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65 años
1957-2022

MEMORIAS

XXXIII National Congress of Biochemistry

October 16-21, 2022 | Mérida, Yucatán.

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1957-2022

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XXXIII National Congress of Biochemistry
October 16-21, 2022 | Mérida, Yucatán.

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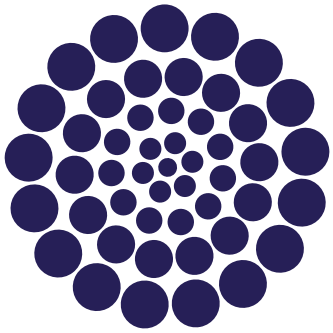

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Dear participants

The organizing committee is pleased to welcome you here in Mérida for the XXXIII National Congress of Biochemistry. This meeting takes place biannually in order to present and discuss new scientific advances in Biochemistry, as well as to promote collaborations on today´s major questions in the field of Neurosciences, Molecular Biology of Fungi, Structure and design of proteins, Quorum sensing, Fluorescence Nanoscopy, Signal Transduction, Bioenergetics and Biomembranes, Plant Development, Emergency vaccines, and new therapies, Virus as experimental molecular tools, among others. Unfortunately, due to the pandemic by SARS-CoV-2, in 2020, our congress had to be canceled, the reason why, we are very excited to be able to have all of you in this meeting in the post-pandemic time.

Mérida, "The White City" was founded by Francisco de Montejo in 1542 over the ruins of T-hò, which means "Place of the five hills", an ancient Mayan settlement, that reminded them of the remains of Mérida in Extremadura, Spain. During the colonial period, stones taken from the Mayan temples were used to build several churches and convents that can be seen in Mérida today. Mérida, located in the Yucatán peninsula, is also close to gorgeous archeological and beautiful natural places. It is an easily accessible cosmopolitan destination connected by air, sea, and land. In 2019, Mérida was designated as a Creative Gastronomic City by UNESCO.

This year, it will be the 65 Anniversary of the SMB, and it is a pleasure to celebrate this occasion with a great academic scientific program for our XXXIII National Congress. The meeting will include plenary lectures from prestigious academic leaders in the field of Biochemistry and Molecular Biology, from single cells to complete animals and plants that will address the state of the art in selected scientific topics. It is highly gratifying to have the valuable participation of distinguished colleagues from Mexico, Spain, USA, Singapore, Australia, Argentina, Canada, Switzerland, and the Czech Republic, interested to meet and interact with their peers, particularly young investigators and students.

We have organized two activities for the students: one that is called "*Having coffee with…*" in which the key speakers will meet with Ph.D. students regarding topics such as: where to send their papers? where to go for postdoctoral training? Among others and the second activity is the "*flash talks*", all you can say about your work in a minute and a half for poster advertising.

Most of the participants in our meeting are students from different Institutions around the country; several of them will attend the Meeting with fellowships. We are sure that all participants will enjoy this meeting due to the high academic quality of the program, as well as to enjoy the beautiful city of Mérida.

Welcome to Mérida 2022!
Ki'imak k óol taale'ex waye'

Teresa Hernández-Sotomayor
SMB President 2021-2023

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GENERAL PROGRAM

XXXIII National Congress of Biochemistry

SUNDAY 16	HRS	MONDAY 17	TUESDAY 18
	8:30 - 10:00	***Plenary Symposia*** *Chair Alicia González* IFC UNAM	***Plenary Symposia*** *Chair Adan Guerrero* IBT UNAM
	10:00 - 11:00	*Patricia León Mejía* IBT UNAM ***Plenary lecture II***	*Alexandra Newton* University of California ***Plenary lecture IV***
	11:00 - 11:30	***COFFEE BREAK***	
	11:30 - 13:00	***Oral Presentations*** 1, 2, 3	***Oral Presentations*** 4, 5, 6 ***& simultaneous Technical Conferences***
	13:00 - 13:15		***Group photo***
Registration 13:00 - 18:00	13:00 - 14:30	***LUNCH***	
	14:30 - 16:15	***Simultaneous Symposia*** 1. Molecular biology fungi and their interactions *Chair: Meritxell Riquelme* 2. Physical-Chemistry, Structure and Design of Proteins. *Chair: Victor Loyola* 3. Systems Neuroscience *Chair: Hugo Merchant*	***Simultaneous Symposia*** 4. Bioenergetics and Biomembranes *Chair: Emma Berta Gutiérrez* 5. Virus as experimental molecular tools *Chair: Luis Vaca* 6. Plant development and specialized metabolism *Chair: Felipe Vázquez*
	16:15 - 16:45	***COFFEE BREAK***	
Opening Ceremony 17:30	16:45 - 17:45	*Mayra de la Torre* CIAD Hidalgo ***Plenary lecture III***	*Erkan Karakas* Vanderbilt School of Medicine PABMB ***Plenary lecture V***
	17:45 - 18:15	***Flash talks***	***Flash talks***
Opening Lecture *Silvia Andrade Silvana* CICY 18:00-19:00 *Alain Filloux* *Nanyang* Tech. Univ. ***Plenary lecture I*** 19:00-20:00	18:15 - 20:15	***Poster Session 1*** Having coffee with... 18:15-19:15 (simultaneous with Posters)	***Poster Session 2*** Having coffee with... 18:15-19:15 (simultaneous with Posters)
Welcome cocktail 20:00-22:00	20:00		***Business session*** 20:00 - 21:00

WEDNESDAY 19	HRS	THURSDAY 20	FRIDAY 21
Plenary Symposia *Chair Enrique Castaño* CICY	8:30-10.00	***Symposia Hispano-Mexicano*** *Chair Agustín Guerrero* CINVESTAV	Out
J. Fernando Peña Ortega INB UNAM ***Plenary lecture VI***	10:00-11:00	*Julio Morán Andrade* IFC UNAM ***Plenary lecture VIII***	
COFFEE BREAK			
Oral Presentations 7, 8, 9 ***& simultaneous*** ***Technical Conferences***	11:30-12:30	*Selene L. Fernández* LANGEBIO Cinvestav ***Plenary lecture IX***	
	12:30-13:00	***Group photo***	
LUNCH			
Simultaneous Symposia 7. Oxidative stress by xenobiotics: toxicity and treatments *Chair: Víctor Calderón* 8. Molecular aspects of bacterial ecology *Chair: Rodolfo García* 9. Betaglycan, a multi-purpose and versatile growth factors co-receptor *Chair: Fernando López Casillas*	14:30-16:30	***Poster Session 4***	
COFFEE BREAK			
José Luis Puente IBT UNAM ***Plenary lecture VII***	17:00-18:00	*Julia Tagüeña* IER, UNAM ***Closing Lecture***	
Flash talks	18:00-18:30	***Final announcements*** ***& closing ceremony***	
Poster Session 3 Having coffee with... 18:15-19:15 (simultaneous with Posters)	18:30-21:00	Free time	
	21:00 - 24:30	***Closing dinner***	

SCIENTIFIC PROGRAM

XXXIII National Congress of Biochemistry

Sunday October 16

17:30-18:00	***Welcome Ceremony*** ***(Gran Salón Yucatán)***
18:00-19:00	***Opening Lecture*** **(Gran Salón Yucatán)** ***Scanning Electron Microscope. A connection between science and art*** IQ. Silvia Andrade Silvana, Centro de Investigación Científica de Yucatán. Chair: Teresa Hernández, Centro de Investigación Científica de Yucatán.
19:00-20:00	***Plenary Lecture I*** **(Gran Salón Yucatán)** ***The Pseudomonas aeruginosa type VI secretion system (T6SS): A bacterial killing machine*** Alain Filloux, Singapore Centre for Environmental Life Sciences Engineering. Nanyang Technological University Chair: Bertha González, Instituto de Fisiología Celular, UNAM.
20:00-22:00	***Welcome Cocktail*** **Terraza and Lobby bar Hotel Fiesta Americana**
	Oral sessions will be held in Fiesta Americana Hotel ***Posters will be exhibited in Hotel Holiday Inn*** **(El Gran Salón and Foyer)**

Monday October 17

8:30-10:00	***Plenary Symposia I*** **(Gran Salón Yucatán)**
	The Ever changing nature of scientific research: four stories Chair: Alicia González Manjarrez, Instituto de Fisiología Celular, UNAM.
	Overlapped genes in bacteriophage Fc02 are transcribed in opposite directions and encode similar activities during the lytic and lysogenic phases in Pseudomonas aeruginosa Gabriel Guarneros Peña, Cinvestav, Zacatenco.
	Divergence of functional transcriptional regulation through the generation of novel hybrid regulators in S. cerevisiae Alicia González Manjarrez, Instituto de Fisiología Celular, UNAM.

	From oxidative stress MAPK signaling to mitochondrial division Jesús Aguirre Linares, Instituto de Fisiología Celular, UNAM.
	Fungal cytokinins, plant growth stimulating compounds or fungal hormones? Alfredo Herrera-Estrella, LANGEBIO, Irapuato.
10:00-11:00	***Plenary Lecture II*** **(Gran Salón Yucatán)** ***Communication makes the difference: the constant dialogue between members of the cell is an essential element for plant development*** Patricia León Mejía, Instituto de Biotecnología, UNAM Chair: Felipe Vázquez Flota, Centro de Investigación Científica de Yucatán
11:00-11:30	***Coffee Break***
11:30-13:00	***Simultaneous oral Sessions 1, 2, 3*** **(Salones Yucatán 1, 2, 3)**
	Yucatán 1 Chair: Edgardo Sepúlveda. CICESE
	Participation of the oncoprotein CagA from Helicobacter pylori in the pancreatic epithelial cells damage Anais Romero-Fabela. Departamento de Infectómica y Patogénesis Molecular. Cinvestav Zacatenco
	Biological and Functional Characterization of the SLC5/STAC Two-Component Signal Transduction Systems Edgardo Sepúlveda. Centro de Investigación Científica y de Educación Superior de Ensenada
	Molecular Cartography of the Salmonella Type III Secretion System Sorting Platform Jose Eduardo Soto. Yale School of Medicine.
	Genomics "microbial dark matter" exploration for antimicrobial discovery Corina-Diana Ceapă. Instituto de Química, UNAM.
	Kinetic characterization of rhizobial bacterias as plant growth promoters (PGPB) in shaken flask and stirred tank Engelberth René Torreblanca Pacheco. Instituto Tecnológico de Tuxtla Gutiérrez

Conformational landscape of the GTPase EFL1 and its implications in the Shwachman-Diamond Syndrome
Nuria Sánchez Puig. Instituto de Química, UNAM.

Yucatán 2
Chair: Elia Diego García. El Colegio de la Frontera Sur

Prolactin regulates H3k9ac and H3k9me2 epigenetic marks and miRNAs expression in bovine mammary epithelial cells during Staphylococcus aureus infection
Marco Antonio Barajas Mendiola. Universidad Michoacana de San Nicolás de Hidalgo

Functional heterologous analysis of allelic variants of human genes potentially driven by natural selection
César Mauricio Campa Álvarez. Unidad de Genómica Avanzada (Langebio), Cinvestav, Irapuato.

Transcriptome analysis of the spider Phonotimpus pennimani reveals novel toxin transcripts
Elia Diego-García. El Colegio de la Frontera Sur.

Abf1 Participates in Cell Cycle Progression and Subtelomeric Silencing in Candida glabrata
Grecia Hernández-Hernández. Instituto Potosino de Investigación Científica y Tecnológica A.C.

Functional characterization of the Tau95 subunit of transcription factor TFIIIC in Trypanosoma brucei
Fabiola Mondragon Rosas. FES Iztacala, UNAM.

Large-scale profiling of ncRNAs in budding yeast longevity
Ericka Moreno-Mendez. Unidad de Genómica Avanzada (Langebio), Cinvestav, Irapuato.

Yucatán 3
Chair: Robert Winkler. LANGEBIO. Cinvestav

Evaluation of endophytic bacteria as plant probiotics in Agave plants
Julio César Maldonado Gómez. Instituto Tecnológico de Tuxtla Gutiérrez.

Structural studies of cell wall biosynthesis of pathogen MRSA. Implications in the antibiotic resistance
Carol Siseth Martínez Caballero. Instituto de Química. UNAM.

	***Changes in induction temperature impacts the structure of recombinant HuGM-CSF inclusion bodies in thermoinducible* E. coli** Norma A. Valdez-Cruz. Instituto de Investigaciones Biomédicas. UNAM.
	Real-time monitoring of volatile organic compounds (VOCs): From basic research to Citizen Science Robert Winkler. Unidad de Genómica Avanzada (Langebio), Cinvestav, Irapuato.
	Litopenaeus vannamei glutathione peroxidases 2 and 4: Responses and modulation during hypoxia and reoxygenation Paulina Estrada Cárdenas. Centro de Investigación en Alimentación y Desarrollo, A.C
	Heterogenous gene expression and splicing in Hypersensitivity Pneumonitis Fibroblasts Ana Lilia Torres Machorro. Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas"
13:00-14:30	***Lunch***
14:30-16:15	***Simultaneous Symposia*** **(Salones Yucatán 1, 2, 3)**
Yucatán 1 1. Molecular biology of fungi and their interactions Chair: Meritxell Riquelme, Centro de Investigación Científica y de Educación Superior de Ensenada.	
	Fungal holobionts: hidden relationships with ecological consequences. Laila Partida Martínez, Cinvestav, Irapuato.
	Exploring the kosmotropy limits in fungi: Aspergillus sydowii as a model of kosmotolerant Ramón Batista García, Universidad Autónoma del Estado de Morelos.
	Exploring natural products from mexican biodiversity Mario Alberto Figueroa Saldívar, Facultad de Química, UNAM.
	Fungal models: can they be the basis of the growth canons of the great fungal diversity? Meritxell Riquelme Pérez, Centro de Investigación Científica y de Educación Superior de Ensenada.

	Yucatán 2 2. Symposium on physical-chemistry, structure and design of proteins In memoriam: Alfredo Torres Larios and Barbarín Arreguín Lozano Chair: Víctor Loyola Vargas, CICY.
	A structural study of an IgE-profilin complex reveals allergen recognition and cross-reactivity information Adela Rodríguez Romero, Instituto de Química, UNAM.
	Polymerases & DNA replication: A tale of bacteria, phages and organelles Luis Gabriel Brieba de Castro, LANGEBIO, Irapuato.
	How are plant peptide hormones perceived by the cells and what determines their signaling specificity? Pedro Jiménez Sandoval, Department of Plant Molecular Biology, University of Lausanne, Switzerland.
	Yucatán 3 3. System Neuroscience Chair: Hugo Merchant Nancy, Instituto de Neurobiología, UNAM.
	Neural interactions mediating cognitive control in prefrontal networks Matthew V. Chafee, Department of Neuroscience, University of Minnesota.
	Regaining our bearings: Neural representations and circuits underlying spatial reorientation Isabel A. Muzzio, Department of Psychological and Brain Sciences, University of Iowa, USA.
	Cortico-striatal circuits for bilaterally coordinated movements Pavel Rueda Orozco, Instituto de Neurobiología, UNAM.
	Brain dynamics in the primate audiomotor circuit during isochronous beat perception and entrainment Hugo Merchant, Instituto de Neurobiología UNAM.
16:15-16:45	***Coffee Break***
16:45-17:45	***Plenary Lecture III*** **(Gran Salón Yucatán)** ***Quorum sensing beyond the signaling molecules*** Mayra de la Torre. Laboratorio de Fisiología Celular y Bioprocesos, CIAD Hidalgo Chair: Jorge Ramírez, IFC UNAM

17:45-18:15	***Flash talks for poster advertising*** **(Gran Salón Yucatán)**
	Memory in transcriptional regulatory dynamics of Escherichia coli in stressful environments Oscar Bruno Aguilar Luviano. Centro de Ciencias Genómicas. UNAM
	The role of non-coding SNPs associated with Alzheimer's disease in neuronal subpopulations of frontal and entorhinal cortex. Erick Cuevas Fernández. Universidad Autónoma del Estado de Morelos
	Detecting recombination in sars-cov by using information theory in a bayesian context Luis Delaye. Cinvestav Irapuato
	Aberrant CLDN6 expression in gastric cancer is associated with enhanced cholesterol metabolism and reduced cytotoxic activity. Sanyog Dwivedi. Facultad de Medicina, UNAM
	Estimation of interaction strengths in the E. coli r egulatory network Jerónimo Martí Vértiz. Centro de Ciencias Genómicas. UNAM
	Genomic analysis of different pathotypes of Colletotrichum lindemuthianum Ma. Irene Morelos-Martínez. Universidad Michoacana de San Nicolas de Hidalgo
	Transcriptomic Analysis of the CM-334/P. capsici/N. aberrans Pathosystem reveals molecular modulation during resistance-breaking response Mariana Romo Castillo. Colegio de Postgraduados
	Redox regulation of the mitophagy receptor Atg32 Ariann E. Mendoza Martínez. Instituto de Fisiología Celular, UNAM
	Hemicellulolytic capacity of different pathotypes of Colletotrichum lindemuthianum in culture with natural substrates Karla Morelia Díaz-Tapia. Universidad Michoacana de San Nicolás de Hidalgo
	Study of the regulation of the Humphreya coffeata terpenome by carbon source Ricardo Alfonso González Hernández. Instituto de Investigaciones Biomédicas, UNAM

Development of a rapid gold nanoparticles-based lateral flow immunoassay for the detection of dengue virus
Cynthia Martinez Liu. Universidad Autónoma de Nuevo Léon

Effects of gold nanoparticles functionalized with polyethyleneimine on the moss Physcomitrium patens
Zuleika Orbe Sosa. Instituto Politécnico Nacional

Design of Self-assembled Antimicrobial Protein-based Nanoparticles
Eddie Guillermo Sánchez Rueda. Instituto de Química, UNAM

Simultaneous Aerobic-Anaerobic Biodegradation Of An Industrial Effluent Of Polymeric Resins With High Phenol Concentration At Different Organic Loading Rates In A Non-Conventional UASB Type Reactor
Jesús Terreros Mecalco. Universidad Tecnológica del Valle de Toluca

The MoBiMS: A miniature mass spectrometer for monitoring volatiles in biological systems
Raúl Alcalde Vázquez. Laboratorio Nacional de Genómica para la Biodiversidad.

Exposure to bis (2-ethylhexyl) phthalate (DEHP) induces oxidative stress in human skeletal muscle cells
Elizabeth Brassea Pérez. Centro de Investigaciones Biológicas Del Noroeste S.C.

Related-Thyroid hormone genes are altered by acute exposure to 2,4-dichlorophenoxyacetic in rat testes
Vanessa Conde Maldonado. Centro de Investigación en Genética y Ambiente.

Kynurenine attenuates mitochondrial depolarization and neuronal cell death AhR-independent way in a Parkinsonian model induced by rotenone exposure.
María Del Rosario García Aguilar. Cinvestav Zacatenco.

Evaluation of the toxic activity of hexanic extract of Sedum morganianum
Cristian Romero Castillo. Universidad Popular Autónoma del Estado de Puebla.

Effects of resveratrol against Giardia lamblia trophozoites through in silico and in vitro approaches
José Roberto Vargas Villanueva. Universidad Autónoma de Coahuila.

18:15-20:15	***Poster Session 1*** ***Will be held in Hotel Holiday Inn* (El Gran Salón and Foyer)** BB BASIC BIOCHEMISTRY I G GENETICS, EPIGENETICS AND GENETIC REGULATION I MU MICROBIOLOGY & VIROLOGY I O OTHERS I ROS REACTIVE OXYGEN SPECIES SB SYSTEMS BIOLOGY & BIOINFORMATICS I TP TOXICOLOGY & PHARMACOLOGY I
18:15-19:15	***Having coffee with….*** **(Salón Celestún)** Paty León, Mayra de la Torre, Alicia González, Alain Filloux

Tuesday October 18

8:30-10:00	***Plenary Symposia II*** **(Gran Salón Yucatán)** ***Fluorescence Nanoscopy*** Chair: Adán Guerrero, Instituto de Biotecnología, UNAM
	Opening: Beyond the limit-fundamentals of super-resolution microscopy Diego L. Delgado Álvarez, CICESE, Baja California.
	Super-resolution imaging reveals the structure disruption of Chromosome Territories 9 and 22 associated with treatment resistance in Chronic Myeloid Leukemia Eunice Fabián Morales, Instituto Nacional de Cancerología.
	Super resolution microscopy reveals dynamic changes in the mouse sperm midpiece Mariano Gabriel Buffone, Instituto de Biología y Medicina Experimental, Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina.
	Nano-deconvolution, opening a new era of fluorescence microscopy Adán O. Guerrero Cárdenas, Laboratorio Nacional de Microscopía Avanzada, Instituto de Biotecnología, UNAM.
10:00-11:00	***Plenary Lecture IV*** **(Gran Salón Yucatán)** ***Protein Kinase C Unbalanced: Deregulated Signaling in Disease*** Alexandra Newton, University of California San Diego. Chair: Agustín Guerrero, Cinvestav, Zacatenco.

11:00-11:30	***Coffee break***
11:30-13:00	***Simultaneous oral Sessions 1, 2, 3*** **(Salones Yucatán 4, 5, 6)**

Yucatán 1
Chair: Luis Antonio Pérez García. Universidad Autónoma de San Luis Potosí

Functional Cyt1Aa is necessary to synergize Bin toxin against Bin-resistant larvae
Nathaly Alexandre do Nascimento. Instituto de Biotecnología, UNAM

Developed a porcine Deltacoronavirus recombinant membrane protein (rM-PDCoV) with potential use in an indirect inmunoenzimatic assay (iELISA) for disease control and prevention
Francisco Jesús Castañeda Montes. Facultad de Medicina Veterinaria y Zootecnia, UNAM.

Computational, structural and inhibitory studies on molecular interactions of the PirABvp toxin from Vibrio parahaemolyticus with their receptor on epithelial cells of shrimp hepatopancreas
Vania Flores Benítez. Universidad Autónoma de Nayarit.

Functional analysis of CSE-8: a hypothetical endoplasmic reticulum protein, chaperone of chitin synthases in Neurospora crassa
Samantha González Téllez. Centro de Investigación Científica y de Educación Superior de Ensenada.

PIR proteins and its functional role on the cell wall of Neurospora crassa
Paul Alejandro Montaño Silva. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco.

Glycosylation of Candida albicans affects its interaction with specific receptors of the cardiac coronary endothelium
Luis Antonio Pérez-García. Universidad Autónoma de San Luis Potosí.

Yucatán 2
Chair: Víctor Aguilar Hernández. CICY

Proteome of Agave angustifolia Haw.: insights about amino acids metabolism in albino plantlets
Mauricio Andrade-Marcial. Unidad de Biotecnología, Centro de Investigación Científica de Yucatán.

Red amaranth (Amaranthus cruentus L.) as a promising source of betalains: an approach of metabolomic profile by UHPLC-MS/MS Orbitrap
Jesús Alfredo Araujo-León. Centro de Investigación Científica de Yucatán.

Isolation and characterization of SARS-CoV-2 neutralizing nanobodies
Dulce Carolina Lugo Gil. Departamento de Bioquímica. Cinvestav Zacatenco.

Molecular bases for the inhibition of the main protease (Mpro) of SARS CoV2
Zaira Pino Dueñas. Universidad Autónoma de Ciudad Juárez.

Exploring the functional role of Slm35 on mitophagy in Saccharomyces cerevisiae
Hilario Ruelas. Instituto de Fisiología Celular. UNAM.

Yucatán 3
Chair: Ernesto Soto-Reyes. Universidad Autónoma Metropolitana

RNA polymerase II pausing contributes to maintain chromatin organization in the chicken erythrocytes
Andrés Penagos Puig. Instituto de Fisiología Celular, UNAM.

Unraveling the secrets of axolotl limb regeneration by the analysis of RNA seq and protein 3D structure prediction
Ernesto Soto-Reyes. Universidad Autónoma Metropolitana Unidad Cuajimalpa.

Characterization of the transcriptional and epigenetic profiles associated with the metabolic memory in vitro
Martí Wilson Verdugo. Instituto de Fisiología Celular, UNAM.

Stress-associated and growth-dependent mutagenesis is divergently regulated by c-di-AMP levels in Bacillus subtilis
Karen Abundiz Yáñez. Division of Natural and Exact Sciences. Universidad de Guanajuato.

Complement receptor 3 (CR3) is activated via an inside-out signalling pathway triggered by CD13 in human macrophages
Laura Díaz Álvarez. Instituto de Investigaciones Biomédicas, UNAM.

Resveratrol inhibits the insulin pathway in liver cells by activating PKC
Karla Daniela Hernández González. Laboratory of Signal Transduction, Department of Biochemistry, Cinvestav IPN.

Technical Conferences (Salón Mérida) Chair: Teresa Hernández. CICY	
11:30-12:00	***Cell culture 3D*** Laura López Bañuelos, UNIPARTS
12:00-12:30	***Transcriptome profile of Aedes aegypti in midgut and salivary glands post DENV-2 infection*** Katherine Laiton-Donato. Centro de Investigación en Salud para el Trópico. MGI–QUÍMICA VALANER
12:30-13:00	***Mentoría de mujeres en STEM, ¿te animas?*** Elizabeth Brassea-Pérez, Mina Königsberg. CIBNOR, La Paz. BC. Universidad Autónoma Metropolitana. Iztapalapa.
13:00-13:15	***Group photo*** **(ESCALINATAS A LA ENTRADA DEL HOTEL FIESTA AMERICANA)**
13:15-14:30	***Lunch***
14:30-16:15	***Simultaneous Symposia*** **(Salones Yucatán 1, 2, 3)**
Yucatán 1 4. Bioenergetics and Biomembranes In Memoriam: Heliodoro Celis Sandoval Chair: Emma Berta Gutiérrez Cirlos Madrid, FES Iztacala, UNAM.	
	All roads lead to mitochondria: mitophagy and stress in Saccharomyces cerevisiae Soledad Funes Argüello, Departamento de Genética Molecular. Instituto de Fisiología Celular, UNAM.
	The bioenergetic machinery of Euglena gracilis Héctor Vicente Miranda Astudillo, Instituto de Investigaciones Biomédicas, UNAM.
	Bacillus subtilis and its respiratory chain: it breaths too Emma Berta Gutiérrez Cirlos Madrid, FES Iztacala, UNAM.
Yucatán 2 5. Virus as experimental molecular tools Chair: Luis Vaca Domínguez, Instituto de Fisiología Celular, UNAM.	
	Use of virus in experimental gene therapy Jose Segovia, Cinvestav, Zacatenco.
	The viruses we use for optogenetic manipulations Fatuel Tecuapetla, Instituto de Fisiología Celular, UNAM.
	Baculovirus display: a novel method for vaccine production Luis Vaca, Instituto de Fisiología Celular, UNAM.

	Yucatán 3 6. Plant development and specialized metabolism Chair: Felipe Augusto Vázquez Flota, CICY.
	Grow or fight: a phospho-switch prioritizes ABCG36/PEN3/ PDR8-mediated transport toward defense Markus Geisler, Department of Biology, University of Fribourg, Suiza.
	The integrate use of metabolomics and transcriptomics as and strategy to identify phytochemicals compounds to use in control pest. Case of Cassia fistula and the ambrosia beetles Enrique Ibarra Laclette, Red de Estudios Moleculares Avanzados, INECOL.
	NTT connects two plant hormonal pathways Nayelli Marsh, Cinvestav, Irapuato.
16:15-16:45	***Coffee break***
16:45-17:45	***Plenary Lecture V*** **(Gran Salón Yucatán)** ***PPABMB Plenary Lecture*** ***Cryo-EM analysis of inositol triphosphate receptor calcium channels*** Erkan Karakas, Vanderbilt School of Medicine, USA. Chair: Agustín Guerrero, Cinvestav, Zacatenco.
17:45-18:15	***Flash talks for poster advertisings*** **(Gran Salón Yucatán)**
	The respiratory chain of Rhodotorula mucilaginosa Paulina Castañeda Tamez. Instituto de Fisiología Celular, UNAM.
	Priming mycobacterial esx-secreted protein B to form a channel-like structure Abril Gijsbers. Instituto de Química, UNAM.
	The human copper transporter 1 (hCTR1) as a possible transporter of Casiopeina III-ia in MDA-MB-231 cells Rogelio Hurtado Alamea. Facultad de Química, UNAM.
	Evaluation of different carbon sources in the production of carotenoids in the yeast Rhodotorula mucilagiosa Ofelia Alejandra Méndez Romero. Instituto de Fisiología Celular, UNAM.
	Hydrogen sulfide synthesis by yeast cysthatione B-synthase is required to survive ER stress Elias Nieto Zaragoza. Instituto de Fisiología Celular, UNAM.
	Study of Complex II biogenesis in Saccharomyces cerevisiae Ulrik Hiram Pedroza Dávila. Instituto de Fisiología Celular, UNAM.

Liver versus Cardiac Mitochondria: Comparison of Some Effectors on the Mitochondrial Permeability Transition Pore
Carolina Ricardez García. Instituto de Fisiología Celular, UNAM.

Evaluation of multifunctional qualities of the rhizobian species Rhizobium sp. ACO-34A as a plant growth promoter rhizobacteria
Víctor Manuel Maranto Gómez. Instituto Tecnológico de Tuxtla Gutiérrez.

Exploring the functional role of the OmpR-type regulators in R. etli
María M. Banda. Centro de Ciencias Genómicas, UNAM.

Influence of OxyR on the expression of phaseolotoxin synthesis genes in Pseudomonas savastanoi pv. phaseolicola NPS3121
Rafael Arnulfo Juárez Navarro. Universidad Autónona de Nayarit.

Serotonin effect in early regeneration of Lumbriculus variegatus
Juana María López Martínez. Facultad de Ciencias Naturales, UAQ.

Alternative CUG Codon Usage in the Halotolerant Yeast Debaryomyces hansenii: An Analysis of Gene Expression Provides New Insights into Adaptation to Extreme Environments
Daniel Ochoa-Gutiérrez. Facultad de Ciencias, UNAM.

An Insight into the novel hybrid regulation complex Rtg3-Nrg1 of Saccharomyces cerevisiae
Edgar Adrián Ramírez González. Instituto de Fisiología Celular, UNAM.

Characterization of Cross-kingdom tRH-target interactions and their role in Trichoderma atroviride-Arabidopsis thaliana mutualistic relationship
Daniel Rafael Saldaña Torres. Instituto Potosino de Investigación Científica y Tecnológica A.C.

Expression of IL-2, IL-4, IL-5, IL-10 and TGFβ genes in patients with COVID-19 in Mexico City
Jennifer Viridiana Sánchez Camacho. Escuela Superior de Medicina, IPN.

Target genes, cell processes and miR-23b-3p effect on HMGB2 expression in cervical cáncer
Gladys Wendy Valente Niño. Universidad Autónoma de Guerrero.

Development of a whole cell biosensor using Bacillus subtilis spores for arsenic detection in water
Luz Idalia Valenzuela García. Centro de Investigación en Materiales Avanzados, Subsede Durango.

	Plant-associated bacteria (PAB): Resources of specialized metabolites Reynaldo Villanueva Enríquez. Instituto de Química, UNAM.
	Characterization of extracellular vesicles released by the parasite Entamoeba histolytica and evaluation of their immunomodulatory effects on human neutrophils Julio César Carrero. Instituto de Investigaciones Biomédicas, UNAM.
	Cellular Immune Response on Cherax quadricarinatus after different immunostimulations Crystal Guluarte. Universidad Nacional Autónoma de México.
	Screening of Agave plants as alternative of α-glucosidase inhibitors source Elia Donají Juárez Niño. CIIDIR. Instituto Politécnico Nacional, Oaxaca.
18:15-20:15	***Poster Session II*** **Will be held in Hotel Holiday Inn (El Gran Salón and Foyer)** BB BASIC BIOCHEMISTRY II BT BIOTECHNOLOGY I G GENETICS, EPIGENETICS AND GENETIC REGULATION II IP IMMUNOLOGY & PARASITOLOGY M MEDICINE, HEALTH & NUTRITION I MV MICROBIOLOGY AND VIROLOGY II
18:15-19:15	***Having coffee with ...*** **(Salón Celestún)** Adán Guerrero, Erkan Karakas, Julio Morán
20:00-21:00	***Business session*** **(Salón Mérida)**

Wednesday October 19

8:30-10:00	***Plenary Symposia III*** **(Gran Salón Yucatán)** ***Novel Research in Gene Regulation*** Chair: Enrique Castaño de la Serna, CICY.
	Nuclear phosphoinositides–new players in regulation of gene expression Pavel Hozak, Institute of Molecular Genetics, Academy of Sciences of the Czech Republic.
	SWI/SNF Chromatin Remodeling Enzymes in Melanocytes and Melanoma Ivana de la Serna, Department of Cell and Cancer Biology, University of Toledo, USA.

	Fibrillarin and non coding RNA in gene architecture and regulation Enrique Castaño, CICY.
10:00 – 11:00	***Plenary Lecture VI*** **(Gran Salón Yucatán)** ***In memoriam: Ricardo Tapia Ibargüengoytia*** ***Exploring the cellular mechanisms of epilepsy: from neurochemistry to electrophysiology and back*** J. Fernando Peña Ortega, Instituto de Neurobiología, UNAM. Chair: Lourdes Massieu, Instituto de Fisiología Celular, UNAM.
11:00 – 11:30	***Coffee break***
11:30 – 13:00	***Simultaneous oral Sessions 7, 8, 9*** **(Salones Yucatán 1, 2, 3,)**
	Yucatán 1 Chair: Adrián Hernández-Díaz Couder. Instituto Nacional de Cardiología "Ignacio Chávez"
	Decreased expression of CB1 receptors in atherosclerosis is associated to a vasorelaxing effect of ACEA on aortic rings María del Rosario Álvarez Valadez. Universidad de Colima.
	Cortactin deficiency induces pancreatic epithelial impairment Abigail Betanzos. Departamento de Infectómica y Patogénesis Molecular. Cinvestav.
	High fructose consumption induces lipid accumulation in adipocytes by regulation of miR-143-5p levels in extracellular vesicles Adrián Hernández-Díaz Couder. Departamento de Inmunología, Instituto Nacional de Cardiología Ignacio Chávez.
	The molecular iodine supplement induces differential antioxidant or proapoptotic Jazmin Lizeth León Pichardo. Instituto de Neurobiología, UNAM.
	The combination of AZD4547 with calcitriol synergistically inhibited BT-474 breast cancer cell proliferation, stemness, and tumorsphere formation Edgar Armando Méndez Pérez. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.
	RANKL signaling in breast cancer stem cells Alejandro Ordaz Ramos. Instituto Nacional de Medicina Genómica.

Biochemical aspects of biotin deficiency in mammals
Antonio Velázquez Arellano. Unidad de Genética de la Nutrición, Instituto de Investigaciones Biomédicas, UNAM

Yucatán 2
Chair: Julio Freyre González. Centro de Ciencias Genómicas. UNAM

Conservation analysis of sequence-divergent lincRNAs in Brassicaceae
Evelia Lorena Coss Navarrete. Unidad de Genómica Avanzada. Langebio. Cinvestav. IPN.

A metanalysis of genomewide aging assays reveals the central modulators of chronological lifespan in budding yeast
Erika Viridiana Cruz Bonilla. Unidad de Genómica Avanzada. Langebio. Cinvestav. IPN.

Advancing global regulatory network inference: an integrative framework
Juan Miguel Escorcia Rodríguez. Centro de Ciencias Genómicas, UNAM.

Transcriptomic composition of venom glands of the recently described Mexican scorpion Centruroides possanii
Patricia Elizabeth García Villalvazo. Universidad de Colima.

Computational modeling of the dynamics of the gut microbiota metabolism
Cristian Mendoza Ortiz. Instituto Nacional de Medicina Genómica.

Regulatory perturbations of ribosome allocation in bacteria reshape the growth proteome with a trade-off in adaptation capacity
José Utrilla Carreri. Centro de Ciencias Genómicas, UNAM.

Yucatán 3
Chair: Pierrick GJ Fournier. CICESE

Neuroendocrine differentiation of lung cancer cells and its effect on the mice immune system
Ricardo Fosado Rodríguez. Facultad de Química, Universidad Autónoma de Querétaro.

Bone microenvironment-suppressed T cells increase bone metastases
Pierrick GJ Fournier. Centro de Investigación Científica y de Educación Superior de Ensenada.

Symmetry is more an antioxidant than an euglycemic advantage
Samuel Álvarez-Almazán. FES Cuautitlán, UNAM.

	Role of pregnancy on insulin-induced vasorelaxation: the influence of angiotensin II receptors Betzabel Rodríguez Reyes. Escuela Superior de Medicina, IPN.
	Repurposing of Metformin and Sodium Oxamate in combination with Doxorubicin, revels intrinsic apoptosis in cervical cancer, in vitro Izamary Delgado-Waldo. Instituto Nacional de Cancerología.
	Global analysis of the cellular mechanism of metformin in a yeast model Jimena Meneses Plascencia. Laboratorio Nacional de Genómica para la Biodiversidad.
Technical Conferences (Salón Mérida) Chair: Arturo Hernández. IFC, UNAM	
11:30-12:00	***Let's establish a new protein purification in one day, from scratch*** Carlos E. Bravo, Field Applications Specialist. BIORAD
12:00-12:30	***Solutions for 3D Cell Cultures*** Alfredo Javier Hernandez Juarez. Corning Life Sciences
12:30-13:00	***The National Laboratory of Channelopathies (LaNCa) of the Institute of Cellular Physiology*** Arturo Hernández Cruz. Instituto de Fisiología Celular, UNAM.
13:00 – 14:30	***Lunch***
14:30 – 16:15	***Simultaneous Symposia*** **(Salones Yucatán 1, 2, 3)**
Yucatán 1 7. Oxidative stress by xenobiotics: toxicity and treatments Chair: José Víctor Calderón Salinas, Cinvestav, Zacatenco.	
	Oxidative stress in metabolisms, poisoning, chemotherapy and radiotherapy: The oxidation for better and for worse José Víctor Calderón Salinas, Cinvestav, Zacatenco.
	Cysteine metabolism and transport in arsenic exposure. María E. Gonsebatt, Instituto de Investigaciones Biomédicas, UNAM.
	Oxidative stress as an inducer of bacterial "persistence" in the origin of mutations resistant to antibiotic Rafael Camacho Carranza, Instituto de Investigaciones Biomédicas, UNAM.

	Yucatán 2 8. Molecular aspects of bacterial ecology Chair: Rodolfo García Contreras, Facultad de Medicina, UNAM.
	Regulation of bacterial virulence by saturated fatty acids Israel Castillo Juárez, Colegio de Postgraduados.
	Plasmid dynamics: from single-cells to microbial communities Rafael Peña Miller, Centro de Ciencias Genómicas, UNAM.
	Plant-bacterial interactions at the root, fostering good relationships by metacommunity lessons Luis David Alcaraz Peraza, Facultad de Ciencias, UNAM.
	Public good exploitation in Pseudomonas aeruginosa Rodolfo García Contreras, Facultad de Medicina, UNAM.
	Yucatán 3 9. Betaglycan, a multi-purpose and versatile growth factor co-receptor Chair: Fernando López Casillas, Instituto de Fisiología Celular, UNAM.
	From betaglycan to TGFBR3L: Deciphering mechanisms of inhibin action Daniel J Bernard, Department of Pharmacology and Therapeutics, McGill University, Montreal, Quebec, Canada.
	Sensitization of cells to TGF-β by the co-receptor betaglycan: structure and mechanism Andrew P Hinck, Department of Structural Biology, University of Pittsburgh, USA.
	Betaglycan's mysterious in vivo affairs Fernando López-Casillas, Instituto de Fisiología Celular, UNAM.
16:15 – 16:45	***Coffee break***
16:45 – 17:45	***Plenary Lecture VII*** **(Gran Salón Yucatán)** ***Unraveling the transcriptional nuances of the chaperone-usher fimbrial operon repertoire of an attaching and effacing bacterial pathogen*** José Luis Puente García. Instituto de Biotecnología, UNAM Chair: Bertha González, Instituto de Fisiología Celular, UNAM
17:45 – 18:15	***Flash talks for poster advertisings*** **(Gran Salón Yucatán)** ***Detection and validation of molecular markers related to the two-way relationship between Renal Cell Carcinoma and Chronic Kidney Disease*** Arijahir Alexis Mancio Cárdenas. Cancerología.

Gastroprotective activity of Callistemon citrinus extract in an induction model of gastric ulcers in obese rats
Jonathan Saúl Piñón-Simental. Universidad Michoacana de San Nicolás Hidalgo.

KCNJ11 and ABCC8 polymorphisms associated to sulfonylurea secondary failure in Type 2 Diabetes Mellitus
Nidia Samara Rodríguez Rivera. UNAM, Facultad de Medicina.

GC/MS Analysis, Antioxidant Activity, and Antimicrobial Effect of Pelargonium peltatum (Geraniaceae)
Gilberto Velázquez-Juárez. Universidad de Guadalajara.

Role of Taurine as a preventive component in Vascular Cognitive Impairment
Andrea Villalobos Villaseñor. Universidad autonoma del estado de Morelos.

Black yeasts from deep-sea sediments of the Gulf of Mexico: cell growth under oligotrophic and hypersaline conditions
Maria Dolores Camacho López. Centro de Investigación Científica y de Educación Superior de Ensenada.

In vitro antagonism, effect on tomato plants in greenhouse and functional genomic analysis of the thermotolerant strain Bacillus velezensis AF12
Salvador Chávez Avila. Universidad Michoacana de San Nicolás de Hidalgo.

Electrochemical immunosensor for the detection of antibodies against an epitope of GP5 protein from PRRS virus.
Luis Enrique Franco Correa. Universidad Michoacana de San Nicolás de Hidalgo.

Molecular evolution of the Spike protein of SARS-CoV-2: evidence of adaptation
Georgina I. López Cortés. Instituto de Investigaciones Biomédicas, UNAM.

T6SS secretion mechanism and novel protein-protein interactions of TecA, a Burkholderia cenocepacia toxin
Julia Monjaras Feria. Queens University Belfast.

Action mechanisms of Rouxiella Badensis SER3 against postharvest fungal pathogens from a genomic perspective
Luzmaria Raquel Morales Cedeño. Universidad Michoacana de San Nicolás de Hidalgo.

Fungal Puzzle Piece: Characterization of Cell Wall Protein ACW-1 in Neurospora crassa
Ana Sofía Ramírez Pelayo. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C.

	Study of prokaryotic diversity and functional markers genes involved in the hydrocarbon degradation and the antibiotic resistance in sediments of the coast of Baja California Ileana Sarahi Ramos Mendoza. Universidad Autónoma de Baja California.
	Extracellular vesicles from Neurospora crassa: vehicles for cell wall-related proteins Daniel Alfonso Salgado-Bautista. Centro de Investigación Científica y de Educación Superior de Ensenada.
	Insights into the mechanism used by a bacterial community to degrade lignocellulose Mónica Noel Sánchez González. Universidad Autónoma de Yucatán.
	Genome mining of Bacillus halotolerans AF23, a thermo- and halotolerant strain with plant growth promoting activities María Fernanda Valencia Marín. Universidad Michoacana de San Nicolás de Hidalgo.
	Prolactin prevents oxidative stress-induced cell death in hippocampal neurons Fernando Macías. Instituto de Neurobiología, UNAM.
	Modulation of Bone Cell Activity and Bone Remodeling by Sulfated Polysaccharides Derived from Brown Algae Jessica Sharlin Landeros Juárez. CICESE.
	Proteomic and molecular study of somatic embryogenesis in Coffea spp. Ana Odetth Quintana Escobar. Centro de Investigación Científica de Yucatán.
	MEDIATOR18 regulates Arabidopsis root system architecture, auxin signaling and is a critical factor for cell viability in root meristems Javier Raya González. Universidad Michoacana de San Nicolás de Hidalgo.
18:15 – 20:15	**Poster Session III** **Will be held in Hotel Holiday Inn (El Gran Salón and Foyer)** BB BASIC BIOCHEMISTRY III G GENETICS, EPIGENETICS AND GENETIC REGULATION III M MEDICINE, HEALTH & NUTRITION II MV MICROBIOLOGY AND VIROLOGY III NN NEUROSCIENCES AND NEUROBIOLOGY ST SIGNAL TRANSDUCTION I
18:15-19:15	**Having coffee with...** **(Salón Celestún)** Ivana de la Serna, Fernando Peña Ortega, José Luis Puente, Selene Fernández

Thursday October 20

8:30-10:00	***Symposia Hispano-Mexicano*** **(Gran Salón Yucatán)** ***Emergency vaccines and new therapies*** Chair: Agustín Guerrero, Cinvestav, Zacatenco.
	Vaccine candidates against coronavirus variants: the role of the Biochemists Beatriz Xoconostle, Departamento de Biotecnología y Bioingeniería. Cinvestav, Zacatenco.
	Interfering the SARS-CoV-2/ACE2 interaction and biophysical characterization of viral spike variants Jerónimo Bravo Sicilia, Instituto de Biomedicina de Valencia-CSIC, España.
	Responding to a pandemic with vaccines: Mexico and the world Laura Alicia Palomares Aguilera, Instituto de Biotecnología, UNAM.
	New frontiers in vaccines and nanotechnology Magdalena Plebanski, RMIT University, Melbourne, Victoria, Australia.
10:00-11:00	***Plenary Lecture VIII*** **(Gran Salón Yucatán)** ***Reactive oxygen species: signaling molecules in neuronal death*** and development Julio Morán Andrade, Instituto de Fisiología Celular, UNAM. Chair: Lourdes Girard, Centro de Ciencias Genómicas, UNAM.
11:00-11:30	***Coffee break***
11:30-12:30	***Plenary Lecture IX*** **(Gran Salón Yucatán)** ***Long non-coding RNAs as evolutionarily fluid chromatin weavers*** Selene L. Fernández-Valverde, LANGEBIO, Irapuato. Chair: Teresa Hernández, CICY.
12:30-13:00	**Group photo** **(ESCALINATAS A LA ENTRADA DEL HOTEL FIESTA AMERICANA)**
13:00 – 14:30	***Lunch***

14:30-16:30	***Poster Session IV*** ***Will be held in Hotel Holiday Inn (El Gran Salón and Foyer)*** BB BASIC BIOCHEMISTRY IV BT BIOTECHNOLOGY II G GENETICS, EPIGENETICS AND GENETIC REGULATION IV O OTHERS II SB SYSTEMS BIOLOGY & BIOINFORMATICS II ST SIGNAL TRANSDUCTION II TP TOXICOLOGY II
17:00-18:00	***Closing Lecture*** **(Gran Salón Yucatán)** ***Science communication for a sustainable future*** Julia Tagüeña. Instituto de Energías Renovables, UNAM Chair: Lourdes Girard, Centro de Ciencias Genómicas, UNAM.
18:00–18:30	***Final announcements and closing ceremony*** ***(Gran Salón Yucatán)***
21:00-24:30	***Farewell dinner*** **(Quinta Montes Molina)**

POSTERS SESSION

XXXIII National Congress of Biochemistry

Posters Session I

Monday October 17, 2022
18:15 – 20:15

BASIC BIOCHEMISTRY I

BB1
Analysis of carotenoids and proline in three variants of achiote (Bixa Orellana) subjected to water stress
Margarita Aguilar-Espinosa. Centro de Investigación Científica de Yucatán A.C.

BB2
Identification and cloning of genes involved in the biosynthesis of betulinic acid in Pentalinon andrieuxii
Alexa Sharai Aguilar Acevedo. Centro de Investigación Científica de Yucatán A.C.

BB3
The peroxisome docking/translocation machinery is developmentally regulated in the fungus Podospora anserina
Beatriz Aguirre López. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB4
Exploring the thermal stability of thermophilic proteins by molecular dynamics
Salomón de Jesús Alas Guardado. Universidad Autónoma Metropolitana Cuajimalpa

BB5
Structural study of catechol 1,2 dioxygenase from Pseudomonas stutzeri
Arisbeth Guadalupe Almeida Juárez. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BB6
Biochemical characterization of components with antimicrobial activity isolated from the venom of endemic scorpions of the State of Chihuahua
Carmen Carolina Alvarado González. Universidad Autónoma de Chihuahua

BB7
The protein phosphatase PP2A and the Casein kinase CKII are expressed in sea urchin spermatozoa
José Daniel Ángeles Salazar. Facultad de Medicina. Universidad Autónoma del Estado de Morelos

BB8
Changes in methyl esterification of pectin in the cell wall of coconut zygotic embryos
Mónica Yanahi Aparicio Ortiz. Centro de Investigación Científica de Yucatán A.C.

BB9
Mammalian CatSper-EFCAB9 is expressed in sea urchin sperm
Fernando Aranda Lozano. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BB10
Participation of intersubunit salt bridges in the stability of glucose-6-phosphate dehydrogenase from Pseudomonas aeruginosa
Edaena Benítez-Rangel. Facultad de Estudios Superiores Iztacala. Universidad Nacional Autónoma de México

BB11
Maltose metabolism controls starch degradation in bean fruit pericarp
Lilia Angélica Bernal Gracida. Facultad de Química. Universidad Nacional Autónoma de México

BB12
Auxin and Cytokinin Cause Major Proteomic Changes for Somatic Embryogenesis in Coffea canephora
Ligia Brito Argáez. Centro de Investigación Científica de Yucatán A.C.

BB13

Effect of the high hydrostatic pressure assisted curing of vanilla beans (Vanilla planifolia) on the total phenolic content and its relationship with the change in color parameters

Génesis V. Buitimea-Cantúa. Escuela de Ingeniería y Ciencias. Tecnológico de Monterrey

BB14

Characterization of a fungal isolate that uses cellulose polymers as a carbon source

Irazú Margarita Calderón-Tinajero. Departamento de Biología. Universidad de Guanajuato

BB15

The Nrg1-Rtg3-Ala repressor complex: the role of the chromatin remodeling in the ALT2 expression profile in S. cerevisie"

Campero-Basaldua José Carlos. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB16

The Nrg1-Rtg3-Ala hybrid repressor complex: Identification of its organization and of the gene circuit under its control

Cecilia Carretero Camberos. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB17

Morphological and molecular control of ES via Ubiquitin-Proteasome in Coffea canephora Pierre ex A. Froehner

Evelyn Arlette Carrillo Bermejo. Centro de Investigación Científica de Yucatán A.C.

BB18

Subcellular localization for an RNA binding protein from Ustilago maydis in Nicotiana benthamiana leaves

Rodrigo Carrillo Solís. Centro de Investigación Científica de Yucatán A.C.

BB19

Biochemical characterization of a glycosyltransferase from Nicotiana tabacum

Arianna Duque Ortiz. Instituto Potosino de Investigación Científica y Tecnológica A.C.

BB20

Expression of Tau protein, an Alzheimer marker, disrupts yeast mitochondrial homeostasis.

Yaisa Castillo Casaña. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB21

BAT1 and BAT2 Functional Diversification: The Role of Subcellular Localization on the Function of Paralogous Genes

Paola Cepeda-García. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB22

Analysis of the effect of insulin resistance on the degradation of branched chain amino acids

Ricardo Benjamín Cervantes Vera. Cinvestav Zacatenco

BB23

Fumarate Reductase a putative component in the alternative mitochondrial respiratory chain of Rhodotorula mucilaginosa.

Natalia Chiquete Felix. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB24

Comparative analysis of the secondary nucleation mechanism between ovalbumin and Moringa oleifera seedling and its inhibition by glucosinolates.

Iván Artemio Corral Guerrero. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

BB25

The pyruvate kinase from the White shrimp Litopenaeus vannamei: gene structure, protein modeling and deduced amino acid sequence

Dalia Guadalupe Cruz Moreno. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB26

Molecular aggregates of β-glucosidase Isoform II from Sechium edule.

Alberto Cruz Rodríguez. Unidad de Bioquímica e Inmunología. Instituto Tecnológico de Oaxaca

BB27

Protoplast isolation and characterization from Argemone mexicana L (Papaveraceae).

Maria Fernanda de la Cruz Velueta. Centro de Investigación Científica de Yucatán A.C.

BB28
Steroidogenesis in JEG-3 cells and progesterone receptors
Paola Diaz Carrillo. Facultad de Medicina. Universidad Nacional Autónoma de México

BB29
Ezrin role in Claudin-9 transfected AGS cells migration
Naresh Esteban Diego Bocanegra. Facultad de Medicina. Universidad Nacional Autónoma de México

BB30
The risk haplotype associated to type 2 diabetes in the SLC16A11 transporter induces changes in its expression
Zuleima Natali Domínguez Velázquez. Departamento de Biotecnología. Cinvestav Zacatenco

GENETICS, EPIGENETICS & GENETIC REGULATION I

G1
Transcriptional regulation of phaC by PhaP5 in Azospirillum brasilense Sp7 for poly-3-hydroxybutyrate (PHB) production
Yovani Aguilar Carrillo. Instituto de Ciencias. Benemérita Universidad Autónoma de Puebla

G2
Effect of 5-azacytidine and trichostatin A on the flavones and flavonols biosynthesis pathway of the albino plant Agave angustifolia Haw
Edder Darío Aguilar Méndez. Centro de Investigación Científica de Yucatán A.C.

G3
Chloroplastic pentatricopeptide repeat proteins (PPR) in albino plantlets of Agave angustifolia Haw. reveal unexpected behavior
Mauricio Andrade Marcial. Unidad de Biotecnología. Centro de Investigación Científica de Yucatán A.C.

G4
MicroRNA miR-142-3P expression in triple-negative breast cancer (TNBC) derived cell lines and its involvement in DNA damage response (DDR) mechanisms
Alberto Aranza-Martínez. FES Iztacala. Universidad Nacional Autónoma de México

G5
Cellular plasticity of radioresistant breast cancer cells favor chemosensitivity
Elena Aréchaga Ocampo. Unidad Cuajimalpa. Universidad Autónoma Metropolitana

G6
Reconstruction of Telomere-Associated Sequences of individual chromosomes of U. maydis by assembling long sequence reads
Cintya Atonal Águila. Instituto de Ciencias. Benemérita Universidad Autónoma de Puebla

G7
The RNA polymerase II subunit NRPB2 is required for indeterminate root development, cell viability, stem cell niche maintenance, and de novo root tip regeneration in Arabidopsis.
Adrián Ávalos Rangel. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

G8
Characterization of microRNA/target regulatory nodes involved in the symbiosis between Arabidopsis thaliana and Piriformospora indica
Ana Karen Ávila Sandoval. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G9
A microRNAs profile predicts gastric preneoplastic lesions progression to gastric cancer
Sergio Ayala Díaz. Universidad Autónoma Metropolitana

G10
High levels of second messenger c-di-AMP positively influence the activation of stringent response and affects mutation frequency rate in Bacillus subtilis.
Víctor Manuel Ayala García. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

G11
Role of SdiA protein in the transcriptional regulation of genes involved in the biosynthesis of the Klebsiella oxytoca tilivalline cytotoxin

Alma Citlalli Balderas Hernandez. Hospital de Pediatría. Centro Médico Nacional Siglo XXI. IMSS

G12
Rhizobium genomic edition using the CRISPR / Cas9 system
Rafael Díaz Méndez. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G13
Methylation profile and expression levels of the ADRA2A gene in post-mortem brain tissue from suicidal subjects.
Marcelo Barraza Salas. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

G14
Genomic engineering in Rhizobium etli: implementation and evaluation of a system based on dCas9
Oussama Bellahsen. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G15
Effect of lncRNA ANRIL on DNA repair in triple negative breast cancer-derived cell lines
Luis Brito-Elias. FES Iztacala. Universidad Nacional Autónoma de México

G16
Centromeric α-satellite non-coding RNA upregulation upon proteasome inhibition: a molecular characterization
Rodrigo E. Cáceres Gutiérrez. IIBO. UNAM. Instituto Nacional de Cancerología

G17
Primpol from A. thaliana is involved in DNA damage tolerance
Laura Daniela Camacho Manriquez. Laboratorio Nacional de Genómica para la Biodiversidad

G18
Towards the identification of the sequences required for the expression of 5S rRNA genes in the early-branched eukaryote Leishmania major
José Andrés Cano Santiago. FES Iztacala. Universidad Nacional Autónoma de México

G19
Bioinformatic selection of transcription factor candidates involved in the regulation of chromoplast biogenesis in Capsicum spp. fruits.
Alejandra Castañeda Marín. Departamento de Ingeniería Genética. Cinvestav IPN Unidad Irapuato

G20
Structural characterization of Transcription Factor Binding Sites of LTTR regulators
Guillermo de Jesus Castillo Cortes. Escuela Superior de Apan. Universidad Autónoma del Estado de Hidalgo

G21
Natural pigment production in response to various stress signals in cell lines of Stenocereus queretaroensis (F.A.C.Weber ex Mathes) Buxb.
Jaime Abelardo Ceja Lopez. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

G22
Stress-induced germ cell apoptosis and stress granules formation upon exposure C. elegans to chemotherapy agents
Andrea Viridiana Cervantes Ayala. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

G23
Identification of polymorphisms of inflammatory genes associated with preterm birth
Jesús Eduardo Chávez Ortega. Facultad de Medicina. UNAM. INMEGEN.

G24
Genetic diversity in Carludovica palmata Ruiz & Pavon in Mexico
Lucia del Carmen Chi Chi. Centro de Investigación Científica de Yucatán A.C.

G25
1-dodecene is a signaling molecule that induces the Oxidative Stress Response in Candida glabrata
Yazmín Contreras-Bravo. Instituto Potosino de Investigación Científica y Tecnológica A.C.

G26
Differential gene expression analysis shows anticancer activity of chalcone in triple-negative breast cancer cells
Eduardo De la Cruz Cano. División Académica de Ciencias Básicas. Universidad Juárez Autónoma de Tabasco

G27
Gene regulation mediated by small RNAs in the cuticle mutant eca2 participates in defense response to fungal pathogen Botrytis cinerea
Carlos De la Rosa Ureña. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MICROBIOLOGY & VIROLOGY I

MV1
Inducible prophages in the genomes of Staphylococcus aureus.
Alan Alejandro Aguayo González. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MV2
The role of phosphate availability on plant growth promotion by the probiotic bacterium Achromobacter sp. 5B1
Joseline Suhail Alejo Guerra. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MV3
Studying tyrosine phosphorylation in ISC pathway proteins
Oscar Manuel Alonso Ambriz. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

MV4
Possible participation of different transport systems for the translocation to the nucleus of two isoforms of fibrillarins in the parasite Trypanosoma cruzi
Arturo Andrade Salas. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

MV5
Molecular basis of enhanced protease activity of Serratia marcescens HU1848
Angel Andrade Torres. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

MV6
In silico and in vitro characterization of the ORF1 encoded protein from the papaya umbra-like virus PMeV-Mx
Jeanin Arguelles Quintal. Centro de Investigación Científica de Yucatán, A.C.

MV7
Manganese metallostasis in Stenotrophomonas maltophilia and its impact on virulence and intracellular survival in phagocytic cells
Fulvia Stefany Argueta Zepeda. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MV8
Antiviral effect of metabolites from Lactobacillus rhamnosus and Chlorella sorokiniana in cells infected with rotavirus
Evangelina Elizama Aros Uzarraga. Universidad de Sonora

MV9
Evaluation of the antimicrobial effect of Thymus vulgaris extract against Staphylococcus epidermidis and Staphylococcus aureus.
Ivonne Estefanía Barbosa Ramírez. Unidad Profesional Interdisciplinaria de Ingenieria. Instituto Politécnico Nacional

MV10
Study on the regulation of depolymerization of the biodegradable bioplastic polyhydroxybutyrate (PHB) in Azotobacter vinelandii
Thalía Barrientos Millán. Instituto de Biotecnología. Universidad Nacional Autónoma de México

MV11
Study of the mechanism of control of C-5 alginate epimerases by the second messenger c-di-GMP: characterization of FleQ as the putative intermediate
Victor V. Barrios Rafael. Instituto de Biotecnología. Universidad Nacional Autónoma de México

MV12
Identification of biosynthetic gene clusters in Acinetobacter pittii strains with possible antifungal activity against Batrachochytrium dendrobatidis and Botrytis cinerea
Elena Bello-López. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MV13
Cystatin C: Antimicrobial and immunoregulatory role in macrophage infected with P. gingivalis Blanca Esther Blancas Luciano. Facultad de Medicina. Universidad Nacional Autónoma de México

MV14
Presence and quantification of Cephalexin (CTX), Sulfamethoxazole (sul1) resistance genes, and hydrocarbon degradation related gene (alkB) on the coast of Baja California
Jesús Tadeo Briseño Guerrero. Instituto de Investigaciones Oceanológicas. Universidad Autónoma de Baja California

MV15
Analysis of the antimicrobial activity of bacteria isolated from native insects of Mexico
Dania Stephanie Brito Beltrán. Instituto de Biotecnología. Universidad Nacional Autónoma de México

MV16
Effect of two mycobacterial proteins on alveolar macrophages activation during Mycobacterium tuberculosis infection
Iris Selene Paredes-González. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

MV17
Antibacterial activity of secreted metabolites from a novel Actinomycete isolated from a Mayan sinkhole
Brian Cárdenas Pérez. Unidad de Química en Sisal. Facultad de Química. Universidad Nacional Autónoma de México

MV18
Evaluation of the antifungal activity of copper (II) sulfate pentahydrate on Moniliophthora roreri
Tania Paulina Carrasco de la Cruz. Universidad Juárez Autónoma de Tabasco

MV19
The thnRDE operon from B. thuringiensis provides immunity to Lactococcus lactis against thurincin H
Luz Edith Casados Vázquez. División de Ciencias de la Vida. Universidad de Guanajuato

MV20
Evaluation and characterization of novel antimicrobials against multidrug-resistant Acinetobacter baumannii
Corina-Diana Ceapă. Instituto de Química. Universidad Nacional Autónoma de México

MV21
Serological evidence of paramyxoviruses related to Porcine orthorubulavirus in Mexican bats
José Luis Cerriteño Sánchez. Instituto Nacional de Investigaciones Forestales Agrícolas y Pecuarias

MV22
Nematicidal activity from lipopeptides produced by Bacillus paralicheniformis
Estefany Thirsa Chavarria Quicaño. Centro de Investigación en Alimentación y Desarrollo, A.C.

MV23
Antibiotic activity of isolated bacteria from a sinkhole located in Sisal, Yucatan
Karla Ortiz-Marcial. Unidad de Química en Sisal, Yucatán. Universidad Nacional Autónoma de México

MV24
Diversity and incidence of endofungal bacteria associated with arbuscular mycorrhizal fungi i n agaves and cacti growing in native arid soil
José Daniel Chávez-González. Departamento de Ingeniería Genética. Cinvestav Irapuato. IPN.

MV25
Effect of osmotic shock on the production of K1 toxin from Saccharomyces cerevisiae
Amairani Chávez Vega. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

MV26
Characterization of the vacuolar proteases of C. auris and their relationship with autophagy
Daniel Clark Flores. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

MV27
RsmA is a central regulator of pyocyanin synthesis and its auto-protective response in Pseudomonas aeruginosa ID4365, an overproducer strain.
Miguel Cocotl-Yañez. Facultad de Medicina. Universidad Nacional Autónoma de México

MU28
Nitrogen availability determines plant growth promotion and the induction of root branching by the probiotic fungus Trichoderma atroviride in Arabidopsis seedlings
Saraí Esparza Reynoso. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MU29
Resistance against inhibition of quorum sensing by autoinducer degrading enzymes
Angel Yahir Estrada Velasco. Facultad de Medicina. Universidad Nacional Autónoma de México

MU30
Roles of RsmA and PqsE on the pyocyanin and alkyl-quinolones synthesis in the marine strain Pseudomonas aeruginosa ID4365.
Misael Josafat Fabian Del Olmo. Facultad de Medicina. Universidad Nacional Autónoma de México

MU31
In silico identification of mutations in the genome of influenza A H1N1 and H3N2 viruses involved in antiviral resistance in Mexico.
Sergio Fierro Torcuato. Facultad de Medicina. Benemérita Universidad Autónoma de Puebla

MU32
Immunomodulatory characterization of peptide GP5T3 from the glycoprotein 5 of the porcine reproductive and respiratory syndrome virus in swine macrophages
Carmen Monserrath Flores García. Escuela Nacional de Estudios Superiores León. Universidad Nacional Autónoma de México

MU33
Antimicrobial activity of cucurmin-chitosan nanocomplexes on clinical isolates of infrequent non-fermenting Gram-negative bacilli species (Achromobacter, Burkholderia, and Stenotrophomonas)
Samantha Maribel Flores-Treviño. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

MU34
Distribution profile of Biosynthetic Gene Clusters in genomes of rhizobacteria strains differing in phytopathogen inhibition and in plant interaction
Saúl Fraire Velázquez. Unidad Académica de Ciencias Biológicas. Universidad Autónoma de Zacatecas

MU35
Genetic diversity and molecular characterization in a set of clinical strains of uropatogenic Escherichia coli producing BLEE.
Viviana Quiroz Luna. Hospital Infantil de México Federico Gómez

MU36
Heterologous expression and characterization of the enzyme encoded by the has gene from Coprinopsis cinerea
Laura Marina Franco-Herrera. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco

MU37
A phage library for antibiotic therapy isolated from the mangrove area located in Sisal, Yucatan
Astrid Franco Iniestra. Unidad de Química en Sisal, Yucatán. Universidad Nacional Autónoma de México

MU38
Identification and characterization of a Two-component Signal Transduction System that Regulates Acetate Utilization in Thermus thermophilus HB27
Gema García. Centro de Investigación Científica y de Educación Superior de Ensenada

MU39
Development of an immunostimulatory complex based on liposomes with glycyrrhizinic acid coupled with recombinant viral proteins of livestock interest.
José Bryan García-Cambrón. Centro Nacional de Investigación Disciplinaria en Microbiología Animal, INIFAP

MU40
Micrococcus luteus LS570 promotes root branching in Arabidopsis via decreasing apical dominance of the primary root and an enhanced auxin response
Elizabeth García Cárdenas. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MU41
Pursuit and characterization of bacteriophages capable of resensitizing multidrug-resistant Pseudomonas aeruginosa strains.

Juan Carlos García Cruz. Facultad de Medicina. Universidad Nacional Autónoma de México

MV42
Antigenicity of PFC chimeric protein (PapG+FimH+CsgA) in serum from pediatric patients with and without UTI
Jesús David García García. Hospital Infantil de México Federico Gómez

OTHERS I

O1
Analysis of cervical cancer extracellular vesicles and its effect on macrophage polarization
Victor Acevedo Sánchez. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

O2
Autophagic flux in atretic oocytes from prepubertal rats
Dafne Bahena Salmerón. Facultad de Ciencias. Universidad Nacional Autónoma de México

O3
Oncogenic role of NM23-H2 in Breast Cancer Cells
Noemi Baranda Avila. Departamento de Investigación Básica. Instituto Nacional de Cancerología

O4
Adaptation to suspension serum-free medium of a CHO cell line producer of recombinant human erythropoietin
Santiago Benavides-López. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O5
Parchment coffee extracts and nopal mucilage an alternative against the fungi growth in cultural heritage materials: stone and wood
Emanuel Bojórquez Quintal. Laboratorio de Análisis y Diagnóstico del Patrimonio. El Colegio de Michoacán

O6
Role of the tryptophan in the protection of human gamma D crystallin from UV radiation damage
Yissell Borges-Rodríguez. Centro de Investigación en Dinámica Celular. Universidad Autónoma del Estado de Morelos

O7
In vitro culture of the ectomycorrhizal fungus Laccaria trichodermophora and its effect on infectivity
Alberto Campos López. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O8
Establishment of a protocol for a three-dimensional culture of cells derived from periodontal ligament
José Juan Can Tec. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

O9
The role of pALT$^{Ink4a/b}$ in resistance to the establishment of cellular senescence
Laura Marianna Cano Mateo. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

O10
Contribution of transcription factors Mfd and GreA in Mismatch (MMR)-Dependent Adaptive Mutagenesis of Bacillus subtilis
Andrea Cantador Gámez. Departamento de Biología. Universidad de Guanajuato

O11
Evaluation of antibacterial activity of MV-L endolysin from phiMR11 phage against methicillin-resistant Staphylococcus aureus
César Salvador Cardona Félix. Centro Interdisciplinario de Ciencias Marinas. Instituto Politécnico Nacional

O12
Symplastic transport participation during the Arabidopsis-Azospirillum interaction

Elizabeth Carrillo-Flores. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

O13

Search for inhibitors to delay the aggregation of crystallin γS induced by UVB radiation.

Kimberly Castañeda Gutierrez. Centro de Investigaciones Químicas. Universidad Autónoma del Estado de Morelos

O14

Cloning and expression of PigMAP protein by recombinant system for its potential use in the evaluation of animal welfare in pigs

Carlos Alfonso Castro Roca. Unidad Xochimilco. Universidad Autónoma Metropolitana

O15

Immunogenicity of a recombinant rHN-PorPU produced by E. coli of Porcine rubulavirus gives protective immunity of litter after challenge

José Luis Cerriteño Sánchez. Centro Nacional de Investigación Disciplinaria en Salud Animal e Inocuidad. Instituto Nacional de Investigaciones Forestales Agricolas y Pecuarias

O16

Characterization of the productive calcium release mode of the endoplasmic reticulum in HeLa cells

Rodrigo Contreras Gaytán. Departamento de Bioquímica. Cinvestav Zacatenco

O17

Presence of S-RNase in the pollen tube cytoplasm triggers Program Cell Death in Nicotiana tabacum?

Yuridia Cruz González Zamora. Facultad de Química. Universidad Nacional Autónoma de México

O18

Hemicellulolytic capacity of different pathotypes of Colletotrichum lindemuthianum in culture with natural substrates

Karla Morelia Díaz-Tapia. Facultad de Medicina Veterinaria y Zootecnia. Universidad Michoacana de San Nicolás de Hidalgo

O19

Kiftherapy: a proposal for cannabidiol-based therapy

Fernando Domínguez Jaimes. Unidad de Estudios Superiores Tultitlán. Universidad Mexiquense del Bicentenario

O20

Application of Principal Component Analysis in an Animal Model of Metabolic Syndrome Induction

Guadalupe Elena Donjuán Loredo. Facultad de Medicina. Universidad Autónoma de San Luis Potosí

O21

Isolation and identification of microalgae from the leachate lagoon of the sanitary landfill of Tuxtla Gutierrez, Chiapas, for use in bioremediation.

Diego Amando Escobar Pacheco. Tecnológico Nacional de México. Instituto Tecnológico de Tuxtla Gutiérrez

O22

Biosynthesis and emission dynamics of camphene in Beauveria pseudobassiana

Verónica del Rosario Frías Negrete. Laboratorio Nacional de Genómica para la Biodiversidad. Cinvestav Unidad Irapuato

O23

Structural and biochemical characterization of components from the scorpion venom Centruroides tecomanus

Alan Roberto Galván Hernádez. Facultad de Ciencias Químicas. Universidad de Colima

O24

Analysis of the occupancy of the transcription factor MEOX2 in the Lung Cancer Epigenome: A Comparative Bioinformatic Analysis

Mariana García Jiménez. FES Iztacala. Universidad Nacional Autónoma de México

O25

AtRAC7/ROP9 small GTPase as a novel negative regulator player in A. thaliana-B. cinerea interaction

Ivette García Soto. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

O26

Phenotypic characterization of lung fibroblasts derived from Mmp8-Mmp13 double knockout mice

María de los Ángeles García Vicente. Facultad de Ciencias. Universidad Nacional Autónoma de México

O27
FTIR analysis of the functionalization of ZnO nanowires for the immobilization of Antibodies
Claudia Erandy Garduño García. Centro de Investigación en Biotecnología Aplicada. Instituto Politécnico Nacional

O28
Study of the regulation of the Humphreya coffeata terpenome by carbon source
Ricardo Alfonso González Hernández. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O29
Simultaneous Aerobic-Anaerobic Biodegradation Of An Industrial Effluent Of Polymeric Resins With High Phenol Concentration At Different Organic Loading Rates In A Non-Conventional UASB Type Reactor
Jesus Terreros Mecalco. Ingeniería en Tecnología Ambiental. Universidad Tecnológica del Valle de Toluca

O30
Inhibition of Colletotrichum gloesporioides with ethanolic extract of Lippia graveolens
Karla Daniela Gutiérrez-Pérez. Universidad Tecnológica de Morelia

O31
Design of Self-assembled Antimicrobial Protein-based Nanoparticles
Eddie Guillermo Sánchez Rueda. Instituto de Química. Universidad Nacional Autónoma de México

O32
Robust and Validated UPLC-MS/MS Method for Assessment L-arginine, ADMA, and L-Citruline Levels in Mexican Pregnant Women with Risk of Preeclampsia
Jessica Hernandez Pineda. Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes

O33
Effects of gold nanoparticles functionalized with polyethyleneimine on the moss Physcomitrium patens
Zuleika Orbe Sosa. Unidad Profesional Interdisciplinaria en Ingeniería y Tecnologías Avanzadas. Instituto Politécnico Nacional

O34
Search for ligand binding sites on FABP4 protein by X-ray crystallography
Maria Fernanda Huerta Anguiano. Instituto Potosino de Investigación Científica y Tecnológica A.C.

O35
Development of a rapid gold nanoparticles-based l ateral flow immunoassay for the detection of dengue virus
Cynthia Martinez Liu. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

REACTIVE OXYGEN SPECIES

ROS1
Association of SOD2 rs4880 polymorphism with non-alcoholic fatty liver disease (NAFLD)
Miriam Fabiola Ayón Pérez. Unidad Académica de Ciencias Químico Biológicas y Farmacéuticas. Universidad Autónoma de Nayarit

ROS2
Comparison of three diets effect on oxidant status and antioxidant capacity in liver and heart in Wistar rats
Miguel Tlacaelel Candelario Domínguez. Universidad Michoacana de San Nicolás de Hidalgo

ROS3
Markers of oxidative stress in postmenopausal women with metabolic syndrome
César Ariel Cruz-Pérez. Instituto Nacional De Perinatología ''Isidro Espinosa De Los Reyes''.

ROS4
Catalase genes expression in response to H2O2 and NaCl is partially regulated by Hog1 MAPK in Debaryomyces hansenii
Ileana de la Fuente Colmenares. Facultad de Ciencias. Universidad Nacional Autónoma de México

ROS5
Respirasome is more susceptible to heavy metal inactivation than free-complex I, but prevent ROS production
Jaime Abraham De Lira Sánchez. Facultad de Medicina. Universidad Nacional Autónoma de México

ROS6
Glucosamine effect on ROS production expression in human dermal microvascular endothelial cells-1
Berenice Fernández Rojas. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

ROS7
Frataxin expression in PC12 and DBTRG-05MG cells in response to chemical hypoxia
Lucero Monserrat Galindo-Moreno. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

ROS8
Role of YwqN and YhdA Oxidoreductases in Bacillus subtilis Oxidative Stress
Beatriz Rufina González Pérez. Departamento de Biología. Universidad de Guanajuato

ROS9
Autophagy adaptor p62 localization during cytotoxic stress in lung epithelial cells
Pamela Esperanza Gutiérrez Chávez. Facultad de Ciencias. Universidad Nacional Autónoma de México

ROS10
Mitochondrial HCN3 potassium channel involvement in autophagy, oxidative stress and apoptosis of rat renal proximal tubule cells
Zinaeli López González. Facultad de Medicina. Universidad Nacional Autónoma de México

ROS11
Evaluating the effect of curcumin on the metacestode of Taenia crassiceps.
José de Jesús Martínez González. Facultad de Medicina. Universidad Nacional Autónoma de México

ROS12
Mfd-dependent processing of 8-OxoG activates a RecA-dependent checkpoint that controls the onset of sporulation in Bacillus subtilis
Lissett E. Martínez Magaña. Departamento de Biología. Universidad de Guanajuato

ROS13
Redox regulation of the mitophagy receptor Atg32
Ariann E. Mendoza-Martínez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ROS14
Role of NusG/NusA in transcriptional mutagenesis of Bacillus subtilis
Edwin Antonio Negrete Duran. Departamento de Biología. Universidad de Guanajuato

ROS15
S-sulfenylation and S-persulfidation in Saccharomyces cerevisiae during cellular growth
Jorge Damián Ramírez Robles. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ROS16
Oxidation of Mitochondrial Calcium Uniporter as a trigger of intracellular Ca2+ mishandling and spontaneous contraction in catecholamine-induced arrhythmia
Felipe Salazar Ramírez. Escuela de Medicina y Ciencias de la Salud. Tecnológico de Monterrey

ROS17
Effect of Apocynin on Expression of Genes Involved in the Antioxidant Response in Diabetic Skeletal Muscle
Elizabeth Sánchez Duarte. Departamento de Ciencias Aplicadas al Trabajo. Universidad de Guanajuato

ROS18
Correlation between circulating cell-free mitochondrial DNA damaged levels and metabolic syndrome factors in a Mexican pediatric population
Mónica Malú Velásquez Esparza. Escuela de Medicina y Ciencias de la Salud. Tecnológico de Monterrey

SYSTEMS BIOLOGY & BIOINFORMATICS I

SB1
Memory in transcriptional regulatory dynamics of Escherichia coli in stressful environments
Oscar Bruno Aguilar Luviano. Center for Genomics Science. Universidad Nacional Autónoma de México

SB2
In silico characterization of BGC´s of Lanthipeptides II located by Genome Mining in Clostridials
Moisés Alejandro Alejo Hernández. Instituto de Química. Universidad Nacional Autónoma de México

SB3
Hormone signaling crosstalk in the Arabidopsis interactome
Lucia Carolina Alzati Ramírez. Instituto Tecnológico Superior de Irapuato

SB4
Structural basis and functional specificity of a cyclo/maltodextrin ABC importer system from Thermoanerobacterales
Jorge Ivan Aranda Caraballo. Universidad de Colima

SB5
Metabolic responses of bacterial communities to discharged xenobiotics by the Chicxulub Ring of Cenotes
Luis Alejandro Ávila-Castro. ENES – Mérida. Universidad Nacional Autónoma de México

SB6
Quest for bacteriophages in soils and rhizospheres from Mexico
Nathalia Badillo Mantilla. Facultad de Ciencias. Universidad Nacional Autónoma de México

SB7
In silico and in vitro study of anti proliferative compounds in breast cancer for PKM2 and HDAC8"
Joselyn Jimena Bahena Montoya. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

SB8
Regulation of transcriptome of trophoblast cells by calcitriol and TGF-b1
David Barrera. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

SB9
Urine and plasma metabolomics revealed endothelial damage in subjects with the coronavirus disease (COVID-19)
Rommel Alejandro Carballo Castañeda. Centro de Investigación Científica y de Educación Superior de Ensenada

SB10
Comparative molecular dynamics simulations of anti-apoptotic Bcl2 protein in apo and holo forms
Luis Alberto Caro-Gómez. Tecnológico de Estudios Superiores de Huixquilucan

SB11
Structural blockade of Omicron's Spike protein by polyphenolic compounds.
Susana Regina Castro Jiménez. Universidad Autónoma Metropolitana–Iztapalapa

SB12
Identification of a conjugative plasmid in Gallibacterium anatis isolated from backyard birds.
María Elena Cobos Justo. Instituto de Ciencias. Universidad Autónoma de Puebla

SB13
Diversity of secondary metabolite biosynthetic gene clusters present in metagenomes of sediments from one sinkhole of Yucatan.
Perla Analuz Contreras de la Rosa. Centro de Investigación Científica de Yucatán A.C.

SB14
In silico prediction of BmVDAC isoforms and their interaction with Bos taurus plasminogen.
Iván Corona Guerrero. Universidad Autónoma de la Ciudad de México

SB15
Sequencing of the Coffea arabica genome and determination of some of its evolutionary characteristics.
Marcos David Couoh Cauich. Centro de Investigación Científica de Yucatán A.C.

SB16
The role of non-coding SNPs associated with Alzheimer's disease in neuronal subpopulations of frontal and entorhinal cortex.
Erick Cuevas Fernández. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

SB17
Assembly patterns and dynamics of synthetic microbial communities based on competitive interactions
Haydee De Luna-Valenciano. Center for Genomic Sciences. Universidad Nacional Autónoma de México

SB18
Detecting recombination in SARS-COV by using information theory in a bayesian context
Luis Delaye. Cinvestav Unidad Irapuato

SB19
Aberrant CLDN6 expression in gastric cancer is associated with enhanced cholesterol metabolism and reduced cytotoxic activity.
Sanyog Dwivedi. Faculty of Medicine. Universidad Nacional Autónoma de México

SB20
Congenital absence of uterus and vagina: a gene interactions analysis based on PPI networks
Fernando Fernández Ramírez. Hospital General de México "Dr. Eduardo Liceaga". Facultad de Ciencias, UNAM

SB21
In silico study of new inhibitors of the human Ornithine decarboxylase
Jessica Georgina Filisola Villaseñor. Cinvestav Zacatenco

SB22
Implications of the crystal structures topology of SARS-CoV-2 main protease (Mpro) in molecular docking
Getulio Flores Tlalpa. ICUAP. Universidad Autónoma de Puebla

SB23
Construction and Analysis of Gene Co-Expression networks of Ustilago maydis
Edgardo Galán Vásquez. Instituto de Investigación en Matemáticas Aplicadas y en Sistemas. Universidad Nacional Autónoma de México

SB24
Prediction of protein-protein interactions and molecular docking of the putative protein Ermp1 from the yeast S. pombe
Dalia González Esparragoza. Instituto de Ciencias. Universidad Autónoma de Puebla

SB25
Analysis of EccD3, ESX3 secretion system component as Mycobacterium tuberculosis drug target.
Ana Laura Granados Tristán. Facultad de Ciencias Biológicas. Universidad Autónoma de Nuevo Léon

SB26
Insights into the coastal microbial antibiotic resistance through a meta-transcriptomic approach in Yucatan
Francisco Alejandro Guillén Chable. UMDI-Sisal, Universidad Nacional Autónoma de México

SB27
Docking analysis on molecular targets and mechanisms of Tau protein in the treatment of frontotemporal dementia
Ana Luisa Hernández Cruz. Escuela Superior de Apan. Universidad Autónoma del Estado de Hidalgo

SB28
Computational study of the T-type voltage-dependent calcium channel (CACNA1G)
Beatriz Hernández Estrada. Facultad de Química. Universidad Autónoma de Querétaro

SB29
Chronic exposure to petroleum-derived hydrocarbons alters the skin bacterial communities and metabolite profiles
Alan Gerardo Hernández-Melgar. Centro de Investigación Científica y de Educación Superior de Ensenada

SB30
CDK-kinase activity inhibition impacts the carbon metabolism in maize germination
Aurora Lara Núñez. Facultad de Química. Universidad Nacional Autónoma de México

SB31
Transcriptomic Analysis of the CM-334/P. capsici/N. aberrans Pathosystem reveals molecular modulation during resistance-breaking response

Mariana Romo Castillo. Colegio de Postgraduados Campus Montecillo

SB32
Genomic analysis of different pathotypes of Colletotrichum lindemuthianum
Ma. Irene Morelos-Martínez. CMEB. Universidad Michoacana de San Nicolás de Hidalgo

SB33
Estimation of interaction strengths in the E. coli regulatory network
Jerónimo Martí Vértiz. Center for Genomic Sciences. Universidad Nacional Autónoma de México

TOXICOLOGY AND PHARMACOLOGY I

TP1
The MoBiMS: A miniature mass spectrometer for monitoring volatiles in biological systems
Raul Alcalde Vazquez. Laboratorio Nacional de Genómica para la Biodiversidad. Cinvestav Irapuato

TP2
5-FU and tamoxifen modify mCRP expression and CSC percentage in SW480 cells
Sofia Alvarez Lorenzo. Facultad de Medicina. Universidad Nacional Autónoma de México

TP3
Aberrant cytokinesis as an alternative mechanism of paclitaxel toxicity in cancer treatment
Marco Alonso Andonegui Elguera. Instituto Nacional de Cancerología

TP4
Expresión of prorenin/renin receptor and its function on cardiovascular system in the offspring of preeclamptic rats
Adriana Yajseel Arenas García. Escuela Superior de Medicina. Instituto Politécnico Nacional

TP5
Non-described itraconazole effect on immunity cells in a murine-eumycetoma treatment
Iván Alejandro Banda-Flores. Facultad de Estudios Profesionales Zona Huasteca. Universidad Autónoma de San Luis Potosí

TP6
Hydrogen sulfide improves vascular dysfunction induced by chronic stress restraint in rats
Jesús Hernan Beltran Ornelas. Departamento de Farmacobiología. Cinvestav Sede Sur

TP7
Exposure to bis (2-ethylhexyl) phthalate (DEHP) induces oxidative stress in human skeletal muscle cells
Elizabeth Brassea Pérez. Centro de Investigaciones Biológicas Del Noroeste S.C.

TP8
Testosterone enhances, via a genomic pathway, airway smooth muscle relaxation induced by salbutamol and theophylline, two drugs useful in the treatment of asthma.
Abril Carbajal García. Facultad de Medicina. Universidad Nacional Autónoma de México

TP9
Related-Thyroid hormone genes are altered by acute exposure to 2,4-dichlorophenoxyacetic in rat testes
Vanessa Conde Maldonado. Universidad Autónoma de Tlaxcala.

TP10
Cytotoxic Effect of Ethanol Extracts of Brazilian Propolis on Human Colorectal Adenocarcinoma Cells
Jesús Antonio Erro Carvajal. Universidad de Sonora

TP11
DNA damage during mitotic slippage as a new mechanism of paclitaxel toxicity
Marco A Escobar-Arrazola. Unidad de Investigación Biomédica en Cáncer, Instituto de Investigaciones Biomédicas. UNAM

TP12
Comparison of Lachesis acrochorda venom composition organism of different biogeographic zones from Colombia
Adrián Marcelo Franco Vásquez. Instituto de Química. Universidad Nacional Autónoma de México

TP13
Kynurenine attenuates mitochondrial depolarization and neuronal cell death AhR-independent way in a Parkinsonian model induced by rotenone exposure.
María Del Rosario García Aguilar. Departamento de Toxicología. Cinvestav Zacatenco

TP14
Punica granatum peel extract affects Giardia lamblia trophozoites cytoskeleton
Mariana Garza Ontiveros. Facultad de Ciencias Químicas. Universidad Autónoma de Coahuila

TP15
NON-contact co-culture for in vitro cytotoxicity assessment of the recombinant anticancer proteins TAT-PTEN-LTU and KLA-PTEN-LTU
Aldo O. González Cruz. Facultad Ciencias Químicas. Universidad Autónoma de Nuevo Léon

TP16
UVB and UVC inhibits cellular processes related to carcinogenesis in cervical cancer cell lines
Angelica Judith Granados López. Unidad Académica de Ciencias Biológicas. Universidad Autónoma de Zacatecas

TP17
Design, production, and evaluation of the recombinant protein E4orf4 linked to the cell penetrating peptide MAP as a new agent against cancer
Javier Hernández Juárez. Facultad de Ciencias Químicas. Universidad Autónoma de Nuevo Léon

TP18
Role of GTPases in the cytoskeleton re-arrangement and cell migration of murine macrophages as a target of organophosphate pesticide residues
David Sebastián Hernández Toledano. Departamento de Toxicología. Cinvestav Zacatenco

TP19
Structural and antimicrobial characterization of the most abundant components from the venom of the scorpion Thorellius intrepidus
Rodrigo Ibarra Vega. Facultad de Química. Universidad de Colima

TP20
Characterization of Ibervillae sonoroe root extracts obtained with different solvents and their cytotoxic activity on glioma cell line.
Judith Yamile Jiménez Pereyra. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez. Universidad Autónoma Metropolitana

TP21
The antipsycotic drug, penfluridol, inhibits Kv10.1 channels
Paulina León Sánchez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

TP22
Biological effect of 4H-Benzo[d][1,3]oxazines in Breast Cancer Cells
Jesús Adrián López. Unidad Académica de Ciencias Biológicas. Universidad Autónoma de Zacatecas

TP23
Leukocyte mTNF-α as a mechanism of adaptation to inflammatory processes in lead-exposed workers: NADPH oxidase as a mediator of oxidative stress
Nadia Cristina López Vanegas. Departamento de Bioquímica. Cinvestav Zacatenco

TP24
Effects of resveratrol against Giardia lamblia trophozoites through in silico and in vitro approaches
José Roberto Vargas Villanueva. Facultad de Ciencias Químicas. Universidad Autónoma de Coahuila

TP25
Potential role of TNF-α and TNFRs in CSCs enrichment induced by Doxorubicin in triple negative breast cancer
María Adriana Medina Mondragón. Facultad de Medicina. Universidad Nacional Autónoma de México

TP26
Evaluation of the toxic activity of hexanic extract of Sedum morganianum
Cristian Romero Castillo. Universidad Popular Autónoma del Estado de Puebla

TP26.1
Metal complexes formed with EDTA, melatonin, and its main metabolites: Computational DFT study and implications for a lead intoxication alternative treatmentJuvencio Robles Garcia. Departamento de Farmacia. Universidad de Guanajuato

Posters Session II

Tuesday October 18, 2022
18:15 – 20:15

BASIC BIOCHEMISTRY II

BB31
The respiratory chain of Rhodotorula mucilaginosa
Paulina Castañeda Tamez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB32
Characterizing the structural sensitivity of plant intrinsically disordered regions in vivo
Constanza Enriquez-Toledo. Facultad de Química. Universidad Nacional Autónoma de México

BB33
Folding and Evolution of a Repeat Protein on the Ribosome
José Arcadio Farías-Rico. Center for Genome Sciences. Universidad Nacional Autónoma de México

BB34
Proteomic approach in coconut fruit ripenig: an insight in amino acid metabolism
Jean Wildort Félix. Centro de Investigación Científica de Yucatán A.C.

BB35
Effect of heat stress on seeds of tolerant and susceptible genotypes of wheat (Triticum aestivum) grown in the Yaqui Valley
Katheryne Fernández Padilla. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB36
Kinetic characterization of respirasomes from Debaryomyces hansenii
Giovanni García Cruz. Facultad de Medicina. Universidad Nacional Autónoma de México

BB37
N-Nitrosodimethylamine regulates claudin expression and invasiveness in gastric cancer cells
Carlos Abraham García García. Facultad de Medicina. Universidad Nacional Autónoma de México

BB38
Acute hypoxia effects on MMPs enzymatic activity and expression in lung adenocarcinoma and squamous carcinoma cells.
Antonio Armando García Hernández. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

BB39
*Transcriptional regulation of glutamate receptors in habanero pepper plants under NaCl stress conditions*Federico García Laynes. Centro de Investigación Científica de Yucatán A.C.

BB40
Rtg1 and its possible role in the formation of the Nrg1-Rtg3-Ala hybrid complex in the yeast Saccharomyces cerevisiae
Janeth Alejandra García Rodríguez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB41
Structural characterization of the Lid of lipase 2 of Pseudomonas alcaligenes
Elena Lizbeth Garcia Villegas. Centro de Investigación en Dinámica Celular. UAEM

BB42
Kinetics of the enzyme Arginine kinase from ticks (Rhipicephalus sanguineus) vector of Rocky Mountain spotter fever (RMSF)
Karina D. García-Orozco. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB43
Effect of glycolysis inhibition on mitochondrial function in human glioblastoma cells
Gigi Abril Garrido-Aguirre. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

BB44
Priming mycobacterial esx-secreted protein B to form a channel-like structure
Abril Gijsbers. Instituto de Química. Universidad Nacional Autónoma de México

BB45
Identification and In Silico Characterization of Novel Helicobacter pylori Glucose-6-Phosphate Dehydrogenase Inhibitors
Saúl Gómez Manzo. Laboratorio de Bioquímica Genética, Instituto Nacional de Pediatría

BB46
Metabolomic analysis of liquid endosperm of Cocos nucifera L. in three stages of maturation
José Rufino Gómez Tah. Centro de Investigación Científica de Yucatán A.C.

BB47
The mean hydrophobicity of OXPHOS proteins is the limiting factor for the allotopic expression of mitochondrial genes
Diego González Halphen. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB48
Proteomic analysis of coconut zygotic embryos at three different stages of development
María Inés Granados Alegría. Centro de Investigación Científica de Yucatán A.C.

BB49
The Hap2-3-5-Gln3 Hybrid Transcriptional Complex: Identification of its Organization and the Gene Circuit Under Your Control
Nancy Yasmin Gutiérrez-Méndez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB50
The Argemone-Corynespora system as model for the study of the contribution of benzylisoquinoline alkaloids in plant-fungus interactions.
Gladys del Carmen Hernández-Eleria. Centro de Investigación Científica de Yucatán A.C.

BB51
Self-assembly of Artificial Virus-Like Nucleocapsids programmed by CRISPR-dCas12
Armando Hernández García. Institute of Chemistry. Universidad Nacional Autónoma de México

BB52
Study of Complex II biogenesis in Saccharomyces cerevisiae
Ulrik Hiram Pedroza Dávila. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB53
Study of the effect of cations on the activity of recombinant LDH-1 and LDH-2 from shrimp Litopenaeus vannamei
Magally Luisa Elena Hernandez Palomares. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB54
Liver versus Cardiac Mitochondria: Comparison of Some Effectors on the Mitochondrial Permeability Transition Pore.
Carolina Ricardez García. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB55
Biochemical characterization of orotate phosphoribosyltransferase from Coffea arabica
Alexis Hinojosa Cruz. Facultad de Química. Universidad Nacional Autónoma de México

BB56
The human copper transporter 1 (hCTR1) as a possible transporter of Casiopeina III-ia in MDA-MB-231 cells
Rogelio Hurtado Alamea. Facultad de Química. Universidad Nacional Autónoma de México

BB57
Cholesterol dependence of Na,K- ATPase enzyme activity of erythrocytes in normal and hyperglycemic blood samples
Aura Matilde Jiménez Garduño. Escuela de Ciencias. Universidad de las Américas Puebla

BB58
Hydrogen sulfide synthesis by yeast cysthatione β-synthase is required to survive ER stress.
Elias Nieto Zaragoza. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB59
Evaluation of the expression of genes encoding pectin methyl esterases in solid endosperm of coconut
Dilery Ahtziry Juárez Monroy. Centro de Investigación Científica de Yucatán A.C.

BB60
Evaluation of different carbon sources in the production of carotenoids in the yeast Rhodotorula mucilagiosa
Ofelia Alejandra Mendez Romero. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BIOTECHNOLOGY I

BT1
Characterization of a chitosan-DNA nanoparticle encoding to somatotropin porcine
María Leticia Almada Leyva. Facultad de Medicina Veterinaria y Zootecnia. Universidad Nacional Autónoma de México

BT2
In silico analysis of the expression of glycosyltransferases in a lignocellulose degrading consortium
Mariana Aurora Almeida Cervera. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

BT3
Metal-binding peptides displayed on the Neurospora crassa mycelium to obtain functionalized surfaces
Francisco Javier Anguiano Melendrez. Biotecnología Industrial. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C.

BT4
Removal of Cr(VI) through a filamentous fungal bioreactor coupled to a biotrickling filter (BLE)
Rogelio Arroyo López. Centro de Innovación Aplicada en Tecnologías Competitivas

BT5
Expression of a new incretin analog in Lactococcus lactis
Isaias Balderas-Renteria. Universidad Autónoma de Nuevo Léon. Institute National de la Recherché Agronomique

BT6
Pseudomonas chlororaphis: a versatile non pathogenic bacterium host for Synthetic Biology
Miguel Angel Bello González. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

BT7
Determination of Crystallographic Structures by Phase Expansion in Fusion Proteins
María Cristina Cardona Echavarría. Centro de Investigación en Dinámica Celular. Universidad Autónoma del Estado de Morelos

BT8
Heterologous expression of a consensus long α-neurotoxin for antibody production against elapid envenomation
Víctor Carpanta Capistran. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BT9
Proteomic analysis of Alicycliphilus denitrificans BQ1 grown on Impranil, a polyester polyurethane coating
Sergio Andres Carreño Florez. Facultad de Química. Universidad Nacional Autónoma de México

BT10
Antigenicity evaluation of P16 protein from genotype A by using naturally infected goats and sheeps plasmas
María Azucena Castañeda Montes. FES Cuautitlán. Universidad Nacional Autónoma de México

BT11
Characterization of small ruminant lentivirus capsid recombinant protein (SRLV-rp25) coupled to immunostimulatory complexes based on glycyrrhizinic acid

María Azucena Castañeda Montes. FES Cuautitlán. Universidad Nacional Autónoma de México

BT12
Low-cost biogas purification system from a full-scale biodigester
Jesús Emiliano Castellanos Sánchez. Facultad de Agronomía. Universidad Autónoma de Chiapas

BT13
Aluminum effect over betalains production in Stenocereus queretaroensis suspension cells
Lizbeth A. Castro-Concha. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

BT14
Advantages of using an automated platform for SARS-COV-2 sequencing in a clinical landscape
Jonathan Cervantes. Laboratorio de Patología Quirúrgica y Citología de Puebla

BT15
Droplet Digital PCR for Analysis of HIV Copy Number Variation
Jonathan Cervantes. Laboratorio de Patología Quirúrgica y Citología de Puebla

BT16
Glycerol kinase driven monophosphorylation of small alcohols
Wendy Escobedo-Hinojosa. Facultad de Química. Universidad Nacional Autónoma de México

BT17
Are the genes NMO2 and NMO5 of Metarhizium brunneum involved in the entomopathogenic process?
Ximena Esquivias Varela. Departamento de Biología. Universidad de Guanajuato

BT18
Heterologous expresion of a rickettsial outer membrane protein
Blanca Elisa Estrada Aguirre. Universidad Autónoma de Chihuahua

BT19
Isolation and Characterization of Thermophilic Microorganisms of Biotechnological Interest of Hot Springs *from San Francisco, Silao, Gto., Mx.*
Jose Maria Fernandez Romero. Unidad Profesional Interdisciplinaria de Ingenieria. Instituto Politécnico Nacional

BT20
A ferrofluid with a dopamine or tetrahydroquinone modified surface for magnetic hyperthermia using Paramecium caudatum
Ximena Alejandra Flores Arévalo. Centro Universitario de la Ciénega. Universidad de Guadalajara

BT21
Biochemical and proteomic analysis from in vitro culture of avocado (Persea americana Mill.)
Rosa María Galaz Avalos. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

BT22
Synthesis of a recombinant RmS-17 polypeptide from Rhipicephalus microplus in the Pichia pastoris expression system
José Bryan García Cambrón. CENID-SAI-INIFAP-Palo Alto

BT23
DNA-Chitosan complexes as non-viral gene carrier: Newcastle Fusion gene nanoparticle formation
Lluvia Isabel García-Córdoba. Universidad Abierta y a Distancia de México-UnADM.

BT24
Identification of genes differentially expressed of Metarhizium during the interaction with insects
Melissa García Fernández. División de Ciencias Naturales y Exactas. Universidad de Guanajuato

BT25
Molecular cloning and functional characterization of banana MaWRKY18, MaWRKY45, MaWRKY60 and MaWRKY70 transcription factors
Sergio García Laynes. Unidad de Biotecnología. Centro de Investigación Científica de Yucatán A.C.

BT26
Role of Wickerhamomyces anomalus β*-glucanase toxin during the interaction of the yeast and phytopathogenic fungus*
María Guadalupe Guerra Sánchez. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

BT27
Monitoring The Crabtree Effect in Yeast Culture Using the MoBiMS Mass Spectrometer System Built
Héctor Guillén-Alonso. Laboratorio Nacional de Genómica para la Biodiversidad. Cinvestav Irapuato

BT28
Xylitol production by Clavispora lusitaniae, a native yeast of mezcal must
David Guzmán Hernández. Departamento de Biotecnología y Bioingeniería. Cinvestav Zacatenco

BT29
Analysis of the Carbohydrate Transport System in Saccharomyces pastorianus
César Ignacio Hernández Vásquez. Facultad de Ciencias Biológicas. Universidad Autónoma de Nuevo Léon

BT30
Analysis of the influence of genes that code for proteins with nitronate monooxygenase activity in the different lifestyles of Metarhizium
Diana Laura Herrera Lino. División de Ciencias Naturales y Exactas. Universidad de Guanajuato

BT31
Generation and characterization of Arabidopsis plants overexpressing the PABN3 and CL15, which are interactors of Glycine-Rich Domain Protein 2
Juan Francisco Jiménez Bremont. Instituto Potosino de Investigación Científica y Tecnológica A.C.

BT32
Evaluation of multifunctional qualities of the rhizobian species Rhizobium sp. ACO-34A as a plant growth promoter rhizobacteria
Víctor Manuel Maranto Gómez. Tecnológico Nacional de México campus Tuxtla Gutiérrez

GENETICS, EPIGENETICS & GENETIC REGULATION II

G28
Exploring the functional role of the OmpR-type regulators in R. etli.
María M. Banda. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G29
Regulation of PGR, PRL, and IGFBP1 gene expression in response to in vitro decidualization in endometrial stromal cells from a patient with endometriosis
Martha Paloma Domínguez Mora. Facultad de Química. Universidad Nacional Autónoma de México

G30
Functional characterization of the NPR1-NPR3 interaction in the Pseudomonas syringae-Arabidopsis thaliana pathosystem
Everardo Jair Flores Cuevas. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G31
Gene co-expression network driven approach to decode the role of miR-122 in triple-negative breast cancer
Mauricio Flores Fortis. Universidad Autónoma Metropolitana Unidad Cuajimalpa

G32
Molecular Basis of Binary Complexes of LysR-Type Transcriptional Regulators
Moisés Alain Flores Hernández. Escuela Superior de Apan. Universidad Autónoma del Estado de Hidalgo

G33
Molecular Characterization and Differential Expression to Hypoxia and Reoxygenation of Hexokinase Isoforms of the Shrimp Litopenaeus vannamei
Marissa Andrea Flores Sauceda. Centro de Investigación en Alimentación y Desarrollo, A.C.

G34
Comparative study of the regulation of autophagy and senescence between mice and naked-mole rats
Berenice Franco-Juárez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

G35
Plant-associated bacteria (PAB): Resources of specialized metabolites.
Reynaldo Villanueva Enríquez. Instituto de Química. Universidad Nacional Autónoma de México

G36
microRNAs contained in hepatoma cells-derived extracellular vesicles modulate miRNA biogenesis elements: a new regulatory mechanism for cell proliferation and migration in HCC.
Rosendo García Carrillo. Centro Universitario de Investigaciones Biomédicas. Universidad de Colima

G37
Development of a whole cell biosensor using Bacillus subtilis spores for arsenic detection in water.
Luz Idalia Valenzuela García. Centro de Investigación en Materiales Avanzados, Subsede Durango

G38
Epigenetic regulation, alternative splicing, and function of AGL19 transcription factor
Berenice García-Ponce. Instituto de Ecología. Universidad Nacional Autónoma de México

G39
Target genes, cell processes and miR-23b-3p effect on HMGB2 expression in cervical cáncer
Gladys Wendy Valente Niño. Facultad de Ciencias Químico Biológicas. Universidad Autónoma de Guerrero

G40
Unraveling the role of the RetCH2128 and RetCH3587 regulators in the R. etli – P. vulgaris symbiosis
Adrian Gonzalez. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G41
Expression of IL-2, IL-4, IL-5, IL-10 and TGFβ genes in patients with covid-19 in Mexico City.
Jennifer Viridiana Sánchez Camacho. Escuela Superior de Medicina. Instituto Politécnico Nacional

G42
Searching for the cognate response regulator of the essential sensor hybrid histidine kinase RdsA in Rhizobium etli
Carmen Guadarrama. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G43
Characterization of Cross-kingdom tRH-target interactions and their role in Trichoderma atroviride-Arabidopsis thaliana mutualistic relationship
Daniel Rafael Saldaña Torres. Instituto Potosino de Investigación Científica y Tecnológica A.C.

G44
The role of JMJ19 and DNA-PrimL genes in Arabidopsis thaliana as potential targets of Trichoderma atroviride small RNA1 during their mutualistic relationship
Eyra Judith Hernández Hernández. División de Biología Molecular. Instituto Potosino de Investigación Científica y Tecnológica A.C.

G45
An Insight into the novel hybrid regulation complex Rtg3-Nrg1 of Saccharomyces cerevisiae
Edgar Adrian Ramirez Gonzalez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

G46
Identification of proteins that interact with the transcriptional repressor Maf1 in the protozoan parasite Leishmania major
Aldo Rodrigo Hernández Zamarripa. FES Iztacala. Universidad Nacional Autónoma de México

G47
Alternative CUG Codon Usage in the Halotolerant Yeast Debaryomyces hansenii: An Analysis of Gene Expression Provides New Insights into Adaptation to Extreme Environments.
Daniel Ochoa-Gutiérrez. Facultad de Ciencias. Universidad Nacional Autónoma de México

G48
Phosphate deficiency activates the Autoregulation of Nodulation Pathway
Mariel Carolina Isidra Arellano. FES Iztacala. Universidad Nacional Autónoma de México

G49
Influence of OxyR on the expression of phaseolotoxin synthesis genes in Pseudomonas savastanoi pv. phaseolicola NPS3121
Rafael Arnulfo Juárez Navarro. Universidad Autónona de Nayarit

G50
Expression of MAL reduces viability of HCC827 human lung cancer cells
Roberto Lara lemus. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

G51
Combination of Metformin, Sodium Oxamate and Doxorubicin induces apoptosis and autophagy in colorectal cancer cells via downregulation HIF-1α
Liliana Leyva Boyso. Laboratorio de Genómica. Instituto Nacional de Cancerología

G52
Serotonin effect in early regeneration of Lumbriculus variegatus
Juana María López Martínez. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

IMMUNOLOGY & PARASITOLOGY

IP1
Effect of testosterone on antioxidant activity and oxidative stress markers in a murine malaria model
Jesús Aguilar Castro. FES Zaragoza. Universidad Nacional Autónoma de México

IP2
EhMyb10 Transcription Factor Interactome: evidence of cotranscriptional regulation
Danna Paola Aguirre Casimiro. Universidad Autónoma de la Ciudad de México

IP3
Mitochondria participation in B cell response against non-bilayer phospholipid arrangements
Giovanna Berenice Barrera Aveleida. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

IP4
Allergenicity profiling of Ligustrum lucidum pollen proteins causing respiratory allergies
Ricardo Neftalí Bravo Rodríguez. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

IP5
DHEA differentially modulates IFN-γ levels in males and females CBA/Ca mice infected with P. berghei ANKA
Fidel Orlando Buendía González. FES Zaragoza. Universidad Nacional Autónoma de México

IP6
Characterization of extracellular vesicles released by the parasite Entamoeba histolytica and evaluation of their immunomodulatory effects on human neutrophils.
Julio César Carrero. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

IP7
DBD-Myb Proteins in E. invadens: Classification and cyst-stage transcription
Elizabeth J. Castañeda-Ortiz. Posgrado en Ciencias Genómicas. Universidad Autónoma de la Ciudad de México

IP8
Oestrogens decrease the number of cytotoxic T lymphocytes and IFN-γ and TNF-α concentration in males *infected with Plasmodium berghei ANKA*
Luis Antonio Cervantes Candelas. FES Zaragoza. Universidad Nacional Autónoma de México

IP9
Antibody-dependent enhancement in dengue virus infection associated with anti-SARS-CoV-2 IgG class antibodies in the coast region of Oaxaca, Mexico.

Elizabeth Cruz Altamirano. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

IP10
EhMyb10 overexpression in E. histolytica: implications during epithelial cell interaction
Patricia Cuellar. Posgrado en Ciencias Genómicas. Universidad Autónoma de la Ciudad de México

IP11
Evaluation of biological activity of butyl and isopropyl quinoxaline-7-carboxylate 1,4-di-N-oxide esters against Entamoeba histolytica.
Juan Pablo Delgadillo Velazco. Escuela Nacional de Medicina y Homeopatia. Instituto Politécnico Nacional

IP12
T-cell immunophenotype and cytokine profiles in pediatric patients infected with Rickettsia rickettsii
Gerardo Pavel Espino-Solis. Facultad de Medicina. Universidad Autónoma de Chihuahua

IP13
Evaluation of myeloid cell activation in pediatric patients with rickettsial and SARS-CoV-2 infections
Mayela Rosario Espinoza Duarte. Facultad de Química. Universidad Autónoma de Chihuahua

IP14
Subunit C82 of RNA polymerase III is essential for cell growth of the human parasite Trypanosoma brucei
Luis E. Florencio Martínez. FES Iztacala. Universidad Nacional Autónoma de México

IP15
Participation of Tgamma/delta lymphocytes in the development of lupus in mouse induced by lipidic particles
Edgar Iván Galarce Sosa. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

IP16
Prolactin exerts dual actions on the inflammatory response of synovial fibroblasts
Jose Fernando García Rodrigo. Instituto de Neurobiología. Universidad Nacional Autónoma de México

IP17
Determination of the presence of amebapores in trophozoites from different species of Entamoeba, using Western-Blot and ELISA
Augusto González Canto. Facultad de Medicina. Universidad Nacional Autónoma de México

IP18
Plasmodium vivax apical membrane antigen 1 I-II from Nicaragua revealed low diversity, moderate differentiation and genetic relationships with Latin American parasites
Lilia González-Cerón. Secretaria de Salud. Instituto Nacional de la Salud Pública

IP19
Cellular Immune Response on Cherax quadricarinatus after different immunostimulations
Crystal Guluarte. Departamento de Bioquímica. Universidad Nacional Autónoma de México

IP20
Degradative profiles of Fibronectin as biomarkers during the progression of the acute and chronic infection with Trypanosoma cruzi
Nora Adriana Hernández Cuevas. Centro de Investigaciones Regionales Dr. Hideyo Noguchi. Universidad Autónoma de Yucatán

IP21
Development of a chimeric recombinant protein against Rabbit Hemorrhagic Disease Virus
Diego Josimar Hernández-Silva. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

IP22
Evaluation of the cross-reactivity of antibodies against DEC-205 receptor in different species
Myriam Rebeca Márquez Chávez. Facultad de Ciencias Químicas e Ingenierías. Universidad Autónoma de Chihuahua

IP23
Proteomic profile of phagocytosis of shrimp Macrobrachium tenellum
Dulce Maria Mateos Guerrero. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

IP24
Activation of intracellular Toll like receptors in combination with vincristine in glioblastoma cells
Orlando Daniel Moedano-Hernández. Hospital Infantil de México Federico Gómez

IP25
Anti-inflammatory response promoted by Trichinella spiralis in an experimental lupus murine model
Christian-Irene Nevárez-Lechuga. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

IP26
Cloning and expression in Nicotiana benthamiana of the ash pollen allergen Fra e 1
Cynthia Lizbeth Nicolás Salazar. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

IP27
Effect of inhibiting p450 aromatase enzyme on the population of macrophages, TNF-α, IFN-γ and IL-10 in CBA/Ca male mice infected with P. berghei ANKA
Teresita de Jesús Nolasco Pérez. FES Zaragoza. Universidad Nacional Autónoma de México

IP28
Cannabinoid receptor 2 modulates FcεRI-dependent activation of mast cells
Rubí Monserrat Osorio Pérez. Departamento de Farmacobiología. Cinvestav Sede Sur. Instituto Politécnico Nacional

IP29
High fructose consumption induces the expression of miR 155-5p in monocytes present in liver and epididymal adipose tissue
Mario Peña Peña. Instituto Nacional de Cardiología

IP30
In silico design of a multi-epitope vaccine construction against Leishmania mexicana
Isis Pérez Concepción. Departamento de Investigaciones Científicas y Tecnológicas. Universidad de Sonora

IP31
Evaluation of the early and convalescent immune response of patients infected by SARS-CoV-2
Horacio Pérez Juárez. Facultad de Medicina. Universidad Nacional Autónoma de México

IP32
Effect of membrane perturbing agents on the secreted activity of acid sphingomyelinase in Entamoeba histolytica.
Fátima Ramírez-Montiel. Departamento de Biología. Universidad de Guanajuato

IP33
Evaluation of the effect of Plectranthus amboinicus essential oil against Entamoeba histolytica.
Juan Mauricio Ramírez Vidal. Escuela Nacional de Medicina y Homeopatia. Instituto Politécnico Nacional

IP34
17beta-estradiol inhibits ICAM-1, VCAM-1, p65 expression and increase expression of antioxidant enzymes induced by amyloid beta 25-35 in microvascular endothelial cells (HMEC-1)
Emma Rodriguez Maldonado. Unidad de Investigación UNAM. Instituto Nacional de Cardiología “Ignacio Chávez”

IP35
Development of anti-human IgA monoclonal antibodies to study of mucosal compartments
Héctor Romero-Ramírez. Departamento de Biomedicina Molecular. Cinvestav. Instituto Politécnico Nacional

IP36
In-silico investigation of surface proteins from Sarcocystis spp. that could cause cross reaction in the serological diagnosis of Toxoplasma gondii
Fernando Aarón Rosas Bruno. FES Iztacala. Universidad Nacional Autónoma de México

IP37
TGF-β in the control of T helper lymphocytes populations in melanoma
Andrés Felipe Sáenz Cabezas. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

IP38
Macrophage migration inhibitor factor contributes to pathology by Plasmodium yoelii 17XL infection
Víctor Hugo Salazar Castañón. FES Zaragoza. Universidad Nacional Autónoma de México

IP39
Participation of conventional dendritic cells by flow cytometry in a mouse model of lupus
Anahi Sotelo Rodríguez. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

IP40
Characterization of the Pescadillo protein in the human pathogen Trypanosoma brucei
Emmanuel Torres Morales. FES Iztacala. Universidad Nacional Autónoma de México

IP41
Effect of prenylated chalcones on Trichomonas vaginalis.
Laura Isabel Vázquez Carrillo. Posgrado en Ciencias Genómicas. Universidad Autónoma de la Ciudad de México

IP42
Klf10 favors Mycobacterium tuberculosis survival by impairing IFN-γ production and preventing macrophages reprograming to Micropinocytosis
Leonor Pérez Martínez. Instituto de Biotecnología, UNAM

MEDICINE, HEALTH & NUTRITION I

M1
Paradoxical Activation of TIMP-3 by MMP-28 in cell migration
Arantxa Melissa Aguilar López. Facultad de Ciencias. Universidad Nacional Autónoma de México

M2
Effect of sialic acids α2-3 and α2-6 stimulation on proliferation and protein synthesis on oral cavity epidermoid cancer cells
Luis Enrique Ambrosio Castillo. Facultad de Odontología. Universidad Autónoma Benito Juárez de Oaxaca

M3
Altered pathways of hypoxia in lung fibroblasts and their relationship with the development of idiopathic pulmonary fibrosis.
Arnoldo Aquino Gálvez. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

M4
Evaluation of the combination of Metformin, Sodium Dichloroacetate and Caffeine as a treatment for Pulmonary Adenocarcinoma under hypoxic conditions
Arnoldo Aquino Gálvez. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

M5
Periodontal Disease Increase the Expression of ACE2 and TMPRSS2 in Oral Epithelium of Diabetes Mellitus Type 2 patients increasing the risk to infection of SARS-CoV-2.
Juan Antonio Arreguin Cano. Facultad de Estomatología. Benemérita Universidad Autónoma de Puebla

M6
Protective Effect on Human Erythrocytes of Annona Muricata L
Ana Paola Balderrama Carmona. Departamento de Ciencias Químico-Biológicas y Agropecuarias. Universidad de Sonora

M7
Acetylation as crucial posttranslational modification in Pulmonary Arterial Hypertension
Judith Bernal-Ramirez. The Institute for Obesity Research. Tecnológico de Monterrey

M8
Nutritional status of a population with a high incidence of chronic kidney disease of unknownetiology in the Eastern part of Michoacan state
Beatriz Cabezas Núñez. Facultad de Ciencias Médicas y Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

M9
Identification of unfolded protein response markers in lungs from Hypersensitivity Pneumonitis patients
Sandra Cabrera Benítez. Facultad de Ciencias. Universidad Nacional Autónoma de México

M10
Autophagy and SPC maintain stemness potential in age-accelerated mice alveolar epithelial cells

Uriel Camacho-Silverio. Facultad de Ciencias. Universidad Nacional Autónoma de México

M11
Involvement of Fusobacterium nucleatum in colorectal carcinoma
Vania Lisset Castillo García. Facultad de Medicina. Benemérita Universidad Autónoma de Puebla

M12
MicroRNAs contained in extracellular vesicles as high sensitivity and specificity biomarkers for hepatocellular carcinoma diagnostic
Luis Alberto Castro Sánchez. Centro Universitario de Investigaciones Biomédicas. Universidad de Colima

M13
Identification of genetic variants of the FTO gene and their association with markers of obesity in the Mexican population.
Alonso Chama Avilés. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

M14
Identification of gene expression signatures associated with cisplatin intrinsic resistance in lung adenocarcinoma cell lines
Rodolfo Luis Chavez Dominguez. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

M15
Changes in mitochondrial dynamics and its modulation by an adenosine derivative in the remodeling stage in a model of myocardial infarction.
Enrique Chávez Jiménez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

M16
Detection and validation of response biomarkers in patients with locally advanced sarcomas: clinical and molecular analysis
Ximena Irán Cortés Fernández. Instituto Nacional de Cancerología

M17
Effect of the consumption of ramón flour on high-fat diet-induced obesity model
Trinidad Eugenia Cu Cañetas. Escuela de Salud. Universidad Modelo

M18
Lack of prolactin receptors leads to precocious intestinal maturation in lactating mice
José Luis Dena Beltrán. Instituto de Neurobiología. Universidad Nacional Autónoma de México

M19
OH-ATRAZINE induce expression syncitin and beta-hCG on the human trophoblast
Pablo Enrique Domínguez López. UIMMR Hospital de Ginecología y Obstetricia No. 4 “Dr. Luis Castelazo Ayala”. IMSS

M20
Impact of miR-155-5p on the fibrotic phenotype of lung fibroblasts in hypersensitivity pneumonitis
Marco Antonio Espina Ordoñez. Facultad de Medicina. Universidad Nacional Autónoma de México

M21
Curcuminoid effects on a model of fatty liver in rats
María Teresa Espinosa García. Facultad de Medicina. Universidad Nacional Autónoma de México

M22
Clinical relevance of the HSP90AA1 and HSP90AB1 expression profile in patients with locally advanced soft tissue sarcoma of the extremities
Angélica Fitta Valdés. Instituto Nacional de Cancerología

M23
Efficacy of a high-protein diet to lower glycemic levels in type 2 diabetes mellitus: a systematic review
María Nelly Flores Hernández. FES Zaragoza. Universidad Nacional Autónoma de México

M24
A vegetal protein and fiber rich nutraceutical ameliorates features of Heart Failure with preserved Ejection Fraction in a mouse model
Jorge Alberto Fragoso-Medina. The Institute for Obesity Research. Tecnológico de Monterrey

M25
Impact of Resistin on migration and invasion phenomena in PC3 prostate cancer cells
Jesús Andrés Frayde Gómez. Facultad de Medicina. Universidad Autónoma de Baja California

M26
Involvement of the eIF4E factor in the mechanism of Doxorubicin resistance in triple-negative breast cancer model
Héctor Frayde Gómez. Facultad de Medicina. Universidad Autónoma de Baja California

M27
Effect of Endocrine Disrupting Compounds in neurons associated to Autism Spectrum Disorder
Gabriela García Cerón. Facultad de Química. Universidad Nacional Autónoma de México

M28
Effect of the coadministration of resveratrol and vitamin C on oxidative status in postmenopausal women with insulin resistance. Randomized clinical trial.
Aline Yunuen García Cortés. Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes

M29
The natural compound α-mangostin inhibits cervical tumor growth
Janice García Quiroz. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

M30
Abnormal mitochondrial calcium content in angiotensin-induced hypertrophy is ameliorated by cannabidiol mimicking PPAR-g activation
Gerardo García-Rivas. Cardiovascular Medicine. Tecnológico de Monterrey

M31
Antitumor effect of a lipid-rich extract from native Mexican avocado seed (Persea americana var. drymifolia) in an in vivo model of murine melanoma
Diana Gabriela Garnica Vélazquez. Facultad de Medicina Veterinaria y Zootecnia. Universidad Michoacana de San Nicolás de Hidalgo

M32
Association of clock gene SNPs with clinical markers of metabolic disorders
María Fernanda Garrido León. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

M33
Search and investigation of associated bacteria in bronchial lavages in Covid patients at The General Hospital "Dr. Miguel Silva.
Mario Javier Gutiérrez Fernández. Universidad Tecnológica de Morelia

M34
Evaluation of the Toll like receptor 2 concentration in the saliva of patients with periodontal disease
Rebeca Guzmán Medrano. Facultad de Odontología. Universidad Autónoma de Chihuahua

M35
Generation of a cellular model to study the capacity of Oleaceae pollen proteins to produce an allergic reaction in vitro
Israel Hernández Aguilar. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

M36
Pharmacokinetics of factor VIII in Mexican patients with hemophilia A
Jesús Hernández Juárez. Facultad de Odontología. Universidad Autónoma Benito Juárez de Oaxaca

M37
FoxO3a in Hypersensitivity Pneumonitis Fibroblasts
Iliana Herrera Fuentes. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

M38
Drug discovery in cancer research: what are we looking for?
Nadia Judith Jacobo Herrera. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

M39
Analysis of effect the bioactive compounds present in foods recommended and non-recommended present in the diet of Mexicans and their relationship with SNPs associated atherosclerosis"
Debora Jimenez Diaz. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

M40
Screening of Agave plants as alternative of α-glucosidase inhibitors source

Elia Donají Juárez Niño. CIIDIR. Unidad Oaxaca. Instituto Politécnico Nacional

M41
Potential effect of brassinosteroids analogs for the prevention of keloid scarring
Marisol Lazcano Rendon. Facultad de Medicina. Benemérita Universidad Autónoma de Puebla

M42
Analysis of the antioxidant effect of ergothioneine in the pathogenesis of Vascular Dementia''
Lizet Guadalupe Leyva García. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

M43
Exercise, metformin, and tBHQ counteract high-fat diet-induced damage in liver mitochondria of middle-age female Wistar rats.
Stefanie Paola López Cervantes. Departamento de Ciencias de la Salud. Universidad Autónoma Metropolitana

M44
Gene expression of ABCG2, SLC22A12, IL-1β, and ALPK1 in peripheral blood leukocytes of primary gout patients were correlated with their comorbidities
Ambar Lopez Macay. División de Neurociencias. Instituto Nacional de Rehabilitación

M45
Clinical-epidemiological profile of a cohort of patients hospitalized with COVID-19 and analysis of polymorphisms in the NOS2 gene (rs2297518, rs2779248 and rs10459953)
Miguel Ángel López Martínez. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

MICROBIOLOGY & VIROLOGY II

MV43
Development of an indirect ELISA with recombinant porcine epidemic diarrhea virus proteins to carry out a seroprevalence study of the virus in pig farms in Mexico.
Eduardo García González. Tecnológico Nacional de México en Celaya

MV44
Production of an antigenic fragment derived from the S protein of the porcine epidemic diarrhea virus, in a Pichia pastoris expression system.
Eduardo García González. Tecnológico Nacional de México en Celaya

MV45
Regulation of virulence factors by quorum sensing in strains belonging to phylogroups 3 and 5 of Pseudomonas aeruginosa
Selene García-Reyes. Institute of Structural Biology. University Grenoble Alpes

MV46
Participation of the microtubular and actin cytoskeleton in the cellular organization during the development of the entomopathogenic fungus Metarhizium brunneum
Abraham A Gasca-Venegas. Departamento de Microbiología. Centro de Investigación Científica y de Educación Superior de Ensenada

MV47
Analysis of antimicrobial resistance genes and MLST population structure of Salmonella enterica strains isolated in Mexico from 2000-2020
Adrián Gómez Baltazar. Facultad de Química. Universidad Autónoma de Querétaro

MV48
Identification of Chlamydia trachomatis genotypes in newborns with respiratory distress
Melissa Daniella Gonzalez Fernandez. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

MV49
Evaluación in silico and in vitro of 4-formyl pyrazole derivatives on the enzyme 3-hydroxy-3methyl glutaryl coenzyme A reductase from Candida glabrata (HMGRCg)
Adilene González Silva. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

MV50
Study of exploitation of exoproteases and population collapses in clinical strains of Pseudomonas aeruginosa
Katya Dafne Guadarrama Orozco. Facultad de Medicina. Universidad Nacional Autónoma de México

MV51
Proteolytic activity of proteins secreted by Ornithobacterium rhinotracheale
Maribel Guerrero-Rangel. FES Iztacala. Universidad Nacional Autónoma de México

MV52
ERIC-PCR typing of clinical strains of sepsis-associated Escherichia coli
Dafne Guillén-Navarro. Hospital Infantil de México "Federico Gómez"

MV53
Characterization of Thioredoxin/Thioredoxin Reductase system of Candida glabrata
Ma. Guadalupe Gutiérrez Escobedo. Instituto Potosino de Investigación Científica y Tecnológica A.C.

MV54
Trichoderma and Plant Growth-Promoting Bacteria, searching for a synergistic interaction with plants
Paulina Guzmán Guzmán. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MV55
Regulation of glycogen synthesis and degradation by quorum sensing in Pseudomonas aeruginosa
Mariel Hernández Garnica. Facultad de Medicina. Universidad Nacional Autónoma de México

MV56
Degradation of chlorpyrifos and lambda cyalothrin by rhizospheric fungi of Typha domingensis plants from Turbio river
Daniella María Joselyn Hernández Pérez. Unidad Profesional Interdisciplinaria de Ingenieria. Instituto Politécnico Nacional

MV57
Participation of the ORFS PA2305 and PA3327 in the virulence of Pseudomonas aeruginosa PAO1
Ximena Hernández Ramos. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MV58
Role of the prophage of the Pseudomonas aeruginosa strain ID4365 in population collapses due to the exploitation of exoproteases from its host
Daniel Huelgas Méndez. Facultad de Medicina. Universidad Nacional Autónoma de México

MV59
The plant beneficial rhizobacterium Achromobacter sp. 5B1 influences root development through auxin signaling and redistribution
Kirán Rubí Jiménez Vázquez. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MV60
Functional and structural studies of two modular antimicrobial endolysins: insights into the potential application in controlling vibriosis in shrimp farms
Oscar Linares-Vergara. Laboratorio de Biología Sintética, Estructural y Molecular. Universidad de Colima

MV61
Seroprevalence of neutralizing antibodies against human and simian adenovirus types, including those used in COVID-19 vaccines, in healthy adults in Mexico.
Raul Eduardo López Antonio. Instituto de Investigación en Ciencias Básicas y Aplicadas. Universidad Autónoma del Estado de Morelos

MV62
Metabolic capacity from Rahnella sp. to degrade xylan, a dominant gut symbiont of Dendroctonus species
Flor Nohemí Rivera Orduña. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

MV63
Screening of phosphate solubilization identifies six Pseudomonas species with contrasting phytostimulation properties in Arabidopsis seedlings
José López Hernández. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

MV64
Phenotypic and genotypic analysis of sequential clinical isolates from Candida glabrata
Ana Lizbeth López Marmolejo. Instituto Potosino de Investigación Científica y Tecnológica A.C.

MV65
Wolbachia pipientis modifies protein expression in Aedes aegypti cells to diminish the susceptibility to dengue virus.
Teresa López Ordóñez. Centro Regional de Investigación en Salud Pública. Instituto Nacional de Salud Pública

MV66
Humoral immune response surveillance in a vaccinated student population trough SARS-CoV-2 Mpro and N proteins
Mónica Gisel López Quiñonez. Universidad Autónoma de Chihuahua

MV67
In-silico analysis of mutations that allow transmission of avian influenza A viruses to humans in Mexico
Melissa Mariana López-Ramos. Facultad de Medicina. Benemérita Universidad Autónoma de Puebla

MV68
Structure and diversity of bacteria and phages communities in the rhizosphere of common bean (Phaseolus vulgaris)
Griselda López Romo. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MV69
The IRF3 and IFI16 components of innate immunity are inhibited in adenovirus-infected cells through their relocalization to viral replication compartments
Regina Malpica. Centro de Investigación en Dinámica Celular. Universidad Autónoma del Estado de Morelos

MV70
Hierarchical protein secretion through the injectisome of enteropathogenic E. coli
Arely Marcos-Vilchis. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

MV71
The Human Adenovirus 36 E4Orf1 protein is sufficient but is not required to induce adipogenesis in infected cells
Verónica Márquez. Centro de Investigación en Dinámica Celular. Universidad Autónoma del Estado de Morelos

MV72
A novel correlative confocal fluorescence and transmission electron microscopy method to characterize extracellular vesicles
Juan Manuel Martínez-Andrade. Centro de Investigación Científica y de Educación Superior de Ensenada

MV73
Cytotoxic activity of isolated bacteria from a Mayan sinkhole located in Sisal, Yucatan
Nahuel Matias Ko. Unidad de Química en Sisal, Yucatán. Universidad Nacional Autónoma de México

MV74
Expression of histone modifying enzymes of Phytophthora capsici during plant-pathogen interaction
Mónica Berenice Rodríguez Rendón. Escuela Nacional de Estudios Superiores León. Universidad Nacional Autónoma de México

MV75
Mannheimia haemolytica OmpH functions as an adhesin
J. Fernando Montes-García. FES Iztacala. Universidad Nacional Autónoma de México

MV76
On the role of the ATPase protein complex in the injectisome of enteropathogenic Escherichia coli
Amin Mora. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

MV77
Identification and characterization of biocontrol agents from amphibians skin against Botrytis cinerea
Yordan J. Romero-Contreras. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

MV78
Implementation and improvement of the CRISPR Cas 12a detection system for SARS-Cov-2 detection
Melissa Daniela Morales Moreno. Instituto de Química. Universidad Nacional Autónoma de México

MV79
From Cap to Collar-How the Endocytic Collar is originated in Neurospora crassa
Rosa R. Mouriño-Pérez. Departamento de Microbiología. Centro de Investigación Científica y de Educación Superior de Ensenada

MV80
The E1B-55KDa oncoprotein regulates adenoviral gene transcription.
Eduardo Mundo Nájera. Centro de Investigación en Dinámica Celular. Universidad Autónoma del Estado de Morelos

MV81
Proteomic analysis reveals the global regulatory effect of the BarA/SirA and CsrB/C systems of Salmonella Typhimurium in conditions relevant for virulence
Jessica Nava Galeana. Instituto de Biotecnología. Universidad Nacional Autónoma de México

MV82
Pigment-producing bacteria isolated from mangroves located in Sisal, Yucatan
Fatima Navarro Cetina. Unidad de Química en Sisal, Yucatán. Universidad Nacional Autónoma de México

Posters Session III

Wednesday October 19, 2022
18:15 – 20:15

BASIC BIOCHEMISTRY III

BB61
Toxicity, identification and visualization of aluminium in plant cells using different advanced microscopy techniques
Ángela Ku González. Centro de Investigación Científica de Yucatán A.C.

BB62
Cellular distribution of alkaloids in Argemone mexicana L.
José Ignacio Laines-Hidalgo. Centro de Investigación Científica de Yucatán A.C.

BB63
Production of a novel bioactive polyketide of marine origin using the metabolic chassis of Escherichia coli
Susana San Juan López-Gutiérrez. LaBioSEM. Universidad de Colima

BB64
The copper transport mediated by the P-type ATPase ctpA is required for enzymes involved in the response to oxidative stress in Mycobacterium tuberculosis
Marcela López Ruíz. Facultad de Ciencias. Universidad Nacional de Colombia

BB65
Inhibition of lecithin-dependent hemolysin of Vibrio parahaemolyticus by metal ions and chemical reagents
Alonso Alexis López-Zavala. Departamento de Ciencias Químico Biológicas. Universidad de Sonora

BB66
Changes in mitochondrial metabolism in metabolically activated macrophages.
Luis Alberto Luévano Martínez. The Institute for Obesity Research. Tecnológico de Monterrey

BB67
USAK, a peptide derived from the C-terminal region of CETPI, modulates in vivo the systemic response to LPS: Proof-of-Concept employing PET
Ismael Luna-Reyes. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB68
Cholesterol dependence of acetylcholinesterase enzyme activity of erythrocytes in normal and hyperglycemic samples
Hassler Stefan Macias Sánchez. Escuela de Ciencias. Universidad de las Américas Puebla

BB69
A computational-experimental approach for the targeted development of fluorogenic substrates and competitive inhibitors of MtMarP protease
Pablo A. Madero-Ayala. Facultad de Ciencias Químicas e Ingenierías. Universidad Autónoma de Baja California

BB70
Agave fructans metabolic profiles in plants of Agave angustifolia Haw. under two different crop management strategies
Ruth Esperanza Márquez-López. Centro Interdisciplinario de Investigación para el Desarrollo Integral Regional. Unidad Oaxaca. Instituto Politécnico Nacional

BB71
Degradation of diesel and gasoline by ligninolytic fungus isolated from contaminated soil
José Antonio Martínez Villalba. Departamento de Bioquímica. Universidad Iberoamericana Torreón

BB72
Effect of chemical inhibitors on the recombinant G6PD: 6PGL fused protein of the parasite Trichomonas vaginalis
Víctor Martínez-Rosas. Instituto Nacional de Pediatría. Instituto Politécnico Nacional

BB73
Spectroscopic analysis of metal ions effect on the aggregation of a 6aJL2R24G protein variant.
María Fernanda Mata Salgado. IICBA. Universidad Autónoma del Estado de Morelos

BB74
Complementary mechanisms that counteract deficiencies in Ca2+ transport mediated by P-type ATPases in Mycobacterium tuberculosis
Milena Maya Hoyos. Facultad de Ciencias. Universidad Nacional de Colombia

BB75
Analysis of the expression of the transcription factor WRINKLED 1 in coconut zygotic embryos at three developmental stages
Damian Alberto Mayo Ruiz. Centro de Investigación Científica de Yucatán A.C.

BB76
A new perspective of protein evolution mechanisms by natural selection and gene drift.
Adriana Julián-Sánchez. Facultad de Medicina. Universidad Nacional Autónoma de México

BB77
Development of a novel virus-like particle (VLP) platform for the display of the SARS-CoV-2 RBD to induce specific immune responses
Angel Homero Miranda Moreno. Instituto de Ciencias Biomédicas. Universidad Autónoma de Ciudad Juárez

BB78
Effect on stability and kinetics of β-hairpin in T. thermophilus HB27 laccase
Beatriz Miranda-Zaragoza. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BB79
The plant mitochondrial homologous recombination
Josué Daniel Mora Garduño. Langebio. Cinvestav

BB80
Biochemical characterization of the bifunctional enzyme G6PD::6PGL of the parasite Giardia lamblia
Laura Eloísa Morales Luna. Posgrado en Ciencias Biológicas. Universidad Nacional Autónoma de México

BB81
Zika virus hijacks dynein for its replication cycle
Edgar Morales Ríos. Departamento de Bioquímica. Cinvestav Zacatenco

BB82
Betaine aldehyde dehydrogenase activity and biomass evaluation in various genotypes of wheat (Triticum aestivum) under heat stress
Grelda Arelí Morán Yañez. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB83
Finding the SLC16A11 substrate by structural modeling
Nicole Justine Moreno Licona. Cinvestav Zacatenco

BB84
Residues in randomized positions contribute to the biochemical properties of designed ankyrin proteins
Diego Nájera Benavides. Instituto Nacional de Pediatría. Universidad Nacional Autónoma de México

BB85
Identification of antimicrobial peptides from scorpion venom of a new species of the genus Mesomexovis
Juana María Jiménez-Vargas. Facultad de Ciencias Químicas. Universidad de Colima

BB86
MAPK and PKA signaling pathways modulate the steroidogenesis in JEG3 cells
Sofía Olvera Sánchez. Facultad de Medicina. Universidad Nacional Autónoma de México

BB87
Molecular dissection of the EscO protein from the injectisome of enteropathogenic Escherichia coli Octavio
Augusto Ontiveros Vivanco. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BB88
Hyperglycemia affects rat sperm hyperactivation and membrane potential
Hiram Pacheco Castillo. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Laura Daniela Palomino Navarrete. Facultad de Química. Universidad Nacional Autónoma de México

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Sergio Gerardo Hernández León. Centro de Investigación en Alimentación y Desarrollo, A.C.

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Floria Lizárraga Sánchez. Instituto Nacional de Medicina Genómica

G54
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Floria Lizárraga Sánchez. Instituto Nacional de Medicina Genómica

G55
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Sarah Melissa Lugo Caro del Castillo. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

G56
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Jesús Monroy Rodríguez. Centro Universitario de Investigaciones Biomédicas. Universidad de Colima

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Jesús Nieto Hernández. Facultad de Ciencias Químicas. Universidad Autónoma de San Luis Potosí

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Luis Fernando Núñez-Becerril. Centro de Investigación Científica de Yucatán A.C.

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Stephanie I. Nuñez-Olvera. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

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Pedro Iván Huerta Venegas. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Norma Angélica Oviedo de Anda. Hospital de Infectología. Centro Médico Nacional La Raza. IMSS

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Emir Alejandro Padilla Padilla. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

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Mario Perez-Medina. ENCB. IPN. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

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Transcriptomic portrait of epigenes in human gliomas
Sofía Plata Burgos. Unidad Cuajimalpa. Universidad Autónoma Metropolitana

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Carmen Quinto. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Single-cell analysis of the Ca2+ signaling genes in breast cancer
Andrés Hernández-Oliveras. Facultad de Medicina. Universidad Nacional Autónoma de México

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Retis-Resendiz Alejandra Monserrat. Facultad de Química. UNAM. Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes

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Anya Miranda Reyes Torres. Facultad de Ciencias. Universidad Nacional Autónoma de México

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Luis Alberto Rivera Rivas. FES Iztacala. Universidad Nacional Autónoma de México

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Julia Gabriela Rivero Manzanilla. Centro de Investigación Científica de Yucatán A.C.

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Mónica Rodríguez Bolaños. Instituto de Ecología. Universidad Nacional Autónoma de México

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Javier Rodríguez Hernández. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

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A long non-coding RNA as a novel regulator of ABA

signaling in Arabidopsis thaliana
Dhamar Gabriela Rodriguez Tenorio. Universidad Autónoma de San Luis Potosí

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Jorge Hiram Romero Estrada. Facultad de Medicina. Universidad Nacional Autónoma de México

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Hernán Romo Casanueva. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

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Miguel Ángel Rosas Paz. Facultad de Ciencias. Universidad Nacional Autónoma de México

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Maria Montserrat Rosendo Vargas. Instituto Potosino de Investigación Científica y Tecnológica A.C.

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Evoli Noemi López Morán. Ciencias Químicas. Benemérita Universidad Autónoma de Puebla

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Silvia Araceli López Morán. Centro de Investigación Biomédica. Tecnológico de Monterrey

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Alejandro Lopez Mejia. Facultad de Medicina. Universidad Nacional Autónoma de México

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Erika Rubí Luis García. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

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Arijahir Alexis Mancio Cárdenas. Instituto Nacional de Cancerología

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Sandra Gabriela May Pérez. División Académica de Ciencias Básicas. Universidad Juárez Autónoma de Tabasco

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Abraham Méndez Fernández. Escuela de Medicina y Ciencias de la Salud. Tecnológico de Monterrey

M53
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Ricardo Miranda Blancas. Facultad de Medicina. Universidad Nacional Autónoma de México

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Josaphat Miguel Montero Vargas. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

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Gabriela Morales-Guadarrama. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

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Julio C Munguía Venegas. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Andrea Muñoz Ayala. Facultad de Medicina. Universidad Autónoma de Baja California

M58

Skeletal muscle mitochondria alterations in the development of heart failure with preserved ejection fraction

Bianca Nieblas. Escuela de Medicina y Ciencias de la Salud. Tecnológico de Monterrey

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Evaluation of the RT-LAMP test for COVID19 in saliva and nasal samples

Manuel Nolasco Quiroga. Clínica Hospital ISSTE Huauchinango. UAMRA-UAT

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Evaluation of single nucleotide polymorphisms associated with the development of vascular dementia in the cellular context of the neurovascular unit

Armando Ocampo del Valle. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

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Carlos Palma Flores. Escuela Superior de Medicina. Instituto Politécnico Nacional

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SNP-food search: A tool for searching bioactive compounds related to single nucleotide polymorphisms

Natalia Paz de Sayve. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

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Detection of NTRK rearrangements by a PCR-based assay for oncology molecular diagnostics.

Cynthia Peñaloza Coronas. Laboratorio de Patología Quirúrgica y Citología de Puebla

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Genomic profiling of a consortium of tumor samples of different origins from Mexican population using NGS.

Cynthia Peñaloza Coronas. Laboratorio de Patología Quirúrgica y Citología de Puebla

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Liver disease associated with cardiac dysfunction in a mouse model of preserved ejection fraction.

Rebeca Pérez Cabeza de Vaca. Hospital Zambrano Hellion. Tecnológico de Monterrey

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Effect of epigenetic drugs valproic acid and hydralazine in metastasis development in NIH 3T3 cells transfected with Ha-rasval12 Gene.

Enrique Pérez Cárdenas. Instituto Nacional de Cancerología

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Pregnancy and GDM effect on vascular GLUT 4 density

Eduardo I Perez Muñoz. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Jonathan Saúl Piñón-Simental. Universidad Michoacana de San Nicolás de Hidalgo

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Raúl Porras Gutiérrez de Velasco. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

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Javier Rodrigo Prado Baeza. Instituto Nacional de Cancerología

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Angel Armando Pulido Capiz. Facultad de Medicina. Universidad Autónoma de Baja California

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Gladys Aurora Pulido Garcia. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

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Luz María Quirino Vela. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

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Adriana Guadalupe Quiroz Reyes. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

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Nancy Araceli Ramirez Gallardo. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Saira Karina Ramirez Thome. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

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Lluvia Iveth Rios Soto. Facultad de Medicina y Nutrición. Universidad Juárez del Estado de Durango

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Cherry Guadalupe Rodriguez Gongora. Centro de Investigaciones Regionales Dr. Hideyo Noguchi. Universidad Autónoma de Yucatán

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Nidia Samara Rodríguez Rivera. Facultad de Medicina. Universidad Nacional Autónoma de México

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Juan Antonio Rojas Murillo. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

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Lessly Monserrat Sánchez Contla. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

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Ana Karina Segovia Parra. Facultad de Medicina y Nutrición. Universidad Juárez del Estado de Durango

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Norma Aurora Stephens Camacho. Departamento de Ciencias Químico-Biológicas y Agropecuarias Universidad de Sonora

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Manuel Tinajero Rodríguez. Subdirección de Investigación Básica. Instituto Nacional de Cancerología

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Tania Valdivia Herrera. Facultad de Ciencias. Universidad Nacional Autónoma de México

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Olga Lidia Valenzuela Limón. Facultad de Ciencias Químicas. Universidad Veracruzana

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Rafael Vargas-Castro. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

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Hilda Vargas Robles. Department of Molecular Biomedicine. Cinvestav Zacatenco

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Javier de Jesús Vasconcelos Ulloa. Instituto de Ingeniería. Universidad Autónoma de Baja California

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Gilberto Velázquez-Juárez. Departamento de Química. Universidad de Guadalajara

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Salvador Chávez Avila. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Cristian Camilo Ortiz Vasco. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Maria Dolores Camacho López. Centro de Investigación Científica y de Educación Superior de Ensenada

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Study of a fungal isolate that uses plastic polymers as carbon source
Martha Lizeth Pérez-Méndez. Departamento de Biología. Universidad de Guanajuato

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Iveth Melissa Quiroz Félix. Universidad de Sonora

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Luis Enrique Franco Correa. Facultad de Medicina Veterinaria y Zootecnia. Universidad Michoacana de San Nicolás de Hidalgo

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Alberto Ramírez Mata. Centro de Investigaciones en Ciencias Microbiologicas. Benemérita Universidad Autónoma de Puebla

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Gerardo Antonio Ramírez Paz y Puente. FES Iztacala. Universidad Nacional Autónoma de México

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Ana Sofía Ramírez Pelayo. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C.

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Ileana Sarahi Ramos Mendoza. Instituto de Investigaciones Oceanológicas. Universidad Autónoma de Baja California

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Xareni Rebollar Juarez. Facultad de Medicina. Universidad Nacional Autónoma de México

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Georgina I. López Cortés. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

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Ulises Emiliano Rodríguez Castrejón. Universidad de Guanajuato

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José Ignacio Rodríguez Ochoa. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Julia Monjaras-Feria. Wellcome-Wolfson Institute of Experimental Medicine. Queen's University Belfast

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Juliana Berenice Rojo Rodriguez. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Luzmaria Raquel Morales Cedeño. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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A novel marine Pseudomonas species with antibacterial activity
Luis Emmanuel Romero González. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Emilio Rosales Olivares. Unidad de Química en Sisal, Yucatán. Universidad Nacional Autónoma de México

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Jose Angel Rubio Miranda. Cinvestav Zacatenco. Instituto Politécnico Nacional

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Jessica Ruiz Escobedo. Instituto de Biotecnología. Universidad Nacional Autónoma de México

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Daniel Alfonso Salgado-Bautista. Centro de Investigación Científica y de Educación Superior de Ensenada

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Mónica Noel Sánchez González. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

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Jesús Ismael Sandoval Díaz. Universidad Juárez Autónoma de Tabasco

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Paola Santos. Facultad de Ciencias. Universidad Nacional de Colombia

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Apolonia Slamet. Universidad Autónoma del Estado de Morelos

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Carla Isabel Tena Fuentes. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Molecular characterization of the long non-coding RNA of PMeV-Mx, a papaya umbra-like virus, through the development of an infectious clone.
Alethia Fernanda Toriz Bravo. Centro de Investigación Científica de Yucatán A.C.

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Mary Carmen Torres Quintero. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

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Yazmin Ugalde Santiago. Universidad Autónoma del Estado de Morelos

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Jennifer Andrea Uribe López. Facultad de Ciencias Naturales. Universidad Autónoma de Querétaro

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Norma Urtiz Estrada. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

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María Fernanda Valencia Marín. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Antimicrobial Capacity of Ethanolic Extracts of Propolis

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Melissa Valenzuela Rincón. Universidad de Sonora

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Julio César Valerdi Negreros. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

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Karina Vazquez Ortiz. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

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Jorge Verdín. Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco, A.C.

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Alvaro Vidal Montiel. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

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Alicia Gabriela Zamora Avilés. Facultad de Medicina Veterinaria y Zootecnia. Universidad Michoacana de San Nicolás de Hidalgo

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Alejandra Zúñiga-Enríquez. Universidad Autónoma del Estado de Morelos

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Miguel Díaz Guerrero. Facultad de Medicina, UNAM

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Giselle del Carmen Alvarez Cirerol. Facultad de Medicina, UNAM

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Alejandro Valdivieso Proaño. Centro de Ciencias Genómicas, UNAM

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David Francisco Aguilar Ávila. Facultad de Medicina. Universidad Nacional Autónoma de México

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Raziel Alejandro Arias Sánchez. Facultad de Ciencias Médicas y Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

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Sleep restriction promotes the A1 astroglial phenotype and increases blood-brain barrier permeability
Jessica Janeth Avilez Avilez. Área Neurociencias. Universidad Autónoma Metropolitana

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Effect of selective inhibition of nuclear export with Selinexor on autophagy and senescence features in an in vitro neuronal aging model.
Lorelei Ayala-Guerrero. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

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Ana Silvia Báez Cordero. Instituto de Neurobiología. Universidad Nacional Autónoma de México

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Boromelatonin ameliorates the cognitive deficit and neuronal loss induced by estrogen deprivation in female rats
Monica Barron Gonzalez. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Guadalupe Bautista Poblet. Hospital de Especialidades. Centro Medico Nacional “Siglo XXI”

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Gisselle Angelica Campos-Martinez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

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Karen Carreto Meneses. Facultad de Ciencias Químicas. Benemérita Universidad Autónoma de Puebla

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José Alfredo Castillo Luna. Facultad de Ciencias Biológicas. Universidad Autónoma de Nuevo Léon

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Gabriela Cruz Carrillo. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

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Karen Stephany Cruz Hernández. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

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Mauricio Domínguez Castro. Instituto Nacional de Perinatologia Isidro Espinosa de los Reyes

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Eunice Dalet Farfán García. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Sleep restriction modifies insulin signaling in the hippocampus of male rats
Jesús Enrique García Aviles. Área de Neurociencias. Universidad Autónoma Metropolitana

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David García Jácome. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Lizbeth E García-Velázquez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

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Edith González Guevara. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

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Perla González Pereyra. Instituto de Neurobiología. Universidad Nacional Autónoma de México

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Christian Guerra Araiza. Centro Médico Nacional "Siglo XXI" IMSS.

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Martín Hernández Lucas. Departamento de Investigación Básica. Instituto Nacional de Geriatria

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Paola Gabriela Hernández Pérez. Escuela Superior de Medicina. Instituto Politécnico Nacional

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Neuron specific enolase as a biomarker of diabetic peripheral neuropathy
Olga Lidia Valenzuela Limón. Faculty of Chemical Sciences. Veracruzana University

NN24
Coadministration of rotenone and manganese to model Parkinson's disease in rats
Maria Teresa Ibarra Gutiérrez. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

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TRPV1 is a noxious sensor regulated by endocannabinoids
Rebeca Juárez-Contreras. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

NN26
Lysosomal alterations during neuronal senescence in an in vitro model
Paulina López-Carrasco. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

NN27
Prolactin prevents oxidative stress-induced cell death in hippocampal neurons
Fernando Macías. Instituto de Neurobiología. Universidad Nacional Autónoma de México

NN28
Histone deacetylase 2 inhibition reverses memory impairment induced by acute stress in mice
Heidy Martínez Pacheco. Instituto de Neurobiología. Universidad Nacional Autónoma de México

NN29
TNF-α receptor antagonism restores pericyte-endothelial cell interactions and improves blood-brain barrier function during sleep restriction
Ma. Fernanda Medina Flores. Universidad Autónoma Metropolitana. Unidad Iztapalapa

NN30
The neuroprotective effect of the endocannabinoid metabolites of cytochrome P450 during the staurosporine-induced neuronal death
Cynthia Navarro Mabarak. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

NN31
Exploring the role of the direct pathway of the basal ganglia in speed control during the execution of motor sequences
Diana Itzel Ortega Romero. Instituto de Neurobiología. Universidad Nacional Autónoma de México

NN32
Encoding visual stimuli by striatal neurons
Job Pérez Becerra. Instituto de Neurobiología. Universidad Nacional Autónoma de México

NN33
Curcumin decreases the protein oxidation in brain of mice fed a hypercaloric diet
Joel Ramírez-Emiliano. Departamento de Ciencias Médicas. Universidad de Guanajuato

NN34
Effect of ketogenic diet on mouse aging
Braulio Ramírez-Ramos. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

NN35
Joint administration of synthetic ligands of TLRs and vincristine in a murine model of medulloblastoma
Guadalupe Rodríguez Santos. Hospital Infantil de México Federico Gómez

NN36
Comparative genomics of TFBSs of LTTR transcription factors.
Hazel Roldán Fernández. Escuela Superior de Apan. Universidad Autónoma del Estado de Hidalgo

NN37
Anti-nociceptive effect of N-acetylcysteine in a rat model of traumatic spinal cord injury
Héctor Alonso Romero Sanchez. Universidad Autónoma Metropolitana. Unidad Xochimilco

NN38
Transcriptional profile of cytokines expressed in mast cells stimulated with S100B, a DAMP associated to neuroinflammation in huntington's disease
Gabriela Saavedra Lanuza. Departamento de Farmacobiología. Cinvestav Sede Sur

NN39
Effect of chronic hypercaloric diet feeding on the inflammatory state, and its relation to cognitive impairment in middle-aged female Wistar rats
Verónica Salas Venegas. Departamento de Ciencia Biológicas y de la Salud. Universidad Autónoma Metropolitana

NN40
A method to interrogate and manipulate pyramidal tract cortico-striatal neurons in rats.
Oswaldo Sánchez-Lobato. Instituto de Neurobiología. Universidad Nacional Autónoma de México

NN41
Immunization with peptide A91 induces neurogenesis at the level of medullary horns in moderately injured rats
Samantha Beatriz Sánchez Noriega. Universidad Anáhuac

NN42
Sulforaphane prevents oxidative damage and cognitive decline in middle-age female and male Wistar rats, but cannot revert previous damage in old individuals
Roberto Santín Márquez. División de Ciencias Biológicas y de la Salud. Universidad Autónoma Metropolitana

NN43
Characterization of rotenone-induced mitochondrial and endolysosomal dysfunction in the cell line SH-SY5Y
Ana Paula Tirado Jiménez. Instituto Nacional de Medicina Genómica

NN44
Antineoplastic effect in human glioma of Riftia Pachyptila extracts and Chemical Profile of compounds
Monica Adriana Torres Ramos. Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez

NN45
Prenatal diet programs the transgenerational heritance of brain structure and anxiety-like behavior in the offspring of rats
Luis Ángel Trujillo Villareal. Facultad de Medicina. Universidad Autónoma de Nuevo Léon

NN46
High levels of circulating Prolactin protect the brain from Diabetes-induced oxidative stress damage
Miriam Nayely Ulloa Zamudio. Instituto de Neurobiología. Universidad Nacional Autónoma de México

SIGNAL TRANSDUCTION AND CELL DIFFERENTIATION I

ST1
Role of intracellular phosphoaminoacid mutants from human alpha1B-adrenergic receptor.
Rocío Alcántara-Hernández. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST2
Differential regulation of Hypoxia-Inducible Factors 1/2/3α over canonical and non-canonical Wnt pathways in colorectal cancer cells
Eduardo Alvarado-Ortiz. Facultad de Medicina. Universidad Nacional Autónoma de México

ST3
Effect of high-glucose in Cx30.2 expression in pancreatic β cells.
Lorelei Larissa Angeles Aguilar. Facultad de Medicina. Universidad Nacional Autónoma de México

ST4
Effect of the nitrogen source in the induction of somatic embryogenesis of Coffea canephora Pierre ex A. Froehner
Centeotl Aragón Rodríguez. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

ST5
The effect of Isoarborinol in adipogenic markers in 3T3-L1 cells
Yesenia Arcos Reyes. Escuela Nacional de Medicina y Homeopatia. Instituto Politécnico Nacional

ST6
PAK 1 Promotes Breast Tumorigenesis Via Phosphorylation and Activation of the Calcium/ Calmodulin-Dependent Protein Kinase II
Luis E. Arias Romero. FES Iztacala. Universidad Nacional Autónoma de México

ST7
Modulation of Bone Cell Activity and Bone Remodeling by Sulfated Polysaccharides Derived from Brown Algae
Jessica Sharlin Landeros Juárez. Centro de Investigación Científica y de Educación Superior de Ensenada

ST8
p32 Promotes a Malignant Phenotype in Colorectal Cancer Cells
María Cristina Castañeda Patlán. Facultad de Medicina. Universidad Nacional Autónoma de México

ST9
Characterization of the function of the PcSNT protein and its role in the cell signaling pathway mediated by heterotrimeric G proteins in Penicillium chrysogenum
Maria Fernanda Cerón Moreno. Universidad Autónoma Metropolitana

ST10
Characterization of TGF-beta-loaded Extracellular Vesicles from Colorectal Cancer Cells
Diana Alondra Coquis Bucio. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST11
Effect of IL-2 in STAT1 phosphorylation in cervical carcinoma lines.
Erika Anayatzin Covarrubias Negrete. FES Zaragoza. Universidad Nacional Autónoma de México

ST12
Urocortin 2/CRF2R mediates Akt and ERK 1/2 activation in 3T3-L1 Adipocytes
Daphne Esperanza Cruz Villarreal. Departamento de Bioquímica. Cinvestav Zacatenco

ST13
Effect of corticotropin-releasing factor (CRF) on ERK 1/2 activation induced by insulin-like growth factor-1 (IGF-1) in CHO-K1 cells
Carlos De Jesus Quiroz. Departamento de Bioquímica. Cinvestav Zacatenco

ST14
Identification and evaluation of the interaction between biomolecules present at the "Manilkara zapota" seeds versus the of P53, P21, Δ-lactoferrin and β-catenin crystalographic structures
Pablo de J. de la Cruz Jiménez. División Académica de Ciencias Básicas. Universidad Juárez Autónoma de Tabasco

ST15
Effects of CBFB inhibition by CRISPR-Cas in breast cancer
Magali Espinosa Castilla. Instituto Nacional de Medicina Genómica

ST16
Regulation of FFA1 receptor interaction with beta-arrestin 2
Emmanuel Flores Espinoza. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST17
Role of TOR signaling pathway in the response to heat stress in corn (Zea mays)
Itzel García Bravo. Facultad de Química. Universidad Nacional Autónoma de México

ST18
MEDIATOR18 regulates Arabidopsis root system architecture, auxin signaling and is a critical factor for cell viability in root meristems
Javier Raya González. Facultad de Químico Farmacobiología. Universidad Michoacana de San Nicolás de Hidalgo

ST19
Adenosine Derivative Treatment Induces Transcriptomic Changes of Hepatocellular Carcinoma by regulating Wnt/β-catenin Signaling
Nuria Guerrero Celis. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST20
Glycine modulation of pro- and anti-inflammatory cytokines and their GPR-6 gene expression in adipogenesis
Rocío Alejandra Gutiérrez Rojas. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

ST21
Effect of the IFC-305 in B-cell Acute Lymphoblastic Leukemia cell lines on the PI3K/Akt/mTOR pathway
Ana María Hernández Jiménez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST22
Lisophosphatidylinositol (LPI) blocks Toll-like receptor (TLR)4-dependent pro-inflammatory and pro-angiogenic cytokine production in mast cells
Alfredo Ibarra-Sánchez. Departamento de Farmacobiología. Cinvestav Sede Sur

ST23
Sea Snails Conotoxins Modulate Bone Cell Activity
Brenda Ivette Iduarte Frias. Centro de Investigación Científica y de Educación Superior de Ensenada

ST24
Proteomic and molecular study of somatic embryogenesis in Coffea spp.
Ana Odetth Quintana Escobar. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

ST25
Chronic Leptin Treatment Induces Epithelial-Mesenchymal Transition in MCF10A Mammary Epithelial Cells
Juan Carlos Juárez Cruz. Facultad de Ciencias Químico Biológicas. Universidad Autónoma de Guerrero

Posters Session IV

Thursday October 20, 2022
14:30 – 16:30

BASIC BIOCHEMISTRY IV

BB91
Crosstalk Between O-GlcNAcylation and CD36 in Macrophages
Yobana Perez Cervera. Facultad de Odontología. Universidad Autónoma Benito Juárez de Oaxaca

BB92
Study of the structural sensitivity to the environment of intrinsically disordered regions in Arabidopsis transcription factors
César Antonio Ponce Diego. Facultad de Química. Universidad Autónoma de Chihuahua

BB93
Effect of 8-Benzyl-1,3,8-Triazaspiro-[4.5]-Decane-2,4-Dione on migration and invasion of PC3 prostatic tumoral cells stimulated with LDLs
Georgina Quintana González. Facultad de Medicina Mexicali. Universidad Autónoma de Baja California

BB94
Effect of pH and temperature on the kinetic parameters of thioredoxin-glutathione reductase from Taenia crassiceps
Juan Luis Rendón. Facultad de Medicina. Universidad Nacional Autónoma de México

BB95
The absence of pyruvate carboxylase and phosphoenolpyruvate carboxylase affect nitrogen fixation in Rhizobium phaseoli
Alma Ruth Reyes González. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

BB96
Characterization of the catalytic capacity of CCD-1 y CCD4-3 at the bixin biosynthesis pathway in Bixa orellana L.
Juana Guadalupe Hernández Reséndiz. Centro de Investigación Científica de Yucatán A.C.

BB97
Genetically encoded fluorescent biosensors to study the relocation of proteins in response to hyperosmotic stress
Esaú-E Rodríguez. Facultad de Química. Universidad Nacional Autónoma de México

BB98
Evaluating Calvin cycle efficiency in potential heat tolerant bread wheat genotypes
Andrea Romero-Reyes. Centro de Investigación en Alimentación y Desarrollo, A.C.

BB99
Mathematical modeling of the reactions catalyzed by an uncommon thermophilic cyclomaltodextrin glucanotranferase
José Gabriel Rosales Castañeda. Facultad de Ingeniería Mecánica y Eléctrica. Universidad de Colima

BB100
Application of ZnO nanoparticles in the reduction of Pb accumulation in corn crops (Zea mays)
José Martín Rosas Castor. Facultad de Ciencias Químicas. Universidad Autónoma de Nuevo Léon

BB101
Determination of the optimal conditions for the activity of betaine aldehyde dehydrogenase against γ-trimethylaminobutyraldehyde
Jesús Alfredo Rosas Rodríguez. Universidad de Sonora. Unidad Regional Sur

BB102
Phytochemical analysis of compounds of therapeutic interest from the extract of mistletoe Psittacanthus calyculatus located in the "Cerro del Palenque" of Purísima del Rincón, Guanajuato and its possible treatment as an antimicrobial agent.
Daniela Sánchez Guevara. Instituto Tecnológico Superior de Purísima del Rincón

BB103
Phytochemical characterization, Angiotensin I-converting enzyme inhibitory and antioxidant activity of Mexican Cordiceps militaris fruiting body ethanolic extract.
Erick Sierra Campos. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

BB104
Analysis of the possible participation of ALDH3H1-1 and SABATH4 genes in bixin biosynthesis in Bixa orellana L.
Diana Laura Sierra Ulín. Centro de Investigación Científica de Yucatán A.C.

BB105
Aldehyde dehydrogenases role in oxidative stress protection in anaerobic microorganisms
Mayel Silva Flores. Departamento de Bioquímica. Instituto Nacional de Cardiología "Ignacio Chávez"

BB106
Analysis of the expression of transcripts encoding oleosins in solid coconut endosperm with different levels of maturity
Blanca Catalina Solís Arias. Centro de Investigación Científica de Yucatán A.C.

BB107
Pregnancy-induced physiological cardiac hypertrophy regulates the expression of perilipin isoforms and PGC-1α in Sprague-Dawley rats
José Guadalupe Soñanez Organis. Ciencias Químico-Biológicas y Agropecuarias. Universidad de Sonora

BB108

Analysis of gene expression: apetala (AP), shaterproof (SHP) and spatula (SPT) in the fruit dehiscence zone of Bixa Orellana L.

Rocío Tamayo García. Centro de Investigación Científica de Yucatán A.C.

BB109

Biochemical characterization of EhHAPp49, an amoebic protein of the HAP-phytase class that exhibits pyrophosphatase activity

Celina Terán Ramírez. School of Chemical Sciences and Engineering. Universidad Autónoma de Baja California

BB110

Metal promiscuity of DapE, a target enzyme for bacterial growth

Manuel Terrazas-López. Universidad Autónoma de Ciudad Juárez

BB111

Heterologous expression of a CCD4 from Bixa orellana L in E.coli cells

Diego Torres-Pech. Centro de Investigación Científica de Yucatán A.C.

BB112

Analysis of the respiratory chain of Bacillus licheniformis as a cyanide-resistant microorganism.

Daniel Uribe-Ramírez. Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional

BB113

Oligomerization of the peptide defensin} J1-1_K45E

Angel David Vargas Burgoa. Centro de Investigación Científica de Yucatán A.C.

BB114

Interrelationship between the cell cycle and glycolysis in maize

Teresa Vargas Cortez. Facultad de Química. Universidad Nacional Autónoma de México

BB115

Effect of β-glucosidase from Chayote (Sechium edule) on the release of volatile compounds in the preparation of blonde ale style beer.

Iliana Vásquez Lara. Unidad de Bioquímica e Inmunología. Instituto Tecnológico de Oaxaca

BB116

Thioredoxin-glutathione reductase from Taenia crassiceps and its ability to generate s uperoxide anion

César Vásquez Lima. Facultad de Medicina. Universidad Nacional Autónoma de México

BB117

H+-ATPases Pma1 and Pma2 from the corn smut basidiomycete Ustilago maydis: a functional analysis

Melissa Vázquez Carrada. Instituto Politécnico Nacional

BB118

Heterologous expression and functional characterization of an aldehyde dehydrogenase (ALDH) potentially involved in bixin biosynthesis

Gabriela Del Carmen Vázquez Gómez. Centro de Investigación Científica de Yucatán A.C.

BB119

A possible involvement of AGCVIII kinases in the phosphorylation of the Argemone mexicana AmABCB1 alkaloid transporter

Felipe Vázquez-Flota. Centro de Investigación Científica de Yucatán A.C.

BB120

Functional characterization of a three-domain pH-adaptive cyclomaltodextrin glucanotransferase

Beatriz Velázquez Cruz. Laboratorio de Agrobiotecnología. Universidad de Colima

BB121

Mgr2 modulates the import of yeast cytosol-synthesized subunit II of cytochrome c oxidase (Cox2) when moving through the TIM23 translocon

Felipe Nieto Panqueva. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

BIOTECHNOLOGY II

BT33
In vitro culture of shoots and calluses of Kalanchoe daigremontiana, as a sustainable source for obtaining metabolites
Gustavo Vicente Leyva Alvarez. Unidad Profesional Interdisciplinaria de Ingeniería. Campus Guanajuato. Instituto Politécnico Nacional

BT34
Study of regulatory proteins in lipolysis: Perilipin 1
Nancy Yaneth Linares García. División de Biología Molecular. Instituto Potosino de Investigación Científica y Tecnológica A.C.

BT35
The effect of punctual mutations on the stability and aggregation state of human CGI-58 protein
Miriam Livier Llamas Garcia. División de Biología Molecular. Instituto Potosino de Investigación Científica y Tecnológica A.C.

BT36
The contribution of the composition, processing, and modifications on the characteristics of natural extracellular matrix gels
Omar Gabriel López Campos. Unidad Profesional Interdisciplinaria de Ingenieria. Instituto Politécnico Nacional

BT37
Disintegrin and derivates activity on integrins
Andrid López Clavijo. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BT38
Comparison of recombinant antibody purification processes by pack-bed and membrane chromatography technique
Francisco E. Lopez Salas. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

BT39
5-hydroxymethyl-2-furaldehyde virulence factor inhibitor in Pseudomonas aeruginosa PA14
Daniela Luis Yong. Centro de Investigación de Micología Aplicada. Universidad Veracruzana

BT40
Effect of Xylaria curta extracts on the regulation of the Las system of P. aeruginosa
Daniela Luis Yong. Centro de Investigación de Micología Aplicada. Universidad Veracruzana

BT41
Antiacetylcholinesterase potential of extracts of carao pulp (Cassia grandis)
Víctor Manrique Fernández. Universidad de Extremadura

BT42
Towards development of a protocol to obtain transgenic Cactaceae plants
Alejandra Lara Vargas. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BT43
Sphingosine 1 phosphate increases testosterone concentration and stimulates theca cells viability
Lydia Marín López.Facultad de Medicina Veterinaria y Zootecnia. Universidad Nacional Autónoma de México

BT44
Acrylamide adsorption on chitin beads
Silvia Martínez Hernández. Unidad de Estudios Superiores Tultitlán. Universidad Mexiquense del Bicentenario

BT45
Implementation of a toluene dioxygenase platform to boost hydrocarbon bioremediation with microbial consortia
Octavio Martínez Martínez. Facultad de Química. Universidad Nacional Autónoma de México

BT46
α-tocopherol production in anaerobic culture by Euglena gracilis
Luis Salvador Meneses Hernández. Instituto Nacional de Cardiología “Ignacio Chávez”

BT47
Systematic modifications of a biosensor based in a

intrinsically disordered protein that tracks the effects of osmotic stress in Arabidopsis thaliana
Guadalupe Itzel Meneses Reyes. Facultad de Química. Universidad Nacional Autónoma de México

BT48
Transcriptome analysis of Persea americana cv. Hass highlights genes involved into zygotic embryogenesis process
Zurisadai Monroy González. Unidad de Bioquímica y Biología Molecular de Plantas. Centro de Investigación Científica de Yucatán A.C.

BT49
Total phenolic content and total triterpenoid content in Ageratina pichichensis and their in vitro cultures
Elizabeth Alejandra Motolinia Alcántara. Universidad Autónoma Metropolitana. Unidad Iztapalapa

BT50
Production of bioethanol from agro-industrial waste by microorganisms isolated from mining waste
Manuel Antonio Naranjo Reyes. Unidad Profesional Interdisciplinaria de Ingenieria. Campus Guanjuato. Instituto Politécnico Nacional

BT51
Xylose reductase NADPH dependent and xylitol dehydrogenase NAD+ dependent from Clavispora lusitaniae
Odilia Pérez-Avalos. Departamento de Biotecnología y Bioingeniería. Cinvestav Zacatenco

BT52
Genetic resources and biotechnology in Habanero pepper (Capsicum chinense Jaqc.) breeding
Gema Pijeira-Fernández. Centro de Investigación Científica de Yucatán

BT53
Nano-micellar technique to improve the quercetin stability
Laura Itzel Quintas Granados. Unidad de Estudios Superiores Tultitlán. Universidad Mexiquense del Bicentenario

BT54
Inhibition of hsa-miR-16a-5p decreases viability and survival of triple-negative breast cancer cells.
Rodolfo Reyes Morales. Laboratorio de Biotecnología Médica y Farmacéutica. Universidad Popular Autónoma del Estado de Puebla

BT55
Genetic transformation of the green microalga Chlamydomonas reinnhardtii with the mNb6-tri gene encoding a trivalent nanobody that neutralizes the SARS-CoV-2 virus
Sandy Giselle Reyes Solian. Unidad de Biotecnología. Centro de Investigación Científica de Yucatán A.C.

BT56
Composition-structure-property relationship in decellularized esophageal matrix obtained from pigs of different ages
Rosalinda Rocha Juache. Unidad Profesional Interdisciplinaria de Ingenieria. Instituto Politécnico Nacional

BT57
Structural appendages of ETEC E9034A promote adherence to intestinal cells
Ricardo Rodríguez Martínez. Laboratorio de Investigación en Bacteriología Intestinal. Hospital Infantil de México Federico Gómez

BT58
Expression of bovine leukemia virus protein p12-p24 of genotype 1
José Hiram Sánchez Gasca. Instituto Nacional de Investigaciones Forestales Agricolas y Pecuarias

BT59
Characterization of the antibiotic effect of supernatants of Streptomyces strains isolated from mining tailings from Guanajuato, Gto.
Juan Francisco Sánchez López. Unidad Profesional Interdisciplinaria de Ingeniería. IPN

BT60
Plasmid recovery from the bacterial inhabitants from the Mayan sinkhole Pol-ac located in Sisal, Yucatan
Nancy Dayan Torres Rodríguez. Unidad de Química Sisal, Yucatán. Facultad de Química. Universidad Nacional Autónoma de México

BT61
Theoretical and experimental analysis of the diagnostic strip design for the rapid detection of Bothrops asper venom in patient serum
Michelle Adelina Toscano Salazar. Instituto de Biotecnología. Universidad Nacional Autónoma de México

BT62
In silico analysis of the expression of nitrogen fixation genes in a lignocellulose degrading consortium
Fátima Gabriela Uicab Canul. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

BT63
Functional characterization of the Carotenoid Cleavage Dioxygenases BoCCD1-1 and BoCCD4-3 from Bixa orellana L. and identification of apocarotenoids with biotechnological potential
Rosa Yazmín Us Camas. Instituto Tecnológico Superior de Calkiní en el Estado de Campeche

BT64
cgigGFP and other fluorescent molecules in Condylactis gigantea
María Vanegas Reza. Instituto de Química. Universidad Nacional Autónoma de México

BT65
Comparative heterologous protein expression of the major allergen of Fraxinus tree pollen
Juan Carlos Vizuet-de-Rueda. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

BT66
Identification and characterization and of algae cell wall degrading specific enzymes from marine actinomycetales
Julian L. Wissner. Unidad de Química en Sisal. Facultad de Química. Universidad Nacional Autónoma de México

BT67
Optimization of the L-lactate oxidase from Aerococcus viridans for electrochemical biosensors
Andrés Zárate-Romero. Centro de Nanociencias y Nanotecnología. Universidad Nacional Autónoma de México

GENETICS, EPIGENETICS & GENETIC REGULATION IV

G78
Transcriptional regulation of StEP, a self- incompatibility gene in Nicotiana
Renata Salcedo-Sánchez. Facultad de Química. Universidad Nacional Autónoma de México

G79
Two glucose-6-phosphatase isoforms are tissue-specific expressed under oxygen-limited and reoxygenation conditions in the shrimp Litopenaeus vannamei
Laura E. Hernández-Aguirre. Centro de Investigación en Alimentación y Desarrollo, A.C.

G80
Quorum sensing molecules control the oxidative stress response in the opportunistic fungal pathogen Candida glabrata
Carlos Ricardo González Ruiz. División Biología Molecular. Instituto Potosino de Investigación Científica y Tecnológica A.C.

G81
miR-193b-3p expression analysis and its possible influence over homologous recombination in triple-negative breast cancer derived cell lines
Julio Alejandro Sánchez-Pérez. FES Iztacala. Universidad Nacional Autónoma de México

G82
Epigenetic regulation and expression of the Ca2+ signaling genes in an Epithelial-Mesenchymal Transition model in breast cancer cell lines
Ana Cecilia Sánchez Trujillo. Facultad de Medicina. Universidad Nacional Autónoma de México

G83
Influence of epidrugs on dental stem cells from

a biochemical and molecular approach
Angelica Anahi Serralta Interian. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

G84
Identifying Genes Devoted to the Cell Death Process in the Gene Regulatory Network of Ustilago maydis
Cinthia U. Soberanes Gutiérrez. Escuela Nacional de Estudios Superiores León. Universidad Nacional Autónoma de México

G85
Long non-coding RNAs and their association with stemness in triple-negative breast cancer
Olivia Téllez Jiménez. Instituto Nacional de Medicina Genómica

G86
Effect of valproic acid on the growth of dental stem cells
Anahí Torres Nájera. Facultad de Ingeniería Química. Universidad Autónoma de Yucatán

G87
Self-modulation of vector promoters by overexpressed bHLH transcription factors
Ana Lilia Torres-Machorro. Laboratorio de Biología Celular. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

G88
Role of HDAC3 on nuclear morphology and profibrotic phenotype in lung fibroblasts.
María Fernanda Toscano Márquez. Facultad de Medicina. Universidad Nacional Autónoma de México

G89
Phenotypic Analysis of insertional mutants of the A.thaliana twinkle primase helicase, SALK_152246, CS855183 WiscDsLox423D2 and SALK_148150
Lilia María de Guadalupe Uribe Ramírez. Laboratorio Nacional de Genómica para la Biodiversidad

G90
Argonaute5 regulates the nodule development in Phaseolus vulgaris
Oswaldo Valdés López. FES Iztacala. Universidad Nacional Autónoma de México

G91
The Application of Ascorbic Acid (AsA) Improves the Quality of Solanum lycopersicum in the Vegetative
Víctor García-Gaytán. Laboratorio de Análisis y Diagnóstico del Patrimonio. El Colegio de Michoacán

G92
Molecular study of the "La" protein in the human pathogen Leishmania major
Sergio García De la Cruz. FES Iztacala. Universidad Nacional Autónoma de México

G93
The mitochondrial genome of healthy mice and humans contains a high diversity of genetic variants
Alfredo Varela-Echavarría. Instituto de Neurobiología. Universidad Nacional Autónoma de México

G94
Identification of genetic variants associated with susceptibility in the development of cervical cancer
María Guadalupe Vargas Solórzano. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

G95
Role of translation factor eIF4E family members during root development under abiotic stress in Arabidopsis thaliana
Ernesto Vázquez Chimalhua. Facultad de Química. Universidad Nacional Autónoma de México

G96
Expression in vitro of two virulence determinants from Avibacterium paragallinarum
Dorcas Flor Ramos Salas. Centro de Investigaciones en Ciencias Microbiologicas. Benemérita Universidad Autónoma de Puebla

G97
Abf1 as an essential protein in Candida glabrata, at different cellular processes

Laura Angélica Vera Salazar. Instituto Potosino de Investigación Científica y Tecnológica A.C.

G98
Identification of genetic alterations that lead to CRLF2 overexpression in pediatric pre-B acute lymphoblastic leukemia
Victoria Vieyra Fuentes. Laboratorio de Genética y Cáncer. Instituto Nacional de Pediatría

G99
Molecular analysis of Tau95 and Tau131, subunits of transcription factor TFIIIC, in the human pathogen Leishmania major
Gino Stefano Villa Delavequia. FES Iztacala. Universidad Nacional Autónoma de México

G100
Evaluation of As2O3, NaAsO2 and Na2HAsO4 on p53 regulation in SiHa, CaLo, C33-A and HaCat cell lines
Ixamail Fraire Soto. Unidad Académica de Ciencias Biológicas. Universidad Autónoma de Zacatecas

G101
Assessing the role of Hog1 in neutral lipid synthesis in the yeast Debaryomyces hansenii
Diana Villarreal-Huerta. Facultad de Ciencias. Universidad Nacional Autónoma de México

G102
Expression profile of six genes involved in neutral lipid synthesis in antarctic yeast Rhodotorula mucilaginosa
Alberto Zamora Bello. Facultad de Ciencias. Universidad Nacional Autónoma de México

G103
Transgenerational effects of glucose exposure over C. elegans behavior
Mariana Zurita Leon. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

G104
Analysis of the alternative sigma factors effect on the genetic expression of the Klebsiella pneumoniae virulence factors
Cecilia Luz Colin Olvera. Unidad de Investigación en Enfermedades Infecciosas. Hospital de Pediatría, Centro Médico Nacional Siglo XXI. IMSS

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O36
Effect of pravastatin on vascular reactivity to phenylephrine in a rat model of preeclampsia
Damián A Madrigal Aguilar. Escuela Superior de Medicina. Instituto Politécnico Nacional

O37
Generation of several high-affinity mAbs anti-Hev b 8 to analyze cross-reactivity among profilin allergens
José Israel Mares Mejía. Instituto de Química. Universidad Nacional Autónoma de México

O38
Design of dsRNA-based fungicides for the control of coffee pathogen Hemileia vastatrix
Maximiliano López Morales. Universidad del Papaloapan, Campus Tuxtepec

O39
Learning and Evaluation in Biochemical Sciences Education
Rebeca Etelvina Milán Chávez. Facultad de Medicina. Universidad Nacional Autónoma de México

O40
Inhibition of Cu(II) induced amyloid fibers formation of the 6aJL2-R24G protein.
Alan Morales Ortiz. Centro de investigación en dinámica celular. Universidad Autónoma del Estado de Morelos

O41
Resonant acoustic mixing to enhance outer-membrane vesicles released by Escherichia coli
Laura María Muñoz Echeverri. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O42
Structural Analysis of Capsicum defensin J1-1 and Expression of J1-1 K45E Variant in Escherichia coli
Gilberto Andrés Muñoz Pérez. Centro de Investigación Científica de Yucatán A.C.

O43
Mitochondrial and peroxisome dynamics during sexual development of Podospora anserina
Raful Navarro Espíndola. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

O44
Effect of chronic stress on epididymal sperm quality and testicular histology
Vanessa Guadalupe Nolasco Garduño. Centro Tlaxcala de Biología de la Conducta. Universidad Autónoma de Tlaxcala

O45
Cellular scaffolds for bone tissue of marine origin
Israel Alfonso Nuñez Tapia. Instituto de Investigaciones en Materiales. Universidad Nacional Autónoma de México

O46
Bioinformatic identification of SCNA associated lncRNAs regulators of tumoral phenotype in colorectal cancer
Héctor Herrera Orozco. FES Iztacala. Universidad Nacional Autónoma de México

O47
DhDIT2, encodes a cytochrome P450 from Debaryomyces hansenii which participates into the degradation of benzo(a)pyrene. A proposal for myco-remediation.
Francisco Padilla-Garfias. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

O48
Antitumoral activity evaluation of methanolic extract of Annona macroprophyllata on colorectal cancer
Eduardo Pérez Arteaga. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

O49
Inhibition of TGF-βs and their receptors by calcitriol in trophoblast cells
Erika Pérez Ortiz. Departamento de Biología de la Reproducción. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

O50
Characterization functional of Kir channels in triple-negative breast cancer
Linley Pammely Prado Celis. Centro Universitario de Investigaciones Biomédicas. Universidad de Colima

O51
Cytokinetic furrow formation promotes DNA damage and expression of p53 targets
Oscar Antonio Ramírez Vega. Instituto Nacional de Cancerología

O52
Elucidation of factors involved in modulating DisA-dependent/independent checkpoint events during germination/outgrowth of Bacillus subtilis spores
Alejandra Rangel Mendoza. Departamento de Biología. Universidad de Guanajuato

O53
Therapeutic effect of laherradurine isolated of Annona macroprophylata on colorectal cancer
Michael Joshue Rendón Barrón. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán

O54
Cardiac T Tubule system remodeling in a diabetic biomodel
Erick Enrique Rivas Oliver. Instituto de Fisiología. Benemérita Universidad Autónoma de Puebla

O55
Evaluation of HPV E1 transcript in extracellular vesicles; presence and transmission to HPV-negative keratinocytes
Ruth Monserrat Rodríguez Hernández. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

O56
Stability of non-symmetric de novo TIM-barrels
Oscar de Jesús Rodríguez Meza. Facultad de Química. Universidad Nacional Autónoma de México

O57
Perilipin isoforms expression is differentially regulated in T4-treated insulin-resistant rat hearts
Guadalupe Itzzel Rodriguez Vazquez. Departamento de Ciencias Químico-Biológicas y Agropecuarias. Universidad de Sonora

O58
Analysis of the protein profile of the flight muscles of Aedes aegypti
José Ángel Rubio Miranda. Departamento de Infectomica y Patogenesis Molecular. Cinvestav Zacatenco

O59
Phytochemical biodirected study of the components with anti-neuraminidase activity present in leaf and flower extracts of Erythrostemon yucatanensis (Greenm).
Nahomi Sáman Hernández. Centro de Investigación Científica de Yucatán A.C.

O60
Bactericidal/permeability increasing protein (BPI) exerts bactericidal activity against Mycobacterium tuberculosis
Silvia Guzmán Beltrán. Instituto Nacional de Enfermedades Respiratorias Ismael Cosio Villegas

O61
3D printed paper spray ionization platform coupled to mass spectrometry for automated chemical analyses
Leonardo Daniel Soto-Rodríguez. Laboratorio Nacional de Genómica para la Biodiversidad. Cinvestav

O62
Using standard optical microscopy to visualize label-free fungal, animal tissue, and plant samples in 3D
Braulio Gutiérrez Medina. División de Materiales Avanzados. Instituto Potosino de Investigación Científica y Tecnológica A.C.

O63
The effect of resveratrol as a radiosensitizer in cervical cancer cell lines through the inhibition of DNA damage repair pathways by homologous recombination (HR) and non-homologous recombination (NHEJ)
Andrea Torres Acosta. Instituto Nacional de Cancerología

O64
Real-time VOC's measurements emitted by Neochloris oleoabundans
Laura Rosina Torres Ortega. Laboratorio Nacional de Genómica para la Biodiversidad. Cinvestav Irapuato

O65
Metabolic features in offspring of mouse mothers with hyperandrogenism
Nayeli Torres Ramírez. Facultad de Ciencias. Universidad Nacional Autónoma de México

O66
Resonant acoustic mixing improves recombinant protein production in Pichia pastoris (Komagataella phaffi) shake flask cultures
Mauricio A. Trujillo-Roldan. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O67
Effect of metformin on the enzyme IDO1 in cervical tissue of the murine model K14E7
Luz del Carmen Valerio Jacome. Departamento de Genética y Biología Molecular. Cinvestav Zacatenco

O68
Biochemical characterization of compounds from Heloderma horridum horridum venom.
Diana I. Zavalza-Galvez. Facultad de Ciencias Químicas. Universidad de Colima

O69
The Oxygen Transfer Rate (OTR), in shake flasks, determines the growth and metabolism of Piscirickettsia salmonis.
Patricio Alejandro Zelada Cordero. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

O70
Metabolic biomarkers of agronomic and quality properties of coffee varieties
Hilda E. Ramos-Aboites. Cinvestav. UGA-Langebio Unidad Irapuato

ST27
Comparison of total phosphorylation in cervical cancer cells cultured in monolayer and in a three-dimensional system
Fernando Abdias López Alva. FES Zaragoza. Universidad Nacional Autónoma de México

ST28
Boric acid orchestrates shoot and root development in Arabidopsis seedlings and improves meristem viability in mediator18 mutants
José López Bucio. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

ST29
Effect of hyperglycemia and inflammation on the macrophage polarization mediated by Resveratrol and D3T
Josué Manríquez Núñez. Departamento de Investigación y Posgrado en Alimentos. Universidad Autónoma de Querétaro

ST30
Effect of Toll-like receptor 4 (TLR-4) activation by LPS on the migratory and proliferative capacity of prostate cancer tumor cells, PC-3.
María de los Ángeles Manzano Hernández. Instituto de Fisiología. Benemérita Universidad Autónoma de Puebla

ST31
Differential effects of fentanyl and methadone on mast cells
Frida Leticia Martínez Cuevas. Departamento de Farmacobiología. Cinvestav Sede Sur

ST32
Interaction between Wnt and lysophosphatidic acid (LPA) receptor signaling pathways in colon cancer
Juan Carlos Martínez Morales. Facultad de Medicina. Universidad Nacional Autónoma de México

ST33
Effect of the IGF-2/IGF-1R complex on the migration capacity of the MDA-MB 231 cells: role of ERβ activation.
Max Alejandro Maximino Rojas. Instituto de Fisiología. Benemérita Universidad Autónoma de Puebla

ST34
Autophagy signaling during germinal cell death in ovaries from prepubertal rats
Israel Muñoz-Velasco. Facultad de Ciencias. Universidad Nacional Autónoma de México

ST35
Role of hydrophobins in asexual spore development in Neurospora crassa
Omar Páez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST36
MlBig1 controls Arf2 activation during Mucor lusitanicus yeast development through the PKA pathway
J. Alberto Patiño Medina. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

ST37
Isolation and characterization of Arabidopsis mutants with enhanced tolerance to serotonin
Ramón Pelagio flores. Universidad Michoacana de San Nicolás de Hidalgo

ST38
Effect of O-GlcNAcylation on AKT phosphorylation in oral cancer cells
Teresa de Jesús Pérez-Cruz. Facultad de Medicina y Cirugía. Universidad Autónoma Benito Juárez de Oaxaca

ST39
Use of DINO-SL to improve a cDNA library for Y2HS in Symbiodinium microadriaticum CassKB8
Tania Islas Flores. Instituto de Ciencias del Mar y Limnología. Universidad Nacional Autónoma de México

ST40
Identification of signaling proteins involved in CD13-mediated cell adhesion and phagocytosis
Kenia Elizabeth Ramos Mexicano. Instituto de

Investigaciones Biomédicas. Universidad Nacional Autónoma de México

ST41

Transcriptional analysis of the Gac/Rsm pathway in Azotobacter vinelandii under nitrogen fixation /non nitrogen fixation condition

Luis Angel García Tejeda. Benemérita Universidad Autónoma de Puebla

ST42

Simultaneous evaluation of changes in intracellular calcium, membrane potential, and intracellular pH during capacitation in human spermatozoa

Emmanuel Rodriguez-Zamarripa. Instituto de Biotecnología. Universidad Nacional Autónoma de México

ST43

Effect of nobiletin on the SCC-9 cell line in the induction of apoptosis and cell migration

Marisol Rosas Martínez. Facultad de Odontología. Universidad Nacional Autónoma de México

ST44

Nobiletin regulates invasion, migration and metastasis in squamous cell carcinoma of the hypopharynx.

Marisol Rosas Martínez. Facultad de Odontología. Universidad Nacional Autónoma de México

ST45

Dissecting the Activation of Group I PAK Kinases by Using a FRET Based Biosensor

Héctor Iván Saldívar Cerón. FES Iztacala. Universidad Nacional Autónoma de México

ST46

Contribution of the mitogen-activated protein kinase Hog1 to the halotolerance of the marine yeast Debaryomyces hansenii

Norma Silvia Sánchez. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST47

Characterization of Non-canonical Wnt signaling in cancer stem cells of colorectal cancer

Miguel Angel Sarabia Sánchez. Facultad de Medicina. Universidad Nacional Autónoma de México

ST48

Increased O-GlcNAcylation promotes IGF-1 receptor/ Phosphatidyl Inositol-3 kinase/Akt pathway in cervical cancer cells

Carlos Josué Solórzano Mata. Universidad Autónoma Benito Juárez de Oaxaca

ST49

TGF-ß/SMAD canonical pathway induces the expression of TAZ (WWTR1) transcriptional cofactor in liver cancer cells

Marcela Sosa Garrocho. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

ST50

Activating the CD95/CD95L pathway induces proliferation in HPV+ cervical cancer cells

Isabel Soto Cruz. FES Zaragoza. Universidad Nacional Autónoma de México

ST51

Role of the GPR30 receptor in the epithelial-mesenchymal transition induced by IL-6 in luminal breast cancer cells

Ana Carolina Tirado Garibay. Facultad de Medicina Veterinaria y Zootecnia. Universidad Michoacana de San Nicolás de Hidalgo

ST52

Evaluation of the anti-adipogenic effect of novel estrogen receptor BETA ligands

María Fernanda Torres Rojas. Escuela Nacional de Medicina y Homeopatia. Instituto Politécnico Nacional

ST53

Biochemical and molecular characterization of a 29 kDa protein from Symbiodinium microadriaticum CassKB8 that is phosphorylated on threonine in response to light

Viviana A. Urban Sosa. Instituto de Ciencias del Mar y Limnología. Universidad Nacional Autónoma de México

ST54

A PTP1B-Cdk3 signaling pathway regulates cell cycle progression through Rb-E2F activation in human glioblastoma cells

Olga Villamar Cruz. FES Iztacala. Universidad Nacional Autónoma de México

ST55
SBiP1 is a chaperone from Symbiodiniaceae that is activated by light and temperature
Marco Antonio Villanueva Méndez. Instituto de Ciencias del Mar y Limnología. Universidad Nacional Autónoma de México

ST56
Evaluation of Akt and NF-κB signaling in MCF-7 cells exposed to sera from obese women treated with Metformin
Alejandro Zentella Dehesa. Instituto de Investigaciones Biomédicas. Universidad Nacional Autónoma de México

SYSTEMS BIOLOGY & BIOINFORMATICS II

SB34
Analysis of genetic biomarkers for atherosclerosis in endothelial cells
María Montserrat Loredo Guillén. IICBA. Universidad Autónoma del Estado de Morelos

SB35
Identification of CRISPR-Cas systems in genomes of Acinetobacter calcoaceticus-Acinetobacter baumannii complex
Jetsi Viridiana Mancilla Rojano. Hospital Infantil de México Federico Gómez

SB36
Exploring the unfolding free energy landscape of the thermophilic β-ATPase subunit by molecular dynamics simulations
Edgar López. Universidad Autónoma Metropolitana

SB37
Characterization of the coupling mechanism of scorpion β-neurotoxins on the voltage-gated sodium channel hNav1.6
Pavel Andrei Montero Domínguez. Instituto de Biotecnología. Universidad Nacional Autónoma de México

SB38
Characterization of the docking mechanism of dopamine agonist on the dopamine receptor 2
Dulce Elena Letras Luna. Universidad Autónoma de Puebla

SB39
In silico analysis of promoters of putative genes encoding chondroitin lyases in Avibacterium paragallinarum
Héctor Hugo Moreno Castillo. Instituto de Ciencias. Universidad Autónoma de Puebla

SB40
Towards the creation of a metabolomics database of terrestrial and marine species in México
Aldo Moreno Ulloa. Centro de Investigación Científica y de Educación Superior de Ensenada

SB41
Repositioning of molecules with potential senolytic activity using virtual screening
Kevin Samael Olascoaga-Del Ángel. Universidad Autónoma Metropolitana–Iztapalapa

SB42
Transcriptomical analysis of floral development of ciricote (Cordia sebestena).
Orlando Emanuel Osorio Pinelo. Unidad de Biotecnología. Centro de Investigación Científica de Yucatán A.C.

SB43
A miRNA-based deep learning model to boost the predictive power of obesity clinical/metabolically markers
Cesaré Ovando-Vázquez. Instituto Potosino de Investigación Científica y Tecnológica A.C.

SB44
Study of changes in the gastrointestinal archaeome and its relationship with cardiovascular risk
Betsy Anaid Peña Ocaña. Instituto Nacional de Cardiología “Ignacio Chávez”

SB45
Parametrization of the FvCB Biochemical Model for C3 Photosynthesis using Bayesian Inference
Uriel G. Pérez Guerrero. ENES León. Universidad Nacional Autónoma de México

SB46
Gene co-expression network and the regulation by the

RNAi machinery during mycoparasitism in Trichoderma atroviride
Camilo Pérez Salazar. UGA – LANGEBIO. Cinvestav Irapuato

SB47
Lea-like proteins in desiccation-tolerant organisms
Diego Pérez Villanueva. Facultad de Química. Universidad Nacional Autónoma de México

SB48
Bioinformatic analysis of the interaction between the human heat shock protein 70 (HSP70) with its target proteins
Luis Ángel Rodríguez García. Universidad Autónoma Metropolitana Cuajimalpa

SB49
Characterization of a Vaccinia virus isolate from an immunocompromised patient with progressive vaccinia in Colombia
Paola Rojas-Estevez. Empresa Nacional Promotora del Desarrollo Territorial

SB50
3'-UTR of the SARS-CoV-2 genome as a possible source of piRNAs
Carlos Romero Díaz. Instituto Tecnológico de Oaxaca

SB51
Exploring the diversity, ecology, and evolution of cyclomaltodextrin glucanotransferases in domains bacteria and archaea
Xitlalli Montserrat Romero Jiménez. Universidad de Colima

SB52
Molecular and biochemical analysis of glutamate receptors family (GLR) in Solanaceae, using the habanero pepper (Capsicum chinense Jacq.) as a model
Fabiola Guadalupe León García. Centro de Investigación Científica de Yucatán A.C.

SB53
The spatial structure in bacteria communities with metabolic interactions because of selection pressures
Sofía Roque Romero. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

SB54
Transcriptional heterogeneity of stationary-phase budding yeast cells
Ivón Elizabeth Salazar Martínez. UGA–LANGEBIO. Cinvestav Irapuato

SB55
Analysis of a polygenetic risk function for Osteosarcoma
Mariana Sánchez Hernández. Facultad de Nutrición. Universidad Autónoma del Estado de Morelos

SB56
Unveiling metabolic traits of Argemone mexicana L. rhizobiome
José Germán Serrano-Gamboa. Centro de Investigación Científica de Yucatán A.C.

SB57
In silico identification of riboswitch motifs within prokaryotic genome codifying sequences reveals recurrent annotation errors
Mariela Serrano Gutiérrez. Instituto de Biotecnología. Universidad Nacional Autónoma de México

SB58
Biological activity estimation of peptides derived from grain through computational prediction algorithms in metabolic diseases
Ana Alondra Sobrevilla Navarro. Centro Universitario de Tonalá. Universidad de Guadalajara

SB59
Study of cross-resistance and collateral sensitivity to beta-lactam antibiotics in an Escherichia coli system with different antibiotic resistance genes TEM
Monica Tapia Rojas. Centro de Ciencias Genómicas. Universidad Nacional Autónoma de México

SB60
Relationship between genes involved in glycerol and triacylglycerol biosynthesis under nitrogen starvation in Chlamydomonas reinhardtii: a bioinformatic analysis
Jorge Antonio Tzec-Interián. Centro de Investigación Científica de Yucatán A.C.

SB61
Biogeochemical functions of bacterial communities inhabiting wetland sediments of the Yucatán Coast

Daniel Adán Vázquez-Carrillo. ENES Mérida. Universidad Nacional Autónoma de México

SB62
Inferring co-expression networks of Arabidopsis thaliana genes during their interaction with Trichoderma spp".
Javier David Vega Arroy. Instituto Potosino de Investigación Científica y Tecnológica A.C.

SB63
Ligand transport analysis of malonate prodrugs through succinate dehydrogenase by Caver Web and CICLOP
Erica Karime Ventura García. Facultad de Ciencias Químicas. Universidad Juárez del Estado de Durango

SB64
Predicting Transcription Factor Candidates that Regulate Genes of the Carotenoid Biosynthetic Pathway in Fruits of Capsicum spp
Maria Guadalupe Villa-Rivera. Cinvestav Irapuato

SB65
A novel motif (Nβ) that leads secretion of lacking signal peptide proteins
Andre Zaragoza Gómez. Facultad de Ciencias. Universidad Nacional Autónoma de México

TOXICOLOGY AND PHARMACOLOGY II

TP27
Determination of the effect of prenylated chalcones on the membrane potential, apoptosis and metabolome of castration-resistant cells in prostate cancer
Marcos Morales Reyna. Centro de Ciencias Genómicas. Universidad Autónoma de la Ciudad de México

TP28
Environmental Cd exposure as a factor risk to insulin resistance development: A peep to insulin secretion mechanisms.
Diana Moroni González. Facultad de Ciencias Químicas. Benemérita Universidad Autónoma de Puebla

TP29
Anti-inflammatory effects of polyphenolic extract of Vitis vinifera pomace on carrageenan induced paw edema
Sendar Daniel Nery-Flores. Facultad de Ciencias Químicas, Universidad Autónoma de Coahuila.

TP30
Morphological characterization and phytochemical evaluation of Callistemon citrinus leaf phytosomes
Luis Gerardo Ortega-Pérez. Instituto de Investigaciones Químico Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

TP31
Sucrose and arsenic induce muscular insulin resistance through different pathways which are muscle-dependent
Juan Pablo Pánico Molina. Instituto de Fisiología Celular. Universidad Nacional Autónoma de México

TP32
Obtaining and evaluating the toxicity of plant extracts of Solanum cervantesii and other species of the Solanaceae family from Huixquilucan, State of Mexico.
Darline Paz-Molares. Tecnológico de Estudios Superiores de Huixquilucan

TP33
Microplastics in tropical gar´s diet (Atractosteus tropicus): effects on enzyme activities
Alejandra Pérez López. División Académica de Ciencias Biológicas. Universidad Juárez Autónoma de Tabasco

TP34
Oxidative stress in Lithobates catesbeianus by test exposure to chlorothalonil
Amparo Celene Razo Estrada. Escuela Nacional de Ciencias Biologicas. Instituto Politécnico Nacional

TP35
Toxicological effects of acute administration of Spathodea campanulata in Wistar Rats
Jose Alberto Martínez Mariano. Facultad de Ciencias Médicas y Biológicas. Universidad Michoacana de San Nicolás de Hidalgo

TP36
The drug combination doxorubicin, metformin and sodium oxamate inhibit cell proliferation through β-catenin inactivation in sarcoma cell lines.
Frida Citlali Rodríguez Izquierdo. FES Iztacala UNAM. Instituto Nacional de Cancerología

TP37
Targeted inhibition of oncogene ERBB2 and related genes of interest in HER2 positive breast cancer cells IGF-1R and ITGB1 due to siRNA activity.
Rodolfo Miranda Espino. Facultad de Ciencias Químicas. Universidad Autónoma de Nuevo Léon

TP38
Apoptotic and autophagic effect of lithium salts in an in vitro model of cervical cancer
Gareth Omar Rostro Alonso. FES Zaragoza. Universidad Nacional Autónoma de México

TP39
Alpha-linolenic acid, an omega-3 polyunsaturated acid protects against indomethacin-induced gastric injury in the rat
Cristina Salinas Nolasco. Escuela Nacional de Medicina y Homeopatía. Instituto Politécnico Nacional

TP40
Collection and Physicochemical Characterization of Expired Acetaminophen
José Angel Sánchez Peregrino. División Académica de Ciencias Básicas. Universidad Juárez Autónoma de Tabasco

TP41
Effect of DHA on oxidative stress and microbiota in a murine model of indomethacin- induced intestinal damage
Martha Ivonne Sánchez Trigueros. Escuela Nacional de Medicina y Homeopatía. Instituto Politécnico Nacional

TP42
Treatment of preeclampsia with metformin: effects in reverting fetal programming of breeding.
Gerardo Abraham Santana Sierra. Escuela Superior de Medicina. Instituto Politécnico Nacional

TP43
Chimera designed with hypothetical activity against Trichomonas vaginalis
José Alberto Santiago de la Cruz. Posgrado en Ciencias Genómicas. Universidad Autónoma de la Ciudad de México

TP44
Particulate matter PM10 affects the mismatch repair (MMR) pathway through SETD2 downregulation
Miguel Santibáñez Andrade. Instituto Nacional de Cancerología

TP45
The antidepressant drug sertraline inhibits Kv4.2 channels
Lorena Beatriz Segura Leal. Centro Universitario de Investigaciones Biomédicas. Universidad de Colima

TP46
Effect of hydrogen sulfide on vascular dysfunction induced by type 2 Diabetes Mellitus in rat thoracic aorta
Diana Laura Silva Velasco. Departamento de Farmacobiología. Cinvestav Sede Sur

TP47
C-phycocyanin prevents impaired AT1, AT2, and Mas receptors expression, endothelial dysfunction, and hypertension caused by chronic kidney disease.
Jorge Alberto Tapia -Martínez. Departamento de Farmacobiología. Cinvestav Sede Sur

TP48
Epicatechin effect in an experimental pre-eclampsia model
Cecilia del Carmen Tufiño Martínez. Escuela Superior de Medicina. Instituto Politécnico Nacional

TP49
Polyphenols inhibit tumor growth and could be used as an alternative for chemo-sensitization in oral cavity and oropharyngeal carcinoma
Heriberto Abraham Valencia González. Instituto de Investigaciones Biomédicas. Instituto Nacional de Cancerología

ABSTRACTS | Conferences Speakers

XXXIII National Congress of Biochemistry

SCANNING ELECTRON MICROSCOPE. A CONNECTION BETWEEN SCIENCE AND ART

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Abstract

"By the help of microscopes, there is nothing so small, as to escape of our inquiry; hence there is a new visible world discovered to the understanding"
Robert Hook

Art and science are apparently different and contrary, however, they are actually two disciplines that are complementary. Art is science and science is art. Everything is interconnected in human knowledge. Since the 15th century, the visual language between science and art has been addressed, being the pioneer the renowned scientist Sir Robert Hooke, with his work MICROGRAPHIA, in which he used an optical microscope to document and disseminate the fascinating world of nature, various scientists left visual testimony of their observations in their long and exciting laboratory observations. The world of the microscope allows us to see other worlds that are there, but many times they are inaccessible to the human eye or it is very segmented diffusion space. The microscopic world surprises with its diversity of shapes, textures and contours, as well as opening the doors to create new and imaginary worlds. At the Yucatan Scientific Research Center, we use a Scanning Electron Microscope, in order to unify the scientific tool with art and nature, to make viewers aware of the beauty of mother nature and its importance not only visual if not on a human level and convey to viewers that when art and science merge, a new vision is created enriched by the visual heritage of our time, just as we broaden the vision of science and generate a broader dialogue between the public space that today all human beings inhabit on this globe.

THE *PSEUDOMONAS AERUGINOSA* TYPE VI SECRETION SYSTEM (T6SS): A BACTERIAL KILLING MACHINE

Alain Filloux
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MRC Centre for Molecular Bacteriology and Infection, SW72AZ, London, United Kingdom
Singapore Centre for Environmental Life Sciences Engineering,
Nanyang Technological University, Singapore 637551, Singapore

Abstract

The Type VI secretion system (T6SS) is a bacterial weapon which delivers toxic effectors to kill competitors or subvert some of their key functions. This nanomachine is thus instrumental for the outcome of bacterial competition in biofilms or polymicrobial systems both in the environment or host. Strikingly, it resembles the tail of bacteriophages. The cytosolic contractile sheath of the T6SS wraps around stacked hexameric rings of Hcp proteins, which form an inner tube. At the tip of this tube is a puncturing device comprising a trimeric VgrG topped by a monomeric PAAR protein.

The toxic effectors are loaded into the machine either by association with the tip (VgrG/PAAR) or with the inner tube (Hcp). This way a cocktail of toxins could be loaded into a single machine and fired at once into a prey. Pseudomonas aeruginosa has three T6SSs (H1-, H2-, H3-T6SS) and can fire a range of ca. a dozen of toxins. Our laboratory has expanded the characterization of this toxin reservoir through various genomic/proteomic approaches so that novel toxins can lead to not yet exploited antimicrobial targets.

The dynamic of the system is entirely based on the elongation/contraction events of the sheath. The sheath elongates from a structure called the baseplate which relies on the initial recruitment of a core protein named TssA. TssA is the least conserved of the core T6SS elements and we found that its association with distinct structural components has a huge impact on the time of residence after elongation and thus speed of firing.

In all T6SS-proficient bacteria may benefit of a very significant advantage in prevailing in polymicrobial population, and the diversity of toxins use can guarantee the success of energetically costing frontal assault. We also observed the existence of multiple T6SSs displaying an obvious diversity in firing dynamics that we propose could contribute to the specialization of the T6SS to suit bacterial lifestyles in diverse environmental niches.

COMMUNICATION MAKES THE DIFFERENCE: THE CONSTANT DIALOGUE BETWEEN MEMBERS OF THE CELL IS AN ESSENTIAL ELEMENT FOR PLANT DEVELOPMENT

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Abstract

Plastids are organelles with diverse specialized functions that are essential for plants, including photosynthesis and the synthesis of a variety of compounds (hormones, amino acids, vitamins, lipids, etc.). Thus, plastids act as metabolic hubs and environmental sensors critical for plant development and survival. The correct plastid differentiation and functionality relies in a coordinated nuclear and organellar gene expression, achieved through the continues communication between the nucleus and the organelle. The nucleus via an anterograde regulation controls plastid development and functionality. In response the plastids communicate their developmental status (biogenic) and functionality (operational), producing diverse signals that impact nuclear gene expression. Anterograde and retrograde regulations create a circuit that is essential, not only for organelle function, but that also impacts overall plant development and environmental responses. Thus, the characterization of the retrograde signals and factors may have an important implication in plant productivity. Our work has defined a new retrograde signal derived from linear carotenoids (ACS1) that affects the expression of hundreds of nuclear genes and that alters leaf morphology, SAM and RAM meristem identities and progression. We have uncovered the order of events in a temporal and spatial context of the ACS-mediated signaling pathway, that involves two consecutive cascades. We have also identified some of the elements that participate in this process, including the GOLDEN2-LIKE (GLK) transcription factor. Our work also aims to understand the evolution of biogenic retrograde signaling and its role during plant terrestrialization using *Marchantia polymorpha* as model. We have analyzed the GLK factor that have been shown to play central functions in different retrograde signaling. We found that the *MpGLK* gene from *M. polymorpha* is a functional orthologue of those from vascular plants, producing ectopic chloroplasts when overexpressed and defective plastids when mutated. Interestingly, our mutant and overexpressing lines exhibit additional developmental phenotypes, previously unknown as part of the GLK functions from Angiosperms, and that are potentially shared with other members of the GARP family that might have been lost in divergent clades. Finally, the expression pattern of the MpGLK was established.

PROTEIN KINASE C UNBALANCED: DEREGULATED SIGNALING IN DISEASE

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Abstract

Protein kinase C (PKC) isozymes that transduce signals from lipid hydrolysis have historically been considered oncoproteins. This stems in large part from the discovery in the early 1980s that tumor-promoting phorbol esters directly activate PKC. Yet three decades of clinical trials using PKC inhibitors in cancer therapies not only failed but, in some cases, worsened patient outcomes. Why has targeting PKC in cancer eluded successful therapies? Our recent findings reframe PKC isozymes as generally having a tumor-suppressive function and suggest that therapeutic strategies should focus on restoring, rather than inhibiting, PKC activity in cancer. In striking contrast, enhanced activity of PKC is associated with degenerative diseases, with gain-of-function variants in PKCalpha identified in Alzheimer's disease and PKCgamma in cerebellar Ataxia Type 14, suggesting that inhibitors for PKC could be repurposed for neurodegenerative diseases. Understanding the molecular mechanisms that control PKC, including upstream regulators such as mTORC2 and the phosphatase PHLPP, informs on how to effectively target this ubiquitous family of kinases in disease

QUORUM SENSING BEYOND THE SIGNALING MOLECULES

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Abstract

In microbial populations, quorum sensing (QS) systems participate in the regulation of specialization processes and control collective behaviors that mediate interactions allowing survival of the species. QS depends on cell density and the binding of signaling molecules to specific intracellular receptors; as the cell concentration increases, the signaling molecules accumulate extracellularly until a critical threshold intracellular concentration of receptor-ligand is reached to regulate the expression of different operons. In a quorum state the microbes behave as social groups, this social behavior implies changes in the genetic expression program compared to genes expressed by the cells at low cells density, which behave as individuals.

While most QS systems are studied as linear processes including autoinducer production-secretion, sensing, and response, the Rap and NprR intracellular QS receptors from *Bacillus* are highly multifunctional and/or redundant, linking signal transduction pathways as well as global expression changes. Multiple studies have shown the genetic and structural basis for the functions of these QS systems, however, the physiological and ecological implications of the integration of different signaling pathways have not been fully addressed. Here we will discuss how these multifunctional receptors switch between functions and connect distinct signaling pathways, as well as the structural changes in the protein upon ligand binding and interaction with other proteins. In addition, we analyze an evolutionary and ecological perspective to understand the multifunctionality and functional redundancy of these QS systems.

CRYO-EM ANALYSIS OF INOSITOL TRIPHOSPHATE RECEPTOR CALCIUM CHANNELS

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Abstract

Cryo-electron microscopy (Cryo-EM) is a powerful technique for studying macromolecules at atomic resolution. In my talk, I will first describe the basic principles of cryo-electron microscopy (Cryo-EM) and its applications in the high-resolution structure determination of proteins. Then, my talk will focus on our latest research on the inositol 1,4,5-triphosphate (IP3) receptors (IP3Rs), a pivotal component of the Ca2+ signaling toolbox in cells.

IP3Rs are intracellular Ca2+ channels, predominantly localized to the ER and activated by the binding of IP3 generated in response to external stimulation of G-protein coupled receptors. Opening of the IP3Rs results in the rapid release of Ca2+ from the ER into the cytoplasm triggering diverse signaling cascades to regulate physiological processes such as learning, fertilization, gene expression, and apoptosis. Dysfunctional IP3Rs cause abnormal Ca2+ signaling and are associated with many diseases, including diabetes, cancer, and neurological disorders.

IP3Rs are activated by IP3 and Ca2+, inhibited by Ca2+ at high concentrations, and potentiated by ATP. However, the underlying molecular mechanisms are unclear due to the lack of structures in the active conformation. I will present new cryo-electron microscopy (cryo-EM) structures of human type-3 IP3R in multiple gating conformations; IP3-ATP bound pre-active states with closed channels, IP3-ATP-Ca2+ bound active state with an open channel, and IP3-ATP-Ca2+ bound inactive state with a closed channel. The structures demonstrate how IP3-induced conformational changes prime the receptor for activation by Ca2+, how Ca2+ binding leads to channel opening, how ATP modulates the activity, and how the pore dilates, providing insights into the long-sought questions regarding the molecular mechanism of the receptor activation and gating. These structures will likely serve as foundations for future experiments addressing biophysical and functional questions related to IP3Rs.

EXPLORING THE CELLULAR MECHANISMS OF EPILEPSY: FROM NEUROCHEMISTRY TO ELECTROPHYSIOLOGY AND BACK

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Abstract

In this presentation I would like to honor Professor Ricardo Tapia. A distinguished member of this Society and a pilar of the Mexican neuroscientific community. I will start describing the work I developed in his laboratory studying the relationships among seizures, extracellular amino acid changes, and neurodegeneration induced by 4-aminopyridine (4-AP; Peña and Tapia 1999), a blocker of transient voltage-dependent K+ channels and a drug that Professor Tapia extensively used to study hyperexcitable states in different brain regions (Tapia et al., 1999). In those studies, we combined a classical neurochemical tool, microdialysis in the hippocampus, a technique pioneered by Professor Tapia in México, with local EEG recordings. A combination introduced by us in México. Then, I will describe my first investigations as an independent researcher in which I returned to the use of 4-AP and compared its effects with those of linopirdine, a blocker of KCNQ2/3 channels, as tools to understand the developmental profile of benign familial neonatal convulsions using electrophysiological recordings in brain slices (Peña and Alavez-Pérez, 2006). I will finish my presentation with new experiments in which I have resumed the use of neurochemical approaches, in this case chemogenetics, to understand the microglial modulation of neural network activity under normal conditions and, of course, under the hyperexcitable states induced by 4-AP. We have revealed that microglia modulate network excitability under basal conditions but also determines the magnitude and persistency of the epileptiform activity induced by 4-AP; offering a new cellular target to control epilepsy. I hope to be able to show a tiny part of the scientific influence that Professor Tapia had on the development of neuroscience, not just by the seminal contributions emerged from his laboratory but from his influence on those of us that have advanced our scientific careers on the experimental approaches and ideas developed by him.

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UNRAVELING THE TRANSCRIPTIONAL NUANCES OF THE CHAPERONE-USHER FIMBRIAL OPERON REPERTOIRE OF AN ATTACHING AND EFFACING BACTERIAL PATHOGEN

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Abstract

Enteropathogenic Escherichia coli (EPEC), enterohemorrhagic E. coli (EHEC) and Citrobacter rodentium represent a family of bacterial pathogens that attach intimately to the intestinal epithelium, destroying the microvilli and forming characteristic lesions called attaching and effacing (A/E). C. rodentium causes, in addition to the A/E lesion, transmissible colonic hyperplasia in mice characterized by hyperproliferation of epithelial cells in the distal part of the colon. In the absence of natural animal models for EPEC and EHEC, mouse infection by C. rodentium has been intensively used as a surrogate model to study different processes associated with the infection caused by these bacteria.

A critical step for successfully establishing a bacterial infection is the initial interaction of the pathogen with the host cells, which is often achieved through filamentous structures known as fimbriae or pili. A/E pathogens have an average of 14 fimbrial operons from the chaperone/usher family. Despite their phylogenetic relationship, the C/U fimbriae provide functional diversity participating in different stages during their transit between an environmental reservoir and the host or from one host to another.

Little is known about the conditions that favor their expression and the molecular bases of the mechanisms that regulate the transcriptional activation of these operons, which, interestingly, are, in most cases, not expressed under laboratory growth conditions, suggesting that strict spatiotemporal control mechanisms ensure the presence of a particular fimbria when is more needed. In this presentation, we will discuss some examples of what we have learned from the work of perseverant, creative and committed young researchers who are laying the groundwork that is advancing our understanding of the diverse regulatory mechanisms controlling the expression of C/U fimbrial operons in A/E pathogens.

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REACTIVE OXYGEN SPECIES: SIGNALING MOLECULES IN NEURONAL DEATH AND DEVELOPMENT

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Abstract:

Reactive oxygen species (ROS) are highly reactive molecules that can induce harmful effects in cells and organisms. Their overproduction has been linked to several diseases and aging. More recently, it was shown that these molecules participate in the regulation of the cell physiology and some pathophysiological processes. It is now accepted that ROS regulate the immune response, the vascular tone, the oxygen concentration and the production of nitric oxide, among others. ROS have also been suggested to play a critical role in the physiology of the nervous system, particularly during some developmental events, including neuronal differentiation, neuritic growth, axonal guidance, proliferation and programmed cell death, as well as in many diseases of the nervous system. Here, we will present in vivo and in vitro experimental evidence showing that ROS are critical signals for the physiology and pathophysiology of the nervous system. We found, for example, that ROS are produced by both mitochondria and the NADPH-oxidase complex (NOX) during neuronal death and that these ROS are necessary as early signals for death to occur. In these regard, we observed, in an *in vivo* model of excitotoxicity, that NOX2 deficient animals showed a marked reduction of the brain damage. We also found that during neuronal death, ROS interact with key proteins related to the activation/inactivation of several signaling pathways, including the MAPK signaling pathway. Our results also show that ROS act through the Akt-TXNIP signaling pathway. This led us to suggest that ROS induce the expression of TXNIP through the activation of the FOXO3 transcription factor by AKT inhibition and that TXNIP expression is necessary to induce neuronal death. We also observed that apoptotic conditions induce an early endoplasmic reticulum calcium release that probably causes an alteration of mitochondrial homeostasis that could be responsible for the observed early ROS production.

Interestingly, ROS and NOX also seem to be critical for neuronal development and differentiation. Developing rats treated with an antioxidant or an inhibitor of NOX induced a significant change in the cerebellar foliation, as well as an alteration in motor behavior. Also, antioxidants and NOX inhibitors reduced the expression of Tau and MAP2 during critical times of cerebellar granule neurons development. On the other hand, our results suggest that H2O2 regulates the axonal growth cone dynamics and filopodia formation. We found that the use of antioxidants and NOX inhibitors impairs axonal growth and that the levels of H2O2 were higher in growing regions

of the axon, such as the axonal growth cones and filopodia. This H2O2 production precedes the observed neurite outgrowth. We propose that the local production of hydrogen peroxide modulate the neurite extension through a modulation of the actin polymerization.

These results reinforce the idea that ROS play a dual role, as signals in neuronal death and in some physiological processes. At early times of development, the production of ROS seems to be critical for neuronal maturation. During a second stage of CGN development, ROS levels allow cell survival, otherwise this would lead to the activation of the programmed cell death.

Key words: Reactive oxygen species, hydrogen peroxide, NOX, redox signaling, nervous system

This work was partially supported by CONACYT (285184) and DGAPA-PAPIIT, UNAM (IN216422)

LONG NON-CODING RNAS AS EVOLUTIONARILY FLUID CHROMATIN WEAVERS

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Abstract:

Long non-coding RNAs (lncRNAs) have recently emerged as prominent elements of the regulatory transactions of eukaryotic genomes. Many of the know regulatory functions of lncRNAs in both animals and plants rely on the rearrangement of chromatin through direct interactions or recruitment of chromatin-modifying elements. In this talk, I will discuss the difficulty in identifying evolutionary conservation in lncRNAs, and how we characterize these evolutionarily volatile elements in the context of their role as regulators of the three-dimensional conformation of nuclear chromatin. I will focus on our findings resulting from the concurrent characterization of transcripts, tridimensional chromatin structure and direct RNA-DNA interactions in closely related plant species.

SCIENCE COMMUNICATION FOR A SUSTAINABLE FUTURE

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Julia Tagüeña is a researcher at the Institute of Renewable Energies of the Universidad Nacional Autónoma de México (UNAM), of which she also served as Director when it was the Energy Research Center. She studied physics at UNAM and obtained a PhD at Oxford University. Her main fields of research are solid-state physics, renewable energies, and science communication. She is a member of the Mexico´s National Research System, with the highest rank, and of different societies such the Mexican Academy of Sciences and the Institute of Physics of UK.

She is a recipient of the "National Communication Award Alejandra Jaidar 2020" and the "Public Understanding and Popularization of Science Award 2021", given by the World Academy of Sciences (TWAS), Latin American and Caribbean Regional Partner (LACREP), November 2021.

OVERLAPPED GENES IN BACTERIOPHAGE FC02 ARE TRANSCRIBED IN OPPOSITE DIRECTIONS AND ENCODE SIMILAR ACTIVITIES DURING THE LYTIC AND LYSOGENIC PHASES IN *PSEUDOMONAS AERUGINOSA*

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Abstract

Studies of temperate bacteriophages' gene expression during the transition from lysogeny to lysis are scarce. To better understand this process, we analyzed the transcriptional changes in the phage genome during the induction of lysogenic bacteria to the lytic cycle. A strain of Pseudomonas aeruginosa PAO1, lysogenic for the temperate phage Fc02(repcIts), carrying a thermosensitive mutation in the phage repressor gene, was used. This mutant maintains lysogeny at 30°C but the repressor is inactivated at 42°C and the lytic cycle is induced giving rise to phage progeny and cell lysis.

Samples were removed from a culture of the lysogen strain PAO1(Fc02repcIts) grown at 30° at various times after induction at 42°. Total RNA was isolated from each sample and processed for strand-specific RNAseq. The results revealed that at 30° the central phage regulatory region displayed extensive bidirectional transcription a feature rarely observed in this region of phage genomes. Transcription from the forward DNA strand was observed at 30° that gradually switched to transcription of the reverse DNA strand after induction to 42°.

As expected, the transcripts at 30° comprise the repressor gene, in agreement with the essentialness of repressor protein to maintain lysogeny. However, upstream to the repressor gene, the transcript contains two so far undescribed ORFs, named as1 and as2. These ORFs, that are overlapped in different frames of the DNA forward strand, presumably are transcribed and translated from a promoter-like sequence and a SD ribosomal recognition region recognized upstream the ORFs. Therefore, they may correspond to novel genes whose mRNA is translated into protein.

Evidence in bacteria harboring plasmid constructs that express as1-as2 gives the cell resistance to infection by other phages, a phenomenon known as exclusion. This is surprising because as1-as2, in turn overlap almost entirely gene 10, transcribed from the DNA reverse strand, that has also been characterized as an exclusion gene.

DIVERGENCE OF FUNCTIONAL TRANSCRIPTIONAL REGULATION THROUGH THE GENERATION OF NOVEL HYBRID REGULATORS IN *S. CEREVISIAE*

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Abstract:

Transcriptional activation responses rely on a repertoire of transcriptional modulators, harboring peculiar domains, which decipher regulatory information through their specific binding to cognate sequences and their capacity to selectively recruit the components of a given transcriptional complex. As opposed to what occurs in modulators composed of a single polypeptide, the finding of regulators composed by various proteins, in which the functional domains are distributed among the different peptides, allowed to pose the proposition that the independent proteins could be used in different combinations with other factors to generate hybrid regulators. Analysis of *GDH1/GDH3* transcriptional diversification showed for the first time that the Hap2-3-5-Gln3 hybrid regulator could be organized from the Hap2-3-5 complex and Gln3 independent activator exchanging the Hap4 activation domain for Gln3, fostering the otherwise inhibited GDH1 and ASN1 induced expression under nitrogen repressive conditions (1, 2). Analysis of the transcription profile of the *ALT1/ALT2* paralogous pair has shown that *ALT2* repression is determined by the action of a novel hybrid regulator, which is organized in the presence of alanine. This novel regulator is constituted by the Nrg1 repressor and the Rtg3 activator forming the Nrg1-Rtg3-alanine hybrid repressor, showing that hybrid regulators, can also be organized by modulators constituted by a single polypeptide. RNA-seq analysis has shown that the Nrg1-Rtg3-alanine hybrid repressor regulates the expression of a group of genes involved in central carbon metabolism and oxidative-reductive processes, constituting a novel gene network. Nrg1 provides the DNA binding domain and recruits the proteins involved in chromatin repressive organization (Tup1), while both, Nrg1 and Rtg3, participate in chromatin organization of their target genes.

Hybrid regulators play an important new role in transcriptional control since these overcome restrictions such as limited nuclear localization, and binding/signaling sensitivity, giving rise to novel regulators triggering specific and refined transcriptional responses to subtle or combined variations of the environment.

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FROM OXIDATIVE STRESS MAPK SIGNALING TO MITOCHONDRIAL DIVISION

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Abstract:

Our group has contributed to establish the role of reactive oxygen species (ROS) as ubiquitous signals that regulate different aspects of development and cell physiology. The study of the roles of the SakA stress MAPK pathway in ROS signaling, in the fungus *Aspergillus nidulans*, led us to uncover different roles for H2O2 in the regulation of mitochondrial division. Indeed, H_2O_2 induces an extensive mitochondrial division that depends on the dynamin-like protein DnmA (Drp1 in animal cells) and its receptor FisA. Although the lack of mitochondrial division has minor effects on respiration, it drastically affects polar growth and development, and results in increased levels of mitochondrial ROS. Moreover, H_2O_2 induces a generalized mitochondrial constriction response, previous to actual division, that involves a gradual depolarization of mitochondria, the participation of Ca^{2+}, and requires a close interaction between mitochondria and the endoplasmic reticulum. Our results support a view of mitochondrial division as the end result of a cascade of signaling events that can be initiated in vivo by H_2O_2.

Our work was supported by grants CONACYT-DFG 277869 and PAPIIT-UNAM IN200719, IV200519 and IN215622.

FUNGAL CYTOKININS, PLANT GROWTH STIMULATING COMPOUNDS OR FUNGAL HORMONES?

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Abstract:

Trichoderma species intimately associate with plant roots, providing several benefits to the host, strengthening immunity, improving root absorptive potential, and conferring protection to environmental stress. *Trichoderma atroviride* produces a series of compounds, including auxins, that modulate root architecture, stimulating primary root growth, formation of lateral roots and root hairs. Because of its intimate interaction with plant and because several phytopathogenic fungi produce cytokinins that are involved in pathogenesis. Therefore, has been assumed that microbes produce cytokinins to facilitate their interaction with plants, since cytokinins are considered plant-specific hormones that play a central role in the regulation of the plant cell cycle and numerous developmental processes. We wondered if these hormones could play a role in a plant-fungus beneficial interaction. Accordingly, we tested if *t. Atroviride* produced cytokinins, and found that it produces several forms of this hormone, being predominant cis-zeatin. Thus, we searched the *t. Atroviride* genome for the presence of cytokinin biosynthesis genes and found that its genome encodes a trna-isopentenyltransferase (trnaipt) and a lonely guy cytokinin activating enzyme (log), in addition to several cytochrome oxidases (p450) that could enabled *trichoderma t*o produce cytokinins. We generated gene replacement mutants in the *t. Atroviride trnaipt* and *log*1 genes, which were no longer capable of producing cytokinins. However, when constructing a phylogenetic tree of the enzymes comparing them with those found in plants and other microbes, we found that many fungi encode the enzymes necessary to produce cytokinins, even though they have no known interaction with plants. Consequently, we wonder if cytokinins could be fungal hormones that play a role in their growth and development. In this talk we will present the evidence indicating that cytokinins play an important role as signaling molecules in growth and development in *t. Atroviride.*

OPENING: BEYOND THE LIMIT–FUNDAMENTALS OF SUPER-RESOLUTION MICROSCOPY

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Abstract:

In the last decade, Super-resolution, or fluorescence nanoscopy, has revolutionized microscopy by breaking the theoretical resolution limit. A variety of techniques that provide resolving power beyond diffraction limit. Structured Illumination Microscopy (SIM), the sample is excited with a known spatially structured pattern of light and relies on the generation of interference patterns and super-resolution information is recovered through mathematical image processing. Stochastically Optical Reconstruction Microscopy (STORM) is based on the stochastic activation of fluorophores at distances larger than the diffraction limit; the fluorophores are not continuously excited, but rather they "blink", reducing the overlapping of their signals and thus increasing resolution. The phenomenon utilized in Fluorescence Fluctuations-Based Super-resolution Microscopy (FF-SRM) is the stochasticity of the number of photons emitted by fluorescent labels over time. These techniques use statistical analysis as the core mechanism to super-resolve the fluorescent molecule distribution, where each molecule independently contributes to fluctuations in the measured fluorescence intensity. A more recent set of super-resolution techniques is Fluorescence Fluctuations-based Super-resolution microscopy (FF-SRM) that, is based on the phenomenon of the stochasticity of the number of photons emitted by fluorescent labels over time. It uses statistical analysis as the core mechanism to super-resolve the fluorescent molecule distribution, where each molecule independently contributes to fluctuations in the measured fluorescence intensity. Nanodeconvolution, or Mean-Shift Super-resolution (MSSR), is based in the Mean Shift Theory and improves the spatial resolution in fluorescence images beyond the diffraction limit up to 1.6 times. It can be applied to a single imaging frame regardless of the type of detector or camera used, and it has been proven in a wide variety of model organisms.

SUPER-RESOLUTION IMAGING REVEALS THE STRUCTURE DISRUPTION OF CHROMOSOME TERRITORIES 9 AND 22 ASSOCIATED WITH TREATMENT RESISTANCE IN CHRONIC MYELOID LEUKEMIA

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Abstract:

Chronic Myeloid Leukemia (CML) originates from a single translocation t(9;22) whose origin has been associated with the topological organization of the nucleus. This rearrangement leads to the fusion of *BCR* and *ABL1* genes giving rise to a chimeric protein with constitutive kinase activity. Tyrosine kinase inhibitors (TKI), such as Imatinib, are used as first-line treatment for CML, though approximately 40% of CML patients do not respond to Imatinib.

In the present study, we performed 3D-FISH and image 3D reconstruction from structured illumination microscopy (SIM) in order to study the 3D organization patterns of the *BCR* and *ABL1* genes, and their chromosome territories (CTs) CT9 and CT22 in CD34+ cells from the bone marrow of CML patients that responded or not to Imatinib.

We found that resistance to TKI treatment in CML is characterized by high levels of CT9 and CT22 structure disruption in CD34+ cells, increased CT volumes (especially for CT22), increased intermingling between CT9 and CT22, and increased occupancy of H3K9ac, an open-chromatin epigenetic mark, in CT22.

We demonstrate the potential of high-resolution imaging, using SIM as a primary tool, to study higher-order chromatin. Taken together, our findings suggest that CT9 and CT22 disruption is a potential predictive marker of response or non-response to therapy in CML, and provide novel insights into the mechanisms underlying resistance to TKI in CML.

SUPER RESOLUTION MICROSCOPY REVEALS DYNAMIC CHANGES IN THE MOUSE SPERM MIDPIECE

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Abstract:

As the mammalian sperm are ejaculated from the male reproductive tract, they are not capable of fertilizing oocytes. In order to gain fertilization competence, they must undergo a series of biochemical and physiological events as they travel across the female tract that are collectively known as capacitation. One of the outcomes of capacitation is the ability to undergo acrosomal exocytosis, a unique secretory event. It occurs as the result of fusion events between the plasma membrane and a specialized vesicle called acrosome. A commonly employed method to assess acrosome exocytosis in single cell imaging is the use of FM dyes, which stain plasma membrane and it allows to follow the dynamics of this unique process. By using this dye, we observed that the mouse sperm midpiece undergoes a decrease in diameter during the acrosome reaction induced either with progesterone, ionomycin or spontaneously. The contraction is initiated in any segment of the midpiece but preferentially begins near the neck. In single-cell super resolution experiments, we also employed Fluo4-AM and SiR-actin to monitor how intracellular calcium and actin dynamics, respectively, are involved in this process. We observed that this contraction is accompanied by an increase in intracellular calcium and a significant change in the F-actin structure located in the midpiece. Taken together, these results demonstrate that after the initiation of the acrosome reaction, the mouse sperm midpiece goes through dynamic and structural changes that could affect the motility pattern of fertilizing sperm.

NANO-DECONVOLUTION, OPENING A NEW ERA OF FLUORESCENCE MICROSCOPY

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Abstract:

We present a novel principle of fluorescence nanoscopy, the Mean Shift Super Resolution microscopy (MSSR) principle, whose algorithmic implementation allows overcoming the diffraction limit of light microscopy by analyzing a single image. We show evidence of the existence of an undescribed spatial resolution limit, alternative to the Abbe's limit, whose information lies in the space of the second derivative of the fluorescence field. A generalized implementation of MSSR allows unveiling hidden nanoscopic features in images collected with any type of fluorescence microscope. We provide applications of MSSR to optical nanoscopy in real time, total internal reflection, confocal and light sheet microscopy. Finally, we show the compatibility of our method with other algorithmic and instrumental super resolution microscopy techniques, extending their capabilities to unattainable resolution regimes aimed to observed cellular function at the nanoscales.

Torres E. et al., Nanoscopic resolution within a single imaging frame. bioRxiv
doi: https://doi.org/10.1101/2021.10.17.464398

NUCLEAR PHOSPHOINOSITIDES–NEW PLAYERS IN REGULATION OF GENE EXPRESSION

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Abstract:

Processes such as gene expression or DNA repair are compartmentalized within eukaryotic nucleus, and nuclear environment contains dynamic membrane-less sub-compartments whose formation is prevalently driven by phase separation. Formation of phase boundaries provides the surface for spatiotemporal control contributing to the high-rate kinetics of crucial processes such as transcription, ribosome maturation, splicing. Our laboratory discovered Nuclear Lipid Islets (NLIs) – globular ~100 nm structures containing PI(4,5)P2 (PIP2) at their periphery which associate with key transcription factors, and showed that NLIs are crucial for efficient Polymerase II transcription. We further observed that nuclear PIP2 distribution is affected by 1,6 hexandiol treatment. To decipher whether the NLIs surface recruits a transcription regulatory proteins through PIP2 molecules in their surface, we employed a proteomic approach based on differential quantitative mass spectrometry (qMS) in combination with super-resolution microscopy. We identified more than 300 NLIs-associated proteins belonging to gene expression (53%) and pre-mRNA splicing (33%). Super-resolution microscopy confirmed that some candidate proteins form foci in nucleoplasm and associate with sub-population of NLIs. Further, our bioinformatical analysis of putative NLIs proteins revealed that majority of them contain Intrinsically Disordered Regions (IDRs). IDRs are known features of proteins undergoing phase separation under in vivo and in vitro conditions. Moreover, we found that the vast majority of these proteins contain K/R rich motifs, which were previously shown as recognition sites for phosphoinositide (PIPs) binding. We hypothesize that NLIs may serve as a structural platform integrating RNA Polymerase II transcription and pre-mRNA splicing by attracting proteins which are prone to form liquid-like particles.

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SWI/SNF CHROMATIN REMODELING ENZYMES IN MELANOCYTES AND MELANOMA

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Abstract:

Epigenetic regulation of chromatin structure is essential for initiating and maintaining tissue-specific gene expression patterns. Disruptions in these normal epigenetic processes can lead to abnormal gene activity and malignant transformation. SWI/SNF chromatin remodeling enzymes are multi-subunit complexes that utilize energy from the hydrolysis of ATP to disrupt chromatin structure and thereby promote accessibility to transcriptional regulators. SWI/SNF complexes contain a central ATPase and 9-12 additional subunits, several of which have bromodomains which are amenable to pharmacological inhibition. SWI/SNF plays a critical role in melanocyte development and in malignant melanoma. Melanocytes are cells in skin, eyes, and mucous membranes that provide protection from ultraviolet radiation by synthesizing the pigment, melanin. Malignant transformation of melanocytes leads to melanoma, an aggressive skin cancer that is resistant to chemotherapeutics. In addition to acquired mutations, the innate ability of melanocytes to migrate and withstand exposure to ultraviolet radiation contributes to the aggressiveness of melanoma and its resistance to chemotherapeutics. Melanocyte-Inducing Transcription Factor (MITF) and SRY-Box Transcription Factor 10 (SOX10) are crucial for the commitment, terminal differentiation, proliferation, and survival of melanocytes. MITF and SOX10 are also required for melanoma proliferation and are associated with resistance to therapeutics. We have determined that SMARCA4, a central ATPase of the SWI/SNF complex and a SWI/SNF subunit, SMARCD1, both interact with MITF and SOX10, and are required for melanocyte development. SOX10 and MITF promote recruitment of the SWI/SNF complex to regulatory regions in order to remodel chromatin structure and facilitate expression of genes that regulate melanocyte function. In melanoma, SMARCA4 promotes resistance to DNA damaging agents through a transcriptional circuitry involving MITF. Bromodomain protein 9 (BRD9) is a Smarca4-interacting subunit that stabilizes SWI/SNF binding at specific genomic loci. Chemical inhibition and CRISPR/CAS9-editing of BRD9 abrogates the expression of tumor-relevant genes and suppresses tumor growth. These findings suggest that the SWI/SNF complex is a potential epigenetic target in melanoma.

FIBRILLARIN AND NON CODING RNA IN GENE ARCHITECTURE AND REGULATION

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Abstract:

During the last decade an advancement into the field of Non coding RNA (ncRNA) from mass sequencing has lead a field that involve them with chromatin and Gene expression. The dynamic aspect in the nuclear structure requires the aid of ncRNA for direct interaction with histone and mediator proteins as well as other molecules including phospholipids to aid in the transport and aggregation of such functional complex. Fibrillarin is primarily nucleolar protein that interacts with several ncRNA either in classical complex like Nop56/58-fibrillarin heterocomplex a core protein complex of the box C/D ribonucleoprotein particles that modify and process ribosomal RNAs. Fibrillarin is a highly conserved S-adenosyl methionine (SAM) dependent methyltransferase. It is the catalytic component of a multi-protein complex that facilitates 2'-O-methylation of ribosomal RNAs, with over 100 modifications essential for accurate and efficient protein synthesis in eukaryotic cells as well as a its involvement in several illness including cancer. However, in non-canonical complexes fibrillarin can interact with several ncRNA like Helena directly and regulate gene regulation. Ribonuclease activity has been added to this multitask protein as part of the mechanism in which may regulate posttranscriptional modifications and RNA processing. Here we show some of the mechanism involve in multiphase control and nucleoli architecture as well as the evolution of this protein along the eukaryotic genomes.

VACCINE CANDIDATES AGAINST CORONAVIRUS VARIANTS: THE ROLE OF THE BIOCHEMISTS

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Abstract:

The Coronaviridae family encompasses several viruses that can cause human diseases ranging from common cold to severe clinical manifestations, such as Middle East Coronavirus Respiratory Syndrome (MERS-CoV), Severe Acute Respiratory Syndrome (SARS-CoV), and COVID-19 (SARS-CoV-2) including the variants of concern Alpha, beta, Delta, and lately, Omicron. SARS-CoV and SARS-CoV-2 coronaviruses employ Spike (S) protein to enter the host cells through interaction with the cellular receptor of the angiotensin-converting enzyme (ACE2) [3]. The Receptor-Binding Domain (RBD) of the Spike (S) protein from SARS-CoV-2 has glycosylation sites but they do not mediate the recognition by the ACE2 receptor. Recombinant antigens NG19 from Wuhan strain and variants of concern (VOC) Alpha/Beta and Delta located within the non-glycosylated S-RBD region were selected and expressed in Escherichia coli. Antigens were then purified by FPLC and employed in preclinical studies to assess their immunogenicity, potency, toxicity and security and special considerations for recombinant antigens, according to the requirements of the regulatory agencies FDA and COFEPRIS. Seroconversion, cellular and humoral response and neutralization capacity assayed in rabbits, mice and Vietnamese pigs demonstrated the capacity of the recombinant antigens to raise a protective response against the virus. The bioengineering of antigen production was developed, consisting in generation of a cell bank, aerobic fed-batch fermentation at 14 L, biomass harvesting by centrifugation, cell lysis by sonication, inclusion body washes, protein solubilization, chromatographic purification by ion exchange, refolding by dialysis, filter sterilization, protein quantification and formulation with the adjuvant $Al(OH)_3$.

As an accelerated emergence of SARS-CoV-2 VOC, an universal vaccine was designed based in extant VOCs, its potential use will be presented to cope with the control of coronaviruses in the human population. This research highlights the usefulness of antigens based on the non-N-glycosylated region of RBD from SARS-CoV-2 for candidate vaccine development.

- Núñez-Muñoz et al., 2021. Vaccines doi: 10.3390/vaccines9080928.
- Fragoso-Saavedra et al. 2022. Front Immunol. doi: 10.3389/fimmu.2022.848054.

INTERFERING THE SARS-COV-2/ACE2 INTERACTION AND BIOPHYSICAL CHARACTERIZATION OF VIRAL SPIKE VARIANTS

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Abstract:

The interaction of the SARS-CoV-2 spike (S) protein (and its Receptor Binding Domain, RBD) with the membrane-bound ACE2 receptor is crucial for viral infection. Based on this interaction we designed a strategy to develop viral entry inhibitors that includes the production/purification of a panel of RBDs and S-proteins representing most viral variants of concern, in silico screening and chemical synthesis of compounds or biophysical and preclinical testing for the evaluation of Spike/ACE2 inhibition. A dedicated protein production facility has been set up allowing the rapid production and characterization of several spike variants and ACE2 as candidate decoys. An interactomics pipeline has been established with the aim of contributing to the biophysical analysis of therapeutic drug candidates targeting this process.

Mutational variants on the spike protein can have a strong impact on the viral infection propertied and we have therefore biophysically and structurally evaluated the impact of different mutations on the SARS-CoV-2 spike protein. Structural characterization has been performed using molecular dynamics and cryoElectron Microscopy. We will present some data on ACE2 candidate decoys and explore some potential mechanisms relating the spike mutation A222V to biologically relevant outcomes.

RESPONDING TO A PANDEMIC WITH VACCINES: MEXICO AND THE WORLD

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Abstract:

I am a scientist in the soul and an engineer in my brain. The COVID-19 pandemic, which has severely hit Mexico with one of the higher mortality rates, highlighted the lack of infrastructure in the country for vaccine development and production. During the last 21 years, I have served as a professional devoted to vaccine development in Chemistry, Manufacturing, and Control aspects of process development. On these topics, as I was appointed as an expert of the Subcommittee for the Evaluation of Biotechnological Products of COFEPRIS for 2013 to 2019, I had the opportunity to be part of the team that constructed the foundations for the evaluation of recombinant vaccines in Mexico. The situation in Mexico remains precarious, but the COVID-19 pandemic has opened many opportunities. We have been filling gaps and contributing with the BSL3 laboratories, the CEPI Centralized Network Laboratory, and the cGMP plant in Hidalgo. Other Mexican groups are also proposing new strategies to fill gaps, such as the National Polytechnic Institute (IPN) graduate program in vaccinology and the collaboration between Laboratorios Liomont and Argentina to produce the ChAdOx AstraZeneca COVID-19 vaccine, which the WHO recently approved. Mexico will emerge stronger from the COVID-19 pandemic, but there are still many limitations. There is not enough personnel expert on vaccine manufacturing, analytics, and development, and many of them emigrate to other countries where there are also limitations. Also, the available infrastructure is not sufficient. Finally, more decisive support from the Mexican government in a strategic plan to nourish the environment for vaccine development and production in Mexico is required. Only when the critical mass for vaccine development exists in Mexico will we stop being totally dependent on others for basic vaccines.

Information taken from Laura A. Palomares (2022) Vaccine manufacturing is essential to ensure access, Human Vaccines & Immunotherapeutics, 18:4, 2060616, DOI: 10.1080/21645515.2022.2060616

NEW FRONTIERS IN VACCINES AND NANOTECHNOLOGY

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Abstract:

The challenge of COVID19 has shown how innovation, specifically the nanotechnologies underlying COVID19 vaccines, can be rapidly harnessed and deployed to address global health. It further emphasized the need to understand how the immune system reacts to nanoparticles generally, as well as emergent infectious diseases, adjuvants and vaccines. Issues such as crossreactivity between COVID19 strains, automimmunity, inflammatory 'cytokine storms' and allergic reactions have come under the spotlight. Herein we will provide an overview of key vaccine development and nanotechnology studies we have been involved in, including how nanoparticles interact with the immune system, and differences in immune profiles elicited by viral vectors like adenovirus, prime-boost approaches, or protein and nucleic acid based nanovaccines. We will also share with our recent work on human clinical trials of Influenza and SARS-COV2 vaccines, including their potential to induce anti-PEG mediated allergies, as well as characterization of immuntiy in patients developing 'long-COVID19'. Understanding how the immune system changes across the lifespan, and how it is different in males and females is further emerging as critical to effective vaccine implementation. We will further share our insights on how to potentially optimize nanovaccine development across such different human target populations. Finally, we will share with you some of our very recent exciting findings on the interplay between immunity and ovarian cancer which as well as offering the possibility of effective vaccination against this cancer, by engaging nanotechnology and lab-on-a-chip devices may offer, for the first time in decades, substantial improvement in the early diagnosis of this highly lethal cancer. The new frontier of personalized vaccines, and tackling diseases hitherto not targeted by vaccines, such as cancers and diabetes, is already here.

FUNGAL HOLOBIONTS: HIDDEN RELATIONSHIPS WITH ECOLOGICAL CONSEQUENCES

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Abstract:

Rhizopus microsporus is an early-diverging fungal species that belongs to the phylum Mucoromycota and it is important in ecology, agriculture, food production and public health.

Our research has revealed that members of *Rhizopus* often establish symbioses with gram-negative beta-proteobacteria from the genus *Mycetohabitans* (*Burkholderia* sensu lato). This vertically-transmitted bacterial symbiont is responsible for the production of toxins that are crucial for the pathogenicity of *R. microsporus*[1,2,3]. Additionally, the endofungal bacteria are essential for the asexual reproduction[4] of their host and also positively affect its sexual cycle, being necessary for abundant zygospore production[5]. After more than a decade since the discovery of this unique bacterial-fungal symbiosis, we now identified new partners: the narnaviruses[6].

In this seminar, I will present some of our most recent results on the role that these bacterial and viral symbionts play in fungal reproduction; how these symbioses affect fungal metabolism, as well as recently described novel Mexican symbiotic *Rhizopus* strains[7] and how they can halp expand our understanding of microbial symbioses and fungal ecology and evolution.

[1]Partida-Martínez & Hertweck. *Nature* 2005. [2]Partida-Martinez & Hertweck *Chembiochem* 2007. [3]Partida-Martinez *et al*., *AEM* 2007. [4]Partida-Martinez *et al*., *Curr Biol* 2007. [5]Mondo *et al*., *Nat Commun* 2017. [6]Espino-Vázquez, *et al*., *ISME* J 2020. [7]Mendoza-Servín *et al*., *in press.*

EXPLORING THE KOSMOTROPY LIMITS IN FUNGI: *ASPERGILLUS SYDOWII* AS A MODEL OF KOSMOTOLERANT

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Abstract:

Although various studies have investigated osmoadaptations of halophilic fungi to saline conditions, only few analyzed the fungal mechanisms occurring at saturated concentrations (NaCl, KCl). Halophilic *Aspergillus sydowii* is a model organism for the study of molecular adaptations of filamentous fungi to hyperosmolarity. For the first time a multi-omics approach (i.e., transcriptomics and metabolomics) was used to compare *A. sydowii* at saturated concentration (a_w=0.75; NaCl and KCl) to optimal salinity (a_w=0.99; 0.5 M NaCl and KCl). Also the analysis included the fungal growth in the presence of sorbitol at a_w=0.75 and a_w=0.99. Analysis revealed 1,842 genes differentially expressed of which 704 were overexpressed at a_w=0.75. Most differentially expressed genes were involved in metabolism and signal transduction. A gene ontology multi-scale network showed that ATP binding constituted the main network node with direct interactions to phosphorelay signal transduction, polysaccharide metabolism and transferase activity. Free amino acids significantly decreased and amino acid metabolism was reprogrammed at a_w=0.75. mRNA transcriptional analysis revealed upregulation of genes involved in methionine and cysteine biosynthesis at extreme water deprivation by NaCl. No modifications of membrane fatty acid composition occurred. Upregulated genes were involved in high-osmolarity glycerol signal transduction pathways, biosynthesis of ß-1,3-glucans and cross membrane ion transporters. Downregulated genes were related to the synthesis of chitin, mannose, cell wall proteins, starvation, pheromone synthesis, and cell cycle. Non-coding RNAs represented the 20% of the total transcripts with 7% classified as long non-coding RNAs (lncRNAs). The 42% and 69% of the total lncRNAs and RNAs encoding transcription factors, respectively, were differentially expressed. A network analysis showed that differentially expressed lncRNAs and RNAs coding transcriptional factors were mainly related to the regulation of metabolic processes, protein phosphorylation, protein kinase activity, and plasma membrane composition. Metabolomic analyses revealed more complex and unknown metabolites at saturated NaCl concentration than at optimal salinity. This study is the first attempt to unravel the molecular ecology of an ascomycetous fungus at extreme water deprivation by NaCl, KCl and sorbitol. This work also represents a pioneer study to investigate the importance of lncRNAs and transcriptional factors in the transcriptomic response to high NaCl stress in halophilic fungi.

EXPLORING NATURAL PRODUCTS FROM MEXICAN BIODIVERSITY

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Abstract:

Natural products (NPs) can be broadly defined as the set of small molecules derived from the environment that are not involved in primary metabolism. Many of today's small molecule therapeutics trace their origins to NPs, which are estimated to provide or inspire the development of 50–70% of all agents in clinical use today. By unveiling new molecular skeletons and inspiring the preparation of semisynthetic and hybrid prototypes, these specialized substances have attracted the attention of scientists and industries related to ecology, food technology, agriculture, bioremediation, drug discovery, among others.

The process of NPs discovery has gradually become more difficult, and the reisolation of known NPs structures is an increasing challenge for the field. Advances in novel strategic approaches are essential for the evolution of NPs chemistry.

In this context, our research group has examined unexplored and unusual source organisms or those from unique environments from Mexico, as an opportunity to find novel NPs. In addition, we have combined classical bioactive-guided isolation and OSMAC approaches, with genetic information and advanced metabolomic techniques, for the discovery of these compounds. Some of the latest discoveries in our research group using this multidisciplinary approach will be presented here.

FUNGAL MODELS: CAN THEY BE THE BASIS OF THE GROWTH CANONS OF THE GREAT FUNGAL DIVERSITY?

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Abstract:

The filamentous fungus Neurospora crassa has been at the vanguard of biochemical and genetics research for over a century. In addition, this fungus has become a magnificent model system to study polarized cell growth. We have used N. crassa to identify and analyze by high-resolution live fluorescence imaging key players of the secretory processes leading to a localized delivery of vesicles involved in cell wall biosynthesis at sites of polarized growth. At the hyphal apices of N. crassa, the Spitzenkörper (SPK) acts as the master choreographer of tip growth. Remarkably, the microvesicles containing chitin synthases (chitosomes) concentrate at the core of the SPK, while macrovesicles containing β-1,3-glucan synthases occupy the outer layer of the SPK. Distinct Rab GTPases are the potential coordinators of the trafficking of the different types of vesicles. Upon fusion of the vesicles with the plasma membrane, both synthases become integrated into the plasma membrane. Recently, we have analyzed cultures of N. crassa to explore release of extracellular vesicles (EVs). We found that the proteome of N. crassa EVs contains enzymes involved in carbohydrate metabolic processes and in oxidative stress responses, circadian clock proteins, cell wall proteins, and cell wall remodeling enzymes. In other fungi, including plant and human pathogens, EVs are released to the external milieu to participate in intercellular communication and virulence-related mechanisms. Our results suggest that in N. crassa EVs could be fundamental as unconventional vehicles for cell wall biogenesis. Our current efforts are investigating the secretory pathways leading to EVs biogenesis.

NEURAL INTERACTIONS MEDIATING COGNITIVE CONTROL IN PREFRONTAL NETWORKS

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Abstract:

To understand the origin of intelligent behavior, we will have to grapple with distributed processing in hierarchical networks that thwart simple structure/function relationships, particularly at a cellular level of scale. Prefrontal cortex is an excellent example. Long associated with cognitive control, neural recording studies in monkeys have established that the abstract neural signals that mediate cognitive control are found distributed between the prefrontal cortex and numerous other brain areas, both cortical and subcortical, that communicate with prefrontal cortex via axonal projections during behavior. Localized function in such a network does not easily reduce to localized patterns of neural activity. Rather, it appears that each cortical area embedded within the network sculpts or modifies patterns of neural activity that appear to emerge everywhere in the network all at once. Functionally dissecting such a system will require learning how the synapses in one cortical area modify distributed neural signals as they pass through one cortical area enroute to others in the network. In this talk, I will describe experimental data from neural recording studies in monkeys that attempt to recover the pattern of synaptically mediated functional interactions between prefrontal neurons and neurons in other brain areas while computations for cognitive control are ongoing. The data will interrogate synaptic mechanisms that mediate these functional interactions, and characterize how functional interactions between prefrontal neurons may fail in schizophrenia, by integrating nonhuman primate drug, mouse genetic, and computational models.

REGAINING OUR BEARINGS: NEURAL REPRESENTATIONS AND CIRCUITS UNDERLYING SPATIAL REORIENTATION

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Abstract:

Reorientation – regaining one's bearings after becoming lost – is a fundamental navigation process wherein the internal sense of direction becomes unreliable, forcing disoriented organisms to only use external cues. Across species the geometry of the surrounding space plays a dominant role in reorientation, even when other directionally informative cues, such as landmarks, are available. Consequently, the modular theory has proposed that reorientation is driven by a cognitive mechanism sensitive to geometry that is impermeant to landmarks. In support of this theory, we have shown that the hippocampal map aligns to the geometry during reorientation. However, the modular theory's exclusive reliance on geometry is limited in situations of contextual ambiguity (identity of a context is unclear). In this scenario, disoriented animals must perform a dual task: 1) recover facing direction within the context (heading retrieval), 2) identify the environment in which they are lost (context recognition). We demonstrate that in relatively unfamiliar surroundings, mice rely on the shape of the layout to compute heading retrieval, while using non-geometric features to perform context recognition. However, with prolonged familiarization with the environment, animals incorporate features to recover heading in order to maximize reward. The neural mechanisms associated with these processes exhibit unique patterns of activity and dynamics. Following disorientation, heading retrieval cells rapidly align to environmental geometry, while context recognition cells align to local features over days, as animals learn their directional value. Firing rate changes integrate these distinct cognitive representations at the neural level. The fast emergence of geometric alignment suggests that layout perception originates in scene processing regions, such as the retrosplenial cortex (RSC). We show that RSC is required for the use of geometry and a long-range GABAergic RSC projection to CA1 inhibits the use of geometric, thereby enhancing landmarks during reorientation. This research uncovers important aspects of navigational architecture.

CORTICO-STRIATAL CIRCUITS FOR BILATERALLY COORDINATED MOVEMENTS

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Abstract:

Movement initiation and control require the orchestrated activity of sensorimotor cortical and subcortical regions. However, the exact contribution of specific pathways and interactions to the final behavioral outcome are still under debate. Here, by combining structural lesions, pathway-specific optogenetic manipulations and freely moving electrophysiological recordings in rats, we studied cortico-striatal interactions in the context of forelimb bilaterally coordinated movements. We provide evidence indicating that bilateral actions are initiated by motor cortical regions where intratelencephalic bilateral cortico-striatal (bcs-IT) projections recruit the sensorimotor striatum to provide stability and duration to already commanded bilateral movements. Furthermore, striatal spiking activity was correlated with movement duration and kinematic parameters of the execution. bcs-IT stimulation affected only the representation of movement duration but spared that of kinematics. Our findings confirm the modular organization of information processing in the striatum and its involvement in moment-to-moment movement control but not initiation or selection.

BRAIN DYNAMICS IN THE PRIMATE AUDIOMOTOR CIRCUIT DURING ISOCHRONOUS BEAT PERCEPTION AND ENTRAINMENT

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The ability to extract the regular pulse in music and to respond in synchrony to this pulse is called beat synchronization and is a natural human behavior exhibited during dancing and musical ensemble playing. Previously, we showed that macaques can predictively entrain to isochronous metronomes, although they have a bias towards visual rather than auditory rhythmic stimuli (Gamez *et al*., 2018). In this study we recorded the simultaneous activity of hundreds of cells in the core (A1) and belt (A2) areas of the auditory cortex as well as in the medial premotor areas (SMA) when monkeys performed both a task that included beat perception (BP) and tapping synchronization (TS) epochs and during passive listening of the metronome. Notably, we found that both A1 and A2 not only showed responses associated with auditory sensation in all tasks, but also neural signals related with active sensing. The latter showed activity that increased during BP and TS with a switch in response phase from sensory driven, tens of ms after the stimulus in the passive condition, to a predictive sensory response during BP and TS. In addition, some A2 neurons showed neural responses aligned to the tapping movements, suggesting that the auditory cortex has access to an internal beat prediction signal, probably coming from the cortical premotor system. Indeed, in SMA we found time-varying single-cell responses which, when projected into a low dimensional space, formed rotatory population neural trajectories that showed two main properties. First, a complete circular loop was formed for each produced interval, converging to a similar state-space location close to the tapping time. The convergence to this neural attractor state could be the internal representation of the pulse that is transmitted as a phasic top-down signal to the auditory areas before each tap. Second, these oscillatory trajectories did not overlap across durations, a signature of temporal scaling; instead, they showed a linear increase in their radius as a function of the target interval (Gamez et al., 2019). These preliminary results give experimental support to the notion of a dynamic interplay between the active sensing signals of the auditory areas and the internal beat representation of medial premotor system during rhythmic perception and entrainment.

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A STRUCTURAL STUDY OF AN IGE-PROFILIN COMPLEX REVEALS ALLERGEN RECOGNITION AND CROSS-REACTIVITY INFORMATION

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Abstract:

Hypersensitivity reactions mediated by immunoglobulins E (IgE) are considered a relevant public health problem in the industrialized world, and an increased prevalence has been reported in developing countries. Asthma and allergic rhinitis are significant diseases in Mexico. Natural rubber latex (NRL) from *Hevea brasiliensis* contains several proteins involved in this type of allergy, which are involved in cross-reactivity against fruits, pollens, and insect venoms. Profilin (Hev b 8) is an excellent example of allergen cross-reactivity. Profilins are 12 to 17 kDa proteins that maintain a high 3D structure and sequence identity. Therefore, cross-reactivity between foods and aeroallergens in patients suffering from respiratory allergies could induce oral-allergy syndrome or even anaphylaxis. We have produced several murine monoclonal antibodies IgG and a novel IgE (mAb 2F5), specific for Hev b 8 [1]. Here, we report the first crystal structures of native murine Fab/IgE structures, with a VH and VL combination that exhibits an authentic pairing in complex with the allergen (Hev b 8). The crystallographic models revealed that the six CDR regions of Fab/IgE interact with the allergen, comprising a rigid paratope-epitope surface of 926 $Å^2$, which includes an extensive network of interactions. Therefore, the IgE exhibits a high affinity for Hev b 8 (Kd = 1.7 nM), even when using high NaCl concentrations in BLI experiments. Remarkably, knowledge of residues at the epitope region and based on cross-reactivity assays using two mutants of the maize profilin (Zea m 12), we propose that this antibody could be a promising tool for developing hypoallergenic profilins. Further studies on the interaction of 2F5 (and other) anti-profilin antibodies with different profilins would help better define critical aspects of cross-reactivity.

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[1] Mares-Mejía I, Martínez-Caballero S, Garay-Canales C, Cano-Sánchez P, Torres-Larios A, Lara-González S, Ortega E, Rodríguez-Romero A. (2016). Sci Rep. 6:32552

Acknowledgments. This work was supported by DGAPA-UNAM (IN208418) and CONACYT CF-2019-87163

POLYMERASES & DNA REPLICATION: A TALE OF BACTERIA, PHAGES AND ORGANELLES

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Abstract:

Plant mitochondria DNA replication is highly diverse. This organelle harbors enzymes with different evolutionary origins that co-evolved to achieve regulated DNA replication. Among the many complexities of DNA replication, DNA replisomes face the inherent problems of selecting a place to start, achieving nucleotide incorporation with uncanny fidelity, and performing coordinated DNA synthesis at high speed. Here we show that plant mitochondria use several mechanisms to solve these problems. We will discuss data that indicate that plant mitochondrial DNA replication starts using multiple priming mechanisms. We will discuss an archetypical bacteriophage-like system present in plant mitochondria and a backup bacteria-like apparatus used to perform homologous recombination at double-stranded DNA breaks.

Furthermore, we will discuss two novel DNA replication routes mediated by Microhomology-mediated end joining and Non-homologous end-joining and how those DNA replication repair systems assist plant mitochondrial DNA replication. We will also discuss the structural adaptations that plant organellar DNA polymerases have evolved to execute DNA repair and DNA replication.

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HOW ARE PLANT PEPTIDE HORMONES PERCEIVED BY THE CELLS AND WHAT DETERMINES THEIR SIGNALING SPECIFICITY?

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Abstract:

As sessile organisms, plants have developed an arsenal of molecular tools that allow them to perceive specific cues and react to the ever-changing conditions of their local environment. Many of those cues are perceived at the plasma membrane by membrane receptor kinases (also called receptor-like kinases, RLKs,) that are capable of transmitting signals from the exterior to the interior of the cell. The RLKs represent one of the largest gene families in the Arabidopsis genome, with more than 610 members. Each RLK is composed of an extracellular domain (ligand-binding domain), a transmembrane helix, and a cytoplasmic kinase domain. The RLKs family can be subdivided according to the architecture of the extracellular domain, with the Leucine-reach repeat ectodomain (LRR), being one of the biggest subgroups with more than 200 members. HAESA-like and CLAVATA1-like are members of the LRR-RLKs subfamily, and control cell separation processes and stem cell homeostasis, by perceiving the sequence-related hormone peptides IDA-like and CLE-like, respectively. How plants perceive and discriminate between molecular cues and what are the mechanisms of signal transduction that plants use to reprogram their cell behavior is still a question that keeps scientists busy and was the inspiration for this work.

Through a series of structural, quantitative biochemistry, and genetic experiments, our work reveals that HAESA-like and CLAVATA1-like receptors use a slightly different configuration in their binding domains to discriminate and specifically bind to their cognate sequence-related but functionally distinct IDA-like and CLV-like peptides, respectively.

ALL ROADS LEAD TO MITOCHONDRIA: MITOPHAGY AND STRESS IN *SACCHAROMYCES CEREVISIAE*

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Abstract:

In most eukaryotic cells mitochondria are essential organelles involved in a great variety of cellular functions. One of the physiological processes linked to mitochondria is aging, a gradual process of damage accumulation that eventually promotes cell death. Aging depends on a balance between mitochondrial biogenesis, function, and degradation. It has been previously shown that in Saccharomyces cerevisiae the mitochondrial protein Slm35 is functionally linked to the TOR signaling pathway, probably playing an important role connecting mitochondrial function with cytosolic responses and cell adaptation to stress and aging. In addition, Slm35 is a negative regulator of mitophagy, the selective form of autophagy that eliminates fragments of the mitochondrial network. Taking all these into account, we hypothesized that Slm35 could function as a sensor that detects metabolic alterations within mitochondria and possibly transfers the damage signal to the key components of the autophagic machinery. To explore the molecular mechanisms underlying the responses previously observed, we analyzed possible transcriptional and translational regulation processes of Slm35 itself as well as the posttranslational modifications of Atg32, the bona fide mitophagy receptor in yeast. Our results indicate that Slm35, whose expression is mainly translationally regulated via the expression of an uORF, could indeed transfer the damage signal to Atg32 and activate mitophagy.

THE BIOENERGETIC MACHINERY OF *EUGLENA GRACILIS*

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Abstract:

Photosynthesis and mitochondrial respiration are the main mechanisms that produce NADH and ATP to feed all the cellular processes in photosynthetic organisms. The transfer of photosynthesis from eukaryotes that belongs to Archaeplastidae (*i.e.* green algae or red algae) to other non-photosynthetic organisms is a spectacular example of evolutionary innovation. This transfer occurred many times upon evolution and gave rise to photosynthetic lineages of high ecological and/or biotechnological significance (*e.g.* diatoms, dinoflagelates, euglens). These organisms are among the most diverse on the planet and they have evolved to adapt to a wide range of environments, nevertheless, information about the complexes involved in the energy production is scare in these lineages.

Here, we characterized the bioenergetic machinery, OXPHOS and light harvesting complexes from *Euglena gracilis*, a secondary green flagellate. Combining 3D gel electrophoresis and two-step chromatographic purification followed by electron microscopy, the presence of atypical subunit composition and additional structural domains, *e.g.* an extra domain located at the tip of the peripheral arm of complex I, a "helmet-like" domain on the top of the cytochrome *c* binding region in complex IV, and a highly divergent geometry of dimeric complex V were observed [1-2]. Despite of these, canonical supramolecular associations into III_2/IV, III_2/IV_2 and I/III_2/IV respirasome were observed. The latter supercomplex was further purified and showed *in-vitro* oxygen consumption independent of the addition of external cytochrome *c* [3].

Additionally, this organism exhibits a low-light adaptation by synthesizing lineage-specific photosystem-associated antenna, named LHCE, containing dramatically red-shifted chlorophyll *a*. Combining phylogenetic, biochemical, structural, and functional studies, we demonstrate the molecular nature of the red-shifted LHCE antenna contributing to both PSII and PSI absorption in light-limiting growth conditions. We further show that LHCE is a mobile antenna, allowing modulating the cross-section of PSII and PSI upon state transitions.

H.U.M.A.´s research is supported by grant IA204122 (PAPIIT, DGAPA, UNAM) and by the Institutional Program (IIBO-UNAM) "The production of biomolecules of biomedical interest in microorganisms".

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BACILLUS SUBTILIS AND ITS RESPIRATORY CHAIN: IT BREATHS TOO

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Abstract:

Bacillus subtilis is a Gram-positive bacterium that lives in the soil and forms endospores as a resistance strategy. *B. subtilis* is an aerobic bacterium that can live in anaerobic conditions with nitrate as a terminal acceptor or fermentation. The respiratory chain has several electron donors in its only membrane: a type 2 NADH dehydrogenase (NDH-2) succinate: quinone reductase (SQR or SDH), a glycerol 3-phosphate dehydrogenase. These complexes reduce a menaquinone 7 (MK-7). From MK-7, the respiratory chain branches to a cytochrome branch (with a b_6c complex, two membrane-bound cytochromes, and a caa_3 oxidase). The other branch is a quinol oxidase branch with an aa_3 oxidase, a *bd*, and a *bb'* oxidase. The b_6c, the caa_3, and the aa_3 complexes contribute to the proton gradient formation. The rest of the complexes do not. We found that the b_6c and caa_3 form a supercomplex in the *B. subtilis* membrane and could be integrated as a "respiratory rope". The membrane-bound cytochromes are also bound to the supercomplex. When the aa_3 oxidase is eliminated, the b_6c+caa_3 supercomplex associates with the SQR, forming a novel supercomplex. This association is possible for a more efficient proton gradient, but also because the reduction of MK-7 by SQR uses the proton gradient for this unfavorable reaction. MK-7 has a low redox potential that could be forming ROS in certain conditions in the cell. We are investigating the formation of ROS by the respiratory chain of *B. subtilis* to discover how this bacterium regulates and avoids the formation of ROS during the reduction/oxidation of MK-7. Another topic to investigate is how NDH-2 works in the membrane and avoids ROS formation because it does not form a supercomplex. Are there other supercomplexes left or hidden? Are there associations with other membrane proteins not part of the respiratory chain? Is the presence of supercomplexes modulated by low oxygen?

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GROW OR FIGHT: A PHOSPHO-SWITCH PRIORITIZES ABCG36/PEN3/PDR8-MEDIATED TRANSPORT TOWARD DEFENSE

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Abstract:

A misbalance between plant growth and defense can result in decimation of a plant population and have therefore important ecological and agricultural consequences. Thus, plants as sessile organisms have evolved refined mechanisms to balance growth-defense tradeoffs. Based on its proposed substrate preferences, the ABC transporter, ABCG36/PDR8/PEN3, from the model plant Arabidopsis stands at the cross-road between growth and defence: recently, ABCG36 was shown to export a few indolic compounds, including the auxin precursor, indole-3-butyric acid (IBA), and to be implicated in the export of the major phytoalexin of Arabidopsis, camalexin.

Here we provide strong evidence that ABCG36 catalyses the direct, ATP-dependent export of camalexin over the plasma membrane, however, most likely in functional interplay with non-camalexin transporting ABCG isoforms. We identify the leucin-rich repeat receptor-like kinase, Auxin-induced LRR Kinase1, ALK1, as a functional kinase to physically interact with and phosphorylate ABCG36. ABCG36 phosphorylation by ALK1 represses unilaterally IBA but not camalexin export leading to a prioritization of ABCG transport toward defense. As a consequence, phospho-dead mutants of ABCG36, like alk1 and abcg36 alleles, are hypersensitive toward infection with the root pathogen, F. oxysporum, caused by elevated fungal progression.

Our findings indicate a novel, direct regulatory circuit between a receptor kinase and an ABC transporter determining transporter substrate specificity. It appears that growth and defense balance decisions in plants are performed on the transporter level by means of a reversible phospho-switch.

THE INTEGRATED USE OF METABOLOMICS AND TRANSCRIPTOMICS AS AND STRATEGY TO IDENTIFY PHYTOCHEMICALS COMPOUNDS TO USE IN CONTROL PEST. CASE OF *CASSIA FISTULA* AND THE AMBROSIA BEETLES

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Abstract:

Ambrosia beetles are a group of wood-boring insects that evolved fungiculture and they have been traditionally considered wood-degraders responsible for accelerating the natural decay of weakened, stressed or recently dead trees. This is due to the fungi which are associated with beetles (mutualistic relationship) are mainly saprophytic. Recent reports, however, have shown that many species of ambrosia beetles could be considered high-risk pests because the associated fungi act as plant pathogenic fungi. This has been observed mainly in those cases in which the beetles are accidentally introduced to new environments in which they found new hosts (invasive pests). Thus far, no effective control strategies for these pests are available, which can be largely attributed to their cryptic lifestyle inside their host trees. In this sense, *Cassia fistula* L., emerges as a study model with enormous potential to mitigate the damage caused by ambrosial complexes. This research project was carried out to demonstrate by in vitro bioassays, the insecticidal and/or antifungal activity of the extracts generated from some organs of *C. fistula* (flowers, pods, stems, and leaves). Fusarium sp. strain INECOL-BM06 and Xyleborus bispinatus Eichhoff (Coleoptera: Curculionidae, Scolytinae) were the organisms used as study cases. Phytochemical compounds presumably responsible for insecticidal and/or antifungal activity were identified by metabolomics analysis while transcriptomic studies were done to identify those genes encoding enzymes that are involved in their biosynthesis.

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NTT CONNECTS TWO PLANT HORMONAL PATHWAYS

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Abstract:

WIP2 / NO TRANSMITTING TRACT (WIP2/NTT) is a zinc finger transcription factor that alters developmental programs in Arabidopsis when overexpressed. The loss of *NTT* function, alone or combined with closely related genes, leads to developmental defects in gynoecia and roots, respectively. Knowing genes that act downstream of NTT can help to understand more about its role in developmental regulation. To find these genes, RNA-seq analyses were performed using separate aerial and root tissues, at different times. Genes that participate in a variety of processes that include hormonal pathways were found to be differentially expressed. The study of these downstream genes led to the finding that NTT acts as a connector of hormonal pathways.

USE OF VIRUS IN EXPERIMENTAL GENE THERAPY

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Abstract:

Gene therapy includes all the interventions that involve the deliberated modification of the genetic material of somatic cells to diagnose, treat or prevent diseases. Many different strategies have been employed to achieve these goals, including: gene transfer, RNA modifications, and more recently gene editing. Since the objective of many of the proposed treatments is the transfer of transgenes to the cells, efficient and safe methods to accomplish these objectives are necessary. Viruses offer these capabilities and have been extensively used, both in preclinical as well as clinical studies. Different virus present diverse properties that can be used for specific treatments and applications, thus they are the most commonly employed vectors in gene therapy. These properties have made virus the preferred systems for gene transfer and they have been used in almost 70% of all gene therapy clinical trials. In this presentation I will provide an overlook of the most frequently used viral vectors, and then show some of the work we have performed in our laboratory.

We have employed different viral vectors (retrovirus, lentivirus, adenovirus) to be employed as experimental treatments for neurodegenerative disorders (Huntington´s and Parkinson´s diseases), and also for cancer treatment, specifically using the expression of Growth Arrest Specific 1 (GAS1) as the therapeutic agent. More recently, we have also started using CRISPR-based technologies, to activate gene expression.

THE VIRUSES WE USE FOR OPTOGENETIC MANIPULATIONS

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Abstract:

Optogenetics is a set of techniques that allow the observation or manipulation of biological processes in order to link such observation/manipulations with the functions of cells. These techniques have become widely used to study all kinds of biological processes, in a wide range of experiments, e.g.: from the polymerization of actin to observing the activity of neurons in the primate's brain. The core of these techniques is in the expression of exogenous proteins that allow the observation/monitoring of the biological processes we want to study. A crucial point for the use of these techniques is the existence of viral vectors that allow the expression of these exogenous proteins in the cells that we want to study. Hence a key point is the appropriate selection of these viral vectors as some are very good in handling big sequences to express proteins but with a low rate of expression and others are too good to express the desired sequences that could end up killing cells due to overexpression.

This presentation will summarize the technical details pros and cons of the different viral vectors used to express light-sensitive proteins into cells to either monitor or manipulate the activity of cells on the different levels of research: studying cellular processes or specific behaviors of animals.

This presentation is supported by the Fronteras de la Ciencia CONACyT grant 154039, the DGAPA-PAPIIT-UNAM grant IN203420 and the Moshinsky fellowship.

BACULOVIRUS DISPLAY: A NOVEL METHOD FOR VACCINE PRODUCTION

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Abstract:

Baculovirus are a large family of viruses comprising over 500 members. These viruses infect a wide variety of insects but are innocuous to humans. The baculovirus expression system combined with insect cell cultures are one of the most effective systems for the expression of proteins of interest due to its high efficiency and large levels of protein production. In fact, many hormones and some vaccines are produced using this expression system. However, the baculoviruses are utilized only as carriers of the protein to be expressed, but the virus itself is not used in any real medical application.

In the present work we show evidence suggesting that the display of proteins on the surface of the baculovirus capsid may provide a useful and powerful tool for vaccine production. We explore the efficiency of display of several proteins of interest, including the S glycoprotein from the SARS-Cov-2 coronavirus, the agent responsible for the recent pandemic.

Baculovirus display is a novel and powerful tool that needs more exploration to validate its future use in vaccine generation and the display of antigens of interest. The journey just begins, and more studies are needed to determine if the antigens are displayed correctly on the surface of the baculovirus and if the postraductional modifications are incorporated into the proteins of interest. Many antigens require glycosylation and other modifications to generate a robust and adequate immune response in the host. The S glycoprotein requires multiple glycosylations for proper expression and folding. Future studies will help to understand the limitations and benefits of baculovirus display.

OXIDATIVE STRESS IN METABOLISMS, POISONING, CHEMOTHERAPY AND RADIOTHERAPY: THE OXIDATION FOR BETTER AND FOR WORSE

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Abstract:

Oxidative processes are essential for life, due to of the oxidoreductant system of energy extraction from nutrients, having oxygen as the final electron acceptor. The oxidants, reactive species and free radicals can be used for different functions including intracellular signaling, although they can also cause oxidative damage, which is directly proportional to the insult and inversely to the defense, generating an oxidative stress with multiple and complex responses that can result in avoiding damage, compensate, contain, repair or irreversible damage that can lead to necrosis, apoptosis or generation of transformed cells and induction of neoplastic cells. In the case of environmental toxicants such as lead, the generation of oxidative metabolites has been found to inhibit different metabolic pathways, resulting in increased cell damage, including apoptosis of erythrocytes (eryptosis) of lead-exposed workers and an antioxidant response that is able to compensate the oxidative damage in erythrocytes, leukocytes, and platelets, preserving function despite the intense insult. Antioxidant treatment of workers has resulted in avoidance of oxidative damage, including less eryptosis and less neurological damage. On the other hand, some chemotherapeutic drugs and ionizing radiation are examples of inducing oxidative insults for cancer treatment, since DNA damage and induction of apoptosis on cell proliferation is the therapeutic effect sought for children with leukemia and women with breast cancer. These treatments generate complex antioxidant responses that may be included in the development and prognosis of the diseases and open the discussion on the use of antioxidants in different phases of treatment for these diseases, where the use of some toxicant privileged by a greater benefit to the patient who otherwise could not be treated in front of a fatal disease. In the seminar we will analyze the analysis of oxidative stress in patients and the use of antioxidant agents in the treatment, with a critical view.

CYSTEIN METABOLISM AND TRANSPORT IN ARSENIC EXPOSURE

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Abstract:

Arsenic (As) is one of the main elements affecting drinking-water quality in Mexico but worldwide. Approximately 2 million Mexicans drink water containing over 0.025 mg As/L, which represents twice the WHO recommended limit (0.010 mg As/L). Exposure to As is associated with skin, lung, and liver (among other) cancers and with immunosuppression and neurotoxicity. Once ingested is quickly absorbed in the gastrointestinal tract and distributed to all organs and tissues. Trivalent As (As3+) enters the cells through GLUT1 and AQP7/9 transporters. At the same time, the pentavalent form (As5+) uses the phosphate transporters in the cell membrane. Inside the cell this form is reduced to As3+ by thioredoxin or GSH and methylated by the As 3 methyltransferase (As3MT) to monomethylated, demethylated and trimethylated forms that will be exported from the cells by MRPs and AQP9. This process consumes GSH and SAM (s-adenosyl methionine as the methyl donor). Using mice models, we have documented that exposure to As depletes GSH pools in many organs, including the central nervous system. Here, we observed that the presence of As modulates the membrane transporters in charge of cystine and cysteine import and the activation of the transsulfuration to provide the cysteine required for GSH synthesis. NFκB and Nrf2 are activated early in the response in the brain cortex. A chronic exposure model shows that over-expression of cystine/glutamate antiporter altered glutamate disposition and ionotropic glutamate expression, leading to impaired learning and memory.

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OXIDATIVE STRESS AS AN INDUCER OF BACTERIAL "PERSISTENCE" IN THE ORIGIN OF MUTATIONS RESISTANT TO ANTIBIOTICS

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Abstract:

Bacterial resistance to antibiotics is a global health problem constantly worsening, so it is essential to determine the mechanisms that cause it. The general experience indicates that the misuse of drugs is the leading cause; however, we propose another possible reason that must be considered to face the problem. Bacteria are capable of giving three types of responses to drug stress: resistance, tolerance, and persistence; where the first involves a genetic change through which it manages to counteract the effect of the drug; in the second response, the bacteria respond with a physiological change that allows it to evade pharmacological action, such as the formation of biofilms, the third response depends on a transient phenotypic state related to an epigenetic trait, in which there is a low rate of cell division and decreased fitness of some cells of the population, which allows them to survive the bactericide (Leibler et al., 2005). During exit from the persistence state, the bacterium goes through a transient state of hypermutability.

Our group has characterized the induction of persistence in Salmonella enterica serovar Typhimurium with different pesticides, including Parathion, Glyphosate, and Azulam. In the survivors, we determined the frequency of auxotrophies, the induction of adaptive mutations, and resistance to various antibiotics. We are currently determining the nature of the mutations involved in antibiotic resistance and the induction of genes typical of the persistence state.

The definition of the mechanisms of induction of the persistence response by pesticides is complex since their structures and mechanisms of action differ. Still, they have in common the induction of oxidative stress, for which we propose the presence of reactive free radicals as the inducer of the response. This proposal is supported by the fact that salicylate is an inducer of both persistence and free oxygen radicals (Dunlop *et al.*, 2017).

This work was supported by the program UNAM-DGAPA-PAPIIT IN204021. The author X.O.R-R is a graduate student at Posgrado en Ciencias de la Producción y Salud Animal in Universidad Nacional Autónoma de México (UNAM) and received the CONACyT fellowship 784236.

Leibler, S., et al., 2005. Bacterial Persistence: a model of survival in changing environments. Genetics. 169(4):1807–1814. doi: 10.1534/genetics.104.035352

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REGULATION OF BACTERIAL VIRULENCE BY SATURATED FATTY ACIDS

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Abstract:

Lipids are the essential biomolecules for life, so their chemical diversity and biological functions have been widely studied. Specifically, fatty acids (FA) are lipids that form a structural part of cells, perform energy storage functions, and act as signal-transducing molecules. Bacteria and archaea are social microorganisms that communicate by *quorum* sensing (QS) to perform various functions.

QS is a complex phenomenon designed to promote the multicellular behavior of unicellular organisms, in which there is coordination at the population level in time and space for the expression of specific phenotypes. The property of FAs as signaling molecules has been recently studied, and their role as communication molecules in various biological and ecological phenomena has been explored (Cortes-López *et al*., 2020).

Currently, there is evidence that FA plays an essential role in controlling biological functions, such as virulence and the production of pigments and proteins, as well as resistance to antibiotics. In this field, saturated FAs have gained notoriety for their role as autoinducers and anti-virulence molecules (Juárez-Rodríguez *et al*., 2021). In such a way, the ecological implications of these discoveries are not yet fully understood, but we are convinced that they will significantly impact the way we understand the role of lipids.

Cortes-López et al (2020). Old acquaintances in a new role: regulation of bacterial communication systems by fatty acids. CRC Press/Taylor & Francis. Pag:47-57. https://doi.org/10.1201/9780429274817.

Juárez-Rodríguez M. et al. (2021). Front. Cell. Infect. Microbiol. (10):879-891. doi: 10.3389/fcimb.2020.597517.

PLASMID DYNAMICS: FROM SINGLE-CELLS TO MICROBIAL COMMUNITIES

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Abstract:

Plasmids are extrachromosomal genetic elements that encode a wide variety of phenotypes and can be maintained in bacterial populations through vertical and horizontal transmission, thus increasing bacterial adaptation to hostile environmental conditions such as those imposed by antimicrobial substances. But a large number of plasmids lack the molecular machinery to stabilize or transfer horizontally through conjugation. In principle, such plasmids would be destined to be lost by segregation in the absence of positive selection, yet small plasmids are ubiquitous in nature. This observation has highlighted the need to develop a more inclusive understanding of the evolutionary benefits that multicopy plasmids provide to their bacterial hosts. In this talk, we will combine mathematical models with single-cell microfluidics and evolutionary experiments to investigate the role plasmids play in the evolution of antibiotic resistance in dynamic environments.

PLANT-BACTERIAL INTERACTIONS AT THE ROOT, FOSTERING GOOD RELATIONSHIPS BY METACOMMUNITY LESSONS

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Abstract:

Bacterial interactions with their host's relevance are out of the question nowadays. Hosts and bacteria are intricate by complex relationships that directly affect the fitness of both participants. Multiple ecological interactions (*e.g.,* mutualism, neutralism, competition) shape the outcome of the relationship. We described and analyzed bacterial diversity from soil and plant roots (rhizosphere and endosphere) of selected plants by shotgun metagenomics and 16S rRNA gene sequencing. We have learned that cultivated, managed plants show lower diversity than wild plants in the same soil substrate [1]. We have successfully transplanted *in situ* microbiomes into greenhouse experiments, conserving the main taxa and genes responsible for plant interactions. The transplanted strategy grants tools to study local bacterial community adaptations and introduce them into non-adapted plants and soil. We tested the concept using historically arid agricultural land microbes, with selection for microbes capable of thriving under dry conditions and establishing successful plant interactions. Contrasting the arid microbiome to humid controls, we identified 199 bacterial genera exclusively found in dry lands and roots of squash plants (*Cucurbita pepo* L.) [2]. Additionally, 2,969 core metagenomic proteins shared no matter conditions for the squash, with an additional set of 924 proteins only found in dry conditions. By plant phenotyping, we correlated bacterial community profiles with plant growth variables. Our work opens ex-situ microbiome conservation and management avenues while highlighting taxa differences and coding genes related to arid adaptations.

Barajas, H. R., *et al*. (2020). Testing the Two-Step Model of Plant Root Microbiome Acquisition Under Multiple Plant Species and Soil Sources. Frontiers in Microbiology, 11, 2445. https://doi.org/10.3389/fmicb.2020.542742

Hernández-Álvarez, C., et al. (2022). Squash root microbiome transplants and metagenomic inspection for in situ arid adaptations. Science of the Total Environment, 805, 150136. https://doi.org/10.1016/j.scitotenv.2021.15013

PUBLIC GOODS EXPLOITATION IN *PSEUDOMONAS AERUGINOSA*

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Abstract:

Pseudomonas aeruginosa is an opportunistic bacterial pathogen that causes difficult to treat local and systemic infections, due its intrinsic tolerance to antibiotics and the production of several virulence factors. Among them diverse exoproteases able to cleave proteins of the connective tissue, such as elastin and collagen, immunoglobulins, iron carrier proteins, etc. and siderophores such as pyoverdine that deliver iron to the bacteria. Due their extracellular action, both exoproteases and siderophores are public goods since they can be utilized by either bacteria that produce them (cooperators) and by non-producers that are considered as social cheaters [1].

In conditions in which the utilization of either exoproteases or siderophores is essential for growth such as media with protein as sole carbon source or media with low iron concentrations, mutants that do not produce them are selected and their proportion in the population increases, sometimes reaching high frequencies that avoid the population growth since cooperators are not longer able to produce enough public goods [1].

Although several works about the exploitation dynamics of public goods in *P. aeruginosa* exists most of them are made with domesticated reference strains such as PA01 and PA14 and using mediums that do not specifically select for non-siderophore producers [2]. In my talk I will show results that deviate from the current models when environmental and clinical strains are used and with media that specifically select non-siderophore producers.

References: 1. Smith P, Schuster M. Public goods and cheating in microbes. 2019.
2. Tostado-Islas O, Mendoza-Ortiz A, Ramírez-García G, Cabrera-Takane ID, Loarca D, Pérez-González C, *et al*. Iron limitation by transferrin promotes simultaneous cheating of pyoverdine and exoprotease in Pseudomonas aeruginosa. ISME J 2021.

FROM BETAGLYCAN TO TGFBR3L: DECIPHERING MECHANISMS OF INHIBIN ACTION

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Abstract:

Reproductive cycles are controlled by hormones from the brain, pituitary gland, and the gonads (ovaries and testes). Gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the synthesis of the gonadotropin hormones, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), from pituitary gonadotrope cells. FSH and LH work in concert on the gonads to regulate gametogenesis and steroidogenesis. The steroids feedback to the brain and pituitary to regulate their own synthesis by inhibiting GnRH, FSH, and LH secretion. The gonads also produce a second class of hormones called the inhibins, which feedback to gonadotrope cells to selectively suppress FSH production. Inhibins are heterodimeric members of the transforming growth factor β (TGFβ) superfamily composed of the inhibin α subunit disulfide linked to the inhibin β*A* or βB subunit to form, respectively, inhibin *A* or B. The inhibin β subunits can homo- or hetero-dimerize to produce the activins (*A*, B, or *A*B), which selectively stimulate FSH synthesis. *A*ccording to current dogma, pituitary gonadotrope cells make activin B, which stimulates FSH in an autocrine or paracrine manner. *A*ctivins bind to activin type II receptors, which then recruit and transphosphorylate activin type I receptors. The activated type I receptors then phosphorylate SM*A*D3, which partners with SM*A*D4 and forkhead box L2 (FOXL2) to drive transcription of the FSHβ subunit gene. Inhibins, in contrast, function as competitive antagonists, binding to activin type II receptors, thereby blocking activin action. Inhibin binding affinity or avidity for activin type II receptors is increased by a co-receptor, betaglycan (also known as the TGFβ type III receptor or TGFBR3). However, when we knocked out betaglycan in gonadotrope cells of mice, inhibin *A*, but not inhibin B antagonism of FSH synthesis was impaired. This suggested that inhibin B might use an alternative co-receptor in gonadotropes. In this lecture, I will discuss our discovery of a novel protein, TGFBR3L, which is exclusively expressed in gonadotrope cells and binds inhibin B, but not inhibin *A*, with high affinity. Loss of Tgfbr3l function leads to increases in FSH levels and litter sizes in female mice. These data suggest that TGFBR3L may be a novel target to regulate fertility.

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SENSITIZATION OF CELLS TO TGF-β BY THE CO-RECEPTOR BETAGLYCAN: STRUCTURE AND MECHANISM

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Abstract:

The TGF-b co-receptor betaglycan (BG) sensitizes cells to the TGF-βs, especially TGF-β2 which binds TbRII weakly. To gain greater insight into the mechanism by which BG potentiates assembly of the signaling complex with TbRI and TbRII, we determined the structure of the BG ectodomain bound to TGF-b using a combination of single-particle Cryo-EM and X-ray crystallography. To do this, the structure of the two component binding domains, BGO and BGZP-C, bound to TGF-b were determined using either Cryo-EM and crystallography or crystallography alone. To ensure that inferences about binding in the context of full-length betaglycan were correct, we also determined, at lower resolution, the structure of the full-length BG ectodomain bound to TGF-b2 using Cryo-EM. To investigate the mechanism, assembly was studied on vesicles using FRET with fluorescently labeled TGF-bs and fluorescently labeled receptors tethered to the vesicles. The Cryo-EM and X-ray structures show that BGO straddles finger 4 of the TGF-β dimer, embracing it with its two β-sandwich domains, without interfering with binding of the adjacent TβRII. The orphan domain extends from the finger 4 towards the center of the TGF-b homodimer, precluding binding of a second molecule of the orphan domain, as well as TbRI. BGZP-C binds to the underside of the TGF-b fingers using the surface of its IgG-like domain in the region adjacent to the FG loop. It blocks binding of both TbRII and TbRI and its FG loop folds into an a-helix, which binds the heel helix of the opposing monomer. The assembly assay shows that in the presence of BG, TGF-b2 and TGF-b3 rapidly bind TbRI and TbRII and partially displace BG. TbRI and TbRII can fully displace BG from TGF-b2 and TGF-b3, but this occurs slowly, especially with TGF-b2. Thus, consistent with the proposed mechanism, BG likely functions by capturing TGF-bs on the membrane, thereby promoting binding of TbRII by increasing the local ligand concentration and by lowering the entropic barrier to complex formation. TbRI is rapidly recruited to the complex, leading to the partial, but not complete displacement of BG. In ongoing investigations, we seek to determine if the complex with partially displaced BG can signal – we are also interested in determining which sub-domain remains bound and if further recruitment of TbRI and full displacement of BG might further potentiate signaling.

Support: This project has received funding from the NIH (GM58670 to APH) and the European Union's Marie Sklodowska-Curie Horizon 2020 research and Innovation Programme (Grant agreement No 893196 to LW).

BETAGLYCAN'S MYSTERIOUS *IN VIVO* AFFAIRS

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Abstract:

It has been 30 years since the cloning of the co-receptor Betaglycan (BG), also known as the type 3 TGF-β receptor (TGFBR3). Although we have a good understanding of many of BG biochemical properties, including its structure and interactions with its ligands and signaling receptors, its *in vivo* functions remain a puzzle. We are still far from accounting how BG many *in vitro* functions impact in the physiology and development of the living organisms.

In this talk we will discuss TGFBR3 gene knock-down (KD) and knock-out (KO) experiments in zebrafish, which have given contrasting results, from embryonic lethality (as in the mouse) to mild non-lethal phenotypes. The BG null zebrafish embryos exhibit a delay in mineralization of the chordocentra, the vertebrae primordium, a process that is partially mediated by TGF-β. We believe that this phenotype is the first *in vivo* example of the BG ligand presentation function amply described *in vitro*. To explain the discrepancy between KD and KO phenotypes we have explored the possibility of a genetic compensation of BG by Endoglin, its highly related co-receptor. Finally, in order to gain insights into what other *in vivo* roles may be played by TGFBR3, we have used immune-histochemistry and the expression of a fluorescent reporter under the control of zebrafish TGFBR3 gene promoter to determine the embryonic patterns of BG gene expression.

Work at F.L.-C.'s lab is supported by grants 254046 (Conacyt) and IN204916 (PAPIIT-UNAM).

ABSTRACTS | Simultaneous Oral

XXXIII National Congress of Biochemistry

STRESS-ASSOCIATED AND GROWTH-DEPENDENT MUTAGENESIS IS DIVERGENTLY REGULATED BY C-DI-AMP LEVELS IN BACILLUS SUBTILIS

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Abstract:

Bacteria have evolved signaling strategies that employ second messengers to rapidly respond to internal and external changes that they encounter in highly competitive environments; among these, the cyclic dinucleotide c-di-AMP has been found to regulate a diversity of physiological processes, mainly in Gram-positive bacteria. However, only a few effectors of this messenger have been identified and characterized to date. Bacillus subtilis relies on three di-Adenylate Cyclases (DACs) to synthesize c-di-AMP, CdaA and DisA, which are synthesized during vegetative growth and CdaS that is involved in spore/germination outgrowth. To escape from growth-limiting conditions, during the post-exponential phase of growth, B. subtilis activates mechanisms that promote genetic variability. This process has been termed stress-associated mutagenesis (SAM) and takes place in non-dividing bacteria when cells are subjected to a nonlethal selective pressure.

Previous results from a proteomic study demonstrated a relationship between nutritional stress and deregulation of DACs and other proteins that degrade or interact with c-di-AMP, suggesting a possible role of this second messenger in B. subtilis SAM. Likewise, a relationship between levels of c-di-AMP and cell survival to DNA damaging agents was found, suggesting a role in DNA repair. Here, we investigated a possible role of c-di-AMP in SAM and growth-associated mutagenesis (GAM). Our results show that in growing cells of B. subtilis YB955 (hisC952, metB25 and leuC427), CdaA and DisA counteract spontaneous and mitomycin-C-induced mutations, while a divergent effect of these DACs is observed in hydrogen peroxide-induced mutagenesis. In contrast, during B. subtilis SAM, DACs are required to promote mutations that allow to escape nutritional stress. These results correlate with intracellular levels of c-di-AMP, which are significantly lower in cdaA and disA deficient strains. The reintegration of functional copies of genes cdaA and/or disA corroborated the observed effects on SAM and GAM. Taken together, these results reveal a novel role for c-di-AMP in DNA repair and generation of genetic diversity in growth-limiting conditions in B. subtilis. Finally, we postulate that this novel function of c-di-AMP can be exerted through proteins that share binding domains for this messenger and play roles in ion transport, transcriptional regulation, as well as oxidative stress protection.

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FUNCTIONAL CYT1AA IS NECESSARY TO SYNERGIZE BIN TOXIN AGAINST BIN-RESISTANT LARVAE

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Abstract:

Toxicity *in vivo* assays showed that the association of *Lysinibacillus sphaericus* (Lsp) Bin toxin with *Bacillus thuringiensis* subsp. *israelensis* (Bti) Cyt1Aa toxin is effective against *Culex quinquefasciatus* resistant to Bin toxin or to *Aedes aegypti* that is naturally refractory to Bin. It is known that Cyt1Aa synergize Cry4 and Cry11 toxins from Bti, by acting as additional receptor. However, the synergistic mechanism between Bin and Cyt1Aa toxins remains unknown. This study aimed to define the mechanism of synergism between Bin and Cyt1Aa toxins against Bin-resistant larvae. For this analysis, we performed bioassays to evaluate the toxicity of mixtures of Bin and Cyt1Aa toxins against resistant larvae, protein interaction assays, and localization of these toxins in the midgut cells using fluorescent labelled proteins and confocal microscopy. In order to evaluate if the Cyt1Aa toxin also acts as a receptor to the Bin toxin, we analyzed the binding-interaction between these toxins by ELISA binding assays showing that these proteins do not interact with each other, indicating that the Cyt1Aa does not act as a receptor of the Bin toxin. In addition, we analyzed if the pore formation activity of Cyt1Aa is necessary for the synergism between these toxins by using a non-toxic Cyt1AaU122E mutant affected in oligomerization and pore formation. The bioassays with mixtures of the different toxins showed that Bin-resistant larvae were susceptible to the combination of Bin and Cyt1Aa but not to the mixture of Bin with the mutant Cyt1AaU122E indicating that pore formation activity of Cyt1Aa is necessary for the synergism with Bin toxin. The analysis of localization in the midgut tissue revealed that the internalization of Bin toxin in the midgut cells of Bin-resistant larvae occurred in the presence of Cyt1Aa but not in the presence of Cyt1AaU122E mutant. These data show that the synergism mechanism between Bin and Cyt1Aa toxins is different from Cyt1Aa with Cry toxins, suggesting that Cyt1Aa synergize Bin toxicity by facilitating its cell internalization through pore formation activity. Our study established the molecular basis of the synergy between Bin and Cyt1Aa, and these findings enlarge our knowledge of their mode of action, which could help to develop improved strategies to cope with insect resistance.

SYMMETRY IS MORE AN ANTIOXIDANT THAN AN EUGLYCEMIC ADVANTAGE

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Abstract:

Thiazolidinediones (TZDs) normalize glucose levels by activating PPARγ in organisms with type 2 diabetes. For this work, 219 new derivatives of TZDs were analyzed in silico and only one candidate was selected for synthesis. This compound called 1G was evaluated for acute oral toxicity in female rats and for control of diabetes-related parameters in a rat model of streptozotocin-induced diabetes. The best compound was chosen considering in silico predictions on pharmacokinetic, pharmacodynamic, and toxicological parameters. Compound 1G was synthesized by a quick and easy Knoevenagel condensation, and the acute oral toxicity was found at a dose greater than 2000 mg/Kg. It apparently produces metabolic effects similar to those of pioglitazone, decreasing glycaemia and triglyceride levels in diabetic animals, without liver damage. Moreover, it did not cause a significant weight gain and tended to reduce polydipsia and polyphagia, while diminishing systemic inflammation related to TNF-α and IL-6. It lowered the level of endogenous antioxidant molecules such as reduced glutathione and glutathione reductase. In conclusion, 1G may be a candidate for further testing as an euglycemic agent capable of preventing inflammation, oxidative stress, and the complications of diabetes.
Álvarez-Almazán S, Navarrete-Vázquez G, Padilla-Martínez II, et al. A new symmetrical thiazolidinedione derivative: In silico design, synthesis, and in vivo evaluation on a streptozotocin-induced rat model of diabetes. Processes. (2021). 9,1294:1-30. DOI: 10.3390/pr9081294.

EXPRESSION OF CB1 RECEPTORS ON AORTIC RINGS IS DECREASED IN ATHEROSCLEROSIS BUT ITS ACTIVATION WITH ACEA CAUSES VASORELAXATION

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Abstract:

Introduction: It has been suggested that dysregulation of the endocannabinoid system is involved in the pathophysiology of atherosclerosis. Some studies have associated the activation of CB1 receptors (CB1R) to an increased atherogenic effect. However, there are no studies that demonstrate the relationship between CB1R with the progression of atherosclerosis and functional alterations of the cardiovascular system. The aim of this study was to determine the correlation between the expression of CB1R with vascular tone and blood pressure in the atherosclerosis progress.

Methodology: Atherosclerosis in rats was induced by treatment for 30 (mild lesions) or 60 days (severe lesions) with an atherogenic "paigen" type diet. CB1R expression and localization in aortic rings was evaluated by immunohistochemical staining and confocal microscopy. Also, the role of CB1R on vascular tension was determined in isometric tension recordings using ACEA (CB1R agonist). Blood pressure (BP) was monitored using a sphygmomanometric method, for 90 min after intravenous administration of ACEA. The data were analyzed by one-way ANOVA and showed as mean ± SEM (n = 8).

Results: CB1R expression in smooth muscle of rat aorta decreased in severe lesions compared with control (0.61 ± 0.07 vs 1 UA, $p < 0.0001$). Moreover, CB1R activation elicited vasorelaxation in aortic rings with mild (82.55 ± 2.40 %; $p = 0.0007$) and severe lesions (85.52 ± 3.31 %; $p = 0.0024$). BP in mild and severe lesions was not modified. Conclusions: Expression of CB1R decreased in severe lesions causing vasorelaxation in aortic rings. This is not associated with changes in BP. However, in mild lesions, results suggest the presence of underlying regulatory mechanisms.

PROTEOME OF *AGAVE ANGUSTIFOLIA* HAW.: INSIGHTS ABOUT AMINO ACIDS METABOLISM IN ALBINO PLANTLETS

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Amino acids (aa) are essential molecules for life because are precursors for the synthesis of proteins and other organic compounds. Their metabolism in plants involves more than one cellular compartment, among which the chloroplast plays a key role. From the 20 essential aa, ten (Arg, Lys, Thr, Leu, Ile, Val, Trp, Phe, Tyr and His) are only synthesized in the plastids and seven (Asp, Cys, Gln, Glu, Gly, Ser and Met) can be synthesized in both chloroplast and other parts of the cell. Despite knowing the roles of aa in plant physiology, little has been assessed in plants with albino phenotypes, lacking chloroplasts. In order to know the impact of the disturbing in chloroplast biogenesis on aa metabolism in albino and variegated somaclonal variants of *Agave angustifolia* Haw., the quantification of the 20 essential aa was carried out in addition to a quantitative proteomic strategy to determine the status of aa biosynthetic pathways. A total of 2,442 different proteins were identified in the proteome of the somaclonal variants, of which 80 correspond to enzymes participating in aa biosynthesis. From these 80, 32 proteins were differentially accumulated (DAPs). On the other hand, the concentration of 16 and 12 of the aa synthesized by the chloroplast were high accumulated in the variegated and albino somaclonal variant, respectively. Surprisingly, our results reveal that in plantlets that lack functional chloroplasts, there is an intense accumulation of aa and key enzymes of the aa biosynthetic pathways in comparison with green plantlets.

RED AMARANTH (*AMARANTHUS CRUENTUS* L.) AS A PROMISING SOURCE OF BETALAINS: AN APPROACH OF METABOLOMIC PROFILE BY UHPLC-MS/MS ORBITRAP

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Amaranth expresses many stunning colors ranging from yellows to reds and violet. This exquisite color spectrum caught the attention of the human in pre-Hispanic times, and different cultures integrated this crop into it is cosmovision as sacred food to deities. Nowadays, the amaranth is a "superfood" because of its health benefits related to nutritional composition and phytochemical content. Regarding phytochemical content, *Amaranthus cruentus* L. is characterized by having large bright red inflorescences rich in betalains, that provide multiple health benefits such as antioxidant, anticancer, hypocholesterolemic, and antibacterial properties.

Betalains have been of particular interest in the food industry, which has been looking for new natural colorants in the last two decades, consequently, to satisfy a demand for more natural products in the food. Today, betanin, the primary pigment source of *Beta vulgaris* L , is the only natural red pigment approved by the Food Drugs Administration and European Union. Therefore, it is promising and exciting to study a new source of betalains as natural colorants with commercial interest; accordingly, our research group has decided to focus on the Amaranthaceae family as a new supply of these pigments.

Regarding to amaranth new betalains investigation, we are using UHPLC-MS/MS with Orbitrap analyzer in order to study the inflorescences of *A. cruentus*, which have a dominant influence on red-violet color. Now, we have studied three varieties of this species and it has been found so far more than 60 betacyanins, betacyanins derivatives, and betaxhantins unreported in literature and new to science.

Amaranthine and isoamaranthine were the most representative compounds when analyzed the betalain profile of *A. cruentus*, followed by betanin, isobetanin, gomphrenin I, and isogomphrenin I, responsible for providing the red-violet color. However, we have found a high concentration of betacyanin derivatives compounds resulted from decarboxylation and dehydrogenation reactions of amaranthine, which are red and more stable than betacyanins. Therefore, these molecules are particularly interesting and should continue be studied by using biochemical and biotechnology applications.

We obtained highly accurate mass measurements and clearly distinguishable between similar chemical structures by conducting High-resolution mass spectrometry (HRMS). Then, it is possible to identify new compounds through de

novo elucidation method, with HRMS when it is combined the HRMS analysis and a sample preparation technique such as Matrix Solid-phase extraction. Now our working team is focused on developing a Mass Spectrometry database of betalains. We include the ion molecular in high-resolution (< 5 ppm), and the ion fragments to establish the mass fingerprint profile for betalains, to find new betalains within Caryophyllales, where they are chemotaxonomic markers.

Finally, since *Amaranthus cruentus* count with big red-violet inflorescences, rich in amaranthine, they can be biotechnologically exploited as a new natural colorant in the food.

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PROLACTIN REGULATES H3K9AC AND H3K9ME2 EPIGENETIC MARKS AND MIRNAS EXPRESSION IN BOVINE MAMMARY EPITHELIAL CELLS DURING *STAPHYLOCOCCUS AUREUS* INFECTION

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Abstract:

Epigenetic mechanisms are essential in the regulation of immune response during infections. Changes in the levels of reproductive hormones, such as prolactin, compromise the mammary gland innate immune response (IIR); however, its effect on epigenetic marks is poorly known. This work explored the epigenetic regulation induced by bovine prolactin (bPRL) on bovine mammary epithelial cells (bMECs) during *Staphylococcus aureus* infection. We determined that the H3K9ac mark decreased (~20%) in bMECs treated with bPRL (12 h, 5 ng/ml) and infected with *S. aureus*, while the H3K9me2 mark was increased (~50%) in the same conditions. Also, this result coincided with an increase (~2.3-fold) in HDAC activity. Moreover, the H3K9ac mark was enriched in the promoter region of IL-1b, IL-10, and BNBD10 genes (~1.5, ~2.5, ~7.5-fold, respectively) in bMECs treated with bPRL, but in bMECs infected was reduced. Likewise, the H3K9me2 mark was enriched in the promoter region of IL-1b and IL-10 genes (~3.5, ~2.5-fold, respectively) in bMECs infected but was inhibited by bPRL. Additionally, the expression of the miRNAs Let-7a-5p, miR-21a, miR-30b, miR-155, and miR-7863 was up-regulated (~2.5, ~1, ~10, ~1.5, ~3.5-fold, respectively) in bMECs infected; however, bPRL induced a down-regulation in the expression of these miRNAs. In conclusion, bPRL induces epigenetic regulation on IIR elements allowing S. aureus to succeed in both persistence and evasion of the host immune response.

CORTACTIN DEFICIENCY INDUCES PANCREATIC EPITHELIAL IMPAIRMENT

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Abstract:

Cortactin is a multifaceted actin-binding protein containing several domains allowing for interaction with other proteins, thus enabling cortactin to fulfill essential roles in diverse actin-related cellular processes, including adhesion and migration. Moreover, homeostasis maintenance of the intestinal barrier is regulated by cortactin; since in cortactin-KO mice, the colon epithelial permeability is increased and the expression and localization of intercellular junctions (IJ) proteins is altered. However, it remains unknown whether absence of cortactin also damages other epithelia, such as pancreas. Therefore, the aim of this work is to analyze the effect of cortactin deficiency on pancreatic IJs proteins of cortactin-KO mice, as well as on the epithelial permeability of a cortactin-depleted ductal pancreatic cell line.

Histologically, the pancreas of KO-mice looks apparently normal, compared with those from WT animals. However, western blot and immunofluorescence analyses of pancreatic tissue revealed that cortactin-deficiency provoked a decrease of filamentous actin, and reduced expression of the IJ proteins (occludin, claudin-1 and ZO-1). Moreover, these proteins relocalized from cellular borders to the cytosol, in the cortactin absence. By contrast, only a slight decrease of E-cadherin was detected, with similar location in WT and KO tissues. To investigate the effect of cortactin on pancreatic epithelial permeability, cortactin-depleted (cortactin-KD) BxPC-3 cells were generated using shRNA and their transepithelial electrical resistance (TEER) was monitored. Cortactin-KD cells exhibited 45% lower TEER than control cells. Accordingly, ICJs proteins were also less expressed and mis-localized.

In conclusion, our results demonstrate that in pancreas, cortactin also participates in the regulation of a proper IJ architecture and epithelial permeability. Thus, cortactin seems to be a critical regulator of epithelial homeostasis in many organs.

FUNCTIONAL HETEROLOGOUS ANALYSIS OF ALLELIC VARIANTS OF HUMAN GENES POTENTIALLY DRIVEN BY NATURAL SELECTION

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Abstract:

The best examples of recent natural selection events in human populations have been discovered in candidate gene studies in which there was a prior selection hypothesis. In addition, genetic variation maps to detect selection signatures in the genome have only been made for current, modern populations1,2. Here, we hypothesize that a global comparative genomic study of ancestral and modern populations will reveal selection signatures in the human genome in an unbiased manner, leading to identifying novel genes under the context of evolutionary adaptation. To this end, we established two populations: the first consisting of 8 hunter-gatherer ancient individuals and the second of current humans from the 1,000 Genomes Project. These populations were compared in nucleotide diversity and in changes of allelic frequencies over time. We found that most of the regions with allelic variations between the compared populations are within the non-coding regions, suggesting that allelic changes occur more frequently in regulatory regions. In addition, single nucleotide polymorphisms were identified in coding regions, with potential for directional selection. To evaluate the functional impact of these changes potentially driven by selection, we propose a model of heterologous expression in S. cerevisiae; this eukaryotic model has been shown to be useful for detecting functional differences between human alleles in protein-coding genes3,4. We will present the comparative phenotypic impacts of candidate variants in genes like the glucose-6-phosphate dehydrogenase (G6PD) and the adenylate kinase 2 (AK2) in “humanized” yeast cells bearing modern and ancestral variants of these genes. Our study sheds light in the functional impacts of genetic changes shaped by selection in recent human history.

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DEVELOPED A PORCINE DELTACORONAVIRUS RECOMBINANT MEMBRANE PROTEIN (RM-PDCOV) WITH POTENTIAL USE IN AN INDIRECT INMUNOENZIMATIC ASSAY (IELISA) FOR DISEASE CONTROL AND PREVENTION

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Abstract:

Porcine Deltacoronavirus (PDCoV) is an enveloped +ssRNA virus that causes acute diarrhea, vomiting, dehydration, and mortality in neonatal piglets. PDCoV was first reported in the US in 2014, co-infecting with porcine epidemic diarrhea virus (PEDV). Therefore, rapid diagnostic tools are necessary for the early detection of infections. The genome size of PDCoV is 25 kb in length encoding for four structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N). M is the most abundant protein in the viral envelope. It is required for the viral assembly process and can induce the production of neutralizing antibodies. Thus, in this study, we cloned, expressed, and purified a PDCoV recombinant M protein (*r*M-PDCoV) with potential use in an indirect inmunoenzimatic assay (iELISA) for disease control and prevention. We obtained the consensus amino acid sequence from 134 sequences available in gene bank from China, USA, Laos, Vietnam, and the Philippines. The Phylogenetic ML tree analysis and the tridimensional model prediction indicate a high conservative level. Then, we obtained a synthetic M protein gene using the consensus nucleotide sequence from 134 sequences. The synthetic gene was cloned into the pETSUMO plasmid and was transformed into *E. coli* BL21 for protein expression. Then, we purify the *r*M-PDCoV using Ni-NTA agarose column with His-tag affinity. The purified protein was identified by a Western blot observing an expected weight signal of 37.7 kDa. To determine the antigenicity and immunogenicity of the rM-PDCoV, three experimental groups of eight BALBc mice 28 days old each were used. In group-2, mice were immunized with *r*M-PDCoV and ISCOM (immunostimulating complex). The mice analysis suggests that ISCOM enhances the *r*M-PDCoV immune response to generate. Finally, the rM-PDCoV was evaluated by iELISA using 62 sera from pig farms to obtain sensitivity and specificity values. Overall, the *r*M-PDCoV developed in this study is suitable to use in immunogenic diagnostic systems.

GENOMICS "MICROBIAL DARK MATTER" EXPLORATION FOR ANTIMICROBIAL DISCOVERY

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Abstract:

The urgent need for novel bioactive compounds is driven by the dramatic global increase in antimicrobial resistance (AMR), considered one of the top ten threats to world public health (WHO, 2021). Antimicrobial discovery is complicated by the lack of data to perform structure-function correlations, thus preventing rediscovery and/or compounds with low activity or high toxicity. Novel antimicrobial chemical classes or mechanisms have not been proposed over the last three decades. While classical research roadmaps can still provide short–term solutions, sustainable strategies to reduce costs and time-to-market are needed, all the while assuring novelty and reduced resistance. Among them, genomic data mining is a field with enormous potential for rapid screening and encountering leads to modern antimicrobial discovery. Some of the advantages of data mining are the ability to predict chemical structures from sequence data, the anticipation of the presence of novel metabolites, the understanding of gene evolution, and the corroboration of data from multiple omics technologies. Based on public gene sequence mining platforms and in silico studies of protein evolution, MicroIQ has predicted that several completely unexplored biosynthetic gene clusters (BGCs) could be extremely interesting as sources of potentially bioactive molecules. The search has been directed by the following criteria: potential antimicrobial activity, new chemical classes and molecules, the absence of immunity (resistance) or virulence genes in or near the biosynthetic gene cluster, a general chemical class with evidence of low antimicrobial resistance and microorganisms of non-pathogenic origin. This strategy pinpointed clusters that produced lantipeptides, siderophores and non-ribosomal peptides. In addition, rationally designed synthetic peptides obtained through collaboration will help establish the baseline for predictions of other synthetic and semi-synthetic derivatives. These and similar molecules have never been characterized, originate from nonpathogenic bacteria of widely diverse origins, and appear to have evolved along the tree of life, indicating that they confer an evolutionary advantage. Confirmation of these predictions in the laboratory and publishing the structure-function correlations obtained will lay the foundation for the identification of novel BGCs and molecules and for the rational design of compounds to have better biological activities and/or less toxicity, finally contributing to limiting AMR in a sustainable way.

CONSERVATION ANALYSIS OF SEQUENCE-DIVERGENT LINCRNAS IN BRASSICACEAE

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Abstract:

In plants, several long intergenic non-coding RNAs (lincRNAs) are known to play important roles in development and stress responses. However, overall annotation and classification of plant lncRNAs is limited, and most lincRNAs lack an annotated biological function. Due to their lack of protein-coding capacity, lincRNAs typically display poor sequence conservation among even closely related species. LincRNAs with functions defined by structural or sequence-specific interactions with other molecules display higher levels of conservation over lincRNAs whose functions are based on proximity to other genes (*cis* regulation).

To identify divergent lincRNAs, we analyzed the conservation of lincRNAs by synteny, microhomology and structural prediction in Brassicaceae. We focused on 4354 lincRNA genes previously identified from >200 public *Arabidopsis thaliana* Col-0 ecotype RNA-seq datasets (Corona-Gomez, *et al*, 2022). Surprisingly, most lincRNA genes (~3400) were conserved by synteny and microhomology across the family. We also analyzed the expression patterns of these lincRNAs in shoot and root tissues of *Arabidopsis thaliana, Brassica rapa, Brassica oleracea, Capsella rubella* and *Thellungiella parvula*. We identified 77 conserved lincRNA genes expressed in both tissues, 7 exclusively expressed in shoots and 4 exclusively expressed in roots, while 1312 conserved lincRNA genes were not expressed in either of these tissues. When we supplemented our results with structural predictions, we obtained 4 lincRNA genes conserved by synteny, microhomology and structure with shoot-restricted and 4 with root-restricted expression.

Our findings provide the first in depth characterization of the evolutionary conservation of lincRNAs beyond sequence conservation in Brassicaceae family and provide new insights into the functions of lncRNAs in different tissues, as well as a set of candidate lncRNAs for future functional studies.

Corona-Gomez, *et al.* 2022. Transcriptome-guided annotation and functional classification of long non-coding RNAs in Arabidopsis thaliana. bioRxiv. doi: https://doi.org/10.1101/2022.04.18.488676

A METANALYSIS OF GENOMEWIDE AGING ASSAYS REVEALS THE CENTRAL MODULATORS OF CHRONOLOGICAL LIFESPAN IN BUDDING YEAST

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Abstract:

The budding yeast Saccharomyces cerevisiae has been widely used as a model to establish which genes and pathways underlie aging and lifespan modulation at the cellular level. Considerable effort has been devoted to carry out genome-wide lifespan assays with knockout mutants in this model organism. While this strategy has been successful in highlighting instances of genes and cellular processes as modulators of lifespan, there are still challenges on identifying cellular processes that consistently modify lifespan and could be appointed as key pathways in lifespan determination. For instance, a previous analysis of three genomewide chronological lifespan assays in yeast showed that there is little consensus across the mutants reported as influencing lifespan. To better understand which are the key modulators of lifespan in yeast, we conducted a computational analysis using 10 genomewide datasets available, which encompase the effects of knockout mutants across different experimental conditions. We thereby interrogate which genes robustly increase or decrease lifespan when disturbed and complemented this analysis with functional interaction networks to disclose the relationships among mutants identified and as a targeted approach to identify other candidate key modulators. We identified, respectively, 21 and 19 functional clusters associated to short and long-lived mutants; we propose these are the key, robust regulators of chronological lifespan in yeast. Unexpectedly, we found several members of the invasive growth/pheromone pathway to have a role on lifespan modulation, specifically on the long-lived phenotype association. To further elucidate on the mechanisms of lifespan modulation through this pathway, we carried out an epistasis lifespan assay with well-established downstream and upstream aging factors. Our study provides an integrated view of the core genetic landscape of lifespan modulation in budding yeast, shedding light into the systems-level mechanisms of aging.

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REPURPOSING OF METFORMIN AND SODIUM OXAMATE IN COMBINATION WITH DOXORUBICIN, REVELS INTRINSIC APOPTOSIS IN CERVICAL CANCER, *IN VITRO*

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Abstract:

Cervical cancer (CC) is a public health problem, being the second most frequent neoplasm in Mexico. CC is associated with human papillomavirus (HPV). The HPV genome is characterized by the presence of the E6 and E7 oncoproteins, which are necessary to maintain the tumor phenotype through the regulation of tumor cell metabolism known as the Warburg effect. Such effect consists of energy metabolism reprogramming to satisfy the concentration of glucose, glutamine, and oxygen to favor cell proliferation and growth. Therefore, being a therapeutic target of great potential. In this study, a therapeutic combination of two repositioned drugs (metformin and sodium oxamate) and the first-line drug, doxorubicin, name triple therapy, was used to inhibit tumor cell metabolism. Metformin (inhibitor of complex I of the electron transport chain), sodium oxamate (inhibitor of lactate dehydrogenase A (LDHA), and doxorubicin (inhibitor of topoisomerase II).

First, we determined the inhibitory concentration 50 of the drugs and combination. Then, we showed that triple therapy inhibited cell migration. Next, we observed that cells exposed to triple therapy revealed the detection of TUNEL, and thus the formation of micronuclei, small extranuclear bodies of chromatid fragments, DNA condensation at the periphery of the nuclear membrane, as well as loss of cell adhesion. We validated the induction of apoptosis by flow cytometry with Annexin V/propidium iodide markers, obtaining high percentages of cells in late apoptosis. Finally, we identified the proteins involved in apoptosis that undergo changes after triple therapy administration. We observed an increase in the detection of proteins such as BAD, BAX, caspase-3, cytochrome C, CD40-R, CD40-L, Fas-R, Fas-L, HTRA2, p21, p27, p53, XIAP, Survivin, HSP27, HSP60, HASP70, and SMAC.

In summary, our research provides new insights into the biological and antiproliferative activities of the combination with metformin, oxamate, and doxorubicin against CC, and may offer a promising therapeutic strategy through triggering the intrinsic pathway of apoptosis.

COMPLEMENT RECEPTOR 3 (CR3) IS ACTIVATED VIA AN INSIDE-OUT SIGNALLING PATHWAY TRIGGERED BY CD13 IN HUMAN MACROPHAGES

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Abstract:

The myelomonocytic marker CD13 (Aminopeptidase N) is considered as a moonlighting protein because of its multiple functions: viral receptor, aminopeptidase, phagocytic receptor, and adhesion molecule[1]. Complement Receptor 3 (CR3) is the most abundant β2 integrin in macrophages, it is also an adhesion molecule and a phagocytic receptor[2]. These proteins can be found together in lipid rafts in the membrane of myeloid cells, which suggests a functional link[3]. In addition, stimulating some phagocytic receptors triggers inside-out signalling cascades that induce an integrin to activate[4]. Therefore, due to their overlapping activities, physical proximity, and the fact that CD13 is a phagocytic receptor that mediates several functions, our rationale was that CD13 stimulation may be able to induce CR3 activation[5]. Thus, the objective of this work was to test this hypothesis and, if confirmed, to propose a sequential mechanistic model for the signalling pathway connecting both receptors. We tackled this task with a hybrid experimental-and-computational approach. Firstly, we confirmed that crosslinking CD13 with monoclonal antibodies induces the activation of CR3 in human monocyte-derived macrophages in a specific fashion. Secondly, using bioinformatic databases, we created a protein interaction network encompassing the closest functional partners of CD13, CR3 and Syk, a non-receptor tyrosine kinase key to signal transduction in myeloid cells. Finally, we proposed a sequential mechanistic model for the CD13-CR3 pathway based on our network and tested it experimentally. Hence, this time- and economy-saving interdisciplinary approach led us to uncover a new CD13-mediated function and to propose a plausible signalling pathway for it. These results have therapeutic potential since CD13 is overexpressed in many cancer types with enhanced metastatic properties, which in turn, could be related to CR3-mediated adhesion.

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TRANSCRIPTOME ANALYSIS OF THE SPIDER *PHONOTIMPUS PENNIMANI* REVEALS NOVEL TOXIN TRANSCRIPTS

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Abstract

Introduction: *Phonotimpus pennimani* (Araneae, Phrurolithidae) is a small-sized (3-5mm) spider endemic to the Tacaná volcano in Chiapas, Mexico, and was described for the first time in 2018 [1]. It is found in soil litter of cloud forests and coffee plantations. Its venom composition has so far not been investigated, partly because it is not a species of medical significance. However, it does have a significant impact on the arthropod populations of its natural habitat. **Methods:** Specimens were collected in Southeastern Mexico (Chiapas) and identified taxonomically by morphological characteristics. A partial sequence from the mitochondrial gene *coxI* was amplified. Sequencing on the Illumina platform of a transcriptome library constructed from 12 adult specimens revealed 25 toxin or toxin-like genes. Transcripts were validated (RT-qPCR) by assessing the differential expression of the toxin-like PpenTox1 transcript and normalising with housekeeping genes. **Results:** Analysis of the *coxI*-gene revealed a similarity to other species of the family Phrurolithidae. Transcriptome analysis also revealed similarity with venom components of species from the families Ctenidae, Lycosidae, and Sicariidae. Expression of the toxin-like PpenTox1 gene was different for each developmental stage (juvenile or adult) and also for both sexes (female or male). Additionally, a partial sequence was obtained for the toxin-like PpenTox1 from DNA. **Conclusion:** Data from the amplification of the mitochondrial *coxI* gene confirmed that *P. pennimani* belongs to the family Phrurolithidae. New genes and transcripts coding for venom components were identified.

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ADVANCING GLOBAL REGULATORY NETWORK INFERENCE: AN INTEGRATIVE FRAMEWORK

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Abstract:

Understanding gene regulation in bacteria through a holistic approach allows us to improve chemical production and unveil structural and evolution principles at system-level[1]. The reconstruction of experimentally-validated global regulatory networks is a highly resource-consuming approach. The computational inference is a still-going challenge that has been mainly addressed from the transcriptomics perspective, obtaining poor results. Network inference based on regulatory binding sites performs better but requires prior knowledge of the regulatory circuitry[2].

We collect current knowledge on bacterial regulation in Abasy Atlas to identify structural principles and conserved regulatory interactions[3]. Then, we extrapolate the information to closely-related organisms with state-of-the-art computational tools, obtaining substantially more promising results[2]. The pipeline is primarily based on the conservation of regulatory binding sites, with the optional application of transcriptomics and functional annotation data for the refinement and interpretation of the results.

Available programs for regulatory network inference require the user to perform multiple steps individually. Our goal is to integrate bioinformatics tools and databases of regulatory interactions, transcriptomics, and gene annotation to perform regulatory network inference from a single genome sequence. The framework also provides the opportunity to employ user algorithms in the pipeline. We use standard performance metrics, network topology, and comparative system-level architecture to assess the results[2].

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LITOPENAEUS VANNAMEI GLUTATHIONE PEROXIDASES 2 AND 4: RESPONSES AND MODULATION DURING HYPOXIA AND REOXYGENATION

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Abstract:

Glutathione peroxidases (GPx) are a large family of antioxidant proteins in most organisms. There are at least eight types of GPx in mammals; five of those are selenoproteins. Glutathione peroxidase 4 (GPx4) is the only GPx capable of reducing phospholipid hydroperoxides from membranes directly [1], and its depletion is lethal in mice [2]. However, there are very few studied invertebrates GPxs and little is known about their molecular responses to stress. The tumor suppressor protein p53, has recently been shown to regulate several antioxidant genes in mammals [3], and some studies suggest that similar mechanisms may regulate the antioxidant responses of invertebrates [4].

The white shrimp *Litopenaeus vannamei* is one of the most worldwide cultivated crustacean species. During their life cycle, this shrimp is subjected to environmental stress, including hypoxia (<2 mg O_2/L). To our knowledge, in this shrimp species, there is only one previous report of GPx. We characterized GPx4 of *L. vannamei* and evaluated the changes in gene expression during hypoxia and p53 knock-down at 1, 6, 24, and 48 h to study the responses to limited oxygen, as well as the role of p53. Furthermore, carbonylated protein content was evaluated as an indicator of oxidative damage. We found a unique GPx4 gene that produces five transcript variants and just two protein isoforms with distinct cellular localization. GPx4 expression changed significantly during short and long-term hypoxia, suggesting that it could be a responsive stress biomarker. Also, p53 knock-down decreased GPx4 expression, indicating that p53 regulates GPx4. Interestingly, carbonylated protein content in the hepatopancreas did not change in response to hypoxia but decreased in p53 knock-down shrimp.

To further study GPxs responses and regulation, we knocked-down GPx4 and evaluated GPx2 expression as well as total GPx and GPx4 enzymatic activity during hypoxia and reoxygenation at 0, 6 and 12 h. Usually, changes and regulation of these enzymes are analyzed separately, however, their relationships are still unclear. Intriguingly, GPx4 and GPx2 had similar changes in expression and surprisingly, GPx4 knock-down appears to induce a negative regulation of GPx2, contrasting to an expected positive compensatory outcome to maintain GPxs function. Although GPx total and GPx4 enzymatic activities were not affected by GPx4 knock-down, there were changes in response to reoxygenation. This study reveals new challenges and inquiries towards the elucidation of the mechanisms that regulate antioxidant responses during stress in crustaceans.

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COMPUTATIONAL, STRUCTURAL AND INHIBITORY STUDIES ON MOLECULAR INTERACTIONS OF THEPIRAB^{VP}TOXIN FROM *VIBRIO PARAHAEMOLYTICUS* WITH THEIR RECEPTOR ON EPITHELIAL CELLS OFSHRIMPHEPATOPANCREAS

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Abstract:

Vibrio parahaemolyticus toxin PirABvp is the major virulence factor exotoxin that contributes to the disruption of the hepatopancreatic epithelium in acute hepatopancreatic necrosis disease in shrimp. There are reports that the PirBvp subunit possesses lectin activity recognizing amino sugars. Also, has been reported that this damage it's through recognition of a specific sugars sequence of the glycoproteins on epithelial cells hepatopancreas. To explore possible sugar specific linked and effects, we performed in silico analysis, comparative structural and inhibitory studies on the A and B subunits with their receptor. Circular dichroism analysis showed highly disordered structures in the absence of octylglucoside, however, when octyl glucoside was used as a ligand to both subunits was observed that only the PirBvp coupled to the ligand and was structurally stable. When ligand-galactose binding assays were performed for the native tetrameric PirABvp complex, an increase in the thermostability of the complex was observed. This data suggest that its necessary a sugar, like galactose, for thermostability of pirABvp complex. In silico analyzes showed that different sugar structures recognizes specific domains of binding in the B subunit. The inhibition of the interaction was observed when were used complexes of sugars and antibodies to inhibits the binding of PirBvp subunit with the hepatopancreas lysate. Altogether, these results suggest the relevance of the interaction of PirBvp with the hepatopancreas in the pathogenesis of acute hepatopancreatic necrosis disease in shrimp.

NEUROENDOCRINE DIFFERENTIATION OF LUNG CANCER CELLS AND ITS EFFECT ON THE MICE IMMUNE SYSTEM

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Abstract:

Lung cancer has the highest mortality among all cancers worldwide. During lung adenocarcinoma development, cells can go through a process called neuroendocrine differentiation (NED), acquiring neural and endocrine properties that affect the tumor microenvironment by releasing specific factors. This phenotype correlates with an increase in metastasis and a lower survival rate of patients. The immune system gets rid of tumor cells through effector cells such as NK cells, monocytes, and lymphocytes, known as peripheral blood mononuclear cells (PBMCs). It was recently shown that the cytolytic capacity of a T-lymphocyte cell line decreases when confronted with differentiated neuroendocrine cancer cells in vitro; however, the cellular and molecular mechanisms involved in this response need to be elucidated. This work aimed to evaluate the effect of neuroendocrine differentiation of adenocarcinoma cells on the activity of mouse PBMCs.

To induce a neuroendocrine phenotype, A549 cells were treated with Forskolin (0.5 mM) and IBMX (0.5 mM) for 72 hours; differentiation was confirmed by identifying the presence of neurite-like projections and neural markers expression (CgA, NSE, and SYP). To evaluate the systemic effects of neuroendocrine differentiation, 10-12 week old male BALB/c mice were IP injected two times either with PBS (control), progenitor A549 cells, or neuroendocrine A549NED cells; 21 days after the first immunization mice were sacrificed, and changes in the profile of immune cells were determined by flow cytometry, as well as changes in the cytokine profile in serum by ELISA assays.

Our results showed that immunizing mice with A549 cancer cells increased the percentage of circulating monocytes. In contrast, injection with PBS or A549NED cells maintained monocyte levels at a basal state. In addition, the pro-inflammatory cytokines IL-2 and IFN-γ, and the anti-inflammatory cytokine IL-10 increased in mice immunized with progenitor A549 cells, suggesting the immune system's ability to mount a regulated response against adenocarcinoma cells, which was not observed in mice immunized with A549NED cells.

These results suggest that neuroendocrine differentiation in cancer cells impairs the proper activation of the immune system, partially contributing to the poor prognosis for patients affected by this pathology.

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BONE MICROENVIRONMENT-SUPPRESSED T CELLS INCREASE OSTEOCLAST FORMATION AND BONE METASTASES IN MICE

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Abstract:

Bone metastases are a highly debilitating complication in more than 70% of patients with advanced breast and prostate cancer, causing fractures, nerve compression, hypercalcemia. Currently approved treatments fail to cure bone metastases or increase patient survival. Immunotherapies activating T cells to fight cancer cells are changing cancer treatment, causing a durable response in some patients. However, it remains unclear whether immunotherapy could benefit patients with bone metastases. The bone microenvironment combines various immunosuppressive factors that could limit its efficacy. Also, T cells could increase bone resorption releasing pro-metastatic growth factors from the bone matrix that can increase cancer cell growth.

Using syngeneic mouse models, we found that bone metastases from 4T1 breast cancer cells contain tumor-infiltrating lymphocyte (TILs) and are increased in normal mice compared to immunodeficient and T-cell depleted mice (x3.6 and x1.6, respectively). This effect seemed caused by the TILs in bone, as T-cell depletion did not affect bone metastases from RM-1 prostate cancer cells that lack TILs and increased the volume of 4T1 orthotopic tumors. T cells from bone metastases expressed the pro-osteoclastic genes *Rankl* and *Tnfa*, and increased osteoclast formation *ex vivo* and *in vivo* at the tumor-bone interface, contributing to bone metastasis development. This pro-osteoclastic effect was specific to inactivated T cells, since activated T cells, secreting IFNɣ and IL-4, actually suppressed osteoclastogenesis, which could benefit patients. Consistently, most T cells in bone metastases were $CD69^-$ or $CD62L^-$. In addition, T cells from 4T1 bone metastases could not be activated in *ex vivo* cultures confirming the presence of immunosuppressive factors in this microenvironment. 4T1 bone metastases were associated with an increase of functional MDSCs, including monocytic-MDSCs that could differentiate to osteoclasts and were more potent T cell-inhibitors. While effective in other models, the PDE-5 inhibitor sildenafil and the bisphosphonate zoledronic acid did not affect the levels of MDSCs in bone metastases or their production of ROS and NO. Seeking other therapeutic targets, we found that 80% of monocytic-MDSCs are $PD\text{-}L1^+$ in bone, which could trigger T-cell suppression since 70% express its receptor, PD-1.

Collectively, our findings identified a new mechanism by which suppressed T cells increase osteoclastogenesis and bone metastases, and also provide a rationale for using immune checkpoint inhibitors since T-cell activation would increase their anti-cancer and their anti-osteoclastic properties.

TRANSCRIPTOMIC COMPOSITION OF VENOM GLANDS OF THE RECENTLY DESCRIBED MEXICAN SCORPION *CENTRUROIDES POSSANII*

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Abstract:

Scorpion venom has been the subject of studies in recent decades due to human deaths caused by poisoning. In the world, each year around one million cases of intoxication are reported and mortality ranges around 3,250 deaths. The scorpions that produce the toxins that most affect mammals are of medical importance and belong to the Buthidae family. In Mexico, the arachnids of this class are of the genus *Centruroides*. In particular, the toxins that act on sodium (Na^+) and potassium (K^+) ion channels are usually the most abundant in the venom and the most studied, since they actively participate during the poisoning process, triggering heart and respiratory failure, edema pulmonary, heart damage and others.

Investigations of protein components of the venom, which basically consist of their isolation and biochemical characterization, have also led to the discovery of their therapeutic and/or biotechnological potential. Thanks to the results of these investigations, today it is known and has been verified the antibacterial, anticancer, analgesic, antitumor, antiviral and insecticide capacity, to mention examples, of some venom proteins and peptides, as well as progress in understanding their receptors or targets of action. To do this, the methodology that has proven to be the most effective is New Generation Sequencing (NGS), which allows a greater number of transcripts to be obtained with a smaller amount of sample and in less time, thus facilitating the identification of more and new components.

The results that we want to share in this National Congress of Biochemistry 2022 consist of the analysis of the Transcriptome of the secretory gland and the venom of the recently reported scorpion *Centruroides possanii*, from the state of Colima, Mexico, in which, up to now, have been found the largest number of transcripts encoding peptides and venom proteins, among all scorpion species, adding a total of 239.

The most abundant components are toxins that act on ion channels (114 transcripts), followed by the category “Other components” with unknown function (62) and enzymes (40). These results suggest, on the one hand, a high toxicity of the venom due to the large number of toxins identified and, on the other hand, they reinforce the need to continue biochemically characterizing the components without annotation, since they represent a wide repertoire of application possibilities.

FUNCTIONAL ANALYSIS OF CSE-8: A HYPOTHETICAL ENDOPLASMIC RETICULUM PROTEIN, CHAPERONE OF CHITIN SYNTHASES IN *NEUROSPORA CRASSA*

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Abstract:

The cell wall of filamentous fungi and yeasts is mainly composed of chitin and glucans. Chitin, although not a major component of the cell wall, is responsible for plasticity and preservation of cell integrity. Chitin synthesis in fungi is carried out by chitin synthases (CHS). The mechanisms involved in CHS biogenesis and trafficking remain largely unknown. In *Saccharomyces cerevisiae*, Chs7p has been identified as CHS chaperone, and it is required for the exit of class 4 chitin synthases from the endoplasmic reticulum (ER). In Neurospora crassa, two proteins orthologous to S. cerevisiae Chs7p were identified: CSE-7 and CSE-8. CSE-7 was characterized as having a key role in the secretion and biogenesis of the class 4 chitin synthase CHS-41. The purpose of this work is the characterization of the hypothetical protein CSE-8 (NCU01814). Δcse-8 strains exhibit a slower growth profile, hyper-branched and wavy hyphae compared to wild-type strains. Furthermore, CSE-8 presumably has an interaction with chitin synthase 5 (CHS-5) of N. crassa, since arrival of CHS-5-GFP at septa and Spitzenkörper is abolished in Δcse-8 strains. Additionally, genetic crosses of Δcse-8 mycelium give rise to few or no mature perithecia, which could indicate the importance of this protein in sexual reproduction processes and its joint activity with class 5 chitin synthases. The results obtained so far suggest the involvement of CSE-8 in the biogenesis and trafficking of chitin synthase 5, which contributes to expand our knowledge about the chitosome secretion machinery in filamentous fungi.

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ABF1 PARTICIPATES IN CELL CYCLE PROGRESSION AND SUBTELOMERIC SILENCING IN *CANDIDA GLABRATA*

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Abstract:

Accurate DNA replication and segregation is key to reproduction and cell viability in all organisms. Autonomously replicating sequence-binding factor 1 (Abf1) is a multifunctional protein that has essential roles in replication, transcription, and regional silencing in the model yeast *Saccharomyces cerevisiae*. In the opportunistic pathogenic fungus *Candida glabrata*, which is closely related to *S. cerevisiae*, at least some of these processes are important for survival within the host, for example, the regulation of transcription of virulence-related genes like those involved in adherence. Adherence of *C. glabrata* to epithelial cells depends primarily on several adhesins encoded by the *EPA genes*. In this work, we found that *CgABF1* is required for silencing near the telomeres, where many *EPA genes* reside. We determined using ChIP-qPCR assays, that Abf1 is recruited at different positions throughout the subtelomeric region of telomere E right where *EPA1, EPA2,* and *EPA3* form a cluster, this might indicate that *Abf1* participates directly in the regulation of expression of these adhesins under specific conditions. *CgAbf1* mediated subtelomeric silencing depends on the 43 C-terminal amino acids. Additionally, we found that abnormal expression, depletion, or overexpression of Abf1, results in defects in nuclear morphology, nuclear segregation, and transit through the cell cycle. In the absence of *ABF1*, cells are arrested in G2 but start cycling again after 9 h, coinciding with the appearance of cells with higher DNA content. Overexpression of *CgABF1* causes defects in nuclear segregation and cell cycle progression. We speculate that these effects could be due to the deregulation of DNA replication.

HIGH FRUCTOSE CONSUMPTION INDUCES LIPID ACCUMULATION IN ADIPOCYTES BY REGULATION OF MIR-143-5P LEVELS IN EXTRACELLULAR VESICLES

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Abstract:

The high fructose intake through sugar-sweetened beverages (SSBs) is related to several metabolic abnormalities, including adipose tissue expansion, and an imbalance in adipokine secretion from adipose tissue. Several reports have studied the adipocyte cellular response to high fructose exposure; however, its endocrine activity has not been fully explored. microRNAs (miRNAs) have emerged as novel paracrine and endocrine signals. Adipocytes can secrete miRNAs in extracellular vesicles (EVs), which transport specific miRNAs as endocrine signals involved in regulating several cellular processes, including adipogenesis. A current study showed that the consumption of fructose in rats induced an increase in levels of miR-143-5p in EVs from plasma and a reduction of miR-223-3p levels. Moreover, the same study reported similar results in adipocytes exposed to fructose. Hence, this study aimed to determine levels of miR-143-5p and miR-223-3p in EVs in plasma from subjects with high and low fructose consumption and to evaluate the function of miR-143-5p in adipocytes exposed to fructose by the antagonism of miR-143-5p. 3T3-L1 adipocytes were transfected with antimiR-155-5p and then exposed to 550 µM of fructose for four days. Lipid accumulation was evaluated by red oil O stained. The expression of genes adipogenic and lipogenic was determined by RT-qPCR. In twenty participants, fructose consumption was assessed using a food frequency questionnaire. The fructose consumption was categorized into two groups: low consumption (< 50 g per day) and high consumption (> 50 g per day). The miR-143-5p and miR-223-3p levels were determined in EVs of plasma by RT-qPCR. In adipocytes, antimiR-143-5p induced a decrease in lipid accumulation in adipocytes exposed to fructose compared with adipocytes only exposed to fructose ($p<0.05$). Also, antimiR-143-5p promoted an increase in *Lpl* expression and a reduction of *Fasn* in adipocytes exposed to fructose compared with adipocytes only exposed to fructose ($p<0.05$). The participants with high consumption of fructose showed high miR-143-5p levels in EVs from plasma compared to those whose with low fructose consumption ($p<0.05$), while the miR-223-3p levels did not show changes. In conclusion, the fructose intake may modulate the miR-143-5p levels in EVs as an endocrine signal involved in lipid accumulation in adipocytes.

RESVERATROL INHIBITS THE INSULIN PATHWAY IN LIVER CELLS BY ACTIVATING PKC

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Abstract:

Resveratrol (RSV) is a polyphenolic compound reported for its multiple benefits in treating cardiovascular diseases, obesity, diabetes mellitus, and cancer. The positive effects of RSV have been mainly associated with its antioxidant activity and with the increase in the expression of proteins that metabolize free radicals and reactive oxygen species (ROS) (Zhang et al., 2021).There are reports about its inhibitory effect on the synthesis of fatty acids and triglycerides, increased expression of glucose transporters (GLUTs), and regulation of glucose and insulin levels, all of them associated with correct signaling of the insulin pathway (Badria, 2019). However, there is controversy about the effect of RSV on specific metabolic tissues and its pro-oxidant effect. In C9 liver cells from normal rat tissue and Hepa 1-6 from mouse hepatoma, we found that RSV affected the insulin pathway at the insulin receptor (IR) level and consequently the PI3K/Akt pathway in both cell types. Conversely, ERK1/2 proteins of the MAPK pathway increased their phosphorylation in C9 cells and were inhibited in Hepa 1-6. These effects were dependent on PKC isoforms, which was corroborated with the inhibitors BIM-I and Gö697, which prevented the effect caused by RSV. In addition, we also observed an increase in Ser-phosphorylation of the IR, an event associated with PKC activity. On the other hand, the effect of RSV and insulin on specific PKC isoforms phosphorylation was analyzed, and we found that RSV caused an increase in Ser729-PKCε, Ser657-PKCα, and Ser643-PKCΔ phosphorylation and promoted the association between IR and PKCα and PKCε. It is possible that the activation of the PKC isoforms is due to the oxidation of cysteines by ROS in the regulatory domain or the catalytic site of PKC, although the interaction between RSV and PKC can also cause their oxidation, therefore, we intend to evaluate in the future the generation of ROS in liver cells by RSV.

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THE MOLECULAR IODINE SUPPLEMENT INDUCES DIFFERENTIAL ANTIOXIDANT OR PROAPOPTOTIC PATHWAYS ON THE HUMAN NEUROBLASTOMA STEM CELLS

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Abstract:

Cancer is one of the leading causes of death in young ages; neuroblastoma (NB) is an extracranial solid tumor of undifferentiated cells of the neural crest. The cancer stem cells (CSC) are the subpopulation with self-renewal capacity, tumorigenicity, chemoresistance, invasiveness and plasticity. CSCs reside in tumor niches and can be studied *in vitro* by their enrichment in neurospheres (low adherence and no differentiating factors). Molecular iodine (I2) exerts antineoplastic effects by inducing apoptotic and differentiation mechanisms in various cancer cells. Its pathways are associated with its oxidant/antioxidant capacity by disrupting the mitochondrial membrane potential (MmpΨ), releasing apoptotic proteins (Bax/Bcl-2), or by activating PPARγ receptors to induce the expression antitumor and differentiation factors. This project aimed to analyze the mechanisms of the mitochondrial pathway that promote the antitumor effects of I2 in CSC and human progenitor neuroblastoma cells.

Briefly, human SK-N-BE(2) NB cells in monolayer (progenitors) and neurospheres (CSC) were used to analyze the effect of 200 µM I2 for 48 h. The results showed that supplementation with I2 significantly decreases cell viability in both models (progenitor and CSC) after 72 h. In addition, I2 increases mitochondrial permeability (I2 934.5 vs. Control 699.4 RFU) of cells in monolayer while in neurospheres, it decreases both MmpΨ canceling the entry of MitoTracker Red (I2 1409 vs. Control 1789 RFU) and the production of O2- ion (MitoSOX; I2 962.0 vs Control 1518 RFU). On the other hand, I2 supplement increases the BAX/BCL-2 apoptotic index as well as NRF2 and Pink1 expression in both models (progenitor and CSCs). The gene levels of AIF and SOD2 were significantly increased with the I2 supplement only in the progenitor model. Further analysis of the nuclear translocation of NRF2 to the nucleus is in progress.

These data suggest that I2 induces antioxidants and/or apoptotic pathways depending on the metabolic status of neuroblastoma cells.

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ISOLATION AND CHARACTERIZATION OF SARS-COV-2 NEUTRALIZING NANOBODIES

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COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. Up to date more than 5,000,000 people around the world have died due to this disease (1). SARS-CoV-2 uses the spike protein (S) to enter the host cells via the receptor binding domain (RBD). The first step in the virus infection process is when RBD interacts directly with human cells through the angiotensin converting enzyme 2 (ACE2) (2). RBD is the major object of study for the antibody-mediated neutralization of its interaction with ACE2. A choice to prevent the interaction between the RBD domain of SARS-CoV-2 and ACE2 are the antibodies produced in camelids that unlike those of mammals are composed of only one heavy chain. The portion of this single chain antibody that recognizes the epitope is the VHH domain, commonly named nanobody (3, 4). One big advantage of these nanobodies is that it can be produced heterologously. Two high affinity nanobodies called H11-D4 and H11-H4 have been identified, isolated and characterized, these are directed to an epitope immediately adjacent and slightly superimposed with the binding region of ACE2 with RBD (5). In our work, the gene of H11-D4 nanobody was sub-cloned into the pRSET-A vector, it was overexpressed using Escherichia coli SoluBL21 strain. Also, directed mutagenesis was performed to obtain the H11-H4 nanobody, substituting the corresponding nucleotides in the plasmid constructed with the gene of the H11-D4 nanobody. Both nanobodies were purified by chromatographic techniques in a FPLC. The final yield for the H11-D4 and H11-H4 nanobodies with histidine flag was 26 and 34 mg/L respectively, whereas for both nanobodies without histidine flag the yield was of 12 mg/L. Through X-ray spectroscopy experiments in the Swiss Light Source Synchrotron it was observed whether the chemical environment surrounding the zinc atom in ACE2 was affected by pre-incubating the RBD with the nanobodies, finding that these inhibit the interaction of RBD with its ligand ACE2. In conclusion, in this work we produced the H11-D4 and H11-H4 nanobodies neutralize the binding of SARS-CoV-2 and some variants with its cellular receptor ACE2. These nanobodies will be used as positive controls in experiments for antibody or chemical-mediated neutralization of the RBD-ACE2 interaction.

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EVALUATION OF ENDOPHYTIC BACTERIA AS PLANT PROBIOTICS IN *AGAVE* PLANTS

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Abstract:

Few are the studies that demonstrate the presence of endophytic bacteria inhabiting agave tissues, however, some of them have reported the presence of different endophytic bacterial genera. The bacterial endophytic community with qualities as plant growth promoting bacteria (PGPB) confers certain benefits that help the host plant to get water, also in nutrients availability and improvements in health. The study of plant probiotic bacteria, specifically in agaves, is scarce. In addition to functional qualities as PGPB, plant probiotic bacteria tend to improve vegetative parameters and soil health. In this work, the isolation and characterization of endophytic bacteria from stem and leaves of *Agave americana* L. was carried out. The genomic DNA of the endophytic strains was extracted and an Enzymatic Restriction Analysis (ARDRA) based on 16S rRNA gene was done to form different groups of genomic profiles. A representative strain from each genomic profile was taken for sequencing and identification. The taxonomic identification showed that bacterial isolates belonged to Pseudomonas, *Xanthomonas*, *Pantoea* and *Bacillus*. The representative strains were conducted to PGPB efficiency measurements and they were evaluated as probiotic bacteria by inoculating *Agave tequilana* at greenhouse. The evaluated bacterial endophytic isolates were able to promote the growth and development of agave plants.

Keywords: *Endophytes, ARDRA, Gen 16S, Plant Probiotics*.

STRUCTURAL STUDIES OF CELL WALL BIOSYNTHESIS OF PATHOGEN MRSA. IMPLICATIONS IN THE ANTIBIOTIC RESISTANCE

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Abstract:

One of the most threatening hospital-associated pathogens is the bacterium *Staphylococcus aureus*, which currently represents a major problem in both the clinical and community settings globally. Several strains exist that are resistant to a wide range of β-lactam antibiotics, known as methicillin-resistant *S. aureus* or MRSA. β-Lactam antibiotics block the synthesis of the bacterial cell wall through inhibition of the transpeptidase activity of Penicillin-Binding Proteins (PBPs). *S. aureus* creates its complex and nearly spherical peptidoglycan with a spare ensemble of only four PBPs, of which two (PBP1 and PBP2) are essential. Addition of a fifth PBP (PBP2a) is a clinically significant antibiotic-resistance mechanism in MRSA.

We have reported the crystal structure of PBP2a in complex with ceftaroline[1] one of the few antibiotics available for treatment of infections by MRSA. We identified an allosteric binding site a remarkable 60 Å distant from the DD-transpeptidase active site that once occupied, a multiresidue conformational change culminates in the opening of the active site to permit substrate entry.

In this work, we have proposed the mechanism of action of a triple combination of a quinazolinone allosteric inhibitor and tazobactam (TZP). The collective effect is the impairment of cell wall biosynthesis, with bactericidal consequence. We demonstrated the efficacy of the triple-drug combination in vivo and in vitro also two crystal structures for complexes of the antibiotics with PBP2a provide support for the proposed mechanism of action[2]. Besides we have presented for the first time an integrative structural biology of the PBP1 providing mechanistic clues about its function and regulation during cell division[3]. In conclusion, out results provide new insights into the complexity of this regulation and pave the way for the development of new compounds that can aid to prevent the expansion of the disease produced by this important pathogen.

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THE COMBINATION OF AZD4547 WITH CALCITRIOL SYNERGISTICALLY INHIBITED BT-474 BREAST CANCER CELL PROLIFERATION, STEMNESS, AND TUMORSPHERE FORMATION

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Abstract:

Fibroblast growth factor receptor (FGFR) overamplification in cancer leads to hyper-activation of target proteins, resulting in increased proliferation. AZD4547, a potent FGFR selective inhibitor, hinders breast cancer cells proliferation. Although luminal B breast tumors may respond to chemotherapy and endocrine therapy, this subtype is associated with poor prognosis and acquired drug resistance. Calcitriol, the vitamin D most active metabolite, exerts anti-neoplastic effects and enhances chemotherapeutic drugs' activity. In this study, we sought to decrease the concentration of AZD4547 needed to inhibit the luminal-B human breast cancer cell line BT-474 proliferation by combining it with calcitriol. Anti-proliferative inhibitory concentrations (IC), combination index, and dose-reduction index were analyzed from sulforhodamine B assays considering the median effect principle of the mass-action law and Chou-Talalay's equations. Western blot and qPCR were used to study FGFR signaling, while the ability of the compounds to inhibit BT-474 cells' tumorigenic capacity was assessed by tumorspheres formation. Results: BT-474 cells were dose-dependently growth-inhibited by calcitriol and AZD4547 (IC_{50} = 2.9 nM and 3.08 µM, respectively). The drug combination elicited a synergistic antiproliferative effect, allowing a 2-fold AZD4547 dose-reduction. Mechanistically, AZD4547 downregulated FGFR1 protein/mRNA expression and phosphorylation, as well as tumorspheres formation-capacity. Calcitriol decreased tumorspheres formation, induced cell surface-attachment and cell-differentiation. Additionally, the compounds reduced ALDH expression, a stemness marker. In conclusion, the drug combination impaired self-aggregation capacity, reduced stemness features and induced cell differentiation. Overall, our results suggest that at low concentration, calcitriol might be a suitable candidate to synergize AZD4547 effects in patients bearing luminal B breast tumors, allowing to reduce its dose and adverse effects.

COMPUTATIONAL MODELING OF THE DYNAMICS OF THE GUT MICROBIOTA METABOLISM

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Abstract:

The dynamics of the gut microbiota are primarily affected by abrupt changes in diet, infection events, and antibiotic therapy. Understanding the mechanisms behind these transitions is critical to generating predictions regarding personalized interventions in these microbial communities. Mathematical modeling allows a holistic study of complex systems like this one, based on data from genomic technologies. Recently, ecological models, such as the compositional Lotka-Volterra (CLV), have been used to represent the growth and interactions between taxa in these systems (Joseph *et al.*, 2020). However, when the metabolism drives compositional changes, these models are limited. In this work, we analyzed the dynamics of the metabolism of the gut microbiota in a longitudinal database through a hybrid model between CLV and flux balance analysis (FBA). To do this, we compared the performance of 4 dynamic models through 'leave-one-out' cross-validation using the RMSE as a proxy of the prediction error. From these evaluations, CLV was chosen for its low RMSE and for the possibility it offers to carry out analyzes directly from relative microbial abundances. Then, we tested two approaches between CLV and MICOM. The latter is an FBA-type computational tool that includes maximization processes and the definition of a balance between community growth and individualized growth of each microorganism (Diener et al., 2020). Finally, from this model, we characterized metabolites produced differentially by these communities and the stability of the enterotypes. Furthermore, we simulated the metabolic response of the system under different disturbances.

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GLOBAL ANALYSIS OF THE CELLULAR MECHANISM OF METFORMIN IN A YEAST MODEL

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Abstract:

Aging is a complex phenotype characterized by a progressive decline of biological functions[1]. In the past few decades, the lifespan expectancy of human has increased, but at the same time aging is considered the primary risk factor of several chronic human pathologies such as cancer, neurodegenerative disease, and others[1]. From this perspective, a major goal of geroscience research is the identification of drugs that improve healthspan by targeting the hallmarks of ageing[2]. One of the most promising compounds is the biguanide metformin, an oral medication employed for treating type 2 diabetes. This antidiabetic drug extends the lifespan of mice, yeast, and nematodes[3,4,5]. While the mechanisms by which this compound exerts its lifespan effects are starting to be characterized, a clear idea of which genes are relevant for its lifespan-extension effect is still missing. Since metformin modulates the cell in a pleiotropic manner, a systems-level study to uncover its lifespan-extension mechanisms is indispensable. Here, we carried out a large-scale functional genomics assay to identify the genetic factors that determine the chronological lifespan extension effect of metformin in the budding yeast *Saccharomyces cerevisiae*. Specifically, we have screened a deletion collection of 1414 knockout strains each lacking one gene with a human ortholog. Our genome-wide analysis provides a global, unbiased view of the genetic determinants, processes, and pathways through which cells respond to metformin, resulting in extended lifespan.

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FUNCTIONAL CHARACTERIZATION OF THE TAU95 SUBUNIT OF TRANSCRIPTION FACTOR TFIIIC IN *TRYPANOSOMA BRUCEI*

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Abstract:

RNA polymerase III (Pol III) transcribes several small RNA molecules that are essential for cell viability, such as tRNAs, 5S rRNA and snRNAs. Accurate transcription initiation by Pol III requires general transcription factors TFIIIA, TFIIIB and TFIIIC. In yeast and higher eucaryotes, TFIIIC is composed of six subunits. Little is known about Pol III transcription in *Trypanosoma brucei* and other trypanosomatids. Until recently, of the three Pol III general transcription factors, only TFIIIB had been found and studied in trypanosomatids. Here we report the identification and characterization of the ortholog of the Tau95 subunit of TFIIIC in *T. brucei* (TbTau95). *In silico* analyses showed that the TbTau95 protein contains the three conserved sequences, and that its predicted 3D structure is very similar to that reported for human Tau95. The inducible knock down of TbTau95 by RNAi had no effect on cell growth, suggesting that this protein is not essential in procyclic forms of *T. brucei*. To identify the proteins that interact with Tau95 in *T. brucei*, we generated cell lines that express PTP-tagged versions of TbTau95. After confirming the correct expression and nuclear localization of the recombinant protein, we carried out tandem affinity purification experiments, and the peptides were identified by mass spectrometry. Among the identified proteins, we found three other subunits of TFIIIC, two of which have not been reported before in trypanosomatids. We also found several subunits of the three RNA polymerases, as well as subunits of some of their transcription factors and regulators. Notably we also identified subunits of the Structural Maintenance of Chromosomes (SMC) complexes cohesin and condensin, which have been reported to interact with TFIIIC in other organisms to carry out extra-transcriptional activities.
This work was supported by grant IN214221 (PAPIIT, UNAM).

PIR PROTEINS AND ITS FUNCTIONAL ROLE ON THE CELL WALL OF NEUROSPORA CRASSA

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Abstract:

Despite the role that some cell wall resident proteins have in the viability of the fungal cell, these proteins have been poorly studied. Morover, the ambiguity in their classification as "structural" has caused a lack of interest in their study. Cell wall proteins are clasified as covalently and non-covalently attached to the cell wall. The covalently-attached group is populated by glycosylphosphatidylinositol-linked proteins (GPI-proteins) and proteins with internal repeats (PIR-proteins). The internal repetitive units of PIR-proteins consist of eight highly conserved amino acids (SQDGQQA). Additionally, they may have a characteristic four cysteine domain at the C-terminus. These characteristics allow the protein to be linked to the CW through an alkali-labile ester bond between a glutamine residue of the repetitive units and β-1,3-glucan or via a disulfide bond between the Cysteine domain to other CWPs. PIR-proteins have only been bioinformatically inferred for three filamentous fungi. In N. crassa, NCU04033 (PIR-1) and NCU07569 (PIR-2) loci encode putative PIR-proteins. To date, neither the diversity nor the function of PIR-proteins in filamentous fungi have been studied. In this work, we aim to analyze the evolutionary history of PIR proteins in fungi and determine the bona fide localization and functional role of these proteins in the cell wall using N. crassa PIR-1 and PIR-2 as models. Evolutionary analysis of PIR proteins suggest that these was an innovation for Ascomycota DIvision. Nevertheless, PIR proteins in Ascomycota classes were unevenly distributed among their species, which suggests gene losing events. Clustering analysis revealed two main groups. The first one matched the classical yeast PIR proteins (four cysteine motifs at the C-terminus, no GPI signal). The second one included PIR proteins from yeast and filamentous fungi. Most of them contained a GPI-signal and diversified cysteine-rich domains. Beside the typical signals of PIR proteins, there were localized unconventional PIR proteins containing additional domains (Hybrid proteins) such as GPI, transmembrane domains, and some other glycosyl hydrolase family 13 (GH13). In order to explore the role of NcPIR proteins in the cell wall, three knock-out (KO) strains Δpir-1, Δpir-2 and Δpir-1/ Δpir-2 were phenotipically analyzed, interestingly, the growth rate of both Δpir-1 and Δpir-2 was higher than that of the WT strain. In addition, cell wall stresors assays results, suggested that these proteins are related to maintenance of cell wall integrity. A 3D model of the protein could help to explain how they are stabilizing the cell wall.

LARGE-SCALE PROFILING OF NCRNAS IN BUDDING YEAST LONGEVITY

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Abstract:

Non-coding RNAs (ncRNA's) are genes that do not code for proteins, but their functions regulate gene expression by different molecular mechanisms. Even though these types of molecules impact the development of organisms and are associated with health and disease states, their relationship with cellular aging is completely unknown. Results in our group have consistently found that deletion of SWR1 (a histone exchange complex) impacts longevity in yeast and in *Drosophila melanogaster.* Given that it has been shown that SWR1 participates in the biogenesis and regulation of ncRNAs, we hypothesized that some ncRNAs participate in the molecular mechanisms that determine yeast longevity, possibly through their interaction with the complex SWR1. Using a genome-wide, intergenic ncRNAs deletion collection we performed large-scale survival assays on a high-throughput robotic station. We analyzed the relative chronological lifespan of 299 ncRNAs deletion strains, revealing an important number of short-lived strains (42), but also few long-lived strains (18). Most of the effects are in tRNAs (23%) and snoRNAs (21%). Interestingly, we also find many cryptic (7%) and stable untranslated transcripts (10%) that affected yeast lifespan. To verify the robustness of our genome-wide test, we validated some of the top hits by flow cytometry (live/dead analysis). Importantly, we obtained a validation rate of ~ 80% for the ncRNAs deletion strains tested by this alternative, small-scale approach. Finally, to shed light on the role of the SWR1 complex in ncRNA biogenesis and aging we generated a double mutant deletion collection (Δ*swr1*-ΔncRNAs) to find epistatic interaction between ncRNAs and a genetic factor that extend the lifespan expectancy. Interestingly, some interactions modified the long-lived SWR1-associated phenotype, suggesting that many ncRNAs are essential for SWR1-induced lifespan extension in budding yeast. Our study represents the first evidence of the functional role of ncRNAs in aging in yeast or any other organism.

RANKL SIGNALING IN BREAST CANCER STEM CELLS

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Abstract:

Introduction: Breast cancer stem cells (BCSCs) are a subpopulation of cells with the ability to self-renewal and differentiate in phenotypically diverse tumor cells. BCSCs have been implicated in treatment resistance and cancer recurrence. RANKL, a cytokine able to bind both RANK and LGR4, has been implicated in the regulation of CSCs. Accumulated evidence has shown that RANKL/RANK signaling induces self-renewal of BCSCs and disrupts differentiation. Recent evidence in osteoclasts has shown that RANKL via LGR4, blocks the RANK signaling and generates an opposite cellular response. Since RANKL/RANK signaling rapidly expands the pool of BCSCs, anti-RANKL inhibitors have increasingly been proposed to eradicate CSCs and treat breast cancer. Nevertheless, RANKL-inhibitor therapies fail to consider the biological effects of disrupting RANKL binding to LGR4. Objective: This project aims to evaluate the effect of RANKL inhibition on stemness of LGR4 low and LGR4 high cells and identify the signaling pathways involved in the RANKL/LGR4 and RANKL/RANK signaling. Methodology: The survival probability of breast tumors expressing low or high RANKL expression was analyzed in a cohort of TCGA. The effect of RANKL inhibition in the stemness was performed in breast cancer cell lines with low and high levels of LGR4. Breast cancer cells overexpressing RANK or LGR4 were treated with RANKL and the transcriptome was evaluated to identify signaling pathways activated by RANKL. Results: Here we show that RANKL could be a good prognosis factor in breast cancer patients with high levels of LGR4. Results indicate that RANKL inhibition in LGR4 low cells was able to decrease the pool of CSCs, however, the inhibition of RANKL in LGR4 high cells fails to decrease the CSCs fraction, promoting growth tumor and enhancing migration and invasion abilities. Data also indicates that when binding RANK, RANKL induces the activation of signaling pathways implicated in stemness, however, the interaction of RANKL/LGR4 results in blockage of these signaling pathways. Conclusions: Our results suggest that RANKL exerts opposite effects on stemness depending on the receptor it binds, these results are supported by differential effects in LGR4 low and LGR4 high cells treated with RANKL inhibitors.

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RNA POLYMERASE II PAUSING CONTRIBUTES TO MAINTAIN CHROMATIN ORGANIZATION IN THE CHICKEN ERYTHROCYTES

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Abstract:

Erythropoiesis in non-mammalian vertebrates like birds gives rise to circulating erythrocytes that retain their nucleus in a highly compacted state. Chicken erythrocytes are often referred to as transcriptionally inactive, although the epigenetic changes and chromatin remodeling that mediate transcriptional repression and the extent of gene silencing during avian terminal erythroid differentiation are not fully understood. Chicken embyronic (eRBC) and adult red blood cells (aRBC) experience a dramatic drop in RNA synthesis rate and undergo extensive chromatin compaction as evidenced by electron micrography. However, a study of the chromatin remodeling and genome organization at high resolution during this process is still lacking.

We have studied the changes in chromatin topology and accessibility that take place during avian terminal erythroid differentiation revealing a complex remodeling process of genome organization. Chromatin accessibility profiling by ATAC-seq and immunofluorescence showed a unique positioning of the accessible chromatin inside the nucleus of aRBC. Open chromatin in the erythrocytes comprises paused promoters of silent genes that retain the RNA polymerase II in a paused state. We performed RNA-seq experiments in eRBC and aRBC and identified a set of genes that remain active in the terminally differentiated erythroid cells, some of them linked to the control of the RNA polymerase II pausing. Finally, we studied the organization of the erythroid genome with a global chromosome conformation capture technology (Hi-C) and found it to be highly compartmentalized and practically devoid of TADs except for regions where the paused RNA pol II contributes to chromatin folding into mini domains. Our results suggest that promoter-proximal pausing of the RNA pol II participates in the transcriptional regulation of the erythroid genome and highlight the role of RNA polymerase in the maintenance of local chromatin organization.

This work was supported by by UNAM Technology Innovation and Research Support Program (PAPIIT) IN207319.

GLYCOSYLATION OF *CANDIDA ALBICANS* AFFECTS ITS INTERACTION WITH SPECIFIC RECEPTORS OF THE CARDIAC CORONARY ENDOTHELIUM

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Abstract:

Candida albicans is a dimorphic fungus that, under immunosuppression of the host, may spread through the bloodstream and reach other organs, including the heart. The cell wall of *C. albicans* is mainly made up of an inner layer of chitin, a network of b-glucans and an outer layer of mannoproteins with N- and O-mannosylated structures. The cell wall of *C. albicans* participates in the interaction with the host, where mannoproteins play an important role in adhesion.

Here, we studied the functional contribution of the N- and O-mannosylated structures of the cell wall of *C. albicans* in the adhesion to the coronary endothelium of the heart. To achieve so, we used an isolated rat heart model (Langendorff model) to measure the cardiac parameters of coronary perfusion pressure (CPP) and left ventricular contraction (LVP) in response to phenylephrine (FE), acetylcholine (aCh) and angiotensin II (Ang II). The responses were measured before and after the application of the treatments that consisted of: *C. albicans* WT yeasts; isolated N-mannans; isolated O-mannans and *C. albicans* pmr1D yeasts, whose phenotype shows shorter N- and O-mannans compared to those of the WT.

Our results showed that *C. albicans* WT alters the PPC and LVP parameters of the heart in response to FE and Ang II, but not aCh. Additionally, isolated O-mannans produced a similar effect as *C. albicans* WT. In contrast, the isolated N-mannans or the *C. albicans* pmr1D strain were not able to alter the response of PPC and LVP. Our data suggest that the adhesion of *C. albicans* occurs specifically to certain receptors in the coronary endothelium and that O-mannans contribute to a greater extent to this adhesion. These data do not rule out that N-mannans play an important role in the interaction with other receptors different from those studied here, so it is essential to continue conducting more studies to elucidate the nature of this interaction and the reason why certain receptors are preferentially bind to one or another structure of the fungal cell wall.

MOLECULAR BASES FOR THE INHIBITION OF THE MAIN PROTEASE (MPRO) OF SARS COV2

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Abstract:

Besides global administration of prophylactic vaccines, control of the evolving "COVID-19" pandemic requires the design and development of new chemotherapeutic antiviral agents that selectively inhibit viral enzymes that are essential for intracellular SARS-CoV-2 replication. The cysteine viral main protease (M^{pro}) is considered among the most promising drug targets, as it is (i) essential for the viral replication complex formation; (ii) recognizes a unique peptide substrate, so mimicking compounds that bind to the active cavity should have few side effects in humans; (iii) low susceptible to accumulate mutations in its coding region, so potential inhibitors should have broad-spectrum activity. This research aims to understand the molecular bases of ligand recognition by Mpro in the context of viral enzyme evolution. FDA-approved compounds that potentially bind to the protease were inferred by molecular docking and were tested for their capacity to inhibit proteolytic enzyme activity of the original strain and a select number of clinically relevant mutations (L89F, K90R, V303I, P132H). Disulfiram (DSF) irreversibly inhibits the enzyme activity in vitro, acting as a competitive inhibitor, while it was also effective in vivo using a heterologous expression chimeric system in E. coli. Captopril and nitazoxanide were also found to interact with Mpro active cavity.

ROLE OF PREGNANCY ON INSULIN-INDUCED VASORELAXATION: THE INFLUENCE OF ANGIOTENSIN II RECEPTORS

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Abstract:

Under physiological conditions, insulin receptor stimulation activates phosphatidyl inositol 3 kinase – protein kinase pathway B (PI3K-Akt) and stimulates endothelial nitric oxide synthase (eNOS) producing vasodilation. Modifications in the insulin signaling cascade are related to pathologies such as insulin resistance and increased vasoconstriction that is associated with the activation of the mitogen-dependent kinases (MAPK) transduction pathway, which favors the production of endothelin 1 (ET-1). Angiotensin II has an important role in regulating vascular tone. Insulin resistance is a feature of pregnancy and is associated with increased levels of angiotensin II (Ang II) and insulin. The aim of this work was to evaluate if pregnancy change insulin-induced vasodilation through changes in Ang II receptors. To prove it, insulin-induced vasorelaxation was assessed in phenylephrine-precontracted aortic rings of pregnant and non-pregnant rats, using a conventional isolated organ preparation. Experiments were performed in thoracic or abdominal aorta rings with or without endothelium in the presence and absence of NG-nitro-L-arginine methyl ester (L-NAME) (10-5 M), losartan (10-7 M), or PD123319 (10-7 M). AT1 and AT2 receptor expressions were detected by immunohistochemistry. Insulin-induced vasodilation was endothelium- and nitric oxide–dependent. Pregnancy diminished vasodilation of the thoracic aorta but increased it in the abdominal segment of the vessel. The insulin's vasorelaxant effect was increased by losartan mainly on the thoracic aorta. PD123319 decreased insulin-induced vasorelaxation mainly in the pregnant rat abdominal aorta. Pregnancy decreased AT1 while increased AT2 receptor expression along the aorta.

In conclusion, pregnancy changes insulin-induced vasorelaxation in a segment dependent way. Moreover, insulin vasodilation is tonically inhibited by AT1 receptors, while AT2 receptors appear to have an insulin-sensitizing effect. The role of pregnancy and Ang II receptors differ depending on the aorta segment. These results shed light on the crosstalk between insulin- Ang II receptors, and on role of pregnancy on the regulation of this interaction.

PARTICIPATION OF THE ONCOPROTEIN CAGA FROM *HELICOBACTER PYLORI* IN THE PANCREATIC EPITHELIAL CELLS DAMAGE

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Abstract:

The *Helicobacter pylori bacterium* affects around half of the world's population. To establish an efficient infection in the gastric epithelium, this pathogen exhibits several virulence factors being the cytotoxin CagA the most widely studied. CagA has been shown to interact with multiple host cell proteins, either depending on its phosphorylation or not, and producing severe cytoskeleton rearrangements, losing of cell polarity, impairing of intercellular junctions and inducing the IL-8 production. In recent years, the *H. pylori* infection has been associated with various pancreatic pathologies, such as acute pancreatitis, pancreatic cancer and diabetes; however, the underlying mechanisms are still unknown. Therefore, the aim of this work is to analyze the effect of CagA on the BxPC-3 pancreatic cells employing two strategies: a recombinant protein (CagA-His) and cagA-depleted bacteria (HpCagA-). The results shown an IC50=28.95 µg/µl for CagA-His over BxPC-3 cells. This protein presented a cytotoxic effect on pancreatic cells in a concentration manner. On the other hand, the HpCagA+ and HpCagA- bacteria strain were genetically characterized by PCR, displaying the presence of the constitutive genes 16s, glmM and UreA; and only the HpCagA+, but not the HpCagA-, strain exhibits the cagA gene. The expression of these genes was confirmed by WB assays, demonstrating that the HpCagA- strain does not express the CagA protein. In addition, by transepithelial electrical resistance assays, it was proved that the pancreatic cells permeability was lesser affected by the infection with the HpCagA- strain, in comparison with the HpCagA+ bacteria. In agreement, the HpCagA+, but not HpCagA-, strain produced alterations in the intercellular junctions proteins, actin and cytoskeleton regulatory proteins. All these findings propose CagA as an important factor for the pancreatic epithelium damage.

EXPLORING THE FUNCTIONAL ROLE OF SLM35 ON MITOPHAGY IN *SACCHAROMYCES CEREVISIAE*

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Due to the fundamental role that mitochondria play in maintaining cellular homeostasis, quality control mechanisms must be in place to ensure the identification and elimination of damaged or excess mitochondria; one of these mechanisms is mitophagy, a form of autophagy that selectively degrades these organelles.

The selective autophagy processes require a receptor to link the cargo to the main autophagy machinery. Atg32 is the mitophagy receptor in the yeast *Saccharomyces cerevisiae*[1,2]. This tail-anchored protein is inserted in the outer mitochondrial membrane, so its N- and C- terminal regions are exposed to the cytoplasm and to the intermembrane space, respectively. The sole presence of Atg32 is not enough to start the mitophagy, as three posttranslational modifications have been implicated in the regulation of the process: the phosphorylation at serines 114 and 119 by casein kinase 2[3], the dephosphorylation by Ppg1 at the same serines[4], and the proteolytic cleavage of the C-terminus by Yme1 in the intermembrane space[5].

The matrix mitochondrial protein Slm35 (*Stress and Longevity-related Mitochondrial factor*) has been proposed as a negative regulator of mitophagy, given that its absence increases the mitophagic flux[6]. Since deletion of the *SLM35* gene increases mitophagy, we wondered whether this increase is related to the post-translational modifications of Atg32, specifically its proteolytic editing. To answer this question, we analyzed the electrophoretic mobility of HA-tagged Atg32 by Western Blot to detect the lower molecular weight version that corresponds to the Yme1-edited form. At the same time, we related the amount of edited Atg32 to the amount of mitophagy when *SLM35* was absent. In this scenario, Slm35 could function as a sensor of metabolic alterations within mitochondria and transfer the damage signal to Atg32 to activate mitophagy.

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CONFORMATIONAL LANDSCAPE OF THE GTPASE EFL1 AND ITS IMPLICATIONS IN THE SHWACHMAN-DIAMOND SYNDROME

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Abstract:

Ribosomes are synthesised through a highly regulated and energetically demanding process. The last cytoplasmic maturation step of the nascent 60S subunit couples the release of the anti-association factor eIF6 (yeast Tif6) with a quality control assessment of the P-site and the GTPase centre by the joint action of the Elongation Factor-like 1 (EFL1) GTPase and its nucleotide exchange factor, the SBDS protein. Defects in the function of any of these two proteins lead to a disease called the Shwachman-Diamond Syndrome (SDS). Mutations prevent the release of eIF6 from the 60S subunit, with the consequent imbalance of mature 60S subunits entering the pool of active translating 80S ribosomes and a decrease in global translation. EFL1 is a molecular motor adopting at least four distinct conformations in solution regulated by SBDS and both guanine nucleotides. The active GTP-bound conformation of EFL1 required for binding to the 60S subunit is largely stabilised by the interaction with SBDS (1). The malfunction of the non-synonymous mutations in EFL1 is unknown, but in most cases, they do not affect its catalytic activity or fold. However, mutations in either SBDS or EFL1 debilitate their interaction preventing the regulation SBDS exerts in the GTPase. SBDS elicits a dissimilar structural and energetic response in the yeast mutant EFL1 R1086Q (equivalent to R1095Q described in SDS patients) compared to that of the wild-type protein. The conformational heat capacity change and corresponding conformational binding entropy of the complexes formed between mutant and wild-type GTPase and SBDS for GTP are of opposite values suggesting a different conformation. Mutation R1086Q has a profound effect on the internal rearrangements necessary to elicit the same conformational change observed in the native EFL1 in response to its effector ligands (2).

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Unpublished results

BIOLOGICAL AND FUNCTIONAL CHARACTERIZATION OF THE SLC5/STAC TWO-COMPONENT SIGNAL TRANSDUCTION SYSTEMS

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The SLC5/STAC histidine kinases comprise a recently identified family of sensor proteins in two-component signal transduction systems (TCSTS), in which the signaling domain is fused to an SLC5 solute symporter domain through a STAC domain. Previously, only two members of this family have been characterized experimentally, the CbrA/B system that regulates the utilization of histidine in Pseudomonas and glucose in Azotobacter, and the CrbS/R system that regulates acetate utilization in Vibrio. We characterized the CrbS/R system in *Pseudomonas fluorescens* SBW25 and through the quantitative proteome analysis of different mutants, we were able to identify a new set of genes under its control and identified a conserved DNA motif in the putative promoter region of acetate-utilization genes in the that is required for the CrbR-mediated transcriptional activation. Moreover, seeking to expand the characterized members of this family, we identified two putative TCSTS in Sinorhizobium fredii NGR234 whose sensor histidine kinases belong to the SLC5/STAC family. We were able to identify the first TCSTS as a CrbS/R homolog that is also needed for growth on acetate, while the second, RpuS/R, is a novel system required for optimal growth on pyruvate. Using RNAseq and transcriptional fusions, we determined that in S. fredii the RpuS/R system upregulates the expression of an operon coding for the pyruvate symporter MctP when pyruvate is the sole carbon source and identified a conserved DNA sequence motif in the putative promoter region of the mctP operon that is essential for the RpuR-mediated transcriptional activation of genes under pyruvate-utilizing conditions. Currently, through the construction and study of chimeric constructs from the proteins we have characterized we are seeking to understand the molecular mechanisms by which the SLC5/STACTCST proteins detect environmental stimuli.

UNRAVELING THE SECRETS OF AXOLOTL LIMB REGENERATION BY THE ANALYSIS OF RNA SEQ AND PROTEIN 3D STRUCTURE PREDICTION

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Abstract:

The axolotl (*Ambystoma mexicanum*) is an organism that has the ability to regenerate most of its tissues and whole-body parts. So, it has become one of the most important model of study in the area of tissue regeneration. Until now, the molecular mechanism related to limb regeneration remains poorly understood. One limitation is that its genome is poorly annotated and there are few sequenced versions of it. Here, we analyzed by RNA-seq 5 juvenile axolotls control limbs and their blastema, compared with two old axolotls' limbs (over eight years old) that lost their limb-regeneration capacity. We found 2743 differentially expressed genes (DEG) between the control limbs and their blastema where most of them were downregulated. We also founded that between juvenile limbs and old limbs there are 172 DEG where the majority were downregulated. In this context, we decided to analyze those genes that showed DEG between old axolotl's limbs vs blastema and we found that 44 genes were DEG, but only 8 genes were overexpressed in blastema and downregulated in old axolotls' limbs. Most of these are involved in processes such as oxidative stress, cell migration, response to vascular damage and bone morphogenesis. An analysis of the 3D structure protein prediction of follistatin-like 1 (Fstl1) show that this protein is conserved in axolotl. Fstl1 is a very important protein in mouse development, where its absence leads to malformations of the respiratory system and postnatal lethality. Our results suggest for the first time a set of axolotl genes that may be involved in tissue regeneration.

MOLECULAR CARTOGRAPHY OF THE *SALMONELLA* TYPE III SECRETION SYSTEM SORTING PLATFORM

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Abstract:

The type III secretion systems (T3SSs) or injectisomes are protein injection nanomachines used by many bacterial pathogens to deliver virulence proteins into a wide range of eukaryotic cells (plants, fungi, mammalian) [1]. A large complex termed the sorting platform, acts from the inside of the bacteria to energize and organize the timely secretion of proteins through the injectisome [2]. Despite the importance of the sorting platform for T3SS function, the mechanisms that drive the assembly of this multi-component structure have not been elucidated. Herein, employing a comprehensive in vivo crosslinking strategy, we monitored the protein-protein interaction network of the entire sorting platform of *Salmonella enterica*. The obtained crosslinks were used as signatures for inter-subunit assembly and combined with systematic genetic deletions allow us to decipher the assembly order of the sorting platform. Insights generated by this study provide major insights on how a complex bacterial nanomachine is built, opening new avenues for the rational design of anti-infective drugs.

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KINETIC CHARACTERIZATION OF RHIZOBIAL BACTERIAS AS PLANT GROWTH PROMOTERS (PGPB) IN SHAKEN FLASK AND STIRRED TANK

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Abstract:

Currently the agricultural sector demands new products and technologies to reduce dependence on agricultural inputs such as chemical fertilizers, in this situation the use of bioinoculants from native rhizobial bacterial strains of the state of Chiapas considered as plant growth promoters (PGPB) represents an alternative to promote the growth and development of crops in the face of high costs and shortages of nitrogenous fertilizers. However, nutritional needs, as well as factors such as pH, temperature, agitation, among others, influence cell growth in production systems at the laboratory and pilot levels. As a first step, the kinetic characterization of three rhizobial bacterial strains was carried out in controlled systems (shaken flask) in order to evaluate the biological quality of the product obtained (biomass) through its cell viability. Subsequently, the scale up process from shaken flask to a stirred tank in an operating volume of 3L was carried out. The effect of three concentrations of carbon source and three levels of mechanical agitation on the growth of the strains was evaluated, additionally the volumetric oxygen transfer coefficient (K_La) for scaling was determined. Cell concentration (CFU/mL), viability percentage (%) and biomass (gr) were considered as response variables. Finally, effectiveness and infectivity tests of the three PGPB rhizobial bacterial strains were carried out on bean plants (*Phaseolus vulgaris*) under bioclimatic chamber conditions.

Keywords: *PGBP bacteria, biofertilizer, bioreactor*.

HETEROGENOUS GENE EXPRESSION AND SPLICING IN HYPERSENSITIVITY PNEUMONITIS FIBROBLASTS

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Hypersensitivity Pneumonitis (HP) is an inflammatory lung disease caused by the inhalation of a wide variety of antigens that induce an exaggerated immunological response in genetically susceptible individuals. HP is the second interstitial lung disease with more admissions at the Instituto Nacional de Enfermedades Respiratorias (INER). Around 40% of the patients develop a chronic stage and evolve to fibrosis, an incurable condition with a high mortality rate.

The immune response in HP is deeply characterized. Many factors have been described to have a role in the development of this and other fibrosing diseases. Most factors have been enlisted in genome-wide assays to have elevated or diminished expression relative to controls or other diseases. Besides global gene expression changes, the pathogenesis of some diseases can also be affected by the altered expression of protein isoforms generated by alternative mRNA splicing. We wondered if this was also relevant for HP.

Aiming to characterize the complex and heterogenous HP gene expression, we evaluated 20 primary HP lung fibroblast cultures derived from patients with contrasting clinical characteristics. The general and splicing isoform expression of seventeen individual targets was analyzed and related to the phenotype of the cultured fibroblasts and the demographic and clinical characteristics of the HP patients. Targets of interest included the innate immune response genes *IFI27* and *AGER*. Adaptive immunity targets consisted of receptors for soluble factors produced by memory T cells, including receptors for IFNγ, IL17, IL4/IL13, and TGFβ, among others.

We found that HP fibroblasts expressed higher levels of mRNA coding for *IFI27* and *PDFGRA* than controls. In contrast, *IL17RC* and *TGFBR3* mRNAs abundance was lower relative to controls. These expression levels correlated with some respiratory function parameters and histologic and tomographic data. We also found that *CXCR4* and *AGER* expressed splicing isoforms that differed between HP patients and controls and were present in patients with specific clinical characteristics. The results presented here are potentially relevant for diagnosis, prognosis, or therapeutics of HP.

STRUCTURAL AND FUNCTIONAL INTERPLAY BETWEEN THE [4FE-4S] CLUSTER AND THE ACTIVE SITE OF MUTYH AND ITS IMPLICATION IN CARCINOGENESIS

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Abstract:

MUTYH is DNA glycosylase in charge of repairing adenine mispaired with 8-oxo-7,8-dihydro-2'-deoxyguanosine (A:OG) via Base Excision Repair. Mutations in *MUTYH* gene are associated to carcinogenesis. Its activity is intrinsically linked to the presence of two metal cofactors, a [4Fe-4S] cluster and a Zinc linchpin motif. A battery of functional studies indicates that both cofactors are absolutely required for proper DNA repair. Actually, 9% of MUTYH cancer-related variants are found within these metallic motifs. In spite of the studies focused on these cofactors, there is not a complete understanding of their function and role in carcinogenesis. To gain knowledge about the structure-activity relationship of the MUTYH we obtained the crystal structure of the first human MUTYH-DNA complex. With this structural information and coevolutionary analysis, we were able to identify a structural connectivity between the [4Fe-4S] cluster and the catalytic pocket through a hydrogen-bond network. The residues that are part of the structural bridge between the [4Fe-4S] cluster and the catalytic pocket are the cysteinyl ligand C290, R241, N238 and the catalytic residue D238. Interestingly all these positions are classified as cancer-associated variants (CAV); C290W, R241Q and N238S. We characterized biochemically these CAVs in MUTYH and found that all of them show loss of glycosylase activity. Binding experiments using an uncleavable adenine 2'-deoxy-2'-fluoroadenosine and abasic site analog tetrahydrofuran across OG show that R241Q and N238S MUTYH mutants, regardless the loss of activity, maintain a high affinity at similar range as WT MUTYH (nM and pM, respectively). The high affinity of R241Q and N236R, and their null glycosylase activity, along with the structure of MUTYH-DNA complex and the coevolutionary data, indicate that the integrity of the hydrogen-bond network that connects the [4Fe-4S] cluster and the catalytic pocket in MUTYH is important for the correct positioning of the catalytic residue D238 and the stabilization of the catalytic pocket architecture. Hence, the pathogenic aspect of these mutations in MUTYH and their implication in cancer can be linked to the disruption of the structural and interplay between both motifs.

REGULATORY PERTURBATIONS OF RIBOSOME ALLOCATION IN BACTERIA RESHAPE THE GROWTH PROTEOME WITH A TRADE-OFF IN ADAPTATION CAPACITY

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Abstract:

Cellular growth is the result of a highly regulated process that demands the allocation of cellular resources towards different tasks. Bacteria have evolved to regulate resource allocation to maximize survival under harsh and changing environments. Here we studied the allocation of ribosomal resources in two sets of strains with regulatory perturbations that increase growth rates in minimal media. Two mutants of *Escherichia coli* K-12 MG1655 with the three stronger ribosomal operon (SQ53: rrnCEH, SQ78: rrnBCH) expression resulted in higher resource allocation to growth and decreased adaptation capacity. These ribosomal operon mutants showed similar phenotype to previously studied *rpoB* mutants. Comparing these two different regulatory perturbations (rRNA promoters or *rpoB* mutations), we show how they reshape the proteome for growth with a concomitant fitness cost. The fast-growing mutants shared downregulation of hedging functions and upregulated growth functions. All of them displayed increased ribosomal content, a longer diauxic shift and a reduced activity of the *aceBAK* operon, indicative of repressed gluconeogenic pathways and suggesting reduced availability of the RNA polymerase for expressing hedging proteome. These results show that the regulation of ribosomal allocation underlies the growth/hedging phenotypes obtained from laboratory evolution experiments.

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CHANGES IN INDUCTION TEMPERATURE IMPACTS THE STRUCTURE OF RECOMBINANT HUGM-CSF INCLUSION BODIES IN THERMOINDUCIBLE *E. COLI*

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Abstract:

The temperature upshift has been widely used as an induction system to produce recombinant proteins (RP´s) in E. coli [1]. Soluble or insoluble RPs can be obtained during overproduction in bacteria [2]. The incorrect protein folding can promote self-aggregation in conjunction with endogenous proteins to form self-assembled aggregates known as inclusion bodies (IBs). Thermoinduction up to 37 ºC could affect recombinant protein (RP) production and metabolism, as well as might impact the RP aggregation. Here, we describe the bioprocess using an E. coli W3110 producer of the recombinant human granulocyte-macrophage colony-stimulating factor (rHuGM-CSF) under the thermoinducible system pL/cI857, applying 39 ºC or 42 ºC after initial culture at 30 ºC. Results indicated that at 39 ºC the production of biomass was intensified with respect to time as well as the acetate accumulation, while the total protein and RP production decreased. At 42 ºC the production of total protein was preferred over biomass accumulation, as well as caused a profound change in the IBs formation, its architecture, and RP content. rHuGM-CSF IBs formed at a higher temperature presented higher disorderly structures compared with IBs formed at 39 ºC enriched in α-helix composition, and amyloidal composition. This study highlights the observation that IBs attain different architectures in response to small changes in environmental conditions, such as the induction temperature. [Thanks to PAPIIT: IN210822].

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BIOCHEMICAL ASPECTS OF BIOTIN DEFICIENCY IN MAMMALS

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Abstract:

Biotin is a vitamin that functions as a cofactor for energy production. In its cycle, biotin is joined to three carboylcses: pyruvate (PC), propionyl-CoA (PCC) and methylcrotonyl-CoA (MCC) by the action of Holocarboxylase Synthetase (HCS). When the carboxylases are degradated, biotin remains joined to a lysine (of its carboxylases) and this compound is known as Biocytin. Through the action of Biotinidase, biocytin is cleaved; lysine is released and biotin is freed and is readied to be reutilized. Our studies were started when we diagnosed a patient with a deficiency of HCS. Later on, our research focused on mammals (rats and mice) and to primary cultures of hepatocyes. In these cultures, we found that biotin regulates the expression of the three carboxylases. In livers of defiecient rats we found, using microarrays, that the mRNAs of the genes for fatty acids oxidation and for gluconegenesis were increased, and those for glycolysis and lipogenesis were diminished. Furthermore, the levels of ATP were reduced and AMP kinase (AMPK) was activated. We also studied the fluxes of synthesis and degadation of fatty acids, using radioactive acetate and palmitate, and measured the amounts of the transcriptional factors ChREBP and SREBP, which were abnormal in biotin deprivation. Additionally, insulin sensitivity was augmented as a consequence of the activation of the intermembrane transporter GLUT-4 by the AMPK, in cutured muscular cells. An important finding was the mitochondrial damage to its structure and function that we found in skeletal and cardiac muscles. All the previous results we observed in biotinidase knockout mice. In conclusion, the above findings help to understand the damages in the human biotinidase deficiency, and contribute to a better understanding of the Metabolic Syndrome.

(All of the above investigations were funded by resarch grants from DGAPA-UNAM and CONACYT)
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CHARACTERIZATION OF THE TRANSCRIPTIONAL AND EPIGENETIC PROFILES ASSOCIATED WITH THE METABOLIC MEMORY *IN VITRO*

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Abstract:

Patients diagnosed with diabetes can achieve good control of blood glucose levels with the aid of pharmacological interventions and lifestyle changes. However, transient exposure to hyperglycemia can still cause long-term damage even after glycemic control is achieved in diabetic patients, a phenomenon known as “metabolic memory”.

The molecular mechanisms behind the metabolic memory are still unknown, but evidence suggests that there is persistent increased oxidative stress and inflammation. In this work we established an *in vitro* metabolic memory model in primary human vascular cells to investigate the effect of transient hyperglycemia in the transcriptomic and epigenetic landscapes of these cells. We exposed human umbilical vein endothelial cells (HUVEC) to three treatments: normal glucose (5.5 mM; 8 days), high glucose (30 mM; 8 days) and metabolic memory (30 mM 4 days; then 5.5 mM 4 days), and then conducted RNA-seq and ATAC-seq experiments in each treatment.

Our results show that both high glucose and metabolic memory treatments induce changes in the expression of genes associated with known pathways altered in diabetes, including oxidative stress and inflammation. Interestingly, we found that transcription factor *NRF3*, a member of the same family of *NRF2*, the master regulator of the antioxidant response, was persistently overexpressed in the metabolic memory treatment. It has been suggested that *NRF3* has antagonistic effects over *NRF2*, thus, we hypothesize that NRF3 could be acting as a repressor of the antioxidant genes in the context of high glucose and the metabolic memory, this through competitive binding to *NRF2* target genes.

In line with this, analysis of the ATAC-seq data revealed an increase in the occupation of the NRF2 motif, which is shared with NRF3, this despite no changes in NRF2 expression. Additionally, motif enrichment analysis of promoters of differentially expressed genes in the metabolic memory treatment showed a significant enrichment for the NRF2 motif. These findings suggest that NRF3 could act as a repressor for the antioxidant system and mantain the metabolic memory.

To corroborate the role of NRF3 in the metabolic memory and its interplay with NRF2, we have conducted knockdown and overexpression experiments and evaluated the subcellular localization and chromatin binding of these transcription factors. With these experiments we aim to determine the molecular mechanisms behind the persistent decrease in expression of antioxidant system genes that occurs in diabetes-associated hyperglycemia, which could result in a new potential target for therapies directed to prevent diabetes complications.

REAL-TIME MONITORING OF VOLATILE ORGANIC COMPOUNDS (VOCS): FROM BASIC RESEARCH TO CITIZEN SCIENCE

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Abstract:

Volatile organic compounds (VOCs) play a central role in ecological interactions, such as plant-plant and plant-microbe communications. The identification and quantification of VOCs in biological systems are challenging. Conventional methods such as gas chromatography (GC) coupled to mass spectrometry (MS) and proton-transfer reaction (PTR)-MS are slow, expensive, and biased. Thus we built a Modular Biological Mass Spectrometer (MoBiMS), which detects a broad range of VOCs between 18 and 154 g/mol without prior enrichment [1]. The system delay time is about 540 ms, which allows for the real-time analysis of (bio)chemical reactions. MoBiMS data are directly comparable with 70 eV spectra (NIST database). We built our prototype with ~60,000 USD, which is about 20 times cheaper than a PTR-MS, and our open-hardware design allows interested research groups to copy and modify the system according to their needs. We also demonstrated the use of the MoBiMS to analyze biological samples in ambient conditions, such as banana smell and tobacco leaves, and monitored the photosynthesis reactions of tomato plants.

Excess levels of VOCs are a severe threat to human health. However, measuring the VOC contamination is costly. Thus, only sparse VOC data are available, even in urban areas. We designed a small Internet-of-Things detector, which is low-cost (~100 USD) and reports the online VOC contamination on multiple spots [2]. The data are stored in a SQL database and can be visualized online. We released hardware design and the software with open source licenses. The MeteoMex platform (http://www.meteomex.com) is suitable for "Citizen Science" projects on environmental protection and agriculture 4.0.

Funding: Conacyt-DFG 2016/277850

[1] Alcalde-Vázquez R, Moreno-Pedraza A, Rosas-Román I, Guillén-Alonso H, Riedel R, Partida-Martínez P, and Winkler R. "MoBiMS: A Modular Miniature Mass Analyzer for the Real-Time Monitoring of Gases and Volatile Compounds in Biological Systems." Microchemical Journal 175: 107090. [2] Winkler, R "MeteoMex: Open Infrastructure for Networked Environmental Monitoring and Agriculture 4.0." PeerJ Computer Science 7: e343.

ABSTRACTS | Technical conferences

XXXIII National Congress of Biochemistry

LET'S ESTABLISH A NEW PROTEIN PURIFICATION IN ONE DAY, FROM SCRATCH

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Abstract:

Achieving a successful method for protein purification usually is a slow, complicated, and frustrating process that consumes plenty of time and resources. Here we present a rapid, practical and unexpensive solution; a design of experiment (DoE) coupled to Stain-free electrophoresis and Image Lab analysis. Bio-Rad´s DoE may solve a problem in just a few hours and provide you of a wide knowledge about the best conditions to bind and elute a protein to/from a specific chromatographic media. Results will direct you to adress the best conditions for binding/eluting according to your own goals: yield, purity and/or activity.

Join us, let's discuss your ideas.

SOLUTIONS FOR 3D CELL CULTURES

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Abstract:

Mammalian cell culture has served as an invaluable tool in cell biology for several decades. Monolayers of adherent cells grown on flat and rigid two-dimensional (2D) substrates, such as polystyrene or glass, have evolved as the mainstay in conventional cell culture systems. Nevertherless, , a multitude of inadequacies associated with 2D culture systems have also emerged, especially with respect to their inability to emulate in vivo conditions and providing physiological relevance.

In the body, nearly all cells in tissues reside in an extracellular matrix (ECM) consisting of a complex three - dimensional (3D) architecture and interact with neighboring cells through biochemical and mechanical cues cell - cell and cell-ECM interactions establish a 3D communication network that maintains the specificity and homeostasis of the tissue.

For more than 25 years, Corning has delivered innovations that have advanced the science of 3D cell culture.

We pioneered the development of novel tools providing easier access to in vivo-like 3D models, such as Corning Matrigel® matrix and Transwell® permeable supports continue to evolving a portfolio of innovative 3D cell culture products, solutions, protocols, and expertise.

Corning present this technical seminat to working with researchers in critical areas like cancer biology, tissue engineering, and regenerative medicine – to help you bring safe, effective drugs and therapies to market in less time with greater certainty.

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THE NATIONAL LABORATORY OF CHANNELOPATHIES (LANCA) OF THE INSTITUTE OF CELLULAR PHYSIOLOGY

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Abstract:

Traducción al Inglés.

Ion channels (ICs) are proteins that regulate the passage of ions (electrically charged atoms) through the cell membrane. These channels are essential for the functioning of all cells in the body, particularly muscle, nerve, and heart cells. The channelopathies are pathological conditions produced by an abnormal function or expression of ICs. Since each small variant in the mutation of an IC can lead to a different disorder, there is a wide variety of channelopathies, which can be due to either the increase or the loss of function of an ion channel and can be acquired or inherited. The National Laboratory of Channelopathies (LaNCa) of the Institute for Cell Physiology has specialized personnel and sophisticated equipment to conduct biophysical, physiological, and pharmacological studies of normal and altered ion channels, in cultured cells and in living tissue slices.

LaNCa incorporates state-of-the-art equipment in electrophysiology, fluorimetry, and microscopy. In addition, it has implemented various assays such as cell cycle, proliferation, invasive migration, cytotoxicity, and cell death. Being a research laboratory, LaNCa is also interested in developing and validating protocols, applicable to the identification of agents with activity on ion channels and disease models that serve as a preclinical platform to evaluate new therapeutic strategies. All the LaNCa's objectives strive to provide reliable and quality data; for this reason, the laboratory is committed to operating under a Quality Management System and has been awarded certificates NMX-CC-9001-IMNC-2015 and ISO 9001: 2015. Moreover, LaNCa provides customized services by designing and developing projects according to the client´s needs.

Currently, LaNCa has strong alliances with several Associated Institutions: The Institutes of Marine Sciences and Limnology, Biotechnology, Biomedical Research and the Preclinical Research Unit (UNIPREC) of the School of Chemistry at UNAM, the University Center for Biomedical Research of the University of Colima, the Monterrey Unit of CINVESTAV-IPN, the National Institute of Cardiology "Ignacio Chávez", the National Institute of Neurology, the Institute of Ophthalmology "Conde de Valenciana" and the Laboratory of Vaccinology and Tropical Viruses of the National School of Biological Sciences of the IPN.

TRANSCRIPTOME PROFILE OF AEDES AEGYPTI IN MIDGUT AND SALIVARY GLANDSPOST DENV-2 INFECTION

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Introduction: Dengue virus (DENV) is the etiological agent of dengue, one of the most important diseases transmitted by vectors, according to the World Health Organization (WHO). Asian/American genotype of Dengue virus type 2 (DENV-2) have been extensively characterized and accumulation of genetic variability of genotype lineages.The virus-host interactions in the different organs are not fully characterized at a functional level, the 14 days post-infection with a specific DENV-2 genotype could be contribute in the vectorial capacity. The aim of this study will be to determinated the transcriptomic profile in midguts and salivary glands of *Aedes aegypti* post DENV-2 infection. **Methodology:** 5 midguts and 9 salivary glands of *Aedes aegypti* infected and uninfected with DENV-2 were evaluated. Quality control was performed using Trim_Galore and all those readings with Q>30 were selected. Filtered reads were then mapped using bowtie2 against the A. aegypti genome from the NCBI database (assembly GCF_002204515.2, NC_035107.1). The RNA-seq profile expression was obtained using htseq-count. Differentially expressed genes (DEG) were identified considering DEG those with a p value <0.05 and log2 Fold Change between -2 to 2 by DESeq2 (version 3.7). Conserved protein domains and associated GO terms were identified using InterProScan (v4.9) including the Pfam, ProSitePatterns, Gene3D, SUPERFAMILY and MobiDBLite databases. The overrepresentation of GO terms in the groups of genes overexpressed and repressed in salivary glands and midguts was analyzed, implementing the ToGo package in R. **Result and discussion:** Ontologies of biological processes (BP), molecular functions (MF) and cellular components (CC) were evaluated. In midgut of the total genes evaluated (2817), 159 genes were over-expressed and 282 genes were repressed. Three significantly enriched were involved positive regulation of transcription, cellular process of protein folding and transmembrane transport. To the repressed three were involved in communication, regulation and response cellular to G protein. In salivary glands of the total genes evaluated (3838), 20 genes were over-expressed and 90 genes were repressed. Two significantly enriched and overexpressed genes were involved in positive regulation of transcription and aminophospholipids transport and two repressed were involved in protein synthesis, and translational initation. **Conclusion:** The study identified different biological processes uncharacterized during DENV-2 infection at the level of the midgut and salivary glands, the transcriptome profile in tissues is essential to understand the extrinsic process of viral infection with a specific genotype and the contribution in the vectorial capacity. Further functional validation of the altered pathways must be implemented.

MENTORÍA DE MUJERES EN STEM, ¿TE ANIMAS?

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Abstract:

En los últimos años ha aumentado la participación de las mujeres en las disciplinas STEM (ciencia, tecnología, ingeniería y matemáticas, por sus siglas en inglés), sin embargo, según la UNESCO sólo el 28% de todos los investigadores del mundo es de sexo femenino (UNESCO, 2019). En México, la brecha de género se ha ido reduciendo a lo largo de los años; no obstante, continúa siendo amplia.

Algunas de las razones por las que hay menos mujeres en puestos de compromiso y liderazgo en STEM son el abandono por acoso y discriminación, presión familiar y social, o bien falta de motivación durante el desarrollo de sus proyectos. Durante su paso por las diferentes diciplinas, una mujer en la ciencia debe compaginar las responsabilidades domésticas de la casa, los hijos, el cuidado de adultos mayores, etc., con el trabajo laboral, lo que representa un gran reto.

En los últimos años se ha visto que tener el apoyo de una mentora o guía que ayude a las investigadoras jóvenes, estudiantes avanzadas de doctorado y postdocs, a lidiar con todos estos obstáculos es de suma importancia para que puedan proseguir con sus carreras en STEM. Asimismo, el ser *mentee* implica una gran responsabilidad y diciplina para la generación de ideas, resolución de problemas y cumplimiento de metas a corto, mediano y largo plazo.

De manera que en esta breve charla invitaremos a las investigadoras que deseen a participar en un curso en línea, donde se ofrecerán herramientas y se fomentarán habilidades para ser mentoras. Esto con el objetivo de poner en práctica lo aprendido y tener una *mentee* a la cual guiar para que se convierta en una líder en STEM.

EBP y MK son mentee y mentora certificadas por el British Council

CELL CULTURE 3D

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Abstract:

Over the years, human has tried to reproduce experimental models, resemble closer to the human organism functioning. Thanks to technology advances, actually, is possible to use 3D cell cultures, in which, cells grow and interact with their environment in three dimensions, getting closer to the cells architecture *in vivo*, providing more reliable and safe results. There are two types of 3D cultures; spheroids and organoids, both are used in studies of cancer, regenerative medicine, toxicology, infectious diseases and drug discovery.

For more than 25 years, Corning has delivered innovations that have advanced the science of 3D cell culture. They pioneered the development of novel tools providing easier access to *in vivo*-like 3D models, such as Corning Matrigel matrix, Transwell permeable supports and Ultra-Low Attachment Surface. Among innovation, they have Corning Matrigel matrix for organoids, Corning spheroid microplate, workflow solutions, Cell Counter and Matribot Bioprinter, as well as, protocols and experience. Cell cultures 3D applications are become broader, not only supports scientific research, but also the industrial sector such as the pharmaceutical and cosmetology industries.

ABSTRACTS | Posters Basic Biochemistry

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IDENTIFICATION AND CLONING OF GENES INVOLVED IN THE BIOSYNTHESIS OF BETULINIC ACID IN *PENTALINON ANDRIEUXII*

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Pentalinon andrieuxii is a native plant of the Yucatan peninsula that has been commonly used in traditional Mayan medicine due to its biological properties and represents a natural source of metabolites with potential application in the pharmaceutical industry. Recently, it has been detected that genetically transformed *P. andrieuxii* plants show an increase in their content of betulinic acid, a natural pentacyclic triterpene type lupane with a variety of biological activities including the inhibition of the human immunodeficiency virus (HIV), properties antibacterial, antimalarial and antitumor. However, many of the genes of the biosynthesis of betulinic acid have not been identified due to the complexity of the biosynthetic pathways of this group of metabolites. The objective of the present work consisted in identifying by homology and phylogenetic analysis the genes involved in the biosynthesis of betulinic acid from the transcriptomes of the leaf and root tissues of young and adult plants of *P. andrieuxii*, from which, five transcripts of genes involved in the biosynthesis of triterpenic acids, including the transcripts of SQS (squalene synthase), SQE (squalene epoxidase), two OSC (oxidosqualenes cyclases) including bAs (β-amyrin synthase) and LUS (lupeol synthase), as well as monooxygenas of the CYP716A subfamily that function as oxidases of the C-28 of triterpenes. Likewise, in silico expression levels were evaluated and the ORFs of the identified genes were amplified with specifically designed oligonucleotides. Finally, the identity of the cloned LUS and SQS genes was verified by sequencing.

ANALYSIS OF CAROTENOIDS AND PROLINE IN THREE VARIANTS OF ACHIOTE (*BIXA ORELLANA*) SUBJECTED TO WATER STRESS

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Abstract:

Bixa orellana L (Achiote) is a tree of great agro-industrial interest due to its seeds, which have a high content of carotenoids, mainly bixin. Carotenoids are synthesized and stored in plastids, they are essential compounds for life, due to the functions they carry out in relation to photosynthesis (Carballo-Uicab *et al*., 2019). The term stress in plant physiology is a biotic or abiotic environmental factor that modifies some physiological process, for example, growth or photosynthesis. Water stress, caused by salinity in the soil, generates reactions in the plant and is reflected in the synthesis and accumulation of proline in the roots and leaves and they suffer alterations in their content of carotenoids and chlorophylls. In addition, salinity due to NaCl is the greatest environmental stress and causes a reduction in crop production (Shao Yen *et al* 2015). In this work, the effect of salt stress on the synthesis of carotenoids and proline in leaves and roots of annatto seedlings of the P12, N4 and N5 variants with 50 mM, 100 mM, and 150 mM sodium chloride was studied. The results show highly variable changes in the concentration of carotenoids, chlorophyll a and b, depending on the NaCl treatment and the control. Likewise, proline accumulated in leaves and roots of the three variants analyzed and its concentration increased with increasing concentration of NaCl applied. The results obtained compared to other species indicate that proline could be an indicator of salt stress in *B. orellana*.

Carballo-Uicab, V. M., Cárdenas-Conejo, Y., Vallejo-Cardona, A. A., Aguilar-Espinosa, M., Rodríguez-Campos, J., Serrano-Posada, H., *et al*. (2019). *Isolation and functional characterization of two dioxygenases putatively involved in bixin biosynthesis in annatto* (*Bixa orellana* L.). PeerJ 7:e7064. doi: 10.7717/peerj.7064

Shao-Yen Chen, Wen-Chang Chi, Ngoc Nam Trinh, Kai-Teng Cheng, Yun-An Chen, Tzu-Chieh Lin, Yu-Chi Lin, Li-Yao Huang, Hao-Jen Huang & Tzen-Yuh Chiang (2015), Alleviation of allelochemical juglone-induced phytotoxicity in tobacco plants by proline, *Journal of Plant Interactions*, Vol. 10, No. 1, 167–172, ISSN: 1742-9145.

THE PEROXISOME DOCKING/TRANSLOCATION MACHINERY IS DEVELOPMENTALLY REGULATED IN THE FUNGUS *PODOSPORA ANSERINA*

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Abstract:

Peroxisomes are dynamic and highly versatile organelles that perform diverse fundamental roles, and that are essential for multiple developmental processes. Peroxisome function relies on the protein constitution of its matrix. Peroxisome matrix protein import depends on two conserved sorting pathways, which are driven by the cycling import receptors Pex5 and Pex7, respectively. These proteins recognize in the cytosol the proteins destined to peroxisomes and conduct their import into the organelle. The import process depends on the peroxisome docking/translocation machinery, which is composed of the peroxisome membrane proteins Pex13 and Pex14 and that constitutes the channel though which proteins are translocated across the peroxisome membrane. In the model fungus *Podospora anserina*, peroxisomes are required for different processes of sexual development, including karyogamy and meiosis initiation. These processes rely on Pex13 but not on Pex14, suggesting the existence of distinct import channels, which contribute to different developmental stages. Here we show that Pex13 abundance in vegetative cells is maintained at relatively low levels by the activity of the E2 ubiquitin-conjugating enzyme Pex4, the E3 ubiquitin-ligase peroxisome RING finger complex, and the peroxin that connects this complex to the docking/translocation machinery (Pex8). Moreover, we found that Pex13 peroxisomal-targeting and abundance also depend on Pex3 and Pex19, which mediate peroxisome membrane biogenesis, and on Pex1 and Pex6, which facilitate import receptor recycling. In addition to this regulation, which is not observed for Pex14, we found that Pex13 is present at higher levels troughout sexual development, where its abundance is further increased in early meiotic (prophase I) cells. These observations show that Pex13 is subject to precise developmental regulation, which involves its selective ubiquitination-dependent removal, and that likely modulates the peroxisome protein translocation system along development.

thath conduct the import of proteins tfurthermore,

This research was supported by grants IA203317 and IV200519 from PAPIIT-DGAPA, UNAM, and 277869 from FONCICYT

EXPLORING THE THERMAL STABILITY OF THERMOPHILIC PROTEINS BY MOLECULAR DYNAMICS

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Abstract:

The study of the thermostability effect in the activity of enzymes has received a great deal of attention for a long time in the literature, due to its importance in industrial applications in food, detergent, cosmetic, textile, and other commercial processes. Proteins have developed different mechanisms relating the sequence, structure, and dynamics to enhance their stability and hence to be functional. Specifically, noncovalent interactions such as hydrogen bonds, ion-pair bonds, and hydrophobic contacts keeping the structure together and packed. However, these factors are not necessarily present in whole proteins, i.e., combinations of one or more structural factors contribute to enhance the protein thermostability. In this way, many efforts have been performed to understand what the molecular interactions are that lead to improved protein thermostability, which have been based on experimental studies, theoretical analyses, and computational simulations. In particular, molecular dynamics (MD) simulation approaches have been very useful for this purpose. Furthermore, the use of MD at different temperatures has proved to be a powerful tool to understand the thermal stability of proteins, as reported in many works. In this work, we present analysis of MD in order to understand the main molecular interactions that provide thermal stability in some thermophile and hyperthermophilic proteins.

STRUCTURAL STUDY OF CATECHOL 1,2- DIOXYGENASE FROM *PSEUDOMONAS STUTZERI*

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Abstract:

One of the enzymes involved in the degradation of aromatic compounds is catechol 1,2- dioxygenase. This intradiol-type dioxygenase is Fe (III) dependent and participates in the oxidation of catechol or other catechol substituents. In this project, we study catechol 1,2- dioxygenase (C12D) from a marine *Pseudomonas stutzeri* strain isolated from the Gulf of Mexico. This species of Pseudomonas was one of the first microorganisms isolated as alkane degraders and has biotechnological relevance in bioremediation processes.

To date, we have purified the enzyme and demonstrated that its quaternary structure varies depending on ionic force (as a trimer in low ionic force and as a dimer when it is higher) also the protein is active even in higher salt concentrations (700 mM NaCl). We have performed some techniques like DLS, Native electrophoresis, and SEC to characterize these oligomeric states of C12D (all these results have been published on (10.3389/fmicb.2020.01100).

In the case of tridimensional structure, all homologous and non-homologous catechol 1,2 dioxygenases deposited in PDB are only in dimeric form, in this work we aim to determine the tridimensional structure of C12D in both oligomeric states by X-ray crystallography and SAXS. In our preliminary results in crystallization trials, the crystals didn't have good quality (higher mosaicity) but we are working on optimizations, and our interest to analyze the samples in solution by SAXS is to elucidate the trimer envelope and determine the difference between dimer-trimer states.

BIOCHEMICAL CHARACTERIZATION OF COMPONENTS WITH ANTIMICROBIAL ACTIVITY ISOLATED FROM THE VENOM OF ENDEMIC SCORPIONS OF THE STATE OF CHIHUAHUA

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Abstract:

Scorpions are one of the oldest arthropods, to date, over 2000 scorpion species have been described which are distributed worldwide, except for Antarctica and North Pole. Mexico possesses highest diversity of scorpions in the world, including medically important scorpion species. The family *Vaejovidae*, which currently includes nearly 240 species, is the most diverse in Mexico. In Chihuahua State have been found at least three species belonging to genus *Chihuahuanus* of which their venom have been not studied. The composition of scorpion venom is highly complex and heterogeneous. Due to the global problem of antimicrobial resistance (AMR) development, new antimicrobial agents are crucially needed. The traditional production of antibiotics has been exhausted, prompting research into alternate antimicrobial strategies. Recently, the spotlight has been oriented on the study of the scorpion-derived antimicrobial peptides (AMPs), which have led to a large number of discoveries that may be of relevance for therapeutic applications and it has been demonstrated that scorpion AMPs can be effectively used as scaffolds to design more specific and less harmful antibiotics. Currently, the study and biochemical characterization of the venom of scorpion species from the State of Chihuahua has taking place, and the results obtained point to the possibility to isolate antimicrobial peptides that can be used effectively against pathogens that are resistant to essentially all of the available antibiotics.

THE PROTEIN PHOSPHATASE PP2A AND THE CASEIN KINASE CKII ARE EXPRESSED IN SEA URCHIN SPERMATOZOA

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Abstract:

The sperm´s goal is to fertilize the egg and to achieve this, they need to swim. Swimming involves intracellular changes in pH, Ca^{2+}, cAMP and protein phosphorylation mediated by the protein kinase dependent of cAMP (PKA) and the kinase activated by diacylglycerol and Ca^{2+} (PKC)[1,2,3,6]. Sea urchin sperm conserves several of the mechanism present in vertebrate animals4. When sea urchins release their gametes into the sea, sperm motility is initiated as pH increases, activating ATPases which drive the flagellum. The sea urchin´s motility is also regulated by sperm activating peptides and chemoattractants from the egg´s external coat like speract5. The protein phosphatase PP2A, has been identified by proteomic analysis as a PKA phosphorylated substrate in flagella samples[1,2,3]. Moreover, an *in-silico* analysis predicts that several proteins from the speract´s signaling cascade are PKA and PKC targets, and that there are phosphorylated predicted sites by casein kinase II (CKII), in proteins like the soluble adenylate cyclase, CatSper 4 and PKC, all of them localized at the flagellum. This suggests the involvement of CKII and PP2A in the sea urchin sperm´s motility. The objective of this project is to determine the participation of CKII and PP2A in the motility of sea urchin. In this project by using Wester-Blot and immunofluorescence experiments, we show that CKII and PP2A are expressed in the sea urchin sperm flagella. Furthermore, the analysis of trajectories of individual cells in the presence of okadaic acid, led us to show PP2A participates in the motility of sea urchin spermatozoa.

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CHANGES IN METHYL ESTERIFICATION OF PECTIN IN THE CELL WALL OF COCONUT ZYGOTIC EMBRYOS

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Abstract:

In non-recalcitrant and climacteric fruits, e.g., tomato, chili pepper, among others, their ripening and maturation are intrinsically related with seed maturation. Moreover, as fruits ripening, their epicarp and mesocarp goes from hard to soft tissues. It is known that those changes in climacteric fruits are accompanied by dynamic changes in their cell wall composition, particularly in the degree of pectin methyl esterification/de-esterification. In case of the seeds from climacteric fruits it has been described that pectin methyl esterification is mainly associated with early events of zygotic embryogenesis, while abundance of de-esterified pectin is present in mature embryos (Pérez-Pastrana et al., 2019). However, during the development of non-climacteric fruits whose mesocarps or endocarps goes to hardness with maturation, e.g., nuts, coconuts, among others, few is known about the dynamics of pectin methyl esterification. In this study, with the goal to analyze how the pectin methyl esterification behaves in coconut immature, intermediate and mature zygotic embryos, an immunohistology analysis was carried out using the monoclonal antibodies JIM5 and JIM7. The first one detects pectin with low degree of methyl esterification, and the second one recognizes highly methyl esterified pectin. Results showed that during the early stages of zygotic embryogenesis, the pectin is mainly methyl de-esterified in the middle lamella of cells. This characteristic is associated with cell wall relaxation and the cell elongation in tissues near to the zygotic embryo. On the other hand, in embryo cells actively dividing, pectin is highly methyl esterified, while in the formation and accumulation of endosperm, as seed maturity increases, the pectin methyl esterification in endosperm cells goes from highly methyl esterified in immature endosperm to methyl de-esterified in mature endosperm. Together, results show that pectin methyl esterification in coconut zygotic embryos and endosperm follow a similar trend to the observed in seeds of climacteric fruits.

MAMMALIAN CATSPER-EFCAB9 IS EXPRESSED IN SEA URCHIN SPERM

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Abstract:

CatSper is a specific calcium ion channel of the sperm flagellum regulated by voltage, cAMP and pH, whose absence in humans causes infertility. In mammals, the complex is composed of at least eleven subunits: four pore-forming (CatSper1-4) and seven accessories (β, Δ, ε, γ, ζ, η and EFCAB9). As EFCAB9 is a subunit that possesses a calcium-binding EF domain like that of calmodulin and CatSperζ a calmodulin-binding IQ motif, the regulatory subcomplex EFCAB9-CatSperζ is formed1, where both subunits interact until the sperm's cytosolic pH becomes alkalinized, causing a dissociation of both proteins and Ca2+ influx.

Sea urchin spermatozoa are the preferred model for studying chemotactic response, a mechanism in which the egg attracts its counterpart by releasing peptides into seawater. CatSper is known to play a crucial role in this phenomenon, since it allows the influx of Ca^{2+} in the flagellum of the sperm that modulates its redirection towards the egg (source of the chemoattractant). In sea urchin sperm, as in mammals, CatSper is expressed in the flagellum in addition to being activated by alkalinization of the cytosol and depolarization of the membrane2. However, since in sea urchin sperm CatSper lacks the CatSperζ subunit, the objective of this project is to verify if EFCAB9 is expressed in the spermatozoa of this organism and if it is part of the complex. The generation of an antibody against a peptide based on the predicted sequence of EFCAB9 from Strongylocentrotus purpuratus genome, allowed us to demonstrate by Dot Blot and Western Blot experiments that EFCAB9 is expressed in *S. purpuratus* and *Lytechinus pictus* sperm.

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PARTICIPATION OF INTERSUBUNIT SALT BRIDGES IN THE STABILITY OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE FROM *PSEUDOMONAS AERUGINOSA*

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Abstract:

The enzyme glucose-6-phosphate dehydrogenase from the bacterium *Pseudomonas aeruginosa* (PaG6PDH) uses $NADP^+$ and NAD^+ with similar preference, and binds glucose-6-phosphate (G6P) showing positive cooperativity. PaG6PDH is dimer-of-dimers homotetramer, and G6P induces a higher structural stability. According to previous data from our group, a putative conformational change induced by G6P binding makes enzyme more resistant to inactivating factors. AlphaFold 2.0 was used to produce a model of the PaG6PDH dimer and a ROSETTA symmetry docking was used to assemble a tetramer, using the human enzyme as reference (PDB 2blh). The model predicts four dimerization salt bridges (DSBs) formed by Glu180-Lys387 pairs, and four tetramerization salt bridges (TSBs) formed by Glu261-Lys264 pairs. THESE FOUR RESIDUES are conserved in 41 out of 44 bacterial G6PDHs and the strong conservation in consistent with a relevant role in the enzyme's structure and/or function. Here, the enzyme kinetics of E180Q and E261Q single PaG6PDH mutants, and its double mutant E180Q/E261Q was studied. All three mutations reduced the affinity for G6P, both as a substrate (K0.5 and Ki), and as a stabilizing ligand (Kd), to a similar extent. The smallest change was observed in the E180Q (2 to 3-fold less than in Wt) and similar effects were found for both E180Q/E261Q and E261Q (3 to 6-fold less than in Wt). The resemblance in the observed changes is consistent with the proposed stabilization of the tetramer induced by G6P binding to the active site. In the presence of G6P, the Wt enzyme is more tolerant to thermal or urea inactivation, and only E180Q retained this feature. By contrast, in both E261Q and in the double mutant the tolerance to thermal or urea inactivation was below that of the Wt in the absence of G6P. The above results suggest a more important role for TSBs than for DSBs in PaG6PDH tetramer stabilization, but from the synergic effect in the double mutant, a participation of DSBs in stability seems probable.

MALTOSE METABOLISM CONTROLS STARCH DEGRADATION IN BEAN FRUIT PERICARP

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Seed development is a process that requires a large amount of metabolic resources

The pods of legume fruits play a crucial role in regulating carbon partitioning to the developing seeds. In a previous study we provide relevant facts for understanding starch accumulation in bean pods. We observed that the sucrose supply remains almost constant during the growth of the seeds. Early in seed development the sucrose surplus is stored as starch, that is degraded after 20 DAA, when the seeds growth became exponential. Therefore, starch accumulation in bean fruit pericarp met the metabolic needs of fast-growing seeds, and it is necessary to understand the characteristics of the starch degradation process. As such, we assessed different enzyme activities and we defined the changes in starch granules during the development of the seeds. We observed that after 20 DAA, fruit pericarp goes into a progressive senescence. However, chloroplasts maintain their integrity, suggesting that starch degradation remains as a compartmentalized process. Starch degradation in bean fruit pericarp is characterized by the increment in the amount of glucose phosphorylated at the C6 position, as well as by a transient increment in maltose and sucrose. These results suggest that the mechanism responsible for starch degradation in bean pods' pericarps is like the one that has been described to occur in leaves. However, unlike in leaves, starch degradation in the bean fruit pericarp is also characterized by a slight reduction in β-amylase activity and a large increment in the activities of cytosolic disproportionating enzyme 2 (DPE2) and glucan phosphorylase enzyme (PHS2). After 20 DAA the starch is phosphorylated so that β-amylase can hydrolyze starch more efficiently, and there is an increment in the velocity of the cytosolic metabolism of the degradation products.

This research was supported by DGAPA-UNAM (PAPIIT-IN226520) and Facultad de Química, UNAM (PAIP 5000-9127).

AUXIN AND CYTOKININ CAUSE MAJOR PROTEOMIC CHANGES FOR SOMATIC EMBRYOGENESIS IN *COFFEA CANEPHORA*

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Abstract:

Somatic embryogenesis (SE) is a cell differentiation process by which some of the somatic cells switch into embryogenic cells. Those cells, later produce somatic embryos with the ability to generate plantlets. Given that competent-embryonic cell formation displays gene expression changes and produces small molecules, proteins inventory might be altered in cells undergoing differentiation to somatic embryos. We use the SE process of C. canephora that yield a high number of embryos as a model to find early regulated proteins involved in the competent-embryonic cell formation. Here, we confirmed that cut-leaf explants cultivation with cytokinin is enough to promote the proliferation of somatic embryos, but auxin- and cytokinin-dependent plantlet pretreatment is required for high yield somatic embryos. Two-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis gels reveal auxin- and cytokinin-dependent regulated proteins in plantlets pretreatment, 41 protein spots with up- and down-abundance. In 14 spots, proteins associated with metabolism and folding of proteins were identified. RPN12 and HSP60 proteins were up-accumulated.

EFFECT OF THE HIGH HYDROSTATIC PRESSURE ASSISTED CURING OF VANILLA BEANS (*VANILLA PLANIFOLIA*) ON THE TOTAL PHENOLIC CONTENT AND ITS RELATIONSHIP WITH THE CHANGE IN COLOR PARAMETERS

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Abstract:

Vanilla bean curing is carried out in a long and very traditional uncontrolled process that involved four stages: killing by thermal treatment, several cycles of sweating-sun drying, and conditioning. During the curing, the flavor, color, and aroma characteristics of vanilla are produced by different enzymatic transformations that take place after the killing, due, it produces a cellular decompartmentalization releasing the enzymes and substrates, including phenolic compounds required for flavor, color, and aroma development. Considering that current methods for vanilla bean curing are long and involve high temperature during the killing, in this work, the high hydrostatic pressure (HHP) a non-thermal technology that also produces cell decompartmentalization, was used to improve phenolic compounds content and its relationship with the change in color parameters L, *a**, and *b** during vanilla beans curing. The HHP-assisted curing process at 50-600 MPa was compared with the scalding at 100ºC/8 s. The total phenolic compounds (TPC) was determined by Folin-Ciocalteau reagent, and the color parameters L (L= 0 (black); L= 100 (white); *a**(+*a*= red, -*a*= green)*;* and *b** (+*b*= yellow, -*b*= blue) were obtained with a spectrophotometer. Results showed that HHP-cured vanilla beans presented higher phenolic content and color parameters values in comparison with the scalded beans. It was observed that after the C1, specifically, from the C3 to C14, a higher phenolic compound increment occurs in the cured vanilla beans, and this transformation was depending on the HHP-treatment and curing cycle. The HHP-treatment at 300 MPa (233 mg GA/g sample dry basis) produced the highest TPC, followed by 200 MPa (203 mg GA/g sample dry basis). This increment was attributed to metabolite decompartmentalization produced by the pressure. Under the HHP-treatment, we proposed that 300 MPa, produced cell wall loosening by crosslinking or depolymerizing cell wall components, leading to phenolic released by rupture of the vacuole, the main storage organelle of these metabolites. The change in color parameters also was dependent on the curing cycle and treatment conditions. The main color transformations in vanilla beans take place in the C3 of the HHP-assisted curing at 300 or 400 MPa suggesting that at least until this curing cycle is required to improve color and phenolic compounds content in cured vanilla beans. And, also suggest that a change in color parameter would be related to the phenolic compounds content in vanilla beans. In conclusion, the HHP could be used to improve phenolic content and color, as well as, to obtain a cured vanilla bean with high quality.

Keywords: Color parameters, high hydrostatic pressure (HHP), vanilla curing.

CHARACTERIZATION OF A FUNGAL ISOLATE THAT USES CELLULOSE POLYMERS AS A CARBON SOURCE

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Abstract:

Cellulose, an essential component of plant cell walls, is the most abundant and used biopolymer on Earth. Its enzymatic degradation is required for its use, mainly by three glycosyl-hydrolases: cellobiohydrolase, endoglucanase, and β-glucosidase. These enzymes work together to transform cellulose into glucose through hydrolysis of the β-1,4 glycosidic bonds and are of great biotechnological interest due to their use in various industrial processes. In the laboratory, we have a fungal isolate recovered from a consortium of microorganisms, which can grow on multiple cellulosic compounds. This work aims to characterize this isolate and determine the battery of enzymes secreted by the fungus to use these polymers as a carbon source. The fungal isolate was cultured on different culture media (YPG-A, PDA, EM, and Sabouraud), showing colonial and microscopic morphological characteristics like fungi of the genera Talaromyes and Penicillium. Subsequently, the fungal isolate was subjected to induction tests with different substrates of cellulosic origin as a carbon source: microcrystalline cellulose (Avicel®), cellophane, carboxymethylcellulose (CMC), and glucose, added (0.03% w/v), to modified Mathur minimal medium (using ammonium chloride as a nitrogen source instead of glutamic acid). Cultures were incubated for two weeks at 28 °C and shaken at 120 rpm. At the end of the incubation, the cell-free supernatant was recovered (3000 g, 10 min, 4 °C), and the secreted protein and the activities of β-glucosidase and cellobiohydrolase were determined using substrates derived from 4-methylumbelliferone. Cellophane was the best inducer of β-glucosidase activity, followed by CMC. In the case of cellobiohydrolase, the best inductor was cellophane, followed by glucose. An important characteristic is that β-glucosidase activity was metabolically repressed, in contrast to what was reported for some Talaromyces species where catabolic repression is not observed. This result implies the molecular characterization of the isolate currently being carried out.

THE NRG1-RTG3-ALA REPRESSOR COMPLEX: THE ROLE OF THE CHROMATIN REMODELING IN THE *ALT2* EXPRESSION PROFILE IN *S. CEREVISIE*

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Abstract:

The yeast *Saccharomyces cerevisiae* duplicated its whole genome (*WGD*), after an allopolyploidization event, which involved mating between two different ancestral yeast species. A large number of the paralogous genes which were conserved by *S. cerevisiae* encode for enzymes involved in carbon or nitrogen metabolism. It has been proposed that selective retention of paralogous genes facilitated the acquisition of a facultative, predominantly fermentative metabolism. *ALT1* and *ALT2* are two paralogous genes that arose as after *WGD*. *Alt1* is the only enzyme capable of catabolizing alanine in *S. cerevisiae*, however, no function has been determined for *Alt2*, even though these two enzymes share 67% sequence identity. Recently, our studies on *ALT1* and *ALT2* functional diversification have suggested the existence of a hybrid transcriptional modulator that could be made up of Nrg1 and Rtg3 (Nrg1-Rtg3). Our results indicate that this complex represses *ALT2* expression only in the presence of alanine as a nitrogen source, suggesting that alanine plays a co-repressor role: Nrg1-Rtg3-Ala. It is worth mentioning that alanine plays a dual role as a co-regulator, since in addition to its function as a presumed negative regulator of *ALT2*, it is required to induce (positive co-regulator) the expression of *ALT1*, forming part of a regulator which has not been identified. This work will allow determining whether, in fact, Nrg1 and Rtg3 form a transcriptional complex, whether alanine plays a role in its organization and, if so, its role in the interaction with chromatin organization and the network of genes whose expression is under its control will be defined. To answer the possible effect of the complex Nrg1-Rtg3-Ala in the *ALT2* expression profile, we determined the expression profile of *ALT2* in the single mutants nrg1Δ and rtg3Δ, in presence of Alanine by qPCR. And in order to know if some proteins are involved directly or indirectly in the complex formation and if these play an important role in chromatin remodeling, we applied Nucleosome Scanning Assay (NuSA) on the *ALT2* promoter. The existence of hybrid regulators such as Nrg1-Rtg3 constitutes a new alternative to study the rewiring process of regulatory networks that could play a crucial role in the selective retention and subfunctionalization of paralogous genes.

THE NRG1-RTG3-ALA HYBRID REPRESSOR COMPLEX: IDENTIFICATION OF ITS ORGANIZATION AND OF THE GENE CIRCUIT UNDER ITS CONTROL

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Abstract:

The study of the response of the yeast *Saccharomyces cerevisiae* to changes in the environment has contributed to the knowledge of the mechanisms that determine transcriptional activation or repression. Transcriptional regulators carry out three basic functions: a) Response to regulatory signals, b) Binding to specific DNA sequences, and b) Promotion of transcriptional induction or repression. *S. cerevisiae* has a single regulator made up of several subunits, this being the HAP complex which is made up of four polypeptides, three of which (Hap2, 3 and 5) form the DNA-binding domain and the fourth subunit (Hap4) which provides the activation domain. The discovery of this complex in 1989 made it possible to propose that yeast could form hybrid transcriptional modulators. The yeast *Saccharomyces cerevisiae* duplicated its entire genome, in an event known as: Whole Genome Duplication (WGD). *ALT1* and *ALT2* are two paralogous genes that arose as after of WGD. Alt1 is the only enzyme capable of catabolizing alanine in *S. cerevisiae*, however, no function has been determined for Alt2, even though these two enzymes share 67% identity at the sequence level. Recently, our studies on *ALT1* and *ALT2* functional diversification have suggested the existence of a hybrid transcriptional modulator that could be made up of Nrg1 and Rtg3 (Nrg1-Rtg3). Our results indicate that this complex represses *ALT2* expression only in the presence of alanine as a nitrogen source, suggesting that alanine plays a co-repressor role: Nrg1-Rtg3-Ala. It is worth mentioning that alanine plays a dual role as a co-regulator, since in addition to its function as a presumed negative regulator of *ALT2*, it is required to induce (positive co-regulator) the expression of *ALT1*, forming part of a regulator which has not been identified. This work will allow to determine whether, in fact, Nrg1 and Rtg3 form a transcriptional complex, whether alanine plays a role in its organization and, if so, its interaction its role on chromatin organization and the network of genes whose expression is under its control will be defined. This analysis constitutes a new alternative to address and understand the rewiring process of regulatory networks that plays a crucial role in the selective retention and subfunctionalization of paralogous genes.

MORPHOLOGICAL AND MOLECULAR CONTROL OF ES *VIA* UBIQUITIN-PROTEASOME IN *COFFEA CANEPHORA* PIERRE EX A. FROEHNER

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Abstract:

Proteolysis is a mechanism of protein degradation by enzymes that has been developed in living organisms to modulate protein homeostasis. The ubiquitin-proteasome pathway (UPS) is one of the main pathways for short-lived protein degradation in eukaryotic cells[1]. Interestingly, in plants the perception and signaling of plant growth regulators (auxins and cytokinins) are modulated by the UPS pathway[2]. Plant growth regulators participate in a wide variety of plant processes and in somatic embryogenesis (SE). SE is an important process due to its biotechnological application for plant propagation. In ES, it has been observed the modulation proteins related to metabolic energy and reactive oxygen species production, transport, and synthesis of plant growth regulators during both the conversion of the somatic cell to an embryogenic cell and maturation of the embryo[3]. Despite the identification and modulation of proteins responsible for the ubiquitination cascade and 26S proteasome subunits during SE induction, it is unknown how protein degradation via the UPS pathway could modulate proteins during the induction of the SE. In this work we used MG-132 for 26S proteasome activity inhibition in explants of *C. canephora* that further utilize in SE. This work will allow us to decipher the contribution of the 26S proteasome in ES. This new knowledge will sport at the molecular bases of ES in *C. canephora* and can be applied in optimization mass propagation and genetic improvement.

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SUBCELLULAR LOCALIZATION FOR AN RNA BINDING PROTEIN FROM *USTILAGO MAYDIS* IN *NICOTIANA BENTHAMIANA* LEAVES

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Abstract:

In eukaryotic organisms the RNA-binding proteins (RBP) play a crucial role for protecting against biotic and abiotic stresses. The RBP's participates in the formation of a ribonucleoprotein (RNP) complexes involved in gene expression. The *UmRrm75* gene from *Ustilago maydis* encodes a SR/RGG protein that contains three RNA recognition motifs and its mRNA levels are induced under peroxide application as well as extreme temperatures. Furthermore, the deletion of the *UmRrm75* gene in *U. maydis* resulted in sensitivity to oxidative and temperature stress. Heterologous expression is a powerful tool for functional and biochemical analyses of genes isolated from diverse organisms. In this work, we observe the subcellular localization of the UmRrm75GFP construction using confocal microscopy under different stress conditions such as: peroxide, boric acid and high and low temperatures. The heterologous expression of *UmRrm75* gene from the fungus *U. maydis* shows evidence of the different subcellular localization under stress conditions in *Nicotiana benthamiana* leaves.

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EXPRESSION OF TAU PROTEIN, AN ALZHEIMER MARKER, DISRUPTS YEAST MITOCHONDRIAL HOMEOSTASIS

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Abstract:

Tau is a microtubule associated protein which is ubiquitously expressed in the human central nervous system. It is involved in a wide variety of cellular processes that are essential for the correct neuronal function. Aggregation of this protein has been linked to neurodegenerative diseases such as Alzheimer. Despite the intense research carried out to date, the mechanisms involved in the Tau's pathogenesis have not been fully characterized. In humans, it appears that Tau can directly interact with cellular organelles such as mitochondria, altering its physiology. In this study we found that the constitutive expression of the 2N4R Tau isoform in the yeast *Saccharomyces* cerevisiae impairs mitochondrial respiration when glucose or ethanol are used as carbon sources. Tau also induces mitochondrial fragmentation and increases mitophagy upon nitrogen starvation. These observations correlate with the mitochondrial localization of a fraction of the expressed Tau protein. In addition, it appears that Tau moderately activates the retrograde yeast program and the response pathway for aggregated heterologous proteins. Our results suggest that the effects of Tau on the yeast mitochondrial physiology could reflect those occurring in human cells where mitochondrial disfunction has been pinpointed as a factor for the establishment of Alzheimer disease.

This work was supported by CONACyT project CF-58550. Y, C-C is a PhD student of the Biochemical Sciences Program, UNAM and received a PhD fellowship from CONACyT (No: 1007708) and was supported by PAEP, UNAM to attend this meeting.

BAT1 AND BAT2 FUNCTIONAL DIVERSIFICATION: THE ROLE OF SUBCELLULAR LOCALIZATION ON THE FUNCTION OF PARALOGOUS GENES

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Abstract:

Saccharomyces cerevisiae has a facultative metabolism, which enables it to thrive in both oxidative and fermentative conditions. It is believed that a major factor in the development of this facultative metabolism was a Whole Genome Duplication which occurred in its evolutionary history, followed by the selective retention of some gene duplicates that have diversified over time. Most of the retained duplicated genes are related to the central carbon metabolism, among them we found the pair of branched-chain aminotransferase enzymes *Bat1* and *Bat2*. Usage of branched chain amino acids as nitrogen source and the synthesis of branched chain amino acids are functions completed only by these two enzymes. Despite their 77% conserved amino acid identity, these enzymes differ in their localization inside the cell; *Bat1* is a mitochondrial protein while *Bat2* is diffused in the cytosol. Also, previous studies in our lab discovered that *BAT1* and *BAT2* have opposite expression profiles. *BAT1* expression is favored in biosynthetic conditions which require synthesis of branched chain amino acids, accordingly, its expression is repressed in the presence of amino acids. On the other hand, *BAT2* expression is favored in catabolic conditions where branched chain amino acids must be used as nitrogen source. Even though both enzymes are capable of degrading and synthesizing amino acids, their expression profiles are correlated with the direction the aminotransferase reaction takes depending on the availability of substrates. Accumulation of alpha-keto acids in the mitochondria could favor biosynthesis of the amino acids, while accumulation of amino acids in the cytosol could favor their catabolism. Our laboratory took interest in discovering if having *Bat1* and *Bat2* in different cellular compartments give *S. cerevisiae* an advantage over having them in the same cellular compartment. To answer this question, we have constructed a yeast mutant library where we have relocalized *Bat1* and *Bat2* to their opposing cellular compartments in the presence or absence of their paralogue. Relocalization was confirmed by confocal microscopy. In order to study the importance of cellular localization of *Bat1* and *Bat2*, we assessed the functional properties of strains by measuring their growth phenotype in biosynthetic and catabolic conditions in the wild type strain and in mutants in which the enzymes were differentially localized.

FUMARATE REDUCTASE A PUTATIVE COMPONENT IN THE ALTERNATIVE MITOCHONDRIAL RESPIRATORY CHAIN OF *RHODOTORULA MUCILAGINOSA*

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Abstract:

Rhodotorula mucilaginosa is a strictly aerobic yeast widely distributed in environments such as ice glaciers, heavily contaminated waters, soils, food, and skin. *Rhodotorula* expresses a branched respiratory chain (RC) containing alternative NAD$^+$oxido-reductases (both ND2i and ND2e) plus an alternative oxidase (AOX) (P. Castañeda-Tamez et al., this meeting). Additionally, we detected a fumarate reductase (FR) that may be part of the branched RC. Under hypoxia or anaerobiosis, FR catalyzes the reduction of fumarate to succinate allowing Complex I to work in the absence of O_2. Complex-I oxidizes NADH and reduces quinone in a proton pumping reaction, while FR reoxidizes quinol and reduces fumarate, yielding succinate, Thus, FR is a key component of anaerobic respiration constituting the final electron acceptor in the *Rhodotorula* RC. FR has been found among bacteria such as *Helicobacter pylori* and *Escherichia coli* as well as in protozoal parasites such as *Trypanosoma*, *Plasmodium*, and *Leishmania*, and in helminths including *C. elegans*. In isolated mitochondria from *Rhodotorula mucilaginosa* a possible FR was detected by clear-activity PAGE and its identity was confirmed by mass spectroscopy. Its expression/activity increased when growing in the non-fermentative carbon source lactate (YPLac). An enzymatic assay for FR detected Complex-I-FR electron-transfer activity in the presence of the chromosome-blocking agents antimycin-A or cyanide. Currently, we are searching for the expression of the alternative quinone (rhodoquinone or plastoquinone) needed for FR activity. FRD may be an important factor for *Rhodotorula* survival in extreme environments, further strengthening the notion that even though Proton/Electron stoichiometry decreases, branched RCs help cells survive under stressful (extreme) conditions.

ANALYSIS OF THE EFFECT OF INSULIN RESISTANCE ON THE DEGRADATION OF BRANCHED CHAIN AMINO ACIDS

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Abstract:

Insulin resistance (IR) is a condition that leads to the development of type 2 diabetes mellitus (T2DM). Recently, metabolomic studies have associated an increase in the serum levels of branched chain amino acids (BCAA's) (leucine, isoleucine and valine) with the development of IR and T2DM[2,3]. This, together with proteomic and transcriptomic studies, that show a decrease in the expression of the enzymes of the catabolic pathway of BCAA's[4], suggest that alterations in the catabolic pathway could be contributing to the increase un BCAAs in serum. Thus, the aim of the present work is to determine if the presence of insulin resistance impairs the BCAA's catabolic pathway, using a targeted metabolomic approach. For this, we induced IR in male C57BL6 mice fed with a high-fat high-sucrose diet (HFHS) for 19 weeks. During this period, we evaluated the development of IR by determining the intraperitoneal glucose (ipGTT) and insulin (ipITT) tolerance curves, and we performed indirect calorimetry. Then, the mice were sacrificed, and several tissues (WAT, BAT, liver, gastrocnemius, kidney and blood) were collected in order to quantify the BCAA's and some of the metabolites from the catabolic pathway by liquid chromatography coupled to mass spectrometry (LC-MS/MS). We observed reduced glucose and insulin tolerance on the HFHS group when comparing the area under the curve (AUC) calculated from the ipGTT and ipITT of the HFHS group versus a control group fed with AIN-93 diet, demonstrating IR development. Moreover, calculating the respiratory exchange ratio (RER) from the analysis by indirect calorimetry, we found that mice from the HFHS group showed reduced metabolic flexibility, compared with the control group which RER even after the administration of BCAAs, was maintained around 0.7 during all the procedure, implaing that this group preferred the use of fatty acids as energy source even with high sucrose on diet. Moreover, the metabolite analysis showed an increase in serum levels of BCAA's and braches chain ketoacids compared with the AIN-93 group, suggesting that the BCAA catabolic pathway is altered in the presence of insulin resistance. At the moment, we are determining the concentration of the metabolites from the BCAA catabolic pathway in the different isolated tissues in order to evaluate the pathway in one by LC-MS/MS.

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THE RESPIRATORY CHAIN OF *RHODOTORULA MUCILAGINOSA*

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Abstract:

The oleaginous yeast *Rhodotorula mucilaginosa* has been isolated from a wide variety of extreme environments, such as high pressure, high salt concentration, low temperature and heavy metal contamination. Carotenoids and lipids produced by *Rhodotorula* are of great interest to the pharmaceutical, cosmetic and biofuel industries. *R. mucilaginosa* has been tested against different types of stress such as osmotic, oxidative and low temperatures, observing an increase in antioxidant enzyme activity and in the production of carotenoids and lipids. In addition, *R. mucilaginosa* is widely used for bioremediation. Several yeast species react to stress modifying the composition of their branched respiratory chains enduring stress situations better. There are few data on the composition of the respiratory chain in *Rhodotorula*, but a branched chain is suggested by its resistance to antimycin A and cyanide, the inhibitors of complexes III and IV of the respiratory chain. Branching could be useful for survival and tolerance to adverse conditions where *R. mucilaginosa* has been isolated. In addition to the canonical complexes I, II, III and IV the *R. mucilaginosa* respiratory chain expresses two type II NADH dehydrogenases, one internal and one external plus the presence of an alternative oxidase (AOX). In addition, the presence of a fumarate reductase is reported. This enzyme may help *Rhodotorula* survive under hypoxic or anaerobic conditions.

COMPARATIVE ANALYSIS OF THE SECONDARY NUCLEATION MECHANISM BETWEEN OVALBUMIN AND *MORINGA OLEIFERA* SEEDLING AND ITS INHIBITION BY GLUCOSINOLATES

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Abstract:

Protein aggregation is a phenomenon by which proteins, under stress conditions, adopt conformations rich in beta sheet, which favors the formation of amyloid structures, these are present in various types of pathologies (1). Among the factors that favor this phenomenon is electromagnetic radiation, which through limited protein denaturation manages to increase the formation of aggregates, in addition to promoting protein glycation through the Maillard reaction (2). The present study aims to identify the nucleation mechanism during the aggregation phenomenon in the *Moringa oleifera* seedling protein fraction (FPPMO) and its comparison with ovalbumin as aggregation control, in addition, the inhibitory capacity of the aqueous leaf extract of *M. oleifera* on the nucleation mechanism by AmyloFitt. Furthermore, using FoldAmyloid, and DictyOGlyc 1.1, it was determinated 13 amyloidogenic regions and 23 glycation sites for ovalbumin and 28 amyloidogenic regions with 11 glycation sites for maturase k were identified as representative protein of FPPMO. With the help of the CB-dock server, it was determined that the glucosinolates in the extract can bind to different aggregation sites through the glycosidic portion of the molecule. The aggregation model was characterized with the help of a domestic microwave and thioflavin T was used for its quantification. It was determined that both fractions follow a secondary nucleation mechanism, and that the extract has an inhibitory effect on the secondary nucleation mechanism by reducing its constant, without significantly reducing the primary nucleation constant. Our results suggest that the glucosinolates present in the *M. oleifera* leaf aqueous extract inhibit the secondary nucleation mechanism of both protein fractions, through various non-covalent interactions. In conclusion, FPPMO aggregates in a similar way to ovalbumin when irradiated by microwaves and the extract avoids this process in both systems.

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THE PYRUVATE KINASE FROM THE WHITE SHRIMP *LITOPENAEUS VANNAMEI*: GENE STRUCTURE, PROTEIN MODELING AND DEDUCED AMINO ACID SEQUENCE

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Abstract:

Litopenaeus vannamei is the main cultivated shrimp species in the world. In natural and farm environments, this shrimp is exposed to environmental hypoxia stress. One of the strategies adopted by shrimp for survival is the metabolic rate regulation under stress. Pyruvate kinase (PK) catalyzes the last reaction of glycolysis and is an important point in the regulation between glycolysis and gluconeogenesis. Compared to mammals, the information in crustaceans about the *PK gene/s,* isoforms, and regulation in response to hypoxia is poorly studied. In this work we analyzed a pyruvate kinase -PK1- gene from *L. vannamei*. *PK1* produces four transcript variants and four polypeptides with slight differences. The PK1 gene has 10 introns, and the deduced proteins have all the domains necessary to code for functional PK. The PK1 gene contains several cis elements for transcription binding factors (TF) in its promoter sequence that are typically involved in environmental stress responses, including NF-kb, HSF, p300, p53 and FoxO, but the classical HRE (hypoxia response element) recognized by HIF-1 was not found. *PKs* have putative sites for reversible phosphorylation and binding to allosteric effectors. Protein homology modeling proposes a homotetramer with catalytic sites in every monomer and a highly conserved structure compared to other organisms. Analysis of expression in response to hypoxia may link transcript variants and polypeptides to cis elements recognizing TF sites found in the *PK1 gene*.

MOLECULAR AGGREGATES OF β-GLUCOSIDASE ISOFORM II FROM *SECHIUM EDULE*

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Abstract:

Numerous plant-derived proteins have been identified that form high molecular weight aggregates. These aggregates are protein multimers that present a non-homogeneous pattern in electrophoresis; in some cases, aggregates greater than 1200 kDa with activity have been observed. In maize β-glucosidase, the presence of aggregates attributed to β-glucosidase Aggregating Factor (BGAF) has been reported, in other proteins, such as myrosinase (β-thioglucosidase) the participation of Myrosinase Binding Proteins (MBP) is observed in the formation of protein aggregates; both factors present lectin activity with an affinity towards glycosylated proteins. In this study, β-glucosidase II from *S. edule* was purified by the method described by Cruz *et al*., after 7 days of incubation the sample was subjected to dissociative electrophoresis and bands corresponding to high molecular weight aggregates were observed. This sample was subjected to agglutination studies and sugar determination. In native electrophoresis at 4.5%, the protein did not enter the separating gel due to the aggregates generated by the protein; likewise, the enzymatic activity was identified, where the gel was incubated in a solution with substrate p-Nitrophenyl-β-D-glucopyranoside 5 mM for 30 minutes, releasing p-nitrophenol, it was also determined that the aggregates maintain the activity up to 75%. These results reinforce what was previously described. β-glucosidase II from *S. edule* presents aggregating activity with high molecular weight products that maintain its enzymatic activity as described by Cruz et al. We discard BGAF and PMB as factors responsible for aggregation based on the amino acid sequence obtained, we think that this property is attributed to the high content of hydrophobic amino acids identified in the β-glucosidase II from *S. edule.*

Translated with www.DeepL.com/Translator (free version)

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PROTOPLAST ISOLATION AND CHARACTERIZATION FROM *ARGEMONE MEXICANA* L (PAPAVERACEAE)

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Abstract:

Argemone mexicana L. (Papaveraceae), commonly known as chicalote in Mexico and Mexican prickly poppy in the US, is a plant widely used in traditional medicine to treat different diseases such as ophthalmia, scabies and cutaneous affections. These bioactive properties are attributed to the presence of wide variety of benzylisoquinoline alkaloids (BIAs) distributed through the plant tissues, mainly sanguinarine and berberine, from the benzophenanthridine and protoberberine BIA groups, respectively. In mature A. mexicana plants, sanguinarine is restricted to the roots and mature seeds, whereas berberine is found in both roots and aerial tissues (leaves and stems; Vázquez-Flota, et al. 2018). Both alkaloids exhibit important medical and industrial applications. Sanguinarine is included in food supplements for livestock, and berberine functions as an insulin sensitizer. The biosynthesis of BIA is a complex process, generally associated to the structure of the plant tissues involved. These tissues often present specialized cells types, for both alkaloid formation and accumulation. However, little is known about how sanguinarine and berberine are allocated in the chicalote cells. Protoplasts represent a very convenient system to study several cellular processes and activities, including cell wall synthesis, cell division, transient gene expression, among others, since they allow better imaging in comparison to cells forming an integrated tissue. Moreover, isolated protoplasts could also be used for the study of special cell types to investigate their specific features (Yoo, S. D., et al., 2007). In this work, we have developed a protocol for the isolation of protoplasts from different tissues of A. mexicana. Incubation of leaf tissues and cell suspension on a lysis solution containing a mix of cellulase, macerozyme and driselase, resulted in the liberation of protoplasts, which upon observation exhibited morphological differences between them. Combined with the fluorescence properties of the A. mexicana alkaloids, protoplasts will be used as a tool on the study of the specific cell types involved in the accumulation of the benzylisoquinoline alkaloids berberine and sanguinarine in these different plant tissues.

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STEROIDOGENESIS IN JEG-3 CELLS AND PROGESTERONE RECEPTORS

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Abstract:

The mechanism of regulation of progesterone (P4) synthesis in the human placenta is unknown. The presence of P4 receptor (PGRMC1) was identified by mass spectrometry in isolated syncytiotrophoblast mitochondria and JEG-3 cells. In this work, we evaluated the possible regulation of steroidogenesis by a mechanism of inhibition by P4, where high levels of P4 modulate its own synthesis through a receptor-ligand system.

JEG-3 cells incubated in the presence or absence of RU486 (15 uM, P4 antagonist) or P4 (10 nM) were used. At 24, 48 and 72 h of incubation, the synthesis of P4 in the culture medium was determined. In other experiments, the cells were incubated for 24 h with RU486 or P4 and subsequently P4 or RU486 were added and incubated for another 24 h. The P4 in the medium was determined by the Elisa method. The P4 receptors PR and PGRMC1 were identified by western blot.

The amount of P4 in the medium in the presence of RU486 decreased by 20% at 24h, reaching control values at 48 and 72h. With the addition of P4, the hormone in the medium increased by 40%, but a decreased was observed at 24 and 48 h reaching the control value. When JEG-3 cells were first incubated for 24 h with RU486 and then P4 was added for another 24 h, the results showed a 20% increase in hormone production; however, when starting the incubation with P4 followed by the addition of RU486, the quantification of the hormone remained like the control. In all conditions, PGRMC1 and a 60 kDa isoform of PR were identified.

The results show that the inhibitor RU486 has a partial inhibitory effect in the first hours of incubation, followed by a recovery of steroidogenic activity. An unexpected result was the P4 decreased in the incubation media through time, with a value close to the control. This result suggests that the hormone is being metabolized into other steroids such as androstenedione or estradiol (preliminary data). Incubation of RU486 followed by P4 increased the P4 production by 20%, which was not observed when the protocol was reversed; suggesting the activation of at least two signaling systems, which together with the P4 receptors could be modulating the cellular steroidogenesis.

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EZRIN ROLE IN CLAUDIN-9 TRANSFECTED AGS CELLS MIGRATION

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Abstract:

Gastric cancer is the fifth most common cancer worldwide and its high mortality rate is due to retarded diagnosis. An evident change during the progression of cancer cells is their modification of the cell structure that includes alterations in their permeability and cell polarity both of which are regulated by claudins, major components of the tight junction structure. Modified claudin expression in gastric cancer epithelia is related with poor prognosis, metastatic potential and tumor recurrence. Claudin-6 or claudin-9 isoforms are abnormally expressed in the AGS cancer cell line conferring them with a higher migration and invasion capacity. Ezrin, an actin linker protein that participate in cellular migration and epithelial-mesenchymal transition, is also deregulated in epithelial cancers. Its cellular relocation from cytoplasm to the perinuclear region and into the newly formed filopodia correlates with poor prognosis. The aim of this study was to assess if Ezrin increased expression in gastric cancer is regulated by claudin 6 or 9. Ezrin expression was evaluated in IL-8 stimulated transfected Cldn-6 and -9 AGS cells; its expression was evaluated by western blot and confocal immunofluorescence, whereas cell migration and invasion by cell wound healing and transwell migration assays. The results with AGS-cldn-9 cells showed that Ezrin expression was significantly increased and that there was an enhanced membrane redistribution in the newly formed filopodia. This suggests that claudin-9 regulates the expression and redistribution of Ezrin favoring cellular migration. More studies are needed to elucidate the signaling pathway involved

Keywords: Gastric cancer, Ezrin, Claudin-9, EMT, filopodia.

THE RISK HAPLOTYPE ASSOCIATED TO TYPE 2 DIABETES IN THE SLC16A11 TRANSPORTER INDUCES CHANGES IN ITS EXPRESSION

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Abstract:

Diabetes has become a global health problem, and Mexico occupies the 6th position with a frequency of 14.1 million people with this disease1. The heritability of diabetes ranges from 25% to 80%1, so the genetic component plays an important role. In 20142, a risk haplotype was identified that explains ~20% of the increase in the prevalence of type 2 diabetes (T2D) in Mexico. This risk haplotype contains 5 single nucleotide polymorphisms (SNPs) located in the coding region of the SLC16A11 gene. This gene encodes for the monocarboxylate transporter (MCT11) and is expressed in liver, salivary glands and thyroid3. Despite the importance of this transporter, the physiological function of MCT11 and its relationship to T2D remains unclear. Previously it has been reported that changes in the expression of the transporter are related to changes in the metabolism of lipids and fatty acids that are associated with T2D3,4, however, the mechanism by which this alteration occurs is unknown. For this, we transiently expressed the wild type of transporter (SLC16A11) and the risk variant (SLC16A11DT2) in the human embryonic kidney cell line HEK293 and in the mouse hepatocyte cell line AML12. Interestingly, we observed that in HEK293 cells, the SLC16A11DT2 expression was 40% lower compared to its control. Besides, a higher effect of the presence of the risk haplotype was observed in AML12 cells where the SLC16A11DT2 expressed 73% less compared to the control. To investigate whether these changes in expression alter the location of the transporter and its variant, we have the perspective of performing indirect immunofluorescence assays.

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BIOCHEMICAL CHARACTERIZATION OF A GLYCOSYLTRANSFERASE FROM *NICOTIANA TABACUM*

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Abstract:

Plant UDP-glycosyltransferases (UGTs) play an important role in the metabolism of xenobiotic compounds and influence the reactivity and solubility of the corresponding aglycones. In this work, we carry out the biochemical characterization of a glycosyltransferase from Nicotiana tabacum NtUGT89A2. The NtUGT89A2 protein was cloned into the pET28 vector for heterologous expression in *E. coli* pLysS cells, followed by purification in three steps: nickel affinity purification, ion exchange purification, and size exclusion purification. We optimized the composition of the purification buffer (50 mM Tris-HCl pH7, 400 mM NaCl), through a thermal stability experiment, resulting in a two-fold increased protein yield compared to non-optimized conditions. Another important finding was that the thermal stability of the protein increased in the presence of UDP-glucose and 2,5 dihydroxybenzoic acid. Dynamic light scattering analysis showed that the NtUGT89A2 protein is found as a monomer in solution with an aggregation temperature of 44 °C. Furthermore, the NtUGT89A2 protein was shown to be active after each purification step. Our results illustrate that the NtUGT89A2 protein is a glycosyltransferase that uses UDP-glucose as the sugar donor substrate and benzoate derivatives as the acceptor substrate.

CHARACTERIZING THE STRUCTURAL SENSITIVITY OF PLANT INTRINSICALLY DISORDERED REGIONS *IN VIVO*

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Abstract:

Intrinsically disordered regions (IDRs) are ubiquitous in all domains of life. While the disordered character of IDRs has been vastly predicted in eukaryotic proteomes, their functional role and regulation in plants are just starting to unveil. Only a small group of plant IDRs have been characterized *in silico* and *in vitro*. These approaches suggest that changes in the physicochemical properties of the environment impact the structure of IDRs, which might, in turn, regulate their function. However, a comprehensive characterization of the structural sensitivity of plant IDRs to changes in the physicochemical environment in a cellular context is currently lacking. Here, we performed bioinformatic analyses to predict environmentally induced conformational changes of different plant IDRs. To characterize the structural sensitivity of plant IDRs in living yeast cells, we fused the open reading frames of a selected group of plant IDRs in between the coding sequences of a Forster Resonance Energy Transfer (FRET) system. Yeast cells expressing the different constructs were subjected to hyperosmotic changes using different osmolytes. The work presented here will contribute to a better understanding of how changes in the environment during stress conditions regulate the structure and function of plant IDRs.

FOLDING AND EVOLUTION OF A REPEAT PROTEIN ON THE RIBOSOME

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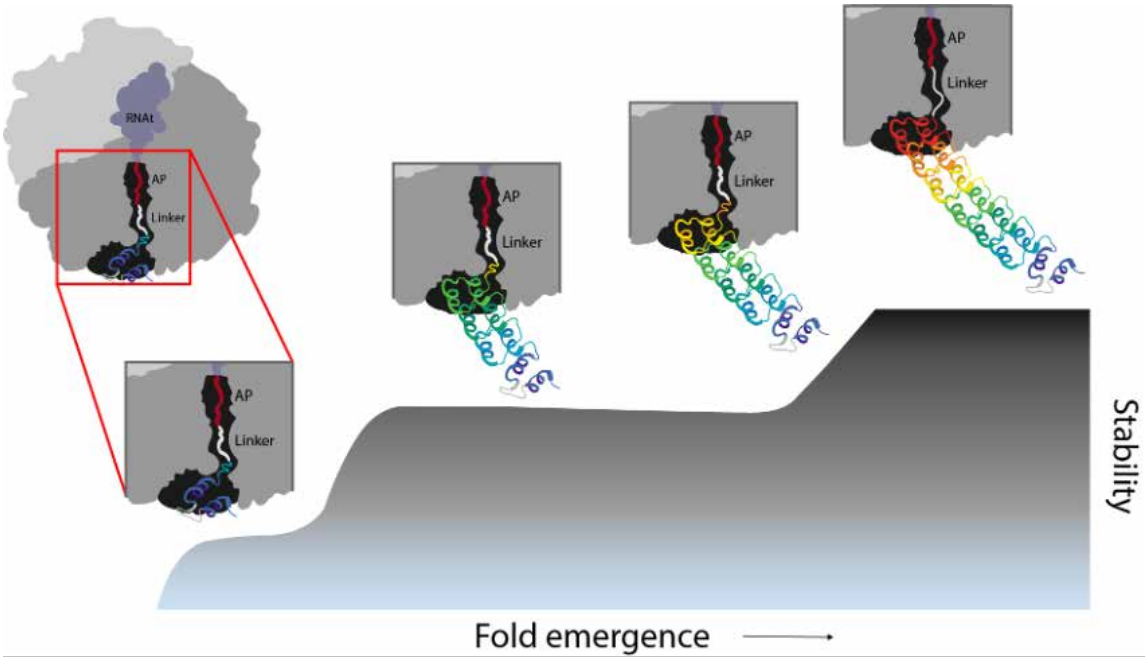
Abstract:

Life on earth is the result of the work of proteins, the cellular nanomachines that fold into elaborated 3D structures to perform their functions. The ribosome synthesizes all the proteins of the biosphere, and many of them begin to fold during translation in a process known as cotranslational folding. In this work we discuss current advances of this field and provide computational and experimental data that highlight the role of ribosome in the evolution of protein structures. First, we used the sequence of the Ankyrin domain from the Drosophila Notch receptor to launch a deep sequence-based search. With this strategy, we found a conserved 33-residue motif shared by different protein folds. Then, to see how the vectorial addition of the motif would generate a full structure we measured the folding on the ribosome of the Ankyrin repeat protein. Not only the on-ribosome folding data is in full agreement with classical in vitro biophysical measurements but also it provides experimental evidence on how folded proteins could have evolved by duplication and fusion of smaller fragments in the RNA world. Overall, we discuss how the ribosomal exit tunnel could be conceptualized as an active site that is under evolutionary pressure to influence protein folding.



PROTEOMIC APPROACH IN COCONUT FRUIT RIPENIG: AN INSIGHT IN AMINO ACID METABOLISM

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The value of coconut three (*Cocos nucifera* L.) and its by-products has gained importance over the centuries, which implies it is used in the manufacture of brushes, ropes, mattress padding and among others. With a coconut fruit production of 60.77 million metric tons per year, the coconut fruit has greatly helped farmers to sustain their staple food, water, and economic sources. Amino acids represent the smallest part of the protein structure; therefore, the composition of amino acids determines the quality of a protein. Coconut proteins contain between 71 to 77% essential amino acids. Amino acids are crucial for the flavor of coconut fruits and also in their embryogenic processes. In order to identify the behavior of proteins related with amino acid metabolism, the proteome of solid endosperm from the immature, intermediate and mature stages from fruits of the green dwarf variety, were studied by high-scale proteomics and tandem mass tag (TMT). 379 proteins were identified, of which 54 were associated to the metabolism of amino acids. This data set represents an insight to proteins contributing to the amino acid metabolism pathways, and enzymes that may be key to the regulation of coconut fruit maturation. An isoenzyme 2 of catalase is a unique protein of the mature stage; while the others were shared between the three stages of maturation. The results of this study can help to understand the mechanism that regulates amino acid metabolism in coconut fruit

EFFECT OF HEAT STRESS ON SEEDS OF TOLERANT AND SUSCEPTIBLE GENOTYPES OF WHEAT (*TRITICUM AESTIVUM*) GROWN IN THE YAQUI VALLEY

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Abstract:

Heat stress affects the development of cereals. The grain-filling stage is sensitive to high temperatures, which decreases the nutrient content in the seeds, this is reflected in seed germination, viability and seedling establishment. Heat stress affects starch synthesizing enzymes, mainly ADP-glucose pyrophosphorylase (AGPase), reducing the content of starch and sucrose in the endosperm of grains. In this work we evaluate the effect of heat stress on wheat seeds from stress-tolerant and stress-susceptible plants. The seeds were obtained from plants sown in three different months: December 2020 (control), January 2021 (LHS) and September 2021 (EHS). Seed germination, vigor and development were monitored, as well as seedling viability and establishment. The starch content of the seeds was measured through the method of Liu, et. al (2011). There were differences between genotypes and month of sown. EHS was the stage with a mayor impact in all the examinated genotypes. The LHS did not show differences with the control group. The genotypes with the highest percentage of germination, vigor, viability, establishment and leaf area, in LHS and EHS were G04, G06 and G13. This indicates that heat stress has an effect in all the parametres analysed.

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KINETIC CHARACTERIZATION OF RESPIRASOMES FROM *DEBARYOMYCES HANSENII*

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Abstract:

Inside the internal mitochondrial membrane, the respiratory complexes could associate into structures called "supercomplexes" which has different stoichiometries. Respirasomes are a type of supercomplexes which has capacity of oxidized the NADH and transfer electrons to oxygen, reducing it into water through complex IV. Simultaneously this process translocates protons from the matrix to the intermembranal space generating a proton motriz force which used the complex V for the ATP synthesis. It has been shown that the interaction between the complexes that form the respirasomes increases their activity and affinity for substrates, also reduces the production of reactive oxygen species (ROS, Reyes-Galindo, M., et al., 2019). Additionally, the regulation of respirasomal NADH:DBQ oxidoreductase activity by the functional communication between complexes I:IV and I:III_2 has been identified. *D. hansenii* is an ascomycete whose halophilic yeast also contains the classic complexes of the respiratory chain, in addition to a cyanide-insensitive alternative oxidase (AOX) and two alternative rotenone-insensitive NADH oxidoreductases. Respiratory complexes have been found in respirasomes with different stoichiometries (Cabrera-Orefice, A., et al., 2014). *D. hansenii* has great importance in the food industry; therefore, it is of interest to study the behavior of the organelles under these conditions, especially the mitochondria and the elements of the electron transport chain. Similarly, it has been seen that under hyperosmolarity conditions, AOX is overexpressed, which suggests a role in the alternate flow of electrons and thus prevent the production of ROS (Garcia-Neto, W., et al., 2017). *D. hansenii* was harvested in YPD medium and for the mitochondria isolation we used the enzymatic method. Briefly, the cells were isolated by differential centrifugation, incubated for one hour with lytic enzymes Zymolyase 20T, then homogenized with a Potter, after centrifuging at 4,667 g the supernatant was recovered and centrifuged at 17,226 g to obtain mitochondria. The supercomplexes and complexes solubilization curve with digitonin showed that the ideal ratio was 3 mg digitonin:1 mg protein; then we made a continuous sucrose gradients in order to isolated the respirasomes. The BN-PAGE analysis of the gradient-fractions showed that respirasomes were located at the bottom of the gradient, while free-complex I was at the middle. These fractions were used for the spectrophotometric characterization of the NADH:DBQ oxidoreductase of the respirasome and free-complex I.

This work is supported by PAPIIT (IN206320) from Universidad Nacional Autónoma de México (UNAM); CONACyT México (87160); MEXUS-CONACyT (CN-20-327). GGC is a PhD student of the Posgrado en Ciencias Biomédicas (312173726) and has a CONACyT scholarship (1103534).

ACUTE HYPOXIA EFFECTS ON MMPS ENZYMATIC ACTIVITY AND EXPRESSION IN LUNG ADENOCARCINOMA AND SQUAMOUS CARCINOMA CELLS

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The objective of the present work was to determine the hypoxia effects on MMPs expression and enzymatic activity in different histologic types of lung cancer cells using acute hypoxia models.

Material and methods: Lung adenocarcinoma (A549, A427, SKLU-1), and squamous carcinoma (Calu-1, SKMES-1) cells were cultured under hypoxic conditions (1% O2) for 6 h and 12 h. Cells that remained in normoxia for each period were considered as controls. After cell incubation, culture medium was taken and MMP- 2 and MMP-9 enzymatic activity was evaluated by zymography and protein expression was assessed by Western Blot. Blotting bands were analyzed by densitometry and results expressed in densitometry units (D.U.).

Results: MMP-2 and MMP-9 enzymatic activity decreased in almost cell lines in hypoxic conditions at 6 h with an increase in some cell lines at 12 h.

MMP-2 and MMP-9 protein expression was different among the examined lung cancer cell lines in normoxia and hypoxia conditions. The highest intensity for the proMMP-2 band was observed in CALU-1 in all conditions examined. ProMMP-2 expression increased in A427, A549 and CALU-1 and decreased in SKMES-1 and SKLU-1 in hypoxic conditions in 6 h. No significant differences were detected in the proMMP-2 expression in A549, SKMES-1 and SKLU-1 at 12 h. The aMMP-2 (active form) was detected in all cells and the highest values were found in CALU-1 in all conditions. Differences between normoxia and hypoxia were observed in SKMES-1, CALU-1 and SKLU-1 at 6 h and among A549, SKMES and SKLU at 12 h. The MMP-9 blotting analysis demonstrated an increase in proMMP-9 (25946.91 ± 3416.7 D.U.) in normoxia compared to hypoxic conditions (56774.9 ± 7566.6 D.U.) at 6 h in A427 cells. ProMMP-9 was augmented in almost all the cells when cells were cultured in a hypoxic environment at 12 h. The aMMP-9 increased in A549 cells in hypoxia (15311.8 ± 2887.8) compared to normoxia (9123.03 ± 1354.02 D.U.) conditions at 6 h. An increment in aMMP-9 was also determined at 12 h (normoxia = 11468.1 ± 2445.6 D.U.; hypoxia = 71570.5 ± 7661.3 D.U.) in A549 cells. No significant differences were observed in the other cell lines. Conclusions: The early effects of hypoxia on MMP-2 and MMP-9 enzymatic activity and protein expression differ among distinct histologic types of lung cancer. These effects are different when cells are exposed to hypoxia at 6h and 12h.

TRANSCRIPTIONAL REGULATION OF GLUTAMATE RECEPTORS IN HABANERO PEPPER PLANTS UNDER NACL STRESS CONDITIONS

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Abstract:

Plant glutamate receptors (GLRs) are a family of transmembrane proteins that were first identified in 1998 in *A*rabidopsis thaliana. Since then great efforts have been made to define the biological function that these proteins have at the organismal level. Until now, the experimental results demonstrate its role in reproductive development, in calcium homeostasis, in the defense response, in the carbon-nitrogen balance, in the response to salt stress, among many other functions. In the response to saline stress, the experimental results allow us to observe that some members of the GLRs family of *A*. thaliana exert a positive effect in the response to NaCl stress. These findings continue to increase knowledge about the mechanisms that the plant exerts when it is under NaCl stress conditions, and is of interest because salinity is a rapidly advancing problem in soils destined for cultivation. The current consequences caused by salinity are the decrease in the production of many crops and in some cases it can lead to total loss when the salinity is severe.

This project addresses the problem of salinity through the study of a family of proteins that initially shows an important role in the strategy of plants to respond to salt stress. The focus is to know how this family of GLRs is transcriptionally regulated under stress conditions by NaCl in a species of economic importance such as habanero pepper. The results obtained allow us to suggest the relationships of some members with the response to NaCl stress and give the opportunity to select such members for studies on how they work molecularly.

KINETICS OF THE ENZYME ARGININE KINASE FROM TICKS (RHIPICEPHALUS SANGUINEUS) VECTOR OF ROCKY MOUNTAIN SPOTTER FEVER (RMSF)

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Abstract:

Studies of substrate-induced conformational changes are crucial to understanding enzyme function, kinetics and inhibition-based drugs. First it is needed to determine experimentally or propose a set of spatial coordinates for the atoms that comprise the enzyme. The arginine kinase (AK) (EC 2.7.3.2) is a crucial enzyme from energetic metabolism from invertebrates, this catalyzes the reversible reaction of the la formation of phosfagen, phosfoarginine. When an organism requires a rapid energy source, ATP can be rapidly synthesized from phosphagens with the reversible reaction from AK and cellular homeostasis is maintain. Biochemically, AK catalyzes the reversible transfer of a phosphate group from phosphoarginine to adenosine diphosphate (ADP), generating adenosine triphosphate (ATP) and arginine.

The ticks infected with the pathogen bacteria *Rickettsia rickettsia*, are the vector of the disease Rocky Mountain spotter fever (RMSF) a deadly disease in America and is an important health problem in Sonora Mexico. To complete its life cycle ticks feeds exclusively of domestic dogs' blood are highly adapted to indoor living but also survive outdoors. Here we report the crystal structure of arginine kinase from *Rhipiceohalus sanguineus* (RsAK) in an open conformation and a model from closed conformation. The Michaelis-Menten kinetics constant was obtained for both substrates ATP and arginine. The kinetics results and structure were compared with other invertebrates' species to understand metabolic process and physiology from ticks *Rhipiceohalus sanguineus*.

N-NITROSODIMETHYLAMINE REGULATES CLAUDIN EXPRESSION AND INVASIVENESS IN GASTRIC CANCER CELLS

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Abstract:

In 2020 gastric cancer was the fifth cause of death worldwide (GLOBOCAN). The exposition to N-nitrosamines specially NDMA, classified as a type 1 carcinogenic agent, is one of the risk factors associated to gastric cancer. NDMA exposition can be exogenic (processed foods) or endogenic (derived from nitrates and nitrites present in processed foods). NDMA is metabolized by CYP 2E1 generating ROS and other carcinogenic metabolites, thus inducing changes that favor cellular migration and the expression of epithelial mesenchymal transition markers.

Alterations of the epithelial tight junctions, specifically claudins, induce changes that supports their metastatic and invasiveness capacity that is normally associated with a worst prognosis. Claudins 1, 2, 4 and 6 expression is regulated by transcription factors like Stat3 and ERK1/2 in response to inflammation processes. So far, the effect of NDMA on claudins is unknown. The aim of this work was to determine the consequences of NDMA exposition on claudin expression and regulation. **Methodology**: AGS cells were exposed to different concentrations of NDMA (0, 5, 10 and 250 µg/ml) for 24 and 48 hours. Claudin-1, -2, -4, -6 expression was evaluated by western blot and immunofluorescence microscopy, CYP2E1 by western blot and its activity by ROS colorimetric assays. The phosphorylation of Stat3 and ERK 1/2 was evaluated by western blot whereas pro inflammatory cytokines mRNA levels was evaluated through RT-PCR. Cell migration and invasion were evaluated by wound healing and invasion assays. **Results:** NDMA induced an increase of claudins 1, 2, 4, 6 after 24 and at 48 hours exposure. Claudin 1 and 6 were mainly localized in the cytoplasm. The level of CYP2E1 and ROS was increased on cells exposed to NDMA for 24 and 48 hours. NDMA induced the activation of Stat3 and ERK1/2. NDMA increased the amount of IL-1β, IL-8 and TNF-α mRNA. An increase in migration and cellular invasion induced by NDMA was also observed. Conclusions: NDMA induces the expression of claudins associated to gastric cancer progression through Stat3 and ERK activation in response to inflammatory cytokines and enhanced ROS production.

RTG1 AND ITS POSSIBLE ROLE IN THE FORMATION OF THE NRG1-RTG3-ALA HYBRID COMPLEX IN THE YEAST *SACCHAROMYCES CEREVISIAE*

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Abstract:

The yeast *Saccharomyces cerevisiae* duplicated its whole genome (WGD), after an allopolyploidization event, which involved mating between two different ancestral yeast species. A large number of the paralogous genes conserved by *S. cerevisiae* encode for enzymes involved in carbon or nitrogen metabolism. It has been proposed that selective retention of paralogous genes facilitated the acquisition of a facultative, predominantly fermentative metabolism. The regulation of nitrogen metabolism in *S. cerevisiae* involves a set of interconnected processes. Previous results from our laboratory have confirmed that *ALT1* encodes for an alanine transaminase located in the mitochondria, while *Alt2* is cytoplasmic and, to date, we do not know what its function is even though *ALT1* and *ALT2* share 67% identity. Our group has also discovered that the expression profile of *ALT1* and *ALT2* is opposite; *ALT1* is induced in the presence of alanine when compared to ammonium, *ALT2* is repressed in the presence of alanine and expressed in ammonium. Furthermore, Nrg1 and Rtg3 do not affect *ALT1* expression, while repressing that of *ALT2*. Previous experiments from our group confirmed that Nrg1 and Rtg3 are part of a hybrid regulator which represses *ALT2* expression using alanine as corepressor. The known function for NRG1 is that it determines the repression of genes negatively regulated by glucose; this implies that Nrg1 recruits remodeling proteins such as the Ssn6-Tup1 complex. In turn, Tup1 interacts with Hda1, a histone deacetylase. Rtg3 is a positive regulator of the retrograde response. Rtg1 and Rtg3 form a dimer located in the cytoplasm. Activation of the retrograde pathway depends on the relocalization of Rtg1-Rtg3 to the nucleus via the phosphatase Rtg2, which dephosphorylates Rtg3. To examine whether Rtg1 is involved in the formation of the Nrg1-Rtg3 hybrid, the mutant rtg1Δ was constructed and, in conjunction with hda1Δ and tup1Δ, we sought to study its possible interaction with the Nrg1-Rtg3 hybrid. After learning the phenotype of the nrg1Δ, rtg1Δ, rtg3Δ, rtg3Δ, hda1Δ and tup1Δ mutants, as well as their partial or complete dependence on amino acids such as glutamic acid, we determined the phenotypes of the mutants when grown under fermentative or respiratory conditions. Our results suggest Nrg1 and Rtg3 play an important role in respiratory metabolism.

STRUCTURAL CHARACTERIZATION OF THE LID OF LIPASE 2 OF PSEUDOMONAS ALCALIGENES

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Abstract:

In recent years, the genome of microorganisms from various habitats, such as industrial waste areas, areas rich in vegetable oils or in soils contaminated with oil. has been analyzed. This has allowed us to identify enzymes with functions that offer enormous potential for various applications in the industrial sector, from catalysis to remediation. Much of this knowledge has been leveled by bacteria of thegenus Pseudomonas, since their metabolic versatility has been involved in a large number of biotechnological applications.

Lipases catalyze the hydrolysis of triacylglycerides whose products are fatty acids and glycerol. These enzymes have a catalytic triad consisting of a serine. an acid residue (glutamic acid or aspartic acid) and a histidine. In addition. lipases have a preserved structure known as a lid. This lid is a mobile element that discovers the active site.

It has been observed that lipase 2 (lip2) of *Pseudomonas alcaligenes* has a sequence identity of 48a with the lipase of P. auroginosa, while the region of the lid has high identity with lids described in other halophilic or psychrophilic bacteria such as *Marinobacter mobilis*, *Oleiphilus messinensis*. *Oleispira antartica* or *Hahellaceae bacterium*. which makes it different from other lipases described until now.

The lip 2 gene of P. alcaligenes was cloned into the Pet 28a vector and was expressed in Escherichia coli BI 21 cells in order to obtain a crystallographic structure that allows us to describe and characterize the possible structural changes of the enzyme, as well as the possible implications of these changes in the stability and catalysis of lip 2 of *P. alcaligenes*.

EFFECT OF GLYCOLYSIS INHIBITION ON MITOCHONDRIAL FUNCTION IN HUMAN GLIOBLASTOMA CELLS

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Introduction. Proliferating glioblastoma (GBM) cells exhibit increased cytoplasmic glycolysis compared to quiescent GBM cells; the last depend more on oxidative phosphorylation. Also, GBM has increased glycolysis and decreased mitochondrial function in the presence of oxygen (Warburg effect). As mitochondria are a focal point of cell death signaling, we explored the mitochondria' response to glycolysis inhibition in proliferating and quiescent GBM cells.

Hypothesis. Inhibition of glycolysis in human GBM cells will increase mitochondrial function and induce the expression of mitochondrial proteins involved in oxidative metabolism.

Objective. To evaluate the effect of glycolytic inhibition on mitochondrial function, protein expression and superoxide anion ($O_2^{\bullet-}$) production in human proliferating and quiescent GBM.

Methodology. Human GBM cells (DBTRG-05MG) were grown in RPMI + 10% FBS. For experimentation, a) proliferating cells, cultured with RPMI + 10% FBS, and b) quiescent cells, cultured with RPMI + 1% FBS, were used. We treated cells with 0-100 µM iodoacetate (IAA) for 30 min, and 24 h later measured cell viability, mitochondrial $O_2^{\bullet-}$ production, expression of mitochondrial proteins (transport electron chain, VDAC, and frataxin), the capacity of ATP synthesis and the activity of mitochondrial complexes.

Results. IAA induced cell death in a concentration-dependent manner, with the effect being more pronounced on proliferating than in quiescent GBM cells. Furthermore, this death is associated with early mitochondrial $O_2^{\bullet-}$ production and the increase in frataxin expression.

Conclusion. Continued research on mitochondrial metabolic reprogramming and its role in maintaining cell homeostasis will be crucial for identifying future cancer therapies.

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PRIMING MYCOBACTERIAL ESX-SECRETED PROTEIN B TO FORM A CHANNEL-LIKE STRUCTURE

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Abstract:

ESX-1 is a major virulence factor of *Mycobacterium tuberculosis*, a secretion machinery directly involved in the survival of the microorganism from the immune system defence (van der Wel *et al.*, 2007). It disrupts the phagosome membrane of the host cell through a contact-dependent mechanism. Recently, the structure of the inner-membrane core complex of the homologous ESX-3 and ESX-5 was resolved; however, the elements involved in the secretion through the outer membrane or those acting on the host cell membrane are unknown (Bunduc *et al.*, 2021). Protein substrates might form this missing element. Here, we describe the oligomerisation process of the ESX-1 substrate EspB, which occurs upon cleavage of its C-terminal region and is favoured by an acidic environment. Cryo-electron microscopy data showed that quaternary structure of EspB is conserved across species, except for the non-pathogenic *M. smegmatis*. EspB assembles into a channel with dimensions and characteristics suitable for the transit of ESX-1 substrates, as shown by the presence of another EspB trapped within. Our results provide insight into the structure and assembly of EspB and suggests a possible function as a structural element of ESX-1 (Gijsbers *et al.*, 2021).

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IDENTIFICATION AND IN SILICO CHARACTERIZATION OF NOVEL HELICOBACTER PYLORI GLUCOSE-6-PHOSPHATE DEHYDROGENASE INHIBITORS

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Abstract:

Helicobacter pylori is a pathogen that can remain in the stomach of an infected person for their entire life. As a result, this leads to the development of severe gastric diseases such as gastric cancer. In addition, current therapies have several problems including antibiotics resistance. Therefore, new practical options to eliminate this bacterium, and its induced affections, are required to avoid morbidity and mortality worldwide. One strategy in the search for new drugs is to detect compounds that inhibit a limiting step in a central metabolic pathway of the pathogen of interest. In this work, we tested 55 compounds to gain insights into their possible use as new inhibitory drugs of *H. pylori* glucose-6-phosphate dehydrogenase (*Hp*G6PD) activity. The compounds YGC-1; MGD-1, MGD-2; TDA-1; and JMM-3 with their respective scaffold 1,3- thiazolidine-2,4-dione; 1H-benzimidazole; 1,3-benzoxazole, morpholine, and biphenylcarbonitrile showed the best inhibitory activity (IC50 = 310, 465, 340, 204 and 304 µM, respectively). We then modeled the HpG6PD protein by homology modeling to conduct an in silico study of the chemical compounds and discovers its possible interactions with the *Hp*G6PD enzyme. We found that compounds can be internalized at the $NADP^+$ catalytic binding site. Hence, they probably exert a competitive inhibitory effect with $NADP^+$ and a non-competitive or uncompetitive effect with G6P, that of the compounds binding far from the enzyme's active site. Based on these findings, the tested compounds inhibiting *Hp*G6PD represent promising novel drug candidates against *H. pylori*.

METABOLOMIC ANALYSIS OF LIQUID ENDOSPERM OF *COCOS NUCIFERA* L. IN THREE STAGES OF MATURATION

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Cocos nucifera L. is the most cultivated palm tree in the world. It is used to obtain both food and raw materials. The most important product is the fruit, from which the liquid endosperm (coconut water) containing high levels of sugars, amino acids and other molecules of nutritional value is extracted. Most of the metabolomics studies conducted on coconut so far have focused on the determination of the fatty acid content of coconut oil and the shelf life of coconut water. Despite the economic importance of this species, the maturation of the coconut is a complex biological process scarcely studied from the metabolic approach; the biochemical changes occurring during fruit maturation are poorly understood. In this study, the liquid endosperms of coconut fruits at three ripening stages were analyzed through a non-targeted metabolomics approach using Ultra High-Performance Liquid Chromatography-Mass Spectrometry (UPLC-MS). A total of 591 m/z signals were detected and classified into 21 categories according to their chemical properties. The principal component analysis (PCA) showed segregation among the samples according to their stage of maturation. Most of the metabolites detected were related to the metabolism of carbohydrates and carboxylic acids. Pathway enrichment analysis showed that carbohydrate metabolism and fatty acid synthesis were the most represented pathways during ripening, followed by those involved in the metabolism of amino acids such as leucine, arginine, and threonine, as well as those acting in the synthesis of phenolic compounds, phytohormones and other secondary metabolites. These results present a first look at the metabolomic profiles of coconut fruit at different stages of maturation.

THE MEAN HYDROPHOBICITY OF OXPHOS PROTEINS IS THE LIMITING FACTOR FOR THE ALLOTOPIC EXPRESSION OF MITOCHONDRIAL GENES

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Allotopic expression involves the transfer of a mitochondrial gene to the nucleus, so its corresponding protein product is internalized into mitochondria and functionally assembled with the correct topology in its proper mitochondrial compartment. It is a promising strategy to develop treatments for mitochondrial-related diseases. We suggest that three main constraints limit the allotopic expression of OXPHOS components: i) the final, functional topology of each membrane-bound OXPHOS subunit; ii) the defined mechanism by which each of the two import complexes of the inner mitochondrial membrane (IMM), i.e., how TIM23 and TIM22, translocate and sort cytosol-synthesized precursors; iii) the mean hydrophobicity (mH) of the transmembrane stretches (TMSs) present in proteins that are destined to the IMM. Using the biological hydrophobicity scale, we assign a mH value and define a "traffic light" color for all TMSs of membrane embedded OXPHOS proteins and predict if they are amenable to be functionally internalized into mitochondria or not. We argue that, because of the mechanistic constraints imposed by the TIM23 and TIM22, it is difficult, if not impossible, for some cytosol synthesized OXPHOS proteins, mainly Cytb, Cox1, Nd1, Nd2, Nd4, Nd5 and Nd6, to reach their final, functional topology. We argue that the design of precursors for allotopic expression must make allowance for mH minimization of highly hydrophobic TMSs.

PROTEOMIC ANALYSIS OF COCONUT ZYGOTIC EMBRYOS AT THREE DIFFERENT STAGES OF DEVELOPMENT

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Abstract:

The coconut palm (*Cocos nucifera* L.) is an oleaginous plant, whose fruit mainly accumulate sugars at immature stages and fatty acids at mature stage. Little is known about the biochemical and molecular mechanisms that govern this behavior (Islas-Flores & Tzec-Simá, 2021). Moreover, the coconut zygotic embryo develops embedded in the solid endosperm. However, it is unclear how the embryo integrates and coordinates their own metabolism with the regulation occurring during the ripening of coconut solid endosperm. This study aims to contribute to the basic knowledge regarding the metabolic regulation that governs the carbohydrate and fatty acid metabolism during zygotic embryo development, in this work, embryos at immature, intermediate and mature stages were obtained from coconut fruits of "Green Dwarf" variety. Protein extraction from the embryos and its analysis in 12% SDS-PAGE gels, showed diverse polypeptide profiles at the different stages. On the other hand, high throughput proteomics analysis using Tandem Mass Tag (TMT) labeling in proteins extracted from zygotic embryos evidenced 541 proteins associated with the immature and intermediate stages, while 540 were in the mature stage. The proteome is different in immature stage compared with intermediate and mature stages. 35% of proteins were involved in metabolic pathways, 10% belongs to carbon metabolism and 2% belong to fatty acid metabolism. Together, results contribute to the global knowledge of the proteomics and metabolism occurring during the development of the coconut zygotic embryo in this recalcitrant and oleaginous plant.

Islas-Flores, I., & Tzec-Simá, M. (2021). Research opportunities on the coconut (*Cocos nucifera* L.) using new technologies. South African Journal of Botany, 141, 414–420. https://doi.org/10.1016/j.sajb.2021.05.030

THE HAP2-3-5-GLN3 HYBRID TRANSCRIPTIONAL COMPLEX: IDENTIFICATION OF ITS ORGANIZATION AND THE GENE CIRCUIT UNDER YOUR CONTROL

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Abstract:

The *S. cerevisiae* transcriptional response to different physiological conditions depends on a repertoire of modulators that decode the information described in the promoters. These regulators are containing two domains: the DNA-binding domain and the activation domain, which can be found in a single polypeptide or in different polypeptides. In yeast, both the DNA-binding and activation domains are present in a single polypeptide. However, there is one exception: the HAP complex, constituted by four polypeptides: Hap2, Hap3, Hap5 which constitute the DNA-binding domain and Hap4 which is the activation domain. Nevertheless, in 19891 it was proposed that yeast could form hybrid transcriptional modulators by creating complexes as Hap2-3-5 (DNA-binding domain) and X (an activation domain which is not Hap4). This new regulator Hap2-3-5-X would elicit a unique response different from that generated by the Hap2-3-5-4 complex. In 2011, our research group discovered the first hybrid modulator consisting of members of the Hap complex binding domain and a foreign factor: Hap2-3-5-Gln3, which had a novel transcriptional role absent in both transcriptional modulators when these work independently[2]. The aim of this study is to determine the organization, targeted gene network, physiologic role and the chromatin interaction of the hybrid transcriptional modulator Hap-2-3-5-Gln3, comparing its properties with those of the native regulators that form it (Hap complex and Gln3). The methodology employed includes techniques such as: Next Generation Sequencing (RNA-seq), Coinmunoprecipitation (CoIP), proteomics and Nucleosome Scanning Assay (NuSA). So far, we are working on the analysis of the interaction of the proteins that make up the complex in presence of repressivew (glutamine) and non-repressive (proline) nitrogen sources; given that the expression of Gln3 is regulated by the quality of the nitrogen source, it is expected that in proline, due to it being a non-repressive nitrogen source, the formation of the complex is null, validating the hypothesis proposed in the present study[2].

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Hernández, H. Aranda C, López G, Riego L, González A 2011 Microbiology,157: 879.

THE *ARGEMONE-CORYNESPORA* SYSTEM AS MODEL FOR THE STUDY OF THE CONTRIBUTION OF BENZYLISOQUINOLINE ALKALOIDS IN PLANT-FUNGUS INTERACTIONS

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Abstract:

Argemone mexicana is widely used in traditional medicine for the treatment of numerous diseases. These properties are mainly attributed to the presence of benzylisoquinoline alkaloids (BIAS), such as sanguinarine and berberine (Rubio-Piña and Vázquez-Flota, 2013). Leaves showing necrotic lesions consistent with fungal infections, were analyzed for alkaloid accumulation revealing the presence of sanguinarine, which is normally absent in the healthy leaves. Sanguinarine accumulation apparently resulted from the preferential use of biosynthetic intermediaries over berberine, since a decrease in the accumulation of the latter was also observed. Four isolates, called AS0044-A to 44-D, were obtained from infected leaves by cultures on PDA medium. Morphological and molecular analysis of these axenic cultures revealed that fungi associated to leaf lesions were *Lasiodiplodia sp*., *Corynespora cassiicola*, *Fusarium solani* and *Cladosporium* sp. When leaves were individually exposed to the isolated fungi, only those challenged with *C. cassiicola*, developed infection symptoms. Necrotic spots were detected on the infection site after two days and lesions continued to expand up to seven days, when leaves were collected for analysis. Retrieval from infected leaves produced *C. cassiicola* as a single isolate, confirming its pathogenic potential on *A. mexicana* and suggesting an opportunistic nature for the other fungus species.

The isolated fungal strain will be molecularly characterized and a model for the study of alkaloid biosynthesis under these conditions will be established. The results obtained will help to elucidate the contribution of BIAS metabolism in the plant-pathogen interaction.

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Rubio-Piña, J., & Vázquez-Flota, F. (2013). Pharmaceutical applications of the benzylisoquinoline alkaloids from Argemone mexicana L. Current Topics in Medicinal Chemistry, 13(17), 2200-2207.

SELF-ASSEMBLY OF ARTIFICIAL VIRUS-LIKE NUCLEOCAPSIDS PROGRAMMED BY CRISPR-DCAS12

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Abstract:

Availability of simple models to investigate the assembly of viral particles could lead to understanding biochemical properties of viral systems and to develop more effective gene delivery systems. So far, some viromimetic polypeptides able to form nanoparticles with nucleic acids have been designed but they still lack important viral properties such as the presence of viral packaging signals. These signals are important because they help to promote self-assembly of coating proteins on their own genomes. In this work, we exploit the programmability of CRISPR-Cas12a system by RNA guised to drive the nucleation and elongated self-assembly of a synthetic polypeptide called “C-S-B” into virus-like particles (VLP) on specific DNA molecules. Positioned CRISPR-Cas12a systems along a DNA template worked out as synthetic packaging signals. They triggered polypeptide self-assembly and full DNA packaging at limiting polypeptide concentrations. This process was further enhanced by fusing to dCas12a a dimerizing domain which further help to polymerize the virus-like polypeptide. This strategy was finally used to discriminate between different DNA templates and promote packaging of specific DNA templates too. Self-assembly of virus-like particles guided by CRISPR-Cas could help to develop programmable biomaterials with applications in biotechnology as well as viromimetic proteins helping to understand viral self-assembly.

PHYSIOLOGICAL AND BIOCHEMICAL EFFECTS OF HEAT STRESS ON BREAD WHEAT PLANTS

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Abstract:

Wheat (*Triticum aestivum* L.) is a major staple and caloric food crop that provides more proteins and calories than any other cereal worldwide. Most of the heat-growing regions in the world experience high-temperature episodes, significantly reducing grain yield and the detrimental effects due to the increasing threat of climate change are expected to be aggravated in the next century. Heat stress (HS) causes adverse alterations in plant growth, metabolism, development, physiological processes, and yield. One of the major consequences of HS is the excess generation of ROS, which leads to oxidative stress. Therefore, the development of HS-tolerant wheat genotypes able to maintain grain yield and quality is crucial to food security and economical profits. Herein, two field experiments: optimal and HS during reproductive stage were performed with 25 CIMMYT and one INIFAP bread wheat genotypes at the Norman E. Borlaug research field in the Yaqui Valley, Sonora, Mexico. Based on grain yield reduction after heat-stress 10 out of 26 genotypes were labeled as heat-tolerant (≤ 700 g) or heat-sensitive (> 700 g) and selected for further analysis. Genotypes 1, 3, 18, parents 22 and 23, and 24 were sensitive while 4, 6, 17 and 26 (control) were tolerant. Genotype 24 had the lowest chlorophyll concentration (µmoles per m^2) and 22 the highest. Only genotype 17 presented significant reduced levels in both Fv/Fm and Eto/Rc fluorescence parameters under HS. Interestingly, in most of the genotypes, catalase activity was reduced in heat-stressed plants, while ascorbate peroxidase activity was increased. Thus, indicating that the latest is preferred in these plants for the H_2O_2 scavenging. Furthermore, the concentration of the osmolyte glycine betaine was higher in all stressed plants.

STUDY OF THE EFFECT OF CATIONS ON THE ACTIVITY OF RECOMBINANT LDH-1 AND LDH-2 FROM SHRIMP LITOPENAEUS VANNAMEI

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Abstract:

There is worrying contamination in the marine environment caused by metals which can provoke changes in the metabolism and therefore in the development and survival of commercial species such as crustaceans. The commercially important shrimp *Litopenaeus vannamei* is one of the species that have adapted to hypoxic environments using lactate dehydrogenase (LDH). LDH is a crucial protein in anaerobic glycolysis. *L. vannamei* has a single LDH gene and by alternative splicing, two subunits, LDH-1 and LDH-2, are generated. Both enzymes have been purified and biochemically characterized. In this work, we analyzed the effect of copper, zinc and cadmium on recombinant LDH-1 and LDH-2. For this purpose, enzymatic assays were performed with both enzymes. The concentrations of the cations were varied, and the dose-response analysis was carried out to obtain the IC_{50} for each metal using the Origin software. Copper did not inhibit either of the two enzymes. Zinc inhibited the LDH-1 with an IC_{50} of 436.2 ± 27.5 µM and LDH-2 of 294.5 ± 21.5 µM. For cadmium, the IC50 was for the LDH-1 of 111.3 ± 0.91 µM and LDH-2 of 85.2 ± 2.5 µM. The effect of zinc and cadmium is higher in LDH-2 with respect to LDH-1. This effect could be explained by the biochemical differences that exist between them and/or the interaction that could exist between the cations and the active site of the enzymes. In conclusion, both enzymes are sensitive to zinc and cadmium cations, which could cause problems in shrimp, as it has already been shown to affect other marine species.

CHARACTERIZATION OF THE CATALYTIC CAPACITY OF CCD-1 Y CCD4-3 AT THE BIXIN BIOSYNTHESIS PATHWAY IN

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Abstract:

Bixa orellana is a plant with a high commercial value because of its primary source of the natural pigment bixin, which is accumulated in the aril of its seeds. In recent years, different proposals about bixin biosynthesis. Thus, Cárdenas-Conejo et al. (2016) have reported several genes from the *B. orellana* transcriptome that code for carotenoid dioxygenase proteins (CCDs) and these have been identified as the responsible for converting lycopene to bixin aldehyde, the first step in the bixin biosynthetic pathway. Based on the background, the approach proposed in this research is to purify the recombinant BoCCD1-1 and BoCCD4-3 enzymes and characterize them by their catalytic capacity to generate bixin aldehyde from lycopene substrate.

Cárdenas-Conejo, Y., Carballo-Uicab, V., Lieberman, M., Aguilar-Espinosa, M., Comai, L., & Rivera-Madrid, R. (2015). De novo transcriptome sequencing in *Bixa orellana* to identify genes involved in methylerythritol phosphate, carotenoid and bixin biosynthesis. BMC Genomics, 16(1), 1–18. https://doi.org/10.1186/s12864-015-2065-4

BIOCHEMICAL CHARACTERIZATION OF OROTATE PHOSPHORIBOSYLTRANSFERASE FROM *COFFEA ARABICA*

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Abstract:

Orotate phosphoribosyltransferase (OPRTase) catalyzes the Mg^{2+}-dependent condensation of the orotic acid (OA) with 5'-phosphorybosilpirofosfate (PRPP) to yield pyrophosphate (PPi) and orotidine 5-'monophosphate (OMP), which is converted by OMP decarboxylase (ODCase) to uridine 5'-monophosphate (UMP), the entry nucleotide to *de novo* biosynthesis of all the pyrimidine nucleotides. In plants, the OPRTase and the ODCase are encoded by a single gene that produces one polypeptide known as UMP synthase.

Coffee is one of the most important agricultural products in Mexico. The *Coffea arabica* species is the one that is cultivated in Mexico, this is associated with a high cup quality, but it is more susceptible to pests and diseases. Therefore, it is very important to avoid plant pathogenic bacteria, such as *Pseudomonas cichorii*.

Previous studies with bacteria, protozoan and fungus have shown the importance of the *de novo* pathway for the synthesis of pyrimidines and its influence on the bacterial virulence. The decrease in pyrimidine nucleotides limits cell proliferation. In an attempt to get a deeper understanding of the role of the OPRTase in the infection of coffee plant infection caused by bacteria, the main goal of this work was to characterize functionally and structurally the UMP synthase of *Coffea arabica*. We obtained the pure recombinant UMP synthase of *C. arabica*. As part of the functional caracterization, we carry out the kinetic studies, finding a K_m value for PRPP very close to the values reported for other OPRTases. Finally, we also obtained the model of the three tridimensional structure of OPRTase from *C. arabica* using AlphaFold.

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THE HUMAN COPPER TRANSPORTER 1 (HCTR1) AS A POSSIBLE TRANSPORTER OF CASIOPEINA III-IA IN MDA-MB-231 CELLS

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Abstract:

Cancer is a generic term used for a large group of diseases characterized by a rapid proliferation of abnormal cells that grow beyond their usual boundaries and wich can invade adjoining tissues. Cancer is the second cause of death worldwide, with an incidence and mortality that grow rapidly. There are several types of cancer treatments however the first line of treatment is based on old therapies that have proven to be effective, such as chemotherapy. Since the discovery of cisplatin the interest for the creation of drugs based on metals started to grow. Casiopeinas are mixed-chelate copper (II) compounds of the general formula [Cu(N-N)(O-O)]NO3 or [Cu(N-N) (O-N)]NO3, where N-N is a substituted aromatic diimine (1,10- phenanthroline or 2,2'-bipyridine), O-N is an α-aminoacidate or peptide and O-O is acetylacetonate or salicylaldehydate. Casiopeinas are designed based on copper, an essential metal for the organism, with the intention of diminishing the negative effects caused by other metallodrugs. Casiopeina III-ia (Cas III-ia) has proved to have good cytotoxic activity in vitro as well as in vivo, wich allowed it to be approved for phase I clinical trials in Mexico. Although several mechanisms to explain their biological activity have been proposed, the mechanisms involved in their transport inside the cell remain unknown. hCTR1 is a homotrimeric membrane protein that acts as the main copper transporter into the cell's citoplasm and has recently gained interest due to it's possible role as a metallodrug transporter. It has been observed that an augmented expression of hCTR1 leads to a greater accumulatiom of platinum drugs, in some cases being able to sensitize normally resistant cell lines, likewise it has been shown that elimination of this transporter renders cells resistant to the effects of these metallodrugs, demonstrating the essential role of this protein in cytotoxic effects. In the present work we studied the cytotoxic effect of Cas III-ia in transfected MDA-MB-231 cells that express a greater concentration of the hCTR1 transporter. The half maximal inhibitory concentration (IC50) for Cas III-ia was determined by sulforhodamine B assay giving a value of 60.98 mM. The MDA-MB-231 cells were transfected using the pWZLblasti-CTR1 plasmid through lipofection with the XfectTM transfection reagent and the change in expression was assessed by western blot 48 hours post transfection. IC50 was determined again in transfected cells giving a value of 62.32 mM. No significant change in the value of IC50 was observed in the transfected cells, suggesting that overexpression of hCTR1 in MDA-MB-231 cells does not increase cell sensitivity to Cas III-ia, however further intracellular accumulation studies might help determine if there is a change in intracellular copper levels.

CHOLESTEROL DEPENDENCE OF NA,K- ATPASE ENZYME ACTIVITY OF ERYTHROCYTES IN NORMAL AND HYPERGLYCEMIC BLOOD SAMPLES

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Abstract:

Background: The prevalence of dyslipidemias in Mexico is about 30-40% and the prevalence of type 2 Diabetes (DM2) is above 15%, both entities represent cardiovascular risk factors and even though the clinical and metabolic consequences of both diseases have been meticulously studied all over the world, it is still much information lacking about their effect on many molecular mechanisms of blood cells, which are continuously exposed to the increased concentrations of lipoproteins and glucose. Erythrocyte Na,K-ATPase (eNKA) is a plasma membrane enzyme in charge of the regulation of intracellular ion concentration, thus affecting volume regulation, water homeostasis, surface area-to-volume ratio and cytoplasmic rheology. All these parameters are involved in erythrocyte deformability and play a key role in different pathologies such as cardiovascular, pulmonary, renal and oncological diseases (1). The excess of cholesterol rich lipoproteins is able to alter the cholesterol content of blood cell membranes, thus affecting the organization and distribution of lipids and proteins with impact in their 3D conformation and function. In addition, the known effects of hyperglycemia on erythrocyte structure and function which also affect membrane fluidity might also contribute to some enzyme dysfunctions and effects could be potentiated when both conditions coexist (2). Aim: In this work we aim to study the effect of plasma membrane compartmentalization of erythrocytes of normal and hyperglycemic samples in a cholesterol dependent manner on eNKA kinetics. Methods: We are going to obtain five samples of normal blood and five samples of normocytic normochromic anemia blood. We are going to add an increasing concentration of LDL to subsets of each sample and incubate for 1h at RT. Afterwards, we are going to isolate and wash the erythrocytes, mix with Lysis buffer for microsomes obtention and perform eNKA activity enzyme with colorimetric tests. Data will be analyzed through statistical methods. Conclusion: It is important to evaluate how hypercholesterolemia and hyperglycemia affect enzyme activity of many blood cells. We are starting our proposal with a first approach on eNKA of red blood cells, however, we aim to expand the enzyme list in a near future, once our methodology is validated.

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IDENTIFICATION OF ANTIMICROBIAL PEPTIDES FROM SCORPION VENOM OF A NEW SPECIES OF THE GENUS MESOMEXOVIS

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Abstract:

Vaejovidae is the most diverse family in North America, with 17 genera and 180 species, including the genus Mesomexovis. In the scorpion venom of this family has been identified peptides with activities antimicrobial, antiviral, antiparasitic, immunomodulators, and analgesic, that can be of interest to the therapeutic area. Antimicrobial resistance is a threat to global health, so there is a need to look for alternatives to generate new antimicrobial agents. We performed a transcriptomic analysis of the venom secretory gland of two female scorpions Mesomexovis sp., a new species endemic of Coquimatlan, Colima. RNA-seq technique was used for the analysis, Genome Analyzer IIx (Illumina, San Diego, CA, USA), and de novo assembly. 22 million reads were obtained with quality of 99.999%. 60 sequences of transcripts code to possible antimicrobial peptides were identified using the BLAST tools in NCBI. These putative peptides were classified in NDBP4 (34%), Scorpine (25%), NDBP5 (18%), NDBP2 (16%), NDBP3 (5%), defensin (2%). Furthermore, we analyzed the peptide profile from the venom of the scorpion Mesomexovis sp., by electrophoresis gels and separated the components using techniques chromatographic as exclusion molecular and reverse-phase HPLC, also the antimicrobial activity of the components isolate was evaluated. The characterization of these putative peptides will allow the generation of the bases for the development of new therapeutic agents that can contend with the worldwide issue of bacterial resistance to antibiotics.

EVALUATION OF THE EXPRESSION OF GENES ENCODING PECTIN METHYL ESTERASES IN SOLID ENDOSPERM OF COCONUT

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Abstract:

Cocos nucifera L, is a plant species of great importance due to the many products that derive from it. As a non-climacteric fruit, during ripening there are several changes that give organoleptic characteristics. A group of enzymes called pectin methyl esterases (PME) are linked to cell wall remodeling. Due to the importance of this group of enzymes, they have been studied in various organisms such as *Arabidopsis thaliana*, *Fragaria vesca* (strawberry), *Malus domestica* (apple), *Prunus mume* (Chinese plum), among others. In the case of the Arecaceae family and specifically in the coconut, there are not many studies that help to understand the molecular processes mediated by the PME in the solid endosperm, the importance of characterizing the expression of PME is due to the fact that the coconut hardens as it matures, a mechanism that is different in other fruits for this reason, in the present work we used bioinformatic tools to identify the PME genes in the coconut genome. Using those genes as templates, DNA primers were designed and synthesized. Using cDNA synthesized from total RNA extracted from immature, intermediate (ripening) and mature solid endosperm and specific primers were used to evaluate by PCR, the expression of PME genes. Results revealed that expression occurred in solid endosperm at the three stages of maturity in tall and dwarf coconuts. Together, results suggest, that PME gene expression play a key role during the softening/ hardening of cell wall development and accumulation of solid endosperm in coconut seeds.

A NEW PERSPECTIVE OF PROTEIN EVOLUTION MECHANISMS BY NATURAL SELECTION AND GENE DRIFT

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Abstract:

One fundamental question in life sciences, with a long and rich history, is explain how proteins/enzymes evolved? Proteins that emerge of new genes provides the raw material for evolutionary innovation that allows organisms to evolve and adapt to environmental changes and eventually give rise to new species. The diversification of life cannot be understood without the evolution and diversification of individual populations and the mechanisms of gene evolution. Interestingly, the historical development of biochemistry and evolutionary theories have run in parallel and interlaced frequently. In this work we describe the most outstanding advances in enzyme/protein properties that allow us to integrate a complete overview to explain how natural selection and gene drift act at a protein/enzyme level. Thus, the historical paradigm "one gene, one enzyme" proposed originally by Beadle and Tatum, and later complemented with Anfinsen's findings to "one gene, one structure, one enzyme", now is changed by a new paradigm like "one gene, several isoproteins/ isoenzymes", assuming that not only can be generated different alternative transcripts from one gene, but also, each alternative protein/enzyme isoform exhibit several conformations in equilibrium, each with the capability to exhibit different functions (usually described as one primary and several secondary functions) that can be subject (permanently) to Natural selection and gene drift. In this way, among the different mechanisms of gene evolution, duplication/divergence actually seems to be the most important because allows the original gene conservation (and their function(s)), but at the same time allows the selection of preexisting secondary function(s) that provide a selective advantage to the organism.

This work was partially supported by UNAM-DGPA PAPIIT grant IN219022. J.C.-C. thanks Programa de Becas Posdoctorales UNAM-DGAPA for a postdoctoral fellowship. E.A. S.-R. is enrolled at the Plan de Estudios Combinados en Medicina (PECEM) program of the Facultad de Medicina at Universidad Nacional Autónoma de México.

TOXICITY, IDENTIFICATION AND VISUALIZATION OF ALUMINIUM IN PLANT CELLS USING DIFFERENT ADVANCED MICROSCOPY TECHNIQUES

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Abstract:

Aluminum (Al), the most abundant metal on earth with 7% among all elements, is ubiquitous and is present in tissue-organs of various plant species, mainly in tropical acid soils. In addition, the toxicity produced by this metal is a factor that limits the productivity of cultivated species. In order to advance studies involving this event, we have used multiple analytical techniques to determine the presence of Al in different plant models; that are of commercial and ecological importance for Mexico. The models studied are: *Coffea arabica*, *Allium fistulosum* (green onion), *Dioon edule* (cycads) and *Opuntia sp* (nopal). The determination of Al has been carried out using the following element mapping techniques: confocal fluorescence microscopy and scanning electron microscopy coupled with energy dispersive X-ray spectroscopy. These techniques are accessible, non-destructive and allow multi-element analysis in biological samples with or without sample preparation [1]. We found that aluminum toxicity affects growth and the production of secondary metabolites [2]. Furthermore, it was studied that the signal transduction mechanisms through which signaling molecules associate with the phosphoinositide signaling pathway are affected by Al stress [3-4]. An overview of the latest results will be presented highlighting the link between biological effects and Al determination in the cell.

Acknowledgements: To Carlos Cruz-Cárdenas (CNRG-INIFAP) and Francisco Barona-Gómez (Langebio–Cinvestav) for their collaboration and plant material donation. Research founded by CONACYT (219893, IFC 2015/035).

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CELLULAR DISTRIBUTION OF ALKALOIDS IN *ARGEMONE MEXICANA* L.

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Abstract:

Argemone mexicana (Papaveracea) is considered a medicinal plant due to the presence of benzylisoquinoline alkaloids (BIAs), produced from tyrosine (Chang, Y., *et al,* 2003). Sanguinarine (benzophenantridine) and berberine (protoberberine) represent the main alkaloids accumulated in this plant, showing a differential tissue distribution. In mature plants, sanguinarine is restricted to roots and mature seeds, whereas berberine is distributed throughout the plant (Rubio-Piña and Vazquez-Flota, 2013). It is not common for alkaloids from these groups to converge in the same species. Synthesis and accumulation of BIA involve the participation of specialized cells in different plant species as it has been shown in *Thalictrum flavum* and *Papaver somniferum* (De Luca and St-Pierre, 2000; Facchini and St-Pierre, 2005). Such cellular distribution has not been established in *A. mexicana* which represents an interesting model due the simultaneous occurrence of alkaloids from these groups. Sanguinarine and berberine, exhibit high chromophoric and fluorescent properties, due to the presence of conjugated double bond systems (Slaninova et al, 2008). Sanguinarine displays a red-orange fluorescence whereas berberine is detected by its blue-greenish emission. These fluoroscopic features allow their detection in fresh tissue sections. In this work, tissue sections from *A. mexicana* leaves, stems, roots and seeds were analyzed by their fluorescence emission using confocal microscopy. Fluorescent signals, corresponding to the emission range of sanguinarine and berberine (ca. 450 nm) were associated to vascular bundles for root, stem, leaf and fruit pericarp, mainly to cell walls xylem vessels. Interestingly, Additionally, signals in root sections were also found in rhizodermis, whereas in seeds, remained restricted to the coats. Interestingly, emission of tissue sections was washed off with methanol. Moreover, vascular bundles also resulted positive to Dragendorff reagent, suggesting supporting their involvement in alkaloid accumulation in *A. mexicana*.

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PRODUCTION OF A NOVEL BIOACTIVE POLYKETIDE OF MARINE ORIGIN USING THE METABOLIC CHASSIS OF *ESCHERICHIA COLI*

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Abstract:

Type III polyketides (PKs III) are β-polyketones with diverse biological activities that are synthesized by type III polyketide synthases (PKS III). Uncultured marine bacteria are emerging as a source of novel bioactive PKs III. In this work, a putative PKS III (ArsMB) encoded in the genome of an uncultured Microbacteriaceae present in a Baltic Sea microbiome was detected by metagenomic mining. Using an inducible biological circuit, including the synthetic *ars*MB and the metabolic chassis of *E. coli* to supply acyl-CoA precursors, the novel PK III was produced in the presence of glucose as a sole carbon source in a mineral medium. Liquid chromatography and NMR spectroscopy analysis showed that the biosynthetic product is a PK III 5-n-alkylresorcinol with intrinsic amphiphilic properties. Antimicrobial tests against the *E. coli* PK III producer, employing a bacteriophage endolysin enzyme that causes bacterial lysis and death by catalyzing the degradation of the peptidoglycan (PG) layer, suggests a key role of the 5-n-alkylresorcinol in the structure of the phospholipid bilayer, influencing the lytic susceptibility. Furthermore, an antioxidant assay showed the ability of the novel PK III to neutralize free radicals. Together, structure determination, biochemical analysis, and bioactive capacity assays of the novel PK III provided valuable information on its functional role in marine microbiomes, the reaction mechanism, and its potential biotechnological applications.

Keywords: *alkylresorcinol; bioactive compound; genomic data mining; prokaryotic engineering*

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THE COPPER TRANSPORT MEDIATED BY THE P-TYPE ATPASE CTPA IS REQUIRED FOR ENZYMES INVOLVED IN THE RESPONSE TO OXIDATIVE STRESS IN MYCOBACTERIUM TUBERCULOSIS

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Abstract:

Mtb has three P1B-type ATPases annotated as possible copper cation transporters, CtpA, CtpB and CtpV [1], which are involved to reduce the internal copper concentration to physiological levels. Possibly, some of these transporters perform alternative functions, such as metalation of periplasmic and membrane proteins [2]. On the other hand, the well-known metalloenzymes superoxide dismutase (SodC), cytochrome oxidase, and multicopper oxidase (MmcO) use copper as cofactor and may be required for overcoming the redox and cupric stress in Mtb [3-5]. In this work, we study the possible link between the copper transport mediated by CtpA with cuproenzyme oxidase activity, and the redox stress response.

We observed that a ctpA mutant strain (MtbΔctpA) displays impairs growth in vitro under oxidative (IC_{50}=724μM H2O2) and nitrosative (IC50=56.6μM Sodium Nitroprusiate) in vitro conditions, compared with the wild type strain MtbH37Ra (WT) IC_{50} 1491 μM H_2O_2 and 152.8 μM SNP. On the other hand, Rt-qPCR experiments showed an increased transcription of mmcO (2 to 3-fold), sodC (5- to 9- fold) and transmembrane cytochrome C oxidase subunit II CtaC (5- to 11-fold) genes in MtbΔctpA, compared to the Mtb WT strain under stress conditions (H_2O_2=1.4 mM or NPS=250μM). However, whole-cell lysates of MtbΔctpA, previously exposed to copper 200 μM for 48 hours, showed slower oxidation of organic substrates (ABTS and pPD) than the showed by lysates of the Mtb WT strain. Finally, the ABTS oxidation was even smaller when MtbΔctpA cells were also exposed to additional stress conditions (1.4mM of H_2O_2 by 3 hours). Altogether results suggest the copper transport mediated by CtpA could be involved in loading Cu^+ into oxidases associated to redox stress response in Mtb.

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INHIBITION OF LECITHIN-DEPENDENT HEMOLYSIN OF *VIBRIO PARAHAEMOLYTICUS* BY METAL IONS AND CHEMICAL REAGENTS

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Abstract:

Lecithin-dependent thermolabile hemolysin (LDH) is a virulence factor excreted by Vibrio parahaemolyticus, a marine bacterium that compromises shrimp farming. In this study, the function of LDH was investigated through its inhibition by metal ions (Mg_{2+}, Ca_{2+}, Mn_{2+}, Co_{2+}, Ni_{2+} and Cu_{2+}) and chemical modification reagents; β-mercaptoethanol (βME), phenylmethylsulfonyl fluoride (PMSF) and diethyl pyrocarbonate (DEPC). LDH was expressed in the Escherichia coli strain BL-21 and purified under denaturing conditions; both enzymatic and hemolytic activity were evaluated. Cu2+, Ni2+, Co2+ and Ca2+ at 1 mM inhibited the LDH esterase activity by 20-95%, while Mg2+ and Mn2+ slightly increase its activity. Also, PMSF and DEPC at 1 mM inhibited the enzymatic activity by 40% and 80%, respectively. Dose-response analysis showed that DEPC was the best-evaluated inhibitor (IC50=0.082 mM), followed by Cu2+ > Co2+ > Ni2+ and PMSF (IC50 = 0.146-1.5 mM). Our results showed that enzymatic activity of LDH from *V.* parahaemolyticus was modulated by metal ions and chemical agents, which could be related to catalytic amino acids residues as Ser153 and/or His393 located in SGNH domain.

CHANGES IN MITOCHONDRIAL METABOLISM IN METABOLICALLY ACTIVATED MACROPHAGES

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Abstract:

Macrophages play a key role in the adaptive immune response. These cells are in the front-line defense against pathogens and participate in tissue remodeling, inflammation and resolution. Depending on the environmental stimulus, macrophages reprogram their metabolism to carry on their cellular functions. In general, activated macrophages are classified in two different stages (although several intermediaries stages are being characterized): a proinflammatory or classic activation (M1 stage) and anti-inflammatory or resolving stage (M2 or alternative activation). Thus, for example, during sepsis, some activating signals like LPS or INF-γ reprogram their metabolism to proinflammatory stages to afront these conditions, secreting mainly cytokines. In the same way, pathophysiological situations like obesity or metabolic syndrome phenocopy several proinflammatory traits observed in classical activation. However, both conditions (classical vs metabolic activation) appear to differ in their metabolic reprograming. Although some key features of metabolic activation (i.e., by lipid overload) are begun to be disclosed, most of the mechanism of metabolic activation are largely unknown. In this work, we used an in vitro model of monocyte-derived macrophages (cell line U937) activation by LPS and palmitic acid in high glucose to unravel the metabolic reprograming of immune cells observed in metabolic syndrome and obesity. We observed that like LPS-stimulation, palmitic acid also induces the release of a similar pattern of proinflammatory cytokines (i.e., TNF-α, IL-6). However, palmitic acid increases the mitochondrial oxidative metabolism when compared to unstimulated (Mo) or classical LPS-activated macrophages (M1). Interestingly, this increase is not accompanied with mitochondrial biogenesis. We also observed elevated glycolytic activity and accumulation of triacylglycerols in lipid bodies. These results suggest that under metabolic activation by palmitic acid, glycolysis is used to produce metabolic intermediaries involved in disposing harmful free fatty acids and, in regulating the metabolic activation stage of macrophages.

USAK, A PEPTIDE DERIVED FROM THE C-TERMINAL REGION OF CETPI, MODULATES *IN VIVO* THE SYSTEMIC RESPONSE TO LPS: PROOF-OF-CONCEPT EMPLOYING PET

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*A*bstract:

Nowadays, infectious diseases have become one of the most concerning situations for public health worldwide. More than 20 million deaths can be associated with sepsis and septic shock every year, both of them considered critical states related to infectious processes. These conditions are characterized by the development of a hyperinflammatory response that overcomes the regulatory mechanisms of inflammation. This unregulated response leads to organic and systemic failures, and eventually death. The establishment of the inflammatory state could be associated with the recognition of immunogenic molecules from pathogens such as Gram-negative bacteria producing lipopolysaccharides (LPS).

In this regard, peptide *USAK* (*USAK*PLS*A*RSPGGRPLSP), a peptide comprising the last 18 amino acids from the C-terminal region of CETPI, a protein originally described by us, has shown important LPS-binding properties *in vitro*, as well as LPS-neutralizing effects *in vivo*.

In this study, we employed Positron Emission Tomography (PET) to analyze changes in metabolism associated with an LPS challenge. 18-Fluorodesoxiglucose ([^{18}F]FDG) has been used as the radiotracer to determine the basal metabolism employing a dwarf rabbit model, following LPS or *USAK*+LPS administration. Experimental animals only treated with LPS, showed an important decrease in [^{18}F]FDG uptake. Nevertheless, attenuation of LPS effects over [^{18}F]FDG uptake was observed in animals treated with *USAK* and LPS. Meanwhile, non-relevant changes were observed in control or *USAK*-treated groups. Interestingly, LPS treatment followed by the administration of peptide *USAK*, resulted in the presence of lower plasma levels of cytokine and pro-inflammatory markers, such as TNFα, IL-1α, IL-1 β, IL-6, IL-8, and MIP-1β, in comparison to the LPS-alone group (1).

Together, these results support the role of peptide *USAK* as an LPS-binding peptide, with potential therapeutic possibilities in sepsis and septic shock.

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CHOLESTEROL DEPENDENCE OF ACETYLCHOLINESTERASE ENZYME ACTIVITY OF ERYTHROCYTES IN NORMAL AND HYPERGLYCEMIC SAMPLES

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Abstract:

Background: The prevalence of dyslipidemias in Mexico is about 30-40% and the prevalence of Diabetes type 2 (DM2) is above 15%, both entities represent cardiovascular risk factors and even though the clinical and metabolic consequences of both diseases have been meticulously studied all over the world, it is still much information lacking about their effect on many mechanisms of blood cells, which are continuously exposed to the increased concentrations of lipoproteins and glucose. Erythrocyte acetylcholinesterase (eAChE) has been described since 1940 and some advances regarding its structure and function have been performed ever since. We now know that eAChE is involved in the nitric oxide (NO) pathway, that its enzyme activity is affected by gender, age, blockage of ACh receptors and different diseases; and it is even used as a biomarker for high blood pressure, glaucoma and neurotoxicity among other diseases (1). The excess of cholesterol rich lipoproteins is able to alter the cholesterol content of blood cell membranes, thus affecting the organization and distribution of lipids and proteins with impact in their 3D conformation and function. In addition, the known effects of hyperglycemia on erythrocyte structure and function which also affect membrane fluidity might also contribute to some enzyme dysfunctions and effects could be potentiated when both conditions coexist (2). **Aim:** In this work we aim to study the effect of plasma membrane compartmentalization of erythrocytes of normal and hyperglycemic samples in a cholesterol dependent manner on eAChE kinetics. **Methods:** We are going to obtain five samples of normal blood and five samples of normocytic normochromic anemia blood. We are going to add an increasing concentration of LDL to subsets of each sample and incubate for 1h at RT. Afterwards, we are going to isolate and wash the erythrocytes, mix with Lysis buffer for microsomes obtention and perform AChE activity enzyme with colorimetric tests. Data will be analyzed through statistical methods. **Conclusion:** It is important to evaluate how hypercholesterolemia and hyperglycemia affect enzyme activity of many blood cells. We are starting our proposal with a first approach on AChE of red blood cells, however, we aim to expand the enzyme list in a near future, once our methodology is validated.

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A COMPUTATIONAL-EXPERIMENTAL APPROACH FOR THE TARGETED DEVELOPMENT OF FLUOROGENIC SUBSTRATES AND COMPETITIVE INHIBITORS OF MTMARP PROTEASE

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Abstract:

Human tuberculosis (TB) remains among the most prevalent infectious diseases worldwide. Mycobacterial acid-resistant protein (MarP) is a transmembrane serine protease that plays a key role in Mycobacterium tuberculosis, the causative agent of TB, promoting bacterial survival within the phagosome milieu of human macrophages.1,2 As a pathologically relevant protein, MtMarP represents a potential target for the rational design of molecules with therapeutic activity against TB. Although the proteolytic activity has already been shown by recombinant MtMarP-assisted hydrolysis of synthetic substrates,3 extensive biochemical characterization is required to gain further insights into the structure-function relationship of the protein. Since GFP is a fluorogenic biosensor with proven effectiveness, we aimed to engineer a GFP-based substrate to analyze the MtMarP proteolytic activity and thus establish the technical basis to develop a protease-specific assay. A computational-designed GFP variant, named GFPCC4, containing the MtMarP-specific cleavage site ARLV↓AWSS (derived from the RipA protein, a physiological substrate),4 was engineered by substituting eight residues of loop 9 (i.e., between β-sheets 9 and 10). GFPCC4 was produced as a 6xHis-tagged recombinant protein in E. coli and purified soluble (but non-fluorescent) under moderate denaturing conditions (2 M urea). Typical protease assays performed under pH-buffered conditions (4.5 and 7.4) and SDS-PAGE analysis showed that GFPCC4 is cleaved efficiently by a recombinant MtMarP protease (in-house produced). So far, it seems feasible to presume that the engineered GFP has potential as a protease-specific substrate. Alternative computational and experimental approaches (independent or combined) to solubilize/refold GFPCC4 from inclusion bodies and design/engineer a novel FRET-based substrate are currently in progress.

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AGAVE FRUCTANS METABOLIC PROFILES IN PLANTS OF *AGAVE ANGUSTIFOLIA* HAW. UNDER TWO DIFFERENT CROP MANAGEMENT STRATEGIES

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Abstract:

In the past years, with the rising global consumption of mezcal, cultivation of *Agave angustifolia* Haw. has grown intensively, prompting to develop new management strategies using chemical inputs for increase crop yield. On the other hand, *A. angustifolia* Haw. has the potential to meet the increasing demand of fructans because, it can also be used as raw material for the production of prebiotics. Although the plant size is apparently advantageous for farmers in terms of amount because larger plants may produce higher usable matter, a large sized plant producing lower amount of fructans is not necessarily a good resource. Therefore, it is necessary to know of the type and concentration of fructans to give alternatives the marketing according to the age and agronomic management of this crop. In this study, we examined fructans fluctuation in plants of *A. angustifolia* Haw. (1 to 3 years-old) using two different crop management strategies on the field: a traditional management without the use of any agrochemical reagents and an intensive agricultural system adding chemical fertilizers. First, we analyzed the plants morphological diversity based in vegetative characters. Subsequently, fructan extracts were analyzed by TLC, FT–IR, and HPAEC–PAD to identify/characterize carbohydrates differences. Analyses of morphological parameters indicated morphological divergence between plants of both cultivation systems. Furthermore, we found that the concentration of simple carbohydrates and fructans changed during plant development. However, concentrations of glucose and fructose did not show significant differences between the two crop managements while sucrose and fructans were more abundant in fertilized plants. Moreover, plants under traditional management showed least amount of fructooligosaccharides (FOS: short DP fructans) and high DP fructans. These results proved that a proper fertilizers management holds a great promise to enhance fructans production making *Agave angustifolia* Haw. a tremendous agave species not only for mezcal but also for prebiotics production.

EFFECT OF CHEMICAL INHIBITORS ON THE RECOMBINANT G6PD::6PGL FUSED PROTEIN OF THE PARASITE *TRICHOMONAS VAGINALIS*

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Abstract:

Trichomoniasis is a sexually transmitted disease (STD) caused by the protozoan *Trichomonas vaginalis*. This infection is very common in the world, with an incidence of around 270 million people affected per year and an estimated prevalence of 8.1% for women and 1.0% for men. *T. vaginalis* uses carbohydrates as its main source of energy, and the glycolytic, pentose phosphate pathway is also important in the metabolism of *T. vaginalis*. In this pathway, glucose-6-phosphate dehydrogenase (G6PD) is a key enzyme that catalyzes the first step. The G6PD protein of *T. vaginalis* differs in length and amino acid sequence with respect to human G6PD because it has been reported that in *T. vaginalis* the gene that codes for G6PD are fused with the gene for 6- phosphogluconolactonase (6PGL) to give rise to a fused G6PD::6PGL enzyme, so the structure of the G6PD::6PGL enzyme is different from that of the human G6PD protein. In this project, the inactivation of the fused recombinant protein G6PD::6PGL of *T. vaginalis* with chemical compounds was studied to propose this protein as a possible pharmacological target, by taking advantage of the differences with the human G6PD enzyme. Functional and structural assays were carried out on the recombinant G6PD::6PGL fused enzyme from the parasite *T. vaginalis*. From a library of 55 chemical compounds, four compounds (JMM-3, CNZ-3, CNZ-17, and MCC-7) were selected that exerted greater than 50% inhibition on the enzyme. Determination of the IC50 calculated for the four compounds indicated values of 155.1, 93, 356, and 260 µM respectively. These IC_{50} values were used to obtain the second-order inactivation constant (k2) of each of them, their reactivity indicated values of 0.32, 0.63, 0.34, and 0.38 M-1s-1 for compounds JMM-3, CNZ- 3, CNZ-17, and MCC-7. Subsequently, a series of structural tests were carried out to determine changes in the secondary and tertiary structure of the G6PD::6PGL protein in the presence of the inhibitors. Circular dichroism assays indicated that the compounds affect the secondary structure of the protein which correlates with the loss of catalytic activity. The evaluation of the tertiary structure of the G6PD::6PGL protein in the presence of the four compounds showed a change in the microenvironment of the tryptophan residues, as well as in the hydrophobic zones when evaluated by intrinsic and extrinsic fluorescence.

DEGRADATION OF DIESEL AND GASOLINE BY LIGNINOLYTIC FUNGUS ISOLATED FROM CONTAMINATED SOIL

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Abstract:

The high demand of fossil fuels in México, such as diesel and gasoline, has caused severe environmental impacts which are reflected in spills on soil and water bodies due to the large volumes handled, poor maintenance and pipeline leaks; as well as fuel theft. One strategy to recover these contaminated sites is bioremediation by microorganisms that reduce the adverse effects of such pollutants. The objective of this study is the isolation, characterization and degradation of contaminants using ligninolytic fungus as an alternative for remediation of diesel and gasoline residue on contaminated sites. Eight strains were isolated from polluted sites, which were then adapted to a contaminated environment and subsequently grown in Minimum Salt Medium (MSM) enriched to 0.5, 1 and 1.5% with the pollutants as the only carbon source. Tween 20 was used as a 1% surfactant. Grown kinetics were performed at 37°C under various conditions (pH 3, 5 and 7) for 30 days to assess their cellular growth (540 nm), the total protein production by Bradford´s method and the MnP enzymatic capacity. The HD strain showed greater results in diesel and gasoline. It also produced the greater amount of total protein count after the 15th day (32 mg/mL). The best degradative results were obtained at 1% for both pollutants, while for mass generation the concentration with best results was 1.5% in both pH 5 and 7. The optimal growth occurred at pH 5 in 72% of the experiments. Microbiological analyses show fungi from the genus Hormographiella spp. and Hormonema spp. By means of gravimetry, the maximum percentage of degradation of 95.63% for gasoline and 53% for diesel was obtained. Both growth and enzymatic activity were modeled with apparent Monod-like kinetics. The kinetic parameters were obtained by the Luus-Jaakola method, showing mathematical similarity with the microbial genera described. It is concluded from this study that the isolated microorganisms show the ability to degrade diesel and gasoline.

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SPECTROSCOPIC ANALYSIS OF METAL IONS EFFECT ON THE AGGREGATION OF A 6AJL2R24G PROTEIN VARIANT

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Abstract:

Light-chain amyloidosis (AL) is one of the most common forms of amyloidosis. It is characterized by the extracellular deposition of variable domain fragments of immunoglobulin light chains. The clinical manifestations of this disease are very varied because the deposits can be found in almost all the organs of the human body causing various failures. Approximately 30% of AL cases contain a λ6a germline and 25% of those cases presents a Glycine at position 24 instead of Arginine (R24G). This mutation causes the protein to be thermodynamically more unstable and to be more amyloidogenic. The recombinant protein 6aJL2-R24G is a good model to study the aggregation pathway of the germline protein 6a. Recently, it was found that the interaction of the 6aJL2-R24G with Cu(II) makes the protein less stable and more prone to form amyloid fibers, however, the effect of other metal ions has not been evaluated yet. Zn(II) is another metal ion that plays a very important role in the aggregation of proteins involved in other amyloidosis. Therefore, in this work, the effect of Zn(II) on the aggregation of 6aJL2-R24G protein was studied using different spectroscopic techniques. Additionally, it has been reported that the protein in the native or fully unfolded state does not form fibrillar aggregates, suggesting the participation of partially unfolded intermediaries in the formation of the fibers. The conformational changes that lead to these intermediaries have not been described yet. The DEER (Double Electron-Electron Resonance) technique allows the distance measurement between multiple paramagnetic labels and can be used to study the protein possible intermediates participating in the fibrillization pathway. In order to study the 6aJL2-R24G aggregation pathway, a site directed mutagenesis was performed to obtain the variant 6aJL2-R24G-S26C-S57C (named as Cys-DM) which is able to bind a paramagnetic label. Since the 6aJL2-R24G protein is very amylodogenic, in this work the effect of the Cys-DM mutation, and the spin labeling was evaluated by different spectroscopic techniques, in the presence and absence of Cu(II).

COMPLEMENTARY MECHANISMS THAT COUNTERACT DEFICIENCIES IN CA^{2+} TRANSPORT MEDIATED BY P-TYPE ATPASES IN *MYCOBACTERIUM TUBERCULOSIS*

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Abstract:

Mycobacterium tuberculosis (*Mtb*), the etiological agent of Tuberculosis, experiences a 4-fold increase in intraphagosomal Ca^{2+} concentration 24 h post-infection.[1] To survive this hostile environment, *Mtb* activates detoxification systems through P-type ATPases, among others, to maintain cellular homeostasis of cations and generate appropriate electrochemical gradients. Specifically, CtpF a Ca^{2+}-ATPase is activated in response to redox stress and hypoxia, conditions faced by *Mtb* during infection [2]. To date, no complementary mechanisms for CtpF are known. Therefore, this study evaluates whether any of the P2-type ATPases (alkaline/alkaline earth metal transporters) genes might be upregulated in the absence of *ctpF* under stress conditions. Consequently, we compared the mRNA levels of P2-type ATPases (*ctpF, ctpH, ctpE*, and *ctpI*) genes in *Mtb*Δ*ctpF* and *Mtb*H37Rv strains during *in vitro* infection of MH-S cells by RT-qPCR. Additionally, the quantification was carried out applying toxic concentrations of Ca^{2+} in *Mtb*Δ*ctpF*.

Our results showed increased transcription of *ctpH* and *ctpE* genes (2- to 5-fold) in *Mtb*Δ*ctpF*, relative to the *Mtb*H37Rv strain during the infection (1 to 7 days post infection). Additionally, the mRNA level of *ctpH* increased 180-fold in the *Mtb*Δ*ctpF* strain after exposure to sublethal doses of Ca^{2+} (2.5 mM), relative to untreated cells. While the expression levels of *ctpI* did not increase in both conditions. This evidence suggests that *Mtb* uses several P2-type ATPases to counteract the *ctpF* deletion and preserve a balanced ion environment in response to stressful conditions within the host. Thus, the ability to modulate ion homeostasis may be a key factor for successful infection.

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ANALYSIS OF THE EXPRESSION OF THE TRANSCRIPTION FACTOR WRINKLED 1 IN COCONUT ZYGOTIC EMBRYOS AT THREE DEVELOPMENTAL STAGES

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Abstract:

The coconut palm (*Cocos nucifera* L.) is a commercially important crop, a member of the Arecaceae family. It produces one of the largest oleaginous fruits in nature, however, it has a small embryo compared to the size of the fruit. At present, there are limited research on gene regulators and metabolic processes related to the maturity of the coconut zygotic embryo, particularly with lipid metabolism. In the present work, the transcription factor WRINKLED1 (WRI1), a member of the APETALA2 (AP2) transcription factor family, was isolated from the coconut zygotic embryo. Reports point to WRI1 as a crucial regulator of genes encoding enzymes involved in vegetable oil biosynthesis. Based on the background, the objective of this work was to carried out bioinformatics analyses, related to conserved regions of the transcription factor WRINKLED1, synthesize specific DNA primers and then determine by qPCR the level of expression of WRI1 in coconut zygotic embryos at different stages of maturity. The results revealed that the amino acid sequence of WRI1 from *Cocos nucifera* L. (designated as CnWRI1) has 342 nucleotides, high degree of amino acid conservation with WRI1 proteins from other species, in particular with members of the Arecaceae family. On the other hand, analyzes of relative expression by conventional PCR, showed that the expression pattern of CnWRI1 in the Pacific Tall variety, decreases as the developmental stages of the zygotic embryos increase, while in the Green Dwarf variety, the greatest sign of expression was found in intermediate stages of maturation. Together, results suggest that WRI1 expression is differentially regulated in both coconut varieties.

EVALUATION OF DIFFERENT CARBON SOURCES IN THE PRODUCTION OF CAROTENOIDS IN THE YEAST *RHODOTORULA MUCILAGIOSA*

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Abstract:

90% of the industrial production of carotenoids implies chemical synthesis. However, this method is highly contaminating as it releases triphenylphosphine oxide, (harmful to human health and the environment). In recent years, the search for natural, efficient, and environmentally friendly options for carotenoid production has experienced a significant increase. Genetically modified Sphingomonas bacteria and *Dunaliella microalgae* are widely used for the microbial production of carotenoids. An alternative is the use of oleaginous yeasts such as Rhodothorula, a pigmented *Cryptococaceae*, widely used as a biotechnological tool due to its easy handling, high biomass production, and ability to grow in extreme environments. Most research on this yeast has focused on increasing the production of these compounds by exposing it to various stressors such as changes in pH, temperature, osmolarity, and UV radiation. However, an unexpensive and efficient alternative could be the modification of the carbon source of the culture medium. The objective of this work was to evaluate the production of carotenoids from *Rhodotorula mucilaginosa* in different carbon sources. We focused on identifying their possible physiological role. Our results showed that when comparing the growth of *R. mucilaginosa* in different media; glucose, mannitol, galactose, and lactate as carbon sources, glucose produced higher biomass. In contrast, carotenoid production increased 78.7% with lactate as a carbon source at the logarithmic growth phase and 65.82% at the stationary phase. Remarkably, inhibiting the carotenoid synthesis pathway led to lower resistance to oxidative stress. Therefore, it is suggested that carotenoids have an important role in resistance to stress.

DEVELOPMENT OF A NOVEL VIRUS-LIKE PARTICLE (VLP) PLATFORM FOR THE DISPLAY OF THE SARS-COV-2 RBD TO INDUCE SPECIFIC IMMUNE RESPONSES

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Abstract:

Facing the current COVID-19 pandemic caused by the emerging SARS-CoV-2 infection, short-term efforts to design, generate, and distribute an effective vaccine capable of inducing specific humoral immune responses against the Spike (S) glycoprotein have resulted in a significant reduction of severe and fatal cases, worldwide. However, these new genetic platforms do not necessarily prevent viral infection following months after inoculation, especially in infants, and cases caused by the new Omicron variant, where the efficacy of prophylactic immunity has been seen as partial. Given this situation, it is necessary to continue research on alternative platforms that could generate long-term immune memory, while remaining economically accessible for countries with limited infrastructure. Virus-like particles (VLPs) derived from repetitive viral capsid proteins with self-assembly property represent an opportunity for the design of symmetric supramolecular scaffolds that could efficiently display and present multiple copies of one or several antigens of medical important pathogens. Notably, VLPs can penetrate germinal center of lymph nodes to induce robust humoral responses. The present project aims to develop and evaluate the structural and immunogenic properties of a "proof-of-concept" VLP platform derived from enterophage HK97, in which each particle displays multiple copies of a non-glycosylated antigenic fragment of the SARS-CoV-2 receptor binding domain (RBD). VLPs were expressed in *E. coli* from HK97-gp5 protein, genetically modified to include an electrostatically complementary adapter peptide, deployed on the surface of the assembled particle for later antigen incorporation. Genetic modification of the C-terminal end of HK97-gp5 does not affect its ability to form capsomeric complexes and self-assembly into spherical VLPs. Furthermore, these added appendages are displayed on the exposed surface of the assembled particle. Immune responses in animals will be evaluated by two-way repeated measure ANOVA.

EFFECT ON STABILITY AND KINETICS OF β-HAIRPIN IN *T. THERMOPHILUS* HB27 LACCASE

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Abstract:

Laccases (benzenediol oxygen oxidoreductases) catalyze the reduction of a dioxygen molecule to two water molecules using four electrons from the substrate. These are versatile enzymes that can use different substrates, such as polyphenols, aminophenols, polyamines, methoxyphenols, and lignins. The catalytic site of laccases is formed by four catalytic coppers (CuT1 CuT2, CuT3a, CuT3β).

Thermus thermophilus HB27 laccase (TthLac) is a highly thermoresistant and mildly alkalophilic enzyme. TthLac possesses catalytic activity against ABTS and syringaldazine as substrates. TthLac (PDB 2XU9) has a β-hairpin (Ala292-Gln307) located above the substrate entry and the CuT1 site. In the present study, we propose that a deletion of β-hairpin will result in increased exposure to the substrate-binding site and, consequently an enhanced catalytic activity.

Mutants in which the hairpin was completely (C1Tth and C2Tth) and partially removed (P2Tth) were designed. Mutants were evaluated by determining kinetic parameters in the presence and absence of free copper. Stability was calculated by analyzing the effect of chaotropic agents on catalytic activity, as well as in the secondary and tertiary structure. The presence of copper was monitored by UV-vis and EPR spectroscopy. Finally, redox potentials were calculated by cyclic voltammetry. All the laccases presented dependence on copper in the reaction medium, displaying 20-1600-fold increases in their catalytic efficiency. Regarding stability, C2Tth showed the highest value with C_m>7M in urea. The wild-type enzyme maintained its structure at higher GdnHCl values (C_m=2.57M). Mutants presented altered spectroscopic signals on the CuT2, CuT3a, CuT3b. The coordination of the copper sites and the modification of the chemical environment of the substrate-binding residues could have been responsible for the kinetic and stability changes in the β-hairpin mutants.

THE PLANT MITOCHONDRIAL HOMOLOGOUS RECOMBINATION

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Abstract:

The DNA in the cell is exposed to a wide variety of damage by physical and chemical agents, which affect its physical constitution, leading to profound biological consequences such as cell death. Mitochondria is the energy production center of the cell and has its own genome, for this reason it is important to maintain the integrity of its mitochondrial DNA (mtDNA). In plant mitochondria, there are mtDNA repair mechanisms, the most important and for which there is more evidence being the homologous recombination (HR) repair mechanism. Recombinases play a central role in HR repair. Arabidopsis has 3 nuclear genes that code for three recombinases: AtRecA1, AtRecA2 and AtRecA3, for which their in vitro biochemical functions and interactions with other HR proteins like AtRecX have not yet been determined that allow understanding on how their activity is regulated.

In the present work we evaluated mitochondrial proteins from Arabidopsis, recombinases an RecX, through single-stranded DNA (ssDNA) affinity assays, ATPase assays by thin-layer chromatography, as well as the inhibition of recombinase ATPase activity by AtRecX.

The results obtained show that Arabidopsis organelle recombinases bind to DNA of non-specific sequence, of different length and structure, have DNA-dependent ATPase activity, which is inhibited by AtRecX, without its domain of unknown function. This inhibition mechanism could be due to protein-protein interaction and competition for ssDNA.

BIOCHEMICAL CHARACTERIZATION OF THE BIFUNCTIONAL ENZYME G6PD::6PGL OF THE PARASITE *GIARDIA LAMBLIA*

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Abstract:

Antecedent: *Giardia lamblia* is an early divergence eukaryote, and has been considered as part of the evolutionary basis of eukaryotes. Among the metabolic routes that it presents, the pentose phosphate pathway (PPP) stands out, through which molecules such as NADPH are generated, which is capable of providing defense against the immune system of its hosts and in this way guaranteeing its survival. Various enzymes are involved in PPP, the first is glucose 6-phosphate dehydrogenase (G6PD) and it plays a very important role at the cellular level since it produces NADPH. A characteristic of the G6PD of G. lamblia is that of presenting fusion with the second enzyme of this pathway, 6-phosphogluconolactonase (6PGL), suggesting that its fusion generates a bifunctional enzyme G6PD::6PGL that favors the efficiency of the pathway. Objective. To determine the bifunctionality of the fused enzyme glucose-6-phosphate dehydrogenase::6-phosphogluconolactonase (G6PD::6PGL) of the parasite *Giardia lamblia*. Material and method. Overexpression and purification of the G6PD:.6PGL fused protein and its individual domains were performed. In addition, the analysis of the catalysis product was carried out by means of mass spectrometry and assay coupled to the 6PGDH enzyme. Results and Conclusions. The findings of the present work demonstrated that the fused enzyme G6PD::6PGL has activity in the 6PGL domain. In addition, the kinetic parameters of the fused enzyme G6PD::6PGL were determined and compared with respect to the individual domain of G6PD. The single 6PGL domain was unstable and could not be purified. It was shown that catalysis is more efficient in the fused G6PD::6PGL enzyme than in the G6PD enzyme isolated individually, suggesting that this enzyme is a bifunctional enzyme. In addition, it was established by enzymatic and MALDI-TOF mass spectrometry assays that the reaction product of the fused G6PD::6PGL enzyme has the compounds; 6-phosphoglucono-d-lactone and 6-phosphogluconate, products of the G6PD and 6PGL domains, respectively.

ZIKA VIRUS HIJACKS DYNEIN FOR ITS REPLICATION CYCLE

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Abstract:

Infection with Zika virus (ZIKV) became a significant health threat since it can spread to the nervous system and can result in death or severe long-term disability[1]. ZIKV belongs to the Flavivirus family that includes also Dengue virus, Yellow Fever virus and West Nile virus. It has been demostrated that Dengue virus binds to the Human cytoplasmic dynein-1 (dynein) but it was no clear whether it binds to the complete Dynein nor if this interaction occurs in an specific time on the virus replication cycle. In this, work we have strong evidence that ZIKV binds to the the heavy chain of Dynein independent of dynactin and cargo adaptor. This is the first non coiled-coil protein that binds to dynein and also, that this protein binds to the NDD, oposite to the dynactin-cargo adaptor binding region[2]. We showed also that this interaction is present in vivo in ZIKV-infected Vero cells in a specific step within the replication cycle, and that the maximum lenght of this interaction is <40 nm by proximity ligation assays. Another evidence for the relationship among the viral and the host proteins is that dynein overexpresses at a highly specific time post ZIKV infection in Vero cells. The ZIKV from infected Vero cells co-immunoprecipitates with dynein. Finally, we disected the region for interaction by selective antobodies and protein engineering resulting that the ZIKV protein that binds to dynein is the envelope protein, and the region of dynein that binds to the virus is the N-terminal dimerization domain. We have two big perspectives from these results 1) To solve the 3D structure of ZIKV with bound dynein by Cryo-EM and 2) To find inhibitor molecules to disrupt this interaction within the cell in order to propose these molecules as tratment for ZIKV infected patients[3].

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BETAINE ALDEHYDE DEHYDROGENASE ACTIVITY AND BIOMASS EVALUATION IN VARIOUS GENOTYPES OF WHEAT (*TRITICUM AESTIVUM*) UNDER HEAT STRESS

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Abstract:

Betaine aldehyde dehydrogenase is the enzyme that catalyzes the last step of the formation of glycine betaine, an osmolyte known to help in the tolerance of plants under abiotic stress. Heat stress has become one of the significant factors that the agricultural system must confront, causing an important reduction in yield and physiological damage to crops. This work examines the activity of betaine aldehyde dehydrogenase and glycine betaine concentration in four bread wheat genotypes under heat stress and its relationship with the capacity to maintain their biomass. Two field experiments were carried out: a control and heat stress during the reproductive stage. Samples for the activity and concentration assays and biomass parameters were taken in these two conditions. The activity of betaine aldehyde dehydrogenase was measured following the oxidation of NAD+ at 340 nm, and the concentration of glycine betaine was measured at 365 nm. The analysis of the biomass parameters shows a general reduction in the spike weight in the stress crops. There was a reduction of seed weight in all genotypes, been genotype 06 the one with a more considerable reduction of seed weight. In all genotypes, the concentration of glycine betaine increased. An increase in betaine aldehyde dehydrogenase activity was observed in genotype 23, which showed lower spike length, weight, and seed number changes. Data suggest that the accumulation of glycine betaine plays a role in the ability of these wheat genotypes to respond to heat stress.

FINDING THE SLC16A11 SUBSTRATE BY STRUCTURAL MODELING

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Abstract:

Diabetes is a chronic degenerative disease of worldwide importance and Mexico is not the exception. Several investigations focused on studying the nature of this disease. In 2014, a study identified a new risk haplotype located in the coding region of the *SLC16A11* gene, associated with type 2 diabetes (T2D) in Mexican population.1 This haplotype contains 5 single nucleotide polymorphisms (SNPs), in which 4 are non-synonymous and 1 synonymous. *SLC16A11* is a member of the monocarboxylate transporters (MCTs) family, however its function and, consequently, the contribution to the T2D etiology is not clearly understood.2 There are studies that have partially characterized the transport of SLC16A11, suggesting pyruvate as its possible substrate3, also relating it to modifications in lipid metabolism1,3. With that in mind, our objective is to characterize *SLC16A11 in silico* to identify possible substrates tested by Docking that will later be corroborated with thermostability tests, previously obtaining the expression and purification of the transporter. We made 22 structural models of *SLC16A11 in silico* seeking for amino acids with the highest probability of appearance inside the transport pore of these models and thereby, propose them as the binding site of *SLC16A11* necessary to perform molecular docking assays. In docking assays, we tested 200 substrates with multiple physicochemical characteristics that could be candidates for transport. Our results have allowed us to identify with two structural models (one of them elaborated with the MCT2 template and the other in AlphaFold2) that the proposed transport pore has hydrophobic characteristics with greater affinity for high molecular weight monocarboxylates, as fatty acids, which would be consistent with the relationship found with lipid metabolism. As a perspective, we will express and purify the SLC16A11 heterologously for biophysics experiments.

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RESIDUES IN RANDOMIZED POSITIONS CONTRIBUTE TO THE BIOCHEMICAL PROPERTIES OF DESIGNED ANKYRIN PROTEINS

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Abstract:

Designed ankyrin proteins are a novel class of therapeutic molecules based on natural ankyrins that mediate protein-protein interactions in virtually all species. Designed ankirins are composed of 33-amino acid repeat modules that form a hydrophobic core sealed by N- and C-terminal capping repeats. In addition, the ankyrin core includes seven random residues that modulate the interaction with its target proteins (1). Several 2- to 6-module designed ankyrins are widely used, especially in biomedical research. However, single-module designed ankyrins were described as unstable and difficult to purify (2). Therefore, in this work, we show the successful purification and biochemical characterization of three single-module designed ankyrins focusing on the features conferred by the randomized amino acids on the stability and biochemical properties of the studied ankyrins.

Objective: To produce three single-module designed ankyrins and evaluate the contribution of different amino acid residues at random positions on their stability and biophysical properties.

Methods: Protein purification was performed by immobilized metal affinity chromatography (IMAC), solubility assays using a centrifugal approach, evaluation of extrinsic fluorescence with ANS, and measurement of thermal stability was carried out by thermal shift assays (TSA).

Results: The three single-module designed ankyrins were successfully purified from the soluble fraction with yields between 15-30 mg per L of cell culture. Designed ankyrin with hydrophobic amino acids in the randomized positions is prone to aggregation and showed the highest extrinsic fluorescence with ANS. Furthermore, charged amino acids in the randomized positions enhance the solubility of designed ankyrins and confer them thermostability, obtaining Tm´s near 60 °C.

Conclusions: The chemical nature of the seven random amino acids of the ankyrin module directly affects its stability and biochemical behavior, allowing these features to be used as a control to modulate its interaction with specific target proteins.

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MGR2 MODULATES THE IMPORT OF YEAST CYTOSOL-SYNTHESIZED SUBUNIT II OF CYTOCHROME C OXIDASE (COX2) WHEN MOVING THROUGH THE TIM23 TRANSLOCON

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Abstract:

The mitochondrial subunit 2 of cytochrome *c* oxidase (CcO), was allotopically expressed in yeast with the point mutation W56→R reducing its hydrophobicity(1). After entering mitochondria, this precursor was proteolytically matured, embedded in the inner mitochondrial membrane (IMM), and functionally assembled into CcO(2). Thus, the Cox2^{W56R} precursor restored growth of a *Δcox2* null mutant in non-fermentable carbon sources. Here, using yeast strains that express a multicopy 2μ plasmid encoding the Cox2^{W56R} precursor (*e:* episomal Cox2^{W56R}), we asked if the overexpression of certain genes could improve the import of this protein into mitochondria, facilitating further growth of the mutant strain in respiratory media(2). Selected genes encoding factors directly or indirectly involved in protein import were overexpressed, and the internalization/maturation/assembly of Cox2^{W56R} was followed. Overexpression of the genes *COX20*, *OXA1*, *TIM22*, increased the levels of mature *e*Cox2^{W56R} in mitochondria and in a less but still important manner from *TOM70*, *MGR2*, *TIM21* and *PSE1*. We further explored the effect of Mgr2, a quality control factor that modulates protein sorting by the TIM23 translocator(3), and followed the import of Cox2^{W56R} expressed either from the multicopy plasmid (*e*Cox2^{W56R}) or from the gene inserted in the nucleus (*n*Cox2^{W56R}) in yeast strains that either lack or overexpress the *MGR2* gene. When the *COX2W56R* gene was expressed in the absence of *MGR2*, the steady-state levels of *n*Cox2^{W56R} slightly decreased. In contrast, when the same gene was expressed from a multicopy plasmid in the absence of *MGR2*, the steady state levels of *e*Cox2^{W56R} were strongly affected. In both cases, overexpression of *MGR2* was of no benefit. We conclude that Cox2^{W56R} is imported through TIM23, in a process that must involve the two known structural/functional forms of the translocator: TIM23^{MOTOR} (lacking Mgr2) and TIM23^{SORT} (containing Mgr2). We propose a model for Cox2^{W56R} biogenesis, where the concerted action of TIM23^{MOTOR} and TIM23^{SORT} is instrumental in correctly sorting the TMS1 and TMS2 of Cox2^{W56R} respectively, allowing the protein to reach its final, functional topology. Mgr2 is instrumental in the lateral release of the TMS2 into the IMM and the concomitant release of the hydrophilic C-terminal domain of Cox2^{W56R} into the mitochondrial intermembrane space. We acknowledge support from PAPIIT-DGAPA-UNAM IN21856.

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HYDROGEN SULFIDE SYNTHESIS BY YEAST CYSTATHIONINE β-SYNTHASE IS REQUIRED TO SURVIVE ER STRESS

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Abstract:

The endoplasmic reticulum (ER) is the main responsible of secretory and membrane proteins biosynthesis. Due to the particular environment of the organelle and reactive oxygen species (ROS) production during protein folding, the ER should maintain a strict homeostasis. When the folding capacity of the ER is exceeded, cells answer through the unfolded protein response (UPR). In yeast, the UPR begins when an unfolded protein binds Kar2p, activating Ire1p. The RNAse domain from Ire1p promotes the alternative splicing of the ER-stress transcription factor Hac1p. Previous studies in our laboratory demonstrated that mutant strain *Dcys4* has a severe growth hindrance during tunicamycin ER-stress induction. CYS4 encodes for the yeast cystathionine β-synthase, which catalyzes the production of cystathionine from serine and homocysteine. Alternatively, Cys4p can produce hydrogen sulfide (H_2S) from either cysteine alone or cysteine plus homocysteine. When and where Cys4p catalyzes the reaction to produce H_2S instead of cystathionine still remains unknown. Hydrogen sulfide is a gasotransmitter that very recently attracted the attention of the scientific community mainly due to the fact that imbalances in its regulation are associated with the prevalence of degenerative diseases like diabetes, fatty liver and Alzheimer's disease.

Here, we found that only Cys4p and not Cys3p shows a sever growth defect when incubated with tunicamycin. However, when we add the amino acid L-cysteine, the *Dcys4* strain recovers its basal growth. To test whether the observed phenotype was due to alterations on the UPR, or something else, we generated the strain *Dcys4Dhac1.* Surprisingly, under ER stress conditions we observed a negative genetic interaction between *CYS4* and *HAC1* genes. Because of the multiple catalytic activities from Cys4p, we hypothesize that the protein should have some regulatory mecanism to produce H_2S at a given time. To test the prior, we generated the mutants C301S and C301Y from Cys4p. Intriguingly, both mutants show different growth phenotypes when inducing ER stress. Also, we found that the activation of the UPR branch from yeast remains functional and its activation is premature on the *Dcys4* strain by following the activation of the promotor region UPRE.

With the above described, we found a novel genetic interaction between a metabolism gene and a gene from the UPR. Besides, we stablished the basis of an endoplasmic reticulum stress regulation mediated by hydrogen sulfide. However, it still remains elusive how the absence of the *CYS4* gene affects the natural homeostasis of the yeast endoplasmic reticulum.

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MAPK AND PKA SIGNALING PATHWAYS MODULATE THE STEROIDOGENESIS IN JEG3 CELLS

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Abstract:

Placental mitochondria have associated the *steroidosome* (contains the enzymes involved in the steroidogenesis), and the *signalosome* (with all the elements of signal transduction) which are necessary for steroidogenesis. However, the mechanism to modulate these multiprotein complexes is unknown. Data from the literature showed that the PKA activity is associated with placental mitochondria and has an important function during the steroidogenic process, since its inhibition with H89 decreases P4 synthesis with changes of protein phosphorylation. Preliminary data also showed that the inhibition of MEK/ERK activity by U0126 diminished the P4 concentration in isolated mitochondria.

To determine whether the PKA or MAPK pathways are involved in steroidogenic control in the human placenta, choriocarcinoma cells (JEG3) were used, which preserve the biochemical characteristics for P4 synthesis.

We use U0126 and Binimetibin (MEK162) to inhibit MEK1/2, and H89 to inhibit PKA. Cells JEG3 were incubated 24 or 48 h and P4 was quantified using an ELISA assay. To identify whether PKA and MAPK signaling cascade work together in the placental steroidogenesis, cells were incubated with H89, U0126 or MEK162 for 24 h followed by the complementary addition with H89, U0126 or MEK162 for other 24 h. The proteins up and downstream of the MAPK cascade were identified and total protein phosphorylation determined by western blot.

The synthesis of P4 decreases approximately 30% in the presence of H89, U0126 or MEK126 at 24 or 48 h. The complementary addition of inhibitors did not modify the P4 synthesis. In both kinds of experiments, the presence of cAMP reestablishes partially the synthesis of P4, suggesting that the PKA pathway has an important participation. The identification of p-MEK and p-Erk in the different experimental conditions showed that MEK1/2 phosphorylation increases in the presence of MEK162, suggesting that a kinase, different from RAF, is associated with the regulation of MEK phosphorylation. It has been reported that PAK, an integrin-activated kinase, can phosphorylate MEK1 at S298, a different RAS phosphorylation site. Also, p-Erk1/2 increases in the presence of cAMP and decreases with U0126 or MEK162, in the same way as P4 synthesis. We suggest that H89 decreases the Ras phosphorylation and therefore the MEK and ERK activity. The effect could be reflected at nuclear level, preventing the

phosphorylation of transcription factors associated with the biosynthesis of steroids such as CREB and c-Jun, negatively modifying the concentration of P4. The results will let us identify proteins of cell signaling which modulate steroidogenesis and further establish a possible mechanism of signal transduction.

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MOLECULAR DISSECTION OF THE ESCO PROTEIN FROM THE INJECTISOME OF ENTEROPATHOGENIC *ESCHERICHIA COLI*

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Abstract:

Enteropathogenic *Escherichia coli* (EPEC) is responsible for diarrheal diseases around the world, especially in low-income countries and it mostly affects children. This pathogen causes a specific histopathology in the gastrointestinal tract which eliminates the microvilli and rearranges the cytoskeleton of the enterocyte. This histopathology is denominated attaching and effacing lesion (AE lesion). The pathogenesis of EPEC is dependent on a Type III Secretion System (T3SS) that is encoded on a chromosomal pathogenicity island known as locus of enterocyte effacement (LEE). The T3SS or injectisome is a nanomolecular complex with a syringe like shape and it is composed of about 20 different proteins. This system is responsible for the translocation of effector virulence proteins into the enterocyte cytosol, which interrupt different signal transduction pathways of the cell to manipulate the cellular physiology to the benefit of the pathogen. The T3SS depends on an ATPase that hydrolyzes ATP to energize the secretion of substrates through the system. The EscO protein is an ATPase activator in the bacterial cytosol which promotes the oligomerization of the ATPase into a hexamer, increasing its catalytic activity. T3SS from other pathogens have shown that the orthologues of EscO (SctO, using the unified nomenclature), shows more than one function. Three principal functions have been associated with SctO which are the efficient activation of the proton-motive force in the export apparatus, the escort of chaperones to the base of the T3SS and the activation of the ATPase. Also, it has been observed that these proteins can interact with the sorting platform, although this interaction does not have an associated function. Hence, in this project it is our interest to determine the regions in EscO where it interacts with chaperones and with the sorting platform to establish the importance of these interactions in the secretion process.

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HYPERGLYCEMIA AFFECTS RAT SPERM HYPERACTIVATION AND MEMBRANE POTENTIAL

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Abstract:

Keywords: spermatozoa, rat, hyperglycemia, diabetes, hyperactivation, hyperpolarization

The newly ejaculated spermatozoa are unable to fertilize the egg, for this they need to experiment biochemical and physiological changes called capacitation. This process includes increases in: the fluidity of the membrane due to the cholesterol removal, the intracellular pH, calcium, bicarbonate and cAMP, in addition, the protein of phosphorylation patterns mediated by PKA, PKC and pY change, the membrane potential hyperpolarizes and the sperm motility change from active to hyperactivated (HA). Only capacitated spermatozoa undergo the acrosomal reaction (AR), a single event of exocytosis essential for fertilization. It is known that alterations in capacitation, HA or AR led to infertility because of various pathophysiological factors, which includes diabetes mellitus (DM). The incidence of DM in males of reproductive age is one of the main reasons why this disease negatively impacts fertility. DM is a systematic, chronic-degenerative disease of a heterogeneous nature, characterized by hyperglycemia, or high blood glucose concentration.

In this work, we use male Wistar rats induced with alloxan (ALX) as model to evaluate how hyperglycemia impacts the sperm hyperactivation and membrane potential. ALX es a diabetogenic agent that impair β-pancreatic cell that produce insulin. Our results show that hyperglycemia decreased body weight and that of the testis and epididymal caudas. Furthermore, the number of total sperm and viability diminish in hyperglycemic rats. Finally, sperm from hyperglycemic rats are hyperpolarized compared with their control, and so not respond to non-physiological inducers of hyperactivation as caffeine, procaine or 4-aminopyridine (4-AP). These results suggest that hyperglycemia alters at least two critical events necessary for the sperm to fertilize the egg, the hyperactivation and membrane potential.

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CHARACTERIZATION OF CHANGES IN THE STRUCTURAL CONFORMATION OF LEA PROTEINS IN DIFFERENT ENVIRONMENTAL SETTINGS AND THEIR POSSIBLE RELATIONSHIP TO THEIR PROTECTIVE FUNCTION

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Abstract:

Due to their sessile nature, land plants are constantly exposed to stressful environments. Plants have evolved strategies to survive in these stressful environments. One of these responses is the accumulation of late embryogenesis abundant (LEA) proteins. LEA proteins lack a well defined three dimensional structure but can change this disordered structural conformation when they undergo changes in their environment, and these changes in the structural conformation of LEA proteins also result in changes in the protective function they exert on other proteins. This suggests that the ability of LEA proteins to change their disordered structural conformation when their environmental surroundings change is related to their protective function. In this work, we chose four LEA proteins from different groups of the model plant *A. thaliana* and we characterized their structural conformation by changing their environmental setting. In silico, by means of Monte Carlo simulations, we were able to characterize the change of the radius of gyration of the proteins of our selected group, by modifying the repulsion of their solution. *In vitro*, using the solution space scanning methodology, we characterized the expansion and compaction of the proteins of our selected group in 21 different osmolytes (denaturing agents, salts, sugars, polymers of different lengths among others). Finally, we expressed the constructs of our selected group in yeast cells and subjected them to hyperosmotic shocks with NaCl, and we measured the changes in their structural conformation using FRET. Our results showed that a protein LEA_4 has greater sensitivity to change its conformation structural using polymers of different lengths and that PvLEA18 has less sensitivity to change its structural confirmation under the same conditions with respect to the other proteins of our select group. In addition, this behavior is reproduced under conditions of hyperosmotic shock *in vivo*. This project will allow us to better understand how LEA protein's function and eventually we may be able to enhance their protective function to benefit not only plants but also organisms under stressful environmental conditions.

STUDY OF COMPLEX II BIOGENESIS IN *SACCHAROMYCES CEREVISIAE*

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Abstract:

Complex II (succinate dehydrogenase) oxidizes succinate into fumarate, transferring electrons to the ubquinone in the respiratory chain (*1*). Complex II is composed by four nuclear encoded subunits: Sdh1 and Sdh2 form the catalytic center in the mitochondrial matrix, while Sdh3 and Sdh4 anchor the complex to the inner membrane and allows the transfer of electrons to ubiquinone (*2*). In *S. cerevisiae*, except for Sdh2, complex II subunits have two versions that arose from a genome duplication event (Sdh1b, Shh3 and Shh4)(*3*). The specific function of these paralogues is not clear (*4*, *5*). We asked what the role of these paralogue subunits is and if complex II subunits (and paralogues) are affected after mutation of other components of the respiratory chain. This is particularly interesting because complex II is the only respiratory complex with all nuclear encoded subunits.

A complexomic assay of yeast mitochondria confirmed that the paralogues are part of complex II(6). In contrast, in a mutant affecting respiratory complex III the paralogues were not detected, and accumulation of complex II with the original described subunits decreased. In addition, an accumulation of assembly intermediaries of CII subunits increased (6). These results suggests that at least complex III activity is necessary to maintain normal levels of complex II and for presence of paralogue subunits of complex II.

We created mitochondrial mutants (lacking mtDNA, or complexes II, III, IV and V) to observe accumulation of the CII subunit Sdh2 as well as the paralogue subunit Shh3. Sdh2 levels were reduced in all mutants, especially in cells lacking mtDNA. Shh3 was not detected in any of the analyzed mutants. Our results demonstrate that complex II biogenesis is regulated by the presence of the other fully assembled respiratory complexes.

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CROSSTALK BETWEEN O-GLCNACYLATION AND CD36 IN MACROPHAGES

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Chronic noncommunicable diseases (CNCDs) currently represent a very high cost for society in various areas. Due to their consequences at different levels, they have been classified as a public health problem. These diseases are favored mainly by unhealthy lifestyles such as poor diet and sedentary lifestyles. These behaviors favor the increase of lipids in the blood. This metabolic risk factor has a great negative impact at the cellular and molecular level in the affected organism. The sterile inflammation in these conditions makes the relationship between the metabolic system and the immune system. In this sense, it is known that aberrant O-GlcNAcylation constitutes a link between metabolism and multiple CNCDs and that macrophages (MΦ) play an essential role in these conditions.

This research aimed to evaluate the levels of O-GlcNAcylation and the expression of CD36 in MΦ J774 stimulated with palmitic acid (PA) and serum from dyslipidemic patients. Initially, the conditions for the stimuli were standardized, and subsequently, the O-GlcNAcylation profile and the protein expression of CD36 and OGT were evaluated The results show that the profile of O-.

GlcNAcylation has similarities with both stimuli. However, a decrease in the level of O- GlcNAcylation was observed in the stimuli sera. OGT expression indicated higher expression in PA treatments.

STUDY OF THE STRUCTURAL SENSITIVITY TO THE ENVIRONMENT OF INTRINSICALLY DISORDERED REGIONS IN ARABIDOPSIS TRANSCRIPTION FACTORS

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Abstract:

Proteins have an important role in cells, having a specifically defined structure that determines their function. However, in the past decades, researchers have discovered proteins that lack a stable secondary or tertiary structure. These proteins are named Intrinsically Disordered Proteins (IDPs) when referring to a complete protein or Intrinsically Disordered Regions (IDRs when a domain of a protein is involved. IDRs possess a characteristic amino acid composition that allows them the capacity to respond rapidly against changes in the physicochemical environment, providing another layer of protein regulation. This idea suggests that the disordered domains of proteins respond to changes in environmental conditions like high osmolarity, causing a conformational shift. Transcription factors of the model plant Arabidopsis thaliana possess high levels of disorder according to recent studies, nonetheless, little is known about the structural sensitivity of its disordered domains. We hypothesize that the structure of the intrinsically disordered regions of a group of transcription factors of Arabidopsis will present a response against effects caused by osmotic shock in vivo. We use different information on IDRs to produce an analysis of the conformational change of the IDRs of a selected group of 21 transcription factors of Arabidopsis and then measure the conformational status using a technique called FRET (Fluorescence Resonance Energy Transfer). We quantified the conformational change of the 21 IDRs in living yeast cells subjected to hyperosmotic stress. The results showed that the structure of transcription factors IDRs have different degrees of response against osmotic shocks in vivo. Currently, we are searching for the determinants of the diverse responses of IDRs using parameters associated with the charge of the IDRs, like the fraction of positive and negative amino acid residues, the total charge, and the mean net charge of the IDR, as well as hydropathy and length. Our findings suggest that a high FRET ratio response is due to a symmetric distribution of the charge throughout the IDR when comparing those IDRs having a non-homogenous charge distribution. Characterization of the different degrees of the response of these IDRs could allow generating new biosensors as a tool that could be used to track physicochemical changes in cells.

EFFECT OF 8-BENZYL-1,3,8-TRIAZASPIRO-[4.5]-DECANE-2,4-DIONE ON MIGRATION AND INVASION OF PC3 PROSTATIC TUMORAL CELLS STIMULATED WITH LDLS

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Introduction. Prostate cancer is the second most common cancer diagnosis and the fifth cause of death worldwide among malignant diseases. In Mexico during the year 2020, an incidence of 26, 742 prostate cancer cases were reported, 70% of which were detected in advanced stages of the disease. Even though several therapeutic approaches exist for prostate cancer treatment, a considerable amount of treated persons will have a relapse of the disease, risk that is increased if the diagnosis is made in advanced stages or if the person has a comorbidity, such as dyslipidemia. Generation of new treatments with the purpose of improving the prognosis of this population group in particular, is of extreme relevance. With continuous research, evidence of new molecules with antineoplastic properties give rise to the possibility of applying such molecules in future patients with prostate cancer. **Objectives**. Characterize the effect of the 8-benzil-1,3,8-triazaspiro-[4.5]-decano-2,4-dione (triazaspirane) against human prostate cancer cells PC3 stimulated with low density lipoproteins (LDL), especifically migration and invasion. **Methodology**. Evaluation of the impact of triazaspiran on the migratory capacity of LDL-stimulated PC3 cells was assessed by scratch wound healing, while invasion was assessed by Matrigel-coated Boyden chamber assays. Results. LDL promotes migration and invasion, whereas triazaspirane inhibits these effects in prostate cancer cell line PC3.

EFFECT OF PH AND TEMPERATURE ON THE KINETIC PARAMETERS OF THIOREDOXIN-GLUTATHIONE REDUCTASE FROM *TAENIA CRASSICEPS*

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Abstract:

Thioredoxin-glutathione reductase (TGR) represents an unusual variant of the high molecular weight Thioredoxin reductase. The enzyme is characterized by the presence of a glutaredoxin-like domain appended at its N-terminal end. Such domain confers to the enzyme the ability to reduce GSSG in a NADPH dependent fashion, in addition to thioredoxin, as well as to catalyze thiol/disulfide exchanges. Although the enzyme is expressed in mammalian testes, it is particularly important in parasitic flatworms, being the only enzyme involved in the reduction of both thioredoxin and GSSG. TGR displays an unusual kinetic behavior with GSSG, showing substrate inhibition followed by reactivation by the product GSH, leading to hysteretic-like progress curves of enzyme activity.

In the present work the effect of both pH and temperature on the kinetic parameters V_m and K_m of the various reductase activities of TGR from *Taenia crassiceps* were analyzed. From the dependence of V_m and the V_m/K_m ratio on pH, the apparent pKa values of both free enzyme and enzyme-substrate complexes were obtained. On the other hand, from the dependence of the turnover number (k_{cat}) on temperature, activation energies for the reduction of thioredoxin, GSSG and the artificial substrate DTNB were determined. Finally, the dependence of the GSSG-dependent substrate inhibition on pH and temperature was also analyzed. The results are discussed in terms of the two-sites ping-pong bi bi kinetic mechanism followed by TGR as well as the catalytic groups present in the redox active centers of the enzyme.

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THE ABSENCE OF PYRUVATE CARBOXYLASE AND PHOSPHOENOLPYRUVATE CARBOXYLASE AFFECT NITROGEN FIXATION IN *RHIZOBIUM PHASEOLI*

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Abstract:

Pyruvate carboxylase (PYC) and phosphoenolpyruvate carboxylase (PEPC) produce oxaloacetate, which is an essential metabolite of the tricarboxylic acids cycle (Koendjbiharie *et al*., 2021). In *Rhizobium etli* CFN42, growth was affected by the absence of PYC in pyruvate and glucose as carbon sources (Dunn *et al*., 1996). In *Rhizobium phaseoli* CIAT652, the PYC mutant showed behavior similar to the CFN42 strain, having an optimal growth in succinate and a deficient growth in pyruvate and glucose. The mutant strains PEPC and PYC-PEPC presented an optimal growth in succinate, while in pyruvate and glucose they were unable to grow. The most drastic effect was observed during symbiosis, where the PYC, PEPC, and PYC-PEPC mutants showed a decrease in nitrogenase activity. These data suggest that these carboxylases are necessary for symbiotic nitrogen fixation in common bean plants.

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LIVER VERSUS CARDIAC MITOCHONDRIA: COMPARISON OF SOME EFFECTORS ON THE MITOCHONDRIAL PERMEABILITY TRANSITION PORE

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Abstract:

Mitochondria play an essential role in bioenergetics and cellular homeostasis, ATP synthesis and death. In aerobic organisms oxidative phosphorylation (OxPhos) is vital for ATP production. In mitochondria, an unspecific channel located in the mitochondrial inner membrane (MIM) called permeability transition pore (mPTP) has large effects on the efficiency of mitochondria to produce ATP and is one of the physiological uncoupling mechanisms [1]. When this channel opens, ion and proton gradients across the inner mitochondrial membrane are depleted, which leads to deficient mitochondrial ATP synthesis, although once irreversibly opened it may lead to cell death [2]. In some mammalian tissues mPTP has transitory opening and is associated with Ca^{2+} homeostasis and cell protection against stress (e.g., cardiomyocytes and myocytes) [3]. However, this mode of opening of mPTP has not been researched in other tissues such as the liver tissue. To explore a possible difference in physiologic role of mPTP for tissues with different lack oxygen tolerance, the reversible opening and closing from the rat liver was compared in the presence of different effectors (Ca^{2+}/EGTA) at different incubation times. We monitored the rate of O_2 consumption, mitochondrial swelling, and the transmembrane potential. Likewise, these experiments were replicated using rat heart to compare the influence of the same effectors in different incubation times. With these results we should elicited the possible different physiological role in these organs.

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GENETICALLY ENCODED FLUORESCENT BIOSENSORS TO STUDY THE RELOCATION OF PROTEINS IN RESPONSE TO HYPEROSMOTIC STRESS

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Abstract:

Cell homeostasis is perturbed when the environment is altered by changes on different physical-chemical properties. One of them is the osmolarity inside the cell. During stress conditions, the osmolarity and macromolecular crowding levels change dramatically. GENETICALLY ENCODED FLUORESCENT BIOSENSORS ARE BIOMOLECULES THAT CAN SENSE EVENTS THAT ARE OCCURRING IN LIVING CELLS. A series of biosensors were designed to study osmotic stress in vivo in the budding yeast *S. cerevisiae* using intrinsically disordered regions (IDRs) and a pair of fluorophores (mCerulean3 as the donor and Citrine as the acceptor). IDRs can be useful to follow how proteins are re-located in response to changes in the intracellular environment. Using confocal microscopy, the response of different IDRs to change in osmolarity (hyperosmotic treatment with 0.5 M NaCl) was followed before and after the treatment. Imaging was done immediately after the treatment with NaCl. In this work, we showed that biosensors are capable to re-localize to different compartments, including liquid-liquid phase separated condensates upon stress. These results will help to understand how hyper-osmotic stress induces the re-location of intracellular proteins.

EVALUATING CALVIN CYCLE EFFICIENCY IN POTENTIAL HEAT TOLERANT BREAD WHEAT GENOTYPES

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Abstract:

The efficiency of photosynthesis is detrimental to crop yield in cereals. However, biochemical limitations under abiotic stress are a bottleneck for crop production in C3 plants, like wheat. Heat stress (HS) can reduce the photosynthetic rate because it affects the carboxylase activity of Rubisco, impacting directly on sugar synthesis and grain yield. In this work, we evaluated the efficiency of the activity of Calvin cycle enzymes in the flag leaf of ten bread wheat genotypes and its impact on yield. Plants were grown in field conditions in the Yaqui Valley, a semi-arid zone, in two planting dates: December 2020 (control) and January 2021 (HS). Chlorophyll fluorescence was measured using a Pocket PEA Chlorophyll fluorometer. Activity of Rubisco, chloroplastic fructose biphosphatase (FBPase) and sucrose phosphate synthase (SPS) were analyzed spectrophotometrically. Maximum PSII efficiency (Fv/Fm) was not affected in any of the genotypes and Rubisco activity increased under HS, indicating an efficient CO_2 fixation. FBPase activity was significantly reduced under HS, whereas the activity of SPS increased in almost all genotypes, except for G01 and G26, suggesting that HS induced changes in carbon distribution in the flag leaf by promoting sucrose synthesis over Calvin cycle regeneration in the chloroplast. At the final harvest stage, total aerial biomass was reduced up to 40% in all ten genotypes by HS. Seed yield was not affected in genotypes G01, G03 and G26, indicating a potential for heat tolerance under the field conditions of Yaqui Valley.

MATHEMATICAL MODELING OF THE REACTIONS CATALYZED BY AN UNCOMMON THERMOPHILIC CYCLOMALTODEXTRIN GLUCANOTRANFERASE

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Abstract:

Cycloglucanotransferase (CGTases) have the exceptional capability to achieve the intramolecular transglycosilation of glucosyl-intermediates from starch (cyclization reaction) to produce cyclic α-(1,4)-linked oligosaccharides or cyclodextrins (CDs). Recently, a novel thermophilic CGTase (CldA) related to Thermoanaerobacterales was characterized. CldA has a hybrid structure and catalytic properties between CGTase and α-amylase never before described. Here we propose a mathematical model of the reactions catalyzed by CldA including reaction specificity to transfer the glucosyl-intermediates to acceptor molecules such as water (hydrolysis activity), and linear oligosaccharides (disproportionation activity, or coupling activity when the glycosyl-intermediate is from CDs), and cyclization reaction. Together with mathematical methods of biological systems, mathematical methods of reduction, as well as parameters estimation using the Markov chain Monte Carlo method, our model adequately describes the kinetics of all 4 reactions of CldA. Moreover, we evaluate hypotheses related to the interactions during the kinetics and the size of carbohydrates substrates. This work provided a valuable tool for modeling the reaction of uncommon CGTases with a remarkable capability of product diversification, opening the opportunity to gain insights into the catalytic mechanism or explain metabolic systems associated with starch metabolism.

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APPLICATION OF ZNO NANOPARTICLES IN THE REDUCTION OF PB ACCUMULATION IN CORN CROPS (ZEA MAYS)

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Abstract:

Lead can be absorbed by high-consumption crops such as corn and pose a risk to human health. In the present work, the effect of ZnO nanoparticles on the Pb accumulation, concentrations of reactive oxygen species and plant growth in corn crops (Zea mays)was studied. A sample of agricultural soil from mining zone in Mexico was enrrichmented to 127 mg/kg of Pb. The modified soil was used in pot experiments for growth in corn crops, which was treated at different concentraions of ZnO nanoparticles (0-3200 mg/kg). The concentration of photosynthetic pigments (chlorophyll (a and b) and carotenes) and the activity of the enzymatic antioxidant catalase was analyzed using UV/vis spectrophotometer. Some micronutrients as such as Zn, Fe, Mn, Ca, Mg, K, P and S was analyzed using optical emission spectroscopy. The Pb concentration in leaves, stem and root was determined by the same method after a acid digestion process and it was used to calculate accumulation factors. The results of the experiments indicated that the treatments with ZnO nanoparticles inhibit the translocation of Pb in the stem and leaf; mainly, and a significant decrement (P=0.05) of its accumulation in roots was observed with the treatment of 400 mg/kg of ZnO nanoparticles. The growth of corn biomass had a negative correlation with Pb accumulation and the micronutrients concentrations were not significantly altered with the treatments. This result sagest that ZnO nanoparticles can be implemented as an amendment in agricultural soils and avoid Pb intake to plant and its transfer to humans.

DETERMINATION OF THE OPTIMAL CONDITIONS FOR THE ACTIVITY OF BETAINE ALDEHYDE DEHYDROGENASE AGAINST γ-TRIMETHYLAMINOBUTYRALDEHYDE

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Abstract:

BADH enzymes have been classified into different families according to their phylogenetic relationship and the specific substrate's recognition. The participation of the Betaine Aldehyde Dehydrogenase in the detoxification of aldehydes and synthesis of the osmolyte and osmoprotectant glycine betaine has been highlighted. To date, the kinetic parameters and optimal conditions of activity for the substrate betaine aldehyde and the coenzyme NAD have been established. The pkBADH has a high affinity for the BA substrate but could recognize other amino aldehydes such as acetaldehyde, butyraldehyde, and glyceraldehyde. However, the activity and optimal conditions regarding the recognition of the substrate γ-trimethylaminobutyraldehyde (γ-TMABA), a precursor in carnitine biosynthesis, have not been determined. Therefore, in the present work, we evaluate the activity of pkBADH against the substrate γ-TMABA to determine activity at different pH, temperatures, and ionic strength, to generate information regarding the role of the enzyme pkBADH in carnitine biosynthesis. Our results indicate that the presence of monovalent cations such as potassium increased the activity values and that pkBADH showed more significant activity against the substrate γ-TMABA in contrast to BA under the conditions used. However, it is necessary to continue with studies such as determining kinetic parameters to define the affinity for the γ-TMABA. substrate.

PHYTOCHEMICAL ANALYSIS OF COMPOUNDS OF THERAPEUTIC INTEREST FROM THE EXTRACT OF MISTLETOE *PSITTACANTHUS CALYCULATUS* LOCATED IN THE "CERRO DEL PALENQUE" OF PURÍSIMA DEL RINCÓN, GUANAJUATO AND ITS POSSIBLE TREATMENT AS AN ANTIMICROBIAL AGENT

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Abstract:

Psittacanthus calyculatus mistletoe is a semi-parasitic plant distributed in central and southern Mexico. It can grow on harvestable plants, wild or cultivated, causing their death. This work seeks to add value to this plant, which is difficult to eradicate and affects plant species of the "Cerro del Palenque" of Purísima del Rincón, Gto. The objective was to obtain a leaf extract for: qualitative phytochemical analysis, quantitative analysis of total phenols and flavonoids, antioxidant and antimicrobial activity. Two methods were used to obtain the extract: aqueous (EA) and a methanol/acetone/water mixture (EMAA). The phytochemical identification was done through reagents that cause changes in coloration and precipitation, evidencing among them the most important: Phenols, Flavonoids, Cardiotonic glycosides, Triterpenes, Amino acids and Alkaloids. Phenols were quantified by Folin-Ciocalteu [1], showing higher concentration (p=0.04) in the EMAA extract than in EA: 114.95 and 68.5 mg gallic acid (GA)/ml of extract, respectively. Flavonoids were quantified by colorimetry showing similar concentrations in both extracts (N.S.) (20.45 and 20.73 mg of (+) catechin/ml of extract, respectively). Antioxidant activity was performed by reduction of 2,2-diphenol-1-picrylhydrazyl (DPPH)[2]. EMAA and EA showed antioxidant activity of 60.2% and 65.2 %, respectively. The IC_{50} presented for the extracts were: 0.112 and 0.111 for EA mg eq. AG/ ml, respectively. The antimicrobial activity of the extract was evaluated in vitro on bacterial growth using Escherichia coli as a model, for this purpose nutrient agar and extract were mixed at different concentrations (0.5, 1, 1.5 and 2 % (v/v)). The inoculum was placed in the center of the Petri dish. For the control, Petri dishes with nutrient agar and bacteria without extract were used. The results show that the extracts presented bacterial inhibition. These results show that Psittacanthus calyculatus possesses bioactive compounds of therapeutic interest and a good antioxidant activity, therefore, it may have a potential use for the inhibition of pathogenic bacteria.
Key words: phytochemicals, antioxidant, inhibition, plant extracts

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PHYTOCHEMICAL CHARACTERIZATION, ANGIOTENSIN I-CONVERTING ENZYME INHIBITORY AND ANTIOXIDANT ACTIVITY OF MEXICAN *CORDICEPS MILITARIS* FRUITING BODY ETHANOLIC EXTRACT

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Abstract:

Angiotensin I converting enzyme (ACE) inhibitors are employed in hypertension treatment (1). Mushrooms have low sodium concentration, which is beneficial for hypertensive patients (2). The present work aimed to proceed to the phytochemical characterization of *Cordyceps militaris* and study of its inhibition of ACE and antioxidant property. In vitro kinetics analysis was done to determine the inhibition of cordycepin and adenosine against ACE. Analysis of protein tunnel combined with molecular docking was carried out to understand the intermolecular interaction between both cordycepin and adenosine with ACE non catalytic site, affecting the normal spatial conformation of ACE and weakening its ability to decompose the substrate. The analysis of the type of interaction that occurs in the ligand binding site in both tunnels was carried out and the molecular modeling information obtained from the Caver web server was used. In the case of cordycepin, the surface binding energy was approximately -5.5 Kcal/mol, this value subsequently decreased over a distance between 2 and 4 Å until reaching a value of -2.7 Kcal/mol. The results showed that ACE inhibitory behavior of both adenosine and cordycepin was mainly due to the interactions of the hydrogen bonds between the compounds and ACE. For the ligand binding site in tunnel 2, the Protein-ligand interaction profiler (PLIP) program reported that adenosine forms eighth hydrogen bonds with residues Lys126A, Lys321A, Arg326A, Cys330A and Val328A. Ser138A forms hydrophobic interaction with adenosine. In contrast, cordycepin forms four hydrogen bonds with residues Trp134D, Thr199B, Met241B and Tyr245B. We also found that the extract showed lower DPPH scavenging activity (IC50 value of 238.9 µg/mL) and ABTS assay was 1.65%. Both cordycepin and adenosine inhibited ACE in noncompetitive manner. Finally, the Ki value for cordycepin and adenosine against ACE was found to be 6.7 and 1.2 µM, respectively. All these findings suggest that *C. militaris* extract are a kind of natural ACE inhibitors.

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ANALYSIS OF THE POSSIBLE PARTICIPATION OF *ALDH3H1-1* AND *SABATH4* GENES IN BIXIN BIOSYNTHESIS IN *BIXA ORELLANA* L.

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Abstract:

Bixa orellana L. is a plant that produces large amounts of bixin, an apocarotenoid which is biosynthesized in all of the plant´s organs, but mainly in the seed´s aril, where it reaches up to 80% of the total carotenoids. Bixin is the second most important apocarotenoid pigment in the world. Currently it is used as a natural pigment in the food, pharmaceutical and cosmetic industries. The relevance of bixin encourage researchers to investigate the biosynthesis pathway of this important apocarotenoid, however, this has not been fully elucidated. In this study, seeds of *B. orellana L* were characterized throughout seven development stages in two accessions with contrasting bixin contents, followed by a quantification of bixin content and an expression analysis performed by qRT-PCR of the *ALDH3H1-1* and *SABATH4* genes through the different stages of seed development. The results revealed that the highest expression levels of these genes coincides with stages with the maximum bixin production, in the immature seeds, mainly in the N4 accession (with a higher bixin production). However, expression levels decay in mature seeds stage, suggesting that biosynthetic activity was lost, even when bixin accumulation could have taken place.

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ALDEHYDE DEHYDROGENASES ROLE IN OXIDATIVE STRESS PROTECTION IN ANAEROBIC MICROORGANISMS

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Abstract:

Strict anaerobic microorganisms are known for their inability to dwell in habitats where oxygen is present, however, several studies reveal that they could be able to express many of the antioxidant defenses used by aerobic microorganisms, thereby being able to tolerate substantial levels of O_2. Aldehyde dehydrogenases (ALDHs) represent an enzyme superfamily responsible for aldehyde oxidation into carboxylic acids by NAD(P)$^+$ reduction. These enzymes are widely distributed among the three domains of life, suggesting an essential role throughout evolution. In their aerobic counterparts this enzymes are considered essential for detoxification of aldehydes produced in the membrane by lipid peroxidation promoted by an increase in reactive oxygen species (ROS). Either as part of their intermediary metabolism or in oxygenation episodes in their habitats, anaerobic microorganisms are exposed to cytotoxic intermediates and ROS. However, ALDHs role in response to oxidative stress protection in this kind of microorganisms has not been widely described, especially in organisms belonging to Archaea domain.

Among Archaea, methanogens stand out as anaerobic microorganisms whose biochemical and genetic analysis suggest that they possess the capacity to develop several mechanisms to contend against oxidative stress. It has been described that *Methanosarcina acetivorans* develops multiple protective mechanisms against oxygen presence and to the oxidative stress associated to it, achieving a decrease in ROS generation in cells pre-adapted to O_2 as well as an increase in the expression of antioxidant machinery to counteract the stress generated. Within this context, *M. acetivorans* could represent a key model organism to elucidate adaptive mechanisms and expression of metabolic intermediary pathways involved in oxidative stress protection, such as the possible expression of ALDHs.

Usage of different carbon sources for growth influences the metabolic profile presented by cells therefore providing differential oxidative stress levels in between carbon sources. Thus, ALDHs activity was measured using different carbon sources as acetate, methanol and triacetylglycerol(TAG). In saturating conditions, activity was detected with benzaldehyde and glycolaldehyde as substrates in every carbon source tested as well as both subcellular fractions, only with NAD$^+$ as cofactor. Activity with acetaldehyde and propionaldehyde as substrates were only detected in cytosolic subcellular fractions of acetate-grown cells, while with phenylaldehyde the activity was not detected in any growth condition. The above suggested not only that there is a different basal expression in accordance to the carbon source provided, but also that different ALDHs isoforms are being expressed. ALDHs activity measurement in cells exposed to external stressor agents will determine whether these enzymes contribute to oxidative stress protection besides of intermediary metabolism.

ANALYSIS OF THE EXPRESSION OF TRANSCRIPTS ENCODING OLEOSINS IN SOLID COCONUT ENDOSPERM WITH DIFFERENT LEVELS OF MATURITY

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Abstract:

Cocos nucifera (L.) is a member of the Aracaceae family, known around the world as a coconut tree. It represents one of the most widely distributed and important crops in the world, this due to the wide use of all parts of the coconut, either to obtain oils and other substances of gastronomic interest, or as a source of fibers for industrial applications. Coconut oil is produced from triacylglycerols (TAGs), accumulated in the form of intracellular lipid droplets (LDs). LDs have a matrix of TAGs covered by a monolayer of phospholipids in which structural proteins called oleosins are embedded. Oleosins are small hydrophobic proteins that form a steric barrier surface to maintain and stabilize the structure of LDs in the cytoplasm. These proteins are encoded by a few genes. The high expression of oils has been described, especially during the embryogenic and immature stages of oilseeds (Huang A. 2018). Given its functions and that the coconut fruit has a high content of TAGs when it has matured, the accumulation of oleosins and the expression of their genes is expected to be gradual and increase during the maturation of the seed. In this study, in coconut fruits of immature, intermediate and ripe stages, dwarf variety, the expression of coconut genes encoding oleosins has been analyzed. It has been seen that the expression is higher in the intermediate stage while it decreases in the mature; however, in both stages the expression is higher with respect to the immature stage. Although preliminary, the results suggest that the expression of these genes correlates with the increase in the accumulation of TAGs in coconut seeds in the intermediate and mature stages.

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PREGNANCY-INDUCED PHYSIOLOGICAL CARDIAC HYPERTROPHY REGULATES THE EXPRESSION OF PERILIPIN ISOFORMS AND PGC-1α IN SPRAGUE-DAWLEY RATS

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Abstract:

Perilipins 1-5 (PLIN) are lipid droplet-associated proteins that participate in regulating lipid storage and metabolism, with PLIN5 isoform are known to form a nuclear complex with the peroxisome proliferator-activated receptor-gamma coactivator 1 alpha (PGC-1α) to regulate lipid metabolism gene expression. Pregnancy-induced physiological cardiac hypertrophy is a reversible process that can change the metabolic programming in the heart. However, the changes in PLIN isoforms expression in response to pregnancy-induced cardiac hypertrophy are not thoroughly studied. In this work, we quantified PLIN isoforms, PGC-1α mRNA and protein abundance as well as triacylglycerol (TAG) and total cholesterol levels in the left ventricle of 3-month-old Sprague-Dawley rats before (non-pregnant, NP), during (late pregnancy, LP), and after pregnancy (postpartum, PP). Compared to NP, the mRNA expression for PLIN1, PLIN2 and PLIN5 increased 9.5-, 28-, and 8-fold in LP, and 7.4-, 18-, and 2.4-fold during PP, respectively. PLIN3 did not change, and PLIN4 was not detected. PGC-1α mRNA expression and protein abundance increased 18- and 11-fold, and 1.5- and 1.2-fold during LP and PP, respectively. TAG and total cholesterol increased 1.5- fold in LP compared to NP, respectively, and returned to basal levels during PP. Here, we present the differential expression of PLIN isoforms in the left ventricle of the heart during pregnancy and postpartum. Our results demonstrate that cardiac PLIN isoforms are differentially regulated during and after pregnancy, suggesting that they may contribute to the regulation of the metabolic shift induced by pregnancy.

ANALYSIS OF GENE EXPRESSION: *APETALA* (*AP*), *SHATERPROOF* (*SHP*) AND *SPATULA* (*SPT*) IN THE FRUIT DEHISCENCE ZONE OF *BIXA ORELLANA* L.

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Abstract:

Bixa orellana L. is a plant that contains a pigment in the aril of its seeds called bixin, which is protected by its fruit, a capsule formed by two valves, joined by the dehiscence zone. When this zone is separated, the seeds are exposed to the environment, leaving them vulnerable to biotic and abiotic factors. For this reason, the expression levels of the *APETALA 2* (*AP2*), *SHATTERPOOF* (*SHP*) and *SPATULA* (*SPT*) genes that are involved in the formation of the dehiscence zone of the fruit of *B. orellana* L. were analyzed taking as reference the transcriptome of *B. orellana* L. (of leaf, mature and immature seed), in different stages of development of two variants, dehiscent (open fruit) and indehiscent (closed fruit); by bioinformatics, by endpoint PCR and by RT-PCR-real time, by lignin deposition and by microscopy. The result determined that the *AP2*, *SHP* and *SPT* genes are expressed in the dehiscence zone of the dehiscent and indehiscent fruits of *Bixa orellana* L. in the six stages of development. It is concluded that the transcription factors *AP2*, *SHP* and *SPT* possibly play an important role in the formation and function of the fruit dehiscence zone of the fruit of *B. orellana* L.

Keywords Bixa orellana, dehiscent, indehiscent, APETALA 2, SHATTERPOOF and SPATULA.

BIOCHEMICAL CHARACTERIZATION OF EHHAPP49, AN AMOEBIC PROTEIN OF THE HAP-PHYTASE CLASS THAT EXHIBITS PYROPHOSPHATASE ACTIVITY

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Abstract:

Phosphatases are hydrolytic enzymes that cleave phosphate groups from biologically important molecules such as proteins, carbohydrates, or lipids. A typical classification sorts them into acid or alkaline based on the pH value for optimum phosphatase activity.1 Entamoeba histolytica, the protozoan parasite causative of human amebiasis, contains a gene (EHI_146950) encoding a 49-kDa protein that shows high similarity to HAP enzymes (i.e., histidine acid phosphatases), named EhHAPp49. Remarkably, this enzyme class exhibits biotechnological and biomedical applications.2 Moreover, EhHAPp49 is a hydrolase found in amoebic phagosomes, suggesting that it plays a key role in the parasitic lifestyle of E. histolytica.3,4 Considering this background, we undertook a study to determine the biochemical features of EhHAPp49 and gain further insights into its structure-function relationship. Colorimetric enzymatic assays using three phosphatase substrates (p-nitrophenyl phosphate, phytic acid, and inorganic pyrophosphate) showed that EhHAPp49 lacks acid phosphatase/phytase activities but exhibits pyrophosphatase activity (optimally at pH 9.0 and 50 °C). In addition, this activity is dependent on Mg+2 cations, and fluoride ions inhibit it. Based on these findings, it seems feasible to presume that EhHAPp49 represents a non-canonical phosphatase that shows pyrophosphatase activity. Furthermore, this study provides the basis for future research on this atypical biocatalyst and its potential application in sustainable agriculture or animal nutrition.

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METAL PROMISCUITY OF DAPE, A TARGET ENZYME FOR BACTERIAL GROWTH

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Abstract:

N-succinyl-L,L-diaminopimelate desuccinylase (DapE) is an amidohydrolase dependent on two zinc metal centers (CM1 and CM2), which catalyzes the breakdown of N-succinyl-L,L-2,6-diaminopimelate into succinate and diaminopimelate. This reaction provides the only source of meso-diaminopimelate and L-lysine, essential amino acids for the transpeptidation of murein chains and formation of peptidoglycan, a polysaccharide essential for bacterial cell wall stability. DapE has been identified as a potential antimicrobial drug target since it is lethal in bacteria such as Helicobacter pylori and Mycobacterium smegmatis upon deletion of the dapE gene, suggesting an important role in cell viability. Since similar metabolic pathways do not exist in humans, anti-DapE inhibitors will possess selective toxicity to bacteria. To develop a drug against DapE requires an understanding of the structural and dynamic basis of the enzyme, as well as the basis underlying its metal promiscuity. This last point is crucial since, the enzyme shows a multipreference for various transition metals, having the ability to catalyze multiple chemical reactions by modifying its second metal center. This is because CM2 could be indispensable for DapE to retain its full catalytic capacity, participate in ligand specificity, or be part of the oxyanion hole, which needs to be assembled to stabilize the intermediate and carry out catalysis. To answer this hypothesis, the crystal structure of the Enterococcus faecium DapE enzyme (EfDapE) was solved by X-ray diffraction at 1.6 Å resolution in the absence of CM2, and EfDapE crystals were obtained in the presence of various transition metals. In addition, the effect of the divalent metal on some of the properties of the enzyme was determined, including its ability to interact with different drugs previously studied, which will allow us in the future to establish how cofactors influence promoting a favorable conformational state for the selection and proposal of future highly efficient antibiotics.

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HETEROLOGOUS EXPRESSION OF *A* CCD4 FROM *BIXA ORELLANA* L IN *E.COLI* CELLS

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Abstract:

Bixa orellana L (Achiote) is a perennial tree species native to the Amazonia and tropicalregions (Moreira *et al*., 2015). Its economic importance lies in the high content of bixin in its seeds (about 80% of total carotenoids). Carotene cleavage dioxygenases (CCD) form a large family of non heme iron-dependent enzymes, involved in the production of a great diversity of apocarotenoids through oxidative cleavage of cyclic and non-cyclic carotenoid double bonds. CCDs have recently been classified into six subfamilies: CCD1, CCD2, CCD4, CCD7, CCD8, and ZAS (zaxinone synthase), which vary in their substrate specificity and cleavage sites. CCD4 enzymes are mainly involved in the regulation of volatile apocarotenoids biosynthesis as well as in the regulation of pigmentation of flower petals, fruits, and seeds (Ko *et al*., 2018). CCD4 enzymes generally have a chloroplast transit peptide in their sequence. Some CCD4 enzymes are associated with the plastoglobules of chloroplasts, where they perform carotenoid cleavage.Express CCD enzymes, identifying their substrates, and the products of their enzymatic activity is essential to understanding carotenoid metabolism and the biological role of apocarotenoids in plants. Here we describe a detailed protocol for the successful cloning of CCD4 gen using GATEWAY technology and their heterologous expression in *E. coli* cells ingineered to produce β-carotene. We also provide a semi-quantitative method for the detection and to determine the consumption level of these carotenoids by high performance liquid.

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ANALYSIS OF THE RESPIRATORY CHAIN OF *BACILLUS LICHENIFORMIS* AS A CYANIDE-RESISTANT MICROORGANISM

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Abstract:

Cyanide is a toxin that binds with the ferric ion of heme a3 in cytochrome c oxidase, causing inhibition in the electron transport of the terminal enzyme and affecting the synthesis of adenosine triphosphate (ATP) and cellular respiration. *Bacillus licheniformis* has been reported as a cyanide-degrading microorganism, which is why it is interesting to see if there are modifications in its respiratory chain that allow the microorganism to survive in the presence of cyanide.

The obtaining of *Bacillus* cell membranes obtained from different growth media was carried out, in a rich medium and minimal alkaline media with nitrogen sources with ammonium sulfate and cyanide. Oxygen consumption graphs were obtained for three classic inhibitors of the respiratory chain, where the ones with the greatest resistance are the membranes obtained from the rich medium. Enzymatic activities for alternating NADH dehydrogenase and succinate dehydrogenase as the first electron acceptors were obtained. Finally, denaturing polyacrylamide gels were made where we obtained different protein bands, obtaining more protein in membranes from the rich medium and less in those that came from a minimal medium with cyanide.

We found differences in oxygen consumption, as well as in enzymatic activities and protein concentration in the membrane depending on the medium in which the cells are obtained.

OLIGOMERIZATION OF THE PEPTIDE DEFENSIN J1-1_K45E

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Plant defensins are a superfamily of antimicrobial peptides with multiple functions described to date. The antibacterial plant defensins are basic, rich cysteine, short (45 to 54 amino acid residues) peptides. (Bleackley *et al*., 2016) In plant immunity defensins have been considered as the first line of innate immune response (Guillén-Chable *et al*., 2017a). Nowdays the resistance to antibiotics that pathogens have acquired in an evolutionary way, hinder the ability to inhibit them (Gachomo *et al*., 2012). Their antimicrobial activity is attractive to design new treatments to deal with bacterial resistance to antibiotics. As described extensively, defensins have a specific interaction with membrane lipids that are important for the biological mode of action on pathogens, interaction with lipids is thought to cause oligomerization and permeabilization of the cells causing death. In our laboratory, the defensin J1-1 from Capsicum fruits expressed in Escherichia coli has shown activity against fungal Pseudomonas aeruginosa. (Guillén-Chable et al., 2017b) The comparison of mutant J1-1_K45E and J1-1 (WT) to form oligomers and lipid concentration dependency for oligomerization are discussed.

INTERRELATIONSHIP BETWEEN THE CELL CYCLE AND GLYCOLYSIS IN MAIZE

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Abstract:

The heterodimer conformed by Cyc/CDK is a key cell cycle regulator whose kinase activity may be modulated by intrinsic and extrinsic inputs. In turn, this heterodimer has multiple phosphorylation targets, some of them still not well characterized. It is not thoroughly established whether the Cyclin/CDK complex can alter its target activities only by physical interaction. Among the phosphorylation targets of some Cyc/CDK complexes, beyond the cell cycle context, are proteins that participate in different metabolic processes, such as enzymes involved in central carbon metabolism. This work explores the interaction of individual members of the Cyc/CDK complex with two enzymes of glycolysis from maize: Hexokinase7 (HXK7) and Glyceraldehyde 3 phosphate dehydrogenase (GAP). *In-silico* phosphorylation prediction unveiled three presumable sites in HXK7, although no canonical site for CDKs phosphorylation was detected in GAP. Both glycolytic enzymes interacted with ZmCycD2;2, ZmCycB1;2, ZmCycB2;1, ZmCDKA;1, as shown in pull-down assays. In addition, Cyc/CDKB complexes obtained by immunoprecipitation phosphorylate both glycolytic enzymes, decreasing their activities. RO-3306 kinase inhibition (specific-CDK inhibitor) and a phosphatase lambda treatment after kinase assay restored the HXK7 activity. At the same time, GAP activity remained down even after phosphatase lambda treatment or in the presence of RO-3306.

Further results suggest that the activity of GAP is negatively modified by increasing CDKB concentrations on the enzymatic assay. Paralleled assays with ZmCycD2;2 or ZmCycB2;1 (as controls) had a null effect on GAP activity. Those results suggest that the cell cycle regulators can modulate glycolysis carbon channeling by at least two different mechanisms.

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EFFECT OF β-GLUCOSIDASE FROM CHAYOTE (SECHIUM EDULE) ON THE RELEASE OF VOLATILE COMPOUNDS IN THE PREPARATION OF BLONDE ALE STYLE BEER

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Abstract:

The presence and release of desirable aromas and flavors (flavor) in alcoholic beverages are considered organoleptic higly relevant attributes. In beer, aromatic compounds such as esters or higher alcohols, mainly, are released in the brewing process from the raw materials used. However, there are other alternatives that can be considered to enhance these attributes, such as the application of enzymes exogenously from different sources (Zhang et al., 2021). β-glucosidases enzymes (E.C.3.2.1.21) participate in the catabolic process of a wide range of carbohydrates, in the hydrolysis of glycosidic bonds linked to glycosides and terminal non-reducing oligosaccharides, and in the release of glucose glycone (Liang et al., 2020). It is worth mentioning that these enzymes are found naturally in a wide spectrum of living beings and plant materials; such as Chayote (Sechium edule), of which evidence of its purification and characterization has already been observed (Cruz-Rodriguez et al., 2020). This work aims to evaluate the effect of the β-glucosidase enzyme from Chayote (Sechium edule) on the release of aromatic compounds in the production process of a Blonde Ale style beer. Two extracts were prepared using Chayote (Sechium edule) as vegetal material to obtain the protein. Two clarified crude extracts were work on; in the first one, we extracted it only with the pulp (ECC) and in the second a buffer solution (ECB) was added to evaluate the difference in the concentration of the desired protein. As a main result, the ECC extract presented a higher protein concentration than the ECB extract. The volume of clarified crude extract was measured for enzymatic activity with 4-nitrophenyl-β-d-glucopyranoside (NPG), protein concentration was determined by the Bradford method using bovine serum albumin (BSA) as standard; assays were performed in duplicate. The brewing process was standardized considering the incorporation of the enzyme together with the hops. Preliminary results are shown.

Zhang *et al*. (2021). Beta-glucosidase activity of wine yeasts and its impacts on wine volatiles and phenolics: A mini-review. Food Microbiology, 100, 103859; Liang, (2020). Glycosidically bound aroma precursors in fruits: A comprehensive review. Critical Reviews in Food Science and Nutrition, 62(1), 215-243; Cruz Rodríguez, *et al*. (2020). Aggregation and molecular properties of β-glucosidase isoform II in chayote (Sechium edule). Molecules, 25(7), 1699.

THIOREDOXIN-GLUTATHIONE REDUCTASE FROM *TAENIA CRASSICEPS* AND ITS ABILITY TO GENERATE SUPEROXIDE ANION

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Abstract

Thioredoxin-glutathione reductase (TGR) is a member of the thioredoxin reductase (TrxRs) family. The members of this family of enzymes share the following characteristics: i) they are homodimeric proteins, ii) its reductase activities are NADPH dependent, iii) a FAD prosthetic group is present per monomer and iv) The redox motif CVNVGC and UC at the N- and C- terminal ends, respectively, are present. Additionally, TGR has an additional glutaredoxin-like domain where another CPYC/S redox center is located. In 2005, it was reported that after irreversible inhibition of HeLa cells TrxR with curcumin, the enzyme switches its activity from antioxidant into a pro-oxidant one, thus acquiring the ability to generate superoxide anion ($O_2^{\bullet-}$). A similar behavior was proposed for inhibited TGR of *Schistosoma mansoni*. In this sense, it is well known fact that enzymes with the capacity to generate $O_2^{\bullet-}$ such as NADPH oxidase and xanthine oxidase, share the presence of an FAD molecule, which suggests the importance of this coenzyme in the mechanism of $O_2^{\bullet-}$ generation. To dissect this mechanism, we used TGR of *Taenia crassiceps* and various inhibitors capable of specifically binding to the various catalytic sites of the enzyme (redox centers), as well as compounds capable of interacting directly with the FAD present. Additionally, the superoxide generating capacity of previously reduced *Tc*TGR in the absence of its disulfide substrate was compared. In both cases, the enzyme can generate ROS, with a higher ability in its reduced form. Our data suggest that superoxide anion generation in flavoproteins is significantly dependent on FAD.

This work was supported by the research grant IN217920 from Dirección General de Asuntos del Personal Académico (DGAPA) UNAM at Universidad Nacional Autónoma de México

H^+-ATPASES PMA1 AND PMA2 FROM THE CORN SMUT BASIDIOMYCETE *USTILAGO MAYDIS*: A FUNCTIONAL ANALYSIS

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Abstract:

Plasma membrane H^+-ATPases of fungi, yeasts, and plants act as proton pumps to generate an electrochemical gradient, which is essential for secondary transport and intracellular pH maintenance. *Saccharomyces cerevisiae* has two genes (PMA1 and PMA2) encoding H^+-ATPases. In contrast, plants have a larger number of genes for H^+-ATPases. In *Ustilago maydis*, a biotrophic basidiomycete that infects corn and teosinte, the presence of two H^+-ATPase-encoding genes has been described, one with high identity to the fungal enzymes (*pma1, UMAG_02851*), and the other similar to the plant H+-ATPases (*pma2, UMAG_01205*). Unlike *S. cerevisiae*, these two genes are expressed jointly in *U. maydis* sporidia. In the present work, mutants lacking one of these genes (Δ*pma1* and Δ*pma2*) were used to characterize the role of each one of these enzymes in *U. maydis* physiology and to obtain some of their kinetic parameters. To approach this goal, classical biochemical assays were performed. The absence of any of these H^+-ATPases did not affect the growth or fungal basal metabolism. Membrane potential tests showed that the activity of a single H^+-ATPase was enough to maintain the proton-motive force. Our results indicated that in *U. maydis*, both H^+-ATPases work jointly in the generation of the electrochemical proton gradient, which is important for the secondary transport of metabolites and regulation of intracellular pH.

Vázquez-Carrada M, Feldbrügge M, Olicón-Hernández DR, Guerra-Sánchez G, Pardo JP. Functional analysis of the plasma membrane H+-ATPases of *Ustilago maydis*. J Fungi. 2022 Jun;8(6):550.

A POSSIBLE INVOLVEMENT OF AGCVIII KINASES IN THE PHOSPHORYLATION OF THE *ARGEMONE MEXICANA* AMABCB1 ALKALOID TRANSPORTER

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Abstract:

Argemone mexicana is a medicinal non-model plant from the Papaveraceae family which accumulates the benzylisoquinoline alkaloids (BIA) sanguinarine and berberine. An ATP Binding Cassette transporter (ABC) B-type transporter, AmABCB1, displaying both berberine and sanguinarine export and import activities, respectively, has been recently isolated from seeds and functionally characterized [1]. Aminoacid sequence analysis revealed the presence of R/KXS and R/KXXS motifs, located within the signature linker domain, which is present in ABCB transporters.

Two putative kinases; AmAGC3-1 and AmAGC2-1, were selected from an *A. mexicana* seedling transcriptome as candidates to phosphorylate AmABCB1. A phylogenetic analysis grouped these candidates with the *Arabidopsis* kinases AtPINOID1 and AtAGC2-2 which have been previously shown to act on R/KXS and R/KXXS motifs of ABCB transporters, modulating their activity [2].

Candidates were isolated from *A. mexicana* plants and characterized for their distribution and activity on different possible protein substrates, including AmABCB1. AmAGC phosphorylation effects on AmABCB1 transport efficiency was also analyzed. In here, we report our findings, discussing potential metabolic engineering applications for pharmaceutical design.

Supported by the National Council of Science and Technology (Mexico; project number: CB-2016-028588) and the University of Fribourg (Fribourg, Switzerland). GS-G is recipient of a SNI 3 research assistantship.

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FUNCTIONAL CHARACTERIZATION OF A THREE-DOMAIN PH-ADAPTIVE CYCLOMALTODEXTRIN GLUCANOTRANSFERASE

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Abstract:

A novel three-domain thermoacidophilic cyclomaltodextrin glucanotransferase (CGTase; named CldA) capable of cyclizing α-(1,4)-glucooligosaccharides from starch to produce functional cyclodextrins (CDs) was recently characterized. Nevertheless, CldA also catalyzes the starch hydrolysis, decreasing the CDs' yield. This work explored different pH conditions, reaction time, protein concentration, presence of ions, and substrate concentration to optimize the CldA cyclization capability. The analysis revealed that the maximum α/β-cyclization activity of CldA is reached at 75 °C, neutral pH, and high starch concentrations (>3%), while the maximum hydrolysis activity is reached at acidic pH regardless of the starch concentration. Furthermore, while the presence of acetate ions increases the general catalysis of CldA, the citrate ions cause inhibition. Thus, under the selected conditions, 50% of CDs are reached (relative to the hydrolysis products) at pH 7.0, while only 25% of CDs proportion is reached at acidic pH (4.0-5.0). Together, these results reveal that it is possible to modulate the specificity of CldA by using different pH values to improve the production of CDs, showing that the enzyme is a promising pH-adaptive biocatalyst for starch transformation.

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Reference

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HETEROLOGOUS EXPRESSION AND FUNCTIONAL CHARACTERIZATION OF AN ALDEHYDE DEHYDROGENASE (ALDH) POTENTIALLY INVOLVED IN BIXIN BIOSYNTHESIS

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Abstract:

Bixa orellana L. is a plant cultivated in tropical areas of South America; it is commercially important in various industries (pharmaceutical, food, textile) due to the red-orange pigment, bixin, accumulated in its seeds. Bixin biosynthesis consists of the sequential reaction of three enzymes (CCDs, ALDH, MET) (Bouvier et al. 2003). Recently investigations of the *Bixa orellana* transcriptome allowed the identification of genes that encode the enzymes CCDs, ALDH, SABATH families potentially involved in the synthesis of bixin (Cárdenas-Conejo *et al*., 2015). Bixin is known to come from the oxidative cleavage of lycopene at the 5-6/5'-6' position catalyzed by carotene dioxygenase enzymes (CCDs), giving rise to bixin aldehyde compound. Furthermore, recent research by Carballo-Uicab *et al*. (2019) demonstrated that BoCCD4-3 is involved in the bixin aldehyde synthesis. However, little is known about the second bixin synthesis reaction involving an ALDHs to produce norbixin. In this study, the coding sequences of BoCCD4-3, ALDH3H1-1 reported from the *B. orellana* transcriptome were optimized in their codons to express them in the recombinant bacteria. This expression system allows us to determine if they can convert bixin aldehyde into norbixin. Additionally, the recombinant proteins obtained will be separated on 12% SDS-PAGE gels, showing their corresponding theoretical mass.

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ABSTRACTS | Posters Biotechnology

XXXIII National Congress of Biochemistry

CHARACTERIZATION OF A CHITOSAN-DNA NANOPARTICLE ENCODING TO SOMATOTROPIN PORCINE.

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Abstract

Recently, use of genic therapy has increased in pharmaceutical to production of hormones or proteins. On porcine industry improve productive efficiency is a challenge of everyday because this result in major earnings. The use of exogen somatotropin as metabolic invigorating has been studied with positive results. However, current extractions methods tend to be expensive and laborious becoming unviable this practice or almost no worthwhile in an industrial way. The administration of naked nucleic acids can have a poor efficiency due to enzyme degradation. Biopolymers have proved nucleic acids protection, one of these is the chitosan, that is a derived of chitin, it showed a good biocompatibility and non-toxic to mammalians.

The present study pretends the characterization of a chitosan-DNA encoding to somatotropin porcine. Nanoparticles was realized with coacervation technique, with three different molecular weight of chitosan. The nanoparticles obtained were named N-PcSoma, which was evaluated with diverse techniques to characterized them. Some of these techniques was digestion tests with restrictions enzymes to prove nucleic acids protection, dissolution rate, encapsulation efficiency, morphologic characteristics by HPLC. In a near future, these N-PcSoma will be study in vitro and in vivo to measure their expression and physiology effect on productive parameters in an animal model.

IN SILICO ANALYSIS OF THE EXPRESSION OF GLYCOSYLTRANSFERASES IN A LIGNOCELLULOSE DEGRADING CONSORTIUM

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Abstract:

Glycosyltransferases (GT) catalyze the synthesis of glycosidic bonds by the transfer of sugar residues from a donor substrate to an acceptor. GTs are involved in important cellular processes such as energy storage, cell wall structure, cell-cell interaction, cell signaling, cell-pathogen interactions, etc[1]. Although GTs play important metabolic roles, the association with membranes, instability in pure form and water solubility difficult the studies[2]. Consortium PM-06 is a microbial community with the capacity to degrade nixtamalized maize pericarp (NMP)[3]. Different metatranscriptomic studies have determined the expression of carbohydrate active enzymes (CAZy) during the degradation of lignocellulose, including a variety of GTs; however, the role of these enzymes is unknown. In this work, the expression of GTs by PM-06 during the degradation of (NMP) was analyzed *in silico*. Results indicate the expression of 327 GTs by *Bacillus, Paenibacillus, Microbacterium* and *Leifsonia.* According to the classification established by the CAZy database, the most abundant families were GT2 (35%), GT4 (23%) and GT51 (8%). A great number of sequences were related to enzymes involved in cell wall synthesis, followed by enzymes synthesizing polymers possibly involved in the adhesion of microbial cells to the insoluble residue. GTs linked to the synthesis of antioxidants such as bacillithiol, and in the metabolism of macrolides were also identified. The results obtained indicate that glycosyltransferases are enzymes that facilitate the function of microorganisms during lignocellulose degradation.

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METAL-BINDING PEPTIDES DISPLAYED ON THE NEUROSPORA CRASSA MYCELIUM TO OBTAIN FUNCTIONALIZED SURFACES

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Abstract:

Contamination of surface water bodies is one of the biggest problems of our time. Metals stand out among the main hazardous wastes dumped by industries. Current conventional processes to remove metals are expensive, therefore, they are not frequently used. An alternative for metals removal is the use of biological systems and their improvement by genetic engineering. Filamentous fungi are an ideal option due to their natural metal-adsorption capabilities and high specific area of mycelium which can be further functionalized by surface protein display approaches. The latter, poorly developed before for filamentous fungi, would consist in the co-translational fusion of a cell wall resident protein of the host to a metal binding peptide, so that the engineered microorganism increases its metal removal capacity.

Here we study the design and development of versatile biofilters based on engineered strains of the filamentous fungus Neurospora crassa that displays aluminum, copper and zinc-binding peptides on their surface, using a native cell wall protein as molecular anchor. Furthermore, to make the system economically sustainable and encourage its application at an industrial scale, the biofilters were coupled to the production of lipids.

After the molecular characterization of homokaryotic engineered strains, and immunolocalization of the displayed peptides, the Zn-binding peptide displaying strain showed a 200% increase of Zn removal, when compared to wild type strains when they were grown in a conventional medium and then exposed to a solution with Zn. The engineered strain also showed an enhanced growth capacity under metal stress conditions.

We are currently working the biofilters design and development. Results that will be shown the presentation day.

This work was supported by FODECIJAL-COECYTJAL, grant 8186-2019 and a CONACYT master in science scholarship to F.A.M..

REMOVAL OF CR(VI) THROUGH A FILAMENTOUS FUNGAL BIOREACTOR COUPLED TO A BIOTRICKLING FILTER (BLE)

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Abstract:

Due the potential health risk associated to the exposition of hexavalent chromium, different biological and physicochemical processes have been developed to remove this pollutant from wastewatera. Nonetheless, when considering the characteristics of water from leather and textile industries, such as high chemical oxygen demand (COD) levels, acidic pH, high concentrations of salts and metals, and the presence of antibioticsb, the use of filamentous fungi can be a good alternative for the biotreatment of metals in this type of effluents.

In the present study, chromium resistant filamentous fungal consortia were isolated from tannery effluent. For this purpose, the activated sludge was cultivated in Petri plates (50% PDA MMM; 20 ppm Cr(VI); pH 5; 28°C). Eight isolated fungal strains were identified as *Cytospora*, *Fusarium*, *Geotrichum* and *Phyllosticta* genera by DNA extraction, amplification and sequencing of the ITS2 region, sequences analysis in the NCBI library database and MEGA software. These consortia were inoculated on an aerobic semibatch bioreactor (1.1 L) at the same conditions of the Petri plates, with the difference that the carbon source was the ethyl acetate outlet emission coming from a BLE outlet airstream. 10-day growth cycles were established to measure changes in pH, chromium concentration and biomass growing. Different tests and growing cycles have demonstrated the ability of the fungal consortium to remove more than 90% of Cr(VI) in solution. Currently, we are establishing the removal mechanisms of the consortium (reduction to Cr(III), bioadsorption and bioabsorption). In the same way, we are determining possible changes on the consortium composition.

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EXPRESSION OF A NEW INCRETIN ANALOG IN *LACTOCOCCUS LACTIS*

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Abstract:

There is a growing group of biopharmaceuticals to treat diabetes that began with insulin and that have been growing over the years; one of them is the glucagon-like peptide-1 (GLP-1) whose incretin function allows increasing sensitivity to insulin by cells. On the other hand, *Lactococcus lactis* is a *Gram-positive* lactic acid bacterium, widely used in the food industry for the production of dairy products, which does not colonize the gastrointestinal tract, does not generate endotoxins or inclusion bodies, has inducible expression vectors in its genome and a great potential to express proteins in the extracellular environment. This ability to secrete proteins is due to the fact that this bacterium has a signal peptide called Usp45 bound to the main protein that is secreted into the extracellular medium[1]. Despite the advances, the great interest in this strain and the potential that GLP-1 has as a drug for diabetes, there are no reported studies comparing the *in-vitro* activity of the extracellular secretion of the signal peptide Usp45 bound to GLP-1. 1 in *Lactococcus lactis*, compared to other signal peptides, as well as conclusive *in-vivo* results, leaving an area of opportunity for research. In the present work, one of these signal peptides called Exp4 (patent FR 2947840) was evaluated, comparing its *in-vitro* efficiency of extracellular secretion in *Lactococcus lactis* against Usp45, both bound to a modified GLP-1 analogue. Plasmids were constructed with the GroESL promoter and the GLP-1 gene modified and fused with the Usp45 and Exp4 export signal peptides, achieving successful transformation of *L. lactis* strains with both constructions. After verifying their identity, the expression of the recombinant peptides was evaluated by means of SDS-PAGE and Dot-blot using an Anti-GLP-1 antibody. Finally, the peptides were evaluated in a murine model induced to hyperglycemia to verify and compare the incretin effect of both constructions. A greater hypoglycemic effect was obtained with the construction made from the Exp4 peptide.

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PSEUDOMONAS CHLORORAPHIS: A VERSATILE NON PATHOGENIC BACTERIUM HOST FOR SYNTHETIC BIOLOGY

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Abstract:

Pseudomonas chlororaphis ATCC 9446, is a non-pathogenic organism that shows potential advantages as a non-conventional host organism for synthetic biology applications. The members of *Pseudomonas genus* show wide substrate consumption capacities, high tolerance to solvents, and high redox potential for reduced compound production. A novel synbio chassis requires molecular tools to express functions in a controlled manner. In this work we developed and characterized molecular tools for inducible heterologous gene expression. We constructed and characterized expression vectors for gene expression under Isopropyl β-d-1-thiogalactopyranoside (IPTG), acyl-homoserine lactone (AHL) and anhydrotetracycline (aTc) inducible promoters. We used the Yellow Fluorescent Protein (YFP) as a reporter of gene expression. These plasmids were designed to be able to exchange YFP for the gene of interest such as the biosynthetic pathway of violacein. YFP and violacein production were evaluated in *P. chlororaphis* and *E. coli* for comparison. The dose-response curve of the different inducers was characterized using YFP fluorescence as a reporter. The relative cost of YFP (in terms of growth rate) production was determined and compared to the cost of expression of YFP in *E. coli*. The ability of *P. chlororaphis* to produce violacein in minimal media with glucose, glycerol and sucrose, in the absence of the violacein biosynthetic pathway precursor (tryptophan), was determined, achieving higher titers compared to *E. coli*, which required the presence of tryptophan as precursor for the production of the metabolite.

DETERMINATION OF CRYSTALLOGRAPHIC STRUCTURES BY PHASE EXPANSION IN FUSION PROTEINS

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Abstract:

Fusion proteins are a type of protein in which two or more protein domains are integrated into one molecule[1]. They are commonly used for purification processes by fusing the protein of interest with a tag[2]. One of the fields where protein purification is used is in protein crystallography, in which the most common is that the tag is removed for the crystal formation[3]. Some authors have shown the usefulness of not removing it because they act as a matrix to facilitate crystallization[4], and can also help solve the structure, as the known to unknown protein phases can be expanded using chain reconstruction programs[1]. In this work, an analysis of the fusion structures of MBP determined in the PDB with free diffraction data was carried out to determine the minimum conditions for the phase expansion of the tag to allow the construction of the rest of the protein, using the program ARP/ wARP5. Coordinates and structure factors obtained from deposits in the PDB were used to determine the structure of the fusion proteins. To determine these coordinates, a molecular replacement was performed in the PHASER MR program[6], using the section corresponding to MBP. Subsequently, the structure factor data obtained from the molecular replacement were used to construct missing chains in ARP/wARP. The analysis was carried out for 53 fusion structures, subsequently carrying out a statistical analysis of the influence of different factors and characteristics of the fusion protein and of the data obtained by X-ray diffraction of the protein crystal on the program's capacity. ARP/ wARP resolves a high percentage of the total protein. It was found that ARP/wARP can reconstruct the fusion protein structures deposited in the PDB from MBP. The analyzes indicate that it is essential that the diffraction data have high resolutions, high values of completeness and multiplicity, in addition to low values of Wilson B factor, crystals with a low solvent content, and other conditions that influence the decrease of the movement inside the protein.

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HETEROLOGOUS EXPRESSION OF A CONSENSUS LONG α-NEUROTOXIN FOR ANTIBODY PRODUCTION AGAINST ELAPID ENVENOMATION

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Abstract:

Envenomation treatments against elapid bites are mostly obtained from immunization of horses using selected regional elapid venoms. The produced polyclonal antibodies from horses have the purpose of neutralizing the most abundant toxic components in such elapid venoms. Long α-neurotoxins (α-LNTXs) in elapid venoms are found in low quantities, and because of this, they generate poor percentages of neutralizing antibodies against them. Consequently, they cause low neutralizing efficiency in most of the commercial antivenoms, which present low effectiveness to neutralize α-LNTXs, and if the neurotoxic effects persist despite the administration of commercial antivenoms, it will be necessary to administer more antivenom doses that can lead to allergic reactions.

To improve the effectiveness of antivenoms, one conception was to produce a consensus α-LNTXs, from well-known α-LNTXs in geographically different elapid venoms, which have been previously reported to have toxic activity. Therefore, selected α-LNTXs from different elapid genus such cobra, coral snakes, and taipan venoms were chosen to propose a consensus α-LNTX. So, in this work, we express in a heterologous manner a consensus α-LNTX to obtain specific antibodies against different elapid venoms containing α-LNTXs to evaluate its ability to neutralize such elapid venoms that present long α-neurotoxins in their venom composition. Therefore, our goal is to generate a broader spectrum elapid antivenom that can neutralize itself or improve commercial antivenoms deficient in α-LNTX neutralization.

PROTEOMIC ANALYSIS OF *ALICYCLIPHILUS DENITRIFICANS* BQ1 GROWN ON IMPRANIL, A POLYESTER POLYURETHANE COATING

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Abstract:

Polyurethane (PU) ranks sixth in the world production of plastics, and the accumulation of plastics waste in landfills has caused a negative environmental impact. Bacteria, fungi, and microbial communities that have the ability to attack PU have been reported. However, even though some enzymatic activities involved in the first attacks to the PU polymer, such as esterases, lipases and proteases, have been reported (1), the metabolic pathways involved in the assimilation of PU degradation, essential knowledge for future biotechnological applications, are unknown. Impranil is a commercial polyester-PU coating, which precursors are 1,6-hexanediol, neopentyl glycol, hexamethylene diisocyanate, and adipic acid (2). This study aims to identify and analyze the proteins displayed by *Alicycliphilus denitrificans* BQ1 during its growth on a mineral medium (MM) containing the commercial PU coating Impranil (MM-Impranil) as the sole carbon source, using shotgun proteomics (3). Proteomic analysis identified 371 differentially expressed proteins of *A. denitrificans* BQ1 during its growth in MM-Impranil. These proteins were associated with the lipid degradation metabolism, pyruvate oxidation, TCA cycle, glyoxylate cycle, and the synthesis of polyhydroxyalkanoates (PHA). Moreover, based on previous analysis where Impranil biodegradation was monitored by gas chromatography coupled to mass spectrometry (GC-MS), in which biodegradation products were identified (4), and by detailed bioinformatic analysis of the putative activities of proteins differentially expressed in Impranil, a biochemical pathway for the intracellular degradation of the initial extracellularly generated products, and their further assimilation in *A. denitrificans* BQ1 is proposed.

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CHARACTERIZATION OF SMALL RUMINANT LENTIVIRUS CAPSID RECOMBINANT PROTEIN (SRLV-RP25) COUPLED TO IMMUNOSTIMULATORY COMPLEXES BASED ON GLYCYRRHIZINIC ACID

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Abstract:

Small Ruminant Lentiviruses (SRLV) infect sheep and goats of all breeds and ages globally, resulting in significant economic losses. In this study, we cloned, expressed and carried out antigenic and immunogenic characterization of SRLV recombinant protein p25 from a B genotype both *in vitro* and *in vivo*, and predicted the antigenic structure of the expressed SRLV-rp25. To do this, we used cDNA from strain FESC-752 to overexpress recombinant SRLV-rp25 protein. We then verified antigenicity *in vitro* by evaluating plasma from goats and sheep naturally infected with SRLV. Six groups of CF1 mice were inoculated with immunostimulatory complexes to evaluate SRLV-rp25 immunogenicity *in vivo*. The complexes used included glycyrrhizinic acid (GA), SRLV-rp25 protein-coupled glycyrrhizinic acid-based liposome complexes (GAL- SRLV-rp25), and glycyrrhizinic acid coupled to protein SRLV-rp25 (GA-SRLV-rp25), SRLV-rp25. We used control groups with ISCOM-M® adjuvant-SRLV-rp25 (ISCOM-M®-SRLV -rp25) formulation as references, and with PBS as a negative control group. The humoral and cellular response were analyzed through ELISAi, and we confirmed efficient expression of the 37.5 KDa recombinant SRLV-rp25. The predicted conformational structure indicates that p25 has similar structural characteristics to other lentiviral capsids. Antigenicity prediction showed eight epitopes distributed throughout p25 surface regions, and immunogenicity analysis revealed that 61% of samples from naturally infected goats and sheep showed immunoreactivity towards SRLV-rp25. The *in vivo* humoral immune response analysis showed that immunostimulatory complexes formed by GAL-SRLV-rp25 and ISCOM-M®-SRLV-rp25 significantly increased antibody production from day 21 until day 35. The cellular immune response analysis showed that groups immunized with GAL-SRLV-rp25 and ISCOM-M®-SRLV-rp25 complexes had no significant difference ($P>0.05$) in IL-10 levels, while the SRLV-rp25 and GAL-SRLV-rp25 groups showed significant differences ($P<0.001$). IFN-γ levels were similar across all groups. Taken together, these results indicate that SRLV-rp25 is antigenic and liposomes formed by GAL-SRLV-rp25 primarily enhance the humoral response and may be candidates for immunogens.

ANTIGENICITY EVALUATION OF P16 PROTEIN FROM GENOTYPE A BY USING NATURALLY INFECTED GOATS AND SHEEPS PLASMAS

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Abstract:

Small Ruminant Lentivirus (SRLV) infects sheep and goats of all breeds and ages throughout the world, resulting in considerable economic losses related to milk production, feed, and low slaughter weight, however, a vaccine that protects against lentiviral infections is not yet available. Based on *env* and *gag* SRLV genes it has been studied sequencies and proteins combinated with adjuvants, resulting in favorable immune response, decreased viral load, and less tissue damage. Therefore, the objective of this project is to design an antigen from a synthetic gene to determine if it is possible to use it in the identification of infected animals and to develop diagnostic systems that include p16 protein of the srlv genotype a2 *gag* gene. To do this, P16 protein was cloned, expressed, and carried out antigenic analysis. To do this, the nucleotide sequence of matrix protein was synthesized by UNIPARTS® using GenBank consensus sequence based on KC155804.1 of A2 genotype, and it was directly cloned into pJET1.2 and subsequently subcloned into PETSUMO1.2 expression vector to overexpress recombinant p16 protein. Finally, protein p16 was purified using nickel affinity columns, and antigenicity was verified *in vitro* by evaluating plasma from goats and sheep naturally infected with SRLV. Results shown correct insert orientation and purified p16 protein integrity, in addition, antigenicity analysis shown 38% of goats and sheep plasma samples presented immunoreactivity to p16 recombinant protein, and some of these samples also shown immunoreactivity to p25 recombinant protein of SRLV genotype B1, which suggest a possible co-infection of both genotypes. Therefore, these results indicated that p16 is an antigenic protein that can be used in the identification of infected animals with SRLV genotype A2 as well as a possible co-infection of SRLV A2 and B1 genotypes.

Castañeda-Montes MA, Cuevas-Romero JS, Cerriteño-Sánchez JL, Garrido-Fariña GI, Ávila-De la Vega L, García-Cambrón JB. Characterization and antigen structural prediction of small ruminant lentivirus capsid recombinant protein (SRLV-rp25) coupled to immunostimulatory complexes based on glycyrrhizinic acid. (Manuscrito en revisión).

LOW-COST BIOGAS PURIFICATION SYSTEM FROM A FULL-SCALE BIODIGESTER

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Abstract:

Anaerobic digestion is a sustainable process for the reduction of greenhouse gases. This process is carried out using a biodigester, where the biogas is generated in a controlled way, that is, 50 to 70% CH_4, 30 to 50% CO_2, < 1% H_2S and impurities. However, CO_2 and H_2S damage devices such as internal combustion engines, grills, gasometers, etc. On the other hand, the high concentration of CO_2 (30-35%) decreases the calorific value of CH_4. Given this problem, this study aims to eliminate impurities from biogas, through the construction of a low-cost purification system for small-scale biodigesters. Therefore, this study is carried out in the pig farm, installed in Villaflores, Chiapas, with a 6 m^3 biodigester operated with pig manure, where filters was be built and tested to remove impurities. A factorial design with four factors is used: Ca $(OH)_2$ (mol/L) to remove CO_2, iron oxide (kg) to remove H2S, activated carbon (kg) to remove moisture, and two levels, height of the filters (40 and 60 cm), where 32 experimental assays were obtained. In this way, it has been observed that the concentration of CO_2 and H_2S has decreased, which will allow the methane, without impurities, to be compressed by a sustainable compression system.

Keywords: Biogas, purification, compression.

ALUMINUM EFFECT OVER BETALAINS PRODUCTION IN *STENOCEREUS QUERETAROENSIS* SUSPENSION CELLS

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Abstract:

Betalains are a type of nitrogen pigments found in plants from the Caryophyllales order, in which we can find *Stenocereus queretaroensis*, whose fruit is called pitaya, that accumulates outstanding quantities of these compounds, which represent an alternative source for natural pigments. Nevertheless, due to their slow development cycle and seasonal nature, the acquirement of natural pigments from these fruits is extremely limited. Therefore, *in vitro* culture systems have been proposed as an alternative production medium for betalains. On the other hand, the use of Al as an inductor of the productivity of these compounds, it´s of great importance in the study of this crop, as it generates knowledge about the physiological response of the plant to this element. The ongoing research has as the general objective to evaluate the Al effect over the betalains content in *S. queretaroensis* suspension cells.

The pitaya suspension cells were cultivated following the methodology described by Miranda-Ham *et al* (1). In the experiments with Al (500 µM), the medium was modified to half of the ionic force and to a pH of 4.3. The content of pigments was determined by the spectrophotometric method, reported by Cai et al (2). For the location analysis and Al distribution in the cell cultures, confocal microscopy was used following the co-location technic, and the microscope FV1000 Olympus with DAPI (l 405) filters, to detect Al, Morin (l 488) and Lumogalion (l 568) and hematoxylin was used for the clear camp images. Suspension cells was treated with AlCl3 500 µM during a culture cycle (16 days), cells were fixed with 4% formaldehyde, washed and incubated with fluorochromes for their microscopic analysis, DAPI was used as nuclear reference.

The betaxanthins in the *S. queretaroensis* suspension cells presents its greatest gathering at the 13th day of the $AlCl_3$ treatment. These results are in accordance with the observations in the confocal microscope and clear camp. It can be observed that the aluminum gathering mainly in the nucleus, nucleolus and nuclear membrane, as well as in the cell wall with a bigger fluorescence intensity at the 13th day of the cycle. The data suggest a possible Al effect over the pigment concentration on these crops.

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DROPLET DIGITAL PCR FOR ANALYSIS OF HIV COPY NUMBER VARIATION

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Abstract:

Even though PCR is the conventional technique for HIV diagnosis in RNA, the Droplet Digital PCR (ddPCR) is a refinement of the conventional polymerase chain reaction (PCR) methods. In ddPCR, DNA/RNA is encapsulated stochastically inside the microdroplets as reaction chambers[1]. A small percentage of the reaction chamber contains one or fewer copies of the DNA or RNA. As with qPCR, ddPCR technology utilizes Taq polymerase in a standard PCR reaction to amplify a target DNA fragment from a complex sample using pre-validated primer or primer/probe assays[2], ddPCR offer the advantage of direct and independent quantification of DNA without standard curves giving more precise and reproducible data versus qPCR especially in the presence of sample contaminants that can partially inhibit Taq polymerase and/or primer annealing for this reason, the QX200 Droplet Digital PCR (ddPCR) system provides absolute quantification of target DNA/RNA molecules for virus as HIV with a reaction cost similar to qPCR[3].

The main objective of this study was a comparison was made between qPCR vs ddPCR in the laboratory of molecular biology of LABOPAT to determine the absolute quantification of samples of patients with HIV, testing was carried out on 8 different samples on 8 replicates to evaluate the correlation between both techniques showing greater sensitivity with ddPCR in comparation with qPCR. The results obtained in this study showed that ddPCR has higher sensitivity and accuracy in copy number detection compared to qPCR technique by 16%, with a confidence interval of 95% and a precision of ±5%.

For this reason, the aim is to incorporate ddPCR as a routine technique in clinical practice for the diagnosis, prognosis, treatment and monitoring of the disease.

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ADVANTAGES OF USING AN AUTOMATED PLATFORM FOR SARS-COV-2 SEQUENCING IN A CLINICAL LANDSCAPE

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Abstract:

In December 2019 the new coronavirus SARS-CoV-2 was responsible for the COVID-19 pandemic which fastly spread around the world. When SARS-CoV-2 was introduced in a new geographic area caused outbreaks that required genomic surveillance and monitoring with the objective of knowing the predominant variant of that area, also identifying other circulating variants and knowing their main genomic alterations (mutational profile) with the purpose of having epidemiological data to improve public health response.

In this sense, the present work used whole-genome sequencing with an automated platform to rapidly and accurately identify the SARS CoV-2 circulating variants in 99 patients of Puebla, Tlaxcala and Mexico City, according to the epidemiological monitoring programs in which LABOPAT participated together with the health secretaries of the state of Puebla and Tlaxcala. Within the main variants detected were Omicron (B.1.1.529 and BA.1 lineages), Delta (B.1.617.2), Gamma (P.1), and Epsilon (B.1.429). Furthermore, sequencing allowed us to detect the mutational profile of each variant and looking for a correlation between the patient symptomatology severity, their SARS-CoV2 vaccination schedule and the analyzed variant.

Finally, we discuss the benefits and advantages of implementing an automated next-generation sequencing (NGS) platforms as a routine test in both public and private health institutions, in such a way to respond effectively to events such as pandemics.

GLYCEROL KINASE DRIVEN MONOPHOSPHORYLATION OF SMALL ALCOHOLS

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Abstract:

Phosphorylation of alcohols plays a fundamental role in living organisms and is valuable for the production of natural products, pharmaceuticals, and organic materials. The described chemical methods to date, for synthesizing phosphate monoesters, require multistep sequences or are limited to specific types of substrates, since harsh reaction conditions are required.

Glycerol kinase (GlpK) from *Escherichia coli* is a suitable biocatalyst to enable the simple production of alcohol phosphate monoesters[1]. GlpK is involved in major metabolic pathways catalyzing the ATP dependent glycerol monophosphorylation[2]. Strikingly, contrary to the expected high specific substrate affinity, this exceptional biocatalyst also enables the direct introduction of a non-protected phosphate group to the hydroxy group of an extensive range of substrates[3]. Nevertheless, the actual product formation from non-natural substrates remains unknown. In order to investigate the biotechnological potential of GlpK to produce small monophosphorylated alcohols, we perform conversions using the short chain alcohols; propane-1,3-diol, (*R*)-(-)-1,2-propanediol, ethane-1,2-diol, and 2-methylpropan-1-ol, as substrates. Our aim was to undoubtedly confirm and quantify the inferred monophosphorylation of the four tested substrates performed by GlpK. Therefore, we established a ^{31}P-NMR method to follow the simultaneous generation of the monophosphorylated product along with the cosubstrate (ATP) consumption [4]. In terms of product formation, from 10 mM substrate, GlpK in comparison to the natural substrate (100%), is capable to generate 80, 50, 20, and five % product for the substrates; propane-1,3-diol, (*R*)-(-)-1,2-propanediol, ethane-1,2-diol, and 2-methylpropan-1-ol, respectively. Our results demonstrate that GlpK displays advantageous catalytic rates suitable for organic synthesis approaches towards the tested substrates in this work, supporting the feasibility of using GlpK as biocatalyst.

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ARE THE GENES NMO2 AND NMO5 OF *METARHIZIUM BRUNNEUM* INVOLVED IN THE ENTOMOPATHOGENIC PROCESS?

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Abstract:

The *NMO2* and *NMO5* genes from *Metarhizium brunneum* code for proteins with activity of nitronate monooxygenases and are differentially expressed during the invasion of the host *Plutella xylostella*. The *NMO5* gene is expressed during the beginning of the infection process; meanwhile, *NMO2* gene is expressed at the end of the infection (1). The phylogenetic analysis showed that these proteins are in different clades. The Nmo2p has similar Km for 1-Nitropropane, 2-Nitropropane, and Nitroethane, like the Ncd-2 from *Neurospora crassa*; meanwhile, Nmo5p prefers 1-Nitropropane and 2-Nitropropane (1). In *N. crassa*, the Ncd-2 function is detoxification of nitroalkanes (2).

In this work, we analyzed the promoter regions of the *NMO2* and *NMO5* genes to understand the different gene expression pattern. Nmo2p and Nmo5p structures were modeled and compared. Additionally, the capacity of the simple null mutants, MbΔnpd2 and MbΔnpd5 of *M. brunneum*, to infect *P. xylostella* larvae was determined.

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HETEROLOGOUS EXPRESION OF A RICKETTSIAL OUTER MEMBRANE PROTEIN

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Abstract:

Rickettsia is a gram-negative bacterium that causes severe diseases in humans, including Rocky Mountain Spotted Fever (RMSF). Recently in Mexico, rickettsiosis became a serious health problem that has been detected mainly in the children population. Diseases caused by rickettsia have re-emerged around the world and is important to highlight in Mexico fourteen species have been described (40% of global diversity) and the most lethal strains were reported on the northern border of Mexico. In Chihuahua, during 2021 74 (27%) cases were reported of RMSF and another rickettsiosis from a total of 275. In Mexico, the fatality rate reaches up to 30%. Currently, patients receive antibiotic treatment with doxycycline, nevertheless, severe cases require intravenous administration. Children manage to survive, unfortunately most of them leave the hospital with long-term sequelae such as neurological failure, damage in liver and kidney and even loss of limbs in consequence to the severe vasculitis. In this work, we have expressed a recombinant protein from the outer membrane of the bacteria in order to be applied for therapeutic and diagnostic purposes.

ISOLATION AND CHARACTERIZATION OF THERMOPHILIC MICROORGANISMS OF BIOTECHNOLOGICAL INTEREST OF HOT SPRINGS FROM SAN FRANCISCO, SILAO,GTO., MX.

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Abstract:

There are environments that can be considered inhospitable to life as it was the case with geothermal waters due to the high amount of dissolved salts, temperature and pH. However, various contributions have shown that these sites are capable of hosting a great variety of life; this class of microorganisms are known as thermophiles since they are able to survive these unconventional conditions**,** such as high temperatures. The interest of these microorganisms lies in the use of their enzymes, which are considered thermostable and are used in several industries to produce paper or food, such as cellulase and amylase. (Sand, 2013, Van den Burg, 2003). This does the research attractive for the discovery of new species in hot springs**,** such as those that are in the community of San Francisco, Silao, Gto., Mx. It began by measuring the temperature of 9 named sites of the A-I which is between 55 and 80 C, in some places the temperature is similar so the sites B, C, D, F and H were selected. The samples were taken in sterile containers of one liter and transported to the "Unidad Profesional Interdisciplinaria de Ingeniería Campus Guanajuato". The samples were processed with filtration to the vacuum and extension in plate inoculating in medium agar LB and broth LB, incubating at 65 C for 48 hours. Subsequently, by means of plate extension, axenic cultures were obtained by inoculation in agar medium, incubating them at 65 C for 18 to 24 h. In this way it was possible to isolate three strains identified as ZH2, ZLC1 and ZVC1 which have a bacillus shape, gram positive, but with different colonial morphology. The ZH2 presents a circular colonial morphology with entire margin, flat, white color and translucent, the ZLC1 is circular with undulate margin, umbonate, rough surface, bright and white color. The ZVC1 is circular, filamentous, flat, shiny and translucent. These strains are capable of producing thermostable enzymes such as amylase and cellulase, after having evaluated them by qualitative tests of starch agar and CMC a positive result was obtained for the presence of visible halos revealed with iodine-lugol and congo red respectively. As future perspective, it will pretended do the evaluated of growth kinetic for determinate the optimal growth temperature and the molecular identification or the enzymes purification.

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A FERROFLUID WITH A DOPAMINE OR TETRAHYDROQUINONE MODIFIED SURFACE FOR MAGNETIC HYPERTHERMIA USING *PARAMECIUM CAUDATUM*

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Abstract:

Super Paramagnetic Iron Oxide Nanoparticles (SPION) have been synthesized by co-precipitation. In order to improve their colloidal properties, SPIONs were coated with dopamine (DA) and tetrahydroquinone (THQ) respectively. The average core diameter of the SPIONs was 13-15 nm and the surface modifications resulted in a good colloidal stability at pH of 4 to 7. Viability studies with the protozoan *Paramecium caudatum* were carried out after 24 h of exposure with SPIONs. These studies demonstrated a half maximal lethal dose for SPION-DA of LD_{50}= 2.0 mg/mL and for SPION-THQ of LD_{50}= 1.0 mg/mL. Additionally, exogenous heating of *P. caudatum* at 42 °C for a short period (15 min), reduced their viability by 50 %. Exogenous heating assays were conducted at temperatures from 37 to 45°C. The conditions for magnetic hyperthermia, always applying a frecuency of 530 kHz and amplitude of 20 mT of the magnetic field for 15 min, were varied in the concentration of added SPIONs (0.5, 1.0, 2.0 and 3.0 mg/mL) and achieved final temperatures of 37 to 45 °C. In contrast to exogenous heating, MHT caused a LD_{50} at 39 °C using only 1.0 mg/mL SPION-DA. The SPION-THQ were more effective: 0.5 mg/mL at already 37 °C reduced cell viability of *P. caudatum* by 50 %. This makes the THQ-coated SPIONs a promising candidate for further MHT studies. Each viability assay was performed using the neutral red uptake test under dark and cold conditions (2–4 °C).

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BIOCHEMICAL AND PROTEOMIC ANALYSIS FROM *IN VITRO* CULTURE OF AVOCADO (*PERSEA AMERICANA MILL.*)

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Abstract:

Avocado (*Persea americana Mill*) is one of the most economically important fruit species worldwide. Mexico is the main producer and exporter. Illnesses are found between the main factors that affect its production. This represents an important phytosanitary risk, causing significant losses that threatens this process. *In vitro* cultivation development by a somatic embryogenesis regeneration system, represents a relevant biotechnological tool that can contribute to the successful attainment of viable plants from difficult propagation or recalcitrant species, just like avocado. This can also contribute to the generation of illness resistant variants by somatic embryogenic avocado cultures. Nevertheless, avocado embryogenic culture regeneration has not been easy; somatic embryos lose their morphogenic competitiveness and viability in the first months after induction depending on their genotype. In addition, the main limiting factor for somatic embryo transformation into seedlings is the incomplete maturation. For this process, a protocol development to support the transformation from somatic embryos to plants it's necessary. To clarify which are the conditional factors of avocado ´s embryogenic culture successful development, in the present study somatic embryogenesis was induced starting from mature avocado zygote embryos resulting in a friable callus. Growth of callus cultures was evaluated through weight as fresh cell weight and dry cell during a 42-day cycle. Incubation in Murashige and Skoog (MS) medium supplemented with Picloram at 0.41 µM as grown regulator and 3 % sucrose was established. Cultures were incubated at 25°C in the dark. During the characterization, 4 phases of culture cycle were identified: 16, 22, 28 and 40 days. This information was used as reference for the auxin and cytokinin analytical determination and the proteomic analysis.

The explicit assessment of growth kinetics is key for proteomic analysis in order to explain somatic embryogenesis through the protein's identification associated with specific morphogenic events. Thus, one can obtain a virtual representation of the steady-state level of protein expression in a cell or tissue preparation under specific metabolic conditions.

SYNTHESIS OF A RECOMBINANT RMS-17 POLYPEPTIDE FROM RHIPICEPHALUS MICROPLUS IN THE PICHIA PASTORIS EXPRESSION SYSTEM

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Abstract:

The aim of this work was to synthesize a recombinant polypeptide from the inferred sequence of Serpin RmS-17 in the Pichia pastoris expression system. By means of an "In silico" assay, a region of interest composed of 435 was selected. In order to identify this region, a pair of specific oligonucleotides was designed for the amplification of the polypeptide, which also contained suitable restriction sites for the enzymes Xba I and Pml I. The obtained product was cloned into the safeguard vector and the insert was released from the vector and purified. The digest was subcloned into the pPICZαB expression vector and the plasmids were purified from competent E. coli Top 10 cells and after restriction analysis confirmed by sequencing. A consensus sequence was obtained that has 99.7% identity with the Porto Alegre strain reported in GenBank. Once the sequencing was obtained, competent Pichia pastoris X33 cells were transformed and characterization tests of the X33/RmS-17 colonies were performed. Subsequently, the expression of the RmS-17 polypeptide was analyzed by electrophoresis under reducing conditions (SDS-PAGE) stained with Coomassie blue and immunodetection was performed by Western Blot. Finally, the induced cells were lysed by mechanical disruption and when analyzing the resulting product, the protein was identified in the first four days of expression using an Anti-Myc antibody.

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DNA-CHITOSAN COMPLEXES AS NON-VIRAL GENE CARRIER: NEWCASTLE FUSION GENE NANOPARTICLE FORMATION

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Abstract:

Newcastle disease is caused by a highly contagious virus. It belongs to avian Paramyxoviruses and it causes huge economic losses in the poultry industry. The use of vaccines can reduce infections and deaths in poultry caused by this virus however, its production can be affected by the presence of mutations. Furthermore, its current production is based on viral replication, causing viral releasing form vaccinated birds. An alternative method is the use of the Newcastle Virus Fusion gene in a gene vaccine format. Gene vaccines have proven to be stable and cheap; however, they require boosters to increase the immune response.

In this investigation it is proposed to optimize the sequence of the Fusion gene, to build the gene by means of overlapping oligos. The sequence was optimized using the codon adaptation index (CAI) generating a sequence with a CAI value greater than 0.7. The optimized F protein gene has a length of 1665 bp and was cloned in the pCDNA3 Myc/His-A expression vector.

It has been reported that the use of chitosan helps protect plasmids from the effect of enzymes present in the extracellular environment, which is why we evaluated the effect of chitosan on the expression of protein F in the HEK 293 cell line.

The development of new routes of administration and protection of gene vaccines will help the development of new vaccines in the veterinary and human sector.

Key words: Newcastle disease, genetic vaccines, nanoparticles.

IDENTIFICATION OF GENES DIFFERENTIALLY EXPRESSED OF *METARHIZIUM* DURING THE INTERACTION WITH INSECTS

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Abstract:

Metarhizium is a fungus well known for its entomopathogenic activity. *Metarhizium* is commercially used in the biological control of pests. Recently was described that it can establish a symbiotic relationship with the root of plants, improving nitrogen uptake, plant growth, and defense against phytopathogens (Stone and Bidochka, 2020).

Given the importance of *Metarhizium* in the biological control of pests, to which its mycorrhizal activity is added, and the importance that organic farming and environmental conservation have acquired, in our laboratory, we are interested in identifying new genes involved in the entomopathogenic process. Many genes involved in the pathogenic process have been described, but several of the genes involved in this process are still unknown and have not been identified. Studying new pathogenicity genes can help design strategies to improve their ability to control pests.

For this purpose, we recovered differentially expressed mRNA during the interaction with *Plutella xylostella* and *Phyllophaga ravida* cuticles. The sequences were analyzed to identify the respective genes in different databases. Among the identified genes are hydrophobin genes which, among other functions, may be involved with the virulence of the fungus towards its host.

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This work was funded by University of Guanajuato, (CIIC 2022, grant No.168/2022).

MOLECULAR CLONING AND FUNCTIONAL CHARACTERIZATION OF BANANA MAWRKY18, MAWRKY45, MAWRKY60 AND MAWRKY70 TRANSCRIPTION FACTORS

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Abstract:

Banana is a staple food for millions of people in Asia and Africa and a source of income in many Latin American countries through exports to U.S. and Europe. However, this crop is affected by fungal pathogens that cause partial or total loss of fruit production. The use of pesticides has been adopted as a conventional control measure; nevertheless, they have negative impacts on the environment and human health. The genetic improvement of the current banana cultivars used for food security represents an attractive alternative to solve these problems since they would not require additional inputs to control the fungal pathogens. In this sense, the transcription factors of the WRKY family represent valuable alternatives for the genetic improvement of banana. The WRKY family of proteins play a key role in plant immunity by activating defense genes. Therefore, the aim of this work was to isolate and characterize four banana *WRKY* genes named as *MaWRKY18*, *MaWRKY45*, *MaWRKY60* and *MaWRKY70*. So far, we have cloned the cDNAs of these four banana *WRKY* genes and performed a comprehensive structural analysis. We have confirmed that these four proteins localize in the nucleus of onion epidermal cells and determined that they all have transactivation activity in yeast. In order to know whether these banana genes have a role in plant immunity we performed a RT-qPCR to measure *MaWRKY18*, *MaWRKY45*, *MaWRKY60* and *MaWRKY70* transcripts levels in response to the defense phytohormones salicylic acid (SA) and methyl jasmonate (MeJA). Interestingly, three genes (*MaWRKY45*, *MaWRKY60* and *MaWRKY70*) were responsive to both hormones but with the highest expression levels in MeJA treatment.

ROLE OF *WICKERHAMOMYCES ANOMALUS* β-GLUCANASE TOXIN DURING THE INTERACTION OF THE YEAST AND PHYTOPATHOGENIC FUNGUS

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Abstract:

The microbial communities are responsible of the biochemical and nutritional changes that occurs in most of the food and fermentable beverages. *Wickerhamomyces anomalus an* Ascomycote yeast has been selected as a biocontrol microorganism to control the growth of several filamentous fungi. In this study we evaluated the effect of *Wickerhamomyces anomalus* during the antagonistic behavior against fungi as *Thielaviopsis paradoxa*, *Colletotrichum gloeosporioides* and *Rhizopus stolonifer*. The yeast was capable to inhibit the growth of filamentous fungi to different degrees, and the most important was the cell wall digestion and spore germination inhibition. We evaluated the use of inactivated fungal biomass as an inducer in complete and minimal culture media for the expression of extracellular enzymes; in YPD cultures, using *T. paradoxa* inactivated biomass as the best inducer, were capable of inhibiting the germination of spores by the action of chitinase and glucanase enzymes according to the expression pattern. In minimal media, only the production of the small killer toxin of 30 kDa with glucanase activity was observed. Focusing on the use of minimal media, the concentrated cell-free extract toxins with β-glucanase activity significantly inhibited spore germination but had no effect on mycelial development which indicates that the biochemical biocontrol mechanism is more complex than cell wall digestion and may include more elements that occur during the yeast-fungus interaction. Understanding the mechanisms of action of biocontrol will allow a better overview of the phenomenon to increase its potential application and improve food quality and production in the agricultural sector.

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MONITORING THE CRABTREE EFFECT IN YEAST CULTURE USING THE MOBIMS MASS SPECTROMETER SYSTEM BUILT

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Abstract:

Saccharomyces cerevisiae presents oxidative growth, under aerobic conditions, transforming glucose source into biomass, CO_2, and water. If glucose exceeds a critical concentration, under aerobic conditions *S. cerevisiae* has an oxide-reductive metabolism, transforming glucose into ethanol. This phenomenon is known as The Crabtree Effect [1].

In 2018, Halbfeld C. continuously monitored Volatile Organic Compounds (VOCs) emitted by *S. cerevisiae*. Using a high-resolution mass spectrometer (SESI-Orbitrap-MS). Sixteen ions were reported as markets of The Crabtree Effect [2].

A more practical and cost-effective monitoring method is desired to be used *in situ* for the industrial application of culture monitoring by VOCs.

Alcalde-Vázquez R. et al. built a modular miniature mass analyzer (MoBiMS) for VOCs monitoring in biological systems. This low-cost system reduces equipment costs by more than 50%. The MoBiMS system is portable and enables real-time analysis [3].

Crabtree effect ion markers can be monitored by a low-resolution mass spectrometer (1 uma). The aim of this work is to show the viability of monitoring VOC markers from the Crabtree effect with the MoBiMS platform. In this way, the analysis could be made *in situ* and directly connected to a bioreactor.

Future work will automate culture monitoring and control. Using predictive models, conditions could be set to maximize products of interest such as ethanol or biomass in this model system.

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XYLITOL PRODUCTION BY *CLAVISPORA LUSITANIAE*, A NATIVE YEAST OF MEZCAL MUST

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Abstract:

Xylitol is a five-carbon sugar alcohol obtained mainly by the enzymatic reduction of xylose, via xylose reductase (XR). Some xylose-assimilating yeasts accumulate xylitol due to an imbalance of cofactors in the redox pathway of assimilation of this pentose. *Clavispora lusitaniae* is a native yeast isolated from mezcal must from Oaxaca, Mexico, and has been observed to grown on xylose as a carbon source under aerobic conditions. This work evaluated the ability of *C. lusitaniae* to produce xylitol from different concentrations of xylose and nitrogen source. An experimental design was carried out to evaluate different concentrations of xylose and yeast extract to find the one with the highest xylitol value. *C. lusitaniae* accumulated 7.2 g L^{-1} of xylitol with a yield of 0.49 gg^{-1} and a productivity of 0.18 g $L^{-1}h^{-1}$ from 20 g L^{-1}. XR activity was also evaluated reaching a specific activity of 15.6 Umg^{-1}, the highest value compared to the other conditions. The results demonstrate that *C. lusitaniae* accumulates xylitol under aerobic conditions and that XR could be induced by its substrate.

Keywords: *Clavispora lusitaniae*, xylose, xylitol, xylose reductase.

ANALYSIS OF THE CARBOHYDRATE TRANSPORT SYSTEM IN *SACCHAROMYCES PASTORIANUS*

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Abstract:

Lager beer, the best selling in the world, is made with yeast strains of S*accharomyces pastorianus* (Sp). Currently, Sp types I and II are recognized, with type I members deficient in maltotriose consumption, an important carbohydrate in brewers' wort. This phenotype is related to fermentation conditions, the presence and copy number variation of maltotriose transporters such as MTY1p, and differential genetic regulation. In this work, we use two lager yeasts. The SpI and SpII strains were grown under the same conditions of temperature, inoculum and culture medium, for which we used YP with 2% maltose (w/v) and wort with 3 and 2% maltotriose and maltose, respectively. Transport rate was determined for both strains under standard conditions. SpII showed 71% and 68% transport for maltose and maltotriose, respectively, compared to SpI. Genomic results showed that SpII contains the MTY1 gene, whereas SpI does not. Global expression analysis showed that the SpII strain had higher activity of the MALx3 genes, positive regulators of the MAL genes. In support of these observations, expression analysis of MALx1, AGT1, MPHx, MTY1 showed that they were present from day 1 in SpII and until day 2 in SpI. Given these data, we can conclude that differential gene regulation is responsible for the observed phenotypes and that fermentation conditions do not play an important role in α-glycoside transport.

ANALYSIS OF THE INFLUENCE OF GENES THAT CODE FOR PROTEINS WITH NITRONATE MONOOXYGENASE ACTIVITY IN THE DIFFERENT LIFESTYLES OF *METARHIZIUM*

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Abstract:

Nitroalkanes are hazardous environmental pollutants due to their toxicity and carcinogenic activity. In nature, 3-nitropropionate (3NPA) and its derivatives are produced as a defense mechanism by many groups of organisms, including bacteria, fungi, insects, and plants[1]. In response to these toxic compounds, several organisms on the phylogenetic scale express genes that code for enzymes involved in the catabolism of nitroalkanes: nitroalkane oxidases (NAOs) and nitronate monooxygenases (NMOs). The genus *Metarhizium* contains in their genome six NMO genes differentially expressed during insect host invasion[2]. The Nitronate Monooxygenase proteins have been involved in detoxification and virulence processes. However, its biological function has not been well described. We perform the individual deletion of the six genes to analyze their possible participation during the growth and differentiation of *Metarhizium,* as well as their possible participation during infection to insects and during interaction with plants.

In this work, we focused on studying the role of the deletion of the *NMO2* gene in the pathogenic interaction with the insects *Plutella xylostella* and *Galleria mellonella*, and in the beneficial interaction with *Sorghum vulgare* (sorgo) and *Brassica oleracea* var. italica (broccoli).

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GENERATION AND CHARACTERIZATION OF ARABIDOPSIS PLANTS OVEREXPRESSING THE PABN3 AND CL15, WHICH ARE INTERACTORS OF GLYCINE-RICH DOMAIN PROTEIN 2

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Abstract:

The *AtGRDP2* gene is expressed during the development and response to salt stress in *Arabidopsis thaliana* plants. Overexpression *AtGRDP2* lines display enhanced growth and development, flowered earlier, and had increased tolerance to abiotic stress, whereas *Atgrdp2* mutants had an opposite phenotype. AtGRDP2 protein is constituted by 3 domains: a DUF1399 located at the N-terminal, a potential RRM in the central region, and a Glycine-rich at the C-terminal. Although AtGRDP2 has been reported to be involved in plant growth and stress response, the mechanism of action is still unknown. In this study, we showed that AtGRDP2 protein has a dual cytosol-nucleus localization in tobacco leaf cells. We identified AtGRDP2 interactors by yeast two-hybrid split ubiquitin assay, which are proteins associated with RNA processing functions such as poly-A binding protein (PABN3), GTP binding elongation factor EF-1α, and plastid ribosomal CL15. Moreover, we generated lines that overexpress the following genes: *PABN3* and *CL15*. Currently, we are challenging these Arabidopsis lines that overexpress the *CL15* or *PABN3* genes under salt stress, and we are also analyzing whether these lines have a differential phenotype in growth.

TOWARDS DEVELOPMENT OF A PROTOCOL TO OBTAIN TRANSGENIC CACTACEAE PLANTS

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Abstract:

The Cactaceae family includes ~1,600 species, most of them are well adapted to arid or semi-arid environments. In the previous work of the laboratory it was reported that many Cactaceae species show determinate growth of the primary root as a consequence of root apical meristem (RAM) exhaustion (Dubrovsky, 1997, Shishkova *et al.,* 2013). Upon RAM exhaustion, all cells of the root apex differentiate and the root stops growing. It has been suggested that the determinate root growth of the primary and lateral roots of Cactaceae represents an evolutionary adaptation, allowing rapid seedling establishment in desert environments. Nevertheless, the mechanisms involved in RAM maintenance and determinate root growth in the Cactaceae family are poorly understood. In order to study genetic regulation of the RAM we aim to develop a protocol to obtain transgenic Cactaceae plants via *in vitro* transformation of explants by *Agrobacterium tumefaciens*, selection of transgenic calli and subsequent plant regeneration. In this work, the initial steps of the development of such a protocol for 2 species with a short life cycle (~ 1.5 years from germination to flowering), *Mammillaria haageana* ssp. *haageana* and *Echinopsis mirabilis,* were performed. We were able to induce and propagate calli of both Cactaceae species, and to regenerate plants from calli of *M. haageana* cultivated for more than a year. Furthermore, for the planned employment of kanamycin as a selective agent in the future transformation experiments, we estimate tolerance of non-transformed calli to this antibiotic. The kanamycin concentration that prevents growth of the non-transformed calli, was higher for *E. mirabilis* than for *M. haageana.*

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IN VITRO CULTURE OF SHOOTS AND CALLUSES OF KALANCHOE DAIGREMONTIANA, AS A SUSTAINABLE SOURCE FOR OBTAINING METABOLITES

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Abstract:

Introduction. The species Kalanchoe daigremontiana Raym.-Hamet. & H. is a Crassulaceae native to Madagascar and has been of interest for the production of various secondary metabolites, such as flavonoids, fatty acids, and bufadienolides, which have been shown to have anti-cancer, immunomodulatory, analgesic, anti-inflammatory, and insecticidal properties. (Herrera et al., 2009, Tkalec et al., 2012) Therefore, the production of secondary metabolites from this plant grown under in vitro conditions represents an opportunity for the production of new drugs sustainably. This cultivation technology also allows biomass and metabolites to be obtained homogeneously and independently of environmental conditions. In this work, an efficient disinfection methodology was evaluated to obtain plant material suitable for inoculation in temporary immersion systems. Methodology. We carry out the disinfection of K. daigremontiana seedlings by modifying the methodology proposed by Ibarra (2017). To finish, a treatment with a NaClO solution at different concentrations (0.25, 0.50, 0.75 and 1.00%) with constant stirring was carried out. The shoots were cultivated in semi-solid MS medium with 1.10 g/L of the culture medium, 7.5 g/L of sucrose and 2 g/L of agar, at a pH of 5.8.Incubating them for 15 days in photoperiods of 16 hours of light/8 hours of darkness at 25. During the inoculation in the temporary immersion system, segments of plant material of approximately 1 cm in length were taken. The concentration of the medium is 2.21 g/L of culture medium and 15 g/L of sucrose, added with different cytokinin treatments (BAP, KIN, 2iP) at a pH of 5.8. The dive is done every 12 hours for 15 minutes. Results. The 0.75% concentration of sodium hypochlorite, the most effective condition, also showing root development and low necrosis in plant tissue. The most suitable hormone concentration for growth in temporary immersion systems was 0.75 mg/L. Conclusions. It is expected to induce callus formation with the use of other hormonal combinations and to evaluate plant physiology through the levels of chlorophyll present in plants grown in SITs.

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STUDY OF REGULATORY PROTEINS IN LIPOLYSIS: PERILIPIN 1

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Abstract:

Neutral lipids are synthesized in most eukaryotic cells and are packaged into lipid droplets (LDs). Lipid droplets have a unique ultrastructure, consisting of a core of neutral lipids such as triglycerides (TAG), which due to their hydrophobic nature are surrounded by a monolayer of phospholipids and integral and peripheral proteins such as Perilipin 1 (PLIN1). Currently, PLIN1 is the most studied member of the perilipin family, playing an important role in the regulation of lipolysis. Under basal conditions, PLIN1 inhibits lipolysis by preventing the access of lipases to the TAGs and recruiting the protein CGI-58, activator of the ATGL lipase, which performs the hydrolysis of the first fatty acid. While under catecholamine-stimulated conditions, PKA phosphorylates PLIN1 and CGI-58, disrupting their interaction and releasing CGI-58, allowing the recruitment of ATGL to initiate TAG degradation. Currently, there is an interest in describing the regulation of the interaction of PLIN1 and CGI-58 and several studies have described that the region of PLIN1 involved in the interaction is the C-terminal. However, no studies have been carried out with purified proteins that allow to know in detail the regulation of the interaction. Therefore, the main goal of this work is to identify key residues in the region of interaction of PLIN1 with CGI-58 and to describe the regulation mechanism by phosphorylation. To achieve this, we are conducting expression experiments of the C-terminal end of PLIN1 (hCot3, L404-522 residues) using a pET28·PPS expression vector in several E. coli BL21 strains. Up to now, the results showed that the hCot3 protein is not expressed in the BL21 (DE3) Star and pLyss strains, while the expression of the recombinant protein was achieved in the BL21 (DE3) CodonPlus strain. The hCot3 construct will be purified by nickel affinity followed by ion exchange and SEC chromatography; this will allow us to initiate protein-protein interaction assays with CGI-58 in the near future.

THE EFFECT OF PUNCTUAL MUTATIONS ON THE STABILITY AND AGGREGATION STATE OF HUMAN CGI-58 PROTEIN

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Abstract:

Lipolysis is a dynamic biochemical process that consists in the degradation of neutral triglycerides stored in lipid droplets (LDs) in response to high energy demand. This process is regulated by catecholamine signaling, which modulates the function of the proteins. Under basal conditions of lipolysis, the peripheral protein Perilipin 1 (PLIN1) is found on the surface of lipid droplets in a complex with CGI-58, the activator protein of ATGL enzyme, which catalyzes the first step of lipolysis. Under stimulated conditions, phosphorylation signaling is triggered by PKA, resulting in the phosphorylation of PLIN1 and CGI-58. Consequently, CGI-58 and PLIN1 interaction is disrupted, allowing CGI-58 to recruit ATGL to the LD to initiate triglyceride hydrolysis. In addition, CGI-58 not only increases the activity of ATGL (20 times in mice) but also extends its regioselectivity to the sn-1 position of the TAG. The interactions of CGI-58 with both PLIN1 and ATGL plays a key role in the regulation of lipolysis. Therefore, in this work, we study the role of the three tryptophan residues at the N-terminus of CGI-58 (W19, W23, and W27), which are involved in LD attachment and ATGL activation by generating a triple tryptophan to alanine mutant 3WA. The phosphomimetization of residue S237 was also investigated by generating the 3WA/S237E mutant. Our experimental results show that tryptophan residues al the N-terminus modulate the oligomerization state of the protein, causing CGI-58 3WA and 3WA/S237E protein versions to be found mainly as a monomer compared to the WT protein, which tends to aggregate. We also found that these mutations increase thermal stability and secondary structure content compared to 3WA, suggesting that phosphorylation plays a role in protein integrity.

THE CONTRIBUTION OF THE COMPOSITION, PROCESSING, AND MODIFICATIONS ON THE CHARACTERISTICS OF NATURAL EXTRACELLULAR MATRIX GELS

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Abstract:

The decellularization processes of mammalian tissues produce extracellular matrix (ECM) scaffolds and their hydrolysates are suitable for generating gels. In this work, ECM gels from bovine Achilles tendon (T) and pericardium (P) were obtained and characterized in terms of their biochemical composition, polymerization kinetics, microstructure, and rheological response. Different tests were performed to optimize the time of both collagen extraction by decellularization and acid hydrolysis. It was studied whether the sterilization of lyophilized scaffolds by ethylene oxide causes a decrease in the ability to form gels (TL and PL). Furthermore, ECM gels were modified with oligourethane prepolymers (O) and colloidal silica particles (S) to generate hybrid gels with improved properties. The results indicate that the proportion of PL in the formulations directly affects the characteristics of the gels, id est, the higher the amount of PL, the longer the time required for gelation, the higher the mass/length ratio and the larger the fiber diameter, the lower storage modulus and higher critical deformation (deformation necessary for gel to flow). It was found that the PL:TL (1:1) gel has characteristics of short gelation time, high mechanical resistance, formation of 149-nm fibers with a mass-to-length ratio of 3.3E+12 Da/cm. This is consistent with superior rheological response compared to the rest of the gels under study. The modification of this gel with O+S generates chemical cross-linking that translates into lower critical deformation and better retention of its elastic properties. These formulations exhibit a degree of crosslinking of 35%, while the mass-to-length ratio increased to 4.2E+12 Da/cm and its critical deformation decreased from 127 to 101%. The gels exhibit viscoelastic properties with the potential to be injectable for gelation in situ, leading to a three-dimensional biomaterial for se in regenerative medicine, biomedicine and tissue engineering.

DISINTEGRIN AND DERIVATES ACTIVITY ON INTEGRINS

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Abstract:

Cell adhesion to the extracellular matrix (ECM) is essential for tissue integrity and cell mobilization. Integrins, through a cavity formed by the heads of their alpha and beta domains, can recognize RGD motifs from proteins present in the ECM, and thus anchor the cytoskeleton of the cell to the ECM. The binding of integrins to their ligands depends primarily on the coordination of a metal ion, usually magnesium, with the aspartate side chain of the RGD motif. Integrins can mediate cell mobilization by attaching and detaching from their ligands, participate in coagulation, promote cell life or death, and can also participate in cancer development processes.

Snake venoms have evolved to be able to digest the tissues of their prey. Disintegrins are proteins present in such venoms that prevent platelet aggregation through their binding to integrins, this is because disintegrins have usually an RGD domain, or another similar domain, that intervene in binding. Different RGD-like motifs can be recognized by different integrins.

In the venom of *Bothrops ammodytoides*, a snake endemic to Argentina, a disintegrin with an MSE motif was found capable of inhibiting the binding of breast cancer cells to the ECM fibronectin, vitronectin and laminin, as well as inhibit the mobilization of these cells.

The purpose of this project is to evaluate the interaction of the MSE motif with integrins through in silico methods, as well as to evaluate the function of the disintegrin and peptides derived from its sequence. So far, by means of molecular dynamics, it has been found that the glutamate of the MSE motif is able to maintain coordination with the metal ion present in the binding site, a manganese, of an alpha(iib)beta(3) integrin structure in a constant manner, but at a greater distance than the aspartate coordination of the RGD motif. Molecular coupling is currently being carried out with the peptides derived from the disintegrin, and work is also being done on the expression of the complete protein and the synthesis of peptides to evaluate their activity on cell lines expressing integrins.

COMPARISON OF RECOMBINANT ANTIBODY PURIFICATION PROCESSES BY PACK-BED AND MEMBRANE CHROMATOGRAPHY TECHNIQUE

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Abstract:

The recombinant antibody (Ab) production involves upstream (growing and harvesting) and downstream (separation) bioprocesses[1,2]. Where this last can account for over 40% of the overall bioprocessing cost, deserving special attention. The affinity capture using protein A chromatography allows the selective recovery of the target molecule where the packed bed is the most used system. The high surface area of the resins used exhibits a good binding capacity. However, high-pressure drops, compaction of the packed bed, and slow intraparticle diffusion can low productivity. Furthermore, the Ab can be modified in its structure during the processes due to the long exposure to aggressive conditions[2]. To overcome these limitations, arise membrane chromatography which uses a transport mechanism toward the binding sites by convention, unlike packed bed, which is by diffusion. Also, the use of membranes allows for working at higher flow rates reducing process time, this is because in the convective mass transport the binding capacity and resolution are independent of the rate flow. The present work compares the recovery efficacy of an Ab between an agarose resin, Praesto® AC, life sciences, and CAT. PR00200, with an average particle size of 85 µm and a microporous cellulose membrane Sartobind® protein A; 2 mL, Sartorius stendim, CAT. 93PRAP06HB-12A, with a pore size of 0.45 µm. The aim is to evaluate which technique is better to obtain Ab when the volume of production and the quantities of Ab are too low at the beginning of the characterization processing. In both cases are used the fabricant recommendation is. The results showed that the membrane Sartobind® protein A purified 2.0 times more protein than resin Praestro®. This preliminary study could be used to continue evaluating both techniques in the scale-up of the purification process.

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EFFECT OF *XYLARIA CURTA* EXTRACTS ON THE REGULATION OF THE LAS SYSTEM OF *P. AERUGINOSA*

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Abstract:

A group of six bacteria known by the acronym ESKAPE has been reported, which can resist many antimicrobials; In addition to developing mainly in hospital environments, the penultimate acronym corresponds to *Pseudomonas aeruginosa*, which has various systems to regulate its virulence, of which quorum sensing (QS) stands out, which is the communication mechanism through autoinducing molecules. The QS is regulated by the hierarchical systems between Las, Rhl and pqs; however, the Las System is the main regulator of gene expression of virulence factors such as: enzymatic activities, pyocyanin production, biofilm formation and elastase, among others. Anti-quorum sensing therapies have focused on identifying molecules that inhibit the LasR receptor, which in this way can inactivate other systems such as Rhl and pqs. The search for new antivirulence compounds has drawn attention to natural compounds. Various fungi have been reported with the capacity to produce secondary metabolites with important biological activities, such is the case of *Xylaria curta*, but so far there are no reports of its antivirulence properties, so the objective of this research was to study an extract (chloroform -methanol) from the culture of *X. curta*, isolated endophytically in oregano leaves (*Origanum vulgare*). Fungal extracts from biomass and broth were obtained and the ability to inhibit; pyocyanin, biofilm and caseinolytic activity at sub-inhibitory concentrations (62.5 to 500 µg/mL). Its ability to decrease LasR transcription by transcriptional fusions with β-galactosidase was also evaluated, using furanone C-30 as a control (Garcia-Contreras *et al.,* 2013). The results indicated that the *X.curta* extract at 250 µg/mL inhibits biofilm formation, caseinolytic activities and pyocyanin production in *P. aeruginosa* PA14. While at a concentration of 7.81 µg/mL the transcription of LasR decreases. This confirms that the fungal extracts do influence the Las System in the regulation of *P. aeruginosa*.

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5-HYDROXYMETHYL-2-FURALDEHYDE VIRULENCE FACTOR INHIBITOR IN *PSEUDOMONAS AERUGINOSA* PA14

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Abstract:

Today antibiotic resistance has been reported as one of the main threats to global health, there are reports that 80% of these infections are caused by *Pseudomonas aeruginosa,* it is considered a nosocomial bacterium and mainly affects immunocompromised patients. Pathogenicity pathways of P. aeruginosa are complex, among them Quorum Sensing (QS) stands out, which is mediated by autoinducer molecules (AI) that regulate population density and allow them to synchronize their gene expression. In this sense, it is extremely important to continue the search for secondary metabolites of fungal origin, which can regulate the growth of pathogenic bacteria or inhibition of bacterial virulence factors. In this way, from a liquid culture of *Idriella* sp. GH5608 was purified and identified as 5-hydroxymethyl-2-furaldehyde (5-HMF) through spectroscopic methods (Espinoza *et al.,* 2008). Subsequently, the inhibition of virulence factors (biofilm, pyocyanin and caseinolytic activity) in *P. aeruginosa* PA14 was evaluated using concentrations of 50, 25 and 12.5 µm/mL of 5-HMF. The results obtained show that 5-HMF (50 µm/mL) decreases biofilm formation and pyocyanin production by more than 50%. In addition, it was able to inhibit the caseinolytic activity in *P. aeruginosa* PA14. This shows that microscopic fungi continue to be an excellent source of antibacterial metabolites.

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ANTIACETYLCHOLINESTERASE POTENTIAL OF EXTRACTS OF CARAO PULP (*CASSIA GRANDIS*)

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Abstract:

Alzheimer's disease is a neurodegenerative disease that currently affects some 46.8 million people worldwide and it is estimated that by 2030 if no drug is created against this disease, it will reach almost 74.7 million. This neurodegeneration is irreversible and is characterized by the formation of fibrillar tangles of hyperphosphorylated Tau protein and the development of senile plaques in the brain. The primary effect of acetylcholinesterase (AChE) is the termination of nerve impulse conduction by hydrolysis of acetylcholine (ACh) at cholinergic synapses. The inhibition of ACh acts as a strategy for the cure of Alzheimer's disease. The essential and fixed oils of certain plants have chemical constituents capable of inhibiting AChE. Among the different plants used is carao (*Cassia grandis*), a plant native to Central America, the Caribbean and the northern region of South America, used in alternative medicine for its metabolites. The objective of this work was to study the inhibitory effect of ACh on different extracts of the pulp of C. grandis (hexanic, chloroformic, ethanolic and methanolic). To determined the potential inhibitor, were taken 25 ml of the working solution (sample dissolved in DMSO 10 mg mL^{-1}) and placed in the wells of an ELISA plate for the positive and negative test control. For the first five column cavities positive control, were added 25 ml eserine solution (10 mg mL^{-1} in Tris / HCl pH 8.0). Were added to each well, 25ul of acetylcholine iodide solution (ATCI), 125µl DTNB solution (5',5-dithio-bis- (2- nitrobenzoate, Sigma), and 50mL of Tris / HCl (50 mM) with bovine serum albumin. the absorbance was measured at 405 nm in 1minute intervals for 8 minutes. 25 uL were added to the solution of AChE (0.226 U/mL) in Tris/ HCl to each well and the absorbance was measured at 405 nm for 10 minutes.The results of inhibition of AChE was The results of acetylcholinesterase inhibition were: (34.45%) for the hexanic extract. (43.21%) for the methanolic extract, (45.56%) for the ethanolic and for the chloroform (48.54%). The 30-50% are moderate inhibitors with importance in humans.

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EVALUATION OF MULTIFUNCTIONAL QUALITIES OF THE RHIZOBIAN SPECIES *RHIZOBIUM* SP. ACO-34A AS A PLANT GROWTH PROMOTER RHIZOBACTERIA

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Abstract:

Nowadays, challenges in agriculture range from the need to satisfy the necessary nutrients for plant growth to the resolution of pollution problems due to the excessive use of chemical fertilizers. Currently, there are several beneficial soil microorganisms, among them, plant growth promoting bacteria (PGPB) have become a very useful strategy for the development of plant biotechnology, as an alternative for sustainable agriculture and to reduce the application of chemical fertilizers. The genus Rhizobium has been widely studied as one of the most important genera that fix atmospheric nitrogen and have the ability to form symbiosis with certain plants in their root zone. Rhizobium sp. ACO-34A, is a native bacterium isolated from the rhizosphere of the agave plant, a non-legume plant species of great importance in Mexico, since it is a precursor of different products such as alcoholic beverages, textile fibers and a rich source of fructan sugars. The present work focused on studying the multifunctional qualities of the bacterial strain ACO-34A, analyzing its ability to synthesize indole acetic acid (IAA), solubilize phosphate and the nitrogenase activity, as well as studying the strain metabolism by using API 20NE and API 20E tests. The results have demonstrated a great adaptability to different carbon sources. Likewise, a study of antibiotic resistance was carried out and differences between ACO-34A and other genetically closest strains were observed.

Keywords: Rhizobium, PGPB, metabolism

SPHINGOSINE 1 PHOSPHATE INCREASES TESTOSTERONE CONCENTRATION AND STIMULATES THECA CELLS VIABILITY

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Abstract:

Luteinizing hormone (LH), induces steroid hormones biosynthesis, it promotes theca cell proliferation and survival. Recent studies in our laboratory indicate that FSH and LH promote sphingosine phosphate production in granulose and theca cells. Respectively, and this sphingolipid increased the percentage of cells in the S and G2/M phases of the cell cycle of bovine granulose cells in culture. With these evidences and considering that S1P regulates the proliferation, survival and steroidogenesis in different cell types, the objective of this study was to demonstrate the participation of S1P in the production of testosterone and viability of bovine theca cells in culture. Ovaries from non-pregnant cows were obtained from a local slaughterhouse, follicles from 4 to 17mm in diameter were dissected, theca cells were obtained and seventy-five thousand viable cells were cultured in 96-well plates, four cultures were made with 6 replicates per well. The cells were incubated with 0, 0.1 and 1uM of S1P in an atmosphere of 5% CO2, at 37°C and 95% humidity for 48 and 96 hours. As a positive control, theca cultures were stimulated with LH (0.02ng/mL and 0.1ng/mL). Testosterone concentrations were determined by ELISA test with the DRG Testosterone commercial kit (EIA-1559) and cell viability by MTT assay. Our results demonstrate for the first time that the addition of 0.1uM and 1uM of S1P to the culture medium increased testosterone concentration and the number of viable bovine theca cells at 96h ($P<0.05$), as occurred when LH (0.1ng/mL) was added to the cultures.

In conclusion, S1P participates in testosterone production and in viability of bovine thece cells in culture and may mediate the biological effects of LH.

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ACRYLAMIDE ADSORPTION ON CHITIN BEADS

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Abstract:

Acrylamide is a chemical neurotoxic and carcinogenic compound present in polyacrylamide and acrylamide copolymers. In addition, acrylamide is one of the main carcinogens in cigarette smoke, with harmful effects throughout the body. Tobacco smoke is the main risk factor for lung cancer and is responsible for more than 85% of lung cancer deaths [1]. Recent investigations reported that acrylamide has a high absorption rate on biomolecules. In this research, we develop a chitin eads for absorption of acrylamide. *Materials and Methods*. We isolate chitin from marine crustaceans wastes by chemical methods to obtain chitin. Shrimp wastes were drying using heat air, following by a decolorization treatment to remove pigments to obtain a colorless product. The chitin was extracted by two major steps, an acidic treatment to dissolve calcium carbonate and an alkaline extraction to solubilize proteins. Finally, the chitin was dissolved in 5 % CH_3COOH for 24. Then, a 2 M NaOH solution was added drop to drop to neutralize the sample. Beads were washed and characterized by microscopy. *Results.* Chitin beads were used to absorb several acrylamide concentrations to determine its maximum capacity. The adsorption isotherm was determined in several pH values (5, 6, 7, and 8). *Conclusion.* The biomolecules as chitin have a great capacity to absorb acrylamide in solution.

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IMPLEMENTATION OF A TOLUENE DIOXYGENASE PLATFORM TO BOOST HYDROCARBON BIOREMEDIATION WITH MICROBIAL CONSORTIA

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Abstract:

Aromatic hydrocarbons (AHs) constitute the most recalcitrant fraction to degrade in crude oil[1]. There is a big concern regarding such compounds since are hazardous substances affecting human health and the ecosystem[2]. The conversion of aromatics to nonaromatic molecules is a challenging reaction, due to the strong stability of the aromatic ring-system[3]. Amazingly, nature have evolved extraordinary enzymes such as Rieske non-heme iron dioxygenases (ROs) that are suitable to circumvent the problem just by introducing molecular oxygen in the aromatic moiety of hydrocarbons[4]. Oil spills can occur both in soils and in aquatic systems as well, threatening the ecosystem equilibrium and resulting in health problems [2]. The most challenging part in bioremediation, to restore hydrocarbon contaminated places, is the activation of the aromatic moiety fraction for the further downstream degradation, until mineralization to CO_2 and H_2O[3]. Several naturally occurring microorganisms are capable to degrade AHs, however the conversion turnover is too low to practically restore oil spills in reasonable time. We focused the scope of this work on the RO toluene dioxygenase (TDO) from *Pseudomonas putida* F1, since this enzymatic system has been tuned for the efficient conversion of several aromatic substrates. For instance, the TDO platform is capable to convert substantial amounts (10 mM) of the monocycle benzene or the bicyclic naphthalene, impressively in matter of hours[5]. Our strategy consists of boosting hydrocarbon degradation by applying the TDO platform prior the microbial consortia addition, in order to activate the aromatic moiety by breaking in advance the aromatic system. In this sense, the downstream degradation steps can be better performed by the microbial consortia since the first step is the limiting one. Our preliminary results have shown that the TDO-Consortia sequential strategy can accelerate up to four times the degradation of benzene and naphthalene. We anticipate that our further kinetic studies will demonstrate the advantages, relevance, and bioremediation potential of our work.

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α-TOCOPHEROL PRODUCTION IN ANAEROBIC CULTURE BY EUGLENA GRACILIS

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Abstract:

Vitamin E is a mixture of 4 tocopherols, and 4 tocotrienols, a-tocopherol is the most active form in human since it accumulates in the tissues for longer times and is the only isoform that is metabolized. Its main biological function is acting as an antioxidant and preventing the oxidation of polyunsaturated fatty acids and proteins, so it is considered an important protective element in the development of diseases related to oxidative processes such as cardiovascular conditions.

The protist *Euglena gracilis* has been widely studied for its great potential in producing metabolites of biotechnological interest as a-tocopherol, regarding the latter it is reported that this isoform corresponds to >90% in Euglena, more than any other organism. Another advantage of Euglena as a biological model is the generation of large amounts of biomass using different external carbon sources such as ethanol and organic acids, glucose, etc, under variable culture conditions such as light/dark, pH ranges from 3 to 8 and even under O_2 limiting conditions.

Precisely when O_2 is limiting, it is known that the concentration of some metabolites such as wax esters, fatty acids and some amino acids increases because their oxidation decreases. Likewise, in anaerobiosis the degradation of paramylon through glycolysis increases, rising the glycolytic flux and therefore some intermediates of this pathway, that are precursors of the alpha-tocopherol synthesis pathway.

Therefore, our objective is to determine whether under conditions of anaerobiosis both metabolic intermediates of the pathway and α-tocopherol increase under O_2 limiting conditions using a mixture of carbon sources with the aim to maintain an exacerbated metabolic state for ROS generation and high biomass.

SYSTEMATIC MODIFICATIONS OF A BIOSENSOR BASED IN A INTRINSICALLY DISORDERED PROTEIN THAT TRACKS THE EFFECTS OF OSMOTIC STRESS IN *ARABIDOPSIS THALIANA*

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Abstract:

Plants are constantly subjected to water deficit conditions. Water deficit leads to hyperosmotic stress conditions in cells. In response to hyperosmotic stress, plants accumulate a group of proteins known as late embryogenesis abundant (LEA) proteins. LEA proteins lack a well-defined three-dimensional structure and are considered intrinsically disordered proteins (IDPs). Recently, our laboratory developed a genetically encoded fluorescent biosensor that is capable of reporting the effects of osmotic stress on different organisms, including yeast, bacteria, plants, and human cell culture. The biosensor, named Sensor Expressing Disordered protein 1 (SED1) uses the *Arabidopsis thaliana* AtLEA4-5 as the sensor domain. This protein dynamically changes its structure depending on the osmolarity and the macromolecular crowding levels of the environment. However, the major limitation that SED1 presents is the inability of reporting osmotic changes in *A. thaliana*. Since AtLEA4-5 is an *A. thaliana* protein, the lack of response could be the result of phosphorylations that might prevent AtLEA4-5 compaction. Also, the donor (mCerulean3) fast photobleaching could directly affect the FRET efficiency. Based on these, we propose to systematically modify certain characteristics of SED1 to generate enhanced versions that are functional in *A. thaliana.* We generated two variants: AtLEA4-5 protein incapable to be phosphorylated (SED1-phosphonull) and a construct with a different FRET pair (mTurquoise2 and mNeonGreen; SED1-mTq2-mNG). These variants were characterized in yeast cells and *N.benthamiana* leaves under hyperosmotic stress conditions. We found that the SED1-mTq2-mNG variant exhibits a FRET change comparable to the original SED1 version in yeast subjected to stress. However, SED1-phosphonull exhibited a lower FRET change than SED1. Our results suggest that SED1-mTq2-mNG is a good candidate for *A. thaliana.* This study will help to obtain a functional biosensor in *A.thaliana* that allows us to dynamically track the effects of osmotic stress in living cells.

TRANSCRIPTOME ANALYSIS OF *PERSEA AMERICANA* CV. HASS HIGHLIGHTS GENES INVOLVED INTO ZYGOTIC EMBRYOGENESIS PROCESS

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Abstract:

Zygotic embryogenesis in higher plants is the developmental process in which the zygote undergoes a series of differentiation events, leading to the formation of a mature embryo. To date, the elucidation of the molecular mechanisms that regulate embryogenesis in plants have not been fully understood. Currently, the use of omics technologies, particularly transcriptomics, allows quantify of changes in gene expression of an organism in different tissues and conditions at a particular moment of time, for this reason, transcriptomic has become a useful tool for the study of embryogenesis in plants. The aim of this work was to identify the genes involved in the development of the zygotic embryo of *Persea americana* cv. Hass by RNA-seq analysis. A total of 24,618 differentially expressed genes (DEGs) was identified during development of the zygotic avocado embryo. Genes involved in auxin homeostasis was identified throughout of embryo growth and development.

TOTAL PHENOLIC CONTENT AND TOTAL TRITERPENOID CONTENT IN *AGERATINA PICHICHENSIS* AND THEIR *IN VITRO* CULTURES

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Abstract:

Introduction: *Ageratina pichinchensis* (Axihuitl) is a medicinal plant that belongs to the Asteraceae family. *A. pichinchensis* is used as a healing, antifungal and for gastritis (1), uses that have been validated by scientific studies, it also has clinical studies that validate its use for the treatment of onychomycosis (2), therefore Axihuitl is an important source of bioactive compounds. The objective of this study was to evaluate the phytochemical profile of wild *A. pichichensis* plant and their *in vitro* cultures.

Methods and materials: The *A. pichichensis* plant was collected in Tepoztlán, state of Morelos, Mexico. From the seeds, *in vitro* plants were obtained and used to obtain callus cultures (30 days old), by means of nodal segment explants cultivated in MS medium with growth regulators, auxin (1-Naphthaleneacetic acid, NAA 1.5 mg/L) and cytokinin (kinetin, KIN 0.1 mg/L). The production of bioactive compounds was evaluated in plant and in vitro cultures by quantification of total phenolic content by the Folin-Ciocalteu reagent (3) and total triterpenoid content by colorimetry (4). All experiments were performed in triplicate and the results are expressed as mean ± standard error. Analyses of variance (Tukey tests, α=0.05) were performed for statistical analysis of experimental data.

Results: Significant differences were obtained in the determination of the total phenolic content. The highest concentration of phenolic compounds was obtained in the plant (100.56 ± 6.83 mg/g), followed by the callus culture (69.31 ± 2.06 mg/g) and to a lesser extent in the plant cultures *in vitro* (14.24 ± 1.71 mg/g). Similar results were obtained in the determination of total triterpenoid content, the highest concentration was in the plant (163.7±16.61 mg/g), followed by the callus culture (120.45±21 mg/g) being lower in the *in vitro* plant cultures (75.28±1.52 mg/g). The production of bioactive compounds was lower in *in vitro* cultures compared to the plant collected from its natural habitat, differences that may be due to the biotic and abiotic stress in which the plant is found in nature activating secondary metabolism as an adaptive response (5).

Conclusion: Based on the results, *in vitro* cultures of A. pichichesis are an alternative to produce bioactive compounds such as phenolic compounds and triterpenes.

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PRODUCTION OF BIOETHANOL FROM AGRO-INDUSTRIAL WASTE BY MICROORGANISMS ISOLATED FROM MINING WASTE

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Abstract:

Introduction. At the national level, the state of Guanajuato contributes 5% of the national production of corn, 13% of wheat and 22% of sorghum, which generates a significant amount of agro-industrial waste [1]. The production of bioethanol can be carried out from lignocellulosic feedstock coming from agro-industrial residues (corn, wheat, and sorghum) [2]. Second-generation bioethanol production involves pre-treatment, saccharification and fermentation of lignocellulosic material. Saccharification consists of the bioconversion of plant material to sugars. This process occurs through the action of microorganisms which presents the cellulosic enzymatic complex that performs the transformation of biopolymers present in vegetal waste to sugars. Another process involved is the fermentation of the sugars to ethanol [3]. In this work, the biodegradation of agro-industrial residues will be analyzed using microorganisms isolated from mining waste in Guanajuato to subsequently produce bioethanol. **Methodology.** We will employ four strains of filamentous fungi previously isolated and identified from one of the mining wastes of Valenciana, Guanajuato. The fungus that will be used are: CH2 (*Cladosporium cladosporoides*), CH6 (*Rhizopus sp.*), CH8(*Penicillium chrysogenum*) and CH10, (*Purpureocillium lilacinum*); likewise, the bacterial strain M7C3 (*Streptomyces badius*) will be used too. The culture of the strains was reactivated from cryopreserved vials at -20 °C. The fungal strains were growing in solid media YPG pH 4.5 and the bacteria was grown in nutrient agar. **Results.** The four fungal strains and the bacteria developed cellulolytic activity. This assay were perform growing microorganisms in carboxymethyl cellulose (CMC) 1% liquid media to detecting sugar production by DNS (dinitrosalicylic acid); the growing in CMC 1% solid media was also used, to determined the colorless zone with Congo red. **Conclusions.** It is expected to verify which of these microorganisms gives better performance for the biodegradation of corn, wheat, and sorghum residues to produce the necessary sugars for its subsequent alcoholic fermentation.

Keywords: bioethanol, microorganisms, mining waste. Acknowledgement: For support to SIP-IPN-20220926.

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XYLOSE REDUCTASE NADPH DEPENDENT AND XYLITOL DEHYDROGENASE NAD+ DEPENDENT FROM *CLAVISPORA LUSITANIAE*

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Abstract:

Clavispora lusitaniae is a yeast that assimilates xylose via the xylose oxidoreduction pathway. However, it has been observed that during the metabolism of this pentose, xylitol accumulates. The activity of the enzymes involved, xylose reductase (XR) and xylitol dehydrogenase (XDH), was assayed using external cofactors to define their affinity for each other. Cell-free crude extracts, xylose and the cofactors NADPH or NADH for XR, and xylitol with $NADP^+$ or NAD^+ as cofactors for XDH were used. XR was found to be NADPH-dependent, and XDH was found to be NAD^+ dependent in this yeast. The catalytic activity of xylose reductase of 1.2 mMol/mL*min and 38 mMol/mL*min was obtained for xylitol dehydrogenase, respectively. In assays with crude intracellular enzyme extracts using 7.5 g /L xylose as substrate and NADPH cofactor, 3.2 g/L ethanol was obtained. While with xylitol as substrate and NAD^+ as a cofactor, 1.8 g/L ethanol was obtained, this reaction became reversible with xylitol as substrate. The last step, catalyzed by alcohol dehydrogenase (ADH), whose catalytic activity was 33 mMol/mL*min, was also studied. The results show that *C. lusitanie* is a candidate to produce bioethanol from hydrolyzed lignocellulose rich in xylose; it can also accumulate xylitol.

Keywords: *Clavispora lusitaniae,* XR, XDH, ADH, NADPH, NADH, NADP+, NAD+.

GENETIC RESOURCES AND BIOTECHNOLOGY IN HABANERO PEPPER (*CAPSICUM CHINENSE* JAQC.) BREEDING

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Abstract:

Habanero pepper is an emblematic crop from Yucatán Peninsula, however, its production in this region is affected by a high incidence of pests derived diseases and also by the genetic variability of planted populations. In this sense, it has been created a number of breeding programs through both conventional and biotechnological methods, in order to obtain and propagate varieties and hybrids with desirable characters as a greater stress resistance and better crop performance. The utilization of *C. chinense* genetic resources has allowed the obtaining of eleven varieties of this specie and multiple hybrid lines with high productivity rates. In the biotech field *Capsicum* breeding has been limited by the recalcitrance of its species to *in vitro* regeneration in plant tissue culture. Although somatic embryogenesis has been successfully induced in *C. chinense*, somatic embryos in advanced stages show morphological, physiological and genetic abnormalities that limit their conversion into plants. Androgenesis is considered an advantageous alternative for obtaining normal embryos from male gametophyte, that give rise to haploid plants that constitute important biotechnological tools. There are reports of androgenesis in *Capsicum* genus, however, *C. chinense* does not yet have an efficient protocol for the induction of this morphogenic process. Therefore, we are currently working on developing an efficient methodology through the optimization of key factors involved in androgenic response.

Factors involved in androgenic response.

NANO-MICELLAR TECHNIQUE TO IMPROVE THE QUERCETIN STABILITY

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Abstract:

Quercetin (Qu) is a flavonoid present in some foods such as fruits, vegetables, nuts, wine, black tea and onion skins, edible vegetables, fruits, and wine, and can prevent free radicals from altering low-density lipoproteins [1]. Qu consumption has been associated to several functions such as anticoagulants, anti-inflammatory, antihypertensive and antihyperglycemic activities. Qu can inhibit lipid peroxidation, which could be useful against cancer cells [2]. However, the antioxidant or prooxidant activity of Qu depends on the redox state of cells and Qu concentration [3]. Evidence suggests that the antioxidant and prooxidant characteristics of Qu may promote the cancer suppression process by analogy with common anticancer drugs, such as doxorubicin, thus contributing to the prevention of tumor growth. In addition, Qu stimulates the induction of apoptosis and leads to cell cycle arrest in cancer cell models [4]. Although Qu has many pharmacological applications, it has not been widely used, perhaps because Qu is insoluble in water and the development of an aqueous formulation of Qu remains difficult, which greatly restricts the clinical application of Qu. Herein, we developed an aqueous formulation of Qu to improve its stability.

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INHIBITION OF HSA-MIR-16A-5P DECREASES VIABILITY AND SURVIVAL OF TRIPLE-NEGATIVE BREAST CANCER CELLS

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Abstract:

In 2020, it is estimated that there were approximately 9 million cancer cases in the world and of these 24.5% were breast cancer alone. Breast cancer is classified into 4 subtypes: Luminal A, Luminal B, HER2+ and triple negative or basal, the latter being the most aggressive.

miRNAs are small non-coding RNAs of approximately 19-25 nucleotides, which inhibit transcription or induce mRNA cleavage. miRNAs are involved in a variety of biological processes including cancer.

Overexpression of hsa-miR-196a correlates with malignancy grades of breast cancer, due to them it has been proposed as a diagnostic marker, furthermore its overexpression has been reported in models of drug resistance in MCF7 breast cancer cells.

In the present work we show that inhibition of miR-196a-5p by using a miRNA mimic decreases viability of MDA-MB-231 cells at 48 h by MTT assay, cell number 24 and 48 h after treatment and inhibits cell migration. The data show that inhibition of hsa-miR-196a is a good study strategy as a therapeutic target.

GENETIC TRANSFORMATION OF THE GREEN MICROALGA *CHLAMYDOMONAS REINNHARDTII* WITH THE *MNB6-TRI* GENE ENCODING A TRIVALENT NANOBODY THAT NEUTRALIZES THE SARS-COV-2 VIRUS

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Abstract:

The SARS-CoV-2 virus has claimed the lives of millions of people and caused the destabilization of the world economy. Biotechnology has provided different strategies to prevent and treat COVID-19, generating products such as mRNA vaccines and monoclonal antibody therapies that have significantly reduced the number of infections and deaths. Monoclonal antibodies have been quite useful to treat COVID-19, however they are expensive to produce. A promising alternative is the nanobody® technology based on the antigen-binding domain of camelid small antibodies. Nanobodies have several advantages over monoclonal antibodies such as their small size (15 kDa), high affinity and low cost of production in microorganisms. Several nanobodies have been developed against SARS-CoV-2, among them, the mNb6-tri stands out as an ultrapotent trivalent nanobody capable of neutralizing the virus by binding to the RBD domain of the spike protein. Among the expression platforms to produce functional therapeutic proteins at low production cost is the green microalga *Chlamydomonas reinhardtii*, which represents a great alternative for the production of nanobodies against SARS-CoV-2. The objective of this project is to generate *C. reinhardtii* transgenic lines capable of producing functional mNb6-tri nanobodies. So far, we have transformed *C. reinhardtii* with *mNb6-tri* using biolistics and detected by PCR 11 transgenic colonies which were positive for the presence of the *mNb6-tri* gene. Six transgenic clones were further analyzed by Southern blot, resulting in the detection of six independent transgenic lines and confirming the integration of the transgene into the *C. reinhardtii* genome. The highest number of transgene copies was found in line L2. The expression levels of *mNb6-tri* in these transgenic lines will be analyzed by RT-qPCR and the binding capacity of recombinant mNb6tri to its target will be assessed by ELISA.

COMPOSITION-STRUCTURE-PROPERTY RELATIONSHIP IN DECELLULARIZED ESOPHAGEAL MATRIX OBTAINED FROM PIGS OF DIFFERENT AGES

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Abstract:

The esophagus is an organ that can be affected by congenital or acquired diseases, whose treatment usually requires its surgical replacement. The natural extracellular matrix is an alternative in the development of homologous biological substitutes. In this work, the decellularization of porcine esophageal tissue obtained from 1-, 21- and 45-days old piglets was carried out by a combination of enzymatic and physicochemical methods. The decellularized scaffolds were evaluated in terms of their residual biochemical composition, microstructure, mechanical properties, and cytotoxicity tests. Furthermore, it was determined whether the use of ECM gel and epoxyeicosatrienoids promote cell growth and proliferation when combined with the esophageal scaffold. The results show that after tissue decellularization there was a significant reduction of DNA and a conservation of fibronectin and glycosaminoglycans in the three age groups. It was evidenced by second-harmonic imaging microscopy the randomly organized collagen fibers in the submucosa and a layer of well -organized fibers in muscular surface of decellularized tissue. It was determined that the mechanical properties of the tissue are not affected after its decellularization. Finally, the cytocompatibility tests showed that the decellularized esophagus by itself allows cell growth, however, when was combined with ECM gel and epoxyeicosatrienoids, the results showed an increase in viability of rabbit primary esophageal epithelial cells.

STRUCTURAL APPENDAGES OF ETEC E9034A PROMOTE ADHERENCE TO INTESTINAL CELLS

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Abstract:

Introduction. *Escherichia coli* enterotoxigenica (ETEC) is the etiologic agent responsible for diarrhea in newborns and children under 5 years, as well as in older adults in developing countries, including to Mexico. ETEC expresses several structural appendages involved in colonization to the intestinal epithelium. **Objective**. Inactivate *cstH*, *lngA* and *fliC* genes in ETEC E9034A strain by homologous recombination, to determine their effect on the adherence to intestinal cells LS174T and HT29. **Methodology**. Single (E9034AΔ*lngA*::km, E9034AΔ*cstH*::km, E9034AΔ*fliC*::cm); double (E9034AΔlngA::kmΔ*fliC*::cm, E9034AΔ*cstH*::kmΔ*fliC*::cm, E9034AΔ*cstH*::kmΔ*lngA*::cm); and triple (E9034A*ΔlngA::km*Δ*cstH*Δ*fliC::*cm) mutants were generated from ETEC E9034A, by the inactivation method in a one-step proposed by Datsenko and Wanner in 2000. . The infection was performed for 4 hours in a partial atmosphere of 5% CO_2. The number of attached bacteria adhered to cell monolayers was quantified by serial dilutions after culturing them on plates with Luria Bertani agar. **Results**. The eight strains showed a low adhesion profile to the LS174T cell line when compared to the HT-29 cell line. Mutation of the *lngA, cstH and fliC* and genes affected the adherence levels significantly to the LS174T cell line when compared to the wild type strain (E9034A); while, the mutant strain in the *fliC* gene did not show a significant difference. E9034AΔ*lngA*Δ*fliC*, E9034AΔ*cstH*Δ*lngA* strains showed a decrease in the number of bacteria adhered to both cell lines, with an adherence level similar to strain E9034AΔ*lngA*. Interestingly, E9034AΔ*cstH*Δ*fliC* strain showed a significant reduction in the number of bacteria adhered to both cell lines when compared with the E9034AΔ*lngA*Δ*fliC*, E9034AΔ*cstH*Δ*lngA* strains Interestingly, the E9034A strain was the one that showed the lowest number of adherent bacteria. **Conclusion.** The *lngA*, *cstH* and *fliC* genes in ETEC E9034A*ΔcstHΔlngAΔfliC* have an important role in the process of adherence to intestinal cells. The low adhesion observed in the LS174Tn cell line compared to the HT-29 cell line, could be as a result of high mucus production.

EXPRESSION OF BOVINE LEUKEMIA VIRUS PROTEIN P12-P24 OF GENOTYPE 1

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Abstract:

Enzootic bovine leukemia (EBL) is an infectious lymphoproliferative disease of cattle, caused by the Bovine Leukemia Virus (BLV). Like other retroviruses, the BLV genome contains the *gag, pol*, and *env* structural genes. The naturally infected animals develop antibodies to *env*-encoded glycoproteins gp51 and gp30 as well as to *gag*-encoded proteins p24 and p15. Ten different genotypes have been classified worldwide. In Mexico, genotypes 1 and 3 of BLV have been identified in cattle destined for dairy production. Currently, there are several commercial kits for AGID and ELISA tests that are based on the use of antigens such as p24 and gp51, all of them foreign-made, these proteins are the most antigenically potent and stimulate the immune response of infected bovines. In the present work, the expression of a double bound protein (p24 and p12) from BLV genotype 1 has been achieved, of which there are no reports so far. The primers were designed that flanked the nucleotide sequence of p24 and p12 proteins, an additional stop codon was included in the reverse design, two colonies had the correct insert and orientation. The expression tests of both colonies were carried out, evaluations were carried out by means of SDS-PAGE gels as well as by Western blot. From the expression test, a molecular weight between 70 to 95 kDa was obtained in its monomeric form, which would correspond to what was expected according to the product of the fusion of both proteins (1112 bp). The study's prospective is to evaluate the efficiency of the BLV recombinant protein P24-12 as an antigen in an ELISA test and to compare the diagnostic efficiency of the test.

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CHARACTERIZATION OF THE ANTIBIOTIC EFFECT OF SUPERNATANTS OF STREPTOMYCES STRAINS ISOLATED FROM MINING TAILINGS FROM GUANAJUATO, GTO.

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Abstract:

Introduction. Bacteria are very ubiquitous microorganisms, capable of surviving in different environments where their growth can be affected by the interaction with other populations of microorganisms (synergistic, antagonistic, etc.), as well as by the physical and chemical characteristics of their environment. As a consequence of these interactions, these microorganisms produce secondary metabolites with varied biological activities, which play an important role in their survival [1]. Bacteria of the *Streptomyces* genus are the main natural source of bioactive secondary metabolites of great importance: antibiotics, antifungals, antiparasitics, antiviral agents, antitumoral agents, immunosuppressants, immunomodulators, plant growth stimulators, enzyme inhibitors, bio-insecticides, siderophores, pigments, herbicides, among others [2, 3]. **Justification.** Microorganisms from mining tailings represent an opportunity to search for metabolites of biotechnological interest. **Results.** So far, *Streptomyces* strains have been isolated from mining tailings in Guanajuato, Gto., which underwent microbiological and molecular identification by PCR amplification of the 16S ribosomal gene for sequencing and identification by bioinformatic analysis. Likewise, it was determined that the supernatants of the *Streptomyces* strains C1M10 and C2M9, showed antimicrobial activity against *Bacillus* sp. **Conclusions.** Growth kinetics will be performed in different culture media of these bacterial strains to determine the growth condition that induces the production of metabolites related to this antimicrobial effect. Finally, using SDS-PAGE gels, the protein profile of the supernatants induced in this antimicrobial activity will be analyzed to detect possible protein bands that correlate with the antibiotic effect detected.

Keywords: *Streptomyces*, bioactive-secondary-metabolites, mining-tailings.

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PLASMID RECOVERY FROM THE BACTERIAL INHABITANTS FROM THE MAYAN SINKHOLEPOL-AC LOCATED IN SISAL, YUCATAN

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Abstract:

Sinkholes, or cenotes from "ts'ono'ot" in Maya, are geological structures of calcareous constitution sculped by millennials. Not to mention that they are also spectacular and peculiar aquatic ecosystems[1]. In some cases, cenotes can be located close enough to the sea, leading to the mix of the underneath fresh water with saltwater. This dynamic conditions in the sinkhole drive special responses in the ecosystem and inhabitant organisms. In microorganisms like bacteria, plasmids are accessories that allow fast adaptations to stressing conditions[2]. From the biotechnological point of view, environmental plasmids are the source of many pathways for biosynthesis or biodegradation processes. In general, plasmids found in nature confer to their hosts beneficial traits that allow them to survive in competitive environments. In the microbial world, one way to compete against other microorganism is via the production of toxins and antibiotics. Another way is by utilizing recalcitrant or unusual substrates that other organisms can't use or by developing resistance to toxic substances such as heavy metals or pesticides, enabling them to survive where others can't. To save energy, these specific degradative capabilities are often tightly regulated in plasmids to be active only in the presence of the target compound[2,3]. These systems are a gold mine for synthetic biology, especially when combined with natural inducible expression systems that allow tuning of metabolic pathways for biosynthetic or biodegradation processes[3,4]. Despite cenotes are a big truistical attraction for exploration, the biotechnological interest for these amazing and prolific ecosystems remains scarce. In order to determine the plasmid diversity harbored by the bacterial inhabitants in a sinkhole, we explored and recollected sediments by scuba diving in a coastal cenote located in Sisal, Yucatan. Sediments were cultured in solid A1-cenote media by the serial dilution method. After 14 days single colonies were subcultured in solid media for macroscopic-microscopic characterization, and in liquid media for biomass production. Grown cultures were harvested and centrifuged to obtain the bacterial pellet which was employed for plasmid extraction and further electrophoretic analysis. We established a customized protocol for plasmid extraction with home-made solutions, since many of the recovered bacteria were Gram-positive, mostly actinomycetes. Currently, we are generating a library of plasmids that will be further sequenced, annotated and analyzed for the presence of operons or genes encoding enzymes for interesting biotechnological processes.

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THEORETICAL AND EXPERIMENTAL ANALYSIS OF THE DIAGNOSTIC STRIP DESIGN FOR THE RAPID DETECTION OF *BOTHROPS ASPER* VENOM IN PATIENT SERUM

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Abstract:

Patient with clinical symptoms of poisoning due to snake bites require an effective diagnose and management as the unknown amount of venom that it needs to be neutralized. The envenomation of snake bites it is a public health issue and therefore it is necessary to develop optimal methods for the treatment. In this work the proposal is the development of the diagnose strip for the lateral flow test that will detect the amount of *B. asper* venom. To support the design, we are using a mathematical model to determine the physicochemical parameters that impact the design of the strip for rapid and timely diagnosis by an essay in sandwich format. The primary antibodies within the test line are polyclonal antibodies extracted from rabbits hyperimmunized with the venom of *B. asper.* These were purified by chromatography based on poison affinity. Specificity was verified in Western-blot and estimation of venom-antibody concentrations was performed by Dot-blot. The values obtained from these experimental results were analyzed in the model, in which three species (conjugate (C_A), fixed antibody in the test area (C_S), and *sandwich* complex (C_{AS}) were considered. According to the evaluated data of the model, it is considered that the variation of the concentrations of fixed antibody and antigen at the experimental level would serve for a better coupling in the design of the strip.

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IN SILICO ANALYSIS OF THE EXPRESSION OF NITROGEN FIXATION GENES IN A LIGNOCELLULOSE DEGRADING CONSORTIUM

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Abstract:

Nitrogen is an essential component of living organisms; however, humans and plants do not have the ability to process the gaseous form (N2) present in the atmosphere. Different microorganisms transform N2 into metabolizable molecules, through different stages of the nitrogen cycle . Diazotrophs are bacteria responsible for carrying out the biological nitrogen fixation (BNF), a process mediated by the nitrogenase system. During the degradation of lignocellulose by microbial consortia, microorganisms establish synergistic relationships to survive. The media used for these purposes are rich in carbohydrates with a low concentration of the nitrogen source. Therefore, at the end of the process the nitrogen concentration limit the microbial survival. Consortium PM-06 is a lignocellulose-degrading microbial community, composed by microorganisms with the ability to fix nitrogen, such as Paenibacillus, Aneurinibacillus and Bacillus . In the present research, the in silico analysis of the expression of genes related to nitrogen fixation in the PM-06 consortium during lignocellulose degradation was performed. The results indicate that at the beginning of the culture (time 0), Paenibacillus macerans expressed the nifB, nifH, nifD, nifK, nifE, nifN, nifX and nifU cluster that includes genes related to nitrogenase and nitrogenase reductase enzymes and proteins involved the biosynthetic process. At the beginning of the culture, cells retain characteristics present in the last stages, where the lack of nutrients and anoxic conditions could predominate. In these stages, the nitrogen fixation would generate compounds that help to the survival and function of the population. These findings indicate that this community could also be used as a fertilizer helping to promote plant growth.

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FUNCTIONAL CHARACTERIZATION OF THE CAROTENOID CLEAVAGE DIOXYGENASES BOCCD1-1 AND BOCCD4-3 FROM *BIXA ORELLANA* L. AND IDENTIFICATION OF APOCAROTENOIDS WITH BIOTECHNOLOGICAL POTENTIAL

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Abstract:

Apocarotenoids are compounds that are derived from the oxidative cleavage of carotenoids. In plants, the Carotenoid Cleavage Dioxygenase (CCD) family of enzymes catalyze the enzymatic cleavage of linear and cyclic carotenoids at their different double bonds, generating a diversity of apocarotenoids. Until now, seven families of CCD enzymes have been reported: NCED, CCD1, CCD2, CCD4, CCD7, CCD8 and ZAS, each one is classified by the type of bond, the carotenoids it cleaves, and the apocarotenoids it produces (Wang et al., 2019). The family of enzymes CCD1 and CCD4 are the most studied and best characterized in plants. Recently, members of the BoCCD1 subfamily: BoCCD1-1, BoCCD1-3, and BoCCD1-4; and the BoCCD4 subfamily: BoCCD4-1, BoCCD4-2, BoCCD4-3, and BoCCD4-4 from Bixa Orellana (annatto or achiote) participate in the first biosynthesis step of bixin, a red-orange pigment present in the aril of the seeds (about 80% of the total carotenoids), widely used in the food, pharmaceutical and cosmetic industries. Furthermore, the results suggest that the enzymes BoCCD1-1 and BoCCD4-3 can cleave lycopene at various double bonds (Rivera-Madrid *et al*., 2016; Us-Camas et al., 2022). Since the enzymes CCD1 and CCD4 can cleave lycopene and other carotenoids such as β-carotene and zeaxanthin at positions 5,6/5',6, 7,6/7',6' and 9,10/9', 10' generating various apocarotenoids, in the present work we carry out the functional analysis of the enzymes BoCCD1-1 and BoCCD4-3 on β-carotene and zeaxanthin, in order to evaluate new potential substrates and find new apocarotenoids produced by these enzymes with possible biotechnological applications for the food, cosmetic and/or pharmaceutical industries. Additionally, this work will allow a better understanding of the biosynthesis mechanisms, as well as the regulation of carotenoid and apocarotenoid pathways in annatto and other plant species rich in these compounds.

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CGIGGFP AND OTHER FLUORESCENT MOLECULES IN CONDYLACTIS GIGANTEA

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Abstract:

Condylactis gigantea, is a marine invertebrate animal belonging to the Cnidaria phylum. These panchronic animals are abundant and very important for maintaining the balance of various aquatic ecosystems, including coral reefs. In addition to their ecological importance, cnidarians are an important source of biotechnological compounds, including fluorescent proteins. Currently, 88% of these molecules come from or were obtained from native proteins isolated from organisms of the Cnidaria phylum.

In the specimens of the C. gigantea anemone from the Mexican Caribbean, we have found five fluorophores, four of them not reported until now, and the green fluorescent protein: cgigGFP (Labas, 2002), of which several spectroscopic characteristics were unknown until this research.

According to spectroscopic analysis and fluorescence microscopy, the compounds present in the tissue of organisms have fluorescent qualities (fluorescence emission, absorbance, quantum yield, etc.), and optimal structural characteristics to become molecules with potential biotechnological use as molecular markers.

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COMPARATIVE HETEROLOGOUS PROTEIN EXPRESSION OF THE MAJOR ALLERGEN OF FRAXINUS TREE POLLEN

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Abstract:

Fraxinus is a tree from the Oleaceae family and is distributed worldwide. In Mexico City, the pollen of *Fraxinus* causes significant respiratory allergies. The major allergen of *Fraxinus* is Fra e 1, which has high homology with other allergens from Oleaceae family. Whole pollen protein extracts are commonly used to diagnose and treat respiratory allergies. However, this extract comprises thousands of non-well characterized proteins which makes the diagnosis inexact. One way to solve this problem is to use allergens expressed and purified from heterologous organisms, such as bacteria and yeasts, which are less expensive and produced more quickly. Unfortunately, these organisms cannot add all plant protein post-translational modifications (PTMs), such as glycosylation. These PTMs sometimes can affect recognition mediated by IgE of patients sensitized. Therefore, we employed bacteria and plants for Fra e 1 expression. We planned to use bacteria for allergens in which PTMs are not important for IgE recognition; meanwhile, plants will be used in allergens where glycosylation is needed. To determine if PTMs are essential for IgE recognition, we expressed Fra e 1 allergen in bacteria (*E. coli* BL21) and plants (*Nicotiana benthamiana*). Fra e 1 gene was codon-optimized and cloned into pMAL-c4x, their expression is under IPTG control for bacterial expression. Additionally, Fra e 1 was amplified by PCR from ash pollen, sequenced, cloned into plant expression vector pCambia 1302, and finally transformed into *Agrobacterium tumefaciens* for plant transformation. Protein extraction was done from bacteria, and *N. benthamiana* leaves and purification of recombinant Fra e 1 was performed with a nickel affinity column (IMAC). Finally, the recombinant allergens will be TEV-digested to remove their Tag. These recombinant allergens will be used in Western-blot using sera from allergic patients to validate whether PTMs are necessary for correct IgE recognition. This will allow us to determine the correct expression organism to produce these allergens.

IDENTIFICATION AND CHARACTERIZATION AND OF ALGAE CELL WALL DEGRADING SPECIFIC ENZYMES FROM MARINE ACTINOMYCETALES

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Abstract:

The focus on algae degradation is more concerning than ever before. From 2014 to the present, massive invasions of the brown macroalgae sargassum (*Sargassum natans* and *Sargassum fluitans*) have been occurring regularly along the Mexican Caribbean coast.[1] These sargassum influxes caused serious environmental, ecological, and economic problems, leading to decreased tourism and the destruction of nearshore flora and fauna.[2]

Thus, it is vital to create an industry, capable of the utilization and valorization of sargassum. The first step of seaweed utilization often involves the hydrolysis of their cell walls, consisting mainly out of cellulose, alginate, fucoidan and other polysaccharides.[3]

One highly interesting source of novel, algae cell wall hydrolyzing carbohydrases, are actinomycetes, which have a fundamental role in the degradation of the complex organic polymers cellulose and chitin.[4,5]

The focus of our work is on the characterization of marine actinomycetes regarding their ability to hydrolyze different polysaccharides. Strains cable of degrading those biopolymers, are further examined on their ability to degrade the cell walls of micro- and macroalgae. Furthermore, the responsible carbohydrases are identified, isolated and enhanced *via* enzyme engineering, to create novel and specific biocatalysts, capable of degrading and valorizing algae. Thus, a highly specific and active carbohydrase is created, capable of degrading algae cell walls at a high turnover.

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OPTIMIZATION OF THE L-LACTATE OXIDASE FROM *AEROCOCCUS VIRIDANS* FOR ELECTROCHEMICAL BIOSENSORS

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Abstract:

The determination of L-lactate concentration is important for sport medicine, but also as a general parameter for health condition. In absence of oxygen and high energetic demand the L-lactate concentration raises and can cause lactic acidosis. Additionally, in food industry is an indicator of bacterial fermentation. There are several reports of electrochemical L-lactate biosensors, they are based on the well characterized enzyme L-lactate oxidase LOx, most of them are second generation biosensors which requires use of electron mediators. LOx is a tetrameric enzyme, which contain a FMN as prosthetic group. The enzyme oxidizes L-lactate to pyruvate, producing also H_2O_2

Two of the main opportunities for improvement of lactate biosensors are: 1, the design of third generation biosensors which allow the direct electron transfer from the enzyme to the electrode, avoiding the use of mediators which in clinical applications can result in toxicity if they diffuse across membrane; 2, the increase of activity at acidic pH values, as the reported LOx enzymes decrease significantly their activity at physiological pH values of sweat, limiting the applicability in wearable devices.

In this work, mutants of the L-lactate oxidase of *Aerococcus viridans* (AvLOx) were designed for: a) Promoting of direct electron transfer to electrodes or b) Modification of the pKa of the catalytic histidine 265. The mutants were evaluated *in silico*, expressed in *E. coli* cultures, purified by several chromatographic steps and kinetically characterized. For third generation biosensors, the mutants were immobilized in electrodes and DET was confirmed by cyclic voltammetry and chronoamperometry. For the case of pH modification, the activity of the mutants was evaluated at different pH values; in combination with chemical crosslinking one of the mutants conserved the 95% of its activity at pH 4.6, compared with the WT which conserves only 30%. Our results demonstrate that through rational design of single mutants, the AvLOx can be optimized to solve issues in biosensing.

ABSTRACTS | Posters Genetics, Epigenetics & Genetic Regulation

XXXIII National Congress of Biochemistry

TRANSCRIPTIONAL REGULATION OF *PHAC* BY PHAP5 IN *AZOSPIRILLUM BRASILENSE* SP7 FOR POLY-3-HYDROXYBUTYRATE (PHB) PRODUCTION

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Abstract:

Phasins (PhaP) are the proteins involved in the regulation of size and number of poly 3-hydroxybutyrate (PHB) granules. Previous studies on phasins have shown that *Azospirillum brasilense* Sp7 has at least 6 phasins (Martínez et al., 2019). Ushimaru et al., (2014) has suggested possible interactions between phasins and Granule Associated Proteins (GAP) such as PHB synthase (PhaC), PHB depolymerase (PhaZ) and regulator proteins (PhaR or PhaM). The interaction between proteins occurs depending on the PHB-producer microorganism.

Instead of phasins are the major proteins covering the PHB granules, there is still not much available information about them in *A. brasilense* Sp7. The aims of this work are to know if PhaP5 phasin and the RpoE gene (σ24) can act together as transcriptional regulators of *phaC* gene during PHB production in *A. brasilense* Sp7.

Using the I-TASSER and SWISS-MODEL servers, 3D structures of PhaP5 and RpoE were generated. For PhaP5, the structure of *Aeromonas hydrophila* $PhaP_{Ahy}$ (PDB number 5IP0) was used as template. For RpoE, the structure of *Rhodobacter sphaeroides* $RpoE_{Rsp}$ (PDB number 2Q1Z) was used. Later, by using the ClusPro 2.0 and HDOCK servers, it was performed a molecular docking to determine the interactions between RpoE (receptor) and PhaP5 (ligand). To evaluate the transcriptional regulation of *phaC*, MEME server was used to obtain the -10 and -35 boxes. A molecular docking protein-DNA was done, using the upstream region of *phaC* (-10 and -35 boxes) as a receptor and PhaP5-RpoE complex as a ligand. The results shown that PhaP5 blocks the binding site of RpoE to DNA, which could affect the transcription of *phaC*. It suggests a possible function of PhaP5 and RpoE repressing the transcription of genes involved in the PHB metabolism under stress-growth conditions.

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EFFECT OF 5-AZACYTIDINE AND TRICHOSTATIN A ON THE FLAVONES AND FLAVONOLS BIOSYNTHESIS PATHWAY OF THE ALBINO PLANT *AGAVE ANGUSTIFOLIA* HAW.

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Abstract:

Epigenetic modifications are reversible changes that alter chromatin structure and gene expression, these changes are shaped by the environment and generate modifications. Among the most studied modifications are DNA methylation and histone post-translational modifications such as acetylation. One way to induce epigenetic changes is using molecules such as 5-azacytidine (5-AzaC) and trichostatin A (TSA). 5-AzaC is an analog of 5-cytosine, which reduces the overall level of DNA methylation, while TSA is an inhibitor of histone deacetylases. In plants, these epigenetic changes can regulate metabolic pathways such as that of flavonoids, which fulfill different functions in the plant such as protection against UV-B light and signaling, to name a few. In Agave angustifolia Haw. In vitro, important differences were found in DNA methylation and histone H3 acetylation between albino plants (A) and green plants (G), which raises the question: is there any relationship between epigenetic changes and the flavonoid biosynthetic pathway in phenotypes G and A of A. angustifolia Haw.? The objective of this work focuses on investigating the effect of AzaC and TSA on the expression of genes involved in the biosynthesis of flavones and flavonols, as well as the accumulation of these compounds in the G and A phenotypes.

CHLOROPLASTIC PENTATRICOPEPTIDE REPEAT PROTEINS (PPR) IN ALBINO PLANTLETS OF *AGAVE ANGUSTIFOLIA* HAW. REVEAL UNEXPECTED BEHAVIOR

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Pentatricopeptide repeat (PPR) proteins are involved in the regulation of RNA metabolism in plastids. Enormous efforts have been made to understand the function and action sites of *PPR* genes in model plants such as *Arabidopsis thaliana*. However, there is little information available on chloroplastic *PPR* genes in non-model plants and less in plants without chloroplasts. A comprehensive and multifactorial bioinformatic strategy was applied to search for putative *PPR* genes in the foliar and meristematic tissues of green and albino plantlets of the non-model plant *Agave angustifolia* Haw. A total of 1,581 *PPR* transcripts were identified, from which 282 were chloroplastic. Leaf tissue in the albino plantlets showed the highest levels of expression of chloroplastic *PPR*s. The prediction for hypothetical targets of 12 PPR sequences in the *A. angustifolia* plastome revealed their action on transcripts related to ribosomes (*rps12*, *rps16*, *rps14* and *rpl33*), photosystems (*psaB*, *psbC* and *psbD*), cytochrome b/f complex (*petA* and *petN*), ATP synthase (*atpA* and *atpE*), transfer RNA (*trnK-UUU* and *trnI-GAU*), plastid-encoded RNA polymerase (*rpoC1*), NADPH dehydrogenase (*ndhG*), and RuBisCO large subunit (*rbcL*). Our results suggest that the expression of *PPR* genes depends on the state of cell differentiation and plastid development. In the case of the albino leaf tissue, which lacks functional chloroplasts, it is possible that anterograde and retrograde signaling networks could be severely compromised, which would lead to a compensatory anterograde response characterized by an increase in the expression of *PPR* genes.

MICRORNA MIR-142-3P EXPRESSION IN TRIPLE-NEGATIVE BREAST CANCER (TNBC) DERIVED CELL LINES AND ITS INVOLVEMENT IN DNA DAMAGE RESPONSE (DDR) MECHANISMS

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Abstract:

Breast Cancer (BC) is the most common type of cancer diagnosed worldwide, and the most common cancer-related cause of death among women. BC is a highly heterogeneous disease, although it can be classified based on the expression levels biomarkers, such as hormonal receptors (Estrogen Receptor (ER) and Progesterone Receptor (PR)), and the Human Epidermal Growth Factor Receptor (HER2). Unlike other types of BC, Triple-Negative Breast Cancer (TNBC) lacks the expression of ER, PR, and HER2; therefore, treatment options against TNBC are limited and it is associated with a poor prognosis and a higher risk of metastasis. Even though TNBC has a better response to chemotherapy, the development of resistance against cytotoxic agents in most TNBC tumors and its high heterogeneity evidenced a necessity for the identification of novel biomarkers. DNA Damage Response (DDR) mechanisms have been identified as possible targets for the development of targeted therapies, particularly Homologous Recombination (HR) has been of special interest due to an HR deficiency observed in TNBC, provoked by mutations in HR proteins, such as BRCA1 and BRCA2. Non-coding RNAs (ncRNAs) have been observed to participate in the regulation of multiple mechanisms in carcinogenesis, including DDR, such as miR-142-3p. It has been reported that miR-142-3p might be involved in the regulation of radioresistance in TNBC cells through its interaction with BRCA2. We have evaluated the expression of miR-142-3p in TNBC-derived cell lines and have observed differential expression levels of miR-142-3p and its targets among the cell lines, which suggests a role for miR-142-3p in the enhanced HR observed in BC.

CELLULAR PLASTICITY OF RADIORESISTANT BREAST CANCER CELLS FAVOR CHEMOSENSITIVITY

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Abstract:

Breast cancer cells exposed to continuous application of radiation frequently undergo molecular and phenotypic changes collectively referred as cellular plasticity. While there is extensive evidence of genetic alterations, the evolution of diverse cell phenotypes and their global transcriptional changes as effective mediators of radioresistance of breast cancer are still poor explored. To elucidate radiation resistant cell phenotypes, we evaluated cell migration, cell survival and apoptosis in an isogenic *in vitro* model of radioresistant breast cancer cells (RR cells). Additionally, we conducted analysis of the global transcriptome changes and gene co-expression networks to evaluate differential expressed genes (DEGs), hub genes and biological pathways enriched to identify key genes related to cell plasticity of the RR cells. We demonstrate that RR-cells enhanced invasiveness, and interestingly, RR cells were significantly sensitive to chemotherapeutic agents by inhibit cell survival and promote apoptosis. We identify DEGs, gene co-expressed networks, hub genes and biological pathways associated to RR phenotypes. DEGs and hub genes detected in the *in vitro* model of radioresistance were differentially predictive for the failure of radiotherapy in breast cancer patients with luminal and triple negative breast cancer (TNBC) tumors subtypes. Additionally, hub genes were also differentially expressed in luminal and TNBC tumors of patients with pathological complete response (pCR) after chemotherapy. In this work we identify several forms of cellular plasticity in radioresistant breast cancer cells and novel gene biomarkers for progression disease after radiotherapy and pCR after chemotherapy in luminal and TNBC patients. These results contribute to understanding the mechanisms underlying cellular plasticity in radiation therapy resistance. The findings opening an opportunity for the design of new treatment schemes for luminal breast cancer and TNBC.

RECONSTRUCTION OF TELOMERE-ASSOCIATED SEQUENCES OF INDIVIDUAL CHROMOSOMES OF *U. MAYDIS* BY ASSEMBLING LONG SEQUENCE READS

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Abstract:

Telomeres and TAS (telomere-associated sequences) are reference points in sequencing assays that indicate the end of the chromosomes has been reached. However, their reconstruction in ordered sequences and the measurement of its size is a difficult task as NGS sequencing platforms and shotgun strategies provide very short reads. Additionally, the massive number of repeated sequences causes failures to measure the actual size of repeated DNA stretches, loss of genetic elements, gaps, and lack of resolution during the assembly. These facts prevent the analysis of molecular mechanisms functioning to protect chromosomes and stabilize genomes.

Genome sequences of *U. maydis* 521 confirm the existence of two main types of TAS, previously named *UTASa* and *UTASb*, reported a limited number of their isoforms and an outline of telomeres and TAS, according to the existing technical and analytical advances. We are interested in elucidating the identity of the genetic elements harbored in each chromosome end of *U. maydis*, intending to know their length, arrange, and organization in each TAS domain. To do this, we choose the reference 521 and PGA2.1 strains, one of which has a low copy number of *UTASa* in its genome. Both genomes were sequenced using the PacBio SEQUEL platform to obtain long reads that allow chromosome ends reconstruction. We obtained 155,813 reads with an average size of 155,817 nt; the quality of the sequences was Q≥ 30. The size of the haploid genome of PGA 2.1 is 22 Mb, was assembled de novo in three steps (cleaning, trimming, and assembly), and 24 contigs were obtained, with N50 of 921,929 and L50 of 7; the G+C content was 53.91%, and the assembly quality (MAUVE) was 54 LCBs. In comparison with the reported fraction of 19.7 Mb from the haploid genome of the 521 strain (GenBank access 237631), the G+C content of 54% let us knew that the chromosome ends of both strains have some sequence variations and translocations on the smallest chromosomes. Third-generation sequencing provides a more powerful tool for whole-genome assembly (including the three structural essential elements of chromosomes) in several species, humans included, to discover the genome's entire function.

THE RNA POLYMERASE II SUBUNIT NRPB2 IS REQUIRED FOR INDETERMINATE ROOT DEVELOPMENT, CELL VIABILITY, STEM CELL NICHE MAINTENANCE, AND DE *NOVO* ROOT TIP REGENERATION IN *ARABIDOPSIS*

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Abstract:

The RNA polymerase II is a macromolecular complex, which drives the biogenesis of coding and non-coding RNAs for gene expression. In this report, we describe new roles for its second-largest subunit, NRPB2, on root organogenesis and regeneration. Down-regulation of NRPB2 activates a determinate developmental program, which correlated with a reduction of mitotic activity, cell elongation, and size of the root apical meristem. Auxin and stem cell niche (SCN) gene expression as well as structural analysis revealed that NRPB2 maintains SCN activity through distribution of PIN transporters in root tissues. Noteworthy, *nrpb2-3* mutants manifest cell death in pro-vascular cells within primary root tips of plants grown in darkness or exposed to light, which triggers the expression of the regeneration gene marker ERF115 in neighbor cells close to damage. Wild-type seedlings regenerated the root tip after excision of the QC and SCN, but *nrpb2-3* mutants did not rebuild the missing tissues, and this process could be genotypified using *pERF115:GFP*, *DR5:GFP* and *WOX5:GFP* reporter constructs. These results show the importance of the transcriptional machinery for root organogenesis, cell viability and regenerative capacity for reconstruction of tissues and organs upon injury.

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CHARACTERIZATION OF MICRORNA/TARGET REGULATORY NODES INVOLVED IN THE SYMBIOSIS BETWEEN *ARABIDOPSIS THALIANA* AND *PIRIFORMOSPORA INDICA*

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Abstract:

Piriformospora indica is a mutualistic symbiotic fungus that colonizes the roots of a wide variety of monocots and dicots plants, including *Arabidopsis thaliana*. This fungus benefits its host plants by promoting their growth, resistance to pathogens and tolerance to abiotic stresses. The molecular mechanisms that control the plant-*P. indica* interaction still require detailed investigation. Such is the case of microRNAs, which are small RNA molecules of 20-22 nt. that regulate important biological processes in plants. So far, microRNAs have been studied in the interaction between *P. indica* and orchids, rice or grass. In order to characterize regulation nodes of microRNAs and their target messenger RNAs in the model plant *A. thaliana* during symbiosis with *P. indica*, in vitro co-culture of both organisms was performed. The corresponding root tissue was used for the analysis of RNAseq, Small RNAseq and Degradome. A list of microRNA/target pairs potentially involved in this symbiosis was established as, for example, miR399/*PHO2*, miR161/*PPR*, miR168/*AGO1*, miR398/*CSD1* and miR157/*SPL*. The function of identified targets is relevant since they are involved in the phosphate homeostasis, defense and stress in plants. Likewise, a different symbiotic phenotype was observed in miR161 mutant plants, compared to the wild type, displaying an altered number of spores. In conclusion, during the symbiosis between *A. thaliana* and *P. indica*, the differential expression of microRNAs and their relation with the corresponding targets was identified. In addition, the analysis of selected mutants showed us that the alteration of the action of microRNAs can affect fungal root sporulation during this interaction.

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A MICRORNAS PROFILE PREDICTS GASTRIC PRENEOPLASTIC LESIONS PROGRESSION TO GASTRIC CANCER

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Abstract:

Gastric cancer (GC) is the result of progressive malignancy of gastric preneoplastic lesions (GPL), mostly associated to *Helicobacter pylori* (*H. pylori*) infection. To date, miRNA expression profiles in the gastric carcinogenesis model have not yet been fully analyzed. The aim of this work was to identify a profile of differentially expressed miRNAs in the progression of gastric carcinogenesis model. We analyzed the miRNomes of preneoplastic lesions available at the European Nucleotide Archive (ENA), and of GC at The Cancer Genome Atlas (TCGA). miRNAs expression levels were analyzed in all preneoplastic lesions from non-active gastritis to GC. Fifteen miRNAs were detected in gastric carcinogenesis progression model. The expression of miR-141-3p, miR-873-5p, miR-429-3p, miR-204-5p, miR-200a-3p, miR-592-5p, miR-146a-5p and miR-368-3p progressively decreased in the gastric carcinogenesis progression model, while miR-122-5p, miR-196b-5p, miR-20b5p, miR-378a-3p, miR-99a-5p, miR-194-5p and miR-101-2-3p were progressively increased. Some of these miRNAs were predictors of overall survival (OS) in GC patients. Additionally, we identify miR-18a-5p significantly up-regulated in GC samples which was associated with better OS in GC patients. miR-18a-5p expression level was analyzed in preneoplastic lesions samples from Mexican patients positive to pathogenic *H. pylori strain* and in the *H. pylori*-AGS cells co-culture. Results showed that miR-18a-5p expression was inhibited in preneoplastic lesions samples from Mexican patients, but it was significantly up-regulated in AGS gastric cancer cells infected by *H. pylori*. In conclusion, these findings collectively revealed a novel miRNAs profile that could predict the progression of preneoplastic lesions to GC. Moreover, miR-18a-5p could be differentially regulate by *H. pylori* in the gastric carcinogenesis model.

HIGH LEVELS OF SECOND MESSENGER C-DI-AMP POSITIVELY INFLUENCE THE ACTIVATION OF STRINGENT RESPONSE AND AFFECTS MUTATION FREQUENCY RATE IN *BACILLUS SUBTILIS*.

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Abstract:

c-di-AMP is a cyclic dinucleotide bacterial second messenger involved in the regulation of a variety of cellular processes named genomic maintenance, stress response, cell wall homeostasis and ions transport. Cellular levels of c-di-AMP are finely regulated by the activity of diadenylate cyclases and phosphodiesterases, both specific for c-di-AMP synthesis and degradation respectively [1].

GdpP is a phosphodiesterase able to hydrolyze a phosphodiester bond from a c-di-AMP molecule, converting this signaling molecule to the inactive form 5'-pApA [2]. Inactivation of GdpP increases c-di-AMP levels in *B. subtilis* and deregulates different metabolic pathways [2]. In addition, it is anticipated that regulation by c-di-AMP may be orchestrated with other nucleotide second messengers such as alarmone (p)ppGpp synthesized by RelA and involved in the bacterial stringent response, and with c-di-GMP, the latter being responsible for defining bacterial lifestyles [4].

In this work, a transcriptional fusion *relA-lacZ* was introduced to locus *relA* of *B. subtilis* and the expression levels of *relA* determined in basal conditions of growth; and, in a genetic background lacking *gdpP* where high levels of c-di-AMP are expected. Expression of *relA* was found to be increased in response to *gdpP* inactivation. Finally, mutation frequency of *gdpP* strain was evaluated and compared to WT strain of *B. subtilis.*

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ROLE OF SDIA PROTEIN IN THE TRANSCRIPTIONAL REGULATION OF GENES INVOLVED IN THE BIOSYNTHESIS OF THE *KLEBSIELLA OXYTOCA* TILIVALLINE CYTOTOXIN

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Abstract:

INTRODUCTION: *Klebsiella oxytoca* is part of the gut microbiota and causes antibiotic-associated hemorrhagic colitis (AAHC) in patients under long treatment with antibiotics[1]. The AAHC is caused by the tilivalline cytotoxin, a non-ribosomal peptide that is synthesized by enzymes encoded in the *aroX* and NPRS operons, which are clustered in a pathogenicity island[2]. The SdiA protein belongs to the "quorum sensing" LuxR transcriptional regulators family and responds to AHLs that are produced by other bacteria and regulates the expression of some virulence genes by binding to the SdiA-box on promoter regions[3]. The role of SdiA on transcriptional regulation of genes involved in the biosynthesis of tilivalline cytotoxin is currently unknown. **OBJETIVE:** To investigate the regulatory role of the SdiA protein in the regulation of genes involved in the biosynthesis of tilivalline cytotoxin. **METHODS:** A mutant was generated from the *K. oxytoca* MIT 09-7231 strain in the gene that codes for the SdiA protein (Δ*sdiA*). The RNA was extracted by the acid phenol method and the gene expression of the genes *aroX* and *npsA* was determined with RT-qPCR. The statistical analysis of the gene expression was determined with One way ANOVA test. **RESULTS:** The expression of both *aroX* and *npsA* genes significantly increased in the Δ*sdiA* strain with respect to the wild-type strain. **CONCLUSIONS:** The transcriptional regulator SdiA acts as repressor of the expression of *aroX* and *npsA* genes, which are involved in the *K. oxytoca* tilivalline cytotoxin biosynthesis.

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METHYLATION PROFILE AND EXPRESSION LEVELS OF THE *ADRA2A* GENE IN POST-MORTEM BRAIN TISSUE FROM SUICIDAL SUBJECTS

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Abstract:

The α2A-adrenergic receptor (*ADRA2A*) has widely associated with mood disorders, particularly depressive conditions, including major depressive disease and suicide [1]. There is strong evidence for an increase of the α2A-adrenoreceptor in the frontal cortex of suicide victims. *Methylation* is a dynamic epigenetic mechanism that has been established by which it can modulate the expression of various genes at cellular times [2].

A case-control study was performed in pairs of 15 subjects per group. RNA extraction was obtained from the prefrontal cortex (PFC) and hypothalamus, and cDNA synthesis was performed. Subsequently, gene expression was evaluated through qPCR, using the B2M gene (β_2-microglobulin) as reference.

MSRE-qPCR assessed *ADRA2A* promoter methylation levels only in cortex samples. Statistical analysis was performed with SPSS v.22 software, considering a value of $p<0.05$. *ADRA2A* gene expression was significantly higher in the frontal cortex of suicidal subjects ($p=0.010$), while in the hypothalamus, there was no difference ($p=0.558$).

Methylation profiles in CPF were lower in cases ($p=0.004$). However, there is no clear correlation between methylation and gene expression ($p=0.105$). When the analysis omitted individuals with a psychiatric history, an inverse correlation between methylation and *ADRA2A* gene expression levels was observed ($p=0.013$).

The results demonstrated a differential expression of the *ADRA2A* gene in CPF of suicidal subjects from Durango. The results demonstrated a differential expression of the *ADRA2A* gene in CPF of suicidal subjects from Durango. This differential expression relates to its promoter region methylation, suggesting that these mechanisms controlled it.

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GENOMIC ENGINEERING IN *RHIZOBIUM ETLI*: IMPLEMENTATION AND EVALUATION OF A SYSTEM BASED ON DCAS9

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Abstract:

Nowadays, the field of genomic engineering is experiencing a new era with the discovery of novel systems called CRISPR-Cas. Besides the use of these systems to generate targeted mutations with high frequency, variants were generated that allow the transcriptional control of specific genes, using dCas9. Unfortunately, no systems have been devised yet for modification of Rhizobiales, including *Rhizobium etli*, a symbiotic nitrogen fixer of the common bean. In this work, we succeeded to implement efficient CRISPR-Cas9 systems for *Rhizobium etli*. The system is based on two compatible plasmids, one harboring a functional Cas9 and the other expressing specific guide RNAs. Initial tests of the system were aimed at generating mutations, instigating double-strand breaks in different targets in the *R. etli* genome, followed by mutagenic repair by NHEJ. Different guide RNAs were constructed against the Red florescent protein gene (inserted in the chromosome of *R. etli*), as well as towards the *argC* gene. Upon coexpression of both the specific guide RNA and Cas9, we observe a high frequency of either non-fluorescent cells or arginine auxotrophs, depending on the guide RNA used. Sequencing of these mutants revealed that these were small deletions in the target genes, caused by NHEJ. Moreover, the cells were analyzed for growth rate and for cell morphology, without detecting any drastic side effects. Furthermore, we generate a dCas9 variant (to allow transcriptional control of specific genes) by introducing a double mutation simultaneously on the catalytic domains RuvC and HNH through different mutational PCRs. Results will be presented about transcriptional control of target genes using dCas9 in *R. etli.*

EFFECT OF LNCRNA ANRIL ON DNA REPAIR IN TRIPLE NEGATIVE BREAST CANCER-DERIVED CELL LINES

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Abstract:

Breast cancer is a multifactorial, heterogeneous disease and, among cancer types, it has the highest incidence and mortality rate in women worldwide. At molecular level, it is classified according to the expression of hormonal receptors (Estrogen, Progesterone and Human epidermal growth factor receptor 2) in Luminal A, Luminal B, HER2, and Triple negative/Basal-Like (TNBC). TNBC represents about 10 to 20% of all diagnosed breast cancer subtypes and is characterized by negative hormonal receptor expression (ES-, PR-, HER2-). This subtype has the worst prognosis, aggressiveness, recurrence, and the lowest survival rate; a targeted therapy is complicated by the absence of receptors. Long non-coding RNAs (lncRNA) are important regulators that do not encode proteins; however, they have important biological functions in the cell. The lncRNA ANRIL (Antisense Noncoding RNA in the INK4 Locus) is a molecular biomarker, over expressed in TNBC that decreases CDKN2A and CDKN2B expression promoting tumor development. The ANRIL expression correlates with diverse molecular processes such as cell cycle regulation, apoptosis, and particularly, homologous recombination repair (HRR); this last mechanism has been proved only in osteosarcoma. DNA repair is relevant in TNBC considering its major genomic instability and association with DNA damage response molecular biomarkers. In this study, we intended to establish whether ANRIL participates directly on the DNA damage response mechanism in TNBC cell lines by evaluating its effect on HRR. We found differential ANRIL expression in TNBC-derived cell lines by RT-qPCR. We manipulated ANRIL expression using siRNAs and the complete cloned transcript. We found differential expression that suggested a role for ANRIL in HRR highlighting its importance in tumorigenesis.

EXPLORING THE FUNCTIONAL ROLE OF THE OMPR-TYPE REGULATORS IN *R. ETLI*

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Abstract:

Members of the OmpR/PhoB family of response regulators (RRs) are highly represented among studied genomes and have been described to be involved in metabolism, stress response, virulence, multidrug resistance, host-microbe interactions, and other regulatory pathways. In *R. etli* CE3, a bacterium that establishes a symbiotic relationship with the common bean plants, the OmpR/PhoB family contains 18 RRs. Only two RRs of this family have been described in *R. e*tli CE3, the regulator of *fix* genes FxkR and the regulator of *vir* genes VirG (1,2). The other 16 RRs are likely to be key regulators of *R. e*tli CE3 physiology, including its capacity to stablish a symbiotic relationship with common bean plants. One of our main interests was to characterize novel regulators whose role was harder to predict by comparative genomics. Hence, using bioinformatic tools, we identified 6 RRs that have orthologues with known functions within the Rhizobiaceae family. As mentioned above, we focused our attention on RRs subgroup with less predictable functions. To unveil phenotypic traits associated with these regulators, we deleted their respective genes and analyzed a variety of behaviors under different conditions.

Interestingly, we were not able to eliminate the genes RHE_CH03010 and RHE_CH03968, suggesting that they are critical for growth. Both genes have a high percentage sequence identity with genes described as essential in *C. cresentus.* We will discuss advances in the characterization of conditional mutants in these genes.

Recently, we reported that the *R. etli* OmpR regulator RetPC57 (3) is a critical player in developing the *R. etli* -common bean symbiosis. We are currently working on characterizing the molecular mechanism employed by this regulator to allow adequate communication between *R. etli* and bean plants. Results in this regard will be presented and discussed.

Acknowledgments. This work was partially supported by PAPIIT-DGAPA (grant IN204320).

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CENTROMERIC α-SATELLITE NON-CODING RNA UPREGULATION UPON PROTEASOME INHIBITION: A MOLECULAR CHARACTERIZATION

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Abstract:

In eukaryotes, correct chromosome segregation requires a strict control of centromeric transcription. Mounting evidence suggests that alterations in such process, or in the abundance of the RNAs transcribed thereof, can be both a cause or a consequence of several abnormal cellular contexts, such as multiple forms of stress, chromosomal instability, and cancer. Furthermore, recent work suggests that the overexpression of centromeric and pericentromeric RNAs can promote resistance to treatment in cancer.

We recently discovered an association between proteasome inhibition and the upregulation of α-satellite repetitive non-coding sequences, which populate human centromeres. The overexpression of such RNAs is linked to the recruitment of the transcription factor NFY to the centromere, and with consequential alterations in proper mitotic progression.

Here, we characterized the transcription of α-satellite RNAs in response to proteasome inhibitors. We treated human cells from different origins (including cancer cell lines) with the proteasome inhibitors MG132 and bortezomib (which is used in the clinic to treat different forms of hematological cancer) in combination with specific RNA polymerase I or RNA polymerase II inhibitors. Remarkably, we demonstrated that α-satellite RNAs can be transcribed by both RNA polymerases and that the contribution of each one of them to α-satellite RNA upregulation depends on the proteasome inhibitor used. Furthermore, we targeted NFY-A with shRNAs and observed an attenuation of the α-satellite RNA upregulation promoted by proteasome inhibitor, establishing a role for NFY-A in α-satellite RNA overexpression upon proteasome inhibition.

These data contribute to the comprehension of the mechanism of centromeric transcription, which is intimately involved with proper chromosome segregation. Moreover, our results could help to lay the foundations to combat the newly discovered treatment resistance promoted by centromeric transcript upregulation in cancer.

PRIMPOL FROM *A. THALIANA* IS INVOLVED IN DNA DAMAGE TOLERANCE

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Abstract:

DNA is subject to chemical insults that can alter or damage its coding potential. For many years several routes to repair DNA have been studied. In 2012 a new player was added to this list: PrimPol. This enzyme has both a primase and a DNA polymerase activities that synthesizes primers ahead of dsDNA break or a DNA lesion, avoiding replication fork collapse. Human PrimPol is widely study in the nucleus and in mitochondria, however this enzyme is barely studied in other organisms. Plants are sessile organism that cope with UV, ROS, metals and a great variety of agents that can damage their DNA. García-Medel et al (2021) was found that PrimPol from Arabidopsis (AtPrimPol) is localized in the nucleus, mitochondria, and chloroplast. However, its role in DNA damage tolerance was not addressed. In this project, with the aim of elucidating whether primpol plays an important role in the response to cell damage. A phenotypic analysis was performed on 3 mutant lines (SALK_052214, SALK_0901163C, CS915202) of *Arabidopsis thaliana* plants subjected to different damage agents, observing a significant difference between the mutant and wild type phenotypes.

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TOWARDS THE IDENTIFICATION OF THE SEQUENCES REQUIRED FOR THE EXPRESSION OF 5S RRNA GENES IN THE EARLY-BRANCHED EUKARYOTE LEISHMANIA MAJOR

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Abstract

RNA polymerase III (Pol III) synthetizes small non-coding RNAs that play key cellular roles, including 5S ribosomal RNA (rRNA), transfer RNAs (tRNAs) and small nuclear RNAs (snRNAs). 5S rRNA is a structural component of the large subunit of ribosomes. Its specific role has not been elucidated, but some studies suggest that it coordinates the functional centers of the ribosome during translation. In X. laevis, the promoter region of 5S rRNA genes is formed by an internal control region integrated by conserved sequences known as box A, intermediate element, and box C. In other organisms, transcription of 5S rRNA genes requires additional sequences. Little is known about Pol III transcription in the protozoan parasite Leishmania, which possesses atypical gene expression mechanisms. For instance, boxes A and B present in a divergently-oriented tRNA-Ala are needed for transcription of the L. major U2 snRNA. Notably, L. major possess only eleven 5S rRNA genes dispersed in the genome and ten of them are associated with at least one tRNA gene. Considering this association, we believe that boxes A and B from the neighbor tRNA genes are important for 5S rRNA transcription. To test this hypothesis, we are currently analyzing by RT-qPCR the transcription of several plasmid constructs after transient transfection of promastigotes. To identify transcripts produced by the transfected plasmids we marked the external 5S rRNA gene by insertion of a 15-nt tag sequence. Furthermore, we are generating specific mutations in our constructs to validate the regions that drive the in vivo transcription of 5S rRNA in L. major.

This work was supported by grant IN214221 (PAPIIT, UNAM)

BIOINFORMATIC SELECTION OF TRANSCRIPTION FACTOR CANDIDATES INVOLVED IN THE REGULATION OF CHROMOPLAST BIOGENESIS IN *CAPSICUM* SPP. FRUITS

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Abstract:

Biogenesis of the chromoplast is a tightly coordinated and regulated process that is synchronized with carotenoid synthesis and fruit ripening; however, the molecular mechanisms that governs this process at the transcriptional level is until now poorly understood. Fibrillin has been associated with chromoplast differentiation due to its structural importance and role in carotenoid storage structures and protein abundance in the chromoplasts during ripening.

The *fibrillin* gene showed an expression profile that was positively correlated with carotenoid biosynthesis and chromoplast biogenesis. We found that this relationship was highly robust and conserved in all 12 accessions available in the *Capsicum* RNA-Seq database named "*Salsa*". We also showed that using an algorithm analysis for transcription factor (TF) - target gene regulation in "*Salsa*" database, coupled with detection of transcription factor-binding sites within the promoter of the target gene (*fibrillin*) leads to the reduction of a large list of candidates to a manageable one that can then be experimentally assayed.

In this study we applied the algorithm to select transcription factor candidates, via co-expression analysis of the Standardized Expression Patterns (SEP), that could regulate the *fibrillin* gene, and that could possibly be involved in the chromoplast biogenesis process. Then, using Virus-Induced Gene Silencing (VIGS) assays with constructs of the selected TF candidates we found that two of these, *CaARF2A* and *CaNAC2,* altered chromoplast biogenesis and carotenoid accumulation in ripening fruits of agroinfected plants. RT-qPCR analysis of the silenced samples showed a significant reduction in the expression of either the TF candidates, of *fibrillin,* and of capsanthin-capsorubin synthase (*CCS*), zeaxanthin epoxidase (*ZEP*) and phytoene synthase (*PSY*), genes that encodes enzymes of the carotenoid biosynthesis suggesting their regulatory role in this pathway.

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STRUCTURAL CHARACTERIZATION OF TRANSCRIPTION FACTOR BINDING SITES OF LTTR REGULATORS

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Abstract:

The LysR-type transcriptional regulators (LTTR) family controls the expression of genes involved in several functional classes and is widely distributed in bacteria and archaea. These regulators bind to specific regions of DNA, called Transcription Factor Binding Sites (TFBSs), acting as dimers of dimers. Although some TFBSs have been identified with experimental methodologies, in many cases the degeneracy of TFBSs leads to unclear results and incorrect interpretations, and therefore the TFBSs remain as good approximations. In this sense, one of the limiting factors for the identification of TFBSs is related to the degeneration or poor conservation of their nucleotide sequences; furthermore, the structural parameters of the TFBSs are frequently not considered. To better define the consensus sequence recognized by LTTR regulators, orthologous intergenic sequences of genes controlled by LTTR regulators, were analyzed. The following molecular biological characteristics were considered for this analysis: symmetry of the TFBSs, length of the sequence, central position with respect to the transcription start site, conservation of the TFBS, interaction with metabolites, genetic organization of the regulator gene with respect to the regulated gene and conformation of the regulator.

Our analysis shows that in the presence of an inducer, the TFs bind to the major grooves of two contiguous inverted repeat regions, termed distal site and proximal site. Each TFBS is 15 to 17 nucleotides long, separated by a half-turn of DNA. The proximal site is located approximately -43 nt upstream the transcriptional start site (TSS), is poorly conserved and overlaps one or two nucleotides of the -35 box of the promoter. The distal site is conserved and is located approximately -63 nt upstream the TSS. According to mutation analysis reported in the literature, TFBSs for LTTR regulators tend to conserve two palindromic sub-motifs, showing that the minor groove nucleotides have less effect on the TF interaction. Finally, it can be mentioned that the molecular biological parameters of TFBSs are important for the characterization of TFBS sequences. The analysis also showed that LTTR family TFs tend to retain two sub-motifs in the TFBS sequences. Therefore, the Tn*11A* rule generally accepted can be extended (Schell, 1993).

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NATURAL PIGMENT PRODUCTION IN RESPONSE TO VARIOUS STRESS SIGNALS IN CELL LINES OF *STENOCEREUS QUERETAROENSIS* (F.A.C.WEBER EX MATHES) BUXB

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Abstract:

Stenocereus queretaroensis is a cactus that has long been used as a food source in central and northern Mexico. Its fruits, commonly called pitayas, biosynthesize high amounts of betalains. These molecules are water-soluble nitrogen compounds; compared to other pigments, such as anthocyanins or carotenoids, betalains stand out for their physicochemical stability in industrial processes. Due to the genetic and environmental factors involved in the biosynthesis and accumulation of secondary metabolites in plants, we used elicitors (SA) osmotressants (PEG 6000 and sucrose), salt (NaCl) and temperature (45 °C) to study the accumulation of betalains in cell cultures of *Stenocereus queretaroensis* fruits. By applying these different stress signals in our model, we obtained color variation for each treatment applied, therefore we objectively measured the color variations using CIELab space. We also confirmed by epifluorescence microscopy the effects of the different stress signals on the subcellular structure. The aim of this work is to understand the regulatory controls that induce the metabolic pathways leading to betalains accumulation. By doing so, we can contribute to the basic knowledge of these metabolic processes and increase the yield of betalains in fruits in the field.

STRESS-INDUCED GERM CELL APOPTOSIS AND STRESS GRANULES FORMATION UPON EXPOSURE *C. ELEGANS* TO CHEMOTHERAPY AGENTS

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Abstract:

The nematode *Caenorhabditis elegans* is an excellent model organism due to its short life cycle, transparency, and gene conservation among other several advantages. In our laboratory, we are studying how germ cells regulate their stress responses. We and other groups have observed that when *C. elegans* germ cells are subjected to stress, germ cell apoptosis is activated and stress granules (SGs) are formed in the gonad (Huelgas-Morales y Salinas 2016, Park et al., 2020). SGs are ribonucleoproteins that are assembled and disassembled dynamically in response to the environmental conditions in a liquid-liquid phase separation manner. The *C. elegans* hermaphrodite gonad is a syncytium that is formed by two symmetrical U-shaped arms that are joined by a common uterus (Corsi et al., 2015). The gonad size and translucence is a perfect "test tube" to observe germ cell death and SGs formation in live animals.

Our aim is to study how *C. elegans* germ cells respond to chemotherapeutic agents like cisplatin, etoposide y paclitaxel to elucidate the mechanisms that regulate these responses. In cancer cell lines, the use of chemotherapeutic agents induces the assembly of SGs which presumably makes them more resistant to the treatments (Park et al., 2020). Additionally SGs can inhibit stress-induced cell death by entrapping proteins involved in apoptosis (Asadi et al., 2021; Park et al., 2020). In *C. elegans*, exposure to cisplatin induces the expression of apoptotic genes like *egl-1* and *ced-13* (García Rodríguez, et al, 2018). We subjected worms to different doses of cisplatin than range from 100 and 150 µg/ml. In preliminary results, we did not observe any effect of cisplatin on worm growth or larval development, but we did find that exposed animals showed low fertility, embryonic lethality, slow down of germ cell proliferation and an increase in apoptosis. Our results show that germ cells are severely affected by cisplatin. However unexpectedly, we did not observe the formation of SGs in the gonad. We will expose animals to higher concentrations of chemotherapy agents to see if we can induce SGs formation to test how these condensates protect germ cells from adverse conditions.

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IDENTIFICATION OF POLYMORPHISMS OF INFLAMMATORY GENES ASSOCIATED WITH PRETERM BIRTH

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Abstract:

According to the WHO, preterm birth (PTB) refers to the birth of a live newborn, which occurs before completing 37 weeks of gestation. It is the most important clinical problem in obstetrics and neonatal medicine. Despite factors such as heredity and racial disparity contributing to the risk of presenting PTB, there are no reports of genetic polymorphisms in Mexico associated with this pathology. **Objective**: To identify polymorphisms (SNPs) in genes that participate in the inflammatory response associated with the development of PTB. **Materials and Methods**: DNA was isolated from saliva samples of 57 women with PTB outcome and 153 at term (TB), according to the suggested protocol "DNA Oragene OG-500", later were verified the quality and integrity of this. A panel with 42 genes associated with the inflammatory response was designed. The "Haloplex" kit was used to capture the designed genes hybridization probes. The enriched DNA probes were sequenced with the Illumina "Miseq" platform, and files with the ". FASTQ" extension were obtained, which were used in the "SureCall" program to identify the genetic variants in cases and controls from the generation of ".VCF" files. Statistical analysis: We evaluated the deviations in the Hardy Weinberg Equilibrium (HWE) for each SNP in the control group, using Pearson's $\chi 2$ test with the "SNPStats" program. In the first analysis, was used a Venn diagram to identify SNPs unique to women with an outcome of PTB and shared SNPs in both study groups. In a second phase, the genotypic and allelic frequency of the minor allele of each SNP in cases and controls were compared to identify its association with PTB. A dominant genetic model was considered for the genotype analysis. Statistical analysis was performed with the "Rstudio" Software; Significant differences were evaluated with the $\chi 2$ statistic ($p<0.05$) and the strength of association with the OR test (95% CI). **Results**: In the first phase of analysis, 115 SNPs were identified in 25 genes only in women with an outcome of PTB. When doing a case-control analysis, 38 SNPs were identified in 12 genes, with a significant difference ($p<0.05$) and association ($OR\geq 2$) for PTB. **Conclusion**: SNPs were identified in genes related to the NOD-type signaling pathway that involves the activation of the inflammasome, as well as that mediated by the activation of NF-κB, which are critical for inflammation, inducing the secretion of cytokines that activate or they inhibit metalloproteinases that intervene in the remodeling of the extracellular matrix of gestational tissues. In this way, identifying the SNPs that alter the inflammation genes can suggest changes in the signaling pathways, causing the outcome to be a preterm or term delivery.

GENETIC DIVERSITY IN CARLUDOVICA PALMATA RUIZ & PAVON IN MEXICO

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Abstract:

Carludovica palmata, an introduced specie cultivated in the northern region of the Campeche, is an importante source of silky and durable fibers for the braiding of the Panama hat and other crafts. The main mechanism of reproduction used by producers is the asexualy propagation by rhizome since seeds apparently are recalcitrant reducing the genetic diversity of the specie and increasing its susceptibly to pathogens attack. To this date there are no estudies about genetic diversity. in *Carludovica palmata.* The aim of this work is to develop estrategies to evaluate the genetic diversity in plants from seeds and plants from rizhome using molecular markers based on conserved regions in eukaryotes (SCoT) and retrotransposons (IRAP). Our results show three molecular markers (IRAP) with polymorphism: NIKITA, SUKKULA and 3'LTR in plants from seeds however SUKKULA is the most polimorfic and therefore is a robust and reproducible candidate for diversity genetic detection in *C. palmata*. Additionally we tested 26 SCoT markers and among them 24 are reproducible and two showed polymorphism (SCoT-5 and SCoT-25). Further statistical analysis are going to validadate our datas and confirm the intraspecific genetic diversity in *C. palmata.*

ANALYSIS OF THE ALTERNATIVE SIGMA FACTORS EFFECT ON THE GENETIC EXPRESSION OF THE *KLEBSIELLA PNEUMONIAE* VIRULENCE FACTORS

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Abstract:

Introduction: *Klebsiella pneumoniae* is an opportunistic pathogen that causes health-associated infections. Some virulence factors present in this pathogen are the capsular polysaccharide, fimbriae, outer membrane proteins, lipopolysaccharide, and the siderophores. The sigma (σ) factors recognize the promoter and participate in the initial stages of transcription; it is known that bacteria have a primary σ factor and a variable number of alternative σ factors, these have been related to regulation of bacterial virulence. The role of alternative σ factors in regulating the expression of *K. pneumoniae* virulence factors is currently unknown.

Objective: To investigate the effect of alternative σ factors on the regulation of virulence factors in *K. pneumoniae*.

Methods: Null mutants were generated from the *K. pneumoniae* 123/01 strain in the *rpoN*, *rpoS*, and *rseA* genes, which code for the σ^N and σ^S factors and anti-σ^E factor. The genetic expression from these strains was determined using RT-qPCR of the virulence factors, as well as the effect on the other σ factors. The effect of the generated mutations on biofilm formation was evaluated by the crystal violet retention method.

Results: The σ^S and σ^N factors negatively regulated the expression of the virulence factors of *K. pneumoniae*, as well as the other σ factors, while the overexpression of σ^E (a consequence of the deletion of the *rseA* gene) positively regulated them. Biofilm formation is not affected in the absence of σ^S nor by the overexpression of σ^E, while the absence of σ^N caused an increase in its production.

Conclusions: The factors σ^N, σ^S, and σ^E regulate the expression of the virulence factors of *K. pneumoniae.*

Deletion of the σ^N factor increased *K. pneumoniae* biofilm formation, but the absence of σ^S factor or the σ^E overexpression did not alter this phenotype.

1-DODECENE IS *A* SIGNALING MOLECULE THAT INDUCES THE OXIDATIVE STRESS RESPONSE IN *CANDIDA GLABRATA*

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Abstract:

Cells respond to environmental changes through reprograming gene expression. During nutritional, osmotic, heat shock or oxidative stress, fungi activate the **E**nvironmental **S**tress **R**esponse (ESR). ESR has two essential elements, a) protein kinase pathways that detect and transmit the information to b) transcriptional factors that reprogram gene transcription. *Candida glabrata* is an opportunistic fungal pathogen that has developed strategies to survive oxidative stress. **R**eactive **O**xygen **S**pecies are neutralized by enzymatic (catalase) and non-enzymatic (glutathione) mechanisms. *C. glabrata* is more resistant to oxidative stress in Stationary Phase. It has been proposed that molecules present in the secretome induce the **O**xidative **S**tress **R**esponse (OSR) within the population. In this work, we determined that at least one of these molecules, C12, triggers a signaling cascade to induce OSR through Yap1 and Skn7 transcriptional factors that that activate *CTA1* (catalase). C12 appears to act through the PK*A* and TOR pathways to regulate *CTA1* expression.

DIFFERENTIAL GENE EXPRESSION ANALYSIS SHOWS ANTICANCER ACTIVITY OF CHALCONE IN TRIPLE-NEGATIVE BREAST CANCER CELLS

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Abstract

Introduction. Triple negative breast cancer (TNBC) is considered an aggressive molecular phenotype, due to the lack of ER and PR expression, as well as the absence of HER-2 amplification. Unlike the other molecular subtypes, TNBC has no effective targeted therapies, so chemotherapy remains the only therapeutic approach in patients suffering from this condition. Chemically, chalcones [(1,3-diaryl)-2-propen-1-one] are compounds consisting of two aryl rings linked together by an αβ-unsaturated ketone. It has been documented that these compounds have anticancer properties, since they modulate gene expression in several mechanisms associated with cell growth, proliferation, and survival. **Objective.** To identify differentially expressed genes that participate in biological processes that could be potentially involved in the anticancer effect of chalcone, using the MDA-MB-231 cell line as a model of this condition. **Methods.** Using a Next-Generation Sequencing (NGS) approach, we compared the transcriptomes of MDA-MB-231 cells treated with the chalcone vs. untreated to identify the genes involved with the anti-cancer effect of chalcone. **Results.** We identified the differential expression of 1,245 mRNAs in various cellular functions associated with cell cycle regulation, transcription/translation, and mitochondrial dysfunction. **Conclusion.** This study indicates that chalcone-treated MDA-MB-231 cells were significantly more likely to show changes in the expression of G1/S cell cycle regulatory genes and apoptosis, which have collectively been linked to a more aggressive breast cancer phenotype, resistance to multiple chemotherapeutic agents as well as increased metastatic potential.

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Shaheen, S., Fawaz, F., Shah, S., & Büsselberg, D. (2018). Differential expression and pathway analysis in drug-resistant triple-negative breast cancer cell lines using RNASeq analysis. *International journal of molecular sciences*, *19*(6), 1810.

GENE REGULATION MEDIATED BY SMALL RNAS IN THE CUTICLE MUTANT ECA2 PARTICIPATES IN DEFENSE RESPONSE TO FUNGAL PATHOGEN BOTRYTIS CINEREA

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Abstract:

Plants are sessile organisms that are subject to several types of environmental stresses, and they have developed different responses to cope adverse conditions. In biotic stress, plants must defend themselves continuously against attack from bacteria, virus, fungi, etc. The first physic barrier between plant and microorganism interaction is the cuticle, which is mainly composed by cutin and waxes. Previous studies showed that *Arabidopsis thaliana* mutants altered in cutin content are resistant to *Botrytis cinerea.* These mutants showed increased permeability and reactive oxygen species (ROS) accumulation in comparison with wildtype plant. Furthermore, a transcriptomic analysis showed that a set of upregulated genes involved in cell wall integrity and accumulation of ROS were shared by cutin mutants (*bdg*, *lacs2-3* and *eca2*), suggesting that these mutants with resistant phenotype can activate other defense pathway. In this work, we focused our attention on *eca2* mutant cuticle-related immunity and if small RNAs (sRNAs) and their target regulation could be required for *B. cinerea* resistance. Briefly, sRNAs are non-coding RNA, approximately 20-24 nt in length. These sRNAs induce gene silencing by incorporating into Argonaute (AGO) proteins and directing the RNA-induced silencing complex (RISC) to target genes by sequence complementarity. To address the participation of sRNAs-targets in the resistance to fungus, we sequenced small RNA libraries from mock- and *B. cinerea*-inoculated leaves in *eca2* and wildtype plants. Our results showed differential expression of sRNAs (such as miRNAs, siRNAs, tRNA-derived sRNA, among others) in these conditions. Performing a target prediction coupled with a transcriptomic analysis, we identified contrasted expression level of small RNAs and their corresponding targets. Finally, we revealed 16 sRNA-target candidates whose regulation occurs exclusively in *eca2* or wildtype. This study aims to characterize the sRNA expression and target regulation that contribute to insight into *eca2* mutant cuticle-related immunity phenotype.

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RHIZOBIUM GENOMIC EDITION USING THE CRISPR / CAS9 SYSTEM

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Abstract:

Rhizobium is a genus of Gram-negative soil bacteria with the ability to fix atmospheric nitrogen in symbiosis with leguminous plants. It is very important to implement novel genetic methodologies that allow us to systematically modify this interesting group of bacteria.

CRISPR/ Cas9 system has become a successful and promising technology for gene-editing. The CRISPR/ Cas9 system from *Streptococcus pyogenes* generates mutations by introducing double stranded breaks in specific genomic positions, directed by the location of designed guide RNAs (1). The resulting double-strand breaks are commonly repaired by homologous recombination, using either identical or altered templates for recombination. Alternatively, some bacteria (including *Rhizobium*) possess a mutation-prone Non Homologous End Joining (NHEJ) system, allowing the introduction of mutations at the site of the break.

Our editing CRISPR/Cas9 system was constructed using a *Xanthomonas*-optimized Cas9 and a binary system of compatible plasmids. One plasmid harbors the guide gRNA (pRhigRNA), and the other carries Cas9 under the control of an inducible promoter (pRhiCas9).

As part of the standardization of our CRISPR-Cas9 system for *Rhizobium* editing, we choose the reporter gene for resistance to Spectinomycin (Sp^R, *addA*) and the wild-type *pyc* chromosomal gene (Pyruvate carboxylase). Using our CRISPR/Cas9 edition methodology in *Rhizobium etli* CFN42, recovered cells showed a mutation efficiency close to 70 percent.

Our findings on genomic editing of *Rhizobium etli* (after at least 3 experiments, and 49 sequenced CRISPR/Cas9 targets), showed that the principal modification after gRNA-Cas9 cutting, were deletions at the 5´end of the cutting site of Cas9, ranging in size from 2 to 285 nt (~76%). The other less frequent modifications were insertion of 1-2 nt in the Cas9 cutting site (~16%), and deletions covering both 5´ and 3´ end of the cutting site of Cas9 (~8%).

These results suggest that our CRISPR/Cas9 edition system, in conjunction with NHEJ, can be systematically used for single step gene-edition of the *Rhizobium* genome, without selective markers.

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REGULATION OF *PGR, PRL, AND IGFBP1* GENE EXPRESSION IN RESPONSE TO IN VITRO DECIDUALIZATION IN ENDOMETRIAL STROMAL CELLS FROM A PATIENT WITH ENDOMETRIOSIS

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Abstract:

Background: Decidualization is a process that plays a central role in establishing and maintaining pregnancy. This process leads to morphological, biochemical and molecular changes in endometrial stromal cells (ESCs) that differentiate into decidual stromal cells (DSC). Decidualization is induced by estradiol (E2), intracellular cyclic adenosine monophosphate (cAMP), and progesterone (P4). P4 acts mainly by binding to its intracellular receptor (PR), encoded by the *PGR* gene, to induce the expression of 4960 genes after in vitro decidualization stimuli. Some of these genes are involved in processes like vascular development, intracellular signaling cascades, and extracellular structure organization.

Endometriosis is a complex gynecologic disease characterized by the growth of eutopic endometrial tissue (glands and ESCs) in areas outside the uterine cavity, forming ectopic lesions. Another feature of this disease is progesterone resistance, which is associated with alterations in the regulation of *PGR-B* isoform expression, leading to inefficient decidualization. The aim of this work was to evaluate the expression of *PGR-AB* (*PGR* isoforms A and B) and *PGR-B* genes, as well as *PRL* and *IGFBP1* genes (biomarkers of decidualization) in response to E2, P4, and cAMP stimulation in primary cultures of ESCs isolated from the eutopic and ectopic tissue of a patient with endometriosis and ESCs from healthy women.

Methodology: Primary cultures of eutopic and ectopic ESCs from a patient with endometriosis and ESCs from control women were stimulated with E2, medroxyprogesterone (MPA), and cAMP for 24 hours to evaluate the expression of *PGR* isoforms and genes encoding for PRL and IGFBP-1 by RT-qPCR.

Results: E2 + MPA + cAMP stimulation increased the expression of *PGR-AB, PGR-B, PRL*, and *IGFBP1* genes in ESCs from healthy women compared to the vehicle ($P<0.05$), while in ESCs isolated from eutopic and ectopic tissue the increment was not statistically significant ($P>0.05$). Moreover, the induction of *IGFBP1* expression

was higher in ESCs from healthy women than those isolated from the ectopic tissue of the patient with endometriosis (P<0.05).

Conclusion: In the present study, we have demonstrated that E2 + MPA + cAMP (a stimulus to induce in vitro decidualization) differentially regulates the expression of *PGR* isoforms and the decidualization biomarkers in eutopic and ectopic ESCs isolated from a patient with endometriosis and women without the disease.

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FUNCTIONAL CHARACTERIZATION OF THE NPR1-NPR3 INTERACTION IN THE PSEUDOMONAS SYRINGAE-ARABIDOPSIS THALIANA PATHOSYSTEM

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Abstract:

The phytohormone salicylic acid (SA) plays a crucial role in activating and regulating multiple responses to biotic and abiotic stresses. Mainly, SA induces systemic acquired resistance (SAR), a mechanism used by plants to resist pathogen attack. In Arabidopsis thaliana, SA is perceived by the NPR1, NPR3, and NPR4 receptors, which are involved in the plant immune response1,2. The NPR1 is the master regulator in SA perception and works as a transcriptional co-activator of pathogenesis-related genes, whereas NPR3 and NPR4 were suggested to function as adaptor proteins of the Cullin ubiquitin E3 ligase to promote NPR1 turnover in an SA-dependent manner2.

The regulatory mechanism between these proteins is complex. Therefore, understanding how their interaction takes place and how different stimuli can modify it allows us to understand better their role in plant immunity. Although the interaction between these proteins has already been analyzed, the interaction domains have not been characterized. This research work is focused on the functional characterization in planta of the domains involved in the NPR1-NPR3 interaction using the Bimolecular Fluorescence Complementation (BiFC) approach. To this aim, the full-length and the sequences encoding for the three major domains of NPR3: the BTB/POZ and ankyrin repeats domains, and the SA binding site of NPR3 were in-frame fused with the GFP C-terminal whereas NPR1 was in-frame fused with the GFP N-terminal. In addition, deletions of only one of the NPR3 domains were done, which allowed us to make a more suitable comparison with the native protein. To investigate the direct interaction between these proteins we used an Agrobacterium-infiltration method for transient expression of destination constructs in leaves of Nicotiana benthamiana. The same constructs generated of NPR3 were fused to full-length GFP, these constructs will be used for the stable transformation of Arabidopsis thaliana plants to evaluate the susceptibility to infection by Pseudomonas syringae.

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GENE CO-EXPRESSION NETWORK DRIVEN APPROACH TO DECODE THE ROLE OF MIR-122 IN TRIPLE-NEGATIVE BREAST CANCER

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Abstract:

MiR-122 has been considered both as tumor suppressor miRNA and oncomiR in breast tumor phenotypes. However, the role of miR-122 in triple-negative breast cancer (TNBC) is still unknown. In this study, the clinical value of miR-122 was used to describe the transcriptomic landscape of TNBC tumors. Low expression levels of miR-122 were associated with poor overall survival (OS) of TNBC patients than those showed higher expression levels of miR-122. We identified gene expression profiles in TNBC tumors expressed lower or higher miR-122. Gene co-expression networks analysis revealed gene modules and hub genes specific in TNBC tumors with low or high miR-122 levels. Gene ontology and KEGG pathways analysis revealed that gene modules in TNBC with gain of miR-122 were related to cell cycle and DNA repair, while in TNBC with loss of miR-122 were enriched in cell cycle, proliferation, apoptosis and activation of cell migration and invasion. The expression of hub genes distinguished TNBC tumors with gain or loss of miR-122 from normal breast tissues. Furthermore, high levels of hub genes were associated with better OS in TNBC patients. Interestingly, the gene co-expression network related to loss of miR-122 were enriched with target genes of miR-122, but this didn't observe in those with gain of miR-122. Target genes of miR-122 are oncogenes mainly associated with cell differentiation-related processes. Finally, 75 genes were identified exclusively associated to loss of miR-122, which are also implicated in cell differentiation. In conclusion, miR-122 could acts as tumor suppressor by control oncogenes in TNBC.

MOLECULAR BASIS OF BINARY COMPLEXES OF LYSR-TYPE TRANSCRIPTIONAL REGULATORS

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Abstract:

The interaction of binary complexes between transcriptional regulators and their binding sites on DNA (BS) has been an important aspect for the understanding of gene regulation in prokaryotes. However, the crystallographic determination of most of the LysR-type Transcriptional Regulators (LTTRs) with its target DNA has not been achieved. The study of these will allow us to know the molecular basis of gene regulation of different regulators of the LTTR family. For this reason, in this study we describe the interaction between the amino acids of orthologous LTTR regulators with the nucleotides of their BS.

Structural analysis of LTTR/DNA proteins, derived from the PDB database, was performed with PyMOL. Results show the coupling between homo-oligomers of BenM/RBS (2BenM/*catB*, 2BenM/*benA*), CbnR/RBS (2CbnR/*cbnA*) and the homotetramer of CbnR/RBS-ABS (4CbnR/*cbnA*). During the analysis, torsion angles, structural geometry, as well as interactions with the phosphate group and hydrogen bonds of the nitrogenous bases were considered. Data indicate that the α3 chains of the amino terminus are inserted into the major grooves of the BS, whereas the interaction with the minor groove of the BS is null. The winged Helix-Turn-Helix motif (HTH) interaction of the α3 chains of each monomer occurs mainly with amino acid residues A28(S28), Q28, R34, Q35 and Q37. These interactions show specific selection with sub-motives in the BS, which correlates with the proposal of an extended motif to the Tn*11A* rule (Oliver, 2016). The extended sub-motifs will allow the identification of degenerate sequences of the proximal sites (ABS2); while the conservation of amino acids in the HTH motif, from LTTR regulators, will favor the prediction of extended motifs in the sequences of Recognition Binding Site (RBS) and Activation Binding Site 1-2 (ABS1-2). The activation mechanism of LTTR regulators requires two binding sites for activation (RBS and ABS2), with the proximal site being highly degenerate (ABS2). In general, this knowledge could provide the fundamental basis to better understand the gene expression mediated by LTTR regulators, which can be used to design anti-infective strategies to combat pathogenic bacteria.

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MOLECULAR CHARACTERIZATION AND DIFFERENTIAL EXPRESSION TO HYPOXIA AND REOXYGENATION OF HEXOKINASE ISOFORMS OF THE SHRIMP *LITOPENAEUS VANNAMEI*

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Abstract:

The white shrimp *Litopenaeus vannamei* is the most cultivated shrimp worldwide, in part as a result of its ability to survive low dissolved oxygen (DO) or hypoxia by adjusting energy metabolism and activating anaerobic glycolysis (Racotta et al., 2002). Hexokinase (HK) is the first enzyme of glycolysis and one key regulation point of the pathway. HK is present in most organisms and in mammals, there are tissue-specific isoforms differentially regulated (Cárdenas et al., 1998). However, little is known about crustacean HKs isoforms. The aim of this study was to characterize the HK isoforms from *L. vannamei* and to analyze their expression in response to hypoxia and reoxygenation. Previously, our group reported one HK sequence from *L. vannamei*; this sequence corresponds to isoform HK1; a second isoform HK2 was annotated in the shrimp genome and transcriptome (Ghaffari et al., 2014; Soñanez-Organis et al., 2011; Zhang et al., 2019). Here we amplified and cloned two HK1 variants from the white shrimp named HK1-long (1,452 bp) and HK1-short (1,302 bp), and one HK2 isoform (1,344 bp). The deduced amino acid sequences of the HK isoforms are highly conserved in sequence and structure with HKs from other species, have similar molecular masses to other invertebrate homologs and are closer phylogenetically to other crustacean HKs. HK1 expression is higher in hepatopancreas, while HK2 is higher in gills, indicating tissue-specificity. Furthermore, severe hypoxia (1 mg/L of DO) decreased total expression of HK1 in hepatopancreas and gills, but reoxygenation (1 h after 12 h of hypoxia) increased the expression to the levels detected in normoxia, while expression of HK2 was affected by hypoxia differentially in both tissues. In hepatopancreas HK2 expression was induced by 6 and 12 h of hypoxia but diminished to normoxia levels after 1 h of reoxygenation. In gills, HK2 expression significantly decreased after 6 and 12 h of hypoxia but was also restored after 1 h of reoxygenation. These results indicate that shrimp HK isoforms expression respond to hypoxia and reoxygenation, in a tissue-specific manner.

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EVALUATION OF AS_2O_3, $NAASO_2$ AND NA_2HASO_4 ON P53 REGULATION IN SIHA, CALO, C33-A AND HACAT CELL LINES

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Abstract:

Chronic exposure to arsenic can bring toxic and carcinogenic effects, however, in recent years As2O3 has been proposed as a therapeutic agent for cancer, as well as other derivatives of this compound. In this study, we investigated the cellular and molecular effects of As2O3, NaAsO2, and NaHAsO4 on HPV positive and negative, tumorigenic, and immortal cells. The cells were treated with each of the compounds from 6.25nM to 10,000nM in concentration and the cell energy was evaluated by means of crystal violet. The effect of As2O3 and NaAsO2 on the cells was produced from 6.25 nM, being greater at 10,000 nM, while for Na2HAsO4 there was no effect on the cell lines. The p53 protein analysis was performed by Western Blot on all Siha, C33-A, CaLo and HaCaT cell lines exposed to As2O3 where an overexpression was obtained in the SiHa and C-33A lines, while with NaAsO2 p53 overexpression was obtained in SiHa, C-33A and CaLo cell lines. The enzymatic activity of Metalloproteinases 2 and 9 was also evaluated by zimography. Therefore, the present study provides information on the effect of As2O3, NaAsO2 and NaHAsO4 compounds on cervical cancer cell lines.

COMPARATIVE STUDY OF THE REGULATION OF AUTOPHAGY AND SENESCENCE BETWEEN MICE AND NAKED-MOLE RATS

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Abstract:

Aging is defined as a progressive decline of physiological functions, leading to the development of age-related diseases and increased probability to die. An accumulation of senescent cells and a decrease in autophagic activity are hallmarks of aging. Cellular senescence is a stable cell cycle arrest, characterized by the expression of antiproliferative proteins $p21^{CIP1}$ and $p16^{INK4A}$, increased activity of senescence associated β-galactosidase activity, decreased expression of lamin B, stabilization of lamin A/C, among other features. Senescent cells are metabolically active and secret a plethora of growth factors, chemokines, cytokines, collectively referred to as senescence associated secretory phenotype or SASP. Cellular senescence is induced by several stimuli, including those that generate DNA damage, and our group showed that dysfunctional autophagy causes neuronal senescence observed in the brain of aged mice and rats. Autophagy is a catabolic process that engulfs and degrades intracellular content such as damaged organelles, aggregated or long-lived proteins or intracellular pathogens, for example. Autophagy is strictly regulated by TFEB and AMPK proteins, among others. TFEB is a transcriptional factor that promotes autophagy and lysosomal biogenesis genes transcription. AMPK is a kinase that phosphorylates and activates ULK and BECN1, both acting at autophagy initiation; interestingly, AMPK is an inhibitor of mTOR, a negative regulator of TFEB and autophagy. Remarkably, the activation of TFEB and AMPK counteract the induction of cellular senescence. Naked mole-rats are eusocial mammals, naturally found in Africa, with the intriguing characteristic of having a longevity of over 30 years and negligible aging. Naked mole-rats live more than 90% of their lives maintaining physiological functions, reproductive success, with no tumour development or other age-related diseases. Naked mole-rats maintain functional autophagy and do not accumulate senescent cells over time, contrary to mice and other species that develop aging. We hypothesize that naked mole-rats maintain a functional autophagy along their life due to a higher activity of TFEB and AMPK. We will present a comparative analysis of the TFEB and AMPK sequence and activity between naked mole-rat and mouse.

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MICRORNAS CONTAINED IN HEPATOMA CELLS-DERIVED EXTRACELLULAR VESICLES MODULATE MIRNA BIOGENESIS ELEMENTS: A NEW REGULATORY MECHANISM FOR CELL PROLIFERATION AND MIGRATION IN HCC

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Abstract:

Liver cancer is the sixth most common type of cancer and the third leading cause of cancer-related death worldwide; it is considered a poor prognosis pathology because its incidence rate is similar to its mortality due to the complex diagnosis and treatment. Hepatocellular carcinoma (HCC) represents de 85% of liver cancer. Therefore, one of the factors involved in HCC development are extracellular vesicles (EVs) —defined as spherical proteolipids of double-layer containing different molecular components—. Subsequently, EVs have an essential role in the progression of HCC by transferring their molecular cargo (proteins and nucleic acids) to other cell types. However, despite the evidence involving EVs in the development of this neoplasia, there is not enough data regarding microRNAs contained in liver tumor cells-derived EVs. Furthermore, the present work evaluated the biological effects of the EVs secreted by HCC cells with diverse differentiation degrees on the proliferation and migration of tumor and non-tumor hepatic cell lines. The miRNAs contained in the VEs contribute predominantly to migration in the well-differentiated and poorly differentiated stages. At the same time, the proteins participate in the regulation of migration in the moderately differentiated and poorly differentiated stages. Also, *in silico* analyzes predict that miRNAs regulate elements of acceptor cell miRNA biogenesis. So, we found that the molecular content of VEs induces the downregulation of miRNAs biogenesis since essential elements of this pathway, such as DROSHA and DICER that decrease their levels with treatment with VEs. Likewise, an association was found between reduced levels of DROSHA, DICER, and enhanced AGO2 expression levels with increased migratory phenotype and cell proliferation. Finally, we propose a mechanism in which the miRNAs of the VEs decrease the levels of DROSHA and DICER, thus triggering the downregulation of the total content of miRNAs in the acceptor cell, and this could lead to an increase in the expression of genes related to cellular processes such as proliferation and migration.

THE APPLICATION OF ASCORBIC ACID (ASA) IMPROVES THE QUALITY OF *SOLANUM LYCOPERSICUM* IN THE VEGETATIVE

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Abstract:

Root biostimulation is a strategy used to improve agricultural sustainability and productivity. As a tool in the optimal development of roots, it participates in the absorption and transport of nutrients, reducing stress factors. The study focused on evaluating the effect of ascorbic acid (AsA) on *Solanum lycopersicum* vegetative development. Three concentrations of AsA applied to the root were evaluated: 100, 200, and 500 (ppm). Root length, plant height, stem diameter, SPAD index, total and individual dry matter content of each organ (root, stem/branches, and leaves), and the total relative percentage of mineral macronutrients absorbed and assimilated were measured. Root length increased by 10.71% and plant height by 5.32% with 100 and 200 ppm AsA. There were no significant differences for stem diameter and SPAD index. The highest values of total and root dry matter were obtained with 200 ppm AsA. Dry matter of leaves and stems/branches was not favored by the application of the treatments. The mineral profile did not show an increase in the total percentage of each element absorbed by treatment. Plant organ mineral content investigations showed that the N, S and Ca accumulated in leaves (39.05%, 66.55%, and 40.32% respectively), P and Mg in roots (36.04% and 54.52% respectively), and K in stems/branches (49.62%).

Keywords: Ascorbic acid, biostimulation, roots, macronutrients, growth, productivity

EPIGENETIC REGULATION, ALTERNATIVE SPLICING, AND FUNCTION OF *AGL19* TRANSCRIPTION FACTOR

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Abstract:

The MADS-box transcription factors participate in developmental processes in all eukaryotes. In plants, they play important roles in integrating internal and environmental signals that affect meristems' post-germination decisions. Therefore, they have different levels of regulation.

The MADS-box *AGAMOUS-LIKE 19* (*AGL19)* participates in flowering transition. *agl19-1* and *agl19-2* mutant alleles showed a late-flowering phenotype, particularly when plants were vernalized (8 weeks at 4 °C), followed by a growing period in short-day photoperiod. Each allele was mutagenized by insertion of a T-DNA into the gene's first long intron, respectively[1].

In this work, we characterized a third mutant allele, *agl19-3,* in which a T-DNA insertion is in the fourth intron. Interestingly, *AGL19* canonical mRNA is detected in the *agl19-1* and *agl19-2* alleles, but not in the third one, at two different plant ages. Furthermore, we unravel alternative splicing (AS) transcripts that accumulate preferentially in *agl19-1* and *-2*. We demonstrated that T-DNA insertions affect chromatin structure, modifying the enrichment of the H3K27me3 repressive mark in this gene's first exon and intron region. Nevertheless, AS transcripts are not T-DNA artifacts because they also accumulate in wild-type plants and in the *curly leaf (clf)* mutant, a gene that codifies for the catalytic subunit of the Polycomb Group (PcG) complex.

Notably, after vernalization, the three alleles showed a similar late-flowering phenotype, probably because of differential expression of the alternative mRNAs that produce truncated proteins or non-coding mRNAs.

Finally, we found two new genes regulated by AGL19 after microarray analysis and RT-qPCR comparing *agl19-3* and wild-type plants, with or without vernalization.

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MOLECULAR STUDY OF THE "LA" PROTEIN IN THE HUMAN PATHOGEN *LEISHMANIA MAJOR*

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Abstract:

Around 1 million new cases of leishmaniasis are reported worldwide each year. This disease is caused by *Leishmania*, a protozoan parasite transmitted to humans by sandflies in tropical and subtropical regions. As a model for molecular biology research, *Leishmania* and other trypanosomatid parasites are interesting because they have atypical gene expression mechanisms, such as polycistronic transcription and trans-splicing. Little is known about RNA polymerase III (Pol III) transcription in these organisms. Unlike other eukaryotes, Pol III in *Leishmania* transcribes all snRNAs, in addition to tRNAs and 5S rRNA. In yeast and vertebrates, the La protein binds to UUU-OH 3' trailers of all Pol III transcripts, protecting them from degradation and promoting proper folding and cytoplasm export. It has been proposed that La also participates in Pol III transcription regulation and ribosome biogenesis. Despite the relevance of La protein, it has not been studied in *Leishmania*. Thus, in the present work we started the molecular characterization of La in *L. major* (LmLa). *In silico* analyses showed the presence of the two distinctive La sequences in LmLa: the La motif and the RNA recognition motif (RRM). Moreover, LmLa has a short basic motif (SBM) in the C-terminal region that is also present in human La (HsLa). Homology modeling revealed that the predicted 3D structure of LmLa is very similar to that of HsLa. A cell line of *L. major* expressing the recombinant protein LmLa attached to the PTP tag was generated and analyzed. Indirect immunofluorescence experiments with this cell line showed that LmLa is mainly a nucleoplasmic protein in promastigotes. Tandem affinity purification experiments followed by mass spectrometry and bioinformatic analyses allowed us to identify several proteins that interact with LmLa. These results will be discussed.

This work was supported by grant IN214221 (PAPIIT, UNAM).

UNRAVELING THE ROLE OF THE RETCH2128 AND RETCH3587 REGULATORS IN THE *R. ETLI – P. VULGARIS* SYMBIOSIS

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Abstract:

The two-component signal transduction systems (TCSs) are the most important signal transduction systems in bacteria to respond, expand and diversify cues to generate adaptability to several environmental conditions implicating changes in gene expression. These systems comprise two proteins, a membrane sensor histidine kinase (HK) and a cognate DNA binding response regulator (RR). Bacterial genomes typically encode multiple (TCSs) according to their genomes and ecological niches. Members of the OmpR/PhoB family of RRs are highly represented. They are involved in metabolism, stress response, virulence, multidrug resistance, and host-microbe interactions, among other processes.

Rhizobia are Gram-negative soil bacteria that fix nitrogen associated with Fabaceae plants (legumes). In *Sinorhizobium meliloti* the participation of the OmpR-type regulators in the control of SNF has been reported. For instance, ChvI and FeuP are necessary for the root infection. PhoB is the regulator of the response to phosphate's limitations and the production of exopolysaccharides (EPSs). CtrA is a master regulator of the cell cycle.

In *R. etli* CE3, the OmpR family contains 18 RRs. Despite the importance and multiple processes where the OmpR regulators participate, only two of them have been characterized. FxkR, the response regulator that controls the microoxic-dependent expression of *fix* genes, and VirG, the response regulator that activates the expression of *vir* genes involved in type IV pili production. Our bioinformatic analysis indicates that six of the *R. etli* CE3 OmpR-like RRs have orthologues with known functions in the Rhizobiaceae family, whereas the remaining have less predictable functions. Therefore, we focused on this group to explore their role. First, we obtained a set of individual mutants where an *ompR* gene was deleted. Our results suggest that RRs RetCH2128 and RetCH3587 are involved in the nitrogen-fixing in symbiosis. Bean plants inoculated with the mutant strains *DRetCH2128* and *DRetCH3587* form fewer nodules and are less efficient to fix nitrogen than plants inoculated with the wild strain. This project aims to decipher the functional role of the RetCH2128 and RetCH3587 regulators in the symbiosis *R. etli-P. vulgaris* as well as establish its molecular mechanism. Results in this regard will be presented.

Acknowledgments. This work was partially supported by PAPIIT-DGAPA (grant IN204320).

QUORUM SENSING MOLECULES CONTROL THE OXIDATIVE STRESS RESPONSE IN THE OPPORTUNISTIC FUNGAL PATHOGEN *CANDIDA GLABRATA*

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Abstract:

Candida glabrata is an important opportunistic fungal pathogen that causes local and disseminated infections in immunocompromised patients. *C. glabrata* has a robust oxidative stress response (OSR) that depends on the metabolic state since stationary-phase (SP) cells are more resistant to oxidative stress compared to logarithmic-phase (LP) cells. It has been proposed that *C. glabrata* cells communicate and modulate the OSR through secreted molecules that activate a network of signal transduction pathways. In this study, we show that BG14 (parental strain) LP cells increase their resistance to oxidative stress when exposed to conditioned medium (CM) from SP cells. This adaptation is mediated by an increase in expression of *CTA1* (catalase I) and the concerted role of stress-related transcription factors Yap1 and Skn7, and partially on the general stress transcription factors Msn2 and Msn4. Interestingly, LP cells exposed to CM of SP cells from *pde2*Δ (High-affinity cyclic AMP phosphodiesterase) or *aro8*Δ *aro9*Δ *aro10*Δ (Aro8 and Aro9 aromatic aminotransferases and Aro10 a phenylpyruvate decarboxylase) showed a reduced resistance to H_2O_2. These data suggest that the synthesis of the protective metabolites from SP cells is controlled by the cAMP-PKA and *ARO* pathways. In addition, LP cells exposed to CM of SP cells from *msn2*Δ *msn4*Δ showed a slight reduction in resistance to H_2O_2 but were more sensitive to H_2O_2 in the presence of CM from *yap1*Δ *skn7*Δ *msn2*Δ *msn4*Δ. We have identified in *C. glabrata* secretome the alkene 1-dodecene (C12) and the aromatic alcohols phenylethanol and tyrosol that could be working as the quorum sensing molecules. Together, these data show that *C. glabrata* quorum-sensing molecules modulates the OSR, an important virulence factor in this fungal pathogen.

SEARCHING FOR THE COGNATE RESPONSE REGULATOR OF THE ESSENTIAL SENSOR HYBRID HISTIDINE KINASE RDSA IN *RHIZOBIUM ETLI*

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Abstract:

Recently, we described a gene encoding an essential sensor hybrid histidine kinase called *rdsA* (after Rhizobium division and shape), located in the secondary chromosome of *Rhizobium etli* CFN42. A conditional knockdown mutation in *rdsA* affects dramatically cell division and shape. Nearly 64% of the cells are spherical cells, instead of the normal bacillary form. Moreover, a large fraction of the cells display abnormal division patterns, affecting polarity of growth and division time. Some of the cells present multiple growth foci. RNAseq analysis of this mutant revealed global changes, with downregulated genes in at least five biological processes: cell division, wall biogenesis, respiration, translation, and motility (1). Unlike other two-component regulation systems, no genes encoding a response regulator was found in the vicinity of *rdsA,* and in fact, no orphan response regulators were identified on the secondary chromosome.

To search for the cognate response regulator of the *rdsA* system, we identified the twenty-five orphan response regulators located on the main chromosome of *R. etli*, using the P2CS Database (http://www.p2cs.org/). Nineteen of these show a high probability of interaction with RdsA, according to ELIHKSIR (https://elihksir.org/). Knockout mutants in each gene were sought, under the rationale that the cognate response regulator would be essential as well. Inactivating mutants were isolated in sixteen of the orphan regulators. The three genes encoding essential response regulators were *ctrA*, *divK* (both controlling cell division and already known to be essential) and RHE_CH03575. Interestingly, a conditional knockdown mutant in gene RHE_CH03575 display a high number of spherical cells (ca. 45%) and problems in cell division. Both phenotypes are reversed upon restoring normal expression of this gene. Experiments are under way to demonstrate interaction of the product of this gene with RdsA, as well as phosphotransfer between these two components.

Martínez-Absalón S, Guadarrama C, Dávalos A, Romero D. 2022. RdsA Is a Global Regulator That Controls Cell Shape and Division in *Rhizobium etli*. Front Microbiol 13:858440.

TWO GLUCOSE-6-PHOSPHATASE ISOFORMS ARE TISSUE-SPECIFIC EXPRESSED UNDER OXYGEN-LIMITED AND REOXYGENATION CONDITIONS IN THE SHRIMP *LITOPENAEUS VANNAMEI*

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Abstract:

Crustaceans face environmental challenges in their habitats. Thus, understanding how these organisms maintain energy homeostasis is crucial for metabolic regulation knowledge under stress. The shrimp *Litopenaeus vannamei* exposed to oxygen-limited conditions induces anaerobic glycolysis and modulates the expression of gluconeogenesis enzymes in tissue- and condition-specific manners[1–3]. Glucose-6-phosphatase (G6Pase) is a key enzyme to maintain blood glucose homeostasis by the last step of gluconeogenesis and glycogenolysis; however, the interplay of these pathways is not fully elucidated in crustaceans. Herein we report the molecular characterization of two G6Pase isoforms from *L. vannamei*, and their regulation *via* the hypoxia-inducible factor 1 (HIF-1) in hypoxia and reoxygenation stresses. The two transcript sequences were obtained and characterized. The amino acid sequences with catalytic amino acids are conserved and have ~35% identity and are phylogenetically close to the corresponding invertebrate homologs. The two isoforms were named as G6Pase1 and G6Pase2. Protein molecular modeling depicts transmembrane proteins with 7 and 8 helices respectively, with the catalytic sites towards the lumen of the endoplasmic reticulum. Expression by RT-qPCR demonstrated that both G6Pases isoforms are tissue-specifically expressed; G6Pase1 is higher in hepatopancreas and has similar levels in gills and muscle in normoxia, in agreement with the enzyme activity, while G6Pase2 is only expressed in hepatopancreas. After HIF-1 knock-down, G6Pase1 is down-regulated in hypoxia but overexpressed in reoxygenation at 3 h of exposure in gills, even though G6Pase2 is down-regulated in both conditions at the same time as in reoxygenation at 48 h but only in hepatopancreas, demonstrating that this transcription factor regulates both isoforms in a condition, time, and tissue specific manner[4].

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THE ROLE OF *JMJ19* AND *DNA-PRIML* GENES IN *ARABIDOPSIS THALIANA* AS POTENTIAL TARGETS OF *TRICHODERMA ATROVIRIDE* SMALL RNA1 DURING THEIR MUTUALISTIC RELATIONSHIP

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Abstract:

Plants are constantly exposed to biotic and abiotic factors affecting their growth and development. In their natural settings, plants are invariably interacting with both, pathogens, and beneficial microorganisms; however, plants have developed several lines of defense, including basal chemical defenses, structural barriers, and innate immunity to counteract pathogens. When pathogens surpass these defense layers, plants trigger sophisticated molecular mechanisms to neutralize pathogen attack, which initiates with the detection of pathogen-associated molecular patterns (PAMP) to activate PAMP-triggered immunity (PTI) that limits the pathogen spreading from the original site of infection. However, some pathogens have developed effector molecules to suppress the PTI. To hinder pathogens, plants employ resistance (R) proteins a kind of intracellular receptors that perceive pathogenic effectors. This defense system is termed effector-triggered immunity (ETI). It has been shown that small RNAs (sRNAs) synthesized by pathogens can act as effectors molecules to suppress plant immunity. *Trichoderma* spp. are plant beneficial fungi that colonize plant roots, conferring beneficial effects by promoting plant growth and inducing the systemic disease resistance. Here, it was predicted that *Arabidopsis JMJ19* (JUMONJI 19) and *DNA-PrimL* (DNA primase large subunit) genes are putative targets of *Trichoderma atroviride* small sRNA1 (*Ta*_sRNA1) during their interaction with the plant. Plant growth stimulation analyses showed that *JMJ19* and *DNA-PrimL* products are potentially positive regulators of plant growth and are not essential for the stimulation of growth by *Trichoderma*. Plant pathogen challenging analyses indicated that the *DNA-PrimL* seems to be a susceptibility gene against both, the bacterial pathogen *Pseudomonas syringae* pv tomato DC3000 and the necrotrophic fungus *Botrytis cinerea*. Furthermore, *DNA-PrimL* is unnecessary to induce the systemic disease resistance against both pathogens by *Trichoderma*. The expression of Arabidopsis marker genes *PR-1a* (systemic acquired resistance) and *PDF1.2* (induced systemic resistance) was higher in *dna-priml* mutant than in wild type plants and that correlated with an enhanced resistance against both pathogens. *JMJ19* seems to plays a role as resistance gene against *P. syringae* pv tomato DC3000. On the other hand, Arabidopsis overexpressing lines of *Ta*_sRNA1 showed different accumulation levels of the *Ta*_sRNA1, which correlated with the downregulation levels of *DNA-PrimL*.

SINGLE-CELL ANALYSIS OF THE Ca^{2+} SIGNALING GENES IN BREAST CANCER

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Abstract:

Calcium ion (Ca^{2+}) signaling regulates major cellular functions such as gene expression, cell cycle, muscle contraction, and apoptosis, among many others, in cell-specific manner.[1] In the context of cancer, Ca^{2+} signaling is involved in tumor initiation and progression, and in the acquisition of metastatic phenotype.[2] Up to date, an estimated 1,670 genes are involved at some point in Ca^{2+} signaling, ranging from genes involved in the maintenance of Ca^{2+} concentrations to Ca^{2+}-dependent transcription factors and Ca^{2+}-activated proteins. Recently, with the analysis of bulk RNA-seq data, we demonstrated that the expression of ~ 10% of the estimated Ca^{2+} signaling genes is altered in breast cancer samples and cell lines. Also, expression results showed breast cancer subtype-specific signatures and an association with the epithelial-to-mesenchymal transition, suggesting that Ca^{2+} signaling could be involved.[3] However, the tumor microenvironment is highly heterogeneous, encompassing a broad range of different cell types. Thus, whether altered Ca^{2+} signaling genes expression is cell-specific in breast cancer remains to be elucidated. The aim of this study is to explore the expression landscape of the Ca^{2+} signaling genes in breast cancer, in cell-specific manner. Through bioinformatic analysis of single-cell RNA-seq data, we explored the expression of all genes involved in Ca^{2+} signaling in cells obtained from different subtypes of breast cancer. Also, with the implementation of trajectory analysis, we analyzed the expression of the Ca^{2+} signaling genes in different tumor progression models.

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IDENTIFICATION OF PROTEINS THAT INTERACT WITH THE TRANSCRIPTIONAL REPRESSOR MAF1 IN THE PROTOZOAN PARASITE *LEISHMANIA MAJOR*

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Abstract:

Leishmania is a flagellated protozoan that belongs to the trypanosomatid family. It is the etiological agent of leishmaniasis, which affects millions of people around the world. *Leishmania* and other trypanosomatids present atypical mechanisms of genetic expression, including polycistronic transcription and the processing of their mRNAs by trans-splicing. In higher eukaryotes, RNA polymerase III (Pol III) is responsible for synthesizing small RNA molecules essential for cell viability, such as tRNAs, 5S rRNA and some snRNAs. Maf1 was originally studied in *S. cerevisiae* as a transcriptional repressor of Pol III in response to multiple stress conditions. It was later found that Maf1 also regulates Pol I and Pol II transcription and that it is involved in several other functions in yeast and other organisms. Little is known about transcriptional regulation in *Leishmania*. By *in silico* analysis, we found that Maf1 in *L. major* (LmMaf1) possesses the three typical sequences of Maf1 orthologs (domains A, B and C). It was also observed that LmMaf1 has a probable globular structure very similar to that of human Maf1. Cell clones of *L. major* expressing the recombinant protein LmMaf1 fused to the PTP tag were generated and analyzed. Tandem affinity purification experiments were performed with them to identify by mass spectrometry the proteins with which LmMaf1 interacts to repress transcription. Proteins previously reported in other organisms as direct interactors of Maf1 were found, such as subunits of the three RNA Polymerases, transcription factors, and a variety of regulators of the localization and action of Maf1, such as kinases, phosphatases, and UPS-related proteins. Thus, proteins with a great diversity of functions were identified, suggesting that Maf1 participates in multiple roles in *Leishmania*. This work was supported by grant IN214221 (PAPIIT, UNAM).

MUTATION OF *MEDIATOR16* PROMOTES PLANT BIOMASS ACCUMULATION AND ROOT GROWTH BY MODULATING AUXIN SIGNALING

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Abstract

The MEDIATOR complex influences the transcription of genes acting as a RNA pol II co-activator. The MED16 subunit has been related to low phosphate sensing in roots, but how it influences the overall plant growth and root development remains unknown. In this study, we compared the root growth of *Arabidopsis* wild-type (WT), and two alleles of *MED16* (*med16-2* and *med16-3*) mutants in vitro. The *MED16* loss-of-function seedlings showed longer primary roots with higher cell division capacity of meristematic cells, and an increased number of lateral roots than WT plants, which correlated with improved biomass accumulation. The auxin response reported by *DR5:GFP* fluorescence was comparable in WT and *med16-2* root tips, but strongly decreased in pericycle cells and lateral root primordia in the mutants. Dose-response analysis supplementing indole-3-acetic acid (IAA), or the auxin transport inhibitor N-1-naphthylphthalamic acid (NPA), indicated normal responses to auxin in the *med16-2* and *med16-3* mutants regarding primary root growth and lateral root formation, but strong resistance to NPA in primary roots, which could be correlated with cell division and elongation. Expression analysis of *pPIN1::PIN1::GFP*, *pPIN3::PIN3::GFP*, *pIAA14:GUS*, *pIAA28:GUS* and *35S:MED16-GFP* suggests that MED16 could mediate auxin signaling. Our data imply that an altered auxin response in the *med16* mutants is not necessarily deleterious for overall growth and developmental patterning and may instead directly regulate basic cellular programs.

PHOSPHATE DEFICIENCY ACTIVATES THE AUTOREGULATION OF NODULATION PATHWAY

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Abstract:

Inhibition of nodule development is one of the main adverse effects of phosphate (Pi) deficiency in legumes. Despite all the efforts made over the last decades to understand how root nodules cope with Pi deficiency, the molecular mechanisms leading to the reduction in nodule number under Pi deficiency remain elusive. In this study, we provide experimental evidence that Pi deficiency activates the Autoregulation of Nodulation (AON) pathway, leading to a reduction in nodule numbers in both common bean and soybean. A transcriptional profile analysis revealed that the expression of the AON-related genes *PvNIN*, *PvRIC1*, *PvRIC2*, and *PvTML* is upregulated under Pi deficiency conditions. The downregulation of the MYB transcription factor *PvPHR1* in common bean roots significantly reduced the expression of these four AON-related genes. Physiological analyses indicated that Pi deficiency does not affect the establishment of the root nodule symbiosis in the supernodulation mutant lines *Pvnark* and *Gmnark*. Reciprocal grafting and split-roots analyses determined that the activation of the AON pathway was required for the inhibitory effect of Pi deficiency. Altogether, these data improve our understanding of the genetic mechanisms controlling the establishment of the root nodule symbiosis under Pi deficiency.

EXPRESSION OF MAL REDUCES VIABILITY OF HCC827 HUMAN LUNG CANCER CELLS

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Abstract:

Epigenetic repression of the **m**yelin **a**nd **l**ymphocyte protein gene (*MAL*) and over-expression of *MUC1* are two well-documented hallmarks of distinct carcinomas. We previously found an inverse relationship between these two proteins in human lung cancer cells, characterized by increased lysosomal degradation of MUC1-C induced by ectopic expression of MAL, and the concomitant decrease of expression of both cyclinD1 and c-myc, because the expression of both proteins is activated by MUC1-C. As these two proteins induce cell-cycle progression and proliferation, we further investigated whether the stable-expression of MAL, could overcome the proliferative effects of MUC1-C in human lung-adenocarcinoma HCC827 cells. Stable MAL-expressing cells were obtained by transfection followed by antibiotic selection. Our results indicated that the viability of MAL-expressing cells after 48 end 96 h of culture were 12.7 and 25% lower than wt cells, respectively. Next, we tested the response of those cells to the ER and genotoxic stresses. We induced ER-stress by treating the cells with 0.5 mM of brefeldin A. After 24h, MAL-expressing cells showed about of 50% les viability compared to wt-cells. On the other hand, the treatment of the cells with increasing concentrations of a genotoxic stressor such cisplatin resulted in 48% of survival of MAL-expressing cells compared with wt-cells. These results account for a negative effect of the over-expression of MAL on the proliferative properties of lung cancer cells HCC827 induced by MUC1-C. Keeping this on mind, we next tested whether the expression of MAL could cause cell cycle arrest. From the flow cytometry profiles, we can conclude that when MAL is expressed, a higher amount of cells remain in G1 phase. Currently we are conducting experiments to see if the expression of MAL induce apoptosis as the mechanism for transformed-cell death.

COMBINATION OF METFORMIN, SODIUM OXAMATE AND DOXORUBICIN INDUCES APOPTOSIS AND AUTOPHAGY IN COLORECTAL CANCER CELLS VIA DOWNREGULATION HIF-1α

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Abstract:

Colorectal cancer (CRC) is the third leading cause of cancer-related death worldwide in both sexes. Current therapies include surgery, chemotherapy, and targeted therapy; however, prolonged exposure to chemical agents induce toxicity in patients and drug resistance. So, we implemented a therapeutic strategy based on the combination of doxorubicin, metformin, and sodium oxamate called triple therapy (Tt). We found that Tt significantly reduced proliferation by inhibiting the mTOR/AKT pathway and promoted apoptosis and autophagy in CRC derived cells compared with doxorubicin. Several autophagy genes were assessed by western blot; ULK1, ATG4, and LC3 II were overexpressed by Tt. Interestingly, ULK1 was the only one autophagy-related protein gradually overexpressed during Tt administration. Thus, we assumed that there was a post-transcriptional mechanism mediating by microRNAs that regulate UKL1 expression during autophagy activation. Through bioinformatics approaches, we ascertained that ULK1 could be targeted by mir-26a, which is overexpressed in advanced stages of CRC. In vitro experiments revealed that overexpression of mir-26a decreased significantly ULK1, mRNA, and protein expression, contrariwise, the Tt recovered ULK1 expression by mir-26a decrease. Due to triple therapy repressed mir-26a expression, we hypothesized this drug combination could be involved in mir-26a transcription regulation. Consequently, we analyzed the mir-26a promoter sequence and found two HIF-1⊠ transcription factor recognition sites. We developed two different HIF-1⊠ stabilization models. Both showed mir-26a overexpression and ULK1 reduction in hypoxic conditions. Immunoprecipitation experiments were performed and HIF-1⊠ enrichment was observed in mir-26a promoter. Surprisingly, Tt diminished HIF-1⊠ detection and restored ULK1 mRNA expression. These results reveal an important regulation mechanism controlled by the signaling that activates HIF-1⊠ and that in turn regulates mir-26a transcription.

MT1-MMP EFFECTS ON BREAST CANCER CELLS TRANSCRIPTOME

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Abstract:

Background/aims: Beyond great research progress, there is still no complete understanding of how breast cancer (BC) develops. Most of patients die because of metastasis and treatment resistance, therefore identification of specific biomarkers is nevertheless needed to overcome these risks. Recent cancer research has focused on the prominent roles of tumor-extracellular matrix (ECM) in almost all aspects of disease progression and, together with the "big data" analysis tools, studies have begun to enlight on ECM contribution across cancer types. Membrane-Type Matrix Metalloproteinase -1 (MT1-MMP), is a key enzyme that modulates cancer progression by the regulation of several cellular processes through proteolytic and non-proteolytic mechanisms. On the other hand, long-non-coding RNA (lncRNA, a class of transcripts with lengths>200nt) have been recognized as key carcinogenesis players. However, it is not known if these molecules participate in MT1-MMP modulated cellular processes. In this study, we aimed to analyze BC cells transcriptome when MT1-MMP is either overexpressed or inhibited, in order to determine a group of lncRNA connected to MT1-MMP functions.

Methods/Results: MCF-7 and MDA-MB-231 BC cell lines were used to overexpress and to inhibit MT1-MMP expression, respectively. RNAseq transcriptome analysis was performed in order to identify differentially expressed transcripts. Significant gene expression changes were assesed by qPCR for 5 coding and 4 non-coding genes. Bioinformatic analysis was employed to analyze signaling pathways and cellular processes upon MT1-MMP modulation. In agreement with previous findings, our results show that biological processes associated with transcription, inflammation, cell death, differentiation and development, among others, are regulated by MT1-MMP expression. Additionally, our results show that the expression of 46 non-coding transcripts was modulated upon MT1-MMP expression, whose possible roles in BC await to be explored. Finally, the present work opens the possibility to study in more detail MT1-MMP roles in BC.

INTEGRATIVE ANALYSIS OF LINC00052 ROLES IN BREAST CANCER CELLS

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Abstract:

Background/aims: Recent studies have shown that long-non-coding RNA (lncRNA, a class of transcripts with lengths>200nt) play key roles in tumor progression. Previous work in our group analyzed whole transcriptome during multicellular spheroid (MCS) formation. Interestingly, the expression of a specific lncRNA, LINC00052, was strongly inhibited[1,2]. In addition, LINC00052 expression is increased in breast cancer (BC) luminal sybtypes in comparison with controls while there is no difference in triple-negative human breast cancer samples[3]. However, LINC00052 functions in breast cancer cells are poorly understood. In this study, we aimed to analyze LINC00052 roles on MCF-7 BC cells.

Methods/Results: Two main strategies were followed to assess this aim. First, with the help of bioinformatic tools, we inferred the molecular mechanism(s) through which LINC00052 acts and modulates cellular processes in breast cancer patients RNA samples. Second, loss of function studies were performed to evaluate LINC00052 relevance in MCF-7 (Luminal BC) cellular processes. Microarray expression assays were done to determine genes and cellular functions modified after LINC00052 knockdown. Next, LINC00052 depletion impact on MCF-7 cellular processes was evaluated. Bioinformatically, we observed that LINC00052 expression relates to BC patient overall survival and that its expression increases in Luminal BC samples in comparison to controls, while it remains low in HER2+ and Basal-like ones. Moreover, LINC00052 expression pairs to some cellular processes and signaling pathways enriched within each BC molecular subtype. Furthermore, experimentally, LINC00052 inhibition modulates cellular processes (migration, DNA repair mechanisms, cell cycle and metabolism) that are key for cancer progression. Finally, to elucidate LINC00052 molecular mechanism, bioinformatically, we inferred that LINC00052 associates with chromatin molecules (H3K4me3, H3K27me3) and cell cycle molecules (E2F4 and CDK6), among others.

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SEROTONIN EFFECT IN EARLY REGENERATION OF *LUMBRICULUS VARIEGATUS*

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Abstract:

Regeneration is a process in which certain organism is capable of restructuring tissues, organs or limbs with the same functionality as the previous lost. This process is usually classified in two types, epimorphosis and morphalaxis. The first, involves the formation of one structure denominated blastema, which is a mass of dedifferentiated cells that promote the formation of de novo structures; on the other hand, morphalaxis is the restructuring of the pre-existing tissues. Within the metazoans, there are groups that present the capacity of total regeneration; among them, we find the phylum of Annelida. *Lumbriculus variegatus* is an aquatic oligochaete which has a marked anterior and posterior regeneration. For this species, it has been described that it presents epimorphic regeneration of the posterior segments and neural morphalaxis. The nervous system is an important mediator in regeneration events because it can produce systemic and local signals that promote the regeneration response. Ones of the local compounds that the nervous system produce are the neurotransmitters and one of this is serotonin. We aimed to evaluate the effect of serotonin in the early regeneration of *L. variegatus*. First, we evaluated the effect of administration of 10 mM serotonin inhibitor 4-Chloro-DL-phenylalanine (PCPA) for the first 14 days-post-amputation (dpa); afterwards, we evaluated the administration of 100 µM of serotonin hydrochloride in the same time lapse. In addition, we analyze the expression of serotonin receptors (5-HT7) in the first days of regeneration. Our results indicate that the administration of PCPA reduced the anterior regeneration since the 5 dpa and the posterior regeneration since 2 dpa. The effect of administration of serotonin hydrochloride also reduces the regeneration in posterior days but in less proportion than in PCPA treatment. This work is a starting point for understanding the role of serotonin in the stimulation of regenerative response in *L. variegatus*.

ANALYSIS OF THE DIFFERENTIAL ASSOCIATION BETWEEN ARGONAUTE PROTEINS AND SMALL RNAS IN THE REGULATION OF LEGUME-RHIZOBIA SYMBIOSIS

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Abstract:

The symbiotic relationship between Rhizobia and leguminous plants (Legume-Rhizobia Symbiosis or LRS) is a process that has been extensively studied to identify the components that participate in its regulation. One of these components is the regulation induced by small RNAs (sRNAs), which guide gene silencing to modulate numerous processes in most eukaryotes; particularly, the plant-microorganism interactions, including the different stages of the LRS.

Argonaute (AGO) family proteins are crucial for the functioning and action mechanisms of sRNAs, being an essential part of the RNA Induced Silencing Complex. Previously, the role of several differentially accumulated sRNAs in LRS had been identified and evaluated, however, little has been studied about their differential association with AGO proteins in this context.

Furthermore, the preferential AGO loading of sRNAs seems to have a significant impact on gene silencing and potentially influence LRS. For example, mechanisms like "microRNA sequestration" make AGO1 and AGO10 compete for miR165/166 association and therefore impair the regulation of transcripts involved in root development.

In the present work, we selected the model legume *Phaseolus vulgaris* in interaction with *Rhizobium etli* to analyze the differential and preferential loading of sRNAs in AGO1 and AGO10. We observed the AGO loading profile of miR166 when comparing 5dpi inoculated plants with non-inoculated controls, giving rise to further study the functional role of this microRNA in the LRS context.

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CONTRIBUTION OF MICRORNAS CONTAINED IN HEPATIC TUMOR CELLS-DERIVED EXTRACELLULAR VESICLES IN THE EXPRESSION REGULATION OF CALCIUM DYNAMICS ELEMENTS IN HEPATOCARCINOMA CELLS

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Abstract:

Hepatocellular carcinoma is the fourth leading cause of cancer death worldwide due to its diagnosis and treatment difficulty. Increases and decreases of Ca^{2+}_i regulate some functions in the hepatocyte through channels, ATPases (pumps), and exchangers. One of the functions of Ca^{2+}_i is associated with the traffic and/or secretion of extracellular vesicles (EVs), which are a heterogeneous group of structures derived from cells, spherical, limited by a lipid bilayer, and can contain various types of biomolecules, among them, nucleic acids. miRNAs are a group of small non-coding RNAs (~22 nt) that mediate post-transcriptional and pre-translational regulation through degradation of messenger RNA and/or translation repression. Additionally, there is no evidence of the participation of vesicular microRNAs in the expression regulation of structures related to Ca^{2+}_i dynamics in HCC cells; so this study aimed to evaluate the involvement of microRNAs contained in hepatic tumor EVs in the expression regulation of elements that modulate Ca^{2+} dynamics in hepatocarcinoma cell lines. We found 5 miRNAs that are shared within the EVs from 5 different tumor cell lines of liver origin and were validated by qRT-PCR from a miRNA microarray implicated in cancer, which had 10 target genes involved in the regulation of Ca^{2+} dynamics; likewise, changes were found in the basal Ca^{2+} concentration of these cell lines under normal conditions and stimulation with EVs. Thus, it´s concluded that miRNAs within the EVs may be modifying the expression of genes related to Ca^{2+} dynamics in liver cancer cell lines.

CHARACTERIZATION OF A LONG NON-CODING RNA WITH AN ETHYLENE REGULATORY PERCEPTION ROLE IN *ARABIDOPSIS THALIANA*

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Abstract:

Ethylene is a phytohormone that regulates many processes during plant development and the response to biotic and abiotic stress conditions. The ethylene perception pathway has been elucidated through the analysis of mutant lines exhibiting an altered phenotype of the triple response This perception begins in the membrane of the endoplasmic reticulum and transduces the signal to the nucleus with the activation of a transcriptional cascade that triggers the activation of several ethylene-responsive genes, where EIN2 plays a central role in this pathway. In the present study, we show the characterization of a long non-coding RNAs (*lncRNA)* located downstream of the *EIN2* gene in the model organism *Arabidopsis thaliana*, and its possible participation in the ethylene perception pathway. The mutant phenotype of *the lncRNA* suggests its participation in the ethylene pathway, showing an altered phenotype in the triple response as well as the deregulation of genes-related to the ethylene response. Furthermore, we found a synteny between the genes of *EIN2* and the *lncRNA* as well as the possible formation of secondary structures present in the *lncRNA*, which is conserved in other organisms suggesting a possible conservation of its function.

ANALYSIS OF GENE EXPRESION AT DIFFERENT STAGES OF CHLOROPLAST DEVELOPMENT OF *AGAVE ANGUSTIFOLIA* HAW.

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Abstract:

The chloroplast is a very important organelle where photosynthesis is carried out in plants. At the early stage, chloroplast can be as small as 0.5µm and when fully development they can reach up to 5µm in size. In our study model *Agave angustifolia* Haw. *in vitro* plants. We offer to understand how the chloroplast genes that we selected of photosystem I and II ((*PsaA, PsaB, PsbA, PsbB, PsbD y PsbH*) are expressed at different stages of chloroplast development of this, since proplastids until mature chloroplast. Knowledge of the genetic information contained in the chloroplast can help us understand its function and mechanisms of action within the cell, as well as the modulation of the expression of key regulators of photosynthesis. The results of this project can be used for other biotechnological application in the future and would represent a successful strategy for gene editing to make photosynthesis more efficient in plants exposed to extreme climates

CO-EXPRESSION NETWORK OF LNCRNAS/MRNAS IN THREE-DIMENSIONAL MICROENVIRONMENT EXACERBATE ESSENTIALS HALLMARKS RELATED TO LUMINAL B BREAST CANCER SUBTYPE

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Abstract:

To have a more functional approach, organotypic 3D cell cultures that more accurately mimic the characteristics of solid tumors in vivo and the tumor microenvironment are required. Currently, studies on the analysis of lncRNAs/mRNAs interactions have not been fully explored in breast cancer cells cultured in 3D microenvironments. In the present research, we studied the expression and potential roles of co-expressed lncRNAs/mRNAs pairs of estrogen receptor- positive luminal B subtype BT-474 breast cancer cells grown in matrix extracellular proteins enriched 3D cultures. Global expression profiling using DNA microarrays identifies 290 upregulated and 183 downregulated lncRNAs in 3D cell cultures. Using a co-expression analysis approach of lncRNAs/mRNA pairs, we identify regulatory axes modulating diverse cancer hallmark such as responses to estrogens, cell proliferation, hypoxia, apical junctions, and resistance to endocrine therapy. In addition, we identified 102 lncRNAs/mRNA correlations in 3D cultures, which were common between TCGA datasets for luminal B breast cancer. Interestingly, we also found a set of mRNAs co-expressed with lncRNAs LINC00847 and CTD -2566J3.1 that showed a modest value as predictors of pathologic complete response (PCR) and overall survival. Finally, both lncRNAs were co-expressed with essential genes for cancer genetic dependencies such as FOXA1 y GINS2. Our findings show that co-expressed lncRNAs/mRNAs pairs, exhibit a high degree of similarity with those found in luminal B breast cancer patients suggesting that they could be adequate pre-clinical tools to identify, not only biomarkers related to endocrine therapy response and PCR, but to understand the biological behavior of cancer cells in 3D microenvironments, which point towards an important contribution of the roles of lncRNAs in organotypic 3D cultures.

Keywords: Breast cancer; 3D cell cultures; lncRNAs; co-regulation networks; therapy response.

INFLUENCE OF OXYR ON THE EXPRESSION OF PHASEOLOTOXIN SYNTHESIS GENES IN PSEUDOMONAS SAVASTANOI PV. PHASEOLICOLA NPS3121

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Abstract:

Halo Blight is a phytopathology that affects to the common bean plants (Phaseolus vulgaris L.) and is caused by the bacterial agent Pseudomonas savastanoi pv. phaseolicola. The main characteristic of this disease is the generation of a chlorotic halo around the necrotic site of the infection, which is produced by action of the phaseolotoxin [N Δ (N'-sulfodiaminophosphinyl)-ornityl-alanyl-homoarginine], the main virulence factor of the bacterium. The genetic information related to the biosynthesis and/or regulation of phaseolotoxin has been located in two pathogenicity islands called cluster Pht and cluster Pbo, which are structured in 23 genes ordered in five transcriptional units and 16 genes distributed in four transcriptional units, respectively. The gene expression of both pathogenicity islands is thermoregulated at 18 °C. Previous studies have demonstrated that oxidative stress influences on the expression of cluster Pht genes and recent evidence of our workgroup has shown the obtention of a phenotype non-toxigenic at 18 °C in a mutated strain in the coding gene for OxyR, global regulator of the oxidative stress. So far, it is unknown the way in which OxyR participates in the production of phaseolotoxin. Based on the above, the objective of this work has been to evaluate the influence of the regulatory protein OxyR on the expression of genes involved in the synthesis and/or regulation of phaseolotoxin. Gene expression analyses of the Pht and Pbo clusters were carried out by the RT-PCR technique using the oxyR- mutant strain of P. savastanoi pv. phaseolicola NPS3121. The results showed that the genic expression of both clusters (Pht and Pbo) is inhibited in the oxyR- mutant background, both at 18 °C and 28 °C. These results demonstrate that the global regulator of oxidative stress OxyR regulates the expression of genes of synthesis and/or regulation of phaseolotoxin in P. savastanoi pv. phaseolicola NPS3121.

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ALTERNATIVE CUG CODON USAGE IN THE HALOTOLERANT YEAST *DEBARYOMYCES HANSENII:* AN ANALYSIS OF GENE EXPRESSION PROVIDES NEW INSIGHTS INTO ADAPTATION TO EXTREME ENVIRONMENTS

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Abstract:

Debaryomyces hansenii is a non-conventional yeast with applications in biotechnology and in the food industry due to its ability to grow in extreme environments of osmolarity, salinity and low temperatures. It grows at 0.6 M NaCl in lab conditions but can be cultivated in media with up to 4 M NaCl. The species also can survive a pH range between 3 and 10. Several studies have focused on characterizing the function of genes that respond to different stress conditions such as salt, pH, and oxidative insults

D. hansenii belongs to the CTG-Ser1 clade, which ambiguously translates CUG codons to Leu (3%) or Ser (97%). CUG ambiguity confers a hypothetical proteome increased by each CUG codon, expanding phenotypic variability and cellular adaptations to face different environments

It has been discovered that the leucine tRNA with the CAG anticodon ($tRNA_{CAG}^{Leu}$) is a hybrid and has sequence modifications that enable the seryl-tRNA synthetase (SerRS) and the leucyl-tRNA synthetase (LeuRS) to recognize it and bind a serine or a leucine in the tRNA, having two forms of the charged tRNA ($tRNA_{CAG}^{Ser}$ and $tRNA_{CAG}^{Leu}$).

In this project, we evaluated cell viability, growth rate and colony switchover. Differential gene expression of $tRNA_{CAG}$, LeuRS, and SerRS genes were detected as response to different ranges of NaCl, pH, and H_2O_2. This is the first study about the hybrid $tRNA_{CAG}$ and aaRS transcriptional rate related to leucylation or serynation of the CUG codon as a response to stress conditions.

DOWNREGULATION OF *CATSPER1* EXPRESSION BY CALMODULIN INHIBITOR (CALMIDAZOLIUM): POSSIBLE IMPLICATIONS FOR FERTILIZATION

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Abstract:

The CatSper channel localizes exclusively in flagella of sperm cells. The Catsper1 protein is essential for the CatSper Channel formation, together with three☒ ☒ pore units, which produces flagellum hyperactivation and confers sperm fertility. *Catsper1* expression is dependent on Sox transcription factors, which can recognize *in vitro* at least three Sox binding sites on the promoter. Sox transcription factors have calmodulin-binding domains for nuclear importation. Calmodulin (CaM) is affected by the specific inhibitor calmidazolium (CMZ), which prevents the nuclear transport of Sox factors. In this work, we assess the regulation of the *Catsper1* promoter *in vivo* by Sox factors in the murine testis and evaluate the effects of the inhibitor calmidazolium on the expression of the *Catsper* genes, motility, and fertility of the sperm. *Catsper1* promotor has significant transcriptional activity *in vivo;* on the contrary, three Sox site mutants in *Catsper1* promotor have reduced transcriptional activity in testis. CaM inhibition affects Sox factor nuclear transport and has notable implications in the expression and production of *Catsper1*, as well as in the motility and fertility capability of sperm. The molecular mechanism described here might conform to the basis of an male contraceptive strategy acting at the transcriptional level by affecting the production of the CatSper channel, a fundamental piece for male fertility.

HIGH-THROUGHPUT SMALL RNA-SEQ ANALYSIS IN THE *ARABIDOPSIS THALIANA* MUTANT *ECA2* IN RESPONSE TO THE FUNGAL PATHOGEN *BOTRYTIS CINEREA*

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Abstract:

In plants, small RNAs (sRNAs), ~19 to 24 nucleotides long, can be classified into two broad categories based on their biogenesis processes: those deriving from a hairpin-shaped folded single stranded RNA precursor (mostly miRNAs) and those deriving from a double stranded RNA precursor (siRNAs). By sequence complementarity certain sRNAs negatively regulate targets either at transcriptional (guiding epigenetic modifications to target genes) or at post-transcriptional level (leading to RNA target slicing or translation repression). Some of these sRNAs are known for having important roles on diverse biological processes including development and stress responses. It has been shown that some sRNAs are part of the interaction regulation between *Arabidopsis thaliana* and the fungal pathogen *Botrytis cinerea*.

In our laboratory, we have previously obtained an *A. thaliana* mutant, called *eca2*, that constitutively expresses *ATL2* (an early-response gene), and which has a more permeable cuticle and is resistant to *B. cinerea* infection. Interested in comparing sRNA expression profiles from wild-type (WT) and *eca2* plants in response to *B. cinerea*, we performed high-throughput small RNA-seq analysis from mock- or *B. cinerea*-treated WT or *eca2* plants. We found that hc-siRNAs (belonging to the siRNA category and exerting their target regulation largely at transcriptional level) are the vast majority from the differentially expressed sRNAs in mock-treated plants, mainly being down regulated in *eca2* plants. We noted that upon *B. cinerea* treatment the majority of sRNAs only up regulated in WT or only up regulated in *eca2* or up regulated in both plants were miRNAs, whereas the majority sRNAs only down regulated in WT were hc-siRNAs.

These results suggest that in unchallenged conditions *eca2* plants could respond more efficiently to the pathogen attack by maintaining a more relaxed chromatin structure; down regulation of hc-siRNAs in WT during *B. cinerea* infection may be a response aimed at achieving the same goal. Further analyses are needed to check if regulation exerted by the up regulated miRNAs upon their targets could also be part of the reasons that make *eca2* a resistant genotype to *B. cinerea* infection.

Financial support: PAPIIT grant number IN203720.

EARLY GENETIC SIGNATURES ASSOCIATED WITH INTRINSIC RESISTANCE IN LUNG ADENOCARCINOMA CELLS PERSISTENT TO TKI TREATMENT

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Abstract:

Lung cancer, the most common malignant tumor, is classified into two groups: non-small-cell lung carcinoma (NSCLC) and small-cell lung carcinoma. From the NSCLC, lung adenocarcinoma is the most frequent histological type and the leading cause of tumor-associated mortality. Despite notable advances in clinical treatment, based on EGFR mutation detection, a significant proportion of patients with lung adenocarcinoma have not shown improved survival rates. Studies have been conducted regarding the resistance mechanisms following TKI administration and have suggested that persistent cells have a notable role in treatment resistance. However, the biological process associated with intrinsic resistance to TKI treatment requires a better understanding.

To analyze the early detection of intrinsic resistance-related transcripts, we exposed lung adenocarcinoma cell lines harboring EGFR mutations to Erlotinib and Osimertinib. After a unique exposure, the transcriptome was sequenced employing an Illumina platform. Transcriptome sequencing was performed on two independent assays, each run-in duplicate. Differential gene expression was tested using the edgeR package, and genes with low abundance were removed. Analyzed genes showing a fold change > |2| and an FDR < 0.05 were differentially expressed. In-silico pathway analysis was performed employing the Clusterprofiler package and KEGG database to identify cellular processes association and interaction networks. Finally, the clinical association was validated using XenaBrowser obtaining overall survival and Kaplan-Meier analysis for each candidate gene.

Persister cells shared three candidate genes associated with the cell cycle processes. XenaBrowser Database analyses suggested that candidate genes have clinical relevance in overall survival. As more targeted therapies are used in clinical practice, knowledge of early prognostic markers is required for better treatment selection. Although our results highlight the potential of these genes as new biomarkers of resistance to initial treatment with TKIs, further studies are needed to validate the clinical relevance of our findings.

TRANSCRIPTOMIC PORTRAIT OF EPIGENES IN HUMAN GLIOMAS

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Abstract:

Gliomas are the most common primary tumors of the central nervous system. Despite having a low incidence, gliomas are usually associated with a poor survival prognosis and high mortality. Glioblastoma Multiforme (GBM), stands out in this group, by being both, the most frequent and most aggressive brain tumors, especially affecting economically active adults. Different molecular mechanisms are involved in this type of neoplasm, including epigenetic processes. Until now, there are no studies focused on globally analyzing genes involved in epigenetic processes known as epigenes. Here, we analyzed public databases of high-throughput RNA sequencing (RNA-seq) of 511 tissue samples of low-grade gliomas and 348 tissue samples of glioblastoma. Also, we analyzed 60 tissue samples RNA-seq of non-neoplastic white matter as control. We found deregulation of several epigenetic processes such as histone enzyme writers, chromatin remodeling proteins, and Polycomb repression complexes, among others. Our results allow to broaden the panorama for the search for biomarkers and/or therapeutic epigenetic targets. These may contribute to a better and more comprehensive understanding to reduce the morbidity and mortality of this disease.

DOWNREGULATION OF COMMON BEAN PHOSPHOLIPASE *PVPLDα2* ALTERS NODULE DEVELOPMENT DURING RHIZOBIAL SYMBIOSIS

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Abstract:

Plant phospholipases Ds (PLDs) are a heterogeneous group of widely distributed enzymes. PLDs participate in several processes, such as responses to abiotic stress and plant-pathogen interactions. Few studies have been carried out on the participation of PLDs in the mutualistic symbioses of plants with microorganisms. One of the most studied symbiotic interactions in plants occurs between legumes and nitrogen-fixing bacteria called rhizobia. In this work, we analize the function of *PvPLDα2*, a gene that encodes a PLD in common bean (*Phaseolus vulgaris* L.), during the symbiotic interaction with *Rhizobium tropici*. Using quantitative PCR assays, high expression of *PvPLDα2* was found in nodules at 14 and 21 days post-inoculation (dpi), compared to uninoculated roots. In addition, strong *PvPLDα2* promoter activity was detected in infected root cortical cells as well as in young and mature nodules. Downregulation of *PvPLDα2* by RNA interference (RNAi) increased the number of nodules at 14 dpi. Importantly, *PvPLDα2*-RNAi roots developed a greater number of multinodules (two or more nodules joined through common tissue) than control roots. Furhermore, RNAi root nodules showed a slight increase in nitrogen fixation rate at 21 dpi. These findings suggest that *PvPLDα2* affects nodule development and shed light on the importance of lipid regulation for rhizobial symbiosis.

AN INSIGHT INTO THE NOVEL HYBRID REGULATION COMPLEX RTG3-NRG1 OF *SACCHAROMYCES CEREVISIAE*

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Abstract:

Transcription factors are direct regulators of gene expression, traditionally these factors are modulated by their nuclear concentration, and activation by phosphorylation or ligand binding, leading to the different signal-transduction pathways. Previous work from our laboratory found a new kind of transcriptional regulator in *S. cerevisiae*, in which Hap2-3-5 DNA-binding domain and Gln3 activation domain form a hybrid modulator to determine the expression of *GDH1* and *ASN1* under repressive nitrogen conditions. That selective transcriptional response is not evoked when the parental regulators (HAP2-3-5-4 and Gln3) act independently. In this study, the Nrg1-Rtg3 hybrid complex was found when while studying the paralogous genes *ALT1* and *ALT2*. Nrg1 inhibits the repression of genes negatively regulated by glucose. Nrg1 works by negatively regulating genes encoding gluconeogenesis enzymes, those implied in the Krebs cycle, and those which metabolize carbon sources other than glucose. Rtg3 and Rtg1 form a transcription complex that activates genes of the retrograde signaling pathway between the mitochondrion and the nucleus as a response to mitochondrial dysfunction, resulting in the induction of antioxidant defenses and stress resistance. The *ALT1* gene encodes an alanine-aminotransferase which catalyzes the transaminase reaction of the amino group from glutamate to pyruvate to form alanine and 2-oxoglutarate. No function has been discovered for *ALT2* yet. Northern Blot analysis showed that alanine induced *ALT1* expression and repressed that of *ALT2*. In both, *nrg1Δ* or *rtg3Δ* mutant strains, *ALT1* expression is not repressed in the presence of alanine, indicating that alanine act as co-regulator of Nrg1 and Rtg3. These data suggested that interaction between Nrg1 and Rtg3 leads to transcriptional *ALT2* repression. We have confirmed the predicted Ntg1-Rtg3 interaction by carrying out co-immunoprecipitation analysis. In addition, preliminary proteomic studies have posed the possibility of the formation of a multiprotein Nrg1-Rtg3 hybrid complex, in which leucine-tRNA ligase (Cdc60), pyruvate kinase 1 (Cdc19), and splicing factor RNA helicase (Prp16) could be included. The Cdc60 protein is related to the Torc1 signal transduction system. In addition, there is *in silico* evidence of Cdc19-Hap2 and Nrg1-Prp16 interactions. This leads to the conclusion that, in the presence of alanine, Nrg1 and Rtg3 form a multiprotein hybrid regulator complex, However. A more detailed analysis will be needed to identify the components of the Nrg1-Rtg3 complex.

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EXPRESSION REGULATION OF THE GENE ENCODING THE PROGESTERONE RECEPTOR IN IMMORTALIZED HUMAN ENDOMETRIAL STROMAL CELLS

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Abstract:

Background: Decidualization is a complex process that involves differentiation of the endometrial stroma to a receptive state, which is required to establish and support pregnancy. This process is initiated by estradiol (E2) during the proliferative phase of the menstrual cycle through the estrogen receptor α (ERα). It has been reported that E2 induces the expression of the gene encoding the progesterone receptor (PGR) in various reproductive tissues such as uterus and breast. Progesterone (P4) and cAMP are major molecules during decidualization in the secretory phase of the menstrual cycle. Recent studies have suggested that PGR expression is regulated by E2, P4, and cAMP signaling in the human endometrium. The aim of the present study was to identify the stimulus that induces PGR expression in human immortalized endometrial stromal cells.

Methods: Immortalized human endometrial stromal cells (T-hESC, ATCC, CRL4003) were stimulated with E2, P4, medroxyprogesterone (MPA) and/or cAMP at different time points to assess the expression of PGR isoforms, PRL, and IGFBP- 1 genes by RT-qPCR. In addition, the morphological cell changes were analyzed by phase-contrast microscopy.

Results: The stimuli with E2 did not generate significant changes in PGR expression in comparison with the vehicle at the different time points evaluated. Stimuli with E2+MPA+AMPc or E2+P4+AMPc significantly increased the expression of total PGR (PGR isoforms A and B) and PGR isoform B at 6 and 24 h compared to the vehicle; the expression of PRL and IGFBP-1 (decidualization biomarkers) was induced only at 24 h. At morphological level, stimuli with E2+MPA+AMPc and E2+P4+AMPc generated decidualized stromal cells after 7 days as previously reported.

Conclusion: In the present study, we have demonstrated that, unlike other cell types, estradiol alone does not induce PGR expression in immortalized human endometrium stromal cells. Interestingly, we have shown that E2+MPA+cAMP (a stimulus to induce in vitro decidualization) induces PGR expression at 6 h and 24 h, confirming that ERα, PGR, and cAMP signaling is involved in the regulation PGR gene expression.

PROTEOMIC ANALYSIS OF THE PHYSICOCHEMICAL PROPERTIES OF *DEBARYOMYCES HANSENII* PROTEINS: A RESULT OF THE ALTERNATIVE CUG CODON USAGE

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Abstract:

The genetic code of organisms is considered practically universal; however, codons can suffer modifications in their structure and alter the way they are translated. An example of an important organism that departs from the premise of the universal genetic code is *Debaryomyces hansenii,* a biotechnologically important yeast belonging to the CTG-Ser1 clade. The CUG codon usually encodes leucine (Leu), a hydrophobic amino acid; although, *D. hansenii* and other CTG-Ser1 clade organisms have acquired the ability to also encode for the polar amino acid serine (Ser). It is not clear what causes this encoding modification in the CUG codon of *D. hansenii*. In this project, the isoelectric and hydropathic properties of the yeast proteome were analyzed, comparing these characteristics when their proteins encode for Leu or Ser to obtain protein alterations dependent on the isoelectric and hydropathic properties. We compare the isoelectric and hydropathic profiles of *D. hansenii* and tracked differences when protein with CUG-encoded residues changed between Leu and Ser. We observed an important difference in the hydropathic profile of the organism when this amino acid change occurs. Therefore, the alternative CUG codon usage directly affects the hydropathy tendency of *D. hansenii* proteins.

ROLE OF MAF1 IN GLOBAL TRANSCRIPTIONAL REGULATION IN THE PROTOZOAN PARASITE *LEISHMANIA MAJOR*

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Abstract

Parasites of the *Leishmania* genus are the causative agents of leishmaniases in tropical regions worldwide. Besides its clinical importance, *Leishmania* is also important for presenting atypical genetic expression mechanisms, such as polycistronic transcription. As in higher eukaryotes, transcription in *Leishmania* is performed by RNA polymerases (RNAP) I, II and III, each one specialized in the synthesis of certain RNA molecules. However, recent work suggests a tight relation and interdependence among all RNAP. Maf1 is a transcription factor that regulates and coordinates the global transcription in vertebrates, acting as a negative regulator of RNAP III transcription. The goal of this work was to elucidate the role of Maf1 in the coordination of the three RNAP in *L. major* by the identification of the genomic regions recognized by Maf1, and by studying the effects of Maf1 overexpression in the abundance of all mRNAs through complete transcriptomic analysis. The results showed that Maf1 recognizes genes transcribed by RNAP I and RNAP II, as well as RNAP III promoter regions. Transcriptomic analysis of Maf1-overexpressed cells revealed a global decrease of the coding transcripts of RNAP III components, as expected for the Maf1 primary activity as negative regulator of RNAP III. Also, we detected a decreased expression of some mRNAs from proteins that regulate RNAP II and RNAP I transcription. Gene Ontology (GO) and KEGG pathway analyses showed the enrichment of transcripts from metabolic proteins, lipid-transporting proteins and proteins involved in fatty acids biosynthesis; and the decrease of transcripts of proteins involved in protein synthesis, amino acid metabolism, genetic expression, and fatty acid degradation. Thus, our findings suggest the role of Maf1 as a global negative transcription regulator in *L. major* and its participation in the regulation of other relevant biological processes of the parasite. This work was supported by grant IN214221 (PAPIIT, UNAM). L.A.R.R thanks to DGAPA-UNAM for his postdoctoral fellowship.

IDENTIFICATION OF TRANSCRIPTION FACTORS ASSOCIATED WITH LYCOPENE CYCLASE GENES IN BIXA ORELLANA L.

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Abstract:

Lycopene cyclase (LCY) genes are a key bifurcation point in the carotenoid synthesis pathway, increasing or decreasing their production. Bixa orellana L. is characterized by producing bixin mainly in its seeds, a red-orange apocarotenoid. However, being a highly heterozygous plant, it generates contrasting phenotypes in pigment production. Our team has identified three morphotypes with different bixin content associated with variation in the expression and SNPs of the Bo-βLCY genes of the transcriptome of the species. The recent sequencing of the genome (not published), gives us the opportunity to explore promoter region sequences that participate in gene regulation by promoting the accumulation of proteins/metabolites. The present study analyzes the transcription factors (TF) associated with the Bo-LCY genes in the B. orellana genome. The cis elements (1,000bp upstream) of each Bo-LCY gene were identified in the PLACE database (Plant Cis-acting Regulatory DNA Elements), as well as the TF associated with them, to generate a data matrix, organized into response categories to stimuli/function. Two important groups of TF involved in essential processes carried out by carotenoids were obtained: photosynthesis (DOFCOREZM, CACTFTPPCA1), reproduction (CAATBOX1, POLLEN1LELAT52) and oxidative system (GT1CONSENSUS, GATABOX), defense against environmental factors (MYCCONSENSUSAT). This study presents to the Bo-LCY genes as differentially regulated with the potential to influence the accumulation of carotenoids, such as bixin, in the contrasting phenotypes of the species.

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FLOWERING TRANSITION WHEN AND WHERE? REGULATION OF *XAANTAL1*

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Abstract:

Flowering is a complex and highly regulated process that ensures that plants flower at the proper time and conditions for reproduction success. *Arabidopsis thaliana,* like many other plants, flowers during the spring-summer seasons; thus, it must detect day-length and temperature rise. Many proteins control long-day signaling, including photoreceptors, circadian-cycle proteins, and the transcription factor CONSTANS (CO). CO induces the "florigen" FLOWERING LOCUS T (FT) that travels from the leaves to the shoot apical meristem (SAM) to induce flowering via its association with the transcription factor FD.

Phytochrome B (PHYB) photoreceptor represses *CO* in the leaves during the daytime, but PHYB is inactivated when temperature increases allowing *FT* transcription.

XAANTAL1 (XAL1) is a MADS-box gene that has an important role in flowering transition. *xal1* mutants have a late-flowering phenotype when they grow under long days at 22°C. In this work, we show that this phenotype is independent of CO regulation and occurs directly at the SAM. Unexpectedly, *XAL1* and several flowering canonical genes are positively regulated by PhyB in shoot apices. Moreover, we found that *xal1* plants have a late-flowering phenotype when they grow in short days with elevated temperatures (27°C). Therefore, XAL1 regulation adds another layer of information to the classical flowering pathways.

This work is supported by PAPIIT-DGAPA (IN206220; IN200920; IN203220; IN211721) and CONACyT (CF-102959; -102987). MRB (CVU 422584) is recipient of a postdoctoral scholarship from CONACyT.

FUNCTIONAL ANALYSIS OF THE MICRORNA MIRNOV223 AND ITS PUTATIVE TARGET *LBD-PHVUL.002G012200.1* IN THE *PHASEOLUS VULGARIS* MODEL DURING SYMBIOSIS WITH *RHIZOBIUM ETLI*

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Abstract:

Common bean, *Phaseolus vulgaris*, is one of the legumes capable of fixing nitrogen thanks to the establishment of a symbiosis with bacteria, called “rhizobia”, which carry a nitrogenase enzyme that reduce atmospheric nitrogen. Each step of the symbiosis between legumes and rhizobia is regulated by various genes. Likewise, some of these genes are post-transcriptionally regulated by different microRNAs. The latter are small non-coding RNA molecules of approximately 20-23 nucleotides. In the Eukaryote Functional Genomics Program, we focus on nodulation regulation by microRNAs. In 2015, using bioinformatic techniques, Formey *et al.* identified a set of microRNAs and their possible targets in *P. vulgaris* genome that have a high probability of being regulators of nodulation. In this analysis, they found new microRNAs never reported before, among which is miRNov223. The specific absence of this microRNA in nodules, compared to the rest of the plant, indicates that miRNov223 probably plays a role in the nodulation regulation process. Thanks to bioinformatic prediction of possible targets for miRNov223, Phvul.002G012200.1 transcript, that codes for a protein with a LOB (Lateral Organ Boundaries) domain (LBD), was determined as the main target candidate. LBDs are regulators of lateral organ growth in plants, and it has been dated that one of these proteins (*LBD16*) is involved in the initial development of nodules in *Medicago truncatula*. Therefore, in this project we focus on functionally analyze the role of miRNov223 and the LBD target in the regulation of the symbiosis between *P. vulgaris* and *R. etli*. We measured the accumulation of miRNov223 and its possible target at key stages of this symbiosis in *P. vulgaris* roots and nodules. For functional analysis, we transformed *P. vulgaris* roots to alter the accumulation or action of the microRNA or the LBD target transcript. The probability that Phvul.002G012200.1 transcript is a genuine target of miRNov223 was evaluated using the 5’RACE technique, testing an eventual microRNA-induced slicing.

Research supported by DGAPA-UNAM IA201522 & CONACYT A1-S-16129

A LONG NON-CODING RNA AS A NOVEL REGULATOR OF ABA SIGNALING IN *ARABIDOPSIS THALIANA*

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Abstract:

Abiotic stresses, such as drought, salinity or heat, have become a major threat for crop plant survival and yield. Full understanding of the mechanisms ensuring plant adaptation to stress can assist in obtaining tolerant varieties. Abscisic acid (ABA), which is the major stress phytohormone, takes part in a plant adaptation to stress through regulation of physiological processes[1]. ABA Insensitive 5 (ABI5) functions in the core ABA signaling through the regulation of the expression of genes that contain the ABSCISIC ACID RESPONSE ELEMENT (ABRE) motif within their promoter region. ABI5 expression is activated by drought and salt stress during seed germination within a short developmental window and its activity causes the inhibition of germination or early seedling growth[2]. In addition, ABI5 activity is regulated at the protein level via protein interaction and posttranslational modification. The AFP (ABI FIVE BINDING PROTEIN) family participates in the control of ABI5 accumulation. It's been reported that AFP1 mediates the proteasomal degradation of ABI5, nonetheless, the mechanism of this regulation is still unknown[3]. Recently, long non-coding RNAs (lncRNAs) have emerged as major products of the eukaryotic transcriptome with regulatory importance and an intergenic lncRNA was identified within *AFP1 locus,* hence we named it as *lincAFP*. The evidence obtained after genotypic and phenotypic analysis in overexpressing and mutant lines of *lincAFP* showed a positive effect on the accumulation of the expression of the neighbor genes *AFP1* and *NTF2* and the participation of this lincRNA in ABA signaling. In this study, we analyzed the effect of *lincAFP* downstream the regulation of its adjacent genes and how this regulation is carried out.

[1]Chen *et al*. Abscisic acid dynamics, signaling, and functions in plants. J Integr Plant Biol. 2020; 62:25.

[2]Skubacz *et al*. The Role and Regulation of ABI5 (ABA-Insensitive 5) in Plant Development, Abiotic Stress Responses and Phytohormone Crosstalk. Front Plant Sci. 2016; 7:1884.

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A NOVEL YY1 BINDING REGION IN CLAUDIN 6 DNA PROMOTER IS REQUIRED FOR THE APPROPRIATE ASSEMBLE OF THE CREB-YY1 COMPLEX

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Abstract:

Gastric cancer represents the fifth cause of death associated with cancer worldwide. Helicobacter pylori (H. pylori) a Gram-negative bacteria, is considered one of the major risk factors associated to gastric cancer; it triggers the carcinogenic process through CagA and VacA oncoproteins. Nevertheless H. pylori lipopolysaccharide (LPS) is another component that participates in this oncogenic process. It has been established that LPS increases the expression of claudin-6 (cldn6) in AGS cells via the ERK1/2 pathway. The expression of claudins is regulated by transcription factors (TF), but the specific TFs that control the expression of cldn6 are unknown. The aim of this project was to identify in AGS cells stimulated with LPS, the TF´s and the DNA sequence in the promoter region where they bind in order to regulate the expression of cldn6. A bioinformatics analysis was initially performed to identify the possible TF´s that regulate cldn6 expression. CREB and YY1 were selected from 14 possible candidates. A further analysis of the cldn6 promoter DNA sequence, revealed that CREB had 17 and YY1 had 9 binding sites, distributed along the cldn6 promoter, that contain 2000 pb in length.

A ChIP assay was performed to locate the precise DNA region where CREB and YY1 bind; the results showed that all the predicted binding sites were occupied by YY1 and CREB, and interestingly, an unexpected YY1 binding region, between 1279-1421 pb, was identified. The latter result suggests that YY1 bridges this distant region and the transcription-starting site thus enhancing claudin 6 transcription in the AGS cell line. Further experimental proof is needed to confirm this hypothesis

REGULATION OF THE *SLM35* GENE UNDER STRESS CONDITIONS IN *SACCHAROMYCES CEREVISIAE*

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Abstract:

The mitochondrial protein Slm35 (*Stress and Longevity-related Mitochondrial factor)* has been linked in *Saccharomyces cerevisiae* with the gene *TOR1* during stress response and life-span regulation. A stress-resistance phenotype appears in yeast lacking *SLM35* or *TOR1*. In contrast, a double mutant is inviable in stress conditions, and its lifespan declines sharply. It has also been reported that Slm35 is a negative regulator of mitophagy in yeast, indicating that this protein is an important component that links stress response, aging, and mitophagy. However, little is known about the regulation of Slm35 itself and how this protein modulates the aforementioned phenomena[1]. The analysis of the 5'-UTR region of *SLM35* revealed sequences predicted to act as stress-related transcription factors recognition sites and a possible upstream open reading frame (uORF), we therefore hypothesized that these elements could regulate mRNA expression and/or protein synthesis in stress conditions. By analysis of the mRNA levels and employing a transcriptional reporter we were able to discard a transcriptional regulation mechanism. Using a strain that expresses a GFP-tagged version of Slm35 we observed an increase of the protein in oxidative stress and stationary phase using glucose as carbon source. In contrast, when the strain was grown using a respiratory carbon source such as lactate or in synthetic medium lacking amino acids, the Slm35-GFP protein levels decreased in an autophagy and mitophagy dependent manner. Furthermore, we observed that the predicted uORF regulates in a positive manner the presence of Slm35, contrary to the repressor characteristic that normally encompass uORFs. All these data suggest that Slm35 and the degradation process of mitophagy share an intricate regulation mechanism.

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NEUTRAL LIPIDS OF THE ANTARCTIC YEAST *RHODOTORULA MUCILAGINOSA*: TRANSCRIPTIONAL REGULATION OF THE ATP CITRATE-LYASE GENE UNDER NITROGEN LIMITATION

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Abstract:

Atp-citrate lyase (Acl) is a cytosolic and nuclear enzyme that cleaves citrate to produce oxaloacetate and acetyl-CoA. Acetyl-CoA is an essential molecule in central metabolism, epigenetic regulation, fatty acid synthesis, etc. Acl is considered a key enzyme in oleaginous microorganisms during the synthesis of fatty acids under nitrogen-limited conditions in the presence of an abundant carbon source. However, limited information is available about the transcriptional regulation of the *ACL* gene in oleaginous yeasts with biotechnological potential. This study evaluated the growth, biomass production, and cell viability of the antarctic yeast *Rhodotorula mucilaginosa* under lipogenic conditions varying the carbon/nitrogen (C/N) ratio. Likewise, the accumulation of neutral lipids and the expression profile of the *RmACL* gene under different lipogenic conditions were analyzed. Our results suggest that nitrogen limitation activates neutral lipid synthesis in the stationary phase (48-72 h). The expression of *RmACL* depends on the C/N ratio during the exponential phase. To understand the transcriptional regulation of *RmACL*, Nucleosome Scanning Assays (NuSA) were performed, allowing to determine a promoter's nucleosomal arrangement. We will discuss the transcriptional regulation of *RmACL* under nitrogen-limited conditions.

THE RNA-DIRECTED DNA METHYLATION MACHINERY IS REQUIRED IN *ARABIDOPSIS* TO MODULATE THE EXPRESSION OF *NSP4* GENE MEDIATED BY *TRICHODERMA*

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Abstract:

Plants have developed several types of defenses that allow them to suppress damage caused by pathogens. At cellular level, the recognition of pathogens triggers a complex defense network in which phytohormones play important roles. In addition, small non-coding RNAs participate in plant defense through RNA-directed DNA Methylation (RdDM). Plants synthesize secondary metabolites called glucosinolates, which are hydrolyzed by myrosinases enzymes and together with specifier proteins, they synthetize antimicrobial molecules involved in the defense of plants against pathogens and insects. Defense mechanisms are also triggered by beneficial microbes such as growth-promoting bacteria and fungi (i.e., *Trichoderma* spp.). Pathogen and beneficial microorganisms trigger the so-called priming response, in which the plant respond fast and strongly to a second infection or a stressful stimulus.

Here, one 24 nucleotide small RNA from Arabidopsis, which is accumulated during *Arabidopsis- Trichoderma* interaction, was predicted to putatively target *NSP4*. *NSP4* codes for one of the five nitrile-specifier proteins that promotes the generation of simple nitriles in the model plant *Arabidopsis thaliana*. To evaluate the role of the sRNA1 and its target, NSP4 from *Arabidopsis thaliana* in the mutualistic interaction with *Trichoderma*, we dissect genetically and molecularly the *NSP4* gene silencing pathway mediated by sRNAs. We demonstrate that *NSP4* participates as putative negative growth regulator in *Arabidopsis*, furthermore, the *nsp4* insertional mutant did not respond to *Trichoderma*-induced priming and was affected in the expression of genes related to Salicylic Acid and Jasmonic Acid/Ethylene. We evaluate *NSP4* gene expression in mutants belonging to the RdDM pathway and realized that *NSP4* expression is regulated in a dependent manner by sRNA-mediated silencing pathways in the presence of *Trichoderma*.

TRANSCRIPTIONAL REGULATION OF *STEP*, A SELF- INCOMPATIBILITY GENE IN NICOTIANA

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Abstract:

In angiosperms with bisexual flowers, self-pollination and self-fertilization are very common events, which lead to inbreeding and after a few generations results in inbreeding depression. Progeny derived from self-crosses may be able to survive and grow in favorable environments but changes in these conditions can interfere with survival given their reduced fitness. Several plant families have developed intraspecific reproductive barriers to prevent self-fertilization and promote out-crossing by recognition of gametes. One extensively studied biochemical barrier is self-incompatibility (SI), in which the pistil rejects pollen from genetically related individuals. Gametophytic self-incompatibility (GSI) in Nicotiana from the Solanaceae family is defined by the specificity determinants S-RNase expressed in pistil and SLF expressed in pollen, where the S-specific interaction and recognition between them inside the pollen tube, may lead to pollen rejection depending on the haplotypes of the cross. To date, the identification of several Modifier Genes (MG) involved in this mechanism has contributed to elucidate the biochemical process, which includes redox regulation and programmed cell death. Additionally, genetic and epigenetic regulation of the specificity determinants and MG takes part on this mechanism and seems to have a crucial role in the maintenance of SI phenotype, but only a few examples have been reported. In this work, we offer a new perspective of maintenance and loss of SI response caused by the genetic regulation of MG, instead of the classical approach to analyze the specificity determinants, here we focus in the MG *StEP*, which is specifically expressed in stigmas of self-incompatible *N. alata* but is not expressed in self-compatible *N. plumbaginifolia.* The *StEP* promoter of *N. alata* contains a region of 220bp that has been deleted in *N. plumbaginifolia*, this region includes a regulatory motif called Box III previously reported in the promoter regions of *SRK* and *SLG* genes of *B. oleracea* which are involved in the sporophytic self-incompatibility (SSI) mechanism of the Brassicaceae family.

CHARACTERIZATION OF CROSS-KINGDOM TRH-TARGET INTERACTIONS AND THEIR ROLE IN *TRICHODERMA ATROVIRIDE-ARABIDOPSIS THALIANA* MUTUALISTIC RELATIONSHIP

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Abstract

Plants and microorganisms have co-evolved molecular mechanisms to establish symbiotic relationships. One of these mechanisms is the use of small RNAs (sRNAs) to modulate gene expression to each other, which is called Cross-kingdom RNA interference (Ck-RNAi). The biogenesis of sRNAs derived from transfer RNAs (tRNAs) has been recently reported, although little is known about their biogenesis and function in gene expression.

We analyzed sRNA-seq and mRNA-seq libraries from the interaction between *Trichoderma atroviride*, a mutualistic fungus, and the model plant *Arabidopsis thaliana* at 48-, 72-, and 96 hours of coculture (hcc). We identified tRNA halves (tRHs), a class of tRNA derived fragments (tRFs), as the main type of sRNA found in both organisms, changing their abundances through time, and presenting Ck targeting. Since sRNAs perform target silencing through a Tri-partite interaction, AGO-sRNA-mRNA, we (i) described how our Ck tRHs would interact with their targets through a k-mer binding approach and (ii) characterized argonaute (AGO) proteins by physicochemical and network properties, to identify similarities with other AGOs that load sRNAs > 22 nt.

We found that Ck tRHs do not have a characteristic mode of binding through 5' to 3' ends, when interacting with their targets. Also, comparing different AGOs at sequence, physicochemical, and network levels, we observed similarities between *T. atroviride* AGOs and AGOs with sRNA cargos ~24-26 nt.

Our results suggest that *A. thaliana* and *T. atroviride* Ck tRHs do not present a characteristic mode of binding to regulate their targets. These Ck tRH targets are related with to metabolism, plant defense, transcription, and translation through 48-96 h of mutualistic interaction. Our results, also suggest that *T. atroviride* AGOs share structural characteristics with transcriptional gene silencing (TGS) AGOs.

Keywords: Symbiosis, Cross-Kingdom, sRNA-seq, Bioinformatics, tRH, RNAi, AGO.

EXPRESSION OF IL-2, IL-4, IL-5, IL-10 AND TGFβGENES IN PATIENTS WITH COVID-19 IN MEXICO CITY

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Abstract:

The COVID-19 pandemic, also known as the coronavirus pandemic, has caused a health emergency due to its high power of transmissibility and for causing fatal effects on the population with chronic diseases.

In recent years the scientific community has studied the virus that originates it in order to understand, diagnose, treat and if possible, prevent its transmission and contagion. The dysregulation of the immune system in this disease could be the key to understanding the fatality of its multisystem effects, predominantly respiratory.

With the aim of studying the pathophysiology, pathogenicity and fatality of COVID-19, this study was carried out during the highest peak of contagion in Mexico, in patients infected and hospitalized in Mexico City. Using information from paraclinical studies such as the National Early Warning Score (NEWS) 2, the D-dimer test and the Cabrini Respiratory Strain Score (CAB-RSS), itself as molecular biomarkers in peripheral blood by determining gene expression of cytokines IL2, IL4, IL5, IL10 and TGF β by real-time PCR and the concentration of the proteins IL1β, IL6, IL10, MCP1 and TNF α.

MIR-193B-3P EXPRESSION ANALYSIS AND ITS POSSIBLE INFLUENCE OVER HOMOLOGOUS RECOMBINATION IN TRIPLE-NEGATIVE BREAST CANCER DERIVED CELL LINES

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Abstract:

Breast cancer is the malignant neoplasm with the highest incidence and a leading cause of death worldwide. It is a heterogeneous disease, and it is classified based on its histologic and molecular characteristics, where triple-negative breast cancer (TNBC) has the highest recurrence, metastasis risk, and mortality rate. TNBC is characterized by the absence of estrogen and progesterone receptors and HER2+; due to these characteristics, TNBC has few therapeutic options, which are usually inefficient. Another critical characteristic of TNBC is the prevalence of mutations in breast cancer susceptibility genes, such as BRCA, and other abnormalities in genes associated with the DNA damage response (DDR); novel therapies are aimed to disrupt these DNA repair processes. Homologous recombination (HR) is one of the primary mechanisms for DNA double-strand break (DSB) repair, and its regulation relies heavily on BRCA. Like virtually every cellular process, DDR is tightly regulated, and mounting evidence supports a pivotal role of non-coding RNAs (ncRNAs) such as microRNAs (miRNA) and long non-coding RNAs (lncRNA) in this regulation. Recent research has revealed two ncRNAs involved in HR: ANRIL, an antisense lncRNA encoded in the CDKN2A/B locus as a positive regulator of DSB repair by HR, and miR-193b-3p, a miRNA transcript encoded in the 16p13.12 region, identify as a tumor suppressor and negative regulator of proteins involved in HR. In this work, we identified a negative correlation between these ncRNAs through a bioinformatic analysis and found differential expression of miR-193b-3b in TNBC-derived cell lines. Our findings suggested an antagonistic role of miR-193b-3p opposite ANRIL with regulatory consequences on HR in TNBC.

EPIGENETIC REGULATION AND EXPRESSION OF THE CA^{2+} SIGNALING GENES IN AN EPITHELIAL-MESENCHYMAL TRANSITION MODEL IN BREAST CANCER CELL LINES

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Abstract:

Breast cancer occupies the second place in mortality among all cancer types, being metastasis involved in ~ 90% of all cases. In breast cancer, metastasis is in part regulated by the Epithelial-Mesenchymal Transition (EMT), where epigenetic mechanisms regulate gene expression to induce the transition between states. Inhibition of epigenetic mechanisms mitigates the acquisition of mesenchymal phenotype in breast cancer cells[1]. Another major mechanism involved in the regulation of the EMT is the calcium ion (Ca^{2+}) signaling. Recently, we demonstrated that the expression of the genes involved in Ca^{2+} signaling is altered in breast cancer samples and cell lines, and their expression is associated with modulation of epigenetic mechanisms[2]. However, is not clear whether the expression of the Ca^{2+} signaling genes is modulated during EMT and whether epigenetic mechanisms are involved in its regulation. Resveratrol (RSV) is a phytoestrogen abundant in grapes and berries. This compound can inhibit histone deacetylases in breast cancer cells resulting in a drop in cell viability[3]. The present work aims to study the changes in expression and the epigenetic regulation of genes involved in Ca^{2+} signaling on an EMT model in breast cancer cell lines treated with RSV through RNA sequencing.

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INFLUENCE OF EPIDRUGS ON DENTAL STEM CELLS FROM A BIOCHEMICAL AND MOLECULAR APPROACH

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Abstract:

Dental stem cells (DSCs) are potent tools for regenerative medicine, tissue engineering, and cell-based therapy because of their multi-lineage differentiation, self-renewal potential, low immunogenicity, capability for expansion, and ease of accessibility [1]. However, the application of DSCs in cell-based therapy may present challenges, such as the low differentiation to another stem cell lineage. Stem cell lineage commitment and differentiation are regulated by an intricate range of environmental factors of which epigenetic influence is vital. Epigenetic modification of DNA and DNA-associated histone proteins has been demonstrated to control cell phenotype and regulate the renewal and pluripotency of stem cell populations.

The activities of the nuclear enzymes, histone deacetylases, are increasingly being recognized as potential targets for pharmacologically inducing stem cell differentiation and dedifferentiation [2]. One attractive strategy that can target epigenetic change is the application of chemical modifiers as epigenetic enzyme inhibitors, termed epidrugs like Trichostatin A (TSA) and valproic acid (VPA). These modifiers have been studied in the induction of epigenetic regulation commitment to another stem cell lineage. In this work, we evaluate the impact of TSA and VPA as epidrugs in dental stem cells to adipogenic commitment as attractive candidates for regulating Histone acetylation and deacetylase enzymes from a biochemical and molecular approach using western blot and qPCR analysis.

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IDENTIFYING GENES DEVOTED TO THE CELL DEATH PROCESS IN THE GENE REGULATORY NETWORK OF *USTILAGO MAYDIS*

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Abstract:

Cell death is a process that can be divided into three morphological patterns: apoptosis, autophagy and necrosis. In fungi, cell death is induced in response to intracellular and extracellular perturbations, such as plant defense molecules, toxins and fungicides, among others. *Ustilago maydis* is a dimorphic fungus used as a model for pathogenic fungi of animals, including humans, and plants. Here, we reconstructed the transcriptional regulatory network of *U. maydis*, through homology inferences by using as templates the well-known gene regulatory networks (GRNs) of *Saccharomyces cerevisiae*, *Aspergillus nidulans* and *Neurospora crassa*. Based on this GRN, we identified transcription factors (TFs) as hubs and functional modules and calculated diverse topological metrics. In addition, we analyzed exhaustively the module related to cell death, with 60 TFs and 108 genes, where diverse cell proliferation, mating-type switching and meiosis, among other functions, were identified. To determine the role of some of these genes, we selected a set of 11 genes for expression analysis by qRT-PCR (sin3, rlm1, aif1, tdh3 [isoform A], tdh3 [isoform B], ald4, mca1, nuc1, tor1, ras1, and atg8) whose homologues in other fungi have been described as central in cell death. These genes were identified as downregulated at 72 h, in agreement with the beginning of the cell death process. Our results can serve as the basis for the study of transcriptional regulation, not only of the cell death process but also of all the cellular processes of *U. maydis*.

Soberanes-Gutiérrez CV, Pérez-Rueda E, Ruíz-Herrera J, Galán-Vásquez E. Identifying Genes Devoted to the Cell Death Process in the Gene Regulatory Network of Ustilago maydis. Front Microbiol. 2021 May 21;12:680290. doi: 10.3389/fmicb.2021.680290. PMID: 34093501; PMCID: PMC8175908.

LONG NON-CODING RNAS AND THEIR ASSOCIATION WITH STEMNESS IN TRIPLE NEGATIVE BREAST CANCER

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Abstract:

Background: Triple negative breast cancer (TNBC) is the most aggressive subtype and represents 15 to 23% of all cases of breast cancer, it is associated with an earlier age of onset of the disease, greater metastatic potential, incidence of relapses, and has a higher percentage of cancer stem cells (CSC). CSC directs the initiation, maintenance, and progression of the disease, and the response to cancer therapy. It is well known that long non-coding RNAs (lncRNAs) are important regulators of the stem population because they regulate the expression of transcription factors that maintain pluripotency and participate in the acquisition and maintenance of chemoresistance, control cell division, and determine cell fate. Therefore, this study aims to identify differentially expressed (DE) lncRNAs in triple-negative tumors (TN) compared to luminal tumors and their possible relationship in the regulation of the stem phenotype. *Methodology*: To identify DE lncRNAs (fold change > 2 or < -2 and FDR < 0.05), we obtained expression data of 2 cohorts of breast cancer patients (n=30 and n=56). Differential expressed lncRNAs were selected in TN tumors compared to luminal tumors. Through bioinformatic analysis, we selected lncRNA DE that correlated positively with the expression of stem cell markers (POU5F1, cKIT, NOTCH1, etc.) and negatively with differentiation markers (MUC1, CDH1, ESR1, etc.). The results were validated in an independent cohort of the TCGA. *Results*: We found 30 DE lncRNAs shared in both cohorts, 25 inhibited and 5 overexpressed in the TN tumors, of these 3 overexpressed lncRNAs correlated positively with markers of stemness and negatively with markers of differentiation and 6 inhibited lncRNAs exhibited an inverse correlation. The differential expression of lncRNAs was confirmed in a TCGA cohort (N=503), obtaining validation of 3 of the 6 inhibited lncRNAs (ENSG00000224559, ENSG00000223808 and ENSG00000232638) and 2 of the 3 overexpressed lncRNAs (ENSG00000280916 and ENSG00000229335).

SELF-MODULATION OF VECTOR PROMOTERS BY OVEREXPRESSED BHLH TRANSCRIPTION FACTORS

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Abstract:

The eukaryotic basic Helix-Loop-Helix transcription factors (bHLH TF) modulate gene expression by binding to the E-box DNA sequences localized in enhancer and promoter regions. TCF3 is a type I bHLH TF or E-protein. It homodimerizes and heterodimerizes with type II tissue-specific bHLH TFs, including ASCL1, TAL2 or SCX. The expression of bHLH TFs is tightly regulated due to their involvement in tissue development and pathologies. One of the most common experimental approaches to assess the function of bHLH TFs is by overexpressing them in different cell types. Our lab overexpresses these factors utilizing adenoviral vectors in lung epithelial cells.

When the bHLH transcription factor TCF3 was overexpressed from a constitutive cytomegalovirus promoter (pCMV) within an adenoviral vector, the expression of itself and of a cotransduced type II bHLH TFs was affected at the mRNA and protein levels. When analyzing gene expression from a second pCMV promoter within the virus, we observed that the bHLH TF TCF3 negatively modulated the pCMV enhancer-promoter expression at the transcriptional level. Furthermore, we found that this effect depended on the multiplicity of infection utilized during the transduction and on the presence of additional bHLH TFs cotransduced with TCF3 viral vectors. Knowledge of the self-regulation by overexpressed bHLH TFs is relevant for all fields utilizing viral vectors to overexpress transcription factors.

EFFECT OF VALPROIC ACID ON THE GROWTH OF DENTAL STEM CELLS

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ABSTRACT:

The use of Stem Cells (STs) in tissue engineering has increased the possibilities of repairing or regenerating tissues and organs. Dental Mesenchymal Stem Cells (DMSCs) are an attractive option from autologous source because they have demonstrated plasticity towards diverse cell lineages and their procurement does not represent ethical conflicts.

Among the DMSCs that can be obtained from the oral cavity are dental pulp mesenchymal stem cells (DPMSCs), which are isolated from pulp tissues of permanent teeth, and dental follicle mesenchymal stem cells (DFMSCs), which are obtained from tissue found between the enamel surrounding the third molar teeth[1].

Currently, the control of cell fate during differentiation of DPMSCs and DFMSCs is a challenge that has been addressed from an epigenetic approach being the modification by histone acetylation one of the most studied strategies in recent years which has made it of interest in our research group.

Histone acetylation is a dynamic process where acetyl groups are added or removed from histones, thereby promoting chromatin remodeling, and allowing the expression or suppression of gene expression associated with a specific lineage. Histone acetylation is mediated by enzymes: histone acetyltransferases (HAT) that add acetyl groups, and histone deacetylases (HDAC) that remove them. Due to the mechanism of action of HDACs[2], they are key to the study of cell proliferation, growth and differentiation processes. One of the strategies that have been addressed is the use of HDAC inhibitors (I-HDACs) such as valproic acid (VPA).

Since the cellular effects of VPA on DPMSCs and DFMSCs cells are unknown, the aim of this study was to evaluate the cell proliferation and cell viability of DPMSCs and DFMSCs exposed to two concentrations of VPA. For this purpose, $2x10^4$ cells/mL of each cell line were seeded in petri dishes and 4 and 8 mM VPA were used in a period of 72 h. Subsequently, cell quantification was performed using the trypan blue method and a photographic record was made of their morphology during their culture with an inverted microscope.

The data obtained show that the concentration of 8 mM VPA generates an important change in the morphology, losing its characteristic fibroblastoide morphology. Likewise, cell proliferation decreases, while viability remains unchanged compared to the control. This could suggest that there is a VPA concentration-dependent relationship in the proliferation and morphology in these cells of dental origin.

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2.- Podobinska, M. et al. (2017) 'Epigenetic Modulation of Stem Cells in Neurodevelopment: The Role of Methylation and Acetylation', Frontiers in Cellular Neuroscience. Vol (11):23

ROLE OF HDAC3 ON NUCLEAR MORPHOLOGY AND PROFIBROTIC PHENOTYPE IN LUNG FIBROBLASTS

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Abstract:

Idiopathic pulmonary fibrosis (IPF) is associated with the activation of fibroblasts, and it may be related to epigenetic changes such as histone acetylation that increase the active transcription. In this context, HDACs are responsible for compacting chromatin by removing acetyl groups. In lung diseases, including pulmonary fibrosis, was reported aberrant HDACs expression, notably HDAC3 increased in IPF fibroblasts, but the impact of its deacetylase activity in these cells remains unexplored. Here, we used IPF and control fibroblasts to determine the influence of HDAC3 on chromatin remodeling and gene expression associated with IPF signature. Additionally, to determine if matrix stiffness modifies HDAC3 expression and function, the cells were grown on hydrogels (HG) of 23 and 1 KPa to mimetic stiffness of a fibrotic lung matrix or normal, respectively. We found that HDAC3 decreased in the nucleus of IPF fibroblasts, which correlated with changes in nucleus size and heterochromatin loss. The inhibition of HDAC3 with RGFP966 in control fibroblasts causes a state of hyperacetylation in H3K9 and provokes an increased expression of profibrotic genes Col1A1, ACTA2, and p21. In controlled stiffness HG, we detected a decrease in nuclear HDAC3 and an increase in fibrotic genes in control fibroblasts when grown in 23 kPa HG compared with 1 kPa HG; however, in IPF fibroblasts, these changes were not observed. Finally, in fibroblasts treated with latrunculin b, we observed that the expression of HDAC3 increases in the nucleus, suggesting that its expression is dependent on the actin filaments. These data indicate that HDAC3 is crucial for maintaining a chromatin structure and normal nucleus morphology. HDAC3 may be considered an antifibrotic molecule and sensitive to mechanical stimuli, so drugs that block cells' ability to sense stiffness could be a potential treatment for IPF.

PHENOTYPIC ANALYSIS OF INSERTIONAL MUTANTS OF THE *A.THALIANA* TWINKLE PRIMASE HELICASE, SALK_152246, CS855183 WISCDSLOX423D2 AND SALK_148150

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Abstract:

DNA replication has been studied since the middle of the 20th century. (Gao et al. 2019). In the *A.thaliana* replisome the helicase-primase (HP) performs the dNTPs hydrolysis, thus allowing the unwinding of the double helix, interacting also with the other proteins present in the plant replisome. However, there are still details that have not been reported on visualizing how a functional replisome is formed and how the concerted synthesis of the leading and lagging strand in a replication fork takes place. In order to elucidate the function of twinkle in the phenotypic expression of *Arabidopsis thaliana*, a genotypic and phenotypic study was performed in the insertional mutants PH1 SALK_152246, PH2 CS855183 WISCDSLOX423D2 and PH3 SALK_148150, where the growth of the plants in each mutant was lower compared to the wild type. In the most evident alterations, in the meristem, some variations were observed in the PH2 insertion, generating a larger amount of leaves and alterations in their shape. In addition, in some individuals the affectations are so severe that they reduce the life span of the plant.

Gao, Y., Cui, Y., Fox, T., Lin, S., Wang, H., de Val, N., & Yang, W. (2019).
Structures and operating principles of the replisome. Science, 363(6429), eaav7003.

ARGONAUTE5 REGULATES THE NODULE DEVELOPMENT IN *PHASEOLUS VULGARIS*

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Abstract:

Both plant- and rhizobia-derived small RNAs play a pivotal role in regulating the root nodule symbiosis in legumes. Small RNAs, in association with Argonaute proteins, tune the expression of genes participating in the nodule development and rhizobial infection. However, the role of Argonaute proteins in this symbiosis has been overlooked. In this study, we provide transcriptional data supporting the notion that Argonaute5 (AGO5) plays a determinant role in the root nodule symbiosis in *Phaseolus vulgaris*. A spatial-temporal transcriptional analysis revealed that the promoter of *PvAGO5* has activity in in root hairs from rhizobia-inoculated roots, nodule primordia and mature nodules. Transcriptional analysis by RNA sequencing revealed that gene silencing of *PvAGO5* affected the expression of genes involved in the biosynthesis of the cell wall and phytohormones involved in the rhizobial infection process and nodule development. We also observed that the expression of genes involved in the plant defense response was upregulated in *PvAGO5*-RNAi mature nodules. PvAGO5 immunoprecipitation-coupled with small RNAs sequencing revealed the small RNAs bounded into AGO5 during the root nodule symbiosis. The data presented shed light on the role that AGO5 may play during the root nodule symbiosis in *P. vulgaris*.

TARGET GENES, CELL PROCESSES AND MIR-23B-3P EFFECT ON HMGB2 EXPRESSION IN CERVICAL CÁNCER

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Abstract:

miR-23b-3p is proposed to be a suppressor tumor in CC, however, the biological processes regulated by its target genes still unknown. The HMGB2 protein regulates the proliferation of CC cells. The decreased expression of miR-23b-3p contrasts with the levels of HMGB2 mRNA, however, the relationship between miR-23b-3p and HMGB2 in CC has not been studied. **Objective:** To identify biological processes regulated by target genes of miR-23b-3p and to evaluate the effect of miRNA on HMGB2 mRNA expression in C-33A and CaSki cells of CC. Material and methods: Target genes of miR-23b-3p were predicted in TargetScan and miRDB. Predicted targets were subjected to GO functional enrichment analysis of KEGG processes and pathways through the DAVID program. The expression of HMGB2 in patients with CC was obtained from the GEPIA and CCLE platforms. C-33A and CaSki cells were transfected with 100 nM mimic of miR-23b-3p for 24 h. RNA was obtained with Trizol from transfected C-33A and CaSki cells and the expression of miR-23b-3p and HMGB2 was determined by RT-qPCR. A value of $p<0.05$ was considered significant. **Results**: Bioinformatic analysis suggests that 785 genes are targets for miR-23b-3p and that of these 101 mRNAs participate in proliferation, 70 in apoptosis and 94 in migration; 18 genes, including HMGB2, have a functional role in these three cellular processes. The 3'UTR region of HMGB2 has 3 MRE sites for miR-23b-3p. HMGB2 expression is significantly augmented in tissues from CC patients. In C-33A and CaSki cells the expression of HMGB2 is significantly higher than in HaCaT. Overexpression of miR-23b-3p decreases HMGB2 expression in C-33A cells, but not in CaSki. **Conclusions:** miR-23b-3p regulates characteristic cancer processes through its target mRNAs. HMGB2 is a likely target of miR-23b-3p that is involved in migration, proliferation, and apoptosis. The results suggest that HMGB2 expression is differentially regulated in C-33A and CaSki cells.

DEVELOPMENT OF A WHOLE CELL BIOSENSOR USING *BACILLUS SUBTILIS* SPORES FOR ARSENIC DETECTION IN WATER

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Abstract:

Arsenic is recognized as a high health risk contaminant [1]. Arsenic contamination strongly affects surface and groundwater, negatively impacting drinking water, and consequently increasing the risk to human health. The limit of arsenic in water for human consumption, established by the WHO and the new Mexican regulation (NOM 127, 2021) is 10 µg/L [2]. Given the geogenic origin of the contamination, in Mexico and specifically in Durango, there are wells supplying water for human consumption that greatly exceed these limits [3].

There are many analytical methods for the detection of As that are usually expensive, handled by specialized personnel and not applicable for the rapid detection of tests applied in situ, and on a large scale [5], so the use of biosensors to perform the detection is a promising alternative due to features such as rapid detection, lower cost and the ability to measure the presence of As [6]

In this study, a whole-cell biosensor for As was developed using the promoter of the ars operon fused to the green fluorescent protein (GFP) in the sporulating bacterium Bacillus subtilis, evaluating the response to As by fluorescence microscopy and fluorescence quantification using a Variouskan Lux plate reader. This biosensor was developed with the purpose of being used in the detection of the presence of arsenic in water in quantities greater than 10 µg/L, and thus having an innovative alternative for in situ detection of the contaminant in water supply sources for human consumption (wells).

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[3] Carrillo-Chávez et al., (2000). *Environmental Geology*, *39*(11), 1295–1303.
[4] Alarcón-Herrera et al., 2001 *Tecnología y ciencias del agua*, *16*(4), 63-70.
[5] Ma et al., 2014 Analytica Chimica Acta, 831, 1-23
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THE MITOCHONDRIAL GENOME OF HEALTHY MICE AND HUMANS CONTAINS A HIGH DIVERSITY OF GENETIC VARIANTS

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Abstract:

Mutations in the mitochondrial genome have been linked to aging in humans, primates and rodents and cause a range of neuromuscular diseases in human. We show here that the mitochondrial genome of embryonic, adult, and aged mouse brain from two different strains contains a diversity of single nucleotide variants and deletions affecting both, coding and non-coding regions with no overt age-related increase in abundance. We also detected both types of variants *de novo* in oocytes and in adult liver and found that in half of the human samples analyzed, over 60% of the mitochondrial genome copies may bear lesions such as a group of base substitutions of low heteroplasmy or clustered intergenic deletions.

IDENTIFICATION OF GENETIC VARIANTS ASSOCIATED WITH SUSCEPTIBILITY IN THE DEVELOPMENT OF CERVICAL CANCER

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Abstract:

Cervical cancer (CC) is a multifactorial disease that originates in cells of the cervix, it initially manifests through preneoplastic lesions. Persistent infection with high-risk Human Papilloma Virus (HR-HPV) is necessary, but not sufficient for the development of CC. The factors that promote the persistence and maintenance of the infection, as well as the pathways that trigger carcinogenesis, are still not fully understood. Susceptibility or resistance to developing this disease may be influenced by individual differences in DNA sequence. However, in CC, it have not been possible to associate the variants present in an only gene with its development.

Know the differences in genetic variation between healthy women and those who develop CC could provide us with more information about the genetic factors involved in the development of this cancer and extensive information can be obtained through massive identification analysis. So, we perform a NGS analysis on genomic DNA samples obtained from cervicovaginal exudates of women with CC. This was performed using a sequencing panel for the analysis of 150 genes that are commonly altered in different types of cancer. We process the 12 samples data trough bioinformatic pipeline for the variant calling analysis. In silico analysis allowed us to identify pathogenic variants and other that could have a direct effect in the gene product. The validation of some of these variants was carried by Sanger sequencing.

Next, we pretend to carry on a genetic association analysis and the design of targeted sequencing panel for the interest variants that which were selected of the previous analysis. For the selection of these variants, we follow three criteria: population data contained in databases, predictive and functional analysis and previous association studies of the variants in cancer. We have selected 45 variants, located in 29 genes. We designed primers for these variants, which are being amplified by conventional PCR in DNA obtained from peripheral blood and cervical samples from women with cervical lesions. This will allow us carry on association and statistical analysis and the design of a target panel.

ROLE OF TRANSLATION FACTOR EIF4E FAMILY MEMBERS DURING ROOT DEVELOPMENT UNDER ABIOTIC STRESS IN *ARABIDOPSIS THALIANA*

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Abstract:

Plant sessile nature demands molecular mechanisms for adaptation to abiotic stress, such as sudden temperature changes, nutrient deprivation or dehydration. One of these relies on rapid adjustment of mRNA translation levels. Around 95% of mRNA are translated in a cap-dependent manner. Translational initial factor eIF4E recognizes the cap structure on mRNA 5' end and serves as initial platform to assemble ribosomes. *Arabidopsis thaliana* isoforms, eIF4E and eIF(iso)4E, have been found necessary during cold responses, since null mutants were more susceptible to freezing challenge than Col-0 WT plants (Salazar-Díaz et al, 2021). Moreover, their expression was up-regulated during cold acclimation at 4º C, along with classical cold response genes *TCF1* and *COR15A*. Interestingly, eIF(iso)4E controls translation of mRNA preferentially expressed in root, such as phosphate transporter 1 (*PHO1*) or sucrose transporter 3 (*SUC3*), and responsive to cold, such as *TCF1* (Martinez-Silva et al., 2012). Nonetheless, root development under stress conditions has not been analyzed in detail in the absence of eIF4E family members. Present ongoing work is focused on the function of eIF4E, eIF(iso)4E and the non-canonical isoform 4E-HP in root growth under control and abiotic stress conditions using the corresponding mutant plants. To mimic abiotic stress, we used jasmonic acid (JA) and abscisic acid (ABA) hormones. Single mutants for either eIF4E isoform displayed reduced root growth under control conditions as compared to Col-0 WT. Root growth further decreased in the presence of JA or ABA for all lines and WT. Especially, the *eif4e* mutant had the lowest root growth in both control and JA or ABA treatments. The translational status of particular mRNAs related to root development, such as *PLETHORA1* and *WOX5*, and other related to stress responses will be assessed through polyribosomal profiling to unravel the role of eIF4E proteins in mRNA metabolism adjustments under stress.

This work is supported by PAPIIT IN218921 (DGAPA), PAIP 5000-9118 (FQ) and by postdoctoral scholarship from DGAPA, UNAM.

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Martínez-Silva A. V., et al. (2012). *PLOS ONE* 7:e31606.

EXPRESSION *IN VITRO* OF TWO VIRULENCE DETERMINANTS FROM *AVIBACTERIUM PARAGALLINARUM*

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Abstract:

Avibacterium paragallinarum is a Gram-negative bacterium of the *Pasteurellaceae* family and is the causative agent of infectious coryza disease in poultry. To have better control strategies for infectious coryza, several genomes of *A. paragallinarum* have been sequenced, these come from recently isolated strains producing respiratory diseases in farm birds and contains several virulence determinants. To know the changes in expression of the virulence factors of two contrasting strains in the laboratory, 2015 and COJ7 strains were selected. These strains vary in their growth rate properties in the culture media recommended for *A. paragallinarum* and were used to determine the level of expression of transcripts of the *fur* and *cdtABC* genes. The first gene is the main controller of internal iron homeostasis and the second is encoding a toxin related to cell damage, both related to pathogenic processes. The expression quantification was done by means of relative qRT-PCR using specific primers with high efficiency, as a response to iron changes. For this, the beta-subunit of RNA pol and *rpo*N genes were also included as constitutive and basal expression markers in *A. paragallinarum*. In this work it was observed that *fur* is a constitutive gene that shows important changes in expression depending on the concentrations of iron supplied in the culture medium. While the *cdt*B gene responds less to iron changes, it does so in a constitutive way with small increases when iron is depleted. This is an important difference that relates to Fur protein and a virulence determinant in *A. paragallinarum*. An *in-silico* study strategy is underway to better understand the transcriptional expression behavior of the genes included in this study

ABF1 AS AN ESSENTIAL PROTEIN IN *CANDIDA GLABRATA*, AT DIFFERENT CELLULAR PROCESSES

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Abstract:

Abf1 or ARS binding factor 1, is a DNA binding protein involved in multiple cellular processes in the yeast *Saccharomyces cerevisiae*, such as the transcriptional regulation of diverse metabolic pathways, DNA replication, silencing of the cryptic mating *loci HML* and *HMR* and DNA damage repair. We have identified the orthologous *CgABF1* gene in the opportunistic fungal pathogen *Candida glabrata*, which is closely related phylogenetically to *S. cerevisiae*, We determined that *Cg*Abf1 is essential for viability and that it participates in the subtelomeric silencing of several *EPA* genes, which code for adhesins and constitute some of the virulence factors of this pathogen. In this work, we sought to determine the function of *Cg*Abf1 in *C. glabrata*. Due to the possible role of *Cg*Abf1 on DNA replication, we determined whether depletion or over-expression of *Cg*Abf1 causes loss of viability. We designed a “shut off” system for *CgABF1* depletion using the *MET3* promoter, which is repressed by the addition of methionine and cysteine. We also generated an over-expressing system in which *CgABF1* is transcribed by the *MT1* promoter, inducible by adding copper to the media. We evaluated the viability in both systems and observed in both, depletion and over-expression of *Cg*Abf1, that there is a dramatic loss of viability even at early time points, and these data correlate with the anormal distribution of nuclei in the cells of both absence and over-expression of *Cg*Abf1. Data from experiments to determine whether Abf1 forms homodimers, using the Bimolecular Fluorescence Complementation system (BiFC) will be presented.

IDENTIFICATION OF GENETIC ALTERATIONS THAT LEAD TO *CRLF2* OVEREXPRESSION IN PEDIATRIC PRE-B ACUTE LYMPHOBLASTIC LEUKEMIA

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Abstract:

Background. Pre-B acute lymphoblastic leukemia (pre-B ALL) is the most common pediatric cancer. Identifying various genetic alterations has made it possible to assign risk stratification to patients. Alterations in the *CRLF2* gene that lead to its overexpression and hyperactivate the JAK/STAT signaling pathway have recently been described; the most common are: a) *P2RY8-CRLF2* gene fusion, b) *IGH-CRLF2* translocation, and c) the less frequent somatic mutation c.695T>G (F232C) in *CRLF2*. It is essential to identify *CRLF2* alterations in pediatric pre-B ALL patients, as they confer an unfavorable prognosis and are helpful in the clinical management of patients.

Aim. To identify *P2RY8-CRLF2*, *IGH-CRLF2*, and *CRLF2* c.695T>G mutation alterations in pediatric patients diagnosed with pre-B ALL overexpressing the *CRLF2* gene.

Methods. We selected 48 bone marrow samples from previously studied pre-B ALL patients with *CRLF2* overexpression; we searched for the *P2RY8-CRLF2* fusion by RT-PCR, the *IGH-CRLF2* translocation by FISH, and the c.695T>G mutation by sequencing a 199bp PCR product flanking the mutation site. We searched for gene variants using the CodonCode Aligner software.

Results. Alterations in the *CRLF2* gene were found in 56% (27/48) of the analyzed patients, thus determining the genetic cause of *CRLF2* overexpression in 27 patients with the following distribution: *P2RY8-CRLF2* fusion in 27% (13/48), *IGH-CRLF2* translocation in 27% (13/48), and c.695T>G mutation in 2% (1/48). The positive sample for the pathogenic *CRLF2* mutation c.695T>G (Phe232Cys) had an allele frequency of 0.38 and corresponded to the patient with the highest gene expression within the cohort. In addition, the polymorphic variants c.730G>A (Val>Met) were found in 8% (4/48) and the intronic mutation 20980C>A in 5% (2/48) of the analyzed samples. We did not find genetic alterations in *CRLF2* in 44% (21/48) of the patients.

Conclusions. *P2RY8-CRLF2*, *IGH-CRLF2*, and the c.695T>G mutation were identified in pediatric patients with pre-B ALL overexpressing the *CRLF2* gene. The identification of these alterations is clinically relevant because of their unfavorable prognostic implications.

MOLECULAR ANALYSIS OF TAU95 AND TAU131, SUBUNITS OF TRANSCRIPTION FACTOR TFIIIC, IN THE HUMAN PATHOGEN *LEISHMANIA MAJOR*

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Abstract:

Leishmania is a protozoan parasite that causes different types of leishmaniasis in tropical regions of the world. It presents atypical mechanisms of gene expression, including polycistronic transcription and maturation of mRNAs by trans-splicing. Eukaryotic transcription is carried out by RNA Polymerases (RNA Pol) I, II and III. RNA Pol III is responsible for the transcription of genes encoding essential small RNA molecules, such as 5S ribosomal RNA (5S rRNA) and transfer RNAs (tRNAs). In yeast and higher eukaryotes, RNA Pol III requires three general transcription factors: TFIIIA, TFIIIB and TFIIIC. In particular, TFIIIC IS A LARGE SIX-SUBUNIT PROTEIN COMPLEX ORGANIZED INTO TWO SUBDOMAINS, TAUA AND TAUB. Notably, in *Leishmania* and other trypanosomatid parasites only TFIIIB has been identified and characterized. The isolation of RNA Pol III transcriptional complexes by tandem affinity purification assays allowed us to identify the orthologs of subunits Tau95 and Tau131 (part of subdomain TauA of TFIIIC) in *L. major*. Bioinformatic analyzes showed that Tau95 possesses the conserved domains found in orthologs from other species: a dimerization domain, a winged helix domain, and a region rich in acidic amino acids. Also, its predicted 3D structure is very similar to the one reported in yeast. Tau131 from *L. major* contains the characteristic tetratricopeptide repeats found in the orthologs from other organisms. To identify the proteins that interact with Tau95 in *L. major*, tandem affinity purifications and mass spectrometry analyses were performed. Among the proteins identified, we found two more subunits of TFIIIC, as well as several RNA Pol subunits, transcriptional regulators and chromatin remodelers. In addition, we are currently analyzing *L. major* cell lines that overexpress Tau131.

This work was supported by grant IN214221 (PAPIIT, UNAM).

PLANT-ASSOCIATED BACTERIA (PAB): RESOURCES OF SPECIALIZED METABOLITES

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Abstract:

In nature, bacteria produce compounds as mechanisms to compete with other microorganisms for the resources available in their ecosystems. Bacteria that emerge victorious from this competition sometimes establish symbiotic relationships with their hosts to achieve a coexistence where both parties benefit. Plant symbiotes have recently drawn attention due to their ability to produce diverse bioactive compounds. In this context, properties that had been attributed to plants may be due to the living organisms that colonize them.

This project proposes the isolation of PAB from plants resident in Mexico and adds their genetic information to a database of 388 public genomes of 59 genera of bacteria isolated from plants, from 42 countries. The media with the best results to cultivate PAB under laboratory conditions and enhance the production of their specialized metabolites were King's Broth and Flour and TWYE. 16 rRNA analysis made it possible to identify at genus level the colonies of bacteria obtained from samples collected from the Valle de los Fantasmas, a protected region around a mining area in San Luis Potosí, Mexico. Different plant tissues were used to differentiate the PAB cultures of bacteria from the same plant, as well as and the epiphytes, endophytes and rhizospheric bacteria. Statistical analysis and genome mining indicated which bacteria are the best producers of compounds with potential biotechnological applications. In addition, the bioinformatic analysis helps us to better understand the behavior of PAB within their hosts and the evolution of the compounds produced to guarantee the persistence of the bacteria and host symbiosis.

ASSESSING THE ROLE OF HOG1 IN NEUTRAL LIPID SYNTHESIS IN THE YEAST DEBARYOMYCES HANSENII

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Abstract:

The metabolism of lipid-accumulating yeasts (oleaginous) has been little studied compared to that of Saccharomyces cerevisiae due to the lack of molecular tools. In S. cerevisiae, MAP kinase ScHog1 can upregulate lipid synthesis. However, it is unknown if this positive regulation is conserved in oleaginous yeasts, which can accumulate more than 20% of dry weight as lipids. Debaryomyces hansenii is an oleaginous yeast that produces neutral lipids (NLs) under conditions of nitrogen limitation in the presence of excess carbon sources. It is unknown whether Hog1 is involved in the de novo lipid synthesis in D. hansenii or other oleaginous yeasts. This study aims to characterize the synthesis of NLs in response to nitrogen limitation and determine if Hog1 contributes to lipid accumulation in D. hansenii. We quantify the production of NLs using the BODIPY probe, which allows us to estimate the intracellular lipids by fluorescence combining spectrofluorometry and flow-cytometry. Our results suggest that the most significant accumulation of NLs occurs during the stationary phase under nitrogen-limited conditions. In the highest lipogenic condition, the expression of several genes involved in the de novo lipid synthesis pathway was analyzed in a Dhhog1Δ mutant. We will discuss the role of DhHog1 in the lipid accumulation of D. hansenii.

EXPRESSION PROFILE OF SIX GENES INVOLVED IN NEUTRAL LIPID SYNTHESIS IN ANTARCTIC YEAST RHODOTORULA MUCILAGINOSA

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Abstract:

Rhodotorula mucilaginosa M94C9 is an oleaginous yeast isolated from Antarctic soil and considered poly-extremotolerant for growth in conditions of cold, osmolarity, salinity, and oligotrophy. This yeast has been reported as capable of accumulating large quantities of neutral lipids in nitrogen-limiting conditions. Nonetheless, the studies of de novo synthesis of fatty acids are scarce since not all of the genes involved have been fully identified in R. mucilaginosa. The primary genes of the synthesis pathway in other yeasts are ACLY, ACC1, FAS1, FAS2, PAH1, and DGA1. In this study, we evaluated growth, biomass, triacylglycerol (TAGs) production, and lipid bodies (LBs) formation in R. mucilaginosa under different conditions of nitrogen availability and excess glucose in the medium. We observed an increase in TAGs production in the nitrogen starvation condition. Also, we found large-size LBs during the stationary phase. Subsequently, we identified the ORFs of the genes above and determined the expression profiles under different lipogenic conditions. Preliminary gene expression analyses during the exponential phase suggest that RmACLY, RmACC1, RmFAS1, and RmFAS2 are up-regulated, whereas RmPAH1 and RmDGA1 (the last of the pathway) are down-regulated. Therefore, the negative regulation of RmPAH1 and RmDGA1 limits the activation of lipogenesis during exponential growth. The expression of RmPAH1 and RmDGA1 during the stationary phase should allow the redirection of carbon metabolism towards lipid production. Understanding the synthesis of the neutral lipids in R. mucilaginosa will broadly impact the oleochemicals industry, such as biofuels.

TRANSGENERATIONAL EFFECTS OF GLUCOSE EXPOSURE OVER C. ELEGANS BEHAVIOR

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Abstract:

Diabetes and obesity are two of the leading causes of health issues worldwide. Both are associated with high caloric diets and a sedentary lifestyle which cause an increase in blood glucose levels. High glucose exposure has negative effects on diverse tissues including the nervous system. Exposure to elevated glucose decreases memory and cognitive function while increasing the risk of neurodegenerative disorders; yet, the mechanisms behind these effects are unclear. Furthermore, the effects of glucose exposure on future generations are not well understood. It is known that nutritional stimuli have effects over future generations that reflect the overall healthspan of the individuals. Using the nematode Caenorhabditis elegans as a model for glucose exposure, we have analyzed the effects of such exposure on associative memory and behavior to odorants. We discovered that glucose exposure impairs associative memory and affects basal chemotaxis. We also defined that glucose-dependent changes on basal chemotaxis are dependent on the transcription factor crh-1 (CREB) as well as the insulin-like pathway. Furthermore, we determined that glucose exposure for one generation causes the phenotypes over conduct to have an intragenerational effect; yet, exposure during multiple generations leads to a transgenerational phenotype. Overall our work highlights the interplay between the nutritional environment and behavior, as well as its consequences in future generations, opening the possibility to characterize the molecular pathways involved in both phenomena.

ABSTRACTS | Posters Immunology & Parasitology

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EFFECT OF TESTOSTERONE ON ANTIOXIDANT ACTIVITY AND OXIDATIVE STRESS MARKERS IN A MURINE MALARIA MODEL

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Abstract:

Malaria is the deadliest parasitic disease on the planet. In the year 2021, 267 million new cases were reported, and it caused 461 thousand deaths. It presents sexual dimorphism; men develop more severe symptoms and higher mortality than women. A probable explanation is the difference in the concentrations of sex hormones, with women presenting higher concentrations of oestradiol than men, while men have a higher concentration of testosterone than women. Testosterone has been shown to induce immunosuppression, which would explain the differences in symptomatology associated with oxidative stress; that in malaria is produced in the cells of the immune response. It is unknown whether testosterone modulates the oxidative stress that constitutes the main route of elimination of *Plasmodium*. Therefore, in this work, the effect of testosterone was determined under different conditions, for which groups of 5 male CBA/Ca mice infected with Plasmodium berghei ANKA were designed with different treatments: No treatment (ST), treated with vehicle (VEH), treated with letrozole; which is an inhibitor of the enzyme that bio transforms testosterone (LET), testosterone-treated (TEST)and vehicle-treated (GX VEH) or testosterone-treated (GX TEST) gonadectomized mice and the enzymatic activity of superoxide antioxidant enzymes was evaluated dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), as well as the concentration of malondialdehyde (MDA), a product of lipid peroxidation, and was contrasted with parasitaemia.

SOD activity increased in intact mice only when treated with testosterone, which decreased MDA concentration. It is likely that the effect of testosterone, in intact mice, is dependent on the concentration of the hormone. On the other hand, the activity of SOD, GPx and CAT increased significantly in gonadectomized mice, whether treated with vehicle or with testosterone, and this did not modify the concentration of MDA. It is likely that the activity of antioxidant enzymes is negatively regulated independently of the concentration of testosterone, secreted by the gonads Regarding parasitaemia, we detected a tendency for parasitaemia to increase as testosterone concentration increases and this effect is reversed by gonadectomy, suggesting that the gonads are necessary for the immunosuppressive effects of testosterone. We conclude that testosterone only modifies the activity of the SOD enzyme in intact mice, which correlates negatively with parasitaemia, likewise, these effects depend on the gonads.

EHMYB10 TRANSCRIPTION FACTOR INTERACTOME: EVIDENCE OF COTRANSCRIPTIONAL REGULATION

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Abstract:

Gene expression is a highly dynamic process that involves many regulating proteins to enable RNA pol II to access promoters. Therefore, several transcription factors (TFs) are needed to activate or inhibit mRNA transcription. During its synthesis, immature mRNA must be processed by co-transcriptional regulation, to allow its exportation to the cytoplasm, where it is translated. Splicing is a complex process that involves almost 150 proteins termed spliceosomal factors (SF); however, additional proteins have been recently identified with a non-splicing function. The Myb transcription factors are proteins recently implicated in transcription regulation and splicing. *Entamoeba histolytica* is an enteric protozoan possessing 8,201 genes, and interestingly almost 30% contain at least one intron, suggesting the presence of co-transcriptional regulation. In addition, EhMyb proteins are the most abundant TFs in this protozoan, which allow us to hypothesize that could regulate some virulence factors needed for host invasion. We previously characterized EhMyb10 and determined the DNA-binding domain (DBD) through EMSA assays. In this work, we performed an *in silico* interactome between EhMyb10 and the *E. histolytica* proteome to determine putative factors binding to this TF. Through the STRING website, we observed that EhMyb10 binds to both transcription and splicing-related proteins. The interactome showed 31 nodes and 260 edges with an e-value of 1.0e-16. Interestingly, one of the proteins bound to EhMyb10 is EhCDC5-like. This protein belongs to the Myb family and has two imperfect R2/R3 repeats, although in *Schizosaccharomyces pombe* its function has been related to spliceosome activation rather than transcription. We also analyzed the primary structure of EhCDC5-like and found a disordered region, as well as, many predicted phosphorylation residues that may be involved in the regulation of the spliceosome active state. In the EhCDC5-like interactome, we found 41 nodes and 756 edges, indicating that the interaction of putative proteins is more likely than those of EhMyb10 binding proteins. In silico, EhCDC5-like binds to many SFs and interestingly to chromatin remodeling proteins. In conclusion, through this bioinformatic analysis, we propose a role for EhMyb10 and EhCDC5-like as a complex during co-transcriptional regulation in this parasite.

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MITOCHONDRIA PARTICIPATION IN B CELL RESPONSE AGAINST NON-BILAYER PHOSPHOLIPID ARRANGEMENTS

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Abstract:

Following antigen challenge, B cells can response through the germinal center pathway and generate IgG antibodies. Anti-lipid IgG antibodies are produced in the immune response against infectious diseases like mycobacterial infections, or in other cases can generate autoimmunity such as anti-non-bilayer phospholipid arrangements (NPAs) antibodies which have been detected in diseases like Systemic Lupus Erythematosus1,2. During these cellular mechanisms, mitochondria undergo metabolic changes associated with the fusion and fission of their membranes which directly influence the mitochondrial membrane potential and plays a crucial role during immune response and in the B cells determination3. We have demonstrated in a murine model which resembles human lupus induced by NPAs, that B cells produce high affinity IgG anti-lipid antibodies. However, the involvement of the mitochondria in this cell lineage in response against lipidic antigens is not known with certainty. Therefore, in this work we studied by flow cytometry the B cell response and the mitochondrial dynamics and membrane potential in female BALB/c mice immunized with NPA-bearing liposomes. We found B1 and plasma cells with fissioned mitochondria and with decreased mitochondrial membrane potential; therefore, these cells metabolism reaches glycolysis. A significant number of B2 cells that mainly respond through the germinal center pathway against the lipidic antigen was found. We also found that the B2 germinal center and memory B cells presented fused mitochondria with increased mitochondrial membrane potential, therefore these cells lead their metabolism to oxidative phosphorylation. Our data suggest that there is a relationship between the in vivo B lineage cells response against a lipidic antigen and the mitochondrial metabolism.

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ALLERGENICITY PROFILING OF *LIGUSTRUM LUCIDUM* POLLEN PROTEINS CAUSING RESPIRATORY ALLERGIES

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Abstract:

Allergic respiratory diseases are a growing health problem in Mexico and the world that affects people's quality of life[1]. Sensitization occurs when the immune system detects an allergen, molecules such as proteins capable of stimulating our immune system. In a recurrence, it causes a chain reaction that generates IgE class antibodies. Allergens can be airborne, such as pollens, fungi, mites, or pet epithelia. Pollen is the male reproductive unit of plants dispersed by insects and wind. The protein composition of pollen is determined genetically and environmentally[2]. Factors such as CO_2 concentration, the incidence of UV light, water availability, and environmental pollution directly influence pollen allergenicity[3]. In addition, intra-species variation may also influence. However, it is unclear how the geographical location influences pollen allergenicity. In this study, we focus on evaluating the variability in the allergenicity protein profile of *Ligustrum lucidum* pollen, a tree widely distributed in Mexico City. Inflorescences of 37 *L. lucidum* trees were collected from May to July 2021 in Mexico City. Then, morphological characterization of pollen was performed, such as exine density, equatorial axis, and polar axis. Finally, to evaluate the IgE binding proteins and their allergenicity according to different collected sites, we used an immunoproteomics approach by dot blot with sera from monosensitive patients. Our results showed high diversity in the morphological traits of *L. lucidum* pollen according to their location. The southeast region has the most significant variance in exine density. This parameter is positively associated with previous pollution rates. Interestingly, samples collected at sites with high pollution levels and under increased stress for trees showed increased allergenicity as assessed by dot-blot. With this study, we aim to contribute to the knowledge of how environmental and pollution factors influence the allergenicity of pollen in cities with high pollution levels.

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DHEA DIFFERENTIALLY MODULATES IFN-γ LEVELS IN MALES AND FEMALES CBA/CA MICE INFECTED WITH *P. BERGHEI* ANKA

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Introduction: Malaria is caused by *Plasmodium,* it is the parasitic disease with the highest mortality in the world. In 2020, 241 million new cases of malaria and 627,000 deaths were reported by The World Health Organization. The severity of disease and mortality in men are higher than in women; in this dimorphic response, sex hormones play an essential role. The hormone DHEA modulates the response of cells of the immune system and cytokines concentration. In addition, patients infected with *Plasmodium* with higher concentrations of DHEA have less parasitemia and higher haemoglobin concentration. In addition, DHEA increases the levels of IFN-γ and IL-10 in plasma, both cytokines are critical to the elimination of *Plasmodium.* However, whether DHEA modulates the IFN-γ and IL-10 concentration in malaria is unknow. The present work aims to determine the relevance of DHEA on sexual dimorphism in malaria, we evaluated whether DHEA differentially modifies pathology levels of IFN-γ and IL-10 in males and females mice infected with *Plasmodium berghei* ANKA (*P. berghei* ANKA). **Methodology:** Intact and gonadectomized (Gx) CBA/Ca male or female mice were treated with 200 µg of DHEA subcutaneously for 5 days. The day after the last administration mice were infected with $1x10^3$ erythrocytes parasitised with *P. berghei* ANKA. Parasitaemia, body weight and haemoglobin concentration were quantified, as well as the concentration of the cytokines IFN-γ and IL-10 in plasma. **Results and Discussion:** DHEA increased the parasitaemia on day 6 post-infection in gonadectomised mice of both sexes. In addition, DHEA decreased body weight only in intact females. Interestingly, DHEA did not modify the haemoglobin concentration in either male or female mice. In addition, DHEA reduced the levels of IFN-γ only in the Gx female which generated a dimorphic pattern. In contrast, DHEA did not change IL-10 concentration of males or females. This finding was unexpected, because has been described to increased the IL-10 synthesis. A probable explanation for this discrepancy is that the inflammatory immune response predominates during the infection with *P. berghei* ANKA. inflammatory response in the infection with *P. berghei* ANKA. The differential effects of DHEA between males and females are relevant because IFN-γ is necessary for the *Plasmodium* clearance, however, is associated with the pathogenesis in malaria. **Conclusions:** DHEA DECREASED THE WEIGHT AND THE IFN-γ, a key cytokine in the immune response against malaria, only in the females. This suggests that the DHEA contribute to the dimorphism sexual in malaria.

CHARACTERIZATION OF EXTRACELLULAR VESICLES RELEASED BY THE PARASITE *ENTAMOEBA HISTOLYTICA* AND EVALUATION OF THEIR IMMUNOMODULATORY EFFECTS ON HUMAN NEUTROPHILS

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Extracellular vesicles (EVs) are structures delimited by a lipid bilayer released into the extracellular space by cells, allowing intercellular communication trough the exchange of numerous molecules that constitute their cargo (soluble and membrane proteins, peptides, carbohydrates, lipids, DNA, and diverse RNA types). EVs are classified according to their subcellular origin and diameter into exosomes, ectosomes, microvesicles and apoptotic bodies. In this work we have isolated EVs released by trophozoites of the human protozoan parasite *E. histolytica*, the causal agent of amoebiasis, alone or in coculture with human neutrophils, and we have determined their effect on the effector mechanisms of these innate immunity cells. Nanoparticle tracking analysis showed that size of amoebic EVs is variable, from less than 50 nm to nearly 600 nm (average 167 nm), whereas neutrophil EVs were more uniform in size, most of them with an average of 136 nm. In cocultures, smaller EVs were identified, most with a size of 98 nm, typical of exosomes. Fusion of amoebic EVs with the membrane of human neutrophil was demonstrated by fluorescence assays in cocultures. Of note, amoebae EVs added to neutrophil-stimulated cultures (with PMA, A23187 ionophore or amoebas), significantly reduced the oxidative burst and delayed the onset time and rate of NET release triggered by all stimuli. In contrast, EVs from amoeba:neutrophil cocultures did not affect ROS production, but did delay NET release. Proteomic analysis of EVs by mass spectrometry revealed a similar protein category distribution in GO analysis, suggesting that differential effects of EVs might be due to differences in individual proteins or others cargo components. These results highlight the importance of EVs-mediated intercellular communication in the outcome of amoebic infection

DBD-MYB PROTEINS IN *E. INVADENS*: CLASSIFICATION AND CYST-STAGE TRANSCRIPTION

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Abstract:

Entamoeba histolytica is an early-branching eukaryote responsible for amoebiasis, the third leading cause of death among protozoan parasitic diseases. The cyst is the infective form for humans that survive in the environment due to a protective, chitin-containing cell wall. After cysts are ingested, parasites excyst in the small intestine to produce the trophozoite form. The trophozoite is the motile and invasive stage that colonizes the intestine. The encystation has been unsuccessfully achieved in vitro and to study this stage, *Entamoeba invadens*, responsible for reptilian amoebiasis has been used as a model. In *E. invadens* its gene expression is differentially modulated during encystation and excystation. The MYB-like DBD is an abundant domain and conforms to one of the largest families of proteins in Entamoeba related to transcriptional regulation. The MYB-like DBD consists of up to four imperfect amino acid sequence repeats (R) of about 52 amino acids, each forming three α-helices with an HTH structure with three regularly spaced tryptophan (or aromatic) residues, forming a hydrophobic core in the three-dimensional structure. The MYB-domain-containing proteins have been described as transcription factors involved in the regulation of gene expression related to encystation in different protozoa parasites. Therefore, in this work, we searched for E. invadens MYB-domain-containing proteins using the Myb DBD of c-Myb (*H. sapiens*) and EhMyb10 (*E. histolytica*) as bait. Forty-four genes encoding for MYB-domain-containing proteins were identified and classified: 24 proteins with a single-repeat 1R and 20 proteins with two repeats (R2R3-Myb proteins) according to an InterproScan motif search. Most proteins have domains that are involved in transcription initiation such as ADA-2, SWI complex I, and Reb1, among others. Expression analysis obtained from the AmoebaDB database showed that some genes are expressed only in the trophozoite stage while others express mainly in the cyst stage. This indicates that MYB transcription factors might regulate the expression of stage-specific proteins and a great variety of cellular processes.

This work is funded by CCyT-UACM (grant CCyT-2021-8)

OESTROGENS DECREASE THE NUMBER OF CYTOTOXIC T LYMPHOCYTES AND IFN-γ AND TNF-α CONCENTRATION IN MALES INFECTED WITH *PLASMODIUM BERGHEI* ANKA

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Introduction: Malaria or paludism caused in 2021, 421 million new cases and 627 thousand deaths (1). Women have less severe symptoms and lower mortality than men. Oestrogens have been reported to be immunopotentiators. In malaria, helper cells, cytotoxic T cells, and NK cells secrete IFN-γ and TNF-α, cytokines that promote parasite clearance by stimulating macrophage phagocytosis. Paradoxically, high concentrations of both cytokines cause severe malaria and increased mortality. In other experimental models it has been described those oestrogens regulate the synthesis of IFN-g and TNF-α (2). Therefore, the purpose of this work is to evaluate the participation of shields on helper T cells, cytotoxic T cells, macrophages and NK cells that produce both cytokines. We will use the strategy of blocking estradiol receptors in vivo with tamoxifen in male mice infected with *Plasmodium berghei* ANKA. This work will contribute to the development of future therapeutic strategies that consider the beneficial effects of oestrogens in men. **Methodology:** 3 groups of 20 4-month-old male mice were treated with vehicle or tamoxifen, in addition to a group without treatment as a control group. Half of the mice in each group were infected with *P. berghei* ANKA and the other half were not infected to serve as a control group. Parasitaemia was assessed daily on Giemsa-stained blood smears. Mice were sacrificed on day 8 post-infection, plasma was obtained to assess cytokine concentration by flow cytometry. In addition, the percentage of helper T cells, cytotoxic T cells, macrophages, and NK cells in the spleen was evaluated by flow cytometry.

Results: Blocking oestrogen receptors with tamoxifen significantly increased parasitaemia on day 8 post-infection compared to control mice, increased plasma concentrations of IFN-γ and TNF-α as well as the number of cytotoxic T lymphocytes compared to control mice treated with vehicle or without treatment. These results show that oestrogens decrease the number of cytotoxic T lymphocytes, which in theory would decrease the concentration of IFN-γ and TNF-α, suggesting that estrogens promote less severe disease. **Conclusion:** Oestrogens regulate the concentration of IFN-γ and TNF-α as well as the number of cytotoxic T lymphocytes in males infected with *P. berghei* ANKA. These findings suggest that the administration of oestrogens or their derivatives should be considered in the future development of therapeutic strategies to reduce mortality in men infected with *Plasmodium*.

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ANTIBODY-DEPENDENT ENHANCEMENT I N DENGUE VIRUS INFECTION ASSOCIATED WITH ANTI-SARS-COV-2 IGG CLASS ANTIBODIES IN THE COAST REGION OF OAXACA, MEXICO

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Abstract:

The antibody-dependent enhancement (ADE) phenomenon, documented in dengue, is favored by IgG antibodies (Ab) that recognize virus envelope proteins and is associated with severe thrombocytopenia. The similarity between SARS-CoV-2 spike proteins and dengue virus envelope proteins has been described in 2020; moreover, in 2021, a fatal case of ADE in dengue favored by anti-SARS-CoV-2 IgG antibodies was reported in India. The aim of the research was to study the ADE phenomenon in patients with SARS-CoV-2 or dengue infection in an endemic dengue area of the Mexican Pacific. We evaluated if the presence of IgG antibodies against Sars-CoV-2 in patients with active dengue infection increase the level of inflammatory biomarkers as high sensitive C reactive protein (Hs-CRP) and ferritin as well if they were associated with a low number of platelets. Also, we evaluated patients with active Sars-CoV-2 infection and presence of IgG antibodies against dengue. The results of anti-dengue Ab, anti-SARS-CoV-2 Ab, blood biometry, ferritin and hs-CRP tests were analyzed in 27 patients from Puerto Escondido, Oaxaca, Mexico. In patients with COVID, the presence of IgG (46.2%) and IgM (15.4%) anti-dengue Ab were observed and they did not show any alteration in the biomarkers. In patients with dengue, IgG (50%) and IgA (21.4%) anti-SARS-CoV-2 antibodies were identified. Patients with dengue and the presence of IgG anti-SARS-CoV-2 Ab, presented the lowest levels of platelets as those observed in the ADE phenomenon. The results obtained suggest the presence of the ADE phenomenon in dengue patients favored by anti SARS-CoV-2 IgG Ab.

EHMYB10 OVEREXPRESSION IN *E. HISTOLYTICA*: IMPLICATIONS DURING epithelial cell interaction

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Abstract:

E. histolytica is the agent responsible for intestinal amebiasis causing almost 100,000 deaths annually worldwide. *E. histolytica* has two stages, trophozoite and cyst. The cyst is the infective form that is ingested in contaminated food and water supplies. The trophozoites are the invasive form that adhere to the surface of the intestinal tissue causing diarrhea and colitis. This infection is due to the expression of virulence factors that participate in phagocytosis, cytolysis and cytoadherence. Myb proteins are one of the most abundant family of transcription factors in *E. histolytica*. These proteins bind DNA through a DBD-MYB domain consisting of three imperfect repeats R1, R2, y R3, characterized by three tryptophans separated by 18 aa each, generating a helix-turn-helix structure. Through transcriptomic analysis, it was observed that *E. histolytica* modulates its gene expression in response to different stimuli, such as hepatic abscess formation, serum deprivation, and interaction with colonic tissue, among others. EhMyb10 belongs to the MybR2R3 family and is a transcription factor of 17.9 kDa that recognizes the canonical Myb Recognition Element (MRE, TAACGG). However, the role of this transcription factor during virulence events remains unknow. By bioinformatic approach, MRE was identified in 826 gene promoters of *E. histolytica*. We then used previously reported RNA-Seq data from basal culture condition and classified the genes according to their expression levels, selecting 162 genes which express similar levels compared to EhMyb10 and in addition, are modulated during intestinal invasion. Finally, we selected 5 genes to analyze the effect of EhMyb10 overexpression and their possible role as virulence factors as well as their importance in transcription regulation. Overexpression was confirmed through RT-PCR, and immunofluorescence assays. To determine the EhMyb10 participation during the *E. histolytica* invasion of host cells, we evaluated the permeability of Caco-2 cells interacted with trophozoites overexpressing EhMyb10. However, no apparent impairment was observed in this intestinal epithelium. This work allows us to determine the importance of transcription factors in the virulence regulation of *E. histolytica,* possibly modulating the transcription of virulence factors or other molecules during epithelial cell interaction.

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EVALUATION OF BIOLOGICAL ACTIVITY OF BUTYL AND ISOPROPYL QUINOXALINE-7-CARBOXYLATE 1,4-DI-N-OXIDE ESTERS AGAINST *ENTAMOEBA HISTOLYTICA*

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Abstract:

Introduction. Amebiasis is a parasitic infection caused by the protozoan *Entamoeba histolytica*. Antiamoebic drugs, such metronidazole and nitazoxanide have been used to treat infection, however, this drugs causes several side effects, and also have mutagenic and carcinogenic properties. Therefore, one important strategy in the development of antiamoebic drugs is the screening of compound libraries such as quinoxaline 1,4-di-N-oxide (QdNOs) derivatives whose have a wide spectrum of biological activities, like antiparasitic. Ethyl and methyl quinoxaline-7-carboxylate 1,4-di-N-oxide derivatives have demonstrated important activity against *Entamoeba histolytica*, due to that, it's necessary to evaluate the effects of molecular changes in the quinoxaline structure. **Objective.** To evaluate the biological activity potential of butyl and isopropyl quinoxaline-7-carboxylate 1,4-di-N-oxide derivatives against *E. histolytica*. **Methods.** Three compounds were evaluated: T-137, T-155 and T-166. Stock solutions of these compounds were prepared by dissolving in dimethyl sulfoxide (DMSO) and then with TYI-S-33 medium. *Entamoeba histolytica* trophozoites ($7.5x10^4$) were exposed to an increasing concentration of each compound for 48 h at 37 °C. IC_{50} was calculated from viability by Neubauer chamber counting. Cytotoxicity of QdNOs (CC_{50}) was evaluated in HFF1 cells and the selectivity index (SI) was determined. **Results and conclusions.** The new butyl and isopropyl quinoxaline-7-carboxylate 1,4-di-N-oxide derivatives showed an IC_{50} of 0.1437 µg/mL, 1.586 µg/mL and 0.5844 µg/mL to T-137, T-155 and T-166 respectively. The incorporation of phenyl (C_6H_5) and methyl (CH_3) substitutions on the quinoxaline ring had better activity than both T-155 and T-166 compounds with methyl and trifluoromethyl (CF_3) susbtitutions. Moreover T-137 showed a better SI value of 3.64 than T-155 and T-166, with 0.1173 and 0.7077. Based on these data we conclude that T-137 and T-166 have better antiamoebic activity than the reference drugs but similar SI value.

Keywords: *Entamoeba histolytica,* Quinoxaline 1,4-di-N-oxide esters, Antiamoebic activity, Butyl, Isopropyl.

T-CELL IMMUNOPHENOTYPE AND CYTOKINE PROFILES IN PEDIATRIC PATIENTS INFECTED WITH *RICKETTSIA RICKETTSII*

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Abstract:

Tick-borne diseases are of public importance from clinical and veterinary perspectives in Mexico, specially the often-neglected Rocky Mountain Spotted Fever (RMSF) caused by the bacteria Rickettsia rickettsii, numbers as high as 273 tick-borne cases have been reported nationwide in Mexico in 2021. The State of Chihuahua reported 76 confirmed cases, of which 59 were caused by RMSF and 17 by another rickettsiosis not specifically identified, owning the prize of the state with the second-highest number of increasing clinical cases reported in this country from 2020 to 2021. Fourteen samples were obtained from children suspected of rickettsial infection, those samples were analyzed from January to December 2021, detecting a prevalence *Rickettsia rickettsii*. The altered clinical hematological and biochemistry analytes in the patients displayed that 100% of the children coursed with elevated liver enzymes and coagulation times, 64% showed leukocytosis due to neutrophilia, 55% of them had thrombocytopenia, lymphopenia and hypoalbuminemia, and 45% showed normocytic normochromic anemia. Statistically significant differences were obtained in the chemokines IL-8, RANTES, CXCL9/MIG and CXCL10/IP-10. Significant differences were observed for IL-1β, IL-6, IL-17, IFNγ and TNFα among the *R. rickettsii* positive group compared to the control group; Finally, significant differences were obtained for all of the subpopulations of CD8+ T lymphocytes when comparing between the groups positive for *R. rickettsii.*

EVALUATION OF MYELOID CELL ACTIVATION IN PEDIATRIC PATIENTS WITH RICKETTSIAL AND SARS-COV-2 INFECTIONS

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Abstract:

The first line of detection and defense against invasive germs is provided by the innate immune system. Myeloid cells of the innate immune system respond differently when challenged with bacteria or viruses. Activation of myeloid cells as monocytes, macrophages, neutrophils, or dendritic cells (DCs), is an early response to infection. When they come into touch with foreign objects, they become activated. Then, they discharge a variety of pro-inflammatory mediators, including cytokines and interferons (IFNs), which are also linked to the production of certain molecules on the surface of immune cells. CD64 expression increases on neutrophils during bacterial infections. Recently an increase in CD169 expression has been discovered on monocytes during viral infections. Thus, the combinatorial detection of CD64 and CD169, respectively, on the surface of neutrophils and monocytes, could be a specific measure for the distinction between the different causes of infections. CD64, CD169, and HLA-DR are activation markers expressed by myeloid cells, such as neutrophils, monocytes, and dendritic cells. The management of infections in the hospital continues to be a limitation due to the identification of infectious causes remains difficult with current techniques. A new combination of two biomarkers, CD64 and CD169, has been proposed as a new rapid flow cytometry technique. In the present work, the expression of activation markers CD164 and CD69 in myeloid cells of childhood patients with bacterial and viral infections was evaluated, and the expression of these same markers in healthy patients was compared in order to determine the differences in the percentages of expression of these markers in the different types of infection.

SUBUNIT C82 OF RNA POLYMERASE III IS ESSENTIAL FOR CELL GROWTH OF THE HUMAN PARASITE *TRYPANOSOMA BRUCEI*

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Abstract

Eukaryotic cells have three different RNA polymerases (Pol). Pol III synthetizes small RNA molecules, such as tRNAs, 5S rRNA and snRNAs, that play key cellular roles. In yeast, Pol III is composed of 17 different subunits, including C82, which is a Pol III-specific subunit that forms a heterotrimer with C34 and C31 that is crucial for transcription initiation at Pol III promoters. Little is known about Pol III transcription in the protozoan parasites *Trypanosoma brucei* and *Leishmania major*, causative agents of African trypanosomiasis and cutaneous leishmaniasis, respectively. *In silico* analyses allowed us to confirm the presence of the C82 typical domains in the orthologs from *L. major* (LmC82) and *T. brucei* (TbC82), despite a relative low sequence identity with human C82 (HsC82). Also, the predicted 3D structure of LmC82 and TbC82 is very similar to the one reported for HsC82. Notably, knock downs by RNAi showed that TbC82 is essential for the growth of procyclic forms of *T. brucei*. Immunofluorescence assays with cellular clones that express the recombinant proteins LmC82-PTP and TbC82-PTP indicated that C82 is a nuclear protein in both parasites. To identify the proteins that associate with LmC82 and TbC82 we performed tandem affinity purification experiments followed by mass spectrometry analysis. In addition to Pol III subunits, among the co-purified proteins we identified four subunits of transcription factor TFIIIC, which was believed to be absent in these parasites. Thus, our results indicate a strong interaction between C82 and TFIIIC during Pol III transcription initiation in trypanosomatids.

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PARTICIPATION OF TGD LYMPHOCYTES IN THE DEVELOPMENT OF LUPUS IN MOUSE INDUCED BY LIPIDIC PARTICLES

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Abstract:

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a variable clinical phenotype, where the mechanisms that lead to its development are not yet fully understood[(1)]. In our research group, we have proposed that SLE and other autoimmune diseases are related to cell membrane alterations; where stable lipidic particles induce the formation of auto-antibodies[(2)]. On the other hand, it has been described that Tgd cells participate in the pathogenesis of SLE by secreting certain cytokines[(3)] and can also respond against lipid antigens. So, in the present work, we study the Tgd cells from mice (BALB/c) with lupus induced by the stabilization of lipidic particles with chloropromazine. We analyze by flow cytometry the activation, proliferation and the stage of the cell cycle of Tgd cells from mice with lupus. We also evaluated by intracellular Flow citometry their response type (Th1, Th2, or Th17) according to the cytokines production and its type of metabolism (glycolysis or oxidative phosphorylation).

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PROLACTIN EXERTS DUAL ACTIONS ON THE INFLAMMATORY RESPONSE OF SYNOVIAL FIBROBLASTS

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Abstract:

Synovial fibroblasts (SF) play a key role in inflammatory joint diseases, such as rheumatoid arthritis (RA), a progressive inflammatory autoimmune disease with articular and systemic manifestations. RA is influenced by reproductive hormones including prolactin (PRL). However, the role of PRL remains controversial since both positive and negative PRL outcomes have been reported in RA. Because SF express the PRL receptor, we used primary cultures of SF to investigate the effect of PRL on the inflammatory response induced by two of the major pro-inflammatory cytokines (IL-1β, TNFα) found in the arthritic joint. SF isolated from the femur/fibula/tibia joint of male C57/BL6 mice were incubated with or without IL-1β (1 ng/mL) or TNFα (10 ng/mL) in the presence or absence of PRL (100 nM). Metabolic activity (MTT colorimetric assay), PRL receptors, proinflammatory mediators (RT-qPCR, Western blot), and nuclear factor-kappa B (NF-κB) signaling (immunofluorescence and Western blot) were evaluated as primary inflammatory endpoints. IL-1β upregulated and TNFα downregulated the expression of the long-form of the PRL receptor in SF. Consistent with this contrasting action, PRL inhibited and stimulated the metabolic activity, the expression of proinflammatory mediators (IL-1β, IL6, inducible nitric oxide synthase), the nuclear translocation of NF-κB and the degradation of the NF-κB inhibitor IkB-β in SF in response to IL-1β and TNFα, respectively. PRL inhibits and stimulates the proinflammatory effect of IL-1β and TNFα in SF, respectively. SF may contribute to the opposing actions of PRL in RA depending on the inflammatory milieu (type of proinflammatory cytokine, level of expression of the PRL receptor, and activation of the NF-κB signaling pathway). On-going in vivo studies are addressing these interactions in the inflamed joint.

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DETERMINATION OF THE PRESENCE OF AMEBAPORES IN TROPHOZOITES FROM DIFFERENT SPECIES OF *ENTAMOEBA*, USING WESTERN-BLOT AND ELISA

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Abstract:

Amoebiasis is caused by *Entamoeba histolytica*, a protozoan parasite that infects the large intestine. It can eventually lead to fatal complications in other organs, especially hepatic amoebiasis. Amoebiasis is one of the principal gastrointestinal diseases in the world and is considered a public health problem in Mexico, where it is endemic. The amebapore, one of the main virulence factors of *Entamoeba histolytica*, is directly linked to the formation of amebic liver abscess (ALA). **Objective**: To determine the presence of amebapores in the trophozoites of virulent and non-virulent *E. histolytica* as well as *E. dispar* and *E. invadens* by means of Western Blot and ELISA. **Materials and Methods:** The three species of *Entamoeba* trophozoites presently evaluated were anexically grown in anaerobic conditions for 72 h. The total extracts from each species were obtained, then resuspended in a buffer solution (10 mM EDTA, 100 µM iodoacetamide, and 0.2 mM E-64) at a dilution of 1:100. Finally, the protein was quantified by the Lowry method and the samples were analyzed by Western Blot and ELISA. **Results:** The analysis by ELISA showed that the corresponding antibody recognized the presence of amoebapores in the virulent and non-virulent *E. histolytica* strains. The antibody titers were similar in both strains (0.5436 and 0.4096, considered 100% and 75.35%, respectively). A lower level of antibody titers was detected in *E. dispar* (0.039), corresponding to 7.2%. Meanwhile, the antibodies were absent in *E. invadens*, which does not infect humans. The ELISA results correlated with those obtained by Western Blot. A molecule in the range of the molecular weight of the amebapore (8.2 kDa) was identified in the two strains of *E. histolytica*, apparently with greater expression in the virulent strain. No protein molecule was visualized in the other two species of the parasite. **Conclusion:** The amebapore was differentially expressed in the four samples herein evaluated (by means of both techniques utilized), finding the highest level in the two *E. histolytica* strains. The most sensitive evaluation was the ELISA test, but Western Blot also showed greater expression for non-virulent *E. histolytica* compared to *E. dispar* and *E. invadens*.

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PLASMODIUM VIVAX APICAL MEMBRANE ANTIGEN 1 $_{I-II}$ FROM NICARAGUA REVEALED LOW DIVERSITY, MODERATE DIFFERENTIATION AND GENETIC RELATIONSHIPS WITH LATIN AMERICAN PARASITES

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Abstract:

In Nicaragua, malaria transmission has historically been a Public health problem. Recently, this country reported 13,220 and 25,505 *malaria* cases in 2019 and 2020, respectively, and *Plasmodium vivax* contributed with 91% and 52% of those cases, respectively. The apical membrane antigen-1 participates in parasite reorientation during the invasion of erythrocytes, and is an important vaccine candidate, aiming to block blood infection and reduce disease severity. In this work, the genetic and antigenic polymorphism of *P. vivax* apical membrane antigen-1 was examined.

Infected blood samples from symptomatic patients with *P. vivax* infection were obtained from different municipalities of Nicaragua, and during 2012-2013. Gene fragment of *pvama1* domains I-II was amplified and sequenced by sanger method. Genetic parameters, neutrality tests, haplotype relationships, genetic structure and amino acid variation were analyzed.

Sixty-five sequences of 915 bp were obtained, and had 19 nonsynonymous and 5 synonymous nucleotide changes. Nicaraguan parasites had low nucleotide and haplotype diversity, high linkage disequilibrium and few recombination events. Tajima´s D and McDonald-Kreitman tests suggest positive and divergent selection. In a median joining network, Nicaraguan haplotypes were separated by 1-26 mutational steps among them and formed at least 2 genetic clusters, and were close-related to other Latin American parasites. Amino acid variation is exposed on the surface of the molecule, and predominates in peptides potentially participating in B cell epitopes.

The results suggest that *P. vivax* from Nicaragua is a moderately differentiated population under contraction. Most amino acid polymorphism laying in predicted B cell epitopes resembled that reported for other Latin American parasites. This information is relevant for vaccine development and epidemiological surveillance.

CELLULAR IMMUNE RESPONSE ON *CHERAX QUADRICARINATUS* AFTER DIFFERENT IMMUNOSTIMULATIONS

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Abstract:

Crayfish (*Cherax quadricarunatus*) is an important species for aquaculture which has seen increases in its production last years. However, infections caused by bacteria such as *Vibrio parahaemolyticus* produce a high economic loss. Immunostimulants such as β-glucans, mannans, LPS, or zymosan (Zym) are alternatives used for control of diseases These immunostimulants are PAMPS recognized by lectins that act as receptors and activating pathways inside hemocytes. This work is aimed at characterizing possible recognition pathway of molecules targets by lectins as zymosan, LPS, or bacteria like *V. parahaemolyticus* strain N16 or *Escherichia coli* BL21A1, and to describe mechanisms implicated and their signalization cascade inside hemocytes. The experiment was carried out as follows: Zym (200 µg/kg), LPS (20 µg/kg), *V. parahaemolyticus* N16 (1×10^7 cells/mL) and *E. coli* BL21A1 (1×10^7 cells/mL) were used for stimulate to crayfish *in vivo* by injection. Samples of hemolymph were taken at 0, 1, 2 and 4 h after stimulation. By flow cytometry was characterized for size and complexity the hemocytes were extracted from the hemolymph. Cellular viability, phagocytosis, ROS, and lectins present in hemocytes were measured by flow cytometry. Humoral parameters were measured in hemocytes by colorimetric techniques for the detection of prophenoloxidase (ProPO), nitric reactive species (RNS), and myeloperoxidase (MPO). The results showed significant differences in cells number, cellular subpopulations, and cell viability of groups treated with Zym, *V. parahaemolyticus* N16 or *E. coli* BL21A1 with respect to group control treated with saline solution or control group. Surprisingly, LPS at low doses showed cellular number reduction after 2 h post-immunostimulation. Phagocytosis was increased significantly after 2 h exposition to *V. parahaemolyticus* N16 or *E. coli* BL21A1-labeled with FITC. These results indicated a cellular activation mediated by semi-granular hemocytes after an immunostimulation with molecules as Zym or bacteria.

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DEGRADATIVE PROFILES OF FIBRONECTIN AS BIOMARKERS DURING THE PROGRESSION OF THE ACUTE AND CHRONIC INFECTION WITH *TRYPANOSOMA CRUZI*

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Abstract:

Chagas disease (American tripanosomiasis), considered as a neglected disease, is caused by the parasite *Trypanosoma cruzi*. It is estimated that approximately 8 million people of the Americas have Chagas disease (CD). Biomarkers (coming from host or parasite) to monitor CD progression as well as the therapeutic response in chronic CD are critically needed, since seronegativization, which may be considered the best indicator of therapeutic cure, takes several years to be observed in adults. Several molecules have been suggested as biomarkers for CD, however, they have to be validated. Taking advantage of mouse models of *Trypanosoma cruzi* infection, we investigated changes in the degradation profile of Fibronectin in plasma.

The degradation profile of Fibronectin was different in the acute phase (15-60 days post-infection (d.p.i.)) compared to the chronic phase of the infection. Furthermore, the degradation profile of Fibronectin between early (60-140 d.p.i.) and late (150-210 d.p.i.) chronic phases was different. Fibronectin fragments of approximately 150, 100, 40 and 30 kDa were identified. The degradation profiles of fibronectin correlated with acute parasitaemia as well as with cardiac parasite burden and tissue damage during the infection. The usefulness of Fibronectin degradation as a biomarker for therapeutic response following benznidazole (BZN) treatment and immunotherapeutic vaccination also was evaluated and a decreased Fibronectin degradation profile was observed upon BZN or a vaccine candidate treatment.

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DEVELOPMENT OF A CHIMERIC RECOMBINANT PROTEIN AGAINST RABBIT HEMORRHAGIC DISEASE VIRUS

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Abstract:

The rabbit hemorrhagic disease (RHD) is an acute, highly contagious, and mortal disease that affects domestic rabbits and wildlife hares. The RHD is caused by a Lagovirus called Rabbit Hemorrhagic Disease Virus (RHDV). The viral genome is a positive single-stranded RNA molecule and contains one gene that codes for a polyprotein that when cleaved results in non-structural proteins and the main capsid protein VP60. Until 2020 Mexico was recognized with disease-free status and there was no approved commercial vaccine; however, a virus attenuated vaccine produced in experimentally infected animals has been used as a strategy for disease control. In 2021 an outbreak was reported in Mexico caused by RHDV-2 that could mean a risk for the cuniculture industry in this country.

This project aimed to develop a recombinant chimeric, multiepitope vaccine against RHDV based on the main capsid protein VP60. Conserved regions of VP60 protein were determined by bioinformatic analysis. The conserved regions were subjected to diverse epitope predicting tools. The predicted epitopes were used to design two chimeric proteins and the respective genes that code for two versions of the same chimeric protein, one of them includes the secretion signal peptide from Thiamine-binding periplasmatic protein from E. coli to promote chimeric protein secretion and solubility. Both genes were cloned and a few clones from each gene were evaluated. Expression tests were performed in small-scale cultures to compare protein patterns expression from both clones and with non-induced cultures from each one as well. A differential protein band that corresponds to the expected molecular weight in soluble non-membrane associated protein samples was observed suggesting that perhaps signal peptide could facilitate chimeric protein secretion. A batch of induced chimeric protein culture was produced in a bioreactor. Bacterial cells were lysed, and recombinant chimeric protein was purified by Fast Pressure Liquid Chromatography with metal ions affinity columns. The desalted purified recombinant chimeric protein in doses of 0, 20, 40, and 60µg was administered in groups of six New Zealand rabbits each and 21 days after first immunization a booster dose with the same protein concentration was applied. Sera samples were taken at 0, 21, and 31 days after the first immunization. Specific antibody production was observed in 31-day samples with no statistical differences within dose concentration ($p<0.05$). Finally, sera from naturally infected animals recognized the recombinant chimeric protein by Western Blot demonstrating that conserved VP60 epitopes occur during the viral infection. Further experiments are needed to confirm that signal peptide promotes recombinant chimeric secretion in control condition cultures and virus neutralization assays as well as to evaluate protective antibody production. This recombinant chimeric protein is a new approach that will contribute to generating a control, prevention, and eradication strategy with the possibility to scale up and reduce costs in vaccine production without involving live animals for virus attenuated vaccine formulation.

EVALUATION OF THE CROSS-REACTIVITY OF ANTIBODIES AGAINST DEC-205 RECEPTOR IN DIFFERENT SPECIES

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Abstract:

Monoclonal antibodies are an instrument for protein identification, targeting, and tracking. These reagents allow us to expand our knowledge towards the characterization of the immune system from species with veterinary interest. Among the cells of the immune system, it is important to study and characterize dendritic cells (DCs), which are known to be the most efficient antigen presenting cells and can regulate, direct the innate and adaptive immune response. They perform this function through C-type lectin receptors highlighting DEC-205, which allows antigen uptake due to its recognition domains for carbohydrates. The main problem we confront in characterizing the immune system is the limited commercial availability of antibodies for certain animal species. Therefore, the objective of this work is to characterize three anti-DEC-205 antibodies, developed against chicken and pig, and to evaluate their recognition capacity with other species. To achieve this, we obtained peripheral blood mononuclear cells from different species (pig, chicken, horse, mouse, and human), incubated separately with three anti-DEC-205 antibodies, two from chicken (2F2 and 4D12) and pig, the cells were acquired by flow cytometer and analyzed with FlowJo V10 software. The results that we obtained is the recognition of the chicken anti-DEC-205 antibody (4D12) to horse mononuclear cells was found. On the other hand, specificity of the porcine anti-DEC-205 antibody was observed for cells of the same species. The limited availability of specific antibodies makes it difficult to study certain species of veterinary interest, which is why the presence of cross-reactivity with the horse indicates that this antibody could be used as a marker for the characterization of equine cells.

PROTEOMIC PROFILE OF PHAGOCYTOSIS OF SHRIMP *MACROBRACHIUM TENELLUM*

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Abstract:

The proteome is defined as the set of proteins expressed by an organism or by a part of it at a given time. On the other hand, proteomics is the science that focuses on the study of protein expression and its changes depending on the biological context, consisting on separation and identification of proteins. The objective of this work was to analyze and describe the proteins present during the phagocytosis process in *M. tenellum*.

For this study, the process of phagocytosis was analyzed, so hemolymph was extracted with anticoagulant (5% Sodium Citrate), then 100 µl of RPMI medium (Roswell Park Memorial Institute) was placed in a chamber for cell culture (Chambers) and 217,500 cells were added and then 50 µl of activators (LPS, Zymosan and β-1,3 glucans) were added and the microscope was observed at 10x. For the proteomic analysis, hemolymph was extracted with anticoagulant (Sodium Citrate 5%), 50µl of immunostimulator (Zymozan) was added and phagocytosis was waited for 10 min, then 5 cycles of heat shock were performed and the extracts of the Proteins were lyophilized and sent for proteomic analysis to Creative Proteomics (Shirley, NY, USA).

It was found that the stimulated hemocytes managed to phagocytose the particles in a period greater than 10 minutes and each of the stages of the phagocytosis process (infection, particle recognition, ingestion or endocytosis and exocytosis) was described. Through proteomic analysis, 80 proteins were analyzed and characterized, of which 22 proteins are exclusive to the phagocytosis process. These proteins were identified in the UniProt and Interprot databases.

In conclusion, the hemocytes stimulated by Zymozan, LPS and PMA manage to phagocytize the particles in a period greater than 10 min and have a greater recognition of pathogens of fungal origin, followed by pathogens of bacterial origin, with semigranular and granular hemocytes being responsible to carry out phagocytosis, a process in which 22 different proteins participate.

ACTIVATION OF INTRACELLULAR TOLL-LIKE RECEPTORS IN COMBINATION WITH VINCRISTINE IN GLIOBLASTOMA CELLS

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Abstract:

Introduction. Glioblastoma is a highly invasive, therapy-resistant primary brain tumor with the highest mortality rate among all primary brain malignancies. Therefore, there is an urgent need to explore the exact molecular mechanisms of glioblastoma progression and develop new and effective treatment strategies to improve patient prognosis. Immunotherapy has become an important part of the treatment of some cancers. The activation of the immune system through Toll-like receptors (TLRs) could be an area of opportunity. The TLR agonists imiquimod, resiquimod (R848) and ODN have been shown to be an effective adjuvant therapy to chemotherapy against several types of cancer. Currently treatment consist of surgical resection followed by chemotherapy and radiotherapy. Vincristine (VCR) is chemotherapeutic medication that inhibits proliferation by depolymerizing mitotic spindles, causing cell cycle arrest and apoptosis.

Material and methods: we use the U373 cell line to determine the effect of TLR activation in combination with VCR on cell viability and migration. We performed flow cytometry assays to corroborate the TLRs expression. We also performed MTT assays to determine the effect of synthetic TLR7, TLR8, and TLR9 agonists (imiquimod, R848, and ODN, respectively; 3 µg/mL) and VCR (200 and 300 ng/mL) on cell viability. We also performed migration assays (wound healing) to determine the effect of the synthetic agonists previous mention (3 µg/ml) and PDTC (200, 300 and 500 µM) on the cell migration.

Results: we confirmed the expression of TLR7 and TLR9 in glioblastoma cells. We also observed a decrease in the viability of glioblastoma cells in the presence of VCR at both concentrations; however, the addition of TLR agonists has no effect. We also performed migration assays with TLR agonists, we observed that the administration of agonists decreases cell migration capacity.

Conclusions: The administration of TLR agonists in combination with VCR does not affect glioblastoma cell viability. However, TLR agonist administration decreased cell migration, mainly imiquimod, which had a significant effect on cell migration.

ANTI-INFLAMMATORY RESPONSE PROMOTED BY *TRICHINELLA SPIRALIS* IN AN EXPERIMENTAL LUPUS MURINE MODEL

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Abstract:

Trichinella spiralis is a nematode that cause trichinelosis which rarely results in patient death[1]. *T. spiralis* induce a Th2-type (anti-inflammatory) response that limit local inflammation. Many studies have therefore focused on this immunomodulation to search for new therapies for pro-inflammatory diseases. Autoimmune diseases arise from the loss of immune tolerance to self-antigens and lead to the attack of the body's own tissues and the development of autoreactive T and B cells[2]. Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that due to a set of alterations in the innate and adaptive immune system triggers an uncontrolled inflammatory process through the generation of autoantibodies and deposition of immune complexes[2]. Our group evaluated the anti-inflammatory properties of the parasite in an experimental murine model of lupus. This model shares similar features with LES, such as the presence of autoantibodies and glomerulonephritis, splenomegaly, arthritis-like joint lesions, alopecia and the facial lesions resembling human malar erythema[3]. In this work, the experimental lupus model was evaluated in groups of mice previously parasitized with *T. spiralis* larvae or immunized with excretory/secretory products (PE/S, muscle larvae proteins and glycoproteins) to find out if they had a therapeutic effect on the progression and outcome of this disease. Six groups of three 4-week-old female BALB/c mice were studied; the first group were untreated mice or negative control (NC), the second and third were the parasitized control (P) and the immunized control (I) respectively; the fourth group was the control of the experimental lupus model (L), the fifth (P+L), consisted of parasitized mice that were subsequently treated for developing experimental lupus and the last group (I+L) consisted of mice immunized with PE/S during four weeks prior to the development of experimental lupus. The presence of pro- (IL-1α, IL-17a, IFN-γ and TNF-α) and anti-inflammatory cytokines (IL-4 and IL-10) in peripheral blood was measured by flow cytometry for six months. In addition, the appearance of characteristic lesions of the lupus model and the detection of anti-*T. spiralis*

antibodies by ELISA were assessed. It was observed that (P+L) and (I+L) groups produced higher amounts of IL-4 and IL-10 compared to the (L) group, which had an impact on the absence of clinical manifestations such as facial lesions, joint lesions and alopecia. In conclusion, *T. spiralis* promoted an anti-inflammatory response in experimental lupus in mice.

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CLONING AND EXPRESSION IN *NICOTIANA BENTHAMIANA* OF THE ASH POLLEN ALLERGEN FRA E 1

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Abstract:

In Mexico, there is a high rate of allergic respiratory diseases caused by the inhalation of pollen from trees of the *Oleaceae* family[1]. Protein extracts from whole pollen are commonly used to diagnose and treat these conditions. However, the extracts comprise thousands of non-well characterized proteins making this method inaccurate for diagnosis and treatment. One solution is to use allergens expressed and purified from heterologous organisms. The common organisms used are bacteria and yeast. Unfortunately, these organisms cannot add all the post-translational modifications found in plants. Fra e 1 is the main allergen in ash pollen, cloned, and expressed in yeast by Barderas in 2005. However, it did not maintain all its post-translational modifications, which affected IgE recognition in sensitized patients[2]. Therefore, we propose an alternative strategy to express Fra e 1 in plants. Briefly, Fra e 1 was amplified from pollen, cloned into the pCAMBIA 1302 vector, and transformed into *Agrobacterium tumefaciens* GV2260. Agroinfiltrations were performed on *Nicotiana benthamiana* leaves, collected, and frozen with liquid nitrogen for protein purification. Until now, we have amplified Fra e 1 directly from native ash pollen. We observed that our protein does not coincide at all with any of the three isoforms reported, which suggests that this Fra e 1 could be a new isoform. We validated the expression of Fra e 1-GFP recombinant by observing the *Nicotiana* leaves under a fluorescence microscope. Currently, Fra e 1 is under the purification process for immunochemical assay.

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EFFECT OF INHIBITING P450 AROMATASE ENZYME ON THE POPULATION OF MACROPHAGES, TNF-A, IFN-G AND IL-10 IN CBA/CA MALE MICE INFECTED WITH *P. BERGHEI ANKA*

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Abstract:

Malaria is the most lethal parasitic disease in the world, it causes higher mortality in men than in women, so it is important to evaluate the participation of testosterone and estradiol in this success. Both hormones are synthesized from cholesterol; however, androgens are converted to estrogens by the enzyme p450 aromatase. In this work, the participation of testosterone in the immune response against *Plasmodium berghei* ANKA was studied, for which testosterone was administered to male CBA/Ca mice, p450 aromatase was inhibited in vivo with letrozole, a competitive and specific inhibitor of the enzyme and infected with *P. berghei* ANKA. It was detected that when testosterone was administered and p450 aromatase was inhibited simultaneously, the concentration of free testosterone and parasitaemia increased. Contrary to expectations, the number of macrophages was not altered by increasing androgen concentration; however, it significantly increased the concentration of TNF-a, a cytokine that contributes to the development of cerebral malaria, and its concentration increases when IFN-g decreases. In addition, the increase in the concentration of free testosterone decreased the concentration of IFN-g and regulated via the increase of IL-10. These results suggest a testosterone-mediated mechanism that explains its immunosuppressive activity and consequently increases the severity of infection with *P. berghei* ANKA. In addition, the release of TNF-a by macrophages and the suppression of IFN-g and IL-10 are probably associated with the lethality of the infection in male mice.

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CANNABINOID RECEPTOR 2 MODULATES FCεRI-DEPENDENT ACTIVATION OF MAST CELLS

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Abstract:

The Type I hypersensitivity (allergic) reactions are exacerbated responses to foreign innocuous agents called allergens. At the begging of these reactions, there is an increase in the production immunoglobulin E (IgE) that is recognized by the high affinity IgE receptor (FceRI) expressed on the plasma membrane of mast cells (MCs). The IgE/FceRI interaction led to sensitization of MCs in a way that, when the allergen (Ag) appears, the formation of Ag/IgE/FceRI aggregates leads to a massive release of proinflammatory components by the MCs in a process known as anaphylactic degranulation. It has been proposed a mechanism in which the endocannabinoids (eCB), a family of bioactive lipids, could participate in the modulation of these responses in an autocrine fashion. This work aims to characterize the specific effect of the cannabinoid receptor 2 (CB_2) on the responses given by the activation of the FceRI receptor in MCs to understand the potential role of eCBs on the control of allergies.

We used primary cultures of bone marrow mast cells (BMMCs) sensitized with monomeric IgE. The presence of eCB receptors in those cells was confirmed by RT-PCR and immunofluorescence. Then, BMMCs were incubated with an agonist and/or an antagonist of the receptor CB_2 before being stimulated with the artificial antigen DNP-HSA. After this, synthesis of cytokine mRNA and degranulation was determined. We found variations on the effects of eCBs on FcεRI-dependent activation of MCs. Also, a constitutively active population of CB2 receptors was detected. Besides those findings, a general inhibitory effect of eCBs was found on cytokine synthesis (TNF, IL-2, IL-3, IL-4, IL-6 and CCL-2) in MCs. To analyze the negative cross-talk between the CB2 and FceRI receptors, activation of key proteins was performed and a decrease on PKC phosphorylation was found in cells pre-treated with the eCB. This work provides a better perspective of the endocannabinoid system in MCs and suggests the possible use of CB2 receptor agonists as a therapeutic approach for Type I hypersensitivity reactions.

HIGH FRUCTOSE CONSUMPTION INDUCES THE EXPRESSION OF MIR 155-5P IN MONOCYTES PRESENT IN LIVER AND EPIDIDYMAL ADIPOSE TISSUE

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Abstract:

High fructose intake through consumption of sugar-sweetened beverages contributes to the development of non-communicable chronic diseases, including obesity, type 2 diabetes, and non-alcoholic fatty liver disease [1]. Also, high fructose intake through consumption of sugar-sweetened beverages increases monocyte exposure to fructose. However, the impact of high fructose exposure on the immune system is poorly understood.

In a study in rats, it was found that high fructose intake promotes an inflammatory phenotype, increasing the production of reactive oxygen species (ROS) in mononuclear cells [4]. In addition, in THP-1 cells exposed to fructose, the inflammatory potential was increased by increasing the expression of IL-1β and CXCL8 [5]. Another study demonstrated that fructose exposure increases the inflammatory profile in LPS-stimulated human monocytes by increasing IL-1β, IL-6, and TNF-α secretion compared to glucose [6]. Therefore, the evidence indicates that fructose can amplify the inflammatory response in monocytes, however, the regulation of inflammation induced by fructose is not fully understood.

MicroRNAs (miRNAs) are non-coding RNA molecules that are involved in the regulation of almost all cellular processes, including inflammation [7]. In particular, miR-155-5p is one of the best characterized miRNAs, which plays an important role in the regulation of the inflammatory response [8]. Overexpression of miR-155-5p in monocytes induced overproduction of proinflammatory cytokines such as TNF-α, IL-6, IL-8, and IL-1β [9]. Furthermore, miR-155 inhibition in monocytes decreases the inflammatory profile through regulation of the TLR4/MyD88/NF-κB signaling pathway [10]. Therefore, the objective of the study was to determine the expression of miR-155-5p in monocytes from rats with high fructose intake. To carry out the present work, male Wistar rats were used, which were exposed to beverages with 20% fructose (w/v) or tap water for eight weeks. The expression of miR-155-5p, Cebpb, Socs-1, Tnfa and IL6 was evaluated in monocytes from fructose-ingested rats by RT-qPCR.

It was found that the expression of miR 155-5p in adipose tissue decreased, as well as the expression of IL-6, in addition no significant changes were obtained in C/EBP-B, SOC1 and enTNF-a. On the other hand, the expression of miR-155-5p in the liver did not have any change. On the other hand, the expression of miR 155 in liver increased the expression in rats with high fructose intake, as well as cebpb, socs1, IL-6, TNF-a.It can be concluded that the consumption of high fructose intake is associated with increased expression of miR-155, as well as its target genes and inflammatory mediator molecules.

IN SILICO DESIGN OF A MULTI-EPITOPE VACCINE CONSTRUCTION AGAINST *LEISHMANIA MEXICANA*

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Abstract:

Leishmania mexicana (*L. mexicana*) is the leading cause of cutaneous Leishmaniasis (CL) in Mesoamerica, a disease for which WHO reported 39,595 new cases in 2020. Currently, there is no licensed vaccine to prevent or treat Leishmaniasis in humans. Furthermore, toxicity and parasite resistance to anti-leishmanial drugs stimulate the research of alternative approaches to disease control. Polytope vaccines elicit cellular and humoral immune responses against various pathogens. Based on this rationale, we designed a multi-epitopic vaccine construction against *L. mexicana* using an immunoinformatics approach. We analyzed the parasite proteome combining VaxiJen 2.0, THMM 2.0, TOPCONS, SecretomeP 1.0 and CELLO2GO servers, from which six probable antigenic proteins were selected and used as input for B and T cells epitopes prediction in the Immune Epitope Database (IEDB). Peptides with higher immunogenicity scores were linked together through CpG oligodeoxynucleotides, resulting in a multi-epitope peptide. An i*n silico* physicochemical characterization showed the molecule is stable, immunogenic, and non-allergenic. In CL, Toll-like receptors (TLR) play a crucial role in linking innate and adaptive immunity; thus we simulated docking studies against TLR-2, 4 and 9 using ClusPro. The results obtained indicate the molecule designed is an interesting candidate to be evaluated in future immunological studies.

EVALUATION OF THE EARLY AND CONVALESCENT IMMUNE RESPONSE OF PATIENTS INFECTED BY SARS-COV-2

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Abstract:

CORONAVIRUS DISEASE 2019 (COVID-19) is a pandemic that affects millions of people around the world. The history of this pandemic is well documented since its appearance and progress in characterizing the humoral immune response to SARS-CoV-2 has been rapid, however areas of uncertainty persist. Our objective was to evaluate the early and convalescent immune response of patients infected by SARS-CoV-2. A longitudinal study design was carried out. The serum were analyzed from: patients with COVID-19 detected by RT-qPCR, who did not require hospitalization (cases); and from clinically healthy individuals with negative RT-qPCR for SARS-CoV-2 (control group). Seroconversion was determined by ELISA using SARS-CoV-2 protein S produced in eukaryotic cells (BHK, HEK, and CHO). The sensitivity and specificity of the ELISA was analyzed by the ROC curve method using Software R. The calculation of the sensitivity and specificity of the test for IgG and IgM was obtained by taking the true positive and true negative sera. A sensitivity of 84.1% and a specificity of 96.7% were obtained in the case of IgM, with a cut-off point of 0.1 and a sensitivity of 100.0% and a specificity of 96.0% in the case of IgG with a cut-off point of 0.2. For the expression of the optical densities of the ELISA, the logarithm of the result expressed in percentage of positivity (PP) was used. PP values for both IgG and IgM were analyzed over seven times (0, 15, 45, 60, 90, 180, 270 days) between the case group and the control group. The cellular response was determined by flow cytometry. Data showed that positivity for IgM lasted up to 45 days and gradually decreased until it disappeared. The IgG antibodies, in most of the positive cases it appeared after 45 days. Most of the volunteers who generated IgG antibodies kept them up to 6 months and only 4% lost them before. In addition, a considerable number of cases were found that did not generate IgM and IgG antibodies throughout the follow-up. We also found a significant increase in IFNa2 production in sera from the group of cases in the acute phase of SARS-CoV-2 infection. The concentration of IFNg, TNFa, IL-6, IL-10, IL-12, IL-18 and IL-23 was higher in the serum of positive patients in the acute phase in contrast to the control group. These indicators related to the immune response associated with the acute phase of the disease, point to the appearance of an early immunoinflammatory response.

KLF10 FAVORS MYCOBACTERIUM TUBERCULOSIS SURVIVAL BY IMPAIRING IFN-γ PRODUCTION AND PREVENTING MACROPHAGES REPROGRAMING TO MICROPINOCYTOSIS

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Abstract:

Mycobacterium tuberculosis has developed diverse mechanisms to survive inside phagocytic cells, such as macrophages. Phagocytosis is a key process in eliminating invading pathogens; thus, M. tuberculosis efficiently disrupts phagosome maturation to ensure infection. However, inflammatory cytokines produced by macrophages in response to early M. tuberculosis infection are key to promoting bacterial clarification. IFN-γ enhances M. tuberculosis engulfment and destruction by reprogramming macrophages from phagocytosis to macropinocytosis. Here, we show that the transcription factor Krüppel-like factor 10 (Klf10) plays a positive role in M. tuberculosis survival and infection by negatively modulating IFN-γ levels. Naïve Klf10-deficient macrophages produce more IFN-γ upon stimulation than wild-type macrophages, thus enhancing bacterial uptake and bactericidal activity achieved by macropinocytosis. Moreover, Klf10−/− macrophages showed cytoplasmic distribution of coronin 1 correlated with increased pseudopod count and length. In agreement with these observations, Klf10−/− mice showed improved bacterial clearance from the lungs and increased viability. Altogether, our data indicate that Klf10 plays a critical role in M. tuberculosis survival by preventing macrophage reprogramming from phagocytosis to macropinocytosis by negatively regulating IFN-γ production upon macrophage infection.

Keywords: inflammation, Mycobacterium tuberculosis, transcription factors.

This work was partially supported by grants from CONACyT (CF-2019 40792 and IFC 2016-2282) and DGAPA-PAPIIT (IN217822 and IN211719).

EFFECT OF MEMBRANE PERTURBING AGENTS ON THE SECRETED ACTIVITY OF ACID SPHINGOMYELINASE IN *ENTAMOEBA HISTOLYTICA*

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Abstract:

The host-amiba relationship is based on a series of interactions between host defense mechanisms and parasite survival strategies. Host cells have diverse mechanisms for pathogen elimination, while Entamoeba histolytica has developed strategies to counteract the host immune response and facilitate its survival. Recently, it has been described that aSMases participate in the repair of lesions in the MP through which Ca2+ internalization occurs, triggering exocytosis of the lysosomes, which upon fusion with the MP secrete aSMase, which hydrolyzes the sphingomyelin of the outer face of the MP generating ceramide, which favors the formation of endosomes to internalize the lesion.

In this work, the involvement of aSMases in the repair of E. histolytica plasma membrane damage caused by different membrane disrupting agents was evaluated. Analysis of the amebic genome showed that it has six genes encoding aSMases, with the EhaSM6 gene being the most transcribed under basal growth conditions and which generates a functional protein. Overexpression of EhaSM6 in trophozoites induces increased secreted activity and tolerance to lysis with pore-forming molecules such as β-Defensin, Magainin II, human complement and streptolysin-O (SLO), in a Ca^{2+} dependent process. Thus, aSMase6 acts as a virulence determinant by repairing the damage caused to its plasma membrane by lytic agents.

EVALUATION OF THE EFFECT OF *PLECTRANTHUS AMBOINICUS* ESSENTIAL OIL AGAINST *ENTAMOEBA HISTOLYTICA*

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Abstract:

Introduction. Amebiasis is a parasitosis and a public health problem in Latin America, caused by the protozoan *Entamoeba histolytica*. This infection can cause serious complications in those who acquire it and some of the drugs of choice used for its treatment, such as metronidazole, have limited therapeutic efficacy, mainly due to the adverse effects that its administration entails. Therefore, the search for new therapeutic options is necessary and the benefits of natural products as a potential source of drugs are well known, among them essential oils, whose components have demonstrated antimicrobial activity. **Objective.** To evaluate *in vitro* the therapeutic potential of the essential oil of *P. amboinicus* against *E. histolytica*. **Methods.** The essential oil was obtained from the leaves of *P. amboinicus* grown in Mexico City and its components were identified by GC-MS. Trophozoites of *E. histolytica* strain HM1-IMSS were exposed to increasing concentrations of the essential oil for 48 h. IC_{50} was calculated from viability by Neubauer chamber counting. Cytotoxicity of the essential oil (CC_{50}) was evaluated in Vero cells by MTT assay and selectivity index (SI) was determined. **Results and conclusions.** The essential oil of *P. amboinicus* grown in Mexico City has the terpenoids caryophyllene oxide, alloaromadendrene oxide, carvacrol, caryophyllene and camphor as major components. The essential oil possesses antiamebic activity with an IC_{50} of 121.7 µg/mL, as well as an SI of 2.99. Based on these data we conclude that the essential oil of *P. amboinicus* has antiamebic activity on the trophozoite stage of the parasite. The observed susceptibility could be related to the structural and metabolic characteristics of this protozoan.

Keywords: *Entamoeba histolytica, Plectranthus amboinicus,* essential oil, IC_{50}, selectivity index.

17BETA-ESTRADIOL INHIBITS ICAM-1, VCAM-1, P65 EXPRESSION AND INCREASE EXPRESSION OF ANTIOXIDANT ENZYMES INDUCED BY AMYLOID BETA 25-35 IN MICROVASCULAR ENDOTHELIAL CELLS (HMEC-1)

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Abstract:

Introduction. Acute myocardial infarction is the main cause of death, it is related to coronary artery atherosclerosis and the incidence increases with age. Amyloid beta-peptide (AB) is identified in the brain of Alzheimer disease (AD) patients and in systemic circulation of healthy individuals. Since AB favors the adhesion and transendothelial migration of monocytic cells on human brain endothelial cells and promotes the oxidative stress in both neurons and vascular cells, particularly endothelial cells, it could be the link between atherosclerosis and AD. The incidence of both disease in women in reproductive age is low, but it increases exponentially in postmenopausal women. 17β-estradiol (E2) inhibits endothelial adhesion molecule expression, it is recognized as antioxidant and it has a role to protect endothelial and neuronal cells of cytotoxicity.

Objective. Our aim was to determine if E2 had an effect on the expression molecules involved in the proinflammatory response induced by amyloid beta 25-35 (AB25-35).

Material and Methods. Endothelial cells (HMEC-1) were treated with, E2(1 ng/ml E2), Aβ25-35(5 uM) and ICI780182 (10mM) as estrogen receptor antagonist. Specific antibodies were used to evaluate the expression of ICAM-1, VCAM-1, p65, eNOS and Akt, SOD1, SO2, GPX4 and catalase by Cytofluorometry and Western blot analysis. U937 monocyte cells were used to do adhesion assay.

Results. Aβ25-35 increase the U937 cells adhesion and also the expression of ICAM-1 and VCAM-1 and p65 on HMEC-1, which was substantially decreased with E2. However Akt, eNOS and all antioxidant enzymes expression was diminished with AB25-35 treatment and it was reverted by E2. ICI780182 did not substantially modify the expression of almost every molecule but on Akt did.

Conclusions. Aβ25-35 enhanced the inflammation increasing adhesion of monocytes and the adhesion molecules and p65 expression on HMEC-1, but E2 decreased that expression trough modify the eNOS/Akt-signaling pathway, in an alfa and beta estrogen receptors independent manner. Aβ25-35 favored the oxidative stress through diminish the antioxidant enzymes expression, but E2 reverted its effect.

DEVELOPMENT OF ANTI-HUMAN IGA MONOCLONAL ANTIBODIES TO STUDY OF MUCOSAL COMPARTMENTS

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Abstract:

Immunoglobulin A (IgA) is the most abundant antibody and humans have two subclasses of IgA (IgA1 and IgA2). IgA1 is predominant in the blood, while IgA2 is more frequent in mucous membranes and secretions (tears, saliva, milk, colostrum, etc). IgA protects the body's mucous membranes, being the first line of defense, neutralizing viruses and toxins, and preventing the adherence and invasion of bacteria and parasites, having an essential role in mucosal immunity.

To obtain monoclonal antibodies for the detection of IgA, we used two protocols of immunization. Two different antigens were used to immunize BALB/c mice. In one group was injected with purified IgA1 from human plasma and another group was inoculated with IgA from human colostrum. We obtained and characterized two hybridomas producing monoclonal antibodies. One of the hybridomas recognized IgA1, and the other recognized both IgA1 and IgA2. Both monoclonals are IgG1 with a light kappa chain. These monoclonal antibodies were useful in quantifying IgA in colostrum as well IgA detection in saliva samples by ELISA, evaluate IgA-secreting cells from human colostrum by flow cytometry and detect bacteria IgA coating. These reagents may be useful to analyze other mucosal compartments and microbiota in humans.

IN-SILICO INVESTIGATION OF SURFACE PROTEINS FROM *SARCOCYSTIS SPP.* THAT COULD CAUSE CROSS REACTION IN THE SEROLOGICAL DIAGNOSIS OF *TOXOPLASMA GONDII*

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Abstract:

Introduction: Epidemiological data estimate that one third of the human population has antibodies against *Toxoplasma gondii* (*Apicomplexa: Sarcocystidae*); however, there is a possibility that the frequency of seropositivity is overestimated because of the presence of cross-reactive antibodies originating from phylogenetically close organisms, such as *Sarcocystis*, which is an insufficiently studied zoonotic parasite.

Objective: In this work, *Sarcocystis spp.* surface proteins were investigated in-silico that could cause cross reaction in the serological diagnosis of *Toxoplasma gondii.*

Methodology: Primary sequences of *Sarcocystis spp*. surface proteins were searched in specialized databases, which were three-dimensionally modeled by two methods, homology and AlphaFold2, and then molecular docking was carried out using ClusPro with a crystallized antibody against the surface antigen 1 (SAG1) of *Toxoplasma gondii*.

Results: 227 primary sequences of *Sarcocystis spp*. were found, of which 23 were complete and corresponded to surface antigens. Of the latter, only 6 sequences better met the requirements for the study. Each sequence was used to generate a homology model and an AlphaFold2 model, yielding a total of 12 three-dimensional models. After performing molecular docking with each *Sarcocystis* protein model and the *Toxoplasma* antibody model, tables of interacting amino acids were made and it was found that a *Sarcocystis spp*. sequence interacted with 77 amino acids of the crystallized *Toxoplasma* antibody; the other 11 *Sarcocystis* sequences interacted with 39 to 68 amino acids of the *Toxoplasma* antibody.

Conclusion: *Sarcocystis neurona* surface antigen 3 (SAG3) modeled by homology is likely to generate cross-reactivity due to the greater number of interacting amino acids. New studies should be carried out to verify the data by experimental methods.

TGF-β IN THE CONTROL OF T HELPER LYMPHOCYTE POPULATIONS IN MELANOMA

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Abstract:

TGF-β is a cytokine enriched in the tumor microenvironment that regulates the differentiation and effector function of T helper cells (Th). For example, TGF-β inhibits the expression of T-bet and GATA3, transcription factors that determine the differentiation to Th1 and Th2 phenotypes. In contrast, TGF-β is required for the differentiation of Th9 and Th17 phenotypes. TGF-β signals through type I and type II TGF-β receptors (TGFβRI and TGFβRII), inducing phosphorylation of the R-Smads (Smad2/3 complex). The R-Smads interact with Smad4, translocating to the nucleus and regulating gene expression. There are different mechanisms of regulation of the pathway, within which we can find regulation at the receptor level, mediated by Smad7, or at the level of the availability of R-Smads, mediated by TIF1γ. Smad7 acts as a negative regulator of the pathway, preventing R-Smad from binding to the TGF-β receptors. TIF1γ can bind to the R-Smads instead of Smad4 and translocate to the nucleus, serving as a positive regulator of the pathway. It can also be a negative regulator promoting the degradation of Smad4. To date, the role of inhibitors of the classic TGF-β pathway such as Smad7 or TIF1γ in T helper lymphocytes in a tumor context has not been described.

Using a murine melanoma model, it was found that TIF1γ deficiency in CD4 cells improves the antitumor response, seen as less tumor growth compared to WT mice. Preliminary results have shown a reduction in the frequency of IFNγ-producing Th1 cells and an increase in Th2, Th9 and Th17 phenotypes, with increased expression of IL-4, IL-13, IL-9 and IL-17A. On the other hand, it was found that the deficiency of Smad7 in CD4 cells worsens antitumor response against melanoma, with larger tumors being observed compared to WT mice. Experiments carried out suggest that this phenotype is accompanied by a lower frequency of Th2 and Th9 cells. Understanding the role of these regulators in the TGF-β pathway in T helper cells in a tumor context can aid in the design of therapeutic strategies against cancer.

MACROPHAGE MIGRATION INHIBITOR FACTOR CONTRIBUTES TO PATHOLOGY BY *PLASMODIUM YOELII* 17XL INFECTION

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Abstract:

Macrophage migration inhibitor factor (MIF) is a cytokine recognized regulator of the inflammatory immune response associated with several immune cells that produce inflammatory cytokines such as IL-1β, IL-6, IL-12, IL-18, and TNF-α. However, the effects of MIF on the immune response in malaria have not been studied. This work aimed to understand the effect of MIF on the immune response and pathogenesis during *Plasmodium* infection. Wild-type (Wt) and MIF knockout (*Mif* $^{-/-}$) BALB/c mice were intravenously infected with 1×10^3 *Plasmodium yoelii* (*Py*) 17XL-parasitized red blood cells. We evaluated parasitemia, survival rates, body weight loss, hemoglobin concentration, spleen-cell proliferation, and the serum concentration of IL-4, IL-10, IL-12, TNF-α, and IFN-γ in *Py*17XL-infected *Mif* $^{-/-}$ and Wt mice at 5 and 7 days postinfection. Our data showed that *Py*17XL-infected Wt mice died 11 days postinfection, while *Mif* $^{-/-}$ mice showed reduced parasitemia, and 58% of mice increased their survival after day 11 postinfection. Interestingly, Mif$^{-/-}$ mice survived until day 21 postinfection; their increased survival was associated with less severe cachexia and anemia and with the production of a Th1/Th2 cytokine combination profile including high levels of IL-12, IL-4, and IL-10, but a significant reduction of IFN-γ in serum. In addition, in response to *Py* 17XL antigen (*Py*Ag), *T. crassiceps* antigen (*Tc*Ag) or *Py*+*Tc*Ag, there were no significant differences in the proliferative response between *Py*17XL-infected *Mif* $^{-/-}$ and Wt splenocytes. These results demonstrate that MIF has an important role in regulating the immune response associated with host pathogenesis and lethality during *Plasmodium* infections.

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PARTICIPATION OF CONVENTIONAL DENDRITIC CELLS BY FLOW CYTOMETRY IN A MOUSE MODEL OF LUPUS

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Abstract:

Dendritic cells (DC) are crucial cells in the induction of immune responses, because they link innate and adaptive immunity. DC mainly participate in the presentation of protein antigens, maintenance of peripheral tolerance and activation of T cells. According to their function and location, DC are subdivided in conventional dendritic cells type 1 and 2 (cDC1 and cDC2), and have been associated with various autoimmune diseases such as Systemic Lupus Erythematosus (SLE)[1,3]. SLE is a multisystem disease of unknown etiology, with loss of tolerance, formation of lipid autoantibodies, complement activation and multisystem damage. Previously in our research group, we developed a lupus mouse (BALB/c, NIH) model by the stabilization of lipidic particles. In this model we demonstrated the production of IgG anti-lipid autoantibodies and other clinical manifestations such as the appearance of malar erythema, common in patients with Lupus[2,4]. In the present study, we analyze by flow cytometry the proportion and cytokine production of cDC1 and cDC2 in mice (BALB/c) with lupus induced by the stabilization of lipidic particles and compare them with healthy mice.

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CHARACTERIZATION OF THE PESCADILLO PROTEIN IN THE HUMAN PATHOGEN *TRYPANOSOMA BRUCEI*

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Abstract:

Human African trypanosomiasis, or sleeping sickness, is a vector-borne disease that is endemic of 36 countries of sub-Saharan Africa and is caused by two subspecies of *Trypanosoma brucei.* This flagellated parasite is interesting to study because it has several biological features that distinguish it from other eukaryotes. One of these peculiarities is the fragmentation of the 28S-type ribosomal RNA chain into two large and four small independent molecules, therefore several differences during ribosome biogenesis in *T. brucei* are expected. Pescadillo (Nop7 in yeast) is an essential element closely related to the synthesis of the 60S ribosomal subunit in *Saccharomyces cerevisiae*. Here, we characterized the Pescadillo orthologue of *T. brucei* (TbPes) using bioinformatic tools. Our *in silico* results showed that TbPes contains the two structural and functional domains, termed Pes N-terminus and BRCT. Amino acid sequence alignments indicate that TbPes is 32.22% identical to the human orthologue. In addition, the predicted three-dimensional architecture of TbPes is highly similar to the *H. sapiens* template. Furthermore, to identify proteins involved in pre-rRNA maturation in *T. brucei*, we produced transgenic parasites that synthetize a recombinant version of TbPes; then we verified the correct expression and nucleolar localization of this protein by Western blot and immunofluorescence microscopy, respectively. TbPes-PTP and associated elements were isolated using tandem affinity chromatography and fractionated by SDS-PAGE. The nature of each band was determined by mass spectrometry and bioinformatic analyses. The work was supported by PAPIIT-UNAM (grant IA204721 to Tomás Nepomuceno Mejía).

EFFECT OF PRENYLATED CHALCONES ON TRICHOMONAS VAGINALIS

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Abstract:

Trichomonas vaginalis is a primitive microaerophilic eukaryotic parasite found in the urogenital tract of humans. This parasite is the causal agent that produces trichomoniasis, the most common non-viral sexually transmitted disease in the world. In Mexico has been reported 16,903 cases in 2021. Trichomoniasis causes in women different symptoms such as vaginal discharge usually with a bad smell and greenish-yellow, dysuria, itching, vulvar irritation, and abdominal pain, vaginal pH rises to 5 or higher. *T. vaginalis* has proteinases that participate in the virulence properties such as a metalloproteinase called TvMP50 involved in the cytotoxicity into the target cells. The drug used for trichomoniasis is metronidazole, but some strains have developed resistance to the nitroimidazoles. Recently, investigations have been carried out in the search for new alternatives in the treatment for this infection, one of them is the use of flavonoid precursor molecules called chalcones (1,3-diaryl), which has been studied. The aim of this work was to evaluate, the effect of 8 prenylated chalcones (PVINA 3CL, PVINA 3F, PVINA 2NO2, PVINA 2Cl, PVONA 3Cl, PVONA 3F, PVONA 3NO2 and PVONA 2Cl) on the viability of *T. vaginalis*, the proteinases activity in substrate on gels SDS-PAGE and the transcript expression of tvmp50 by RT-PCR semiquantitative. The data showed that the PVINA 3CL had IC_{50} of 29.24μg/ml, the PVINA 3F had IC_{50} 25.18μg/ml, PVINA 2NO2 had IC_{50} of 41.92 μg/ml and PVINA 2Cl had IC50 of 87.11μg/ml on T. vaginalis viability, and the adhesion levels of the parasites treated with the prenylated chalcones into the HeLa cells diminished. The proteinases zymograms showed that the PVINA 3F reduced the TvMP50 activity and diminished the tvmp50 transcript. We determined by Molecular Docking the interaction of PVINA 3F with TVMP50. Theses prenylated chalcones could be used as a new chemotherapeutic agent for treatment of trichomoniasis.

ABSTRACTS | Poster Medicine, Health & Nutrition

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PARADOXICAL ACTIVATION OF TIMP-3 BY MMP-28 IN CELL MIGRATION

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Abstract:

Matrix metalloproteinases (MMPs) are zinc dependent proteins that degrade components of the extracellular matrix, and activate other MMPs or diverse mediators, like growth factors, cytokines and chemokines. MMP-28 is increased in the epithelium of Idiopathic Pulmonary Fibrosis (IPF), an epithelial-driven age-associated disease with very low lifespan. This enzyme induces an invasive and migratory phenotype in the human alveolar epithelial cell line A549 and in the rat alveolar epithelial cell line RLE. In addition, the MMP-28 mutant KQ-MMP28, an intracellular enzyme allegedly not recognized by furin, increases migration, while EA-MMP28, an enzyme with a mutation in its catalytic site, does not. The aim of this study is to analyze which proteases or protease inhibitors are activated by MMP-28 to induce the observed migratory phenotype. Results: Through arrays of proteases and their inhibitors, it was discovered that MMP-28 changes the expression of Tissue Inhibitor of Metallo-Proteinases (TIMPs) and MMP-2 (gelatinase A). Western blots and zymograms were used to validate the results and it was observed that in A549 cells that overexpressed MMP-28, there is a significant increase of TIMP-3, TIMP-1 and MMP-2. There were not differences in the expression of MT1-MMP. These changes were the same in the cells that overexpressed KQ-MMP28, suggesting that the results are due to the intracellular enzyme. The levels of these targets in EA-MMP28 overexpressing cells are the same as in empty vector transfected cells. The RLE cells expressing MMP-28, also increase the expression of TIMP-1 and TIMP-3; however, the expression of MMP-2 does not change, but the expression of MMP-9 (gelatinase B) does. TIMP-3 also increases at mRNA level, unlike MMP-2. Therefore, using siRNAs, the level of TIMP-3 will be decreased, and it will be analyzed if the increase in the gelatinases and the migratory phenotype depend on this inhibitor, in an overexpressed MMP-28 epithelial context. Besides, scRNAseq data shows that IPF fibroblasts overexpress TIMP-3 and MMP-2; consequently, it will be a new opportunity to evaluate if this possible new activation mechanism for gelatinase A is present in another cell type in IPF.

EFFECT OF SIALIC ACIDS α2-3 AND α2-6 STIMULATION ON PROLIFERATION AND PROTEIN SYNTHESIS ON ORAL CAVITY EPIDERMOID CANCER CELLS

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Abstract:

Introduction: Oral squamous cell carcinoma (OSCC) in México has a high mortality rate due to the fact that patients recieve treatment at advanced stages. Several molecular changes occurr in cellular transformation/ progression, such as glycosylation, especifically sialic acid (Neuc5Ac). Sialylation is a process that is altered in neoplastic cell with an increase in structures ending in Neuc5Ac-α2-3 and a decrease of Neuc5Ac-α2-3, favoring invasion and metastasis. To study the effect on proliferation and protein synthesis by stimulation of –α2-3 and –α2-6 sialic acids with lectins (MAA and SNA respectively) in SCC-152 and HaCaT cells. Methodology: SCC-152 and HaCaT cell were cultured under conventional conditions, and Neuc5Ac-α2-3/-α2-3 expression was assessed by immunocytochemistry. Subsequently, cells were deprived and incubated for 24 hours with different concentrations of MAA and SNA lectin, finally, morphology protein concetration, electrophoretic profile and cell proliferation were evaluated. Results and Discussion: SCC-152 and HaCaT cells expressed both sialic acids bu immunocytochemistry. Lectin stimulation assays showed no changes in cell morphology; however, an increase in protein concentración was observed in SCC-152 cells compared to HaCaT with SNA lectin, while there was a decrease in protein quantification in both cells with MAA lectin. Finally, an increase in SCC-152 proliferation was found with both lectins with greater effect by SNA, interestingly, this effect was also observed in HaCaT cells. Conclusions: Neuc5Ac-α2-6 favors protein synthesis in tumor cells that would favor proliferation, so it cpuld be associated with invasion and metástasis, it is necessary to purify and characterize the proteins expressinf the modification.

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EVALUATION OF THE COMBINATION OF METFORMIN, SODIUM DICHLOROACETATE AND CAFFEINE AS A TREATMENT FOR PULMONARY ADENOCARCINOMA UNDER HYPOXIC CONDITIONS

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Abstract:

Background: Lung cancer represents the second most common type of cancer and the highest mortality worldwide; adenocarcinoma is the one with the highest incidence of its subtypes. The hypoxic tumor microenvironment (in solid tumors) derived from insufficient cell perfusion may be due to the high rate of cell growth that helps to perpetuate said hypoxia, this condition within the tumor cells favors metabolic and cellular reprogramming (Warburg Effect), and this has been associated with tumor resistance to chemotherapeutic drugs and even radiotherapy. Hence, the **objective** of this work was to evaluate whether Metformin, Sodium Dichloroacetate (DCA), and Caffeine affect cell viability because these drugs have the potential to reverse metabolic reprogramming. **Methods:** Two commercial cell lines BEAS-2B (bronchial epithelium) and HCC827 (lung adenocarcinoma), were used; initially, oxygen consumption was evaluated, and later they were treated with different doses of metformin, DCA, and caffeine under hypoxic and normoxic conditions. The violet crystal technique was used to evaluate cell viability, the effect percentage was determined, and finally, a combination of the concentrations with the best effects was tested to evaluate the possible pharmacological interaction. Cell growth comparisons between different culture conditions were analyzed using the Mann-Whitney "U" test. **Results:** Regarding oxygen consumption, the HCC827 line presented a metabolism with a tendency to oxidation, unlike BEAS-2B. Statistically significant differences were observed when evaluating cell viability at all concentrations (normoxia vs. hypoxia) of the three drugs in both cell lines. However, statistically, significant differences were observed at higher doses when evaluating the pharmacological effect. Finally, when performing the holographic analysis, the combination of metformin at 7.5954 mM/caffeine at 2.1397 mM was the only one that presented the sum of the pharmacological effect under normoxic conditions. **Conclusion:** Our results point to hypoxia as a drug resistance factor (reported by other authors) regardless of the drug used; however, the metformin/caffeine combination could be a therapy with summative or adjuvant purposes in the treatment of lung cancer; therefore, it is necessary to carry out complementary techniques to confirm our findings.

ALTERED PATHWAYS OF HYPOXIA IN LUNG FIBROBLASTS AND THEIR RELATIONSHIP WITH THE DEVELOPMENT OF IDIOPATHIC PULMONARY FIBROSIS

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Abstract:

BACKGROUND. Idiopathic pulmonary fibrosis (IPF) is a progressive, irreversible, and usually fatal disease of unknown etiology. Hypoxia has been described as a determining factor in the development and progression of this disease. However, the role of hypoxia is still unclear. Therefore, this work aimed to elucidate the signature of hypoxia in the transcriptomic circuitry of IPF-derived fibroblasts.

METHODS. We performed the transcriptomic analysis with the Clariom™ D assay, human (Applied Biosystems™, Cat: 902923), on two primary healthy fibroblast cell lines (NOVA, NHLF) and three derived from IPF patient lungs that underwent 48-hour of normoxia or hypoxia, all experiments were performed in triplicate.

RESULTS. Analyzes showed the classical pathways enriched by hypoxia in healthy or fibrotic fibroblasts using EnrichR. However, differences in gene overexpression of metabolic pathways were observed in fibrotic fibroblasts, showing some heterogeneity between fibrotic cell lines; hypoxia-related pathways that were downregulated are a unique opportunity to explore.

CONCLUSION. The differences in the gene expression of fibroblasts in both oxygenation conditions are few. In specific pathways, the differences will allow us to establish the appropriate hypotheses to clarify the role of hypoxia in the development of IPF.

PERIODONTAL DISEASE INCREASE THE EXPRESSION OF ACE2 AND TMPRSS2 IN ORAL EPITHELIUM OF DIABETES MELLITUS TYPE 2 PATIENTS INCREASING THE RISK TO INFECTION OF SARS-COV-2

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Abstract:

Recently has been reported that the most critical cases of COVID-19 are in patients with comorbidities such as Type 2 Diabetes Mellitus (T2DM) and hypertension. Likewise, we have identified that SARS-CoV-2 uses the angiotensin-converting receptor 2 (ACE2) and the transmembrane protein serine 2 (TMPRSS2) to infection of human cells. In this sense, periodontal disease has a bidirectional relationship with T2DM increasing the inflammation, neutrophil activity, and cytokine release. Therefore, the periodontal disease in T2DM could increase the expression of ACE2 and TMPRSS2 in the oral epithelium increasing the risk of infection of SARS-CoV-2. Methods: Following clinical examination, the patients were classified into four groups according to the presence of periodontal disease and present of T2DM: periodontal health (PH) (PH-non-T2DM, PH- T2DM) and periodontal disease (PD) (P-non-T2DM, PD-T2DM). Blood, whole saliva samples (WSS), and epithelial cells were collected from each patient. Blood samples were used for polymorphonuclear cells count determination, while WSS was used to determine UFC of streptococcus and Staphylococcus, and the epithelial cells were used to evaluate the ACE2 and TMPRSS2 expression by immunohistochemistry

Results: Of the 105 patients analyzed, PH-non-T2DM (30) PH- T2DM (19) and PD-non-T2DM (30), PD-T2DM (26). PD-T2DM group has a significant increase in the percentage of plaque, pocket probing depth, and clinical attachment loss ($p<0.001$) compared to PH-PP group. Microbiologically PD-T2DM and PH-T2DM exhibited significantly higher UFC for Streptococcus than non-T2DM. likewise, PD-T2DM and PH-T2DM exhibited significantly lower in UFC of Staphylococcus than non-T2DM. The expression of ACE2 and TMPRSS2 was increased in oral epithelium cells from PD-T2DM and PH-T2DM patients compared to PH non-T2DM. Conclusions: T2DM patients have a distinct alteration in periodontal tissue were identified, including an increased clinical attachment loss and levels of expression of ACE2 and TMPRSS2 in epithelium oral cells. This evidence could be suggested that the periodontal disease in T2DM increases the risk of infection of SARS-CoV-2

PROTECTIVE EFFECT ON HUMAN ERYTHROCYTES OF *ANNONA MURICATA* L

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Abstract:

Among the plant species used in traditional Mexican medicine is soursop (*Annona. muricata* L.). In Mexico, the leaves of *A. muricata* L. are used to treat various diseases, such as gastric cancer, stomach pain, and bronchitis. The phenolic compounds present in this plant are considered responsible for antioxidant activity; additionally, different studies have shown the presence of flavonoids and lipophilic antioxidant compounds. However, no studies evaluating the antioxidant effect of soursop leaves on human erythrocytes have been reported, in this context, part of this research was evaluating their antioxidant effects (inhibition of hemolysis) on human erythrocytes of *Annona muricata* L. leaves. The leaves of *A. muricata* L. were obtained in Nayarit, Mexico. The dried and powdered leaves were used to prepare ethanolic and aqueous extracts. Hemolysis was induced by the radical AAPH [2-2'-azobis (2-amidinopropane) dihydrochloride]. For the assay, was proved erythrocyte suspension, the soursop extracts, and the AAPH. The results were expressed as a percentage of inhibition. *A. muricata* leaf extracts on human erythrocytes, it was observed that the AEE had a greater protective capacity since a value of 51.21 ± 0.36% inhibition of hemolysis. In contrast, the aqueous extract showed a lower protective capacity because of a hemolysis inhibition value of 4.16 ± 0.13%. Flavonoids' contents could be related to the protection of cell membranes because they interrupt the interaction of the phospholipid components and inhibit their oxidation may explain the protective effect of soursop leaf extracts evaluated in this study. Extracts from the leaves of *A. muricata* have a nutraceutical application because of anti-hemolytic activity, mainly in ethanolic extracts.

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ACETYLATION AS CRUCIAL POSTTRANSLATIONAL MODIFICATION IN PULMONARY ARTERIAL HYPERTENSION

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Abstract:

Pulmonary arterial hypertension (PAH) is the leading cause of right ventricle (RV) dysfunction. Recently, our group showed that mitochondrial protein hyperacetylation contributed to RV myocytes' energetic impairment. Upregulation of mitochondrial deacetylase enzyme sirtuin 3 (SIRT3) preserved RV myocyte function. Additionally, SIRT3 loss-of-function polymorphism has been found in peripheral mononuclear cells (PMNC) in PAH patients. This study is aimed to explore a possible relationship between protein acetylation profile, expression of Sirtuins, and clinical parameters in PMNCs from PAH patients. We studied a cohort of 20 healthy volunteers and 40 patients with idiopathic PAH that have been stable for three months with no acute auricular fibrillation. Exclusion criteria for PAH patients included type 2 diabetes, ischemic cardiomyopathy, and systemic arterial hypertension. RNA and protein were extracted from buffy coat samples using Trizol and RIPA, respectively. RT-qPCR was used to analyze critical enzymes that control the acetylome. Additionally, western blot was used to quantify acetylation protein levels and sirtuins expression. In PMNCs from PAH, patients' essential proteins that control acetylation were modified. Exploring the correlations between posttranslational modifications and activation of sirtuins in patients with PAH may help develop new approaches to address the progression and severity of the disease.

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NUTRITIONAL STATUS OF A POPULATION WITH A HIGH INCIDENCE OF CHRONIC KIDNEY DISEASE OF UNKNOWN ETIOLOGY IN THE EASTERN PART OF MICHOACAN STATE

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Abstract:

The evaluation of the nutritional status is useful to identify needs, deficiencies or excesses of nutrients in order to ensure a better quality of life in people with a chronic disease, such as chronic kidney disease of unknown etiology (CKDu). This disease does not have a known cause; however, it is associated with environmental contaminants, such as heavy metals or nephrotoxic toxins, such as the mycotoxin Ochratoxin A. About 9% of the adult population of the state of Michoacan suffers from this disease, with a 3 to 1 incidence in the eastern part of the state. Therefore, it is important to know if their diet could be contributing to the disease. **Objective:** To determine the nutritional status of a population in the Municipality of Hidalgo, Michoacán. **Methodology:** 28 participants over 18 years of age were recruited with a diagnosis of CKDu and without renal disease from the Municipality of Hidalgo, Michoacán. They answered two questionnaires, one related to their medical history and the other, related to the frequency of food consumption; weight and height were also recorded. **Results:** Participants were classified into 2 groups: 1) 17 without kidney disease and 2) 11 with CKDu. Both groups were found to have a high intake of lipids, adequate intake of carbohydrates and low intake of proteins and minerals such as calcium, selenium, iron and potassium, and vitamins D and E. In contrast, vitamin C intake exceeded the RDI. With respect to phosphorus, the mean of group 2 is within the RDI but the mean of group 1 exceeded the RDI by 571 mg. In both groups sodium was within the RDI (<2500 and <2300 mg/day, respectively). Some participants of group 1 showed symptoms of compromised renal function. **Conclusion:** Both groups present nutritional deficiencies, particularly CKDu patients; therefore, they require supplementation and other interventions.

Keywords: Nutritional status, chronic kidney disease of unknown etiology

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IDENTIFICATION OF UNFOLDED PROTEIN RESPONSE MARKERS IN LUNGS FROM HYPERSENSITIVITY PNEUMONITIS PATIENTS

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Abstract:

Several types of cytotoxic damage disrupts protein folding in the endoplasmic reticulum (ER), causes ER stress, and activates a signaling network called the unfolded protein response (UPR). The UPR is controlled by three ER-transmembrane stress sensors, namely inositol-requiring enzyme 1α (IRE1α), pancreatic endoplasmic reticulum kinase (PERK) and activating transcription factor 6 (ATF6). ER stress biomarkers has been found elevated mainly in epithelial cells from lungs of patients with Idiopathic Pulmonary Fibrosis (IPF), a chronic and progressive aging-associated disease of unknown etiology. However the role of ER stress and UPR activation in Hypersensitivity Pneumonitis (HP), another fibrotic disease, has not been described before. HP is a complex syndrome caused by the inhalation of a variety of antigens in susceptible and sensitized individuals characterized by an exaggerated humoral and cellular immune response. We explored by immunohistochemistry the localization of the ER-resident chaperone BIP/GRP78 (78-kDa glucose-regulated protein), X-box-binding protein (XBP1) and the pro-apoptotic activity of C/EBP homologous protein (CHOP) in lung tissues from control subjects and HP patients. In control lungs, we observed low positive staining for Bip and XBP1 in some macrophages and epithelial bronchial cells, whereas other cell types were negative. Conversely, a strong Bip, XBP1 and CHOP positive staining was observed in hypertrophic and hyperplastic alveolar epithelial cells, and in the epithelium from respiratory bronchioles between bridging fibrosis, in the lungs of patients with HP. Also we observed intense positive staining for Bip, XBP1 and CHOP in alveolar and interstitial macrophages and in some neutrophils in the lungs of patients with HP. A significant increase in proteins from the UPR signaling network in the lungs from HP patients compared to control lungs was observed. Our data suggest that ER stress and UPR activation could be involved in the pathogenesis of Hypersensitivity Pneumonitis.

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AUTOPHAGY AND SPC MAINTAIN STEMNESS POTENTIAL IN AGE-ACCELERATED MICE ALVEOLAR EPITHELIAL CELLS

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Abstract:

Alveolar epithelial type 2 cells (AEC2) play an important role in lung regeneration acting as facultative progenitor cells. However, during aging the regenerative capacity of the epithelium is compromised, declining along with other biological mechanisms. For example, in idiopathic pulmonary fibrosis these cells have a detrimental shift in autophagy activity associated with aging[1]. Among the factors involved during aging, the deterioration of autophagy is highlighted since it causes loss of function and survival of stem cells[2]. Therefore, it is of central importance to know if the alterations caused by aging prevent alveolar regeneration and the exhaustion of stem cells. The aim of this project was to analyze the relationship between autophagy and regeneration during aging to better understand their role in the pathophysiology of age-associated lung diseases. Methods: To assess the effect of aging in this study, we used the Zmpste24 deficient mouse that has a similar phenotype of accelerated aging as progeria syndrome. In this mouse, aging is caused by a defect in the nuclear lamina and the phenotype is acquired gradually. Thus, at 16 weeks a strong aged phenotype is established. We tested the role of aging in epithelial regeneration by a tridimensional culture of lung organoids. Epithelial cells were positively selected with EpCAM by magnetic beads. Immunofluorescence (IF) and qPCR were performed to compare and evaluate SPC levels and autophagy of these cells. Results: Although at 16 weeks Zmpste24 deficient mice show characteristics such as weight loss, hair gray, and a decreased lifespan versus WT, isolated AEC2 cells showed an increase in autophagy activity and SPC expression when compared to WT cells. In addition, they are capable of forming organoids in number and size similar to the WT and young KO mice. All these features are present when epithelial cells are cocultured with mesenchymal cells derived from WT mice. Conclusion: Alveolar epithelial type 2 cells from aged mice (Zmpste24-/-) maintain regeneration capacity *in vitro,* which appears to link SPC and autophagy.

1 Bueno, M. et al. *J Clin Invest* .125, 521–538 (2015).

2 García-Prat. et al. *Nature.* 529, 37-42 (2016)

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INVOLVEMENT OF FUSOBACTERIUM NUCLEATUM IN COLORECTAL CARCINOMA

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Abstracto:

Introduction: Colorectal carcinoma (CRC) is the most frequently diagnosed cancer and the second cause of death from cancer in United States, in México 15,000 cases are diagnosed annually, when the diagnosis is timely, 9 out of 10 patients manage to remit the illness. There are several factor that increase the probability of developing cancer, such as: genetics, age, sex, race, adenomatous polyps, inflammatory bowel disease, obesity, smoking, nutrition, etc. Currently the microbiota plays an important role in the predisposition to this disease, among the main bacterias of microbiota is *Fusobacterium nucleatum*, a gram negative anaerobe from the oral microbiota. *Fusobacterium nucleatum* manintains a symbiotic relationship with its host, but is an opportunistic pathogen too capable of causing different diseases including CRC where a strong association has been found with the development, growth, progression, prognosis, resistance to treatment and recurrence of cancer. **Methods**: a compilation of scientific publications was made whose inclusion criteria were their publication in indexed journals, ad hoc databases as PUBMED an Google Schoolars were used, the keyword used for the search were *Fusobacterium* and colorectal cancer. **Results:** *F. nucleatum* was associated with the evasion of NK cell- mediated tumor cell lysis through the interaction of FAP2 with the NK receptor inhibitor TIGIT. In colorectal cancer patients with F. nucleatum recurrence was observed after chemotherapy, due to the LPS-TLR4 interaction which altered the response to chemotherapy. Likewise, it promoted the appearance of mutations in the genome, as well as metastatic dissemination. In another group of patients, it influenced the malignant transformation of adenomas to carcinomas since it promoted a proinflammatory environment rich in ROS. Patients with high levels of intratumoral *F. nucleatum* showed a lower survival. **Conclusion:** *F. nucleatum* is closely related to the mechanisms that activate and promote CRC, so its study is of the utmost importance. Currently an early fecal marker is proposed as detection method of appearance an development of CRC, this will allow predicting the progression, prognosis and recurrence of the disease.

MICRORNAS CONTAINED IN EXTRACELLULAR VESICLES AS HIGH SENSITIVITY AND SPECIFICITY BIOMARKERS FOR HEPATOCELLULAR CARCINOMA DIAGNOSTIC

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Abstract:

Hepatocellular carcinoma (HCC) is the sixth most frequent neoplasia and the third cause of cancer mortality worldwide. The HCC research is of great interest in oncology because the percentage of incidence and mortality are similar. Therefore, early diagnosis of this pathology can significantly improve the clinical prognosis of patients. Several studies have shown that Extracellular Vesicles (EVs) —spherical double-layer proteolipids containing various molecular components, including proteins and microRNAs— are increased in the HCC blood of patients. We cultured a non-tumoral liver cell line and five hepatoma cell lines with distinct differentiation stages. Next, the conditioned mediums were subjected to differential centrifugation to obtain EVs-enriched fractions and then were effectuated to physical and molecular characterization. Our results indicated that miR-183-5p, miR-19a-3p, miR-148b-3p, miR-34a-5p, and miR-215-5p are common miRNAs contained in EVs secreted by hepatoma cell lines. Consequently, we developed a DEN-induced HCC rat model for determining the miRNA expression in circulating plasma EVs. The results showed that miRNA expression levels are significantly higher in plasma circulating EVs obtained from DEN-treated rats compared with control rats. Then, we evaluated the miRNA expression in EVs-derived HCC patients with different clinicopathological features and healthy volunteers. qPCR data analysis exhibited a significantly high miRNA relative expression of all evaluated microRNAs in plasma circulating EVs of HCC patients compared to EVs of the control subjects. Furthermore, we validated the diagnostic accuracy of miRNAs as HCC biomarkers by ROC curves of every miRNA in HCC patients compared to a control group. These results suggested that the analyzed miRNAs provided promising AUC, sensitivity, specificity, accuracy, and LR values for discriminating HCC patients from healthy subjects. Finally, for increased the diagnostic test capacity of analyzed miRNAs, we determined the optimal biomarkers combinations through combiROC. These results suggested that combining these five analyzed miRNAs provided a new diagnostic panel for detecting HCC.

IDENTIFICATION OF GENETIC VARIANTS OF THE FTO GENE AND THEIR ASSOCIATION WITH MARKERS OF OBESITY IN THE MEXICAN POPULATION

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Abstract:

The FTO gene is a gene located at locus 16q12.2, which has been associated with the presence of obesity in several studies. Similarly, the specific association of various single nucleotide polymorphisms (SNP) of this gene and the presence of obesity in humans has been studied. For this reason, this work focuses on the identification and association of genetic variants of FTO with markers of obesity in the Mexican population. For the above, a sample of 638 subjects of both sexes, participants in the SUSLUD-UAQ program was taken. From this evaluation, the clinical variables of waist circumference, BMI, body fat %, serum levels of triglycerides and total energy consumption were taken, as well as a whole blood sample from which the genomic DNA was extracted with a commercial kit and identified 100 genetic variants of the FTO gene by isothermal PCR. The data was analyzed using the statistical program IBM SPSS Statistics V21, in which descriptive statistical analyzes were performed to determine the prevalence and genetic frequencies and binary logistic regressions adjusted for sex and age were performed to determine the association between clinical variables and SNP. 51.6% were female and 48.4% male; 30.9% had a high waist circumference; 7.4% obesity and 25.1% overweight according to their BMI; 46.9% a high fat; 18.2% high triglyceride levels and 44.7% an energy intake above the median (2400 kcal). Of the 100 genetic variants analyzed, 8 variants were not found to be present in at least 1% of the population. The additive analysis for the dominant model showed significant associations with various clinical variants, among which risk associations between a BMI>30 kg/m2 and the rs10852523 (OR=2.998), rs61743972 (OR=2.395), and rs7203572 (OR=2.395) stand out. OR=1898); likewise, a risk association was observed between high levels of triglycerides and the rs4389136 (OR=1.692). On the other hand, a significant association of protection was also found between the rs74449711 (OR=0.080), rs74018195 (OR=0.113) and rs17820328 (OR= 0.414) with energy consumption greater than 2400 kcal, also an association between a high fat percentage and the SNPs rs9934504 (OR=0.560), and rs17819033 (OR=0.576). The results obtained show clear associations between clinical markers of obesity and FTO polymorphisms reported in other populations and the Mexican population, as well as others never reported before, which allows expanding the investigations of SNP of said gene and its relationship with obesity.

IDENTIFICATION OF GENE EXPRESSION SIGNATURES ASSOCIATED WITH CISPLATIN INTRINSIC RESISTANCE IN LUNG ADENOCARCINOMA CELL LINES

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Abstract:

The use of doublet platinum-based chemotherapy, using cisplatin (CDDP), is the standard care treatment for lung adenocarcinoma. However, not all patients respond to CDDP therapy because of intrinsic resistance. In this setting, drug-tolerant persister cells (DTPs) are those resisting the initial drug insult. Although acquired resistance to CDDP in lung adenocarcinoma has been extensively described, few studies have investigated the mechanisms leading to DTPs associated with intrinsic resistance to CDDP.

Methods: We examined the cytotoxic effect of CDDP by measuring the percentage of cell death following exposure on lung adenocarcinoma cell lines A549, H1299, H1573, and 3B1A (patient-derived). In CDDP-DTPs, we sequenced the transcriptome to identify differentially expressed genes. Expression of candidate genes was validated by RT-qPCR. The clinical relevance of candidate genes was analyzed using two independent cohorts of CDDP-treated patients.

Results: The lung adenocarcinoma cell lines exhibited distinct degrees of sensitivity to CDDP since different percentages of dead cells were detected. Bioinformatic analysis revealed that the transcriptome of CDDP-DTPs was negatively enriched with genes involved in WNT and cell cycle pathways. Contrariwise, oxidative phosphorylation and metabolic degradation of drugs were positively enriched. Unsupervised hierarchical clustering using expression of differentially expressed (DE) genes revealed that cell lines clustered according to CDDP sensitivity. Interaction network analysis of DE genes resulted in the identification of three highly connected sub-modules involved in chromatin remodeling, cell cycle, PI3K, and MAPK pathways. Survival analysis of hub genes showed that expression of *SOCS1, GADD45A, MLLT3, NR2F2, TET3, TAF4,* and *NCOA3* was associated with overall survival in CDDP-treated patients.

Conclusion: In lung adenocarcinoma cell lines, altered expression of genes involved in oxidative metabolism and reduced proliferation rate contributes to intrinsic resistance to CDDP. The association of expression with the survival of patients indicates that these genes could be employed as biomarkers or potential targets to improve survival of patients.

CHANGES IN MITOCHONDRIAL DYNAMICS AND ITS MODULATION BY AN ADENOSINE DERIVATIVE IN THE REMODELING STAGE IN AN EXPERIMENTAL MODEL OF MYOCARDIAL INFARCTION

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Abstract:

In Mexico, the second cause of death is heart disease, among them the acute myocardial infarction, which is caused by ischemic necrosis induced by vascular occlusion induced by rupture or erosion of an atherosclerotic plaque that produces reduced blood flow in the coronary artery and oxygen levels. In an experimental model of myocardial infarction induced with isoproterenol (Iso), sequential changes in energy metabolism have been demonstrated in the stages of pre-infarction (12 h), infarction (24 h), and 72 h after administration of Iso. In addition, it was shown that in the postinfarction stage, oxygen consumption and mitochondrial membrane potential cannot be recovered. Because the energy demand of the heart is high, it is necessary for the mitochondria to perform their function properly. Therefore, the objective of this work was to study histological changes and mitochondrial dynamics one month after infarction, in the remodeling stage, and the possible protective effect of the adenosine derivative IFC-305, which has previously been shown to have the ability to recover mitochondrial function. Four groups of Wistar rats were formed: 1) the control group, to which saline was administered i.p.; 2) In the second group, the infarction was induced by the administration of Iso (85 mg/Kg s.c.) and saline was administered i.p. as a vehicle; 3) The third group received Iso (85 mg/Kg s.c.) and subsequently treated with the IFC-305 compound (50 mg/kg/day i.p. for 1 month); 4) The last group was administered only with IFC-305 (50 mg/kg/day i.p. for 1 month). Rats were randomly taken to confirm infarction induction by histological analysis at 96 h after Iso administration. In addition, it was confirmed by electron microscopy that there are mitochondrial morphological alterations. This work shows alterations in mitochondrial activity possibly as a consequence of the remodeling process of cardiac tissue. As shown in electron microscopy, the proteins responsible for regulating the processes of mitochondrial dynamics show the persistence of fission compared to mitochondrial fusion. The IFC-305 compound is capable of regulating these alterations and may be an adjunct in the treatment of the sequelae of a myocardial infarction.

DETECTION AND VALIDATION OF RESPONSE BIOMARKERS IN PATIENTS WITH LOCALLY ADVANCED SARCOMAS: CLINICAL AND MOLECULAR ANALYSIS

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Abstract:

Soft-Tissue Sarcoma (STS) is a heterogeneous group of neoplasms of mesenchymal cells and has a characteristically source number of connective tissues. About 50%-60% of sarcomas arise from extremities, which originates mainly in the limbs and has a high degree of metastasis, furthermore, it shows a great histologic subtype diversity. The standard treatment for STS locally advanced in extremities (LAE) is surgery combined with neoadjuvant or adjuvant therapies based on chemotherapy and radiation and/or isolated limb perfusion (ILP). Both therapies have a high recurrence and progression rate while successes are rare. Due to the, and the high degree of heterogeneity that this kind of cancer presents, there has been a rise in the use of precision medicine for the treatment of STS LAE. The development of studies which allow us to identify molecules that could work as possible biomarkers for diagnosis and prediction of the response to current therapy become necessary. In 2017, Dancsok et al. studied eight molecules that regulate the signaling pathways associated with the resistance in STS treatment. The found molecules were: the PDGFR-β, mTOR, Notch, β- catenina, Hedgehog , MDM2, DDX3 and Hsp90; all of this seem participate in the development of resistance mechanisms to different kinds of therapy. Aim: In the present study, we evaluate the response to combined chemotherapy and radiotherapy against PAE therapy in a cohort of patients with STS LAE with expression profile of six molecules associated with the therapy resistance in STS. Methods: A cohort of patients was established from a database given by the skin and soft parts department of NCI, México. The expression profile of the proposed molecules was determined by immunohistochemistry and the association of the clinical variables of interest was analyzed. Immunohistochemistry was performed from our panel of 6 molecules associated with the therapy resistance in STS: HSP90, HSP90α, HSP90β, p-mTOR ser2448, p-Akt ser473 and β-cateniResults: Hsp90 was found expressed at the cytoplasm level in epithelioid sarcoma, in clear cell sarcoma and primitive neuroectodermal sarcoma and at the nuclear level in pleomorphic sarcoma, synovial sarcoma, liposarcoma and spindle cell sarcoma. On the other hand, p-mTOR ser2448 was found at the cytoplasmic level in epithelioid sarcoma and synovial sarcoma and, interestingly, at the nuclear level, it was found in pleomorphic sarcoma and myxoid liposarcoma. Likewise, p-Akt ser473 was found at the cytoplasmic level in epithelioid sarcoma and in myxoid liposarcoma, being found at the nuclear level in pleomorphic sarcoma. Similarly, β-catenin was found at the nuclear level in spindle cell sarcoma, this one being the last protein to be standardized. p53 protein showed higher expression in several STS histologic subtypes. The expression profile between the five molecules evaluated allow to identify patients subgroup with STS LAE with worse prognosis and therapy resistance in STS LAE subjected to chemotherapy and radiotherapy versus PAE therapy.

EFFECT OF THE CONSUMPTION OF RAMÓN FLOUR ON HIGH-FAT DIET-INDUCED OBESITY MODEL

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Abstract:

Ramón seed (Brosimum alicastrum Swartz) is a traditional food in Mexico, it contained fiber, protein, and bioactive compound, which are related with beneficial effects on health1,2. Obesity is a public health of Mexico, and it is related with multiple factors such as glucose intolerance, insulin resistance, nonalcoholic fatty liver disease and dyslipidemia3. Objective: To determine the effect of the consumption of ramón flour (RF) on high-fat diet-induced obesity model. Methods: Twenty male BALB/c strain mice were divided in 4 groups based on diet consumption (n=5): Control (C): AIN-93 control diet4; C+RF: control diet adjusted with 30% ramón flour; HFD: high-fat diet + sugar in water, and HFD+RF: high-fat diet adjusted with 30% of ramón flour + sugar in water; diets were consumed for 90 days. Results: No differences were observed in body weight among groups. HFD+RF showed lower glucose concentrations on OGTT at 60 min (162 ± 14.2 vs 216 ± 22.8 mg/dL, $P<0.05$) and 90 min (124 ± 5.67 vs 182 ± 17.5 mg/dL, $P<0.01$) compared to HFD. On serum biochemical parameters, HFD+RF had lower concentration of total cholesterol (148 ± 4.37 vs 228 ± 5.44 mg/dL, $P<0.05$) and ALT (11.4 ± 2.41 vs 35.2 ± 3.64 U/mL, $P<0.01$) compared to HFD; and C+RF group showed lowest concentration of total cholesterol and triglycerides ($P<0.05$). Analysis of different weight tissues showed that HFD group had greater amount of white adipose tissue (WAT) compared to the HFD+RF (1.55 ± 0.26 vs 0.82 ± 0.18 g, $P<0.05$). Also, only the HFD group presented lipid vacuoles on liver histology. Conclusions: Consumption of RF decreases glucose and cholesterol level and decreased the accumulation in liver on high-fat diet-induced obesity model.

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LACK OF PROLACTIN RECEPTORS LEADS TO PRECOCIOUS INTESTINAL MATURATION IN LACTATING MICE

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Abstract:

Postnatal gut maturation is a gradual process that involves changes to provide major absorption selection between milk molecules and exogenous antigens. The immature epithelium responds to milk components and acts as an interface with the neonatal immune system. Prolactin (PRL) is a pleiotropic pituitary hormone present in maternal milk in high quantities. Milk PRL is a bioactive component able to ameliorate metabolic alterations in pups nursed by dams on a high fat diet during lactation. However, the tissue targets that mediate milk PRL actions on the offspring are unknown. We hypothesized that milk PRL regulates intestinal epithelium maturation, acting through its receptors present in the gut of lactating pups. To test this, we measured gene expression by RT-qPCR of neonatal (immature) and adult-type (mature) epithelium on proximal small intestine (duodenum and jejunum) of lactating PRL receptor null mice (Prlr-KO) and their wild type (Prlr-WT) pairs at postnatal days (PD) 7, 14 and 21. As markers of neonatal epithelium (Neo-Ep) we evaluated Lactase *(Lct)*, Argininosuccinate synthetase 1 *(Ass1)* and neonatal-Fc-receptor *(Fcrn).* Whereas markers of adult epithelium (Ad-Ep) were Sucrase isomaltase *(Si)* and Adenosine desaminase 1 (*Ada1)*. Significant changes were observed between genotypes at PD14. Duodenum of Prlr-KO showed reduced expression of markers of Neo-Ep *Lct* and *Fcrn* compared to Prlr-WT. Whereas, the jejunum of Prlr-KO showed higher expression of markers of Ad-Ep, *Si* and *Ada1,* and lower expression of markers of Neo-Ep *Lct*, *Ass1* and *Fcrn* than Prlr-WT PD14. Thus, Prlr-KO at PD14 show a phenotype of precocious intestinal epithelium maturation, an event that could lead to adverse health consequences, such as poor digestion of lactose. In addition, low expression of Ass1 in jejunum of Prlr-KO may lead to reduced arginine synthesis, an amino acid important for tissue growth and repair. Neo-Ep shows high expression of Fcrn that binds and improves transcytosis of immunoglobulin G (IgG) from milk leading to acquisition of passive immunity from the mother. Lower expression of Fcrn in proximal small intestine of Prlr-KO PD14 could lead to reduced passive immunity. In summary, these results support that milk PRL modulates enterocytes maturation, avoiding precocious intestinal maturation. Hence, milk PRL may be a regulator of the neonatal immune system-gut axis.

Key words: Enterocytes maturation, lactating pups, milk prolactin.

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OH-ATRAZINE INDUCE EXPRESSION SYNCITIN AND β-HCG ON THE HUMAN TROPHOBLAST

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Abstract:

Introduction: The pesticide Atrazine belongs to the 2-chloro-s-triazine family of herbicides. It is one of the most used herbicides worldwide, has been detected as one of the main pesticide contaminants of groundwater and surface water. Thus, the arbitrary and indiscriminate use of atrazine in the areas of agricultural cultivation, represents a great risk of contamination of the aquifer mantles. During pregnancy, the endocrine disrupter chemicals (EDCs), have adverse effects on human placenta. It has been shown that atrazine decreases the synthesis of hCG protein in human trophoblastic cells, therefore, are greatly exposed to environmental polluting chemicals which gain access to maternal blood. Nowaday known that syncitin, play an important role in the proliferation and differentiation of trophoblasts, key event in the formation of the hemato-placentary. In this way any alteration of the mechanism can be associated with abortions and fetal growth restriction.

Objective: The present study was designed to determine the effects of atrazine in vitro, on human trophoblast, using the trophoblast-derived choriocarcinoma BeWo line cell.

Material and methods: The choriocarcinoma-derived BeWo cell line ($1.5X10^3$/well) were seed into 96-well microplates for the viability test using comercial CytoTox 96 assay kit. To determine effect of atrazine on human trophoblast, ($5X10^4$cells/well) were seed into 24-well plates containing 1 mL of DMEM culture medium with the atrazine at concentrations ranging from $1X10^{-5}$ to 10 micromolar (mM), for 48 hours. The total RNA content was extracted using the phenol-chloroform method and a Nanodrop Spectrophotometer was used to determine RNA quantity. Each sample was reverse transcribed to cDNA using the Invitrogen retrotranscription kit. Specific primers for genes syncitin and bhCG, were designed through the web application Primer BLAST.

Results: The exposure of trophoblasts to different concentrations of OH-atrazine (pM–mM), did not affect cell viability during 72 h. We observe the expression of both genes increases in the rank of atrazine concentration that are reported in various body fluids in humans.

Conclusion: The present study brings to the light important effects on human trophoblast exerted by environmental polluting chemicals. OH-Atrazine there was an inducter effect on the mRNA syncitin and bhCG in the human trophoblast. Is interesting since this imbalance can alter the processes of implantation and placentation in pregnant women exposed to the herbicide and potentially, contribute to the development of pathologies such as intrauterine growth retardation and preeclampsia. The effects sustained at concentrations as low as pM raise great concern about the environmental risk to pregnancy, pointing to the need for protecting development of the foetus from the toxic effects of EDCs.

IMPACT OF MIR-155-5P ON THE FIBROTIC PHENOTYPE OF LUNG FIBROBLASTS IN HYPERSENSITIVITY PNEUMONITIS

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Abstract:

Hypersensitivity Pneumonitis (HP) is a complex syndrome characterized by an exacerbated immune response that affects lung parenchyma and may evolve into progressive fibrosis (PF). The deregulation of microRNAs (miRNAs) and genes have been involved with the pathogenesis of multiple interstitial lung diseases (ILDs). Despite the role that the miRNAs play in lung fibrosis, their involvement in HP remains unexplored. Using an integrated analysis on microarray and RNA-seq of HP profiles, we identified differentially expressed (DE)-miRNAs and DE genes (DEGs) associated with HP. From DEGs in HP lungs, we identified microRNA-155-5p (miR-155-5p) and other 17 novel miRNAs that could regulate DEGs in HP lungs to respect control and idiopathic pulmonary fibrosis (IPF) lungs. Primary lung fibroblasts were used to evaluate *in vitro* the role of miR-155-5p in HP. We found that HP fibroblasts have higher levels of miR-155-5p, present high proliferative capacity, and have less senescence markers than IPF fibroblasts. The exogenous miR-155-5p expression increased the proliferation rate, decreased TP53INP1 expression, and its migratory capacity, while miR-155-5p inhibition reduced proliferation and increased the senescence markers. In addition, IL-17 and IL-4 stimulated the miR-155-5p expression in HP fibroblasts. Our findings suggest that the inflammatory environment in HP lung promotes miR-155-5p expression in lung fibroblasts which regulates specific features in HP fibroblasts, which may be a critical difference with IPF fibroblasts.

CURCUMINOID EFFECTS ON A MODEL OF FATTY LIVER IN RATS

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Abstract:

Introduction: Curcumin is a polyphenol found in turmeric and has been reported to have antioxidant, anti-inflammatory, and hepatoprotective properties, among others. Polyphenols rich diet would be beneficial for the treatment of metabolic diseases, such as, metabolic syndrome, and non-alcoholic fatty liver disease. This work summarizes the influence of oral supplementation with curcumin or diacetyl curcumin on non-alcoholic fatty liver disease and dyslipidemia induced by high-fat and high cholesterol diet (HFD).

Methods: Twenty-four male Wistar rats (180-200g) were fed on HFD diet (27% more fat than control), by 10 weeks. At the 4th week were treated with curcumin (C) and diacetyl curcumin (A) suspended in soybean oil, with rodent-appropriate orogastric tube.

The groups were the follow:

I. ND, Group, fed on normal-control diet for rodents and 0.5 mL soybean oil.

II. HFD, high fat diet and 0.5 mL soybean oil.

III. HFD+C, high fat diet+ curcumin (100 mg/0.5mL soybean oil)

IV. HFD+A, high fat diet+ diacetyl curcumin (50 mg/0.5 mL soybean oil)

At the end of the experimental time, the rats were euthanized, obtaining blood, liver and retroperitoneal fat.

In both blood and liver were measured: triacylglycerols (TAG), total cholesterol (TC), glucose and thiobarbituric acid reactive substances (TBARS). Retroperitoneal fat, wet liver weight, as well as the body weight, were determined gravimetrically.

Results

The increase in body weight at the end of the experimental time was not different among the groups. The percentage of retroperitoneal fat was lower in curcuminoid-treated rats versus HFD.

In plasma, there were no changes among the groups on each metabolite analyzed.

The most important effects of curcuminoids (HFD+C and HFD+A groups) was on the liver, especially on the concentration of total lipids, TC, TAG and TBARS, observing significant differences as compared to the HFD group.

Therefore, the results have shown a protective and antioxidant effects of curcuminoids against the development of non-alcoholic fatty liver disease.

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CLINICAL RELEVANCE OF THE *HSP90AA1* AND *HSP90AB1* EXPRESSION PROFILE IN PATIENTS WITH LOCALLY ADVANCED SOFT TISSUE SARCOMA OF THE EXTREMITIES

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Abstract:

Soft-Tissue Sarcoma (STS) is a neoplasm of mesenchymal cells and has a characteristically source number of connective tissues with more than 70 histological subtypes. About 50%-60% of sarcomas arise from extremities, which originates mainly in the limbs and has a high degree of metastasis. The standard treatment for STS locally advanced in extremities is surgery combined with neoadjuvant or adjuvant therapies based on chemo and radiotherapy (CT/RT) and/or isolated limb perfusion (ILP). Both therapies have a high recurrence and progression rate while successes are rare. Become necessary the development of studies which allows us to identify molecules that work as biomarkers for prediction of the response to current therapy. In 2017, Dancsok et al. studied eight molecules that regulate the signaling pathways associated with the resistance in STS treatment. Molecules found were the PDGFR-β, mTOR, Notch, β-catenin, Hedgehog, MDM2, DDX3 and Hsp90. Moreover, Ernst et al. In 2015, the overexpression of HSP90 isoforms were related *HSP90AB1* with the radioresistance, being that multiple HSP90 client proteins orchestrating characteristics of the malignant phenotype, including angiogenesis, invasiveness, and metastasis. **Aim:** To evaluate the response to combined CT/RT against ILP therapy with the mRNA expression level of HSP90 isoforms to identify its independent role with resistance therapy in STS locally advanced in extremities. **Methods**: A cohort of patients was established from a database given by the skin and soft parts department of NCI, México. mRNA expression level of HSP90 isoforms was determined by qRT-PCR from formalin-fixed, paraffin-embedded tissue sections (FFPE) and the association of the clinical variables: survival, tumor size, prognosis, clinical stage, cell subtype and response to treatment. **Results:** The expression profile between HSP90 isoforms its related to the clinical variables of interest was analyzed, further allow to identify patients subgroup with STS locally advanced in extremities with worse prognosis and therapy resistance in subjected to CT/RT versus ILP therapy.

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EFFICACY OF A HIGH-PROTEIN DIET TO LOWER GLYCEMIC LEVELS IN TYPE 2 DIABETES MELLITUS: A SYSTEMATIC REVIEW

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Abstract:

Diabetes is a metabolic disease with a high worldwide prevalence, and an important factor of mortality and disability in the population. Complications can be reduced or prevented with lifestyle changes in physical activity, dietary habits and smoking cessation. High-protein diets (HPD, >30% or >1.0 g/Kg/day) decrease glycemia in part due to their content of branched-chain amino acids (BCAAs), mainly leucine. Leucine (and other BCAAs) improve glucose metabolism by directly signaling in the Mediobasal Hypothalamus (MBH), increasing liver insulin sensitivity. To determine the effectiveness of a HPD to lower hyperglycemia, we analyzed the results of published clinical studies focusing on the levels of fasting plasma glucose (FPG) and/or glycosylated hemoglobin (HbA1c) in patients with type 2 diabetes mellitus (T2DM). We carried out a systematic search for clinical studies assessing HPDs. We searched 5 databases (Scopus, Web of Science, PubMed, Epistemonikos and Cochrane) collecting 179 articles, and finally selected 8 articles to further analyze their results. Among the 8 studies analyzed, in 4 of them HPD caused a decrease in FPG in a range of 0.3 to 2.5 mmol/L, a higher level than with a CD, which caused a small drop from 0.03 to 2.2 mmol/L. Meanwhile, in 5 of the 8 studies, HPD induced a decrease of HbA1c between 0.29 to 1.8%, while CD values decreased between 0.05 to 1.3%. The rest of the studies reported unchanged values. On first look, it could be thought that the HPD values does not provide a very clear outcome compated to the CD group, however, upon furhter analysis of the glycemic profile, a clear benefit emerges. In conclusion, HPDs are a better alternative than CDs to reduce hyperglycemia in patients with T2DM. For this porpoise, are especially useful the so-called Paleolithic diets, due to its higher quality protein of animal and vegetal sources, excluding grains, dairy products, salt, refined fats and added sugars.

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A VEGETAL PROTEIN AND FIBER RICH NUTRACEUTICAL AMELIORATES FEATURES OF HEART FAILURE WITH PRESERVED EJECTION FRACTION IN A MOUSE MODEL

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Abstract:

Among cardiovascular diseases, prevalence of Heart Failure with preserved Ejection Fraction (HFpEF) is particularly relevant and several models trying to recapitulate its effects have been developed. Recently, (Schiattarella et al., 2019) developed a mouse model which exhibits most of the features related to human HFpEF. Since many of the characteristics of cardiovascular diseases are related to metabolic disorders and nutraceuticals are a promising alternative to counteract some of these features, we intervened diet of HFpEF mice with a protein and fiber rich nutraceutical of vegetal origin. The HFpEF model we used is based on a high fat diet (HFD) combined with L-NAME administration during 8 weeks, once this time passed, we alternated the HFD with the nutraceutical during 4 weeks. During the intervention we found that caloric intake from HFD was 51 % less than that of regular chow, from nutraceutical was 39 % less than that of regular chow and 57 % less than that of HFD. At the end of intervention, we measured several parameters from mice plasma and found that nutraceutical consumption increased triglycerides circulation in both control and HFpEF groups. Serum cholesterol was increased by the HFpEF diet but also by the nutraceutical consumption, besides, nutraceutical preferentially increased High Density Lipoprotein circulating levels in both control and HFpEF groups. Although cardiac hypertrophy was not detected by means of cardiomyocyte transversal area, BNP expression was increased in HFpEF mice but nutraceutical consumption reduced this increment. Regarding the known systemic inflammation present in cardiovascular diseases and metabolic syndrome, we measured cytokines expression in heart through qRT-PCR and found that Il1β mRNA was only reduced in the HFpEF group intervened with the nutraceutical. Il6 levels were diminished by the HFpEF treatment and in a greater extent by the nutraceutical alone or in combination with the HFpEF treatment. Finally, Tnfα mRNA was increased in the HFpEF group and nutraceutical reversed this increment. In conclusion, the dietary intervention with a vegetal nutraceutical rich in protein and fiber reduced some of the deleterious features of HFpEF possibly by altering inflammatory pattern. Exploration of appetite related hormones are needed to better understand the mechanism of action.

Schiattarella, G. G., Altamirano, F., Tong, D., French, K. M., Villalobos, E., Kim, S. Y., Luo, X., Jiang, N., May, H. I., Wang, Z. V., Hill, T. M., Mammen, P. P. A., Huang, J., Lee, D. I., Hahn, V. S., Sharma, K., Kass, D. A., Lavandero, S., Gillette, T. G., & Hill, J. A. (2019). Nitrosative stress drives heart failure with preserved ejection fraction. *Nature 2019 568:7752*, *568*(7752), 351–356. https://doi.org/10.1038/s41586-019-1100-z

INVOLVEMENT OF THE EIF4E FACTOR IN THE MECHANISM OF DOXORUBICIN RESISTANCE IN TRIPLE-NEGATIVE BREAST CANCER MODEL

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Abstract:

Breast cancer is the most common malignancy and is one of the leading causes of cancer mortality in women worldwide. Tumors with triple-negative features are highly aggressive and have a relatively short life expectancy. Chemotherapy with anthracyclines is the standard treatment for this type of cancer; however, one of the main problems is chemoresistance, which has been demonstrated in several types of cancer, achieved by the overexpression of efflux bombs. The latter relates to an increase in the translational capacity of cancer cells [1,2]. Previous work of our group has shown that in a triple-negative breast cancer cell (TNBC) model, PDCD4 expression is downregulated in a cell line treated with doxorubicin, a drug of the anthracycline family. These cells show increased invasiveness and notably, the levels of eIF4F complex formation were higher, which is composed of eIF4A, eIF4E, and eIF4G proteins. eIF4E factor represents a pharmacological target that may be critical in the chemoresistance processes associated with the overexpression of efflux pumps such as ABC transporters, particularly the ABCC family. Therefore, our project aims to elucidate the association of the translation process of the eIF4E factor with the overexpression of ABC transporters. Our protocol aimed to generate doxorubicin chemoresistant MDA-MB-231 cells, we evaluated their cellular behavior through scratch-wound assays, where we observed an increase in cell migration in resistant cells, as well as an increase in secretion and activity of metalloproteases 2 and 9; we are also evaluating the effect of eIF4E inhibition by 4E1RCat on cell migration and metalloproteases secretion and activity. On the other hand, we characterized the expression of the eIF4E factor as well as the expression of specific ABC transporters, by western blot and qPCR techniques. Data suggest that the eIF4E factor es implied in the chemoresistance and its inhibition could sensitize the resistant cells.

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IMPACT OF RESISTIN ON MIGRATION AND INVASION PHENOMENA IN PC3 PROSTATE CANCER CELLS

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Abstract:

Introduction: Prostate cancer is the second most common cancer diagnosis and the fifth cause of death worldwide among malignant diseases. In Mexico during the year 2020, an incidence of 26, 742 prostate cancer cases were reported, 70% of which were detected in advanced stages of the disease. Resistin is a protein rich in cysteine residues secreted by resident macrophages of adipose tissue and is associated with tumor progression. Transduction pathways that are mediated by Resistin have been described in various types of cancer cells, including signaling through toll-like receptor 4 (TLR4), and activation of the PI3K/Akt/NF⊠B pathway (1). In line with this notion, it has been observed that Resistin expression levels are elevated in high-grade prostate tumor tissue; while in low-grade tissue or with benign prostatic hyperplasia, the expression of this protein was significantly lower (2). **Objective:** Characterize the role of Resistin on migration and invasion in PC3 prostate cancer cells. **Methodology:** PC3 cell cultures were stimulated with increasing concentrations of Resistin. Cell migration was evaluated by scratch wound assays, while invasion was determined by Matrigel-coated Boyden chambers. MMP-2 secretion was evaluated by zymography. **Results:** In the present study, we show that treatment of PC3 cells with Resistin promotes an increase in migration and invasion, accompanied by an increase in MMP-2 secretion. **Conclusions:** In summary, our data demonstrate that Resistin induces migration and invasion in PC3 prostate cancer cells.

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EFFECT OF ENDOCRINE DISRUPTING COMPOUNDS IN NEURONS ASSOCIATED TO AUTISM SPECTRUM DISORDER

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Abstract:

Autism Spectrum Disorder (ASD) is a neurocognitive disorder characterized by atypical social interaction due to unknown etiology. Recently, ASD has been proposed to be associated to redox imbalance in neurons caused by involuntary fetal exposure to Endocrine Disrupting Compounds (EDCs) during pregnancy or early life-stages. EDCs can be found in food. Their origin is diverse (e.g. packaging, irrigation water, etc.) and although they are found in low concentrations (ppm or ppb) they are capable of altering endocrine functions, leading to the production of oxidative stress and causing changes in the ratio of metabolites related to methionine synthase (MS) activity.

In the present work, the viability of neuronal cell cultures was evaluated in vitro with the most common EDCs reported in food: phthalates and bisphenol A (BPA) at different concentrations. Cultures were exposed to EDCs in 24 h treatments in order to identify the specific MS activity.

As a result, enzymatic activity of MS was reduced up 66%, namely 3-fold in comparison to cultures that were not exposed to EDCs. Our results demonstrate that some endocrine disrupting compounds in food can significantly reduce the enzymatic activity of methionine synthase in neurons, leading to possible changes associated with autism.

EFFECT OF THE COADMINISTRATION OF RESVERATROL AND VITAMIN C ON OXIDATIVE STATUS IN POSTMENOPAUSAL WOMEN WITH INSULIN RESISTANCE. RANDOMIZED CLINICAL TRIAL

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Abstract:

BACKGROUND: IN POSTMENOPAUSAL WOMEN, DUE TO ENDOCRINE changes, there is an increase in oxidative stress that predisposes them to the early manifestation of fragility syndrome, as well as cardiovascular and metabolic alterations that represent comorbidity with chronic degenerative diseases. Postmenopausal women constitute an ideal model of study, due to the set of the effects produced by aging; There is also a tendency to increase adipose tissue that favors an increase in the body mass index (BMI), going from a normal state to overweight and obesity, approximately a weight increase of 0.5-1 kg per year, with an increase in abdominal fat and loss of peripheral lean mass, which generates an increase in insulin resistance, total cholesterol, triglycerides and increases the risk of type 2 diabetes mellitus and cardiovascular disease, which represent the main cause of morbidity and mortality in women older than 50 years. Sixty-one percent of women in this stage require a primary therapeutic strategy to counteract the oxidative effect and insulin resistance due to the decrease in estrogen. **Objective:** To evaluate the effect of the combined administration of resveratrol and vitamin C on insulin resistance and antioxidant capacity in postmenopausal women. **Material and methods:** A randomized, double-blind, longitudinal, quasi-experimental and prospective clinical study was conducted. A total of 46 postmenopausal women between 50 and 60 years of age with insulin resistance were included. The participants were divided into 3 groups: Group A: Resveratrol, n=13; Group B: Resveratrol + vitamin C, n=19 and Group C: Vitamin C, n=14. **Results:** Compared between before and after antioxidants, group B showed a statistically significant difference (p=0.10), which represents a 28% decrease in lipohydroperoxides. Regarding the product malondialdehyde (MDA), the three groups showed a statistically significant difference, observing a decrease of 25% (p=0.0007), 24% (p=0.002), and 38% (p=0.0001), of MDA, respectively. In relation to protein damage, the three groups presented a statistically significant difference, being the most representative group C with a decrease of 36% (p=0.0001). While in the total antioxidant capacity there was a significant increase of 22% and 28% in group B and C, respectively. Finally, in insulin resistance (HOMA-IR), no significant differences were observed. **Conclusion:** Supplementation with the antioxidant combination significantly decreased lipohydroperoxides and protein carbonylation in postmenopausal women with insulin resistance. Moreover, increases the total antioxidant capacity by up to 28%. On the other hand, resveratrol and vitamin C do not have significant effects on insulin resistance.

ABNORMAL MITOCHONDRIAL CALCIUM CONTENT IN ANGIOTENSIN-INDUCED HYPERTROPHY IS AMELIORATED BY CANNABIDIOL MIMICKING PPAR-G ACTIVATION

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Abtract:

Cardiac hypertrophy is a relevant component in heart failure with reduced ejection fraction (HFrEF), hence its wide attention as a molecular target and the interest to study its molecular mechanism in both *in vitro* and *in vivo* models. It has been suggested that PPAR-g activation may counteract cardiac hypertrophy nevertheless it is not clear whether cannabidiol (CBD) may recruit such mechanisms while preventing it. Here, we investigated the disturbances in mitochondrial calcium associated with the angiotensin related hypertrophy in cardiac cells and the consequences on cardiac mitochondria from a HFrEF murine model, where a CBD intervention may affect those disturbances intracellular calcium handling. First, hypertrophy on cardiac revealed a 3-fold increase in mitochondrial calcium associated with an overexpression of the mitochondrial calcium uniporter (MCU).Under this condition, respiratory control ratio was reduced 30% concomitant with a reduction of calcium retention capacity. Activation of PPAR-g with rosiglitazone prevented cardiac hypertrophy and reduced MCU overexpression. CBD intervention mimicked most of the PPAR-g activation: reduced hypertrophy, reduced MCU overexpression and intra mitochondrial calcium content, thus improving calcium retention capacity. In conclusion, CBD may counteract cardiac hypertrophy by relying on the PPAR-g activation, making it a molecule of interest for future research regarding cardiac hypertrophy

THE NATURAL COMPOUND α-MANGOSTIN INHIBITS CERVICAL TUMOR GROWTH

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Abstract:

Background: Cervical cancer is a significant public health problem, ranking among the most prevalent tumors in women worldwide. It is one of the leading causes of cancer mortality, and its systemic therapy exhibits considerable side effects. Previously we determined that the natural xanthone α-mangostin inhibited C33a, HeLa, SiHa, and CaSki cervical cancer cells proliferation. **Objective:** Based on the above, we aimed to evaluate *in vivo* the antitumoral effects of AM in a murine cervical cancer model. **Methods:** The tumorigenicity of C33a, HeLa, SiHa, and CaSki cell lines was assessed in BALBc *nu/nu* athymic female mice by subcutaneously injecting 2 x 10^6 cells in both hind limbs of each mouse. SiHa-tumor bearing mice were treated with oral α-mangostin (8 mg/kg body weight) or its vehicle (0.1% of DMSO) daily for one month. The tumor length (L) and width (W) were measured thrice weekly with a caliper to calculate the tumor volume (TV) with the formula $TV = LxW^2/2$. **Results:** The cell lines C33a, SiHa, and HeLa induce the formation of tumors in mice. CaSki cell line did not form tumors in our model. The α-mangostin effects were assessed in SiHa tumor-bearing mice, whose tumoral growth was significantly inhibited by the natural compound. No adverse side-effects of the treatment on the animals' well-being were detected, as assessed by clinical and behavioral changes such as weight loss, modification of locomotor activity, and anxiety. **Conclusion:** These results suggest that α-mangostin is an effective antitumoral agent in cervical cancer and provides the basis for further studies to test this natural compound *per se* or as an adjuvant to the conventional therapy in cervical cancer tumors. Supported by CONACyT México, grant A1-S-10749 from LD and by funds from Departamento de Biología de la Reproducción del INCMNSZ.

ANTITUMOR EFFECT OF A LIPID-RICH EXTRACT FROM NATIVE MEXICAN AVOCADO SEED (*PERSEA AMERICANA* VAR. DRYMIFOLIA) IN AN *IN VIVO* MODEL OF MURINE MELANOMA

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Abstract:

Human melanoma is responsible for 80% of skin cancer deaths. Also, 30-90% of melanoma patients treated with conventional anticancer therapies do not respond favorably to treatment or eventually relapse. Therefore, natural compounds have been considered as alternatives to fight cancer and to reduce the side effects of anticancer therapies. We have previously shown that a lipid extract from Mexican native avocado seed (LEAS) (*Persea americana* var. drymifolia) is cytotoxic against various cancer cell lines, including murine melanoma B16-F0, by inducing apoptosis. Hence, we determined the antitumor effect of LEAS on a subcutaneous xenograft murine melanoma model. Mice with melanoma were injected intraperitoneally with LEAS (5 mg/ml) every four days (a total of four doses). They were examined every two days and weighed, and tumor size was registered until they were euthanized (20 days). LEAS treatment caused a significant decrease in the mass and volume of tumors (80-90% of reduction) with respect to control mice. Also, there were no significant differences in the weights of kidney, spleen, and heart organs. Likewise, we do not observe differences in the clinical parameters. These results suggest that the lipid extract from Mexican native avocado seed contains bioactive molecules that can affect the progression of melanoma cancer.

ASSOCIATION OF CLOCK GENE SNPS WITH CLINICAL MARKERS OF METABOLIC DISORDERS

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Abstract:

INTRODUCTION. THE CIRCADIAN RHYTHM IS A CYCLE THAT INCLUDES 24 hours a day, in which the systemic processes that must be carried out in the states of sleep and wakefulness (light/dark cycle) are differentiated, these ones have an impact on the physiological homeostasis of the organism.

This cycle is genetically determined by a set of genes and proteins, which create and control the different cellular and molecular processes fundamental to life, allowing the generation of the concordance between the exterior and interior of the organism. *Methodology.* 346 new students of the University Health Service of Universidad Autónoma de Querétaro (SU Salud-UAQ) were analyzed and anthropometric, body composition, biochemical and clinical data were obtained. Their eating habits were evaluated through a self-administered questionnaire.

Genomic DNA was extracted from the blood samples using a commercial kit simultaneously with an isothermal PCR for the ARNTL, CLOCK, PER1, PER2, CRY1, MTNR1B and NR1D2 genes (74 SNPs).Means and standard deviations were determined for numerical variables, for category traits genetic frequencies were calculated and to determine the strength of association between SNPs and metabolic variables logistic regressions adjusted to age and sex were used through the SPSS Statistics v26 program. *Results.* 58% of women (n=201) and 42% of men (n=145) were found, with an average age of 18.9 ± 1.5 years. As expected, a significant difference was found in anthropometric, body composition and dietary variables, however, glucose concentrations were higher in men (85.7 7.5 mg/dL) compared to women (82.1 8.6 mg/dL). 25 of the total SNPs analyzed, showed a statistically significant association with metabolic alterations, being ARNT gene the one with the highest number of associations with metabolic alterations. The rs10832027 variant was found to be associated with RI (OR=2.4), the rs2278749 with TG 150 mg/dL (OR=2.3), the rs1982350 with overweight (OR=1.8), while the PER2 gene variants (rs58574366) (OR=3.9) and CRY1 (rs1056560, rs1861591) (OR=2.8, OR=1.5 respectively) were associated with serum total cholesterol 200mg/dL. According to eating habits, the rs10832027 variant was associated with a later meal consumption (OR=2.0) and high carbohydrate intake (OR=1.9). *Conclusion.* The results of this study show the association between the genes of the circadian system and metabolic alterations in young adults.

SEARCH AND INVESTIGATION OF ASSOCIATED BACTERIA IN BRONCHIAL LAVAGES IN COVID PATIENTS AT THE GENERAL HOSPITAL "DR. MIGUEL SILVA

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Abstract:

Introduction. The positivity in bronchial lavages of patients with COVID19 at the Dr. Miguel Silva General Hospital, in the period from May to August 2021, increased, so it is relevant to characterize and classify the bacteria isolated from these patients, determine the average age, with more frequently to infections, classifying the cultures that were observed with more cases and the bacteria that were more resistant to antibiotics is relevant. The investigation, description and classification of the bacteria found in the respiratory system of COVID patients, helps to offer better pharmacological treatments, as well as help in decision-making in critical processes that involve special procedures such as endotracheal intubation for the connection of respirators. mechanical and that drugs have a synergistic effect with vaccines to solve these infections in patients.

Objetive. Characterize the different microorganisms found in the bronchial lavage of patients with COVID in the period from May to August 2021.

Materials and methods. In 92 cultures of Bronchial Lavage, samples of fluid from the pleural space are analyzed to determine if it contains bacteria, Routine microbiological studies such as Gram staining and cultures in Enriched media for microorganisms, and Antigen detection tests, molecular techniques and antibiograms are performed for identification. to determine sensitivity

Results. 12% of patients with a positive diagnosis of SARS COVID-19 who underwent bronchial lavage in the period January-May 2021, had at least one diagnosis with an associated pathology other than COVID-19, The male gender in patients were more prone. The microorganism most associated with SARS-COV2 infection was Acinetobacter baumannii. After bronchial lavage culture, the presence of bacterial resistance was observed in a significant percentage of 14.1%.

Conclusions. Acinetobacter baumannii appeared more frequently in the Bronchial Lavage in patients in 12% according to the consulted bibliographies, it was observed that it stands out more frequently in patients with 50 years of age or older in Mexico.

EVALUATION OF THE TOLL LIKE RECEPTOR 2 CONCENTRATION IN THE SALIVA OF PATIENTS WITH PERIODONTAL DISEASE

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Abstract:

Background: Periodontal disease is one of the most frequent chronic oral illness and is characterized by mild to severe immune-mediated destruction of dental supporting tissues. Salivary Toll like receptor 2 (TLR-2) is an immunological factor influencing the development of inflammatory alterations such as chronic periodontitis. The goal of this work was to evaluate the probable association between the salivary concentration of TLR-2 and the occurrence and severity of periodontal disease. Methods: Thirty patients diagnosed with periodontal disease were enrolled in this study. Periodontal status was evaluated using the Community Periodontal Index of Treatment Needs (CPITN) and patients were classified as having mild, moderate, or severe disease. 1.5 ml of unstimulated whole saliva of each patient was collected before and two months after periodontal treatment. Salivary TLR-2 concentration was measured with an enzyme-linked immunosorbent assay. Data were analyzed by Kruskal-Wallis, Mann Whitney tests and Pearson correlation coefficient. $P<0.05$ was considered significant. Results: The mean TLR-2 salivary concentration in patients in the severe disease group (11.38 +/- 1.43 ng/ml) was significantly higher than mean concentration in the moderate (5.79 +/- 0.74 ng/ml) and mild (2.01 +/- 0.85 ng/ml) disease groups ($P=0.0002$ and $P=0.0001$, respectively). Similarly, significant difference was found between the moderate and mild disease groups ($P=0.0352$). Positive correlation was observed between periodontal inflammation index and TLR-2 concentration ($r=0.767$). TLR-2 concentrations before periodontal treatment were significantly higher than after periodontal treatment ($P=0.0005$). Conclusion: These results suggest a relationship between presence and severity of periodontal disease and salivary TLR-2 concentration and reveal the potential value of this concentration as a progression marker in periodontal inflammation.

GENERATION OF A CELLULAR MODEL TO STUDY THE CAPACITY OF OLEACEAE POLLEN PROTEINS TO PRODUCE AN ALLERGIC REACTION *IN VITRO*

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Abstract:

Every year during the flowering season, the pollen of some tree species, such as the Oleaceae family, can produce allergic reactions in people living in cities with high levels of pollution. During an allergic reaction, IgE antibodies are produced in response to the allergens present in the pollen. IgE binds to allergens to activate cells involved in the immune response, where the FcεRI receptor of mast cells must recognize these allergens to carry out degranulation and release the mediators of the inflammatory process (1). In diagnostic, sensitive patients are challenged with protein extracts from whole pollen *in vivo* (skin prick test). The principal disadvantage of this test is that specialized doctors must carry that out, with the probability of provoking anaphylactic shock in the patient. To resolve this, we propose to generate a model with humanized rat basophilic leukemia cells (RBL-2H3) to study the ability of pollen proteins from the Oleaceae family to elicit an IgE reaction *in vitro* using the serum of sensitized patients. Until now, RBL-2H3 cells were transfected with two vectors that encode the α-chain of the human IgE receptor and a reporter gene (GFP) for cell degranulation. This model will be validated using total protein extracts of Oleaceae tree pollen and sera from sensitive patients that contain IgE. Through the GFP reporter gene, the degranulation will be validated by microscopic fluorescence or qPCR. Shortly, this model will also help us validate which pollen proteins can generate an allergic reaction in sensitive patients of trees of the Oleaceae family.

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PHARMACOKINETICS OF FACTOR VIII IN MEXICAN PATIENTS WITH HEMOPHILIA A

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Abstract:

Introduction. Treatment of severe hemophilia A (HA) patients requires the substitution of deficient factor VIII (FVIII). To reach this, an optimal dose of FVIII should be given based on pharmacokinetic (PK) analysis[1,2]. In Mexico, FVIII-PK is not used. Therefore, the aim of this study was to determine for the first time the PK parameters of FVIII in Mexican patients with severe HA. **Methods.** Fifteen samples from severe HA patients under prophylactic treatment were analyzed. In addition, we included the samples from 15 HA patients with obesity. FVIII activity was determinate (one-stage clotting assay) before and after 0.25, 0.5, 1.0, 4.0, 8.0, 12 and 48 h after infusion of a standardized dose of FVIII (40 UI/kg). We used the WinNolin software to establish a mono and bi-compartmental model. We determined the parameters: area under the curve, maximum activity (A_{max}), *in vivo* recovery (IVR), distribution volume, half-life time, mean residence time, clearance, minimum activity, and elimination constant. **Results.** FVIII-PK was highly variable between patients, with results suggesting a likely over dosage of FVIII. Bi-compartmental model showed better results for FVIII behaviour than monocompartmental model. On the other hand, obese patients showed A_{max} and IVR values under the expected values affecting other parameters. **Conclusions.** FVIII-PK differs between HA patients a fact that suggests that FVIII dose should personalize independently of the body weight. Differences in the PK parameters between study groups suggest that FVIII in obese patients has low bioavailability than non-obese patients, maybe due to differences in plasma distribution of FVIII or perhaps, to the action of non-neutralizing antibodies or FVIII inhibitors in very low titers.

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FOXO3A IN HYPERSENSITIVITY PNEUMONITIS FIBROBLASTS

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Abstract:

Hypersensitivity Pneumonitis (HP) is an inflammatory lung disease caused by inhaling different antigens that induce an exaggerated immunological response. Chronic patients may progress to a fibrotic form that may mimic some features of idiopathic pulmonary fibrosis, leading to loss of lung architecture, reduced quality of life, and death. However, the specific cellular and molecular characteristics of HP remain unclear. Proliferative fibroblasts play a pivotal role in pulmonary fibrosis as they are responsible for the aberrant accumulation of extracellular matrix. In IPF fibroblasts, low levels of transcription factor FoxO3a promote resistance to apoptosis. Still, the presence and activity of FoxO3a and its possible impact on the pathological phenotype of fibroblasts in Nh are unknown. In lung fibroblasts from patients with IPF and NH, we analyze the presence and localization of FoxO3a by immunofluorescence and the protein levels by WB. In FPI fibroblasts, the immunostaining corroborated the existence of FoxO3a in the nucleus and cytoplasm, and additionally, slight staining for acetylated FoxO3a that is exclusively nuclear was also detected. Interestingly, in HP fibroblasts, we observed the opposite, and the results obtained indicate an increase of total and acetylated FoxO3a in the nucleus and cytoplasm of the cells. Additionally, analysis of cell fractions by western blot confirmed that in HP fibroblasts, there is a significant increase in total FoxO3a in the nuclear and cytoplasmic fraction and of acetylated protein in the nuclear fraction. FoxO3a deacetylation is a critical event that modifies the expression of multiple genes dependent on this factor and may be mediated by deacetylases such as sirtuins. In contrast to IPF fibroblasts, we found that Sirt1 is significantly increased in NH fibroblasts. These results indicate that in HP, there is an upregulation of FoxO3a that could be part of a distinctive signature of fibroblasts in this disease and opens a window to analyze its impact on the regulation of genes dependent on this factor, such as CDKN1A, SOD2-1 or IGFBP1 that can modify the phenotype of these cells.

DRUG DISCOVERY IN CANCER RESEARCH: WHAT ARE WE LOOKING FOR?

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Abstract:

Searching for new molecules for cancer treatment is a priority in the biomedicine area. Due to the cancer cell characteristics, complexity, uncontrolled proliferation, aberrant metabolism among others; emerges the necessity to constantly obtain new molecules that target specific cancer mechanisms. An opportunity area for drug discovery relies on nature. Medicinal plants have been a source of metabolites with different biological activities against several diseases including cancer.

Successful examples of antineoplastic drugs from natural origin currently used are taxanes, vinca alkaloids, podophyllotoxins, etoposides, and anthracyclines. Their mechanisms of action include DNA synthesis inhibition, topoisomerase inhibitors, tubulin-binding agents, and apoptosis induction. As seen, these drugs target different hallmarks of cancer; however, cancer cells could generate chemoresistance, or severe side effects for the patients. In this scenario, the investigation of other molecules is crucial to give patients alternatives for treatment.

Our research group focuses on the search for new or known molecules as anti-cancer drugs to select those compounds implicated in different mechanisms of action that target the *hallmarks* of cancer. In the last decade, our work has been interested in autophagy as a cell death process in cancer cells. As part of our newest findings, are the acetogenins as autophagy promotors that leads cancer cells to apoptosis. Acetogenins are metabolites unique to the Annonaceae family known to be cytotoxic, antimalarial, antimicrobial, apoptotic, and pesticidal.

Autophagy is a conserved process in eukaryotic cells that maintains cellular homeostasis. It starts in response to a stress stimulus, commonly nutrient deprivation. Thus, the cell survives by the degradation of macromolecules and organelles through lysosomal degeneration. In cancer, autophagy acts as a survival mechanism to avoid cytotoxicity caused by antineoplastic drugs or could lead to cell death by apoptosis when the autophagy flux is kept. In this scenario, what we search for, are molecules that induce autophagy and apoptosis in cancer cells. So far, we have identified laherradurin, an acetogenin, and the methanol extract of the plant *Annona macroprophyllata* as autophagy inducers in HCT116 colon cancer cells by the hyperlipidation of the protein LC3. Moreover, laherradurin showed antitumor activity *in vivo*, significantly reducing the number of tumors and side effects compared to the drug reference cisplatin. These facts indicate that autophagy in cancer is a worth strategy for novel therapies and nature could be a source of chemical structures with such activity.

ANALYSIS OF EFFECT THE BIOACTIVE COMPOUNDS PRESENT IN FOODS RECOMMENDED AND NON-RECOMMENDEDPRESENT IN THE DIET OF MEXICANS AND THEIR RELATIONSHIP WITH SNPS ASSOCIATED ATHEROSCLEROSIS"

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Abstract:

Cardiovascular diseases (CVD) are sufferings-degenerative that represent an unsustainable expense for health systems collapsed in our time, for that reason are considered a health and economic problem in Mexico and the world. Represent the first places of mortality, so their attention is a priority. According to the WHO are 17.9 million deaths worldwide and only in Latin America 2 million annually. In Mexico, it is the second cause of death with 113,899 fatal events, impacting 26% of the population CVD includes systemic arterial hypertension, ischemic heart disease, heart failure, degenerative calcific aortic valve stenosis, and congenital heart disease, and principally atherosclerosis (AT). This pathology affects blood vessels such as arteries of large and medium-size. Its development is due to the formation and accumulation of lipids that give rise to plaques in the arterial lumen. The consequences of these plaques cause loss of vascular elasticity decreased blood flow and increased pressure in the arteries. This condition can lead to collapse or detachment from the plaques into the vascular system. Where eventually can cause an ischemic event that results in stroke or myocardial infarction. Several factors contribute to the development of At, these could be divide into modifiable, those that are a consequence of the lifestyle that each person carries, and not modifiable, those that derive from genetic and/or environmental alterations. The outcome is usually lethal with a high incidence in the fourth decade of population life. Previously, in the laboratory, it has been identified single nucleotide polymorphisms (SNPs) as a strategy to influence a health response to the prevention of AT. This work aims to associate the effect of these SNPs in a cellular process in a no disease versus a diseased state. This will be possible if we defined the pathology concerning the metabolic role associated with a bioactive compound (BC), which are biologically active substances that can modulate or have an effect on metabolic processes resulting in the promotion of better health conditions. From this point of view, we looking for promoting a better health condition between the identified SNPs, their role in the metabolism of AT, and the food with the BC identified. This research will focus on the Mexican population through the National Health and Nutrition Survey (ENSANUT 2018) which reports the recommended and non-recommended foods present in their diet National Health and Nutrition Survey, in this way, we can propose a specific dietary guideline that decreases the development of AT.

SCREENING OF *AGAVE* PLANTS AS ALTERNATIVE OF α-GLUCOSIDASE INHIBITORS SOURCE

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Abstract:

Type 2 diabetes mellitus (T2DM) is a chronic degenerative disorder responsible for 1.5 million deaths in 2019 worldwide and is characterized by resistance to the normal effects of insulin and a gradual inability of the pancreas to produce it (IDF, 2019). This disease can be treated by inhibiting α-glucosidase which results in delayed carbohydrate absorption in the gastrointestinal tract and thus postprandial hypoglycemia (Jarald et al., 2008). However, it is known that commercial α-glucosidase inhibitors such as acarbose and voglibose present adverse effects; therefore, alternatives with fewer side effects have been sought, for example, medicinal plants as a source of active compounds (Escandón-Rivera et al., 2020) including *A*gave potatorum Zucc (Galindo-*U*argas, 2022). Therefore, the objective of the present work was to analyze the inhibitory potential of the different *A*gave species available in the *U*alles Centrales and Mixteca regions of Oaxaca. Based on the results and previous work of the group, the aim is to contribute to the search for new drugs to combat type 2 diabetes mellitus, to provide alternative uses for ornamental agave species and to revalue the waste generated in the mezcal industry. For this purpose, an aqueous extract was obtained by infusion of fresh leaves (100 g) of 13 agave species and then a bioautographic assay was performed at different concentrations with acarbose as a positive control. The results showed that the 13 agave species evaluated contain secondary metabolites capable of inhibiting a-glucosidase in a concentration-dependent manner. The results makes *A*gave as potential alternative source of bioactive compounfs for the treatment of T2DM.

Key words: *A*gave, bioautography, ethnomedicine, Diabetes Mellitus type 2.

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POTENTIAL EFFECT OF BRASSINOSTEROIDS ANALOGS FOR THE PREVENTION OF KELOID SCARRING

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Abstract:

Keloids are benign scars that protrude beyond the borders of a wound edge and present with a nodular, rubbery appearance. They are caused by lesions in the dermis involving any inflammatory process. Keloids occur after an abnormal healing process. For example, exacerbated inflammation, excessive collagen and extracellular matrix deposition, dysregulated fibroblast growth and excessive wound contraction.

The TGF-β1/Smad signaling pathway has been reported to be involved in the healing process, participates in the differentiation of fibroblasts to myofibroblasts, regulates the deposition of collagen I and III in the extracellular matrix, and inhibits collagenase function. Elevated levels of TGF-β1 and Col-1 have been observed during keloid scarring. A dysregulation in this pathway induces keloid formation. However, MAPK/Erk, p38, JNK, nuclear factor-kb and PI-3K/Akt signaling pathways have also been reported to be involved in TGF-β1 function.

Brassinosteroids are polyhydroxylated 5-cholestane phytohormones that are involved in various plant processes, such as cell division, photomorphogenesis, xylem differentiation, reproduction, etc. Structurally they are similar with the steroid hormones of humans. Brassinosteroids have therapeutic effects against various diseases. However, to synthesize brassinosteroids, a large amount of pollen, seeds and leaves is required. Therefore, it is convenient to work with analogues that have a potential healing activity, whose synthesis cost is low, and the dose required to see the effect is also low.

Recently, the research laboratory of the botanical garden of the Institute of Sciences of the Benemérita Universidad Autónoma de Puebla synthesized brassinosteroid analogues which will be tested to inhibit some of the proteins involved in the process of keloid formation. This will be done using bioinformatics programs and *in vitro* and *in vivo* tests.

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ANALYSIS OF THE ANTIOXIDANT EFFECT OF ERGOTHIONEINE IN THE PATHOGENESIS OF VASCULAR DEMENTIA

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Abstract

Vascular dementia (VD) is described as a type of cognitive decline that is related to cerebrovascular events. Resulting in loss of synaptic connections and cell death. These processes lead to the impairment of two or more cognitive domains. In 2019, the United Nations (UN) reported that 55.2 million people in the world with dementia; National Health Survey (ENSANUT) publicized that Mexico had a prevalence of 7.9% of cases. Current diagnostic methods are inaccurate. Likewise, the VD treatment is not very sensitive and specific and is prescribed once complications appear. Early detection of this pathology and personalized treatment are important, considering the individual's genetic information, the identification of single nucleotide polymorphisms (SNPs) described in genome-wide association studies (GWAS), metabolic function and impact on health of the bioactive compounds (BC) present in food. The relationship between metabolic processes and BC has been described. Studies such as the one proposed by Wojciech Grodzicki and Katarzyna Dziendzikowska. ENSANUT offers an overview of the health and nutrition conditions of a representative sample of the Mexican population, showing the frequency of consumption of recommended and non-recommended foods. This project aims to analyze the role of BC present in Mexican food associated with the pathophysiology of VD, taking integrating the genetic variants reported in GWAS, giving a proposal for specific foods that could impact in this pathology. We use the bioinformatic tools SVA (1), SNP-FS (2) and Nutri plot (3). The data derived from this project suggest the participation of ergothioneine present in foods such as mushrooms, kidney beans and oat bran, with an antioxidant and anti-inflammatory effect, such as the relationship with endothelial cells in the brain. This suggests a positive role in preventing VD decline.

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EXERCISE, METFORMIN, AND TBHQ COUNTERACT HIGH-FAT DIET-INDUCED DAMAGE IN LIVER MITOCHONDRIA OF MIDDLE-AGE FEMALE WISTAR RATS

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Abstract:

Obesity is defined as an energy imbalance between calories consumed and calories expended.

This condition has been related to a higher risk of developing metabolic diseases and about 90% of obese people progress to Non-Alcoholic Fatty Liver Disease (NALFD). NAFLD is characterized by fat accumulation in hepatocytes and can progress to NASH, cirrhosis, or liver cancer. Mitochondria are key organelles in energy generation, but in NAFLD mitochondrial function is altered; the ability to generate energy decreases and ROS generation increases. Among the interventions that have been used to reverse these effects, aerobic exercise stands out. Our working group has shown that the combined treatment of metformin (MTF) and tertbutylhydroquinone (tBHQ), along with an exercise training routine prevents part of the deterioration associated with aging. So, our aim was to evaluate the effect of exercise in combination with MTF and tBHQ to counteract mitochondrial damage in the liver during obesity. Hence, Wistar female rats were subjected to a high-fat diet (HFD) from 21 days of age until 15 months. The treated groups performed a fartlek-type exercise and received MTF and tBHQ from 10 to 15 months of age. Our results showed that the combined treatment of exercise + MTF + tBHQ increased ATP synthesis, OXPHOS complexes activity, recovered the membrane potential, decreased ROS production, and increased AMPK and PGC1a expression.

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GENE EXPRESSION OF ABCG2, SLC22A12, IL-1β, AND ALPK1 IN PERIPHERAL BLOOD LEUKOCYTES OF PRIMARY GOUT PATIENTS WERE CORRELATED WITH THEIR COMORBIDITIES

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Abstract:

Genes ABCG2, SLC22A12, and ALPK1 have been strongly associated with dysfunction of urate metabolism in patients with gout, but it is unknown how these transporters are expressed in patients with acute or chronic gout. Our objective was to analyze the gene expression of urate transporters and inflammation genes in peripherial blood from gout patients and controls, to determinate if the metabolic profile of gout patients can influence at the gene expression profile. Our objective was to analyze the expression of urate transporters ABCG2, SLC22A12 and inflammation molecules ALPK1 and IL-1β in peripheral blood leukocytes from gout patients and to compare them with their metabolic profile and with the gene expression of people without gout and without hyperuricemia. Methods. A total of 36 chronic and acute patients and 52 controls were recruited, ABCG2, SLC22A12, IL-1β and ALPK1 gene expression was evaluated by quantitative real-time PCR. Correlations of gene expression with clinical and laboratory parameters of patients were also analyzed. Results. IL-1β was significantly increased in PBMCs of patients when compared with their PMNLs ($p<0.05$). A significant increase in ABCG2 and IL-1β were found in PMNLs from patients compared to controls ($p<0.05$). Correlations of gene expression in patients were related to levels of serum uric acid (sUA), serum creatinine, CRP, triglycerides, BMI, kidney disease, hypertension, and metabolic syndrome. Conclusions. Our data suggest that the leukocyte cells of the patients respond to the presence hyperuricemia and comorbidities expressing ABCG2 and IL-1β genes differentially compared to normouricemic and non disease state. Hyperuricemia, dyslipidemias and obesity should stimulate the differential gene expression of peripheral blood leukocytes (neutrophils and monocytes) even in an asymptomatic state.

CLINICAL-EPIDEMIOLOGICAL PROFILE OF A COHORT OF PATIENTS HOSPITALIZED WITH COVID-19 AND ANALYSIS OF POLYMORPHISMS IN THE NOS2 GENE (RS2297518, RS2779248 AND RS10459953)

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Abstract:

Background: Coronavirus disease 2019 (COVID-19) is a viral infection caused by SARS-CoV-2. The manifestations, susceptibility and outcome of the population depends on the individual's history, genetic susceptibility, age and comorbidities. Studies have shown that polymorphisms in the *NOS2 gene* are correlated with susceptibility and severity of respiratory diseases, such as tuberculosis, influenza and asthma[1]. The purpose of this work was to associate the genetic profile of polymorphisms of the *NOS2 gene (rs2297518, rs2779248 y rs10459953)*[2] to predict an outcome in patients with COVID-19 and future complications that may arise. **Methods:** This is an observational, descriptive and cohort study. We included hospitalized patients with COVID-19 in the year 2020, and the data that was obtained include: comorbidities, manifestations, laboratory variables, complications, and treatment. **Results:** At the end of the study, 548 patients with COVID-19 were included, 370 were men (67%) and 178 women (33%), the age range was 17 to 86 years old, with an average of 57 . The population was classified in mild/moderate with 130 patients (25%), severe 89 (16.2%) and critical disease 321 (73.3%). The hospitalization days were from 1 to 256 days, with an average of 27 days. The most common comorbidities were diabetes mellitus type 2 166 (30.2%) and hypertension 174 (31.7%), 253 (46.2%) of the subjects had septic shock, and 213 (38.9%) died from COVID -19. The genotyping of the population with the rs2779248 probe showed genotype TT 301 (54%), CT 214 (39%) CC 31 (5%), under the dominant model TT 301 (54%) CT+CC 245 (45%). Multivariate analysis showed an association between the type CT+CC polymorphism [HR:.76, (95%CI:.61-.95, p=0.16], age adjusted [HR:.98, (95%CI:. 97-.98) p=0.001], male [HR:.75, (95%CI:.60-.94, p=0.015] Hypertension [HR:.93, (95%CI:.72-.1.2 , p=0.63] DM2 [HR:.96, (95%CI:.77-.1.2, p=0.77] with mortality during hospitalization in the patients. The other two polymorphisms were analyzed without finding statistically significant results. Conclusions: The rs2779248 polymorphism under the dominant inheritance model (CT+CC) in the NOS2 gene was presented as a protective factor for mortality in patients hospitalized with COVID-19.

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THE ROLE OF HYPOXIA INDUCIBLE FACTOR 3A IN COLON CANCER

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Abstract:

Colorectal cancer is one of the most common malignant neoplasms in terms of incidence around the world and is the second cause of death from cancer. Hypoxia is a hallmark of the tumor microenvironment. Cellular adaptation to hypoxia is primarily mediated by a family of transcriptional regulators: HIF-1α, HIF-2α, and HIF-3α. In contrast to HIF-1α and HIF-2α, a specific role for HIF-3α in cancer biology has not yet been established. The aim of this study is to elucidate the role of HIF-3α in colon cancer.

Three lines of malignant colorectal cancer (RKO, SW480 and SW620), one non-malignant (112CON), normal tissue and tumor tissue derived from colon cancer patients were evaluated to examine HIF-3α expression by Western Blot. Data Analysis from *Progno Scan* was carried out to analyze the correlation between HIF-3α mRNA expression and cancer progression. Knockdown of HIF-3α expression was carried out using a lentiviral system in the three malignant cells to investigate the effects of its silencing on malignant phenotype maintenance: cell viability, colony formation, b-catenin-transcriptional activity activation and in the basal autophagia activity. We found that HIF-3a is overexpressed under normoxic conditions in all cell cancer lines and tumor tissue sample compared with non-malignant cells and normal epithelium tissue. Kaplan-Maier analysis showed that overexpression of HIF-3a correlates with a patient's lower survival rate and a poor prognosis with different cancer types (P>0.05). Cell viability was decreased in all three malignant lines with HIF-3a knockdown compared with control HIF-3a expressing cells. Consistent with this, Annexin-V evaluation showed an increase in apoptotic rate in cells depleted of HIF-3a compared to control cells. In addition, HIF-3 silencing also decreased clonogenic capacity, increased basal autophagy and increased activation of canonical Wnt pathway in colon cancer cells.

EFFECT OF BONT/A IN THE MURINE MODEL OF TRIPLE-NEGATIVE BREAST CANCER AS A POSSIBLE ANTI-TUMOUR TREATMENT INVOLVING THE SV2A RECEPTOR

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Abstract:

OBJECTIVE. Analyze the expression of the SV2A receptor in 4T1 cancer cells and evaluate the effect of the BoNT/A on tumour progression in the triple negative breast cancer model in BALB/c mice.

MATERIALS AND METHODS. Mouse breast cancer cells 4T1 triple negative (ATCC® CRL2539™), human breast cancer cells MDA-MB-231 (ATCC® HTB-26), and glioblastoma cells U87 (ATCC® HTB-14™) were used as positive control. Cells were fixed and stained for vesicle release receptor SV2A by flow cytometry (FACS CANTO II). In addition, their location and distribution were analyzed in a Zeiss epifluorescence microscope with the ApoTome 2 system. Concerning the in vivo model; breast cancer was generated in BALB/c mice by inoculating 4T1 cells ($5x10^4$) once the tumor reached an approximate size of $30mm^3$, BoNT/A was administered intratumorally at doses: 0.25U, 0.5U and 1U and the effect of the toxin for 24 days determining: tumor size, animal weight gain, food intake and hematic biometry (HB).

RESULTS. Flow cytometry showed an overexpression of SV2A in triple negative MDA-MB-231 and 4T1 cells. This protein was found in the membrane of two cell types, not showing differences in its distribution. In the U87 positive control, as expected, the receptor was clearly present. On the other hand, *in vivo*, BoNT/A doses of 0.5U and 1U decreased the size of the tumor and spleen in mice with breast cancer, in addition, the number of neutrophils and monocytes was reduced. For erythrocytes, lymphocytes and platelets, no statistically significant difference was observed with treatment.

CONCLUSION. For the first time, the presence and overexpression of the SV2A receptor in the 4T1 murine breast cancer cell line is described, as our group has reported for the MDA-MB-231[1] cell line and biopsies[2] with this type of cancer. These results open the possibility of using the BoNT/A, which is the specific binder of SV2A, as a possible adjuvant treatment in triple-negative breast cancer, since in the model the proinflammatory cells in the peripheral blood have decreased. In addition, not adverse side effects on the health of mice, reflected in its weight, food intake and other HB parameters, were observed.

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MITOCHONDRIAL DYNAMICS CHARACTERIZATION IN PMBC FROM A PAH COHORT

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Abstract:

Pulmonary arterial hypertension (PAH) is characterized by vasoconstriction and vascular remodeling. An important pathological feature is inflammation and infiltration of immune cells in PAH lesions, which modulate the disease performance. Important differences have been found in immune cells population and impaired response in peripheral blood mononuclear cell (PMBC) from PAH patients and control[1]. After PBMC activation, its metabolic demands increase along with changes in electron transport chain, redox-related enzymes, mitochondrial dynamics (fusion/fission) and mitophagy[2]. Mitochondrial dynamics is crucial to maintain the balance of energetic demands and consequently the regulation of metabolism. For this reason, it is important to explore if immunophenotypically changes are related to mitochondria dynamics changes in PBMC form PAH patients. We conducted a retrospective cohort study in subjects with newly or previously diagnosed PAH and matching controls. PMBC were isolated from whole blood. To recognize the cell populations, an immunophenotypic profile was performed. A noticeable hyporreactivity was found in all T lymphocytes subsets (T cells CD3+ -24.8 %, T helper -22.4 % and T cytotoxic -30.5% change vs control) represented by a low expression of the CD69 activation marker. Furthermore, mitochondrial quality control was explored using qPCR and Western Blot techniques. It was observed that PAH PMBCs have a predominance for fission pathway noted by a significantly increased gene expression of DRP1 levels expressed as mean fold change (1.169 ± 0.5439 SEM) and increased DRP1/OPA1 ratio (6.015 ± 1.640 SEM) compared to control. In addition, a significant increase in TFAM mean fold change gene expression (4.896 ± 1.650 SEM) and increased levels of mtDNA (3.510 ± 1.217 SEM) indicate mitochondria biogenesis. These results suggests that mitochondria quality control, particularly, DRP1-mediated fission determines the response of lymphocyte cell populations and inflammation during PAH.

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EFFECT OF IFC-305 ON MITOCHONDRIAL FUNCTION IN AN EXPERIMENTAL MODEL OF BLEOMYCIN-INDUCED PULMONARY FIBROSIS

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Abstract:

Pulmonary fibrosis is the final result of several diseases characterized by the expansion of the fibroblasts population, exaggerated accumulation of extracellular matrix and destruction of lung parenchyma. Previous studies have shown that the compound derived from adenosine IFC-305 has a protective effect on the cirrhosis hepatocellular carcinoma model. This effect has been associated with a restoration of mitochondrial function and reduction of expression of proteins related to the development of fibrosis [1]. Recently, we have found that the fibroblasts from Idiopathic Pulmonary Fibrosis show mitochondrial dysfunction [2]. The aim of this study was to analyze the potential therapeutic effect of IFC-305 in the murine model of pulmonary fibrosis. **Method:** Male wild-type mice of 8 weeks of age were instilled with bleomycin and one week later they were administrated with IFC-305 (50 mg/kg) for 3 weeks every other day. We isolated the mitochondria of the lungs and measured several parameters Bleomycin-induced lung damage and collagen deposition were evaluated with Masson`s trichrome stain and determination of hydroxyproline. **Results:** The levels of collagen were decreased with IFC-305. The compound significantly increased the activity of complex I and ATP production and improved the oxygen consumption rate induced by Glutamate/Malate. **Conclusion:** Our results suggest that IFC-305 may be a potential therapeutic agent for pulmonary fibrosis. More experiments are in process.

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DETECTION AND VALIDATION OF MOLECULAR MARKERS RELATED TO THE TWO-WAY RELATIONSHIP BETWEEN RENAL CELL CARCINOMA AND CHRONIC KIDNEY DISEASE

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Abstract:

Renal Cell Carcinoma (RCC) stands for the 10th and has the highest mortality rate amongst genitourinary cancers. Clear Cell Renal Cell Carcinoma (ccRCC) is the most common histological subtype. Almost all the familiar cases of ccRCC comes from a loss of heterozygosity in the Von Hippel Lindau (VHL) disease gene. Moreover, nearly all the spontaneous cases of ccRCC have a mutation of this gene in early phases. Due to this link between the CCR tumorigenesis and the VHL inactivating mutation, it has become a biomarker for prognosis of the ccRCC. Other molecules have been reported as biomarkers for CCR; those, among others, are the VHL target HIF-1α, and his target gene VEGF. Some interesting emerging molecules as biomarkers are the Hsp90 family, which participate in the proper folding and functioning of many "client" proteins including VHL, HIF-1α and VEGF. The CCR's first line treatment is the nephrectomy. Although many patients don't recur within 18 months after the nephrectomy, many patients develop Chronic Kidney Disease (CKD) if not already suffer at the moment of the surgery. This disease is a common comorbidity in oncological patients, representing 20-30% of the cases. The diagnostic method of the CKD includes the serum creatinine and albumin and the estimated Glomerular Filtration Rate (eGFR). Unfortunately, these parameters only change in the last phases of the disease. The strongest relation between CCR and CKD appears between the decrease of the eGFR and the ccRCC. This finding widens the possible mechanisms to study the biological fundaments of the CCR and CKD relationship (Onconefrology). Therefore, it is necessary to identify and determine a biomarker panel for both CCR and CKD associated to the relationship between these diseases. Methods. With paraffine embedded tissues we determine the suggested biomarkers through IHQ and WB and analyze the association between relative expression and clinical variables of interest. Results. As a first approach to understand the relation between fibrosis and CKD we analyzed the fibrosis percentage in both tissues: normal tissue (TN) and tumoral tissue (TC). We found an augmented fibrosis in TN when compared to TC. Moreover, this augmented fibrosis was associated to a greater risk to suffer and develop CKD. On the other hand, TC showed a low percentage of fibrosis when assayed the tumoral size (according to TNM classification) T3 and the cancer progression. These findings suggest that fibrosis is a preventive event that stops the tumor development. Referring to the molecules analyzed, PAX8 showed an increased expression level as the tumor size increase. The same tendency was observed in the Fuhrman Grade variable; suggesting that an increased level of

PAX8 is associated to an advanced grade of disease. pVHL can distinguish TC from TN with a lower expression in TC. This low expression was observed in the patients with metastasis at diagnosis. HSF1 protein showed an increased level in TC, but there wasn´t a significative difference when compared to TN because this tissue is altered due to the nearby to TC and tissue fibrosis. HSF1 also was increased in a higher Fuhrman grade suggesting these levels are associated to a poor prognosis. It has been reported that his main target gene Hsp90 has many implications for cancer and these activities depends on the isoform evaluated. In this study, Hsp90β showed a low expression level on the patients with metastasis, suggesting this Hsp90 isoform could be a suppressor of cancer due to his role in the adaptation to response to cellular stress. These molecules showed an important role in the prognosis and cancer progression; therefore, we encourage the evaluation and validation of these molecules in the clinic through a less invasive technique as liquid biopsies.

EFFECT OF ACUTE CONSUMPTION OF PIPERINE AND COCOA ON BIOCHEMICAL PARAMETERS AND OXIDATIVE DAMAGE

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Abstract:

The consumption of cocoa, rich in flavonoids, suggests health benefits such as a reduction in the risk of suffering from chronic diseases (cardiovascular diseases, metabolic disorders, and cancer). However, the low intestinal absorption of flavonoids is one of the problems related to their consumption. Recent reports mention that the consumption of piperine, present in pepper, improves the absorption of flavonoids from food. It has been shown that the supply of turmeric with piperine increases the bioavailability of curcumin in the blood, improving its therapeutic activity. However, there are no reports of the effect of piperine on cocoa flavonoids. In this sense, the objective of the study was to evaluate the effect of pepper piperine on the absorption of cocoa flavonoids in biochemical parameters and markers of oxidative damage. Twenty-two people participated in this study, after signing the informed consent. The average age to be included was 21 years. A case-control study was conducted, in which each participant was their own control. The study was carried out in two stages separated by a week between each stage for each participant. Stage I (acute consumption of cocoa) and Stage II (acute consumption of cocoa + piperine) with blood samples obtained at 0, 1, and 2 hours after food consumption. Biochemical parameters (Glucose, Cholesterol, Triglycerides, HDL-Cholesterol, LDL-Cholesterol, Uric Acid, Albumin, and Total Protein), markers of oxidative damage (lipoperoxidation, MDA), antioxidant defense (Thiol groups) were determined, and the content of Total Phenols. The results showed a decrease in the parameters evaluated, similar between cocoa and cocoa with piperine. Similarly, the marker of lipid peroxidation decreased in the consumption of cocoa with piperine compared to that of cocoa.

DISTINCTIVE PHENOTYPIC AND TRANSCRIPTOMIC SIGNATURES BETWEEN HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFPEF) AND HEART FAILURE WITH REDUCED EJECTION FRACTION (HFREF)

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Abstract:

Heart failure (HF) represents a leading cause of death and disability worldwide. Nearly half of the cases of heart failure are constituted by heart failure with preserved ejection fraction (HFpEF), which is predicted to soon become the predominant form of HF. Despite the growing pharmacotherapeutic armamentarium for heart failure with reduced ejection fraction (HFrEF), HFpEF shows refractory for most treatments to manage HF. Thus, we aimed to compare two preclinical models of HF (HFpEF vs. HFrEF) in terms of their phenotype, functional features and transcriptomic signatures in order to uncover differences that could guide further exploration of potential therapeutic molecules. HFrEF model consisted of mice exposed concomitantly to angiotensin II and L-NAME. For the HFpEF model, a group of mice was exposed to a high-fat diet combined with L-NAME. Heart function was invasively evaluated, and the heart was retrieved for histopathological and molecular processing. Both HFrEF and HFpEF animals presented alterations regarding the function of the left ventricle, encompassing an increase in systolic and diastolic pressures, and a high stiffness index. As expected, HFrEF mice exhibited a pronounced loss of ejection fraction, while no differences were found in the HFpEF model. Structurally, cross-sectional area of the cardiomyocytes was almost two times higher in HFrEF animals, compared with controls, whereas only a modest increase was observed in the HFpEF mice. While transcripts of BNP and COLL1 were both overexpressed in the hearts of HFrEF mice, no changes in expression of these remodeling markers were found in HFpEF animals. Moreover, inflammation was explored evaluating expression of proinflammatory cytokines (IL-1B, IL-6, TNF) and anti-inflammatory IL-10. Results suggest comparable levels of inflammation in the hearts of both HFrEF and HFpEF mice. Finally, next generation-based RNA-seq yielded 1339 differentially-expressed genes (FDR<0.05, Fold Change>2) for HFpEF animals, compared with controls. Top over-represented ontological terms included several terms related to extracellular matrix composition, heart development, immune system processes and mitochondrial metabolism. Further verification of altered respiratory function and fibrosis is guaranteed, but transcriptomic data could guide pharmacological approaches to focus on these phenomena in order to improve our pathological understanding of HFpEF.

DETERMINATION AND ANALYSIS OF THE CRYSTALLOGRAPHY STRUCTURE OF RECOMBINANT SIGMA GLUTATHIONE TRANSFERASE FROM *TAENIA SOLIUM*

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Abstract:

Taenia solium is a parasite of the class Cestoda, responsible for two diseases in humans: taeniasis and cysticercosis, but neurocysticercosis (NCC) is the leading cause of non-congenital epilepsy in the world [1]. In Mexico, the cost of managing, treatment, and diagnosis patients with NCC was approximately US$54 million in 2015 [3], and some patients do not respond to current available treatments. This parasite is endemic in underdeveloped countries, however, in developed countries where this disease was considered to have been eradicated, cases of NCC have already been reported due to the migration of people from endemic areas [4]. The success of the establishment of the parasite is related to its defense mechanisms that inactivate the elements of the host immune response and its high tolerance to oxidative stress, where glutathione transferases play an important role [4]. Glutathione transferases (GSTs) are a family of enzymes highly expressed in cells, which are part of the phase II detoxification process and catalyze the conjugation of glutathione to various endo- and exo-electrophilic substrates [5]. This conjugation produces soluble compounds and substrates for export mechanisms, such as P-glycoprotein and multidrug resistance-associated protein [13]. GSTs are the main xenobiotic detoxification system in helminths since they have minimal activity of both cytochrome P450 and glutathione peroxidase, in addition to lacking catalase. Therefore, obtaining the crystallographic structure of *Taenia solium* Glutathione transferase sigma (*Ts*GSTS) will give us the possibility of screening commercial drug libraries to find leading molecules that in future research will serve for the rational design of specific inhibitors for *Ts*GSTS, which will allow not altering the activity of the GSTs of their hosts, as has already been shown for Ts26GST.

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AN ALTERNATIVE METHOD FOR THE CHARACTERIZATION OF RESPIRATORY ALLERGY-CAUSING POLLEN ALLERGENS

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Abstract:

Respiratory allergies are critical medical conditions affecting almost 20% of the world's population. The most prevalent are asthma and allergic rhinitis, which directly impact the patient's quality of life. One of the leading causes of these diseases is the inhalation of pollen, whose proteins (allergens) can induce an IgE-mediated hypersensitive reaction. However, pollen allergens are not fully characterized, making diagnosis and treatment difficult in clinical practice. Routine characterization of pollen allergens involves extracting proteins and separation by two-dimensional gel electrophoresis (2-DE) coupled with immunoblotting employing sera from sensitized patients. Then, the identification of immunoreactive proteins is made by mass-spectrometry. Nevertheless, this technique can only identify allergens in their primary structure due to SDS-PAGE conditions. Therefore, we propose an alternative method to characterize pollen allergens based on co-immunoprecipitation (co-IP). This technique uses target protein-specific antibodies to capture proteins of interest indirectly. For this work, we tested the co-IP of the complex formed by IgE-allergens from sera of patients sensitized to *Ligustrum lucidum*, an allergenic tree at CDMX. In the first step, we employed a mouse monoclonal antibody against human IgE conjugated with agarose to precipitate the total IgE of the allergic patients. At the same time, a total pollen protein extract obtained by a phenol-modified method was clarified with the same antibody to reduce nonspecific interactions. After, we incubated overnight the complex anti-IgE-human IgE with total pollen proteins. Once washed to remove unbound proteins, the samples were eluted from the beaded agarose with urea buffer for quantification and electrophoresis. Finally, analysis by LC-MS/MS for protein sequencing identified the major pollen allergen Lig v 1, among other potential allergens. This alternative method has advantages, such as characterizing low abundance allergenic proteins not identified yet. Also, proteins in their native state preserve the structure and the post-translational modifications crucial for IgE binding.

VASCULOGENIC MIMICRY IN TRIPLE-NEGATIVE BREAST CANCER CELLS IS INHIBITED BY CALCITRIOL AND CURCUMIN BY BLOCKING THE PI3K/AKT PATHWAY

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Abstract:

Neo-vascularization is essential for tumor growth and dissemination. The formation of channel-like structures by cancer cells, namely vasculogenic mimicry (VM), is generally associated with epithelial-to-mesenchymal transition, metastasis, and resistance to therapy in highly aggressive tumors, such as those with a triple-negative breast cancer (TNBC) phenotype. The role of cancer-endothelium interaction on the formation of the tumor microcirculatory network and the effect of natural products for VM therapeutic purposes remain poorly investigated. To address these issues, we developed an *in vitro* VM model by co-culturing human endothelial cells (EAhy.926) with TNBC cells (MBCDF-T or HCC-1806), and studied the effects of curcumin, a natural phytochemical, and calcitriol, the active vitamin D metabolite, on VM formation. We considered these compounds given previous studies showing that their combination abrogated TNBC tumor growth and angiogenesis *in vivo*. Results: Co-culture of EAhy.926 with MBCDF-T, HCC-1806, and trophoblast cells, triggered tubular-like structures formation, suggesting the participation of endothelium in both pathological and physiological VM. Tube-like structures formation was accompanied by increased VEGFR2 and FGFR1 expression, as well as upregulation of pro-angiogenic molecules in the co-cultures. Interestingly, TNBC cells VM capacity was inhibited by calcitriol and to a lesser extent by curcumin; however, their combination further inhibited VM. Mechanistically, treatments inhibited the phosphorylation of several proteins, including those involved in the FGFR/PI3K/Akt pathway. Specific pharmacological inhibition of FGFR or PI3K suggested that this is the main signaling pathway involved in VM of TNBC cells. Our results support the possibility of using these natural compounds as adjuvants for VM inactivation in patients with highly malignant tumors inherently capable of forming VM or in patients with ongoing anti-angiogenic therapy.

PREECLAMPSIA DECREASES INSULIN-INDUCED VASOCONSTRICTION AND VASODILATION IN RAT AORTA

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Abstract:

The average percentage of women suffering from preeclampsia is between 10 and 14%. Insulin resistance and Angiotensin II concentrations are increased in this disease. It is not known if this condition modifies the vascular response tu insulin. The objective of this work was to evaluate if insulin decreases insulin induced vasorelaxation in a rat model of preeclampsia. Using a conventional isolated organ bath, thoracic and abdominal aorta rings from heathy pregnant or PE rats were stimulated with phenilephrine in the presence or absence of insulin 100mM. Also, aorta rigns precontracted with Phe were relaxed with an increasing concentrations of insulin. PE aorta rings showed a significant increase in Phenylephrine (Fe)-induced contractility compared with healthy pregnant and non-pregnant groups. When the curves were run in the presence of insulin [100 mIU/mL], the contraction induced with phenylephrine was reduced in all groups, but particularly in the PE group mainly in the presence of endothelium. The PE group developed a lower relaxation to insulin compared to healthy pregnant and non-pregnant groups, both in the thoracic and abdominal aorta. In rings without endothelium, the relaxing effect of insulin was equally diminished in all groups. Resuts suggest insulin has a more vasorelaxant effect in the thoracic aorta in an endothelium independent way. Also, increased vasocosntriction produced bay PE is particularly sensible to insulin.

TAMOXIFEN METABOLITE TREATMENT PROMOTES THE TRANSITION OF MCF-7 ESTROGEN RECEPTOR-POSITIVE BREAST CANCER CELLS TO TRIPLE-NEGATIVE PHENOTYPE

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Abstract:

Introduction: Breast cancer is the most common malignancy in women worldwide. In 2020 it had approximately an incidence of 2 million cases and caused 6 thousand deaths (WHO, 2020). Currently, the main subtypes are estrogen receptor (ER) positive, human epidermal growth factor receptor type 2 (HER2), and triple-negative with no expression of hormonal receptors. 80% of breast cancer tumors are ER-positive, for these cases indicated neoadjuvant treatment in premenopausal women is tamoxifen, a prodrug that leads to the *in vivo* generation of its main active metabolites 4-hydroxytamoxifen (4OH-Tam) and 4-hydroxy-N-desmethyl-tamoxifen (Endoxifen). Although tamoxifen therapy is highly effective, it is common for patients to develop resistance and treatment failure. Recurrent and metastatic tumors can differ in hormonal receptor status in comparison with the primary tumor, getting it necessary to make changes in pharmacological strategy. Determining the mechanism behind these phenotypic changes allows the proposal of new strategies and pharmacological targets. **Objectives:** Characterize a chemoresistant RE+ breast cancer model generated from MCF7 cells treated with 4OH-Tam and Endoxifen. **Methodology:** Generation of cellular variants resistant to 4OH-Tam and Endoxifen. Characterization of hormonal receptors expression and migratory capacity by scratch wound healing assay in the chemoresistant model. **Results:** Chemorresistant cells have a phenotype similar to triple-negative subtype with a diminished hormonal receptor and an increased migratory capacity, in addition to an important change in its morphology. Results indicate that resistant cells developed epithelial-mesenchymal transitions (EMT) and suggest the nuclear factor erythroid 2-related factor 2 (NRF2) may have a crucial role, condition associated with endoplasmic reticulum stress. Nrf2 modulation could represent a pharmacological target in recurrent cases of breast cancer.

World Health Organization. (2020). *Cancer Today*. Retrieved from Global Cancer Observatory: https://gco.iarc.fr

SKELETAL MUSCLE MITOCHONDRIA ALTERATIONS IN THE DEVELOPMENT OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

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Abstract:

Heart failure (HF) with preserved ejection fraction (HFpEF) represents more than 50% of total HF cases with no available treatment options[1]. Exercise intolerance is a key manifestation of HFpEF as it presents as an early persistent symptom and is considered a major determinant of reduced quality of life in these patients[2]. Noncardiac mechanisms for reduced aerobic capacity have been proposed, especially skeletal muscle (SM) alterations and a loss of its mass, known as atrophy[2,3]. The complex clinical phenotype that characterizes HFpEF stem from the presence of multiple comorbidities[4] which are associated with important metabolic alterations leading to insulin resistance and mitochondrial dysfunction in the heart and the SM[5]. The main objective of this project is to evaluate mitochondrial function alterations and atrophy development in gastrocnemius and soleus muscle during progression of HFpEF in a preclinical mice model. All procedures were approved by the animal use and care committee (Protocol #2020-009). 8-week-old male C57BL/6 mice were randomly assigned to a HFpEF group where they were given a high-fat diet (60%) and L-NAME during 5, 8 and 12 weeks, and compared with a control group. At the end of each period and after fasting for 4 hours, EF had no changes (61% vs 62%, p>0.05 for all groups), while EDP (end-diastolic pressure) was increased in the 8 (5.7 ± 0.51 vs 8.4 ± 0.31, p=0.002) and the 12 weeks HFpEF groups (2.5 ± 1.01 vs 5.8 ± 0.86, p=0.03). Then, skeletal muscle fibers were isolated to evaluate mitochondrial function by high-resolution respirometry, a representative trace is shown below for the 5 weeks group. Additionally, relative gene expression of mitochondrial dynamics, biogenesis, and mitophagy processes and mtDNA content by qPCR were performed, which was increased in the 5 weeks group (p=0.01) and decreased in the 8 (p=0.04) and 12 (p=0.01) HFpEF groups. Signs of SM atrophy were evaluated by histological analysis and the expression of atrophy-related genes. Data are expressed as the mean ± standard error; unpaired t-test was performed for comparison between groups.

[1]Pfeffer, MA. et al, Circulation research 2019; 124(11):1598-1617. [2]Dhakal BP. et al, Circulation. Heart Failure 2015; 8(2):286-294. [3]Wood, N. *et al*, ESC heart failure 2021; 8(1):3-15. [4]Streng, KW. et al, International journal of cardiology 2018; 271:132-139. [5]Saotome, M. *et al*, International journal of molecular sciences 2019; 20(14). 3552. [6]Schiattarella, GG. et al, Nature 2019; 568(7752):351-356.

EVALUATION OF THE RT-LAMP TEST FOR COVID19 IN SALIVA AND NASAL SAMPLES

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Abstract:

At the beginning of 2019 a new viral strain was discovered; early 2020, the new respiratory disease called COVID-19 was spread around worldwide becoming a serious health problem. The molecular test that was implemented was RT-PCR, which is widely proven for diagnosis, however the cases were so many that it became very difficult to diagnose adequately also in a short time. For instance in Mexico, the infrastructure for this type of technique was not enough to cover the demand, especially in regions far from metropolitan areas. The goal for this study was to implement and evaluate the RT-LAMP technique for diagnosis COVID, in patients of a secondary care hospital, in saliva and nasal samples. Study design: cross-sectional, comparative and analytical. In this study we analyzed 3 groups of patients: one positive with symptoms of COVID-19 (analyzed by PCR), another positive asymptomatic group, and a control group (negative of COVID). Five samples were taken from each patient, 2 nasopharyngeal, 2 nasal and 1 saliva. The PCR and the antigen test were performed with nasopharyngeal samples, the RT-LAMP and another antigen test were performed with the two nasals, and the RT-LAMP and the antigen test were performed again with the saliva test. It should be noted that there are different variants of RT-LAMP, we decided to implement the test without extraction of genetic material for two reasons, some works comment that it improves its efficiency and specificity; the other reason is that in remote places there are not necessary equipment to perform RNA extraction. 128 samples were analyzed, 55 with symptoms, 32 asymptomatic and 41 controls, most of the patients age range from 19 to 39 years being mostly female. 73% of the CTs for the PCR were in a range from 21 to 30.9. The results of the RT-LAMP in nasal and saliva were similar, 2 false positives and 1 false negative were observed, presenting a sensitivity of 97.75 and a specificity of 93.20. The results found have high sensitivity and specificity, especially for asymptomatic patients. It is important to point out that the RT-LAMP test, in addition to determine saliva samples (non-invasive test for patients), can also be determined in remote regions, since it can be easily implemented with basic molecular biology equipment.

EVALUATION OF SINGLE NUCLEOTIDE POLYMORPHISMS ASSOCIATED WITH THE DEVELOPMENT OF VASCULAR DEMENTIA IN THE CELLULAR CONTEXT OF THE NEUROVASCULAR UNIT

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Abstract:

Vascular dementia is a neurological disease characterized by the declive of at least one cognitive domain of the patient. Its origin is related to a set of cardiovascular pathologies that limit the supply of oxygen and glucose to the central nervous system. Within these nosological entities is atherosclerosis, which is a chronic inflammatory disease of the blood vessels, characterized by the deposition of low-density lipoproteins in the intimal layer of the arteries, generating a lesion called atheroma. It has been proposed that the obstruction of blood flow in the brain is mediated by the formation of thrombi derived from the rupture of the atherosclerotic plaque. The following question was raised in this project. Is it possible to know the relationship of genetic variants associated with atherosclerosis with the development of vascular dementia in the cellular context of the neurovascular unit? To answer this problem, a seek for single nucleotide polymorphisms derived from genome-wide association studies for both diseases was made using the SVA v0.11 algorithm. Subsequently, the type of genetic variant and its topology in the genome was determined. The cell line of the neurovascular unit associated with each polymorphism was identified using SCRAD v0.9, which is a text-mining tool. Likewise, the relationship of these variants with metabolism was evaluated through the information from the REACTOME database. Finally, an *in silico* characterization of the effect of the variants present in genes at the protein level was carried out using POLYPHEN2, PROVEAN, and SIFT. The data presented in this project identify oligodendrocytes and astrocytes as the head cell types in the development of vascular dementia. In the same way, it is detailed that the variants found participate in the metabolic pathways of extracellular matrix degradation, demyelination, and cell death. Highlighting that these events can play an essential role in the etiology of the disease.

(-)-EPICATECHIN MODULATES THE EXPRESSION OF MYOMIRS IMPLICATED IN EXERCISE RESPONSE IN MOUSE SKELETAL MUSCLE

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Abstract

The flavanol (–)-epicatechin has been classified as an exercise mimetic. Besides, several miRNAs play a role in modulating the adaptation of the muscle to different training protocols. However, notwithstanding all information, few studies aimed to determine if (–)-epicatechin can modify the expression of miRNAs related to skeletal muscle development and regeneration. Mice were treated for fifteen days by oral gavage with the flavanol (–)-epicatechin. After treatment, the gastrocnemius of the mice was dissected, and total RNA was extracted. The expression of miR-133, -204, -206, -223, -486, and -491 was evaluated by qRT-PCR. We also used bioinformatic analysis to predict the participation of these miRNAs in different skeletal muscle signal transduction pathways. Additionally, we analyzed the level of MyoD and MyoG myogenic proteins by Western blot and evaluated the transversal area of muscle fibers stained with E&H. (–)-Epicatechin upregulated the expression of miR-133, -204, -206, -223, and -491 significantly, which was associated with an increase in the level of the myogenic proteins MyoD and MyoG and an augment in the fiber size. The bioinformatic analysis showed that the studied miRNAs might participate in different signal transduction pathways related to muscle development and adaptation. Our results showed that (–)-epicatechin upregulated miRNAs that participate in skeletal exercise muscle adaptation, induced muscle hypertrophy, and increased the level of myogenic proteins MyoD and MyoG.

SNP-FOOD SEARCH: A TOOL FOR SEARCHING BIOACTIVE COMPOUNDS RELATED TO SINGLE NUCLEOTIDE POLYMORPHISMS

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Abstract:

A genome-wide association study (GWAS) is an approach used in genetic research to associate specific variations (1). Among these variations are single-nucleotide polymorphisms (SNPs). By identifying them, they can be used to understand how genes contribute to the disease; in this way better prevention and treatment strategies can be developed (2). The analysis of information for the understanding of genes and food interactions is complex. For this reason, the need arises to develop a bioinformatic tool relevant to the field of nutrition, specifically with the study of bioactive compounds (BCs) that are chemical substances that are found in small quantities in all living beings and are associated with the promotion and prevention of pathologies (3). From data mining, a BCs search tool associated with SNP and metabolic pathways, which we call SNP-FOOD SEARCH (SNP-fs), was automated. The input search elements are the identifiers of the SNPs, to obtain information about the gene, the metabolic pathway, the bioactive compounds, and the food where the identified compounds are located. It uses specialized databases: Genecode, Reactome, foodb, PubChem and USDA to retrieve data (4) Bioinformatics tools make an important contribution to science, for example, SISTEMATX that provides information about secondary metabolites and their structure. (5) While SNP-fs allows to identify the relationship between the BCs of the SNPs, as well as the related foods and the metabolic pathways involved. Validation of the experimentation: An association analysis was performed between oxidative stress SNPs and Alzheimer's disease (AD). Diadzein is a BCs belonging to the isoflavones present in soy products. One gram of soy protein contains about 150 mg; it is involved as a free radical scavenger and is a protective antioxidant in AD. Finally, from this tool, it is intended to study at the level of medicine and precision nutrition the possible influence of BCs on specific diseases.

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GENOMIC PROFILING OF A CONSORTIUM OF TUMOR SAMPLES OF DIFFERENT ORIGINS FROM MEXICAN POPULATION USING NGS

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Abstract:

Precision medicine has made tremendous progress in recent years. Particular attention has been paid to molecular diagnosis and targeted treatment strategies that focus on the mutational profile of cancer patients. Unfortunately, in Mexico, efforts to know the diversity and mutation frequency of the highest incidence tumors in the Mexican population have not yet reached the scale to generate important population-level data. In addition, the cost of advanced diagnostic technologies such as next-generation sequencing is too high, since most of them are manufactured outside the country, making it impossible to achieve affordable costs to incorporate these procedures into the diagnostic process of cancer patients.

For this reason, through the acquisition of an automated next-generation sequencing platform, our laboratory has carried out the sequencing of 89 samples of solid tumors of different origins, including lung, breast, pancreas, central nervous system, colon, liver, and skin tumors, in order to establish the mutational profile of these samples in the Mexican population and find similarities and differences between our data and international databases. The preliminary results have served us to establish a basis for tumor diversity in the country. It is intended to continue this project until we reach a sample of not less than 500 patients.

In addition, we performed an evaluation of the platform itself under the requirements of the clinical setting, where response times are critical for decision making and medical management of cancer patients. The information obtained not only contributes to the construction of databases targeted to the Mexican population, but also expands the knowledge of genomic profiling of tumors of different origins. Finally, the evaluation and economic viability of this project has been carried out in order to create a more accessible diagnostic panel compared to the options currently available on the market, in conjunction with the ability to process samples within the country without the risk associated with exporting samples.

World Health Organization. (2020). México. In International Agency for Research on Cancer. Retrieved from https://gco.iarc.fr/today/data/factsheets/populations/484-mexico-fact-sheets.pdf

DETECTION OF NTRK REARRANGEMENTS BY A PCR-BASED ASSAY FOR ONCOLOGY MOLECULAR DIAGNOSTICS

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Abstract:

Cancer is one of the diseases with the highest incidence and mortality rate in the world. In 2020 alone, 195,499 new cases were diagnosed, and 90,222 deaths were recorded in Mexico *(Globocan, 2020).* Thanks to molecular diagnostic techniques, it is now possible to study biomarkers relevant to the diagnosis, prognosis and treatment of cancer patients. In recent years, the medical and scientific community has paid particular attention to the study of alterations in NTRK genes 1,2 and 3, because although the frequency of occurrence of these alterations is relatively low, patients treated with inhibitors of the NTRK tyrosine kinase domain have shown a better response compared to conventional treatment.

Similarly, the challenge of molecular biology is to provide a functional assay for the simultaneous detection of multiple alterations at a price affordable to the general public, especially in this Latin American scenario where advanced technologies such as next-generation sequencing are not the best option due to their operational costs. In response to this problem, we developed a PCR-based assay; the design of which has been shown to be effective in detecting fusions with NTRK1, with attempts to replicate the design for NTRK 2 and 3. Primer design took into account that overexpression of the tyrosine kinase domain is a consequence of NTRK1 rearrangements, which can be absolutely quantified using a digital PCR system; likewise, the translocated region of the gene exhibits a loss of expression that can also be visualized compared with expression of both sections in healthy tissue. Preliminary results show a successful design for both regions. The design was tested in healthy tissue and a positive control for NTRK 1 fusion. This showed the difference in expression of the generated amplicons, successfully confirming the logic of the primer design by real-time PCR. To improve the results, the primer set corresponding to the tyrosine kinase domain will be optimized, as the aim is to increase the specificity of this domain for NTRK1 and distinguish it from other tyrosine kinase domains to eventually transfer it to the digital PCR platform and include them into a panel of relevant biomarkers to diagnostic and treatment of cancer patients.

Peñaloza Coronas, C., Montilla Fonseca, S.M. and Sánchez, M.L. (2022), Response to clinical evaluation of the effectiveness of fusion-induced asymmetric transcription assay-based reverse transcription droplet digital PCR for ALK detection in formalin-fixed paraffin-embedded samples from lung cancer. Thoracic Cancer, 13: 146-146. https://doi.org/10.1111/1759-7714.14241

World Health Organization. (2020). México. In International Agency for Research on Cancer. Retrieved from https://gco.iarc.fr/today/data/factsheets/populations/484-mexico-fact-sheets.pdf

EFFECT OF EPIGENETIC DRUGS VALPROIC ACID AND HYDRALAZINE IN METASTASIS DEVELOPMENT IN NIH 3T3 CELLS TRANSFECTED WITH *HA-RAS*^{VAL12} GENE

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Abstract:

The metastasis development it is a multi-stage process where the tumor cell dissemination results in the establishment of secondary tumors at distant locations. The hydralazine and valproic acid (HV), two repositioned drugs, they are DNA methyltransferase inhibitor and histone deacetylase inhibitor (respectively). This combination of drugs has shown clinical activity in several neoplasic tumors, and they are able to upregulate some anti-metastatic genes. It is well known that oncogene *Ras* is associated to metastasis. The aim of present study was evaluate the potential role of this drug combination as antimetastatic therapy in *Ha-ras*^{val12} transfected NIH3T3 cells *in vivo*, and evaluate some invasion parameters *in vitro*. The results showed HV treatment have a strong growth inhibitory effect in NIH3T3-ras, and reduce 50% the cell motility and chemotaxis in comparison with parental cell line. However HV increases gelatinase activity of MMP-2. HV inhibits invasion in vitro with Matrigel (6-fold). Treatment of Balb/C nu/nu mice with hydralazine, valproic acid or their combination in pharmacologic dose, and inyected with with NIH3T3-ras cells, led to a strong antimetastatic effect: reduce the number (6 times less) and the size of metastatic lung nodules (75% less), and reduce the number of animals with metastasis (2/6 vs 7/7 animals). No clear correlation was found in the expression changes of the 80 pro- and antimetastatic genes with HV treatment, however some genes involved in cell motility were modified (Onto-tools), which was validated by western blot. Not changes in TET1, -2 or -3 was observed with the treatment, these proteins are asociated to active DNA demethylation.

Conclusion: Hydralazine and valproic acid, two repositioned drugs as epigenetic agents, exhibit antimetastatic effects in vitro and in vivo and hold potential for cancer treatment. The meaning of our results is limited by the use of the model of *Ha-ras*-transfected murine cells. Therefore, additional research on human tumor models for metastasis are needed. The present study was supported by CONACyT, grant No. A1-S-43144.

PREGNANCY AND GDM EFFECT ON VASCULAR GLUT 4 DENSITY

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Abstract:

Insulin resistance characteristic of pregnancy worsens if pregnancy is complicated by gestational diabetes mellitus. GLUT4 translocation is mainly insulin-dependent but there is scarce information about changes in vascular smooth muscle associated to insulin resistance. Also, a decrease in GLUT4 density has been associated with hypertension. The aim of this work was to assess if pregnancy and GDM change the density of GLUT4 transporters in the rat aorta. The experiments for detecting the GLUT4 density by means of direct immunofluorescence prepared by the “en face” method were performed using the thoracic and abdominal portions of the aorta from non-pregnant or pregnant rats fed with standard (SD) or hypercaloric (HD) diet for 7 or 9 weeks. The results showed that the GLUT4 density is not different between the thoracic and abdominal segments of non pregnant rats on standard diet, but it was decreased ($P<0.001$) in the group on hypercaloric diet. Pregnancy SD increased GLUT4 density only in the abdominal segment ($P<0.001$), but hypercaloric diet during pregnancy (GDM) markedly diminished GLUT4 density in both aorta segments ($P<0.001$). These results suggest that pregnancy increases insulin PI3K pathway and glucose metabolism mainly in the vascular territory proximal to the maternal-fetal circulation. Gestational diabetes mellitus reverses the vascular adaptations of pregnancy, favoring a pro-hypertensive condition.

LIVER DISEASE ASSOCIATED WITH CARDIAC DYSFUNCTION IN A MOUSE MODEL OF PRESERVED EJECTION FRACTION

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Abstract: Many patients with Non-Alcoholic Fatty Liver Disease (NAFLD) and non-alcoholic steatosis have ventricular heart disease that often manifests clinically as HFpEF. A recent prospective study on outpatients with HFpEF indicates that the prevalence of NAFLD could reach 50% and that half of them could have advanced fibrosis. Despite being frequent, the molecular and cellular mechanisms are still unknown and do not have a specific treatment. The experimental induction of HFpEF has been achieved by a model of cardiometabolic disease induced by hypertension and a high-fat diet, which produces ventricular dysfunction and systemic modifications, physiologically mimicking what occurs in the metabolic syndrome. This model has widely characterized cardiac dysfunction. However, it is unknown if NAFLD is recapitulated in this model, similar to patients with HFpEF.

Objective: To determine if the metabolic changes in our model of HFpEF show NAFLD and underlying mechanisms.

Method: We analyzed C57BL6 mice in two groups, controls and with HFpEF, for which serum and liver tissue were extracted. With the serum, the parameters of HDL, LDL, TG, ALT, AST, albumin, protein, and as well as in liver tissue, the presence of steatosis and fibrosis with H / E and Masson were evaluated. Triacylglycerols (TG) and cholesterol were quantified, as well as the evaluation of mitochondrial function, oxidative stress markers, inflammatory markers, and hepatic expression of genes associated with fatty acids, cholesterol, and bile acid metabolism.

Results: Our model of HFpEF presented alterations regarding the function of the left ventricle, impairment in diastolic pressures, high stiffness index, and pulmonary congestion. As expected, HFpEF mice exhibited no differences in ejection fraction. The cross-sectional area of the cardiomyocytes showed hypertrophy and increased expression in natriuretic peptides, indicating pathological remodeling. Liver tissue micrographs showed the presence of micronodular steatosis in animals with HFpEF without forming fibrotic bridges or changes at the parenchyma level. We observed a significant difference between groups for serum values of TG and LDL. Likewise, a notable increase in TG accumulation in liver tissue is observed. However, this accumulation of lipids does not induce remarkable mitochondrial damage as respiratory control, and mitochondrial phosphorylating efficiency close to that of control animals are observed.

Conclusions: As a result of a high-fat diet and hypertension, dyslipidemia was demonstrated. The absence of noticeable changes in mitochondrial function between the two groups is independent of intracellular lipid overaccumulation. This would indicate that although histological features of steatosis are observed at the cellular level, liver damage suggests an early stage of NAFLD associated with HFpEF.

GASTROPROTECTIVE ACTIVITY OF CALLISTEMON CITRINUS EXTRACT IN AN INDUCTION MODEL OF GASTRIC ULCERS IN OBESE RATS

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Abstract:

Obesity is a disease caused mainly by excessive consumption of food with a high caloric intake, decreased physical activity and genetic predisposition which contributes its development. This condition presented several complications as cardiovascular diseases, type II diabetes mellitus, hypertension, fatty liver and some types of cancer as gastric, giving rise to a poor quality of life. The inadequate intake of drugs as non-steroidal anti-inflammatory NSAIDs (diclofenac, ibuprofen, indomethacin, celecoxib), causes gastric and intestinal mucosa damage generating injury and malfunction of the organs involved in the absorption and assimilation of food. Therefore, looking for natural products with biological activity and few side effects is important. Callistemon citrinus has been reported to have several biological activities as antioxidant, antimicrobial, hepatoprotective and chemoprotective against colon cancer. Among the compounds that give it these properties are terpenes and phenols. To date, there are no reports that correlate with intake of high fat and sugar diet and the predisposition to more easily generate gastric ulcers. The aim of this study is to determine the gastroprotective effect of Callistemon citrinus leaf extract in a model of obesity for 15 weeks and the intake of NSAID as indomethacin. 30 Wistar rats (Rattus norvegicus) were randomized in 6 experimental groups (n=5). Group 1 (control) rats fed with normal pellet rodent; Group 2: High fat sucrose diet (HFSD) fed with a diet with caloric intake of 5.37 kcal/g; Group 3: (HFSD + C. citrinus), rats received HFSD plus C. citrinus leaf extract (250 mg/kg) once a day by oral gavage; Group 4: Indomethacin single dose of 30 mg/kg orally; Group 5: C. citrinus single dose of 250 mg/kg + IND and Group 6: Omeprazol single dose of 30 mg/kg + IND. All groups were fasted for 24 h prior to indomethacin administration. The results showed a decreased weight gain, morphological and biochemical parameters in the HFSD + C. citrinus as compared with the HFSD group. In addition, the extract decreased gastric lesions caused by indomethacin, reduced the activity of the myeloperoxidase, cyclooxygenase-2 and 5-lipoxygenase and inflammatory biomarkers as TNFα, IL-6, AOPP, leptin and adiponectin caused by obesity and the use of indomethacin.

NOVEL *LIGUSTRUM LUCIDUM* POLLEN PROTEINS CAUSING RESPIRATORY ALLERGIES IN POLYSENSITIVE PATIENTS

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Abstract:

Introduction: The *Ligustrum lucidum* belongs to the Oleaceae family, one of the world's most allergenic and distributed family plants. Due to its ornamental cultivation, trees of *L. lucidum* are widely distributed in the world; for example, in Mexico City, it is one of the main cultivated species. Inhalation of aeroallergens causes approximately 40% of respiratory allergies, and the pollen of *L. lucidum* is a significant cause. Respiratory allergies manifest symptoms such as rhinitis, runny nose, nasal congestion, and conjunctivitis, which can seriously damage patients' quality life. This work aims to characterize the *L. lucidum* pollen proteins that cause respiratory allergies in polysensitive patients.

Methods: Total proteins were extracted from *L. lucidum* pollen using a modified phenol extraction method and separated by two-dimensional gel electrophoresis (2-DE) for immunoblotting. Sera from seven polysensitive patients for *L. lucidum* was collected as a source of the Ig-E antibodies for western blot. Finally, for identification, immunoreactive proteins were cut and analyzed by liquid chromatography coupled to mass spectrometry (LC-MS/MS).

Results: *L. lucidum* pollen proteins characterized by 2-DE showed more than 200 spots in a pI 3-10, of which 24 spots showed immunoreactivity with a pool of sera from polysensitive patients. We identified six proteins with allergenic potential such as Pectinesterase (Fra e 11), UDP-arabinopyranose mutase, Major pollen allergen Ole e 1, Glucan endo-1_3-beta-D-glucosidase (Fra e 9), Allergen Fra e 1 and Major pollen allergen Lig v 1. Interestingly, we identified 22 novel proteins not previously associated with allergic reactions, such as Malate dehydrogenase, Glyceraldehyde 3-phosphate dehydrogenase, Flavanone 3-hydroxylase, Fructose-bisphosphate aldolase, among others. These proteins could be responsible for the cross-reactivity with pollen from other Oleaceae family trees.

Conclusions: Knowing the *L. lucidum* pollen proteins that cause allergies in polysensitive patients is imperative for developing more effective diagnostic methods and treatments.

IMMUNOHISTOCHEMICAL CHARACTERIZATION OF THREE-DIMENSIONAL CELL CULTURE MODEL FROM RENAL CELL CARCINOMA.

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Abstract:

Cancer is one of the major public health problems worldwide, being the second leading cause of death around the world. Both genetic factors and microenvironmental components enhancing the development, progression and metastasis processes of malignant cells, besides contributing to the acquisition of intratumor heterogeneity. All of these features represent the major hurdles in the search of new effective and safer treatments. Three-dimensional (3D) cell culture models have changed the paradigm of preclinical cancer research as they more closely resemble the complex tissue environment and architecture of human solid tumors than in conventional bidimensional (2D) cell cultures. Among 3D cell culture models, spheroids and organoids represent the most versatile and promising models in that they can recapitulate the heterogeneity and pathophysiology of human cancers, among other things, because they show the formation of 3 zones with different metabolic characteristics and the presence of different gradients both nutrients and oxygen. **Methods**: Since 3D cell cultures models mimic the tumoral microenvironment, the structure and biology and physical properties of solid tumors, we proposed the generation of different 3D cell cultures derived from cells of renal cell carcinoma (RCC) to get a model that we can used to explore de mechanism behind the development and response to drugs process and give us a more real approach to what happens in human tumors. In this project, we used a combination of two methods of spheroids scaffold-free formation: liquid overlay and agitation by spinner flask. We accomplished two different 3D cell cultures from two renal carcinoma cell lines, each one with different tumorigenicity, the 786-O cell line and ACHN cell line. The spheroid formation was monitoring each 24 hours during all time formation. At the same time, a formalin fixed paraffin-embedded protocol was performed for spheroids with the aim of identifying the expression of specific molecules that enable recognizes the three distinctive zones of a 3D cell culture: the peripheral and metabolically active zone, the middle quiescent zone, and the necrotic center zone. **Results**: Both cell lines of renal cell carcinoma were capable to form spheroids, subjected to different culture conditions. The ACHN spheroids showed a longer lifetime and bigger size than 786-O spheroids. The immunohistochemical and western blot characterization showed a differential expression of three molecular markers (Ki67, p27, HIF1a), that we can use to define the metabolic state of different zones or layers of the spheroids, give us a global image of the spheroid´s architecture and maturation. **Conclusions**: An important highlight, is that marker´s expression change in relation to the maturation time of the spheroid and its size, in young spheroids the presence of p27 and HIF1a y lesser than older and is necessary that the size of spheroid be more than 200 micrometers in order to present the three metabolic zones.

INTERACTION OF NATURAL MOLECULES IN AN ENDOXIFEN AND 4-OH-TAMOXIFEN RESISTANCE ER+ BREAST CANCER MODEL

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Abstract:

Approximately 80% of breast cancer cases are estrogen receptor-positive (ER+) (Ferlay J, Ervik M, 2020), and are sensitive to hormonal treatment (tamoxifen). Tumor cells resistant to tamoxifen could increase the expression of the eukaryotic initiation factor 4F (eIF4F) complex. Among the most effective targets that have been studied, since it is an essential subunit of the eIF4F complex, is the factor eIF4A. Several small molecules such as rocaglates, hippuristanol, and pateamine A, have been reported to inhibit eIF4A (Sai Kiran Naineni, 2020). We propose the use of cryptotanshinone and auraptene molecules to sensitize resistant cells to the most active metabolites derived of tamoxifen, 4-hydroxytamoxifen, and endoxifen. Among the most relevant results obtained was the generation of cellular variants resistant to 4-hydroxytamoxifen and endoxifen. The concomitant treatments of 4-OH tamoxifen and endoxifen generated synergy with the Auraptene molecule, which induced sensitization on tamoxifen metabolites-resistant cells, as well as in RE+ parental cells. This phenomenon was not registered in triple-negative breast cancer cells. Our preliminary data showed the interaction between the overexpressed eIF4A protein and the auraptene and cryptotanshinone molecules, data supported by molecular docking. This suggests that the interaction of Auraptene with eIF4A may inhibit the activity of the eIF4F complex, promoting the sensitization of chemoresistant and parental ER+ cells.

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Sai Kiran Naineni, Rayelle Itoua Maïga, Regina Cencic, Andrea A. Putnam, Luis A. Amador, Abimael D. Rodriguez, Eckhard Jankowsky, Jerry Pelletier. A comparative study of small molecules targeting eIF4A RNA. (2020) May; 26(5): 541–549. doi: 10.1261/rna.072884.119

DETERMINATION OF CARDIOMETABOLIC RISK IN MEDICAL STUDENTS

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Abstract:

Introduction: Cardiometabolic risk (CMR), refers to the overall risk for developing cardiovascular disease (CVD) and type 2 Diabetes Mellitus (DM2), which are associated with risk factors such as abdominal obesity, insulin resistance, among others. Abdominal fat, particularly visceral or ectopic adiposity and insulin resistance are the main contributors to CMR. Several anthropometric measurements help to determine the risk of presenting chronic diseases, which show a better correlation with biochemical and clinical values present in individuals with CMR. **Objective:** To determine the cardiometabolic risk by means of anthropometric formulas in medical students in the city of Oaxaca de Juárez. **Methodology:** Correlational, non-experimental cross-sectional study, n= (56), medical students aged 18 to 23 years, who signed the consent form. The Nutritional History instrument was applied, biochemical blood tests were performed to determine glucose, cholesterol, triglycerides, and HbA1c, anthropometric measurements of weight, height, hip-hip circumference were taken, and analyzed with descriptive statistics and the correlation statistics of Spearman's Rho, Pearson, and Kendall's Tau. **Results:** 50% were men and 50% women, the prevalence of CMR was 26.8% for the WHtR formula and 91.1% with low risk for the WHR formula, according to the BMI 66.1% were normal weight, followed by 21.4% overweight and 7.4% underweight, 4% overweight and 7.1% obese, according to laboratory tests the mean HbA1c was 35.73 mg/dl and A1c 47.02mg/dl, glucose 98.46mg/dl, triglycerides 142.72mg/dl and cholesterol 168.50mg/dl. **Conclusions:** there is a significant relationship between anthropometric variables and laboratory levels.

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CARDIOMETABOLIC RISK ASSESS BY ANTHROPOMETRIC MEASUREMENTS

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Abstract:

Introduction: Cardiomebolic risk refers to risk factors that increase the probability of developing vascular events and chronic diseases. Mexico has a high prevalence of morbidity and mortality of chronic degenerative diseases that are considered a global epidemic. Recent studies determined that using formulas and anthropometric measurements helps determine the risk of chronic diseases. Anthropometric measurements and formulas are easy, inexpensive, and non-invasive that help to know the current health status of the population. **Objective:** Relating anthropometric measurements to lipid profile, glucose, and glycated hemoglobin a1c in medical students. **Methodology:** fifty-six men and women with Body Mass Index (BMIs, kg/m^2) between 15 to >30kg/m^2, in age of between 18-23 age who were medical students recruited from Oaxaca city, Mexico. Subjects were free of metabolic diseases (diabetes, coronary heart disease and hypercholesterolemia). We applied the nutritional medical history instrument. And measured body weight, waist and hip circumference, height, neck, thigh was measured following the procedures adopted of on the standardization of anthropometric measurements. Formulas were made waist-to-height ratio (WHtR), waist-to-hip ratio (WHR) finally the equation "Deep abdominal AT (cm^2). Pearson's, Tau Kendall, and Rho of Spearman correlation coefficients. **Results:** Mean of waist was 77.14 cm ± 9.94, hip 96.45 cm ± 9.30, neck 33.16 ±3.45, thigh 47.43 ± 5.68, fat percentage 28.84% ±10.74, muscle percentage 31.43% ±8.02 and for the AT it was 34.63 cm^2 and the CMR was 26.8%, according to laboratory levels the mean glucose was 98.46 mg/dl ± 9.94, cholesterol 168.50mg/dl ± 28.01, triglycerides 142.74 mg /dl ± 37.09 and for HbA1c 35.73mg/dl ±149.91. A correlation (Rho of Spearman, Tau Kendall, Pearson´s) was found between the lipid profile and the anthropometric variables, the percentage of fat and muscle did not present a correlation with the laboratory values. **Conclusion:** We show that there is a correlation between anthropometric formulas and laboratory levels.

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MESENCHYMAL STEM CELLS-TRAIL AS A STRATEGY IN COLORECTAL CANCER

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Abstract:

Colorectal cancer (CRC) is the third cause of cancer and the second cause of cancer-related death [1]. The main cancer therapies include surgery, chemotherapy, and radiotherapy. However, these have limitations, such as adverse effects and chemoresistance [2]. One new therapeutic option that has emerged is mesenchymal stem cells (MSC) due to their properties of self-proliferation, migration to the tumor microenvironment, and immunoregulation [3]. Moreover, they can be genetically modified with antitumoral proteins [4]. The TNF-related apoptosis-inducing ligand (TRAIL) is a protein that activates apoptosis in tumoral cells by expressing the TRAIL death receptors DR4 and DR5 [99]. This study evaluated chemosensitivity and TRAIL sensitivity in CRC cell lines and developed an MSC model that produces TRAIL. First, we determined chemosensitivity to 5-fluorouracil, oxaliplatin, and irinotecan in CACO2 and CMT-93 CRC lines. TRAIL or chemotherapy sensitivity was analyzed by the ATP-CRA luminescence reaction. TRAIL receptors (DR5) were analyzed by immunofluorescence. MSC were isolated from mice bone marrow (BM-MSC) and genetically modified with lentiviral vectors to express TRAIL and green fluorescent protein as a reporter. TRAIL protein was evaluated by Western Blot and ELISA. Our results showed that CRC cell lines expressed TRAIL receptor DR5 in 86.32 ± 5.78 % in CACO2 cells and 68.92 ± 5.21 % in CMT-93 cells. Moreover, recombinant TRAIL induced cell death in CACO2 and CMT-93 cell lines. We classified CACO2 as chemoresistant and CMT-93 as chemosensitive. BM-MSC were isolated, characterized, and genetically modified, showing a media concentration of 327.1 pg/mL. The monomeric band was identified by Western blot. Thus, BM-MSC are a promissory vector to TRAIL delivery, representing another therapeutic strategy as TRAIL can induce cell death in chemoresistant cancer cells.

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BACTERIAL CYCLODIPEPTIDES IMPACTED THE MEVALONATE AND CHOLESTEROL PATHWAYS IN HELA CELLS OF HUMAN CERVIX ADENOCARCINOMA

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Abstract:

The incidence of human cervix adenocarcinoma caused by papillomavirus is the third most common cancer among women. Cyclodipeptides (CDPs) are organic compounds produced by bacteria. These have attracted for their antibacterial, antifungal, and anticancer activity; considering them as potential to be used as new drugs. In this work the cytotoxic activity of the CDPs produced by *Pseudomonas aeruginosa* PAO1 bacterium was analyzed in HeLa cells of human cervix adenocarcinoma as study model. Results indicate that CDPs blocking the PI3K/Akt/mTOR pathway but downstream responses comprising gene expression remain unstudied. Seeking to understand the cytotoxic and anti-proliferative effects of CDPs in HeLa cells, a global RNA-Seq analysis was performed. Interestingly, transcriptomic analysis revealed the participation of genes of the mevalonate and cholesterol biosynthesis pathways; in agreement with this observation, total cholesterol diminished, confirming the blockage of the cholesterol synthesis. The expression of some genes of the mevalonate and cholesterol synthesis such as HMGS1, HMGCR, IDI1, SQLE, MSMO1, SREBF1, and SOAT1 was up-regulated by CDPs exposure. Accordingly, metabolites of the mevalonate pathway were accumulated in HeLa cultures treated with CDPs and the cholesterol content significantly decreased in both cells and supernatants. The finding suggests that the metabolism of cholesterol is crucial for the occurrence of cervix adenocarcinoma, and the blockade of the sterol synthesis as an anti-proliferative mechanism of the bacterial CDPs, represents a reasonable chemotherapeutic drug target to explore.

IL-17/HBD-2 CONCENTRATIONS IN TOTAL SALIVA IN PERIODONTITIS AND RHEUMATOID ARTHRITIS

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Abstract:

Periodontitis (P) and Rheumatoid Arthritis (RA) are chronic inflammatory diseases characterized by the destruction of periodontal tissue, articular bone and cartilage, respectively, in which IL-17 participates. This cytokine is produced by various leukocytes and participates in the differentiation, activation and maturation of osteoclasts, causing the destruction of connective and bone tissue (periodontal tissues). However, it also promotes the integrity of the epithelial barrier, as well as the production of antimicrobial peptides (AP). Among them, beta-defensin 2 (hBD-2) is involved in gingival homeostasis, as well as in periodontal disease, however, it is unknown how IL-17 and hBD-2 are found in patients with both pathologies in advanced stages. The objective of this study was to determine the concentration of IL-17 and hBD-2 in saliva of patients with P and advanced RA. From unstimulated saliva samples before and after periodontal treatment, with a diagnosis of Stage IV Periodontitis, grade C, generalized, RA and psoriasis, IL-17 and hBD-2 were quantified by ELISA. Our results showed that IL-17 levels before treatment were lower compared to those obtained in post-treatment and in the periodontally healthy control. For hBD-2, the concentration was higher before treatment compared to quantification after treatment, as well as control. IL-17 is a proinflammatory cytokine whose role in immunopathogenesis in P, RA has been identified; however, our results are interesting, since IL-17 decreases after treatment, data that agree with what was reported by Rodríguez -Montaño et al., 2021. In this sense, the concentrations of hBD-2 in patients with these characteristics have not been reported, so the regulation mechanisms must be clarified.

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BENZIMIDAZOLE DERIVATIVES AS INHIBITORS OF SHIKIMATE KINASE FROM METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

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Abstract:

Introduction: Bacterial infections are a serious threat to our population. It is estimated that by the year 2050 one of the main causes of death will be due to infections by multiresistant bacteria. World Health Organization has recognized methicillin-resistant Staphylococcus aureus (MRSA) as an important threat since it causes serious hospital acquired and community acquired infections. Therefore, the development of new treatments against this bacterium is a priority. Enzymes of the shikimate pathway are considered as excellent targets for new antibiotic development, in particular shikimate kinase (SK), which catalyzes the conversion of shikimate to shikimate-3-phosphate, is considered an important target given its essentiality for bacterial survival.

Objective: To obtain and characterize methicillin-resistant *Staphylococcus* aureus shikimate kinase (SaSK) inhibitors through *in vitro* enzymatic assays.

Methodology: An initial screening was performed with SaSK and a benzimidazole derivatives chemical library which consisted of 161 compounds. These small molecules were assayed at a starting concentration of 200 µM. Afterwards, the two most potent compounds were selected for biochemical characterization by performing curves at different concentrations of each substrate (namely ATP and shikimate (SHK)) and fixed concentrations of each compound to obtain their mode of inhibition.

Results: Out of the 161 compounds, 72 did not inhibited SaSK, 73 showed limited inhibition ranging from 5-20 %, 14 compounds inhibited 30-40%, and two of them, compounds **1** and **7** showed a 56% and 52% SaSK inhibition at 80 µM and 100 µM respectively. Therefore, each compound was characterized to obtain their mode of inhibition. The results showed that compound **1** presented an uncompetitive behavior against SHK and a mixed type against ATP. On the other hand, compound **7** showed an uncompetitive behavior against SHK and a noncompetitive against ATP.

Conclusions: These results provide information about new potential inhibitors against SaSK and could be used as hits to obtain new antibacterial drugs.

ROLE OF TLR2, TLR4 AND TLR9 RECEPTORS IN PLATELET AGGREGATION IN TYPE 2 DIABETES

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Abstract:

Type 2 diabetes (T2D) is a metabolic disorder characterized by hyperglycemia, a consequence of relative insulin deficiency, due to pancreatic β-cell dysfunction. In 2014, the WHO reported 422 million people over 18 years of age with diabetes, of which 95% were type 2. Hyperglycemia alters glucose homeostasis causing oxidative stress, alterations in cell signaling, decreased availability of nitric oxide, increased production of thromboxane, and activation of AP-1, tissue factor, plasminogen activator protein and NF-κB. The latter is part of the Toll-like receptors (TLRs) signaling pathway, such as TLR2, TLR4 and TLR9, which have been related to platelet hyperactivity and intravascular alterations, leading to the development of atherogenesis. Platelets aggregate at the site of atherosclerotic plaque rupture or endothelial erosion, stimulating thrombus formation and promoting atherosclerosis. Objective: To analyze the role of TLR2, TLR4 and TLR9 and its relationship with platelet alterations in patients with T2D. Methodology. A total of 31 diabetic patients and 31 healthy controls from Yucatan, aged 30 to 65 years old, were recruited. From 10 mL of peripheral blood, complete blood cytometry, serum levels of glucose, total cholesterol, HDL-c, LDL-c, triglycerides were performed. From platelet-rich plasma, platelet aggregation was determined by light transmission, and the expression in platelets of TLR2, TLR4, TLR9, and MyD88 and NF-κB signaling proteins, by flow cytometry. Results. No significant differences were found in platelet aggregation or activation between patients and controls; however, a tendency to decrease in aggregation times in diabetic was observed. Expression levels of TLR2, TLR4, MyD88 and NF-κB did not show significant differences between groups; however, TLR9 expression was higher in controls (47.31±27.06) than patients (30.87±29.06). We found positive correlation between aggregation time and MyD88 expression (p=0.0340) in T2D patients, but negative correlation with TLR2 (p=0.456), TLR4 (p=0.0043), MyD88 (p=0.0455) and NF-κB (p=0.0495), expression and mean fluorescence intensity of TLR2 (p=0.0400), MyD88 (p=0.0.43) and NF-κB (p=0.0201) was observed in controls. TLR9 did not show correlation with aggregation time. Conclusion. TLR2 and TLR4 signalling pathways might be involved in platelet aggregation in Yucatan population, but not in T2D patients, probably because treatment with metformin could be altering platelet activation and aggregation. Further studies involving patients with different medication should be done.

KCNJ11 AND *ABCC8* POLYMORPHISMS ASSOCIATED TO SULFONYLUREA SECONDARY FAILURE IN TYPE 2 DIABETES MELLITUS

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Abstract:

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia, insulin resistance, and a relative insulin deficiency it represents a serious public health issue in our country, with increasing prevalence (1). There are mutations on pharmacological or metabolic target genes involved in variations to treatment response. Sulfonylureas remain a common treatment in Mexico mainly combined with metformin. Glucotoxicity and lipotoxicity associated with T2DM progression and sulfonylureas prolonged use can cause apoptosis in β-pancreatic cells, so that treatment may lose effectiveness over time, this phenomenon is known as sulfonylurea secondary failure (2), defined as the lack of glycemic control expressed as levels of glycosylated hemoglobin (HbA1c) greater than 7.0% after 12 months of treatment with sulfonylureas alone or combination (3). Sulfonylurea secondary failure timing is very variable, may be genetic factors involved in this variation. There are many polymorphisms associated with sulfonylurea response (4) as the ones in ATP dependent potassium channels (KATP) coded by *KCNJ11 and ABCC8 genes*.

We conducted a study that included 183 T2DM patients treated with metformin, glibenclamide or combination from Mixcoac and Portales Health Centers of Benito Juárez Health Jurisdiction in Mexico City. Genotyped for the polymorphisms: rs5219 (*KCNJ11* E23K), rs757110 (*ABCC8* S1369A) and rs1799854 (*ABCC8* -3C/T). Biochemical and anthropometric data were collected from the clinical record. Association of polymorphisms with treatment response was looked finding that patients who present the GG genotype of *KCNJ11* E23K presented a significantly higher risk of being in non-glycemic control in a shorter period (odd ratio; OR 3.066) and the homozygous and heterozygous genotypes containing the alleles G-E23K, A-S1369A and C -3C/T presented significant OR with respect to the recessive genotypes with respect to disease time progression. So, we propose these alleles may be related to sulphonylurea secondary.

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COCULTURE OF NEURONS AND SCHWANN CELLS DERIVED FROM MESENCHYMAL STEM CELLS OF HUMAN ADIPOSE TISSUE, AS POTENCIAL CELL THERAPY FOR DEMYELINATING DISEASES

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Abstract:

A demyelinating disease is any condition that causes damage to the myelin sheath resulting in neurological problems. One of the main therapeutic approaches focuses on inducing or enhancing remyelination and/or regenerating or replacing neurons to establish neuronal connectivity and achieve functional recovery. The therapeutic potential of Schwann cells in combination with drugs related to myelin synthesis, such as complex B, is currently being studied to remyelinate unprotected axons and restore nerve function. In this study, we evaluated the coculture of SCHWANN CELLS AND DIFFERENTIATED NEURONS FROM HUMAN MESENCHYMAL STEM CELLS OBTAINED FROM ADIPOSE TISSUE (MSC-ATh) with or without complex B. First, we isolated, expanded, and characterized MSC-ATh using CD34, CD90, and CD105 surface markers. Subsequently, MSC-ATh were differentiated into neurons by culture media with bFGF and Forskolin. Differentiation to Schwann cells was achieved by culture media with ATRA, Forskolin, bFGF, PDGF, and HRG. The differentiation process was validated by immunocytochemistry staining with surface markers such as neurofilaments for neurons and GFAP, S100 protein, and PBM for Schwann cells. To determine the amount of complex B necessary for cell culture experiments, we determined the mean cytotoxic concentration 50 by cytotoxic assay measuring intracellular ATP. The myelinating potential of the coculture of neurons and Schwann cells with or without B complex was verified at 7 and 14 days by immunocytochemical staining using neurofilament, S100 protein, and PBM markers. The results without complex B on day 14 showed an increase of 12% in the expression of S100, 23.9% in the expression of PBM, and 8.83% in the expression of NF compared to day 7. Also, our results with B complex showed an increase of 27.63% for s100, 19.4% for PBM, and 15.9% for NF compared to day 7. Coculture of neurons and Schwann cells with or without complex B significantly differed in PBM and S-100 expression. In conclusion, the coculture of SCHWANN CELLS AND DIFFERENTIATED NEURONS FROM MSC-ATh WITH B complex could be a good therapeutic approach to inducing neuron axon remyelination in demyelinating diseases.

IMPACT OF BIOACTIVE COMPOUNDS PRESENT IN FOODS AVAILABLE IN MEXICO ON OXIDATIVE STRESSMETABOLISM AND ALZHEIMER'S DISEASE GENETIC VARIANTS ASSOCIATED

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Abstract:

Alzheimer's disease (AD) is a type of dementia characterized by slow and progressive neurodegeneration, the formation and accumulation of neuritic plaques and neurofibrillary tangles in brain cells. The global investment for the treatment of this disease is more than 200 million pesos per year and it is estimated that it will double by 2030. In the Systems Biology and Translational Medicine laboratory, by artificial intelligence strategies such as data mining and supervised machine learning have been identified single nucleotide polymorphisms (SNPs)(1) associated with AD and oxidative stress (OS). Since the last decade these genetic variants have become very relevant as they have provided clues to complex disease questions. There are several publications that support the hypothesis that OS metabolism is a phenomenon that occurs in the early stages of AD and may directlytrigger Tau hyperphosphorylation. OS is a state in which elevated levels of reactive oxygen species (ROS) are generated in cells, and as a consequence, antioxidant mechanisms are insufficient to reduce the potential damaging impact of ROS, that is related related to the presence of Aβ. It has been reported that the bioactive compounds (BC) influence the pathological processes of AD, since they reduce the levels and phosphorylation of Aβ and tau, preventing their aggregation. A BC are essential and non essential compounds (e.g., vitamins or polyphenols) present in any living being, and can be shown to have an effect on human health. BC are also referred as nutraceuticals that reflects their effect in the human diet due their biological activity. They also avoid an OS, have anti- inflammatory activity, provide protection to cellular structures and inhibit neuronal apoptosis. However, the variability of the genes that make up the metabolic pathways associated with AD has been poorly studied. In this project the principal aim is to provide clues on how the effect of these variantsassociated with AD and OS impact through gain or loss of function or modification of metabolism in the genomic context of an individual belonging to a specific population. We hypothesize that this information will be relevant to propose the role of BC on gene product and their effect on metabolic pathways associated with OS and AD.

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FINDING HITS FOR TYPE 2 DIABETES DRUG DESIGN. CHARACTERIZATION OF PROTEIN TYROSINE PHOSPHATASE 1B INHIBITORS

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Abstract:

Introduction: Type 2 diabetes is a chronic-degenerative disease manifesting multiple alterations in the glucose homeostasis including impaired insulin secretion and decreased sensitivity of insulin-dependent organs to this hormone. Currently there are multiple therapeutic options for the treatment for type 2 diabetes, nevertheless, they show limited long-term efficacy, as well as adverse effects, which limits their use. Therefore, it is urgent to develop new treatment alternatives. In this context, protein tyrosine phosphatase 1 B (PTP1B), a negative regulator from insulin signal transduction pathway, has been considered an excellent target for antidiabetic drug design.

Objective: To characterize PTP1B inhibitors which can serve as hits to design a new drug against type 2 diabetes.

Methodology: In the present work, a chemical library composed by 109 benzimidazole derivatives, was evaluated to determine the inhibition capability of these compounds in PTP1B. The four most potent compounds were characterized, first, the concentration that inhibits 50% of enzyme activity (IC50) was determined through curves at different inhibitor concentration. Furthermore, their inhibition mechanism was obtained varying substrate concentration at different fixed inhibitor concentrations.

Results: The data showed that the IC50 values obtained were of 9, 9, 12 and 18 μM for compound **1**, **2**, **3** and **4**, respectively. In respect to their inhibition mechanism, compounds **1**, **2** and **3** showed a noncompetitive inhibition mode, whilst compound **4** was a mixed-type inhibitor. These findings indicate that the four compounds can bind both the free enzyme and the enzyme-substrate complex. Furthermore, in the case of noncompetitive inhibitors, these showed the same affinity for both.

Conclusions: The four inhibitors reported her are good hits that provide structural and kinetic information that can be used to develop a new drug against type 2 diabetes.

SUCRALOSE INCREASE THE MACROPHAGE INFLAMMATORY RESPONSE AND ALTERS THE PATTERN OF ADIPOKINES IN DIFFERENTIATED ADIPOCYTES OF THE PCS-210-010 CELL LINE

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Abstract:

Sucralose is a non-nutritive sweetener recognized by membrane taste receptors known as sweet taste receptors. These receptors are responsive to identifying sweet molecules in oral tissues and other extraoral tissues where the exact role outside the gustatory systems is still elusive. Sucralose is considered a safe additive because it is eliminated 24 h before consumption; however, its bioaccumulation in adipose tissue was evidenced. On adipose tissue are embedded immune system cells involved in developing low-grade systemic inflammation, like macrophages. To date, there is not enough information to show whether sweeteners potentiate inflammatory processes by altering the function of cells in tissue and/or contribute to the development of metabolic pathologies. Considering that sucralose may impact metabolic disease development, our research is related to an inflammatory response in stimulated macrophages and mature adipocytes. This work shows the relative mRNA expression of TAS1R2 and TAS1R3 genes by qPCR in human visceral adipose tissues (VAT), macrophages, and adipocytes differentiated from PCS-010-210 human cell line; also we determine om stimulated macrophages the concentration of the chemokine IP-10 by ELISA; and finally we determine the effect of sucralose on adipocyte fat lipid accumulation by oil red staining, as well the concentration of adipokine and cytokine in our culture by flux cytometer at two phases of maturation process at 96 at 192h. Our results demonstrate the presence of TAS1R2 and TAS1R3 mRNA transcripts in all samples being TAS1R3 mRNA expression higher than TAS1R2. The effect of sucralose on differentiated macrophages shows an increase in the concentration of the chemokine IP-10 could induce its polarization to M1. Finally, on adipocytes, cytokines and adipokines concentration decreased with sucralose stimuli. In conclusion Sucralose can increase an inflammatory response on macrophages but impair the response of cytokines and adipokines on mature adipocytes.

ROLE OF CD54 IN THE METASTATIC CAPACITY OF GASTRIC CANCER STEM CELLS

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Abstract:

Gastric cancer is the fourth leading cause of cancer death in the world (Sung et al., 2021). One of the theories that support these high mortality rates, is the presence of cancer stem cells (CSC), which have the potential of self-renewal and cell differentiation, as well as a greater tumorigenic capacity (Eun, Ham, & Kim, 2017). In our research group, we identified CD24+CD44+CD326+CD54+ phenotype cells isolated from patients with gastric cancer. Interestingly, this phenotype was absent in cells isolated from patients without gastric cancer, who presented a population with a CD24+CD44+CD326+CD54- phenotype. Furthermore, in addition to demonstrate that CD24+CD44+CD326+CD54+ subset are true gastric cancer stem cells (GCSC), these cells derived of tumorspheres from the AGS cell line possess a higher ability to metastasize in a zebrafish model. Our aim is to explore the role of CD54 in these GCSC; for this purpose, we have isolated GCSCs from the AGS cell line by cell sorting and generated a GCSC-CD54KO by CRISPRCas9. Then, with the CD44+CD24+CD326+CD54 knockout (KO) cell line we will evaluate their ability to migrate, invade and tumorigenic capacity in a zebrafish model, this will help us to gather more evidence to elucidate the role of CD54 in the tumorigenic capacity of GCSC and will support our proposal to use it as a therapeutic and prognostic marker of Gastric Cancer.

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ANALYSIS OF LINE-1 RETROTRANSPOSON AS A SENESCENCE MARKER IN ACCELERATED AGING MICE

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Abstract:

Idiopathic Pulmonary Fibrosis (IPF) is a chronic, progressive, irreversible and usually lethal interstitial lung disease, of unknown etiology and very limited therapeutic options. The main risk factor and driving force of this disease is aging[1]. Most of the hallmarks of accelerated aging have been identified in IPF lungs, including cellular senescence[2]. Cellular senescence is a cellular state characterized by an irreversible cell cycle arrest, resistance to apoptosis, an altered metabolism, and the development of a senescence-associated secretory phenotype (SASP)[3]. It can be triggered by DNA damage, telomere shortening and activation of transposable elements (TE). TEs are nucleic acid sequences that can move from one place to another in the genome, for example, Long Interspersed Element-1 (LINE-1) is the only active autonomous retrotransposon (constitutes 17% of the human genome) and its activity can cause mutagenesis, DNA damage and genomic instability[4]. The aim of this study was to determine if the LINE-1 element is found in lung senescent cells in an accelerated aging model. Methods: Zmpste24 deficient mouse was used as an accelerated aging model, which has a similar phenotype as Hutchinson-Gilford progeria syndrome. The aging phenotype is caused by a defect in the nuclear lamina and it is acquired gradually. Thus, at 4-weeks of age the knockout mouse is identical to the wild-type mouse, while at 16 weeks a strong aged phenotype is established. Zmpste24 -/- mouse lung tissue and fibroblasts were isolated. Cellular senescence was assessed by SA β-galactosidase essays and by examining the expression of known marker p16 via Immunohistochemistry (IHC) and Immunofluorescence (IF). Markers p16 and p21 were also evaluated via qPCR. LINE-1 expression was assessed by IHC, IF and by qPCR. Additionally, LINE-1 protein was examined in mouse lung tissue and human IPF lung tissue by IHC. Results: As expected, we observed a significant increase in fibroblasts senescence in KO mice compared to their WT counterparts by β-galactosidase activity and p16. We found LINE-1 activity to be colocalized with β-galactosidase in Zmpste24 -/- mouse fibroblasts, suggesting a link between LINE-1 and cellular senescence. Remarkably, LINE-1 was also found to be activated in human IPF lung tissue. Conclusions: LINE-1 could be a novel marker of cellular senescence associated with age-related lung diseases.

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ASSOCIATION BETWEEN THE PROSTATE SPECIFIC ANTIGEN AND OTHERS BIOCHEMICAL PARAMETERS IN A MEXICAN POPULATION SAMPLE IN VERACRUZ

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Abstract:

In Mexico, prostate cancer has become one of the biggest public health problems, being the third leading cause of death after cardiovascular disease and diabetes. More than 60% of patients are asymptomatic and the diagnosis is established by the increase of prostate-specific antigen (PSA) concentrations, therefore, higher problem that arises is that 70% of cases are detected in advanced stages. Currently, there are several molecular markers for the detection of prostate cancer, however, these are expensive and not easily accessible. Studies by Ferron et al (2019) suggest that neutrophil, platelet, and eosinophil ratios to lymphocytes predict improved Gleason score in low-risk prostate cancer patients. With this antecedent, the question arises that other biochemical parameter could be altered by PSA increase. Objective: evaluate the relationship of biochemical parameters with prostate-specific antigen concentrations in the Omealca Veracruz population. Methods: A retrospective study was conducted by reviewing the log of a Private Laboratory in Omealca, Veracruz, for a year and a half. Criteria inclusion were subjects over 40 who attend the laboratory to perform PSA test among other laboratory studies. Blood biometrics results performed in a hematological analyzer were collected, as well as clinical chemistry analyses determined by spectrophotometric methods and PSA was quantified by an immunoenzymatic trial. Statistical analyses were made in Stata 17 software, having a statistical significance value of $p<0.05$. Results: During study period, 120 men attended to be realized the prostate-specific antigen, obtaining values from 0.11 to 49.2 ng/mL, where 15% (n=18) had high levels of PSA (mean 16 ± 15 ng/mL), that were associated with increases in eosinophils proportion ($p<0.05$). Linear regression analyses show a positive correlation of PSA levels with total protein ($r=0.57$ $p<0.05$), amylase ($r=0.78$ $p<0.01$) and lipase ($r=0.86$ $p<0.01$) serum concentrations. Conclusion: Eosinophil count, the total proteins, amylase, and lipase seric, could be useful in the assessment of prostate alterations, because inexpensive and easily available tests.

EXPERIMENTAL COLITIS IS ATTENUATED BY CARDIOPROTECTIVE DIET SUPPLEMENTATION THAT REDUCES OXIDATIVE STRESS, INFLAMMATION, AND MUCOSAL DAMAGE

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Abstract:

Inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD) are multifactorial, relapsing disorders of the gastrointestinal tract. However, the etiology is still poorly understood but involves altered immune responses, epithelial dysfunction, environmental factors, and nutrition. Recently, we have shown that the diet supplement corabion has cardioprotective effects due to reduction of oxidative stress and inflammation. Since oxidative stress and inflammation are also prominent risk factors in IBD, we speculated that corabion also has beneficial effects on experimental colitis. Colitis was induced in male mice by administration of 3.5% (w/v) dextran sulfate sodium (DSS) in drinking water for a period of 3 or 7 days with or without daily gavage feeding of corabion consisting of vitamin C, vitamin E, L-arginine, and eicosapentaenoic and docosahexaenoic acid. We found that corabion administration attenuated DSS-induced colon shortening, tissue damage, and disease activity index during the onset of colitis. Mechanistically, these effects could be explained by reduced neutrophil recruitment, oxidative stress, production of proinflammatory cytokines, and internalization of the junctional proteins ZO-1 and E-cadherin leading to less edema formation. Thus, corabion may be a useful diet supplement for the management of chronic inflammatory intestinal disorders such as IBD.

THE XANTHONE α-MANGOSTIN SYNERGICALLY ENHANCES TAMOXIFEN ANTIPROLIFERATIVE ACTIVITY IN ESTROGEN RECEPTOR POSITIVE BREAST CANCER CELLS

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Abstract:

Breast cancer is the most commonly occurring neoplasia in women worldwide. Tamoxifen, a selective estrogen receptor modulator, has been the traditional standard care to treat hormone receptor-positive breast cancer stages. However, this drug significantly enhances the risk of developing endometrial cancer, thromboembolic events, and neuropsychiatric effects, encouraging the development of effective drugs with lower side effects. The search for novel plant-derived anticancer compounds is being conducted to study their potential to enhance classical chemotherapy and targeted therapy. This approach aims to destroy tumor cells while sparing normal cells and reducing undesirable adverse effects. Herein, we aimed to evaluate whether α-mangostin, a natural antineoplastic compound from mangosteen fruit, could increase the anticancer effect of tamoxifen in the estrogen receptor-positive breast cancer cell lines MCF-7 and T-47D, allowing dose reduction. The sulforhodamine-B assay evaluated cell proliferation, inhibitory concentrations, and potency from dose-response curves, followed by analysis of their pharmacological interaction using the combination-index method and dose-reduction index. The results showed that each compound alone inhibited cell proliferation in a concentration-dependent manner; however, when tamoxifen and α-mangostin were used simultaneously, a synergistic antiproliferative effect was observed. The dose-reduction index indicated that this combination has the potential to decrease tamoxifen dosage in breast cancer cells. Hence, α-mangostin could be employed as an effective co-adjuvant for tamoxifen in treating estrogen receptor-positive breast cancer patients. Supported by CONACyT México, grant A1-S-10749 from LD.

EVALUATION OF TWO TRIAZASPIRANES AS INHIBITORS OF MIGRATION AND INVASION IN PROSTATE CANCER CELLS PC3

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Abstract:

Introduction: Cancer is a very important problem currently, because of the complexity of establishing an effective treatment. In 2020, according to the Globocan report, 19,292,789 new cases and 9,958,133 deaths were registered due to the disease (1). In present, cancer is considered as a heterogeneous disease, highly variable due to the constant change of its molecular components. It is important to elucidate the principles on which tumor progression/carcinogenesis develops, characterized by an increase in proliferation, induction of angiogenesis, as well as the generation of invasion and metastasis, among other characteristics (2). **Objective:** The purpose of this work is to evaluate the activity of two triazaspirans as inhibitors of migration and invasion processes in PC3 prostatic tumor epithelial cells, through a possible negative regulation of the FAK/Src signal transduction pathway, and a decrease in the secretion of MMP-2 and MMP-9. **Methodology:** A molecular docking analysis was performed using the Moe 2008.10 program. Using the proposed triazaspirans against the proteins of interest FAK and Src. The effect of triazaspirans on cancer migration and invasion was evaluated by scratch wound closure and matrigel-coated Boyden chamber assay, respectively. In addition, the Western Blot technique was used to quantify protein expression in p-FAK, p-Src, E-cadherin and N-cadherin proteins, besides the zymography technique to observe the secretion of MMP-2 and MMP-9. **Results:** The molecular docking showed interactions in regions of interest of the FAK and Src proteins, in the biological activity assays an inhibitory effect on cell migration and invasion was demonstrated, accompanied by decreased phosphorylation levels of p-FAK and p-Src. In addition, we observed a decrease in the secretion of MMP-2 and MMP-9 **Conclusions:** Triazaspiran-type molecules have important inhibitory effects on the mechanisms associated with metastasis in PC3 prostate tumor cells.

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GC/MS ANALYSIS, ANTIOXIDANT ACTIVITY, AND ANTIMICROBIAL EFFECT OF *PELARGONIUM PELTATUM* (GERANIACEAE)

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Abstract:

In recent years, the increase in antibiotic resistance demands searching for new compounds with antimicrobial activity. Phytochemicals found in plants offer an alternative to this problem. The genus Pelargonium contains several species; some have commercial use in traditional medicine such as *P. sinoides*, and others such as *P. peltatum* are little studied but have promising potential for various applications such as phytopharmaceuticals. In this work, we characterized the ethanolic freeze-dried extracts (FDEs) of five tissues (root, stem, leaf, and two types of flowers) and the ethyl acetate fractions from leaf (Lf-EtOAc) and flower (Fwr-EtOAc) of *P. peltatum* through the analysis by thin-layer chromatography (T.L.C.), gas chromatography coupled to mass spectrometry (GC-MS), phytochemicals quantification, antioxidant capacity, and antimicrobial activity. After the first round of analysis, it was observed that the FDE-Leaf and FDE-Flower showed higher antioxidant and antimicrobial activities compared to the other FDEs, for which FDE-Leaf and FDE-Flower were fractionated and analyzed in a second round. The antioxidant activity determined by ABTS showed that Lf-EtOAc and Fwr-EtOAc had the lowest IC50 values with 27.15 ± 1.04 and 28.11 ± 1.3 µg/mL, respectively. The content of total polyphenols was 264.57 ± 7.73 for Lf-EtOAc and 105.39 ± 4.04 mg G.A./g FDE for Fwr-EtOAc. Regarding the content of flavonoid, Lf-EtOAc and Fw-EtOAc had the highest concentration with 34.4 ± 1.06 and 29.45 ± 1.09 mg Q.E./g FDE. In addition, the minimum inhibitory concentration (M.I.C.) of antimicrobial activity was evaluated: Lf-EtOAc and Fwr-EtOAc were effective at 31.2 µg/mL for Staphylococcus aureus and 62.5 µg/mL for *Salmonella enterica*, while for the *Enterococcus feacalis* strain, Fwr-EtOAc presented 31.2 µg/mL of M.I.C. According to the GC-MS analysis, the main compounds were 1,2,3-Benzenetriol (Pyrogallol), with 77.38% of relative abundance in the Lf-EtOAc and 71.24% in the Fwr-EtOAc, followed by ethyl gallate (13.10%) in the Fwr-EtOAc and (*Z*)-9-Octadecenamide (13.63% and 6.75%) in both Lf-EtOAc and Fwr-EtOAc, respectively.

ROLE OF TAURINE AS A PREVENTIVE COMPONENT IN VASCULAR COGNITIVE IMPAIRMENT

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Abstract:

Vascular Dementia (VD) or Vascular Cognitive Impairment (VCI) has been described as a clinical syndrome derived from cardiovascular risk factors with alterations in at least one cognitive domain. This pathology is the second most common dementia, representing 15% of the cases of dementia diagnosed annually. In Mexico, an incidence of 16.9 per 1000 people/year is reported for the urban region and 34.2 per 1,000 people/year for the rural area, with an average of 25.55 per 1,000 people per year, showing a prevalence of 7.9%. The current diagnosis is made at the late stage of the disease since the presence of the clinical picture is necessary. For this reason, the need arises to seek methodologies that allow the timely screening. Precision medicine suggests using single nucleotide polymorphisms (SNPs) derived from genome-wide association studies (GWAS) to identify risk *loci* in disease pathogenesis. Concerning food, it has been described that nourishment and dietary patterns play a significant role in the development or prevention of different nosological entities. Macarro, et al., propose the intake of citrus fruits such as oranges and olive leaves due to a low intake of acidogenic foods (meat, fish, cheese, rice, and cereals) and a high intake of alkaline foods such as fruits, vegetables, and legumes for the reduction of cardiometabolic disorders. In this way, it has been suggested that the bioactive compounds present in the Mexican diet may play a crucial role in the prevention of vascular dementia. However, there is no record to date of how bioactive compounds participate in the pathogenesis of vascular cognitive decline. For this reason, this project aimed to identify the role of bioactive compounds in the pathogenesis of vascular dementia. The following methodology was used to accomplish the aim. Through the Automated Variant Selection algorithm (SVA)$_{(1)}$ the SNPs present in GWAS for VD were identified, as well as the associated genes. Next, the metabolic pathways related to the genes were evaluated, based on the information deposited in the Reactome database. With these data, the SNP-FS$_{(2)}$ algorithm was used to determine the bioactive compounds and their health effects associated with the identified SNPs. Finally, based on the Nutri_plot$_{(3)}$ algorithm, we observed the frequency with which the Mexican population consumes foods that present the identified bioactive compounds. The results found detail the participation of taurine in vasodilation processes, LDL reduction, and cholesterol mobilization. As well as metabolic pathways Presynaptic depolarization and calcium channel opening. These are key processes in the pathogenesis of vascular dementia. Therefore, it is suggested that taurine may have a modulating effect on the pathogenesis of vascular dementia.

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ABSTRACTS | Posters Microbiology & Virology

XXXIII National Congress of Biochemistry

INDUCIBLE PROPHAGES IN THE GENOMES OF *STAPHYLOCOCCUS AUREUS*

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Abstract:

Phages have an important role in microbial biology. The presence of prophages is associated with genes encoding for virulence factors and resistance to antibiotics. Here, we investigate the frequency of prophages in *Staphylococcus aureus* (Sa) and their relationship with methicillin-resistant *S. aureus* (MRSA), biofilm formation, and their clinical origin. We obtained a collection of 180 Sa (MRSA and MSSA) from four third-level health units in Mexico City. A total of 16 out of 180 Sa strains showed an inducible prophage after treating all strains with mitomycin C treatment. Additionally, these inducible phages presented a narrow host range of infections on a selected set of 40 Sa strains. However, bioinformatic prediction of prophages from 100 Sa strain sequences in the collection revealed that 107 of 452 (23.67%) were complete prophages. These results indicate that even though the completeness of the prophage identified by the prediction, only a minor set of Sa prophages are still active.

To know if the Sa active prophages obtained in this work belong to a specific Sa Clonal Complex (CC) and are worldwide distributed, we downloaded 993 complete Sa genomes from the GenBank. They belong to different CC´s and countries. Prophage predictions were performed for all the Sa from the GB, and high-quality predictions were used for genomic comparison. From the predicted high and medium quality prophages, a viral classification based on protein clusters was performed using vConTACT. This analysis showed that our Sa predicted, and inducible prophage genomes are mainly within a large international group of prophages. This analysis showed that our predicted and inducible Sa prophage genomes fall into 31 clusters, which are within a large international group of prophages.

THE ROLE OF PHOSPHATE AVAILABILITY ON PLANT GROWTH PROMOTION BY THE PROBIOTIC BACTERIUM ACHROMOBACTER SP. 5B1

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Abstract:

Achromobacter sp. 5B1 is a bacterial strain isolated from *Prosopis* sp. (mezquite) rhizosphere that grows in a saline environment with the property of improving growth and productivity of *Arabidopsis* seedlings. Root inoculation with the bacterium enhanced both the auxin response and transport within the root tip and caused an agravitropic behavior and the formation of turns and coils that primes pericycle cells to develop more lateral root primordia[1]. Here, we investigated the contribution of phosphate nutrition in plant biomass production and changes in root system architecture in Arabidopsis WT seedlings and in mutants related to low phosphate (Pi) sensing *smb3*, *almt1* and *stop1.* Application of increasing concentrations of Pi increased the root and shoot biomass production by the bacterium, which correlated with massive formation of new root branches with more absorptive potential, and this response was disturbed in the low Pi-related mutants. Compared to wild-type plants, *smb3*, *almt1* and *stop1* mutants had reduced primary root deviation from the gravity vector and diminished coil formation, which impacts in the overall root branching process. Our results indicate the dependence of phosphate nutrition and signaling by *Achromobacter* sp. 5B1 to influence directional root growth, a trait that contributes to development and adaptation to the environment.

Keywords: Rhizobacteria, root architecture, biomass distribution, phosphate.

STUDYING TYROSINE PHOSPHORYLATION IN ISC PATHWAY PROTEINS

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Abstract:

Protein tyrosine phosphorylation is an important post-translational modification (PTM) that enables cell adaptation to environment changing conditions. In bacteria, this dynamic and reversible PTM is mainly achieved by the concerted activity of bacterial tyrosine kinases (BY-kinases) and tyrosine phosphatases (PTP). In Proteobacteria, most PTP belong to the low molecular weight (LMW)-PTP family. During the last two decades bacterial tyrosine phosphorylation has gained attention, as it has been implicated in stress responses, DNA metabolism, cell division, pathogenesis, transcriptional regulation and exopolysaccharides (EPS) synthesis. Accordingly, most BY-kinases and LMW-PTP encoding genes are located in operons directing EPS metabolism. However, we have noticed the prevalence of a LMW-PTP encoded next to the ISC operon across all members of the order *Burkholderiales*. Products of ISC operon are responsible for the synthesis and assembly of the iron-sulfur (Fe-S) clusters, ubiquitous cofactors required for crucial biological processes including respiration and photosynthesis. By using as a model the opportunistic pathogen *Burkholderia cenocepacia* and the LMW-PTP associated to the ISC system, BPtpA, here we evaluated tyrosine phosphorylation by focusing in the scaffold protein IscU and the chaperone HscA. Tyrosine phosphorylation was assessed through Western blot and mass spectrometry. Protein-protein interaction between BPtpA and ISC proteins was evaluated by bacterial two hybrid and pull-down assays. Current efforts are under way to determinate if BPtpA can achieve dephosphorylation of IscU and HscA proteins.

CHARACTERIZATION OF THE PRESENCE AND ACTIVITY OF EFFLUX PUMPS SYSTEMS IN PSEUDOMONAS AERUGINOSA MULTIDRUG RESISTANCE STRAINS AND IDENTIFICATION OF PUTATIVE INHIBITOR COMPOUNDS

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Abstract:

Bacterial infections represent an important cause of morbidity and mortality worldwide, especially in hospitalized patients or with pathologies that compromise their immune system.

Among the multiple resistance mechanisms of *P. aeruginosa*, there are activated efflux pumps systems which respond to extracellular stress and provide resistance to antibiotics. Common adaptations leading to regulation of efflux pumps causing overexpression are found in many multidrug resistance strains.

Therefore, the present work focuses on the identification and characterization of the different systems pumps activated and the implementation of a phenotypic method to identify activity of the main efflux pumps with ethidium bromide as a potential substrate.

Population to study: The clinical isolate strains (10) used in the following project were provided by the Instituto Nacional de Rehabilitación (INR) and come from burn patients in the intensive care unit, as well as other hospital wards, as well as mutant strains for the pyoverdine production system (*ΔpvdS, ΔpvdR*) and for the main efflux pump system (*ΔmexA, ΔnalD*).

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POSSIBLE PARTICIPATION OF DIFFERENT TRANSPORT SYSTEMS FOR THE TRANSLOCATION TO THE NUCLEUS OF TWO ISOFORMS OF FIBRILLARINS IN THE PARASITE *TRYPANOSOMA CRUZI*

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Abstract:

Ribosomal biogenesis and nuclear import of proteins are fundamental processes in eukaryotes. These processes have been mostly studied in model organisms such as yeast and mammalian cells. Our group conducts research focused on ribosomal biogenesis and nucleolar dynamics in *Trypanosoma cruzi*. This microorganism is a protozoan of the Trypanosomatida order, its medical importance is due to the fact that it is the etiological agent of Chagas disease.

Fibrillarin is an essential subunit of ribonucleoprotein complexes that guide and catalyze the methylation of specific residues in rRNA precursors. These events occur during ribosome biogenesis and occur universally in the nucleolus of eukaryotic organisms. For about 7 years we have been interested in the fibrillarin biology of *T. cruzi*. We know that in this organism fibrillarin is represented by two isoforms, with 69% identity and 80% similarity, in an apparently redundant molecular system (TcFib 1 and TcFib 2). Both proteins are expressed as nucleolar proteins. It is of our interest to investigate whether there is any domain in the fibrillarins of *T. cruzi* that could function as a nuclear localization signal in this important pathogen. For this reason, we began the analysis of the intracellular localization of both *T. cruzi* fibrillarin isoforms, expressed in transgenic lines as fluorescent chimeras (fusions with EGFP). The analysis of serial deletions in this experimental system showed us that the two fibrillarin isoforms have a differential dependence on the presence of their amino terminal formed by a region rich in glycine and arginine residues, GAR region. That is, TcFib 1, unlike TcFib 2, does not require this amino-terminal region for its import into the nucleus, suggesting that there are two molecular pathways of import. There is then the possibility that the two fibrillarins are differentially translocated in different physiological conditions to the nucleus of *T. cruzi*; situation that would imply that the TcFib1 and TcFib2 molecular system is not entirely redundant. Preliminary data from cell treated with ivermectin suggest that the classical importin alpha and importin beta pathway is not involved in the nuclear transport of these proteins.

MOLECULAR BASIS OF ENHANCED PROTEASE ACTIVITY OF *SERRATIA MARCESCENS* HU1848

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Abstract:

Serratia marcescens is a ubiquitous microorganism from order *Enterobacterales*. During last decades this bacterium has gained attention as an emerging pathogen associated with different clinical conditions. Cytotoxic capabilities of *S. marcescens* have been mostly attributed to its proteolytic activity. And, depending on the *Serratia* isolate, up to five serralysin family proteases can be encoded within genome. Here, we evaluate the protease production of two multi-drug resistant *S. marcescens* strains (HU1848 and SmUNAM836), isolated from bronchial expectorations at two Mexican health care institutions. A higher proteolytic activity, as well as related phenotypes, were determined in strain HU1848. Zymography analysis indicated the presence of at least two and three proteases in supernatants of HU1848 and SmUNAM836, respectively. Proteases PrtS and SlpD were identified by mass spectrometry from supernatant samples. Moreover, quantitative PCR revealed higher transcript levels of the transcriptional regulator *eepR* in HU1848 related to SmUNAM836. Several nucleotide substitutions were noticed in the *eepR* promoter of HU1848. By electrophoretic mobility-shift assays we are comparing the DNA binding capabilities of the repressors, CRP and HexS for the *eepR* promoter of both strains. Overall, our study brings clarification to the hyper-proteolytic phenotype of HU1848 strain and to the *eepR* repressors binding sites, also anticipates the use of such DNA region as a feasible predictor of high levels of proteases and other secondary metabolites in related *S. marcescens* strains.

IN SILICO AND IN VITRO CHARACTERIZATION OF THE ORF1 ENCODED PROTEIN FROM THE PAPAYA UMBRA-LIKE VIRUS PMEV-MX

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Abstract:

Papaya Meleira or "sticky" disease was reported for the first time in Brazil in 1989, it is proposed to be caused by the double infection of a dsRNA virus related to totiviruses called Papaya meleira virus (PMeV) and virus of ssRNA genome phylogenetically to umbraviruses, called PMeV2. In 2012, we identified a new virus which shares 60 % nucleotide identity with PMeV2, in papaya plants exhibiting meleira symptoms at the Yucatan Peninsula. In 2015, a third umbra-like virus was reported in papaya plants from Ecuador, associated to the Papaya ring spot virus. The genomic organization of these viruses consists of two open reading frames (ORF1 and ORF2) and a long non-coding RNA. ORF2 encodes an RNA-dependent RNA polymerase (RdRP) with 42% identity to the RdRPs of umbraviruses, while ORF1 encodes a protein of unknown function. In order to gain knowledge on P-ORF1 function, in the present work P-ORF1 was characterized using bioinformatic and experimental approaches. In-silico analysis suggest that this protein is a new class of viral movement protein, sharing some signatures with the well-described umbravirus movement protein P-ORF3, such as: nuclear localization signal, RNA binding, transmembrane trend with no prevalence of integration to the plasma membrane, and an intrinsically disordered region associated with transient interaction with multiple molecules. Advances in the expression and purification of the recombinant protein in E. coli and assays to corroborate the information obtained under in-silico analysis will be presented at the meeting.

MANGANESE METALLOSTASIS IN STENOTROPHOMONAS MALTOPHILIA AND ITS IMPACT ON VIRULENCE AND INTRACELLULAR SURVIVAL IN PHAGOCYTIC CELLS

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Abstract:

The objective of this research project is to identify genes underlying the manganese (MnII) homeostasis in Stenotrophomonas maltophilia and reveal their roles in virulence using Gallleria mellonella larvae as an alternative host, and its impact on intracellular survival in the free-living amoeba Acanthamoeba castellanii, a professional phagocyte.

Transition metals, such as (MnII), are trace elements required by all types of living organisms as structural and catalytic cofactors for numerous proteins. They play also key roles in electron transport, due to their redox potential1. In recent years, compelling evidence has accumulated on the central role of transition metals in virulence2. Professional phagocytes of the innate immune system of vertebrates subject invading microbes to nutritional stress of Fe and Mn, severely limiting their availability in tissues and in macrophage phagosomes and poisoning phagocytosed microbes with excess Zn and Cu3. These defense mechanisms are ancient, being present even in free-living unicellular phagocytes such as the social amoeba Dictyostellium discoideum4. Regarding S. maltophilia, there are only a few studies on the in vitro physiological adaptation to Fe deficiency or excess and the formation of biofilms5,6. In the present proposal we study the metallostasis of Mn(II) that, in addition of the catalytic and structural functions mentioned above, is particularly important in containing oxidative stress7. Using comparative genomics and bioinformatic approaches, we identified a likely mini MntR-regulon conserved in S. maltophilia, consisting of the metalloregulator MntR, the MntH importer and MntP exporter. Plasmids expressing transcriptional fusions to GFP demonstrate that mntH and mntP are down- and upregulated, respectively, at increasing Mn concentrations. An mntP deletion mutant has shown Mn sensibility in vitro and displays attenuated virulence in G. mellonella and the mntP::GFP fusion has shown to be expressed in A. castellanii phagosomes by fluorescence microscopy.

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ANTIVIRAL EFFECT OF METABOLITES FROM *LACTOBACILLUS RHAMNOSUS* AND *CHLORELLA SOROKINIANA* IN CELLS INFECTED WITH ROTAVIRUS

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Abstract:

The probiotic *Lactobacillus rhamnosus* has been related to the prevention and treatment of diseases caused by rotavirus, because it participates in the stimulation of the host's immune system. Additionally, the protective potential of probiotics can be increased by incorporating substances called prebiotics, such as the microalgae *Chlorella sorokiniana*. In the present work, the antiviral effect of the metabolites of the probiotic *L. rhamnosus* and the prebiotic *C. sorokiniana* was evaluated in HT-29 cells infected with rotavirus Wa at the level of INF-alpha expression. HT-29 cells were infected with rotavirus Wa (MOI 0.01) and subsequently treated with metabolites from *L. rhamnosus* and/or *C. sorokiniana*, mRNA extraction was performed, followed by cDNA synthesis and amplification of INF-alpha by quantitative PCR. The results indicated that in cells infected with rotavirus and treated with *C. sorokiniana* the percentage of infectivity was reduced to 5%, while in HT-29 cells treated with *L. rhamnosus* the viral titer decreased to 20%, while in the combination of both, the percentage of infectivity dropped to 2%. Likewise, an increase in INF-alpha was observed in HT-29 cells treated with *C. sorokiniana* (1.8 times) and *L. rhamnosus* (5.26 times). The combination of prebiotic and probiotic showed an elevated expression of INF-alpha 77.11 times higher. In conclusion, the combination of *C. sorokiniana* and *L. rhamnosus* induces the activation of the cellular antiviral response, which makes it possible to reduce the cytopathic effect caused by rotavirus.

EVALUATION OF THE ANTIMICROBIAL EFFECT OF *THYMUS VULGARIS* EXTRACT AGAINST *STAPHYLOCOCCUS EPIDERMIDIS* AND *STAPHYLOCOCCUS AUREUS*

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Abstract:

Thymus vulgaris, commonly known as thyme, is an aromatic plant of dry soil, native to the Western Mediterranean countries, widely used in the culinary field. In the 19th century, when antibiotics were not yet discovered, thyme was considered an effective disinfectant. The leaves of the plant have multiple properties, including anti-inflammatory, spasmolytic, antifungal, antiviral, antioxidant, and a significant antibacterial effect, both for Gram-positive and Gram-negative bacteria. Currently, the use of natural products has been considered an alternative to reduce the use of antibiotics to treat mild and moderate ailments. In this project we worked with two Gram-positive bacteria present in the skin microbiota and easily propagated: *Staphylococcus epidermidis* ATCC 12228 and *Staphylococcus aureus* ATCC 25923. The extracts of T. vulgaris were obtained by the reflux method, using two different solvents (water and 96% ethanol), obtaining a final concentration of 1g/ml for both types of extracts. The evaluation of the antimicrobial capacity of the extracts was done by disc sensitivity tests, using the Kirby Bauer method. The results obtained show an inhibition halo of 21 and 16 mm for *S. epidermidis* with the aqueous and ethanolic extracts, respectively. On the other hand, an inhibition halo of 19 and 14 mm was observed for *S. aureus* with the aqueous and ethanolic extract, respectively. This demonstrates the antibiotic property of both extracts; however, the aqueous extract presented a greater antibacterial activity for the microorganisms tested; being considered a good alternative for the treatment of ailments caused by these microorganisms.

STUDY ON THE REGULATION OF DEPOLYMERIZATION OF THE BIODEGRADABLE BIOPLASTIC POLYHYDROXYBUTYRATE (PHB) IN AZOTOBACTER VINELANDII

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Abstract:

Polyhydroxyalkanoates (PHA) are polyesters produced by various archaea and bacteria as reserve of carbon, energy and reducing power. These polymers are intracellularly accumulated under conditions of carbon source excess with limitation of nitrogen, phosphorous or oxygen, and are mobilized (utilized) when the carbon source is scarce. The importance of these compounds in industry is that they can be used to manufacture biodegradable plastics to replace petroleum-based plastics. A. vinelandii is a bacterium capable of producing high amounts of polyhydroxybutyrate (PHB), the most common PHA, and its synthesis starts from two molecules of acetyl-CoA, through three enzymatic steps catalyzed by β-ketothiolase, acetoacetyl-CoA reductase and PHB synthase, encoded by the phbA, phbB and phbC genes, respectively. PHB mobilization (degradation) is carried out by the enzymes PHB depolymerase, hydroxybutyrate dehydrogenase, succinyl-CoA transferase and, again, β-ketothiolase. Although these two processes occur simultaneously, giving rise to a synthesis/mobilization cycle, some mechanism is needed to control the balance of this cycle, thus favoring synthesis or degradation, depending on the metabolic conditions. Some regulators of the PHB biosynthetic genes are known in A. vinelandii but nothing is known about the control of PHB degradation.

In this work, we show that the A. vinelandii protein PhbF is one of the regulators involved in biosynthesis process, acting as repressor of the expression of phbP1 gene, that encodes a phasin, a granule-associated protein that affects the size and number of granules. PhbF regulates phbP1 by binding to a site on the phbP1 promoter. A similar binding site is found in the intergenic region shared by phbZ1 gene, that encodes a PHB depolymerase, and the phasin gene phbP2 (probably involved in biosynthesis). The participation of PhbF regulator in the control of mobilization process was demonstrated by the analysis of phbZ1 gene expression in both wild type and phbF- strains through qRT-PCR and phbZ1-gusA transcriptional fusions. An increase in phbZ1 expression was observed in the phbF mutant, and the analysis of its PHB accumulation phenotype showed a decrease of polymer accumulation with respect to the wild type. The results show that PhbF is a negative regulator of both phasine protein expression and PHB depolymerization in this bacterium.

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STUDY OF THE MECHANISM OF CONTROL OF C-5 ALGINATE EPIMERASES BY THE SECOND MESSENGER C-DI-GMP: CHARACTERIZATION OF FLEQ AS THE PUTATIVE INTERMEDIATE

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Abstract:

A. vinelandii is a free-living, Gram-negative bacterium. It produces the linear polysaccharide alginate, composed of mannuronic (M) and guluronic (G) residues. The proportion and distribution of these residues determine its physicochemical traits. Higher G content favors the gelling properties of the polymer. When environmental conditions are adverse, *A. vinelandii* undergoes a process of cell differentiation for the formation of desiccation-resistant cysts. The central body of the cyst is covered by a cell envelope, containing alginates with a high proportion of G residues, which are essential for desiccation resistance. The G residues of the polymer is derived from the activity of extracellular C-5 epimerases, AlgE1-6 (1), catalyzing the conversion of M to G residues. Previous work in our laboratory demonstrated that the second messenger c-di-GMP exerts a positive effect on the transcription of *algE1-6* genes. Reduced levels of this second messenger abrogated *algE1-6* mRNA accumulation and impaired the formation of desiccation-resistance cysts (2).

FleQ is a c-di-GMP effector acting as a repressor or activator of its target genes, depending on the intracellular concentrations of c-di-GMP. Bioinformatic analysis suggested that FleQ might be the intermediary in the regulation of *algE1-6* by c-di-GMP, as potential FleQ binding sites were identified in the promoter regions of these genes; this constitutes the central question of the present study. The positive effect of c-di-GMP on *algE1-6* expression was confirmed by Western Blot assay as in the presence of artificially reduced levels of c-di-GMP the extracellular AlgE1-6 proteins were not detected. Results of a transcriptomic analysis (RNAseq) of the *fleQ*$^-$ mutant suggested that this regulator acts as a repressor of *algE1-6* transcription, as the mRNA levels of *algE4* and *algE6* were higher in the absence of FleQ. This negative effect is investigated by using *gusA* transcriptional fusions and qPCR analysis. The existence of alternative regulatory pathways for the control of *algE1-6* by c-di-GMP is currently being explored.

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IDENTIFICATION OF BIOSYNTHETIC GENE CLUSTERS IN *ACINETOBACTER PITTII* STRAINS WITH POSSIBLE ANTIFUNGAL ACTIVITY AGAINST *BATRACHOCHYTRIUM DENDROBATIDIS* AND *BOTRYTIS CINEREA*

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Abstract:

INTRODUCTION: Biocontrol has been focused on the study and use of microorganisms uniquely isolated from animals or the affected plant to manage pests and diseases, this is why we are looking for compounds against Chytridiomycosis, a lethal fungal disease caused by *Batrachochytrium dendrobatidis* (Bd), responsible for many of the recent population declines and extinctions of amphibians all over the world and against *Botrytis cinerea* (gray mold) is one of the most widespread and destructive fungal diseases of horticultural crops. **OBJECTIVE:** To determine the chemical nature of antifungal compounds against the fungi Bd and *B. cinerea* produced by strains of *A. pittii* isolated from amphibians and clinical samples, and to identify the genetic differences between strains producing and not producing these compounds. **MATERIAL AND METHODS:** 2 *A. pittii* strains were isolated from the skin of neotropical amphibians from Panama and 8 clinical strains were selected and tested against Bd and *B. cinerea*. Genomes were sequenced with the DNABseq platform, BGI, and MinION (Oxford, Nanopore), and genome comparison was performed with Roary. Biosynthetic clusters were identified with AntiSMASH and BigScape. **RESULTS:** Amphibian strains showed to inhibit or retard the growth of both fungi better than clinical strains, comparative genomics yielded that amphibian strains possess 308 unique genes that were not found in clinical strains, of which 243 encode for hypothetical proteins and 65 that are assigned a function. 12 biosynthetic clusters were detected among the 10 *A.pittii* strains, highlighting those that are NRPS/hserlactone, Arylpolyene, RiPP-like, Tropodithietic-acid, Betalactone, Redox-cofactor, Siderophore, RRE-containing, Hserlactone, NRPS-like. Almost all BGCs showed similarities corresponding to predicted compounds with possible antimicrobial activity, the amphibian strains possess a cluster encoding an arylpolyene that was not found in the clinical strains, however, there is not enough *in silico* information indicating the type of compound being produced, is interesting to know more about this cluster and the metabolic pathways in which it participates. Interestingly, the amphibian cluster showed similarity to a cluster predicted with AntiSmash in an *A. pittii* strain isolated from fish. **CONCLUSION:** Amphibian strains of *A. pittii* play an important role in protecting against their pathogens but can also retard the growth of other plant pathogens, and it is shown that the gene content of the bacterium can be modified depending on the environment in which it is found.

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CYSTATIN C: ANTIMICROBIAL AND IMMUNOREGULATOR ROLE IN MACROPHAGE INFECTED WITH *P. GINGIVALIS*

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Abstract:

Background: Periodontitis is a chronic infectious disease, characterized by an exacerbated inflammatory response and progressive loss of supporting tissues. *P. gingivalis* is a key etiological agent in periodontitis. The macrophages population accounts for 5 to 30% of the inflammatory infiltrate of patients with periodontitis**.** Monocytes localized in the inflammatory infiltrate could be differentiated into M1 macrophages, which induce inflammatory mediators such as IL-1β, IL-6, IL-8, TNF-α, and the inducible nitric oxide synthase enzyme (iNOS), amplifying the inflammatory response. Furthermore, IL-1β and TNF-α increase the expression of matrix metalloproteinases (MMPs), and active osteoclasts which are essential for bone destruction.

Cystatin C an antimicrobial peptide with immunoregulatory activity participates in decreasing cytokine production such as IL-1β and TNF-α and induces macrophage polarization to M2 phenotype, which favors anti-inflammatory cytokine production such as IL-10. The aim of this study was to assess the effect of Cystatin C on the production of inflammatory and anti-inflammatory cytokines, the release of ROS and NO, and cell apoptosis induced by *P. gingivalis* in infected macrophages.

Design: Macrophages were obtained from peripheral blood monocytes. Cells were infected with *P. gingivalis* (MOI:1:100) for 3 h and subsequently stimulated with Cystatin C (2.5 µg/ml) for 24 h. The intracellular localization of *P. gingivalis* and Cystatin C by immunofluorescence and immuno-gold-TEM, was evaluated. The intracellular antimicrobial activity of Cystatin C in infected macrophages by counting Colony Forming Units (CFU), was determined. The production of TNF-α, IL-1β, and IL-10 by ELISA, was assessed. To determine the ROS production, cells were incubated with 2',7'-dichlorodihydrofluorescein diacetate (H2DCFDA). The concentration of nitrite in supernatants with the Griess reaction was assessed. Cell death by TUNEL, Annexin V, and caspase 3 was determined.

Results. Cystatin C is internalized in infected macrophages and localized in plasma membrane, cytoplasm, and nucleus. Furthermore, Cystatin C reduces the intracellular bacterial load of *P. gingivalis* on infected macrophages. A decrease in the production of pro-inflammatory mediators such as TNF-α, and IL-1β, and an increase in anti-inflammatory IL-10 cytokine and ROS production were also observed., whereas

downregulation of NO in macrophages, was detected. Interestingly, Cystatin C decreases cell death in infected macrophages.

Conclusions. Cystatin C is internalized by infected macrophages and exerts antimicrobial and immunoregulatory activity, observed by the inhibition of *P. gingivalis* intracellular growth, a decrease of inflammatory cytokines, and NO. It also favors an anti-inflammatory response through the production of IL-10 and the inhibition of cell apoptosis. These findings highlighted the importance of understanding Cystatin C properties.

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PRESENCE AND QUANTIFICATION OF CEPHALEXIN (*CTX*), SULFAMETHOXAZOLE (*SUL1*) RESISTANCE GENES, AND HYDROCARBON DEGRADATION RELATED GENE (*ALKB*) ON THE COAST OF BAJA CALIFORNIA

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Abstract:

Nowadays, ocean pollution is a worldwide relevant topic due to its high impact on the environment. Some pollutants immediately affect the ecosystems, such as hydrocarbons, which are carcinogenic and toxic substances able to pass through the trophic chain. Other contaminants are the so-called “emergent”, whose poor regulation causes mid and long-term damage, resulting in catastrophic effects for both humans and nature. An example of these pollutants is antibiotics, that when released into the sea, cause bacteria to acquire antibiotic resistance genes (ARGs).

The coast of Baja California is a zone with high anthropogenic activities and untreated sewage released. Hydrocarbons (many of them listed as priority pollutants) and antibiotics (emergent pollutants) can harm the microbiota composition and the health of these sites. Functional marker genes can be used to monitor the health of coastal environments. Total DNA from 34 samples from marine sediments obtained along the coast of Baja California was analyzed by amplifying the functional molecular markers *CTX*, *sul1,* and *alkB* genes associated with cephalexin resistance, sulfamethoxazole resistance, and alkane biodegradation, respectively. The results showed that *sul1* and *CTX* amplicons were detected in 16 and 22 sampling areas, respectively. In contrast, *alkB* amplicons are associated with 14 sampling sites. The amplified genes’ location coincides with areas close to Wastewater treatment plants. qPCR analysis will also be added to corroborate and quantify the previously obtained results

The results allowed us to elucidate if there is a relationship between the marker genes analyzed and the areas with evidence of high anthropogenic activity.

ANALYSIS OF THE ANTIMICROBIAL ACTIVITY OF BACTERIA ISOLATED FROM NATIVE INSECTS OF MEXICO

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Abstract:

Currently, Antimicrobial Resistance (AMR) represents one of the most serious health problems for humanity. In 2019, there were an estimated 4.95 million deaths associated with and 1.27 million deaths attributable to antibiotics-resistant bacterial (Murray *et al.,* 2022). The World Health Organization (WHO) established a global action plan for the control of AMR, with a major objective being the development of new antibiotics and new antibacterial strategies (OMS, 2016). Different studies have reported that the microbiota of insects is a source with great potential for the identification of antimicrobials and other bioactive compounds. Bacteria from insects produce antimicrobial compounds that are not produced by the same species from soil or plants, which indicates a specialization of the bacteria from insects (Chevrette *et al.*, 2019). In this project we are evaluating the antibacterial activity of a collection of bacterial strains isolated from different native insects of Mexico, such as the maguey worm *Aegiale hesperiaris*, the cochineal *Dactylopius coccus* and the ant *Atta mexicana*. Interestingly, we have found distinct bacterial strains from the insects that inhibit the growth of pathogenic bacteria from the ESKAPE group: *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and/or *Staphylococcus aureus*. Therefore, our results show the potential of the Mexican biodiversity to identify new antibacterial compounds.

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BLACK YEASTS FROM DEEP-SEA SEDIMENTS OF THE GULF OF MEXICO: CELL GROWTH UNDER OLIGOTROPHIC AND HYPERSALINE CONDITIONS

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Abstract:

Black yeasts are among the most successful extremophiles and extreme-tolerant organisms. Some of them have been isolated from hypersaline aquatic environments, where NaCl concentrations range from 3 to 30%. Their slow growth, high melanin production, and unconventional cell division cycles are thought to confer them survival advantages. In this study we characterized morphogenesis of three black yeasts isolated from deep-sea sediments of the Gulf of Mexico (GoM) under salinity stress and oligotrophy. ITS and LSU regions sequencing allowed the identification of the strains as *Salinomyces thailandica* (*St*), *Neophaeotheca triangularis* (*Nt*), and *Neophaeotheca salicorniae* (*Ns*). Modified Czapek Dox medium amended with different concentrations of glucose, sea salts, NaCl, and melanin inhibitors was used for all assays. During the early 72 h of growth, *St* grew as yeasts with unilateral or bilateral budding as the main forms of cell division. Pseudohyphae appeared later in medium with £10% of NaCl. *Nt* and *Ns* produced muriform cells that developed endoconidia and pseudohyphae. *Nt* remained in a yeast-like state in medium without or low concentrations of NaCl, whereas in medium with £10% of NaCl, it made pseudohyphae, that produced endoconidia. In contrast, *Ns* produced pseudohyphae in all salt concentrations, but it developed faster in medium without salts and in non-oligotrophic medium. In general, growth división in the three species was faster in oligotrophic media. In addition, the melanin inhibitor phthalide induced changes in cell morphology, and inhibited the production of pseudohyphae and of extracellular polymeric substances. The results obtained indicate that the salinity, oligotrophy, and melanin are factors that influence cell growth, cell cycles, and morphology. This project demonstrates the plasticity of these species to adapt to different extreme conditions such as those found in the deep-sea sediments of the GoM.

ANTIBACTERIAL ACTIVITY OF SECRETED METABOLITES FROM A NOVEL ACTINOMYCETE ISOLATED FROM A MAYAN SINKHOLE

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Abstract:

Actinomycetes are fascinating microorganisms resembling fungi but keeping the genetic advantages and simplicity of bacteria. Many of them are well renown for their prolific capability to produce secondary metabolites with antibiotic activity[1]. Despite Actinomycetes are ubiquitous, the most studied and better characterized ones are isolated from soil. Therefore, a plethora a Actinomycetes from unexplored environments are still yet to be discovered. Sinkholes are not only captivating but indeed prolific ecosystems harboring microorganisms with different metabolic features than the terrestrial ones [2]. In this work, we focus on characterizing in terms of metabolite profile, antibacterial activity, and taxonomic assignation an actinomycete strain isolated from the Mayan sinkhole named "Pol-ac", located in Sisal, Yucatan. Sinkhole sediments were collected by scuba diving and employed to prepared serial dilution cultures in solid selective A1 marine media. After two weeks incubations, A single colony displaying actinomycete features was isolated from the rest of the grown microorganism and inoculated in A1 marine broth. After 14 days of incubation, the obtained supernatant was exhaustively extracted with ethyl acetate and rotaevaporated *in vacuo* until dryness. The obtained crude extract was tested for antibacterial activity, according to the M07-A10 document from the Clinical & Laboratory Standards Institute[3], resulting remarkably active against *Staphylococcus aureus* ATCC 25923 (Minimal Inhibitory Concentration = 200 µg/mL). The metabolite profile of the crude extract was analyzed using a HPLC Agilent 1260 II system equipped with a C18 column (Agilent Eclipse XDB-C18, 5 µm, 4.6 × 150 mm, Santa Clara, US), operated at isothermal conditions at 30ºC, at 0.8 mL min^{-1} flow and using an elution gradient. The results of the metabolic profile showed three main compounds, which can be possibly responsible for the antibiotic activity. For the taxonomic assignations of the actinomycete strain, the genomic DNA was isolated and employed as template for the amplification of the whole 16S rRNA gene and further sequencing. Results indicated that the isolated Actinomycete is a novel Streptomyces strain not previously annotated in the NCBI database.

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EVALUATION OF THE ANTIFUNGAL ACTIVITY OF COPPER (II) SULFATE PENTAHYDRATE ON MONILIOPHTHORA RORERI

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Abstract:

Copper (II) sulfate pentahydrate is a compound commonly used in the agricultural industry for its fungicidal (protective) action and is the main component of "Bordeaux mixture", a mixture used to treat the cocoa disease called "black spot or cocoa moniliasis" caused by infection with the fungus Moniliophthora roreri. The indiscriminate use of this "Bordeaux mixture" has increased copper concentrations in agricultural areas and there are regions that, due to "uses and customs", prepare it up to 10 times more concentrated than the recommended effective dose. In this context, it is necessary to determine whether the high proportions of copper sulfate used by farmers have their origin in phenomena related to antifungal resistance. The objective of this project is to evaluate the fungicidal effect of copper sulfate used in a cocoa-growing region of Comalcalco, Tabasco, and to determine if Moniliophthora roreri shows any degree of resistance with respect to the reported effective concentrations. The methodology included the collection of cocoa pods in a field comprising 2 ha located in Ranchería Miguel Hidalgo (18º16'06.2ºN 93º21'09.5ºW) in the municipality of Comalcalco, Tabasco. Specimens collected included those visibly infected by the fungus or with external symptoms of the disease and others without apparent damage. These specimens were collected, transported and stored in plastic bags at room temperature (31ºC). For the growth and isolation of Moniliophthora roreri, three nutrient media will be evaluated: potato dextrose agar, sabouraud agar and oat agar with exposure to different concentrations of copper sulfate and exposure times (7-15 days), all in constant incubation at 25ºC (±3ºC). Identification of the fungus will be made by optical and stereoscopic microscopy according to its macroscopic and microscopic characteristics in the presence of specific dyes such as lactophenol blue.

THE *THNRDE* OPERON FROM *B. THURINGIENSIS* PROVIDES IMMUNITY TO *LACTOCOCCUS LACTIS* AGAINST THURINCIN H

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Abstract:

Lactococcus lactis is a lactic acid bacterium of great importance for the food industry. Due to the GRAS status of *L. lactis*, systems have been designed for the expression of recombinant proteins of biotechnological interest. A peptide with biotechnological importance is the bacteriocin thurincin H, which has many favorable characteristics to be used as a bioconservative in food. It has been reported that it needs at least nine genes for its biosynthesis, within these the *thnRDE* genes provide immunity to the native producer strain. The objective of this work was to integrate these genes into the *L. lactis* strain to make it resistant to thurincin H and to be able to produce it in the future. To achieve this, the *thnRDE* genes were cloned into a vector for *L. lactis* and transformed into the sensitive strain. It was possible to obtain a strain of *L. lactis* resistant to thurincina H that can be used for its safe heterologous production.

EVALUATION AND CHARACTERIZATION OF NOVEL ANTIMICROBIALS AGAINST MULTIDRUG-RESISTANT *ACINETOBACTER BAUMANNII*

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Abstract:

Antimicrobial resistance (AR) poses a serious global threat of increasing concern to human, animal, and environmental health, due to the emergence, spread and persistence of multidrug-resistant (MDR) bacteria or "superbacteria" such as Acinetobacter baumannii. Due to its ability to rapidly develop resistance through intrinsic and acquired mechanisms, the treatments available to treat infections are increasingly limited. For this reason, it has been classified as an ESKAPE pathogen; carbapenem-resistant A. baumannii is considered by the World Health Organization as a number one critical priority pathogen for which new therapies are urgently required. In Mexico, studies reported that A. baumannii has a higher drug resistance compared to the worldwide average, which is alarming because almost there aren't therapeutic options available, and because a mortality rate of over 25% has been reported due to infections associated with this pathogen.

For all these reasons and to contribute to the growing understanding of drug resistance in Mexico, this project evaluated a wide range of compounds that have been discovered or synthesized at the Institute of Chemistry – UNAM, tested them against multiresistant Acinetobacter baumannii isolated recently from Mexico and analyzed their response to these possible novel antimicrobials. The antimicrobial evaluation was performed with the broth microdilution method according to the guidelines of the Clinical and Laboratory Standards Institute, and the activities were compared to clinically relevant drugs. In addition, the panel of Acinetobacter baumannii strains were characterized for their phenotypic profiles of resistance to clinically relevant drugs.

Considering the current lack of interest and resources dedicated to innovative antimicrobial discovery, the implementation of such high throughput assays complements other efforts (such as genomic data mining and structure-function relationship studies) to increase the chances for breakthrough findings and reduce the time and financial weight needed to walk the first steps towards innovation in the antimicrobial field.

SEROLOGICAL EVIDENCE OF PARAMYXOVIRUSES RELATED TO PORCINE ORTHORUBULAVIRUS IN MEXICAN BATS

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Abstract:

Over the past years, a number of zoonotic and vector-borne viral diseases have emerged in Southeast Asia and the Western Pacific, with fruit bats as a wildlife reservoir. Bats have been implicated in numerous new emerging infectious diseases, through its role as reservoirs for viruses with the ability to occasionally cross species barriers. One family of viruses with a particularly strong link to bats is *Paramyxoviridae*. Bats seem to be an ancient reservoir of many paramyxovirus taxa, and it is possible to find a variety of paramyxovirus lineages in most bat families. In America, retrospective analyses have shown the presence of two different paramyxoviruses from the genus *Orthorubulavirus*. In this report, we showed the presence of antibodies to *Porcine orthorubulavirus* (PRUV) in Mexican bats using a serological approach. A total of 42 bats, belonging to seven different species, were sampled from two different refuges/caves, located near to a pig fattening area where spontaneous outbreaks of PRUV had occurred. Analysis by serum-virus neutralizing and immunoperoxidase monolayer assay revealed the presence of antibodies in fifteen out of 42 investigated bats (i.e. 35%), six of them were also positive by *Paramyxoviridae* family using PCR assay targeting the L gene of paramyxoviruses. Three additional bat samples (two insectivorous and one haematophagus) were positive using a semi-nested PCR targeting the L gene of the *Paramyxovirinae* subfamily *Avulavirus-Rubulavirus* genus. One Sequence and phylogenetic analysis showed a genetic relationship between *Porcine orthorubulavirus* and bat paramyxovirus (GenBank MT636875–BatMxPUV). Infectious virus was not isolated from any samples. Antibody and antigen detection of this virus in different bats species is important for our understanding of PRUV ecology, evolution and mechanism of cross-species transmission. These findings support the hypothesis that bats could act as a reservoir for interspecies transmission of certain *paramyxoviruses*.

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NEMATICIDAL ACTIVITY FROM LIPOPEPTIDES PRODUCED BY *BACILLUS PARALICHENIFORMIS*

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Abstract:

Root-knot nematodes (mainly *Meloidogyne* genus) are plant parasites damaging roots of agricultural crops severely. As an alternative to synthetic chemical nematicides, the use of microorganisms and/or their metabolites are investigated[1]. For instance, species from *Bacillus* genus stands out, since they are natural antagonists against bacteria, fungi and nematodes[2]. Nowadays, there are already *Bacillus*-based nematicides on the market (*B. pumilus, B. subtilis,* among others). However, there is not an exhaustive characterization about *Bacillus* nematicidal metabolites, hindering the development and commercialization of *Bacillus*-based bionematicides[1,2]. Previous research suggests that cyclic lipopeptides (LPs), synthesized by *Bacillus* species are molecules that may be involved in the nematode control, since their antifungal and antibacterial activities have been demonstrated[3].

A native novel *B. paralicheniformis* strain, showed a high nematode control capacity, both *in vitro* and *in vivo* tests against *M. incognita*; although until now, LPs' involved in the nematicidal activity (NA) were unknown. Therefore, the objective of this work was to identify and characterize their active LPs through bioguided procedures, employing *Caernohabditis elegans* as model nematode. A crude lipopeptide extract (CLE) was obtained from *B. paralicheniformis* fermented broth, and its NA was estimated as median lethal dose (LD_{50}). The CLE components were fractionated by semi-preparative thin layer chromatography and the active LPs were characterized by electrospray ionization mass spectrometry (ESI-MS). The estimated LD_{50} was 3.8 mg/mL, observing that *B. paralicheniformis* synthesize several families of LPs such as: fengycin A (C_{14}-C_{17}), fengycin B (C_{16}-C_{17}), surfactin (C_{15}-C_{17}), and lichenysin (C_{12}, C_{13}, C_{14}, and C_{16}), being the most polar fraction containing fengycins, the most active too (100% larvae mortality). This is the first comprehensive study reporting LPs produced by *B. paralicheniformis*, the nematicidal activity from lichenysins, as well as the LPs' structure-function relationship.

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IN VITRO ANTAGONISM, EFFECT ON TOMATO PLANTS IN GREENHOUSE AND FUNCTIONAL GENOMIC ANALYSIS OF THE THERMOTOLERANT STRAIN *BACILLUS VELEZENSIS* AF12

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Abstract:

The increase in temperature and fungal infections reduce agricultural production, in addition, they threaten food security due to the projections of temperature increase in the next 50 years[1]. The indiscriminate application of fungicides is the most effective technique against phytopathogens, however, it causes environmental pollution. Bacterial bioinoculants are a promising alternative[2], particularly those that are thermotolerant and can act at high temperatures. In this research project, the thermotolerance and antagonism of 48 bacteria isolated from soils affected by underground fires were evaluated. The isolates were identified by sequencing the 16s rRNA gene, the genus *Bacillus* was predominant. The antagonistic activity by diffusible compounds was carried out against *Botrytis cinerea*, *Fusarium brachygibbosum, Geotrichum candidum* and *Botrytis* sp.. The AF12 strain showed the best ability to inhibit mycelial growth, with a 42%, 18%, 41%, 52%, respectively. Therefore, it was selected for plant assays and functional genomic analysis. Under greenhouse conditions, its effect on tomato plants inoculated with *F. oxysporum* was evaluated. The AF12 strain increased the fresh and dry weight of the stem. The genome of AF12 was sequenced, which consists of a 3.9 MB chromosome. It was taxonomically identified as *Bacillus velezensis* using the Average Nucleotide Identity (ANI) and Genome-to-Genome Distance Calculator (GGDC) algorithms with similarity values of 98.15% and 98.52%, respectively. A genomic scrutiny revealed that it possesses groups of genes with high similarity to those that code for antifungal compounds, such as fengycine. It also has genes involved in thermotolerance and production of indole acetic acid, siderophores and phosphate solubilization. These results suggest that *B. velezensis* AF12 is an excellent option as a biocontrol agent and plant growth promoter, because it presents various action mechanisms. However, it is unknown if AF12 maintains its antagonistic activity at higher temperatures and if it modifies its physiology as an adaptive response. Therefore, the antagonism, growth kinetics, membrane components and phospholipid synthesis at 28, 32, 35, 37, 45 and 50°C are being analyzed.

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DIVERSITY AND INCIDENCE OF ENDOFUNGAL BACTERIA ASSOCIATED WITH ARBUSCULAR MYCORRHIZAL FUNGI IN AGAVES AND CACTI GROWING IN NATIVE ARID SOIL

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Abstract:

Arbuscular mycorrhizal fungi (AMF) form mutualistic associations with the roots of 70-80% of all terrestrial plants, improving plant nutrition and alleviating biotic and abiotic stress. In recent years, the study of AMF and their endofungal bacteria (EB) has revealed two main symbiotic lineages: Betaproteobacteria (*Burkholderia*-related) and Mollicutes (*Mycoplasma*-related). However, diverse bacterial communities loosely or strictly associated with AMF spores have been reported. Studies from our research group have shed light into the composition and diversity of microbial communities associated with wild and cultivated agaves and cacti in arid and semiarid regions of Central and North America. Noteworthy, sequences of AMF were detected with low abundance (<1%) in all below-ground compartments of native agaves and cacti. In contrast, the cultivated *A. tequilana* was devoid of AMF. Here, we examined the colonization and taxonomic diversity of AMF associated with micro-propagated plants of *A. tequilana, A. salmiana,* and *M. geometrizans* growing in a native arid soil. Our experiments show that root colonization was greater in both agaves reaching 78% of colonization in 12 months, while being only 21% in *M. geometrizans*. Amplicon sequencing of the ITS2 region revealed 64 OTUs associated with AMF, being the genus *Ambispora* the most abundant. For the first time, we identified the presence of 502 bacterial OTUs associated with the spores of AMF from an arid soil. These findings suggest that AMF associated with agaves and cacti potentially harbor diverse bacterial communities that include members of the Mycoplasmatales, Rhizobiales and Pseudomonadales.

On-going research will reveal if novel and strict AMF-bacteria associations exist, and if these symbioses help plants to thrive in arid ecosystems.

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EFFECT OF OSMOTIC SHOCK ON THE PRODUCTION OF *K1* TOXIN FROM *SACCHAROMYCES CEREVISIAE*

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Abstract:

One of the phenotypes of the model organism Saccharomyces cerevisiae is the one called *Killer+* or *K1*. It is infected by dsRNA satellite viruses, which results in the production of a toxin capable of killing sensitive strains, called *K1*[1, 2]. Its structure, processing to mature protein and its molecular target, which has been called the potassium channel, TOK1[3], are currently known.

The binding of the toxin to this channel increases its probability of opening for a longer time, causing a large flow of ions out of the cell[1]. The Killer toxin (*K1*) is of great importance at the biomedical level, since it has been seen in different studies that it is not only capable of killing other species of yeast[4], but also multiple bacterial species with medical importance[5].

Recently, *S. cerevisiae* added one more advantage to its list. Previous studies have documented that it has the ability to modify its cell wall and regulate its volume by reducing it by up to 2/3 in response to an osmotic shock; whereas, if the cell is returned to an isotonic medium, it recovers its original volume and shape. This experiment gave the guideline to prove that aquaporins were participating in the process, because if the yeast lacks any of them (AQY1, AQY2), it is unable to regulate its volume[6,7].

This led us to generate an osmotic shock in toxin-producing strains, firstly, to verify that they maintain the capacity to regulate their volume and, secondly, to quantify the production of *K1* in response to an osmotic shock with the purpose of discovering new environmental conditions at which a greater or lesser production of toxin is obtained for said biomedical approach.

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CHARACTERIZATION OF THE VACUOLAR PROTEASES OF *C. AURIS* AND THEIR RELATIONSHIP WITH AUTOPHAGY

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Abstract:

C. auris is a multidrug-resistant pathogen, which has been linked to the healthcare-associated infections, being capable of causing fungemia mainly in immunocompromised patients with a fatality rate of 50%, registering approximately 400,000 cases per year. Moreover, molecular studies have allowed to classify *C. auris* based on its genetic information and geographic distribution in different clades. In México, the first case of invasive candidiasis due to *C. auris* on a Monterrey hospital was made public in 2020. That same year, different epidemiological organizations issued an epidemiological alert, describing the fungus as a public health problem. On the other hand, the vacuolar proteolytic system of yeasts plays a role in different physiological functions, including their virulence, morphogenesis, maintenance of homeostasis and turnover of senescent or non-functional organelles and proteins. Interestingly, all these processes have been associated to autophagy. This mechanism gives the cell the ability to survive on different microenvironments and stress inducers. This process is mediated by autophagy related genes (ATGs) involved in the formation of the autophagosome, which is degraded by vacuolar proteases for the subsequent reuse of monomeric and oligomeric structures. To study the vacuolar proteases of *C. auris* will allow to know the role of these enzymes in autophagy and other related processes. In this work, a search for the most likely putative vacuolar proteases genes in the *C. auris* genomes of two different strains, one from Spain (*C. auris* 49, Clade III) and the other form Mexico (*C. auris* 201498, Clade IV), was performed. Additionally, an *in silico* analysis of the primary, secondary and tertiary structure of the deduced proteins was performed. Specific activity was also determined by substrate affinity and inhibition profile of their enzyme extracts as well as the expression level of autophagy-related genes and vacuolar proteases by RT-qPCR at different stages of the growth curve. Finally, both enzyme activation and expression in non-proliferating media deficient in nitrogen and carbon sources were measured.

RSMA IS A CENTRAL REGULATOR OF PYOCYANIN SYNTHESIS AND ITS AUTO-PROTECTIVE RESPONSE IN *PSEUDOMONAS AERUGINOSA* ID4365, AN OVERPRODUCER STRAIN

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Abstract:

Pyocyanin is a phenazine with redox activity produced by *Pseudomonas aeruginosa* that is harmful to other bacteria and eukaryotic organisms by generating reactive oxygen species. Gene regulation of pyocyanin synthesis and its auto-protective response against pyocyanin has been addressed in the PAO1 and PA14 strains. Here, we determined how RsmA regulates pyocyanin synthesis in *P. aeruginosa* ID4365, an overproducer strain, and what is the protective response to avoid self-damage. We found that, in the PPGAS medium, *rsmA* inactivation increases pyocyanin production compared with the wild-type strains ID4365, PAO, and PA14. We showed that RsmA regulates inversely the expression of both *phz* operons involved in pyocyanin synthesis; particularly the *phz2* operon is positively regulated at the transcriptional level indirectly through MvaU. Also, RsmA negatively regulates *phzM* and *phzS* expression, which code for the accessory enzymes to produce pyocyanin. Furthermore, we showed that RsmA positively regulates the translation of the sigma factor RpoS, and the expression of *rpoS* under an independent promoter decreases pyocyanin production in the IDrsmA strain. Finally, we found that the levels of 512 proteins are affected in the *rsmA* mutant, and some of them are related to avoiding the self-damage produced by pyocyanin. These results indicate that RsmA is a master regulator of pyocyanin synthesis and also of its auto-protective response.

CURCUMIN INHIBITS THE SECRETION OF TYPE III EFFECTORS FROM PSEUDOMONAS AERUGINOSA

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Abstract:

Antibiotic resistance of bacterial pathogens is a worldwide critical health problem, great efforts are aimed toward addressing this problem to preventing and treating infections of multidrug resistant bacteria (MDR) by replacing the conventional approach of antibiotic use with anti-virulence therapies. Disrupt the production of virulence factors, bacterial adhesion to the target cell, biofilm formation and protein secretion systems involved in pathogenesis constitute the major strategic approach against MDR bacteria such as *P. aeruginosa*. The virulence factors in this pathogen are stringently regulated by Quorum Sensing (QS), which allows the bacteria reprogram gene expression accordingly its population density. The timing expression of virulence factors at high bacterial density enables the pathogen colonization and promoting the establishment of the infection. Hereby the Type III secretion system (T3SS) plays a key role in *Pseudomonas* pathogenesis since it is responsible for the injection of virulence proteins named effectors directly to the cytoplasm of the target cell.

Our research group is interested in the use of curcumin, a yellow pigment found in the roots of the edible plant Curcuma longa and widely used in the food and cosmetic industries, as an inhibitor of *P. aeruginosa* pathogenesis. Our data support that the most significant inhibitory effect of curcumin was observed on ExoS and ExoU secretion of T3SS from PA01, PA14 reference strains and four clinical isolates.

NITROGEN AVAILABILITY DETERMINES PLANT GROWTH PROMOTION AND THE INDUCTION OF ROOT BRANCHING BY THE PROBIOTIC FUNGUS *TRICHODERMA ATROVIRIDE* IN *ARABIDOPSIS* SEEDLINGS

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Abstract

Plant growth-promoting fungi are integral components of the root microbiome that help the host resist biotic and abiotic stress while improving nutrient acquisition. *Trichoderma atroviride* is a common inhabitant of the rhizosphere, which establishes a perdurable symbiosis with plants through the emission of volatiles, diffusible compounds, and robust colonization. Currently, little is known on how the environment influences the *Trichoderma*–plant interaction. In this report, we assessed plant growth and root architectural reconfiguration of *Arabidopsis* seedlings grown in physical contact with *T. atroviride* under contrasting nitrate and ammonium availability. The shoot and root biomass accumulation and lateral root formation triggered by the fungus required high nitrogen supplements and involved nitrate reduction via AtNIA1 and NIA2. Ammonium supplementation did not restore biomass production boosted by *T. atroviride* in *nia1nia2* double mutant, but instead fungal inoculation increased nitric oxide accumulation in *Arabidopsis* primary root tips depending upon nitrate supplements. N deprived seedlings were largely resistant to the effects of nitric oxide donor SNP triggering lateral root formation. *T. atroviride* enhanced expression of *CHL1:GUS* in root tips, particularly under high N supplements and required an intact CHL1 nitrate transporter to promote lateral root formation in *Arabidopsis* seedlings. These data imply that the developmental programs strengthened by *Trichoderma* and the underlying growth promotion in plants are dependent upon adequate nutrition and may involve nitric oxide as a second messenger.

RESISTANCE AGAINST INHIBITION OF QUORUM SENSING BY AUTOINDUCER DEGRADING ENZYMES

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Abstract:

Pseudomonas aeruginosa is a bacterium of clinical importance, it belongs to the ESKAPE, which has been defined by its clinical importance and high resistance to antibiotics[1]. It is associated with ventilator-associated pneumonia, surgical site infections, wound and burn infections. *P. aeruginosa* has an arsenal of virulence factors that allow it to colonize and cause infection in its host[2]. Among them, elastase (metalloprotease capable of destroying different proteins such as collagen, among others); alkaline protease (zinc-dependent metalloprotease that inhibits phagocytosis, among others)[3,4], and pyocyanin, which promotes oxidative stress, delays the inflammatory response due to damage to neutrophils[4]. These virulence factors are regulated by cell-cell communication, called quorum sensing (QS), which allows bacteria to estimate their population density and activate virulence when a high density has been reached[5].

P. aeruginosa has three mechanisms of QS systems, two of them mediated by signals such as N-acyl homoserine lactones (AHLs), Las and Rhl, each one is made up of three elements: a synthase (LasI and RhlI), a signal receptor (LasR and RhlR) and an autoinducing signal (N-3-oxo-dodecanoyl-L-homoserine and N-butyryl-homoserine lactone respectively)[4,5]. These two systems are hierarchically organized, with the LasIR system activating RhlIR, each of which controls the expression of different virulence factors. Strategies such as “quorum quenching” (QQ) have been proposed, which consists of blocking or inhibiting QS by obstructing the function of autoinducing synthases, signal receptors or by degrading autoinducers by two enzymatic strategies: interrupting the lactone ring through a lactonase or through cleavage of the acyl tail by acylases[4,6].

Ones of the molecules that have been described that have a QQ activity is the C-30 furanone that blocks the LasR[7] receptor and the enzyme lactonase AiiM[4]; for the first resistance systems have been described in *P. aeruginosa*, but none have been described resistance to QS inhibitory enzymes yet[7]. In the present work, it was evaluated whether *P. aeruginosa* can develop resistance to one of these self-inducing degrading enzymes.

In this project, it was found that growth in minimal medium with M9 salts added with 1% adenosine is adequate to inhibit growth and QS, with this condition it is possible to obtain resistance against QS inhibitors that don’t inhibit growth. In

the specific case of *P. aeruginosa* PAO1, growth curves were made in M9 medium with adenosine with 2 concentrations of the enzyme AiiM, colonies were isolated (expected to be resistant to the QQ activity of the enzyme) and only two presented a persistent resistance, since when measuring the phenotypes of caseinolytic activity and pyocyanin in the presence of lactonase AiiM, they present a similar activity to the PAO1 strain without enzyme, and their production of long-chain AHL is not affected in the presence of AiiM.

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ROLES OF RSMA AND PQSE ON THE PYOCYANIN AND ALKYL-QUINOLONES SYNTHESIS IN THE MARINE STRAIN *PSEUDOMONAS AERUGINOSA* ID4365

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Abstract:

Pseudomonas aeruginosa is an opportunistic pathogen that produces several virulence factors such as rhamnolipids, elastase, and pyocyanin. Pyocyanin synthesis is controlled at the transcriptional level by the three-quorum sensing systems Las, Rhl, and Pqs. The Pqs system depends on the production and detection of alkyl-quinolones (AQs). AQs are produced by enzymes encoded by the operons *pqsABCDE* and *phnAB* whose transcription is dependent on the PqsR regulator. In addition, it has been shown that in the clinic strain *P. aeruginosa* PAO1 the PqsE protein, whose gene is expressed within the operon that produces AQs, is essential in the production of pyocyanin. Pyocyanin synthesis is also regulated at the post-transcriptional level by RsmA which is part of the Rsm system. In *P. aeruginosa* ID4365, a marine strain that overproduces pyocyanin, *rsmA* inactivation increases pyocyanin synthesis but decreases AQs production suggesting that *pqsABCDE* operon expression is downregulated. These data suggest that PqsE is dispensable for pyocyanin production and that RsmA positively regulates AQs production. In this work, the effect of the *pqsE* mutation on pyocyanin synthesis and also the regulation of RsmA on key genes for AQs synthesis such as *pqsA, phnA,* and *pqsR* was studied. The results obtained demonstrate that PqsE is essential for the synthesis of pyocyanin in the wild-type strain ID4365 since its inactivation abolishes its production. However, *pqsE* inactivation in the *rsmA* mutant strain reduces pyocyanin synthesis but still is able to produce it, indicating that in this condition PqsE is not essential for pyocyanin production. On the other hand, regarding the regulation of the synthesis of AQs, the experimental data obtained by transcriptional fusions suggest that RsmA positively regulates the expression of *pqsA* and negatively that of *pqsR*. Nevertheless, these data will be complemented with translational fusions to confirm that this regulation is at the transcriptional level which suggests an indirect regulation.

IN SILICO IDENTIFICATION OF MUTATIONS IN THE GENOME OF INFLUENZA A H1N1 AND H3N2 VIRUSES INVOLVED IN ANTIVIRAL RESISTANCE IN MEXICO

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Abstract:

Background: Influenza A viruses belong to the Orthomyxoviridae family, are RNA-genome, enveloped, spherical viruses, causing seasonal epidemics and sometimes pandemics. Treatments for infection with this virus include M2 proton channel inhibitors, neuraminidase (NA) inhibitors, and more recently polymerase (PA) complex inhibitors. As viruses have a RNA genome, they undergo mutations in each replicative cycle, some of these mutations occur at sites where the antiviral binds to the NA or PA protein, causing them to be less sensitive to the effect of antivirals. In this work we analyzed the presence of mutations that confer resistance to antivirals in influenza A viruses circulating in Mexico.

Methods: We obtained 59 mutations for NA (33 mutations for N1 and 26 mutations for N2) and 15 mutations for the PA gene, which were experimentally reported in the literature. The NA and PA sequences of the seasonal H1N1, H1N1 pdm09 and H3N2 subtypes isolated in Mexico from 2000-2022 were obtained from the Flu Database Research gene bank. Sequence alignments and mutation detection were performed using BioEdit 7.2 and UGENE.

Results: 361 H1N1 virus NA sequences, 78 H3N2 subtype NA sequences, 223 H1N1 subtype PA protein sequences and 67 H3N2 subtype PA protein sequences were analyzed. A total of 6 mutations were identified in the NA of the H1N1 subtype including H275Y (5.57%), S247N (0.24%), D199N (0.24%), V106I (33.9%), N248D (57.14%),

D214G (2.91). For the H3N2 subtype, 4 mutations Q136K (2.04%), D151N (8.16%), D151V (2.04%) and V215I (87.76%) were identified. The total number of sequences with more than one mutation is 139 for H1N1 and 2 for H3N2. These reported mutations confer resistance to oseltamivir, peramivir and/or zanamivir. In the case of PA protein sequences, there were no mutations conferring resistance to baloxivir-marboxyl.

Conclusion: Although circulating strains of influenza A virus resistant to neuraminidase inhibitors were found in Mexico, this does not yet represent a threat to public health, since they are not found in a high percentage circulating in the population. However, genetic surveillance should be established to monitor the presence of these and other mutations that increase the pathogenicity or virulence of this type of virus.

IMMUNOMODULATORY CHARACTERIZATION OF PEPTIDE GP5T3 FROM THE GLYCOPROTEIN 5 OF THE PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS IN SWINE MACROPHAGES

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Abstract:

The innate immune response against RNA viruses is essential to induce early signals that could limit viral pathogenesis and will activate the adaptive immune response to clear the viral infection. The porcine reproductive and respiratory syndrome virus (PRRSV) represents a model to understand the innate immune signaling mechanisms that could trigger viral clearance or enable persistence in swine. Experimental evidence shows that viral glycoproteins can bind Toll-like receptor 4 (TLR4) and induce the activation of nuclear factor kappa B (NF-kB) (Olejnik et al., 2018) and nuclear factor of activated T cells (NFAT) (Liang et al., 2017) to enhance the expression of proinflammatory cytokines. We have studied the immunomodulatory potential of peptides from PRRSV-GP5 in mouse macrophages and showed that the peptides induce the expression of interferon (IFN) -alfa, IFN-beta, and IL-12, and this overexpression correlates with the activation of the NF-kB signaling pathway. Furthermore, it is essential to assess the immunomodulatory effects of the peptides in swine macrophages and evaluate the role of TLR4 and NFAT in the signaling cascade that induces the expression of antiviral cytokines. **Objective:** To evaluate the immunomodulatory effect of peptide GP5T3 from GP5 of PRRSV, alone or encapsulated in Poly(methacrylic acid) (PMA) nanoparticles, by quantifying the expression of TLR4 and IFN-alfa in swine macrophages, to elucidate the innate immune signaling pathways involved in a protective antiviral response against PRRSV. **Methodology:** Swine macrophages 3D4/31 were stimulated with GP5T3 alone or encapsulated in PMA (GP5T3-PMA) nanoparticles, and control stimulants dexamethasone and lipopolysaccharide (LPS). The expression of TLR4 and IFN-alfa was evaluated by RT-qPCR at 2- and 8-hours post-stimulation. **Results:** GP5T3 alone and GPT3-PMA induced the overexpression of TLR4 and IFN-alfa at 2 hours post-stimulation. At 8 hours post-stimulation, only GP5T3 alone induced the overexpression of IFN-alfa. **Discussion and conclusion**: The overexpression of TLR4 and IFN-alfa by GP5T3 suggests that GP5 of PRRSV triggers the activation of innate immune signaling pathways with antiviral effects. This probe of concept experiment supports further analysis of the activation of the NFAT signaling pathway and the expression of additional antiviral cytokines, such as INF-gamma. ***Acknowledgments:*** This project was carried out under the grant PAPIIT- IA208322 from DGAPA-UNAM.

ANTIMICROBIAL ACTIVITY OF CUCURMIN-CHITOSAN NANOCOMPLEXES ON CLINICAL ISOLATES OF INFREQUENT NON-FERMENTING GRAM-NEGATIVE BACILLI SPECIES (*ACHROMOBACTER*, *BURKHOLDERIA*, AND *STENOTROPHOMONAS*)

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Abstract:

Background: Infrequent non-fermenting Gram-negative bacteria such as *Achromobacter*, *Burkholderia*, and *Stenotrophomonas* species are increasing the rate of healthcare-associated infections, often with high morbidity and mortality.[1-2] These pathogens can also show drug resistance to several first-line drugs used for their treatment, such as trimethoprim-sulfamethoxazole (TMP-SXT).[3-4] There is a need to search for alternative treatment options. The aim of this study was to determine the effect of curcumin-chitosan nanocomplexes on clinical isolates of infrequent non-fermenting Gram-negative bacilli. **Material and methods**: Clinical isolates of *Achromobacter xylosoxidans*, *Burkholderia contaminans,* and *Stenotrophomonas maltophilia* were obtained from a third-level hospital in Nuevo Leon, Mexico. Isolates were identified by MALDI-TOF mass spectrometry and end-point PCR and sequencing. Antimicrobial susceptibility tests were determined by broth microdilution. Nanocomplexes were prepared by co-precipitation of magnetic nanoparticles (MNP) and encapsulation by ionic gelation with cucurmin (CUR) and chitosan (CHI) using tripolyphosphate of pentasodium (TPP) as a crosslinker. The effect of CUR, CHI/TPP, CHI/TPP/MNP, CUR/CHI/TPP/NPM, and CUR/CHI/TPP/NPM/TMP-SXT was assessed on the bacterial isolates by broth microdilution. **Results**: The minimum inhibitory concentration (MIC) obtained of *A. xylosoxidans* (1/19 µg/mL), *B. contaminans* (4/76 µg/mL), and *S. maltophilia* (16/304 µg/mL) to TMP-SXT denoted resistance in all three species. The exposure to different concentrations (1—300 µg/mL) of CUR/CHI/TPP/NPM did not show antimicrobial activity. However, the addition of borderline-susceptible concentrations of TMP-SXT (0.06/1.18 and 2/38 µg/mL) to CUR/CHI/TPP/NPM (MIC=0.5 µg/mL) improved the susceptibility levels to TMP-SXT. **Conclusions**: *Achromobacter*, *Burkholderia*, and *Stenotrophomonas* clinical isolates changed their susceptibility to trimethoprim-sulfamethoxazole after exposure with cucurmin-chitosan nanocomplexes, highlighting the need to assess these potential treatment options.

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DISTRIBUTION PROFILE OF BIOSYNTHETIC GENE CLUSTERS IN GENOMES OF RHIZOBACTERIA STRAINS DIFFERING IN PHYTOPATHOGEN INHIBITION AND IN PLANT INTERACTION

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Abstract:

In rhizosphere bacteria there are some species that act as biocontrol agents against phytopathogens and at the same time associate with the root in plants to promote their growth and activate defense response. The phenotype of these bacteria should correlate with genetic characteristics throughout the genome. Biosynthetic gene clusters (BGCs) contain groups of genes responsible for the biosynthesis of secondary metabolites including antibiotics to inhibit competing microorganisms and metabolites for other diverse biological functions. In the present work, the objective was to analyze the presence of BGCs for antibiotics in the genome of 4 rhizosphere and soil bacteria, bacteria that differentially distinguished in the inhibition of 4 pathogens that cause root rot in chili and in friendly or hostile behavior in the interaction with the plant root. In the genome of bacteria of the genus *Bacillus* and *Paenibacillus*, it was analyzed with bioinformatic tools to identify the specificities of BGCs, their respective antibiotics produced and the possible correlation with respect to pathogen inhibition behavior and interaction with the plant in the root. In results, the bacteria with the better performance of pathogen inhibition and virulent behavior in roots, a *Bacillus* sp. with more than 16% of its genome is devoted to BGCs for antibiotic biosynthesis, 30% of these are totally unknown, with no similarity to known BGCs, with between 4 and 14 BGCs shared and 18 BGCs not shared with the other three bacteria, in the non-shared BGCs are those that biosynthesize bacilisin, butyrosin A/B and others still with unknown function. In two *Paenibacillus* strains, between 6 and 14% of their genome is occupied by DNA for BGCs, exhibiting great differences between these strains in this respect. In the least capable bacterium against pathogens, only 4% of the genome is destined for BGCs. Non-ribosomal peptide synthetases (NRPS) and polyketide synthases (PKS) are the largest number of BGCs found in the genome of three of these rhizobacteria with good performance against pathogens studied here.

ELECTROCHEMICAL IMMUNOSENSOR FOR THE DETECTION OF ANTIBODIES AGAINST AN EPITOPE OF GP5 PROTEIN FROM PRRS VIRUS

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Abstract:

The virus responsible for porcine reproductive and respiratory syndrome (PRRSV) is a pathogen that causes high mortality in sows from all ages. PRRSV is a virus with single-stranded RNA genome, encoding a total of 10 structural proteins and 16 non-structural proteins. GP5 structural protein have the main epitopes that induce the production of neutralizing antibodies. Data from our group showed that a peptide (conservated epitope) from GP5 protein, can induce a strong and prolonged response mediated by antigen-specific antibodies, called GP5-B. The most common diagnostic method to quantified antibodies in serum anti- PRRSV is ELISA test, but these is expensive and requires sample transportation to the laboratory. On the other hand, immunosensors are viable diagnostic alternative in which antigen-antibody interaction can be quantitatively determined immediately. **Objective**: Development of a prototype of the sensitive and specific electrochemical immunosensor for the quantification of antibodies against PRRSV. **Methods**: Electrodes functionalization was characterized binding viral peptide and unspecific blocking protein. Electrochemical behavior of the immunosensor was analyzed by cyclic voltammetry and electrochemical impedance spectroscopy. Balb/c mice were immunized with GP5-B peptide binding to carrier protein BSA. Serum from mice were collected 45 days after immunization. **Results**: The anti-PRRSV antibody sensor was able to recognize the antigen-antibody interaction, with a detection limit of 0.6 ng/ml, a sensitivity of 100%, and a specificity of at least 93%. Considering all the data, the new immunosensor can be used for the diagnosis of antibodies against the PRRS virus.

Acknowledgments

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HETEROLOGOUS EXPRESSION AND CHARACTERIZATION OF THE ENZYME ENCODED BY THE HAS GENE FROM COPRINOPSIS CINEREA

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Abstract

Hyaluronic acid (HA) is a very important polysaccharide; it can be found in vertebrates, some bacteria, viruses, and the yeast Cryptococcus neoformans. HA plays essential biological roles, it is involved in cell proliferation, differentiation, and tissue repair, among others. It is also used in pharmaceutic, cosmetic, and orthopedic industries. The enzyme that performs the synthesis of HA is the Hyaluronic Acid Synthase (HAS), which is a transmembrane protein belonging to the processive glycosyltransferase family (GT2). Recently, we found bioinformatic evidence of putative HASs in filamentous fungi, among which Coprinopsis cinerea HAS (Cc-HAS, CC1G_02369) showed 82% identity against C. neoformans HAS (CPS1p, CNAG_04320). However, so far there is no empirical evidence of a bona fide HAS in filamentous fungi. In this research, we aim to provide further evidence and demonstrate that C. cinerea putative HAS is able to produce HA as a first step to understand its biological role. To reach this objective, we first performed a structural analysis to compare the Alpha-fold predicted structure of Cc-HAS against some already characterized HASs (from C. neoformans, Streptococcus pyogenes, S. equisimilis, Mus musculus and Chlorella virus), as well as other processive glycosyltransferases such as chitin synthases (CHS) and cellulose synthases (CS). In addition, we heterologously expressed Cc-HAS together with the C. neoformans UDPG-DH (Cn-UDPGDH), necessary to synthetize a precursor of the HA, in the yeast Saccharomyces cerevisiae. S. cerevisiae is an ideal expression host because is completely unable to synthetize HA by itself and allows the characterization of Cc-HAS without purifying it. The structural models obtained for Cc-HAS and Cn-HAS were almost identical to each other (RMS: 1 Å), supporting functional homology. It was also found that the pore of fungal HASs is composed of 3 helixes, unlike those of bacteria (4 helixes) and animal (6 helixes) HASs. Moreover, fungal HASs were more similar to CHSs than the CSs, which is consistent with the hypothesis that HAS may have evolved from an CHS. To elucidate the catalytic activity of Cc-HAS, a double transformant (MFCcHAS) expressing Cc-HAS and Cn-UDPGDH was obtained and characterized. After expression induction, a Western Blot (anti-V5-HRP) confirmed the expression of Cn-UDPGDH in our system, which showed the expected size of 56 KDa in the cytosolic fraction. In addition, to confirm the cellular localization of both enzymes, an immunofluorescence assay was performed using Anti-V5-Alexa555 antibodies, which showed the presence of the proteins in the yeast cells. We are still working on the heterologous Cc-HAS expression system set up. The latter results will be presented during the congress. This work is being supported by CONACYT-Ciencia de Frontera 2019, grant 552259.

A PHAGE LIBRARY FOR ANTIBIOTIC THERAPY ISOLATED FROM THE MANGROVE AREA LOCATED IN SISAL, YUCATAN

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Abstract:

Bacteriophages, or in short phages, are simple, yet incredibly diverse, non-living biological entities consisting of DNA or RNA enclosed within a protein capsid[1]. These viruses infect and replicate only in bacterial cells[2]. They are ubiquitous in the environment and play an important ecological role controlling bacteria populations. They are extremely diverse in size, morphology, and genomic organization[1]. These bacteria-specific viruses have been used as a treatment against pathogens such as *Shigella dysenteriae* as early as 1919[2]. Currently, there is a growing interest on phage therapy due to the global problematic regarding antibiotic resistance that we have been facing in the last years. It is widely known that bacteria inhabit almost everywhere in every ecological niche, similarly, phages exist in all niches wherever their hosts are present, including hypersaline environments, polar regions, deserts, on and within organisms other than bacteria, fresh and sea water, and soil[3]. The peninsula of Yucatan harbors astonishing, not to mention amazingly diverse mangrove hypersaline ecosystems, however scarcely explored for the search of bacteriophages. Such ecosystems are natural control systems, providing barriers from flooding, hurricanes, they help control soil erosion, and are considered to be biofilters for water[3]. In order to generate a library of isolated bacteriophages from these ecosystems, we recollected sediment samples from mangrove niches located in Sisal, Yucatan. Sediments were resuspended in phage buffer (1:10 w/v), centrifuged at 5,000 rpm for 10 min. Supernatants were recovered and filtered employing 0.20 µm sterile syringe filters to obtain the bacteriophage suspension. We employed a diverse set of ATCC pathogens with the aim to obtain a substantial range of active bacteriophages against different strains. Phage detection and count was performed according to the double agar overlay assay, which allows localized phage-host contact in a confined environment (Petri dish) containing two layers of agar on top of each other, resulting in a so-called lawn. If a phage is capable of infecting the tested bacterium, clear spots or plaques appear on the lawn, containing lysed bacteria and phage particles[4]. At the moment, we have successfully isolated active bacteriophages against *E. coli*, *E. faecalis*, *P. putida*, and *K. pneumoniae*. Our current findings indicate that our library will continue expanding.

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DEVELOPMENT OF AN IMMUNOSTIMULATORY COMPLEX BASED ON LIPOSOMES WITH GLYCYRRHIZINIC ACID COUPLED WITH RECOMBINANT VIRAL PROTEINS OF LIVESTOCK INTEREST

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Abstract:

Currently, the development of vaccines has been one of the most important challenges due to the appearance and reappearance of diseases. In the livestock sector, viral diseases cause great economic damage. Vaccines (of the recombinant type) are made with an antigen of recombinant origin and an adjuvant, which together will generate a strong immune response. The **objective** of this work is to develop an immunostimulant complex (antigen plus adjuvant) with potential use as a vaccine in the livestock sector. **Methodology**. Liposomes were developed using the lipid film method (KÖNNINGS *ET AL*., 2002). A mixture of phospholipids, cholesterol and glycyrrhizinic acid was made in a 2:1:2 ratio, respectively, homogenized at 15000 rpm and subsequently filtered at 0.8, 0.45 and 0.2 µm. The liposomes were stored at 4°C. *Orthorubulavirus porcine* recombinant HN protein (rHN-PorPV) (CUEVAS-ROMERO *ET AL*., 2016) was used as antigen and a 5:5 mixture (5 µg of adjuvant and 5 µg of protein) was made. The size, shape and stability of the complex were evaluated by TEM and Zeta potential. To determine the immunogenicity, BALB/c mice at 21 days of age were immunized (5 ug /mice) with 2 doses at 0 and 14 days, until 35 days. Tail blood samples were taken from the mice every 7 days post immunization (until euthanasia). The kinetics of antibody production was evaluated by indirect ELISA assay. **Results**. The size and shape analysis showed pleomorphic liposomes with a size ranging between 60-200 nm, while stability analysis indicated that the liposomes were stable (-28 mV). The kinetic of antibody production showed that the mice inoculated with the immunostimulatory complex produced considerably more antibodies compared to the negative control and the group inoculated with the protein alone. **Conclusion**. In this work, we produced stable liposomes coupled with a recombinant rHN-PorPV antigen. These results showed that the liposomes complex can generate a strong immune response in animal models, which indicates that it can potentially be used as an adjuvant for vaccines against infectious diseases in the livestock sector.

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Micrococcus luteus LS570 promotes root branching in *Arabidopsis* via decreasing apical dominance of the primary root and an enhanced auxin response

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Abstract:

The interaction of plant roots with bacteria is influenced by chemical signaling, where auxins play a critical role. Auxins exert positive or negative influences on the plant traits responsible of root architecture configuration such as root elongation and branching and root hair formation, but how bacteria that modify the plant auxin response promote or repress growth, as well as root structure remains unknown. Here, we isolated and identified via molecular and electronic microscopy analysis a *Micrococcus luteus* LS570 strain as a plant growth promoter that halts primary root elongation in *Arabidopsis* seedlings and strongly triggers root branching and absorptive potential. The root biomass was exacerbated following root contact with bacterial streaks, and this correlated with inducible expression of auxin-related gene markers *DR5:GUS* and *DR5:GFP*. Cellular and structural analyses of root growth zones indicated that the bacterium inhibits both cell division and elongation within primary root tips, disrupting apical dominance, and as a consequence differentiation programs at the pericycle and epidermis, respectively, triggers the formation of longer and denser lateral roots and root hairs. Using *Arabidopsis* mutants defective on auxin signaling elements, our study uncovers a critical role of the auxin response factors ARF7 and ARF19, and canonical auxin receptors in mediating both the primary root and lateral root response to *M. luteus* LS570. Our report provides very basic information into how actinobacteria interact with plants and direct evidence that the bacterial genus *Micrococcus* influences the cellular and physiological plant programs ultimately responsible of biomass partitioning.

Keywords: Rhizobacteria, root architecture, biomass distribution, auxin, mitosis.

García-Cárdenas E, Ortíz-Castro R, Ruíz-Herrera León Francisco, Valencia-Cantero Eduardo, López-Bucio José. 2021. *Micrococcus luteus* LS570 promotes root branching in *Arabidopsis* via decreasing apical dominance of the primary root and an enhanced auxin respponse. *Protoplasma*. https://doi.org/10.1007/s00709-021-01724-z

PURSUIT AND CHARACTERIZATION OF BACTERIOPHAGES CAPABLE OF RESENSITIZING MULTIDRUG-RESISTANT *PSEUDOMONAS AERUGINOSA* STRAINS

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Abstract:

The discovery of antibiotics is widely recognized as one of the most successful developments in the history of medicine; however, their overuse and misuse have contributed to the increasing phenomenon of bacterial resistance.

Pseudomonas aeruginosa is a multidrug resistant (MDR) bacterium with one of the highest morbidity and mortality rates, for that reason the World Health Organization (WHO) has urged for the development of new therapeutical strategies against this opportunistic pathogen. One promising therapeutic strategy is phage therapy which consist in the use of lytic viruses that infect bacteria called bacteriophages (or phages for short), in the treatment of a clinically relevant infection (1).

Bacteria can develop resistance to phages through different mechanisms, the most common consists in the loss or mutation of the structures on the surface of the bacteria where the phage receptors are located. This phenomenon can also undergo a reduction in the virulence of the bacterium or allow the resensitization of MDR bacteria to antibiotics, as some researchers have observed (2).

For that reason, in this project we aim to isolate and characterize phages capable of resensitizing MDR *P. aeruginosa* strains to antibiotics by obtaining phage resistant clones.

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ANTIGENICITY OF PFC CHIMERIC PROTEIN (PAPG+FIMH+CSGA) IN SERUM FROM PEDIATRIC PATIENTS WITH AND WITHOUT UTI

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Abstract:

Introduction. Uropathogenic *Escherichia coli* (UPEC) is the main agent of urinary tract infections (UTI). The pathogenicity of UPEC involves the expression of virulence and fitness factors associated with bacterial establishment in urinary tract, such as adhesins: FimH (F), CsgA (C) and PapG (P). There is not an effective vaccine for UTI prevention, therefore, the use of these three adhesins as a chimeric protein (PFC) is proposed to evaluate the antigenicity level and its possible use as a vaccine against UTI by UPEC.

Aim. Purify the chimeric protein PFC by affinity chromatography and evaluate by Enzyme-Linked ImmunoSorbent Assay (ELISA) the levels of IgG and IgA in serum from pediatric patients with UPEC-positive UTI, UPEC-negative UTI and serum without UTI.

Material and methods. *E. coli* strain BL21 DE3 was transformed with pLATE31 as vector expression, the expression of the chimeric protein was induced with IPTG and it was purified under denaturing conditions. In addition, SDS-PAGE and Western Blot were performed to verify protein identity; subsequently, it was dialyzed and quantified. Finally, ELISA assays were performed to evaluate the IgA and IgG levels from 42 serum, divided into 14 samples for each of the following three groups: 1) Pediatric patients with UPEC-positive UTI, 2) Pediatric patients with UPEC-negative UTI and 3) Pediatric patients without UTI. Statistic significant differences was determinated by Student´s t test.

Results. Serum from pediatric patients with UPEC-positive UTI presented a significantly higher level of IgA ($p=0.0008$) and IgG ($p=0.0046$), compared with serum from pediatric patients with UPEC-negative UTI; as well as levels of IgA ($p=0.0023$) and IgG ($p<0.0001$) from patients without UTI.

Conclusion. The PFC was an antigenic protein and was recognized primarily by IgA and IgG from pediatric patients with UPEC-positive UTI.

IDENTIFICATION AND CHARACTERIZATION OF A TWO-COMPONENT SIGNAL TRANSDUCTION SYSTEM THAT REGULATES ACETATE UTILIZATION IN *THERMUS THERMOPHILUS* HB27

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Abstract:

Two-component signal transduction systems (TCSTS) play an important role in the perception and transmission of signals to generate a response to environmental stimuli in bacteria, fungi, and plants. They are commonly comprised of a sensing histidine kinase (HK) protein, that detects the stimulus, and a response regulatory (RR) protein, that activates the cellular response. Recently, a new family of bacterial TCSTS called SLC5/STAC, in which the HK is linked to a solute symporter within the same peptidic-chain, has been described. Only three members of this family have been experimentally characterized, the CrbS/R system that regulates acetate utilization in *Vibrio* and *Pseudomonas*; the CbrA/B system that regulates histidine utilization in *Pseudomonas*; and the RpuS/R system that regulates pyruvate utilization in *Sinorhizobium*. Seeking to expand knowledge of the SLC5/STAC family beyond the Proteobacteria, we identified the putative TCSTS *TTH_RS04215/TTH_RS04210*, in the *Deinococcota Thermus thermophilus* HB27. While *TTH_RS04215* is annotated as a sensing HK belonging to the SLC5/STAC family, *TTH_RS04210* is predicted to be a response regulatory protein. Interestingly, the genes coding for both proteins are located in an operon together with six other genes whose annotation suggests that they are involved in signal transduction or solute transport processes. To determine the function of this two-component system we constructed, by allelic exchange with a Kanamycin resistance cassette, two mutant strains in the *TTH_RS04215* and *TTH_RS04210* genes. Subsequently, using utilization assays and growth curves we determined that, unlike the wild-type strain, both mutants were unable to utilize acetate as a sole carbon source. We are currently characterizing the other genes that make up the operon to determine if they are involved in the transport or utilization of acetate in *Thermus thermophilus*.

PRODUCTION OF AN ANTIGENIC FRAGMENT DERIVED FROM THE S PROTEIN OF THE PORCINE EPIDEMIC DIARRHEA VIRUS, IN A *PICHIA PASTORIS* EXPRESSION SYSTEM

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Abstract:

Porcine epidemic diarrhea (PED) is a disease with a mortality rate of at least 80% in piglets, the responsible etiological agent is an RNA coronavirus, named porcine epidemic diarrhea virus (PEDv). Commercial vaccines are not effective against strains that currently circulates in Mexico and their high costs make their application difficult. For this reason, the generation of candidate biologics to immunize pigs against PEDv is important. The aim in this work is produce the antigenic domain CTD of the S protein of PEDv, in a *Pichia pastoris* expression system.

In this study, the biological material used was cDNA obtained from pigs samples with signs of PED from one outbreak in Michoacán. The cDNA was used as a template to amplify the CTD S by PCR, the amplification product was cloned in pJET 1.2/blunt plasmid and, subcloned into the expression vector pPICZαB. The transformation of *Pichia pastoris* X-33 was carried out with pPICZαB/CTD-S linearized with *Pme*I. The colonies obtained were characterized and used in an expression test in BMMY medium, the cells free medium was analyzed by SDS-PAGE and Western blot.

The PCR product obtained was amplified at an alignment temperature of 64 °C, with 958 bp. Cloning was achieved in the pJET 1.2/blunt vector, as well as subcloning in pPICZαB and were characterization by sequencing. Colonies of *Pichia pastoris* X33 transformed with pPICZαB/CTD-S were obtained. The cells free mediums obtained were analyzed in polyacrylamide gel electrophoresis and an overexpression band was observed at 41 kDa after 96 h with methanol (0.5%), corresponding to the CTD recombinant protein of PEDv and with western blot test, the presence of the protein was confirmed.

Finally, in this work, we successfully obtained *P. pastoris* strains that produce CTD recombinant protein of PEDv for produce a biological candidate to immunize pigs against PEDv in Mexico, in addition to generating a production system scalable to bioreactor.

DEVELOPMENT OF AN INDIRECT ELISA WITH RECOMBINANT PORCINE EPIDEMIC DIARRHEA VIRUS PROTEINS TO CARRY OUT A SEROPREVALENCE STUDY OF THE VIRUS IN PIG FARMS IN MEXICO

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Abstract:

Porcine epidemic diarrhea (PED) is a disease with a mortality rate of at least 80% in piglets, the responsible etiological agent is an RNA coronavirus, called porcine epidemic diarrhea virus (PEDv). The spike (S) protein has higher antigenicity than any of the others PEDv proteins, and anti-S antibodies detected in PEDv-infected pigs persist longer than others antibodies. Thus, the domain NTD of S protein was produced due to has higher antigenicity, the detection was done developing an indirect ELISA. The aim in this work is: Develop an indirect ELISA using a fragment of the S protein of DEPv.

The NTD-S protein was obtaining recombinantly, in an expression system *E. coli* BL21, the protein was purified through affinity chromatography (IMAC). The purified protein, was used as antigen for test in western blot serum of infected animals with DEPv from a pig farm of Abasolo, Guanajuato. Then, for to begin the standardization 30 serums were positives, meanwhile for the negative serum was used a collection serum, being 29 negative of 30 serum tested. Therefore, with the positive and negative serum was standardized the conditions for the indirect ELISA. The final conditions were: 75 ng of antigen for each well, 1:200 dilution serum, 1:10000 α-pig-HRP conjugate, the blocking was with 5% non-fat milk in PBS-tween buffer (20 Mm tris-HCl, pH 8, 0.15 m NaCl, 0.05% tween 20) at 37°c for 1 h with moderate agitation, TMB as revelation solution during 30 min and H_2SO_4 2M as stop solution, the samples were measured to 450 nm.

The final conditions obtained for this research was: 100% sensivity, 95% specificity and cut off 0.2. Finally, this research promise to development a diagnostic system effective for DEP in Mexico for to help, to prevent and control the disease.

REGULATION OF VIRULENCE FACTORS BY QUORUM SENSING IN STRAINS BELONGING TO PHYLOGROUPS 3 AND 5 OF *PSEUDOMONAS AERUGINOSA*

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Abstract:

Pseudomonas aeruginosa (PA) is an opportunistic pathogen with clinical and environmental isolates classified into 5 phylogenetic groups, the group 1 and 2, are represented by the reference strains PAO1 and PA14, respectively; the group 3 and 5 are represented by the PA7 and PA39-like strains, respectively (1) and no references strains of group 4 is yet reported (1).

The strains belonging to groups 3 and 5 have genotypes and phenotypes differences with respect to the reference strains PAO1 and PA14, that include deletions in the *rhlC*, *phzH* genes (2), the lack of the entire type III secretion system-encoding locus and the production of the exotoxin ExlA (3, 4).

PA produces a panoply of exoproducts some of them recognized as virulence factors (VF). The most studied are pyocyanin, elastase LasB and rhamnolipids; their expression is regulated by a mechanism called quorum sensing (QS) (5), that depends on cellular density. Currently the synthesis of VF by QS has been extensively studied in PAO1 and PA14 strains. However, several strains of groups 3 and 5 of PA produce variable quantities and combination of exoproducts suggesting a different regulation by QS with respect to the reference strains.

To obtain a general overview of the regulation of virulence in PA, we undertook a global phenotypic characterization of available group 3 and 5 strains in comparison to reference strains. Phenotypic characterization will be correlated with genotypes to draw a comprehensive picture on virulence potential and regulatory circuits in those unusual group of pathogens. The objective is to provide the biomedical sciences with new therapeutic targets to attack infections caused by PA of any phylogenetic group.

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PARTICIPATION OF THE MICROTUBULAR AND ACTIN CYTOSKELETON IN THE CELLULAR ORGANIZATION DURING THE DEVELOPMENT OF THE ENTOMOPATHOGENIC FUNGUS *METARHIZIUM BRUNNEUM*

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Abstract:

Metarhizium is a genus of fungi well known for its role as an entomopathogenic able to infect many insect species. This fungus also can form other beneficial interactions with plants as an endophyte. While interacting with either insects or plants, the fungus must defy different barriers and toxic compounds, which trigger events of cell differentiation and organelle-transport to achieve homeostasis. In fungi, cell polarity is an essential process for proper growth and morphogenesis. Microtubules and actin cytoskeleton are essential to maintain cell shape and the intracellular transport of organelles, such as vesicles, mitochondria, peroxisomes, lipid droplets, among others. To describe the role of the actin and microtubular cytoskeleton in the intracellular organization of *M. brunneum*, we used the anti-microtubules drug benomyl (BML) and the anti-actin drug latrunculin B (Lat B). We determined the concentration that inhibited mycelial growth rate by 50% (LC50) of each anti-cytoskeleton drugs. These concentrations were used to assess if microtubules and actin are performing as scaffolds to transport organelles. Peroxisomes labeled with the protein KAT-GFP, were observed as bright fluorescent spots evenly distributed along the hypha. Peroxisomes moved in anterograde and retrograde fashion at different speeds. Exposure to Lat B did not affect peroxisomes movement but distribution was abnormal. In the presence of BML, peroxisomes decreased their number of moving fluorescent particles in addition to having an abnormal distribution. Lipid droplets stained with BODYPI were observed as fluorescent particles localized throughout the hypha with slow anterograde and retrograde motion. In cells treated with BML, lipid droplets remained static and started to accumulate throughout the hypha, while in cell treated with Lat B, lipid droplets have oscillatory movement, with some of them moving short distances. The AVC stained with FM4-64, showed localization in the apical dome, moving in the growth direction, with BML treatment AVC was smaller, and under Lat B treatment AVC was no visible. Mitochondria stained with MitoTracker Green were observed as long filaments distributed throughout the hyphae, and their positioning was altered by depolymerizing the Mts. We concluded that microtubules are involved in chitosomes, peroxisomes and lipid droplets transport and actin is necessary for peroxisomes, lipid droplets and mitochondria positioning.

ANALYSIS OF ANTIMICROBIAL RESISTANCE GENES AND MLST POPULATION STRUCTURE OF *SALMONELLA ENTERICA* STRAINS ISOLATED IN MEXICO FROM 2000-2020

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Abstract:

Salmonella enterica represents one of the most frequent causal agents of food contamination associated to gastroenteritis. Despite this, there are few studies in Mexico that focus on the molecular epidemiology of *S. enterica*. Therefore, the aim of this work was to evaluate the MLST population structure and the presence of AMR genes in genome assemblies of *S. enterica* from Mexico available in public databases. A total of 2,561 genome assemblies from Mexico were downloaded from EnteroBase. A total of 171 different serovars were found in Mexico. The five most frequent serovars found were Newport (8.51%), Oranienburg (7.03%), Anatum (5.78%), Typhimurium (5.12%) and Infantis (4.57%). Using the 7-gene MLST scheme, a total of 287 Sequence Type (ST) clustered in 128 eBurst Groups (eBG) were found in Mexico. The most frequent ST were ST23 (Oranienburg), ST64 (Anatum) and ST32 (Infantis). Using the core genome MLST scheme, 132 HC2000 and 195 HC900 hierarchical clusters were found. The most frequent HC2000 cluster was HC2000_2 (n=256), which fell into five HC900 clusters and five distinct serovars [HC900_2: Typhimurium and its monophasic variant (n=136), HC900_79: Saintpaul (n=88), HC900_1898: Reading (n=23), HC900_536: Heidelberg (n=6) and HC900_1299: Coeln (n=3)]. A total of 638 (24.9%) *S. enterica* genome assemblies presented at least one AMR gene and in 1,923 (75.1%) no AMR genes were detected. The *Salmonella* genome assemblies analyzed contained from 1 to 17 AMR genes. A total of 78 different AMR genes belonging to 13 antimicrobial classes were found. The most frequent class was aminoglycosides (31.76%). This class also showed the highest gene diversity, with 25 different genes related to aminoglycoside resistance. The second most frequent class was tetracyclines (12.53%), with 6 different genes. Our results highlight the relevance of continuing the surveillance system of *Salmonella* in Mexico and improve it by the use of WGS analysis tools to generate data useful to better evaluate the potential risk of the circulating *Salmonella* strains for human health.

IDENTIFICATION OF *CHLAMYDIA TRACHOMATIS* GENOTYPES IN NEWBORNS WITH RESPIRATORY DISTRESS

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Abstract:

Chlamydia trachomatis is the most common bacterial sexually transmitted infection worldwide, which can be classified into biovars or pathotypes according to the clinical manifestation that can cause: trachoma, caused by the A-C genotypes; not invasive genitourinary infections, caused by the D-K genotypes; and the lymphogranuloma venereum, caused by L1-L3 genotypes. In Mexico, the epidemiological studies of *Chlamydia trachomatis* focus mainly on the incidence and prevalence of this microorganism in female sex workers, pregnant women, infertile women, women with clinical symptoms that require gynecological care, and in men whose partners are sterile, being the genotype F the most important. However, there is no study that reveals the *Chlamydia trachomatis* genotypes that causes respiratory tract infection and conjunctivitis in mexican newborns.

In this work, 79 samples such as bronchial aspirates (53), nasopharyngeal swabs (10) and conjunctival swabs (16) from neonatal patients with a previous diagnosis of *Chlamydia trachomatis* infection [363 samples of 1062 (34.18%)], treated at the National Institute of Perinatology (Instituto Nacional de Perinatología) between January first, 2016, to January first, 2020 were analyzed. The *ompA* gene (gene of the Main Outer Membrane Protein MOMP) was amplified by endpoint PCR in 40 samples (50.6%) and was used for genotyping by the restriction fragments of polymorphic length (RFLP) method as well as real-time PCR coupled to Melting Curve (qPCR-MC). The associations between the genotypes and the clinical data of the newborn were developed with a relative risk analysis using Fisher's exact test.

The results showed that the genotype with the highest prevalence in neonates was I with 35% (14/40), followed by genotype E with 32.5% (13/40), D with 17.5% (7/40), F with 12.5% (5/40), and L2 with 2.5% (1/40). The clinical analysis showed that genotype D was associated with neonatal sepsis (p = 0.017, RR = 5.83 (95% CI 1.51-25.985), genotype E was associated with an Apgar value of 7 at 5 minutes (p = 0.021).

In conclusion, the *Chlamydia trachomatis* genotypes identified in newborns with respiratory distress were, I in 35%, E in 32.5%, D in 17.5%, F in 12.5%, and L2 in 2.5%. The genotype D was associated with the development of neonatal sepsis, while genotype E was associated with an Apgar value of 7 at 5 minutes.

EVALUACIÓN *IN SILICO* AND *IN VITRO* OF 4-FORMYL PYRAZOLE DERIVATIVES ON THE ENZYME 3-HYDROXY-3METHYL GLUTARYL COENZYME *A* REDUCTASE FROM *CANDIDA GLABRATA* (HMGRCG)

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Abstract:

Currently, the yeasts of the genus *Candida* have been the causative agents of multiple fungal infections in hospitalization units, with *Candida glabrata* being the most frequent species followed by *Candida albicans*. Likewise, in the recent pandemic, cases of fungal co-infection were reported in patients who had the SARS-CoV-2 virus. In addition to this, resistance mechanisms continue to be manifested by the reference drugs used, such as azoles. Due to this, it is necessary to search for new compounds with targets other than azoles. One of these targets proposed by our research group has been the enzyme HMGR from *C. glabrata*, which is known to be involved in the ergosterol synthesis pathway in fungi. For this reason, in this work, the evaluation of the growth and ergosterol synthesis of 12 pyrazole derivatives obtained by chemical synthesis on *C. glabrata* CB138 was carried out, as well as a study of molecular docking and inhibition of enzymatic activity of the recombinant enzyme. HMGRCg. The results obtained showed that such compounds inhibited the growth and ergosterol synthesis of *C. glabrata*. Furthermore, it was shown that such compounds recognized amino acid residues of the active site of such enzyme and inhibited the activity of the recombinant enzyme HMGRCg. In conclusion, these findings suggest that such derivatives could be proposed as an alternative in antifungal therapy by inhibiting growth, ergosterol synthesis and HMGRCg activity.

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STUDY OF EXPLOITATION OF EXOPROTEASES AND POPULATION COLLAPSES IN CLINICAL STRAINS OF *PSEUDOMONAS AERUGINOSA*

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Abstract:

Pseudomonas aeruginosa has a QS-sensing LasRI system in which its autoinducer N-3-oxo-dodecanoyl-homoserine lactone controls the production of a wide variety of extracellular enzymes and metabolites (1). In the PAO1 and PA14 strains, this system activates several genes, among them that of elastase (enzyme responsible for the degradation of elastic fibers) whose production allows the colonization of certain tissues, such as in the lungs of individuals with cystic fibrosis and also the inactivation of certain elements of the immune response; another QS system they have is RhlRI, whose inducer is N-butanoyl-L-homoserine lactone. The RhlR regulon contains several genes and overlaps with the LasR regulon. There is also a non-AHL (acyl-homoserine lactone) signaling system called the Pseudomonas quinolone signal system (PQS), 2-heptyl-3hydroxy-4-quinolone, and the PQS synthesis operon that is responsible for several alkylquinolones (1).Pseudomonas aeruginosa is a primary bacterial model for studying cooperative behaviors. The exploitation of a public good, such as exoproteases, siderophores, surfactants, bioluminescence, among others, provides benefits to an entire bacterial population thanks to the action of the cooperators, however the cheaters do nothing for the population, cheat and take advantage of these benefits by prospering in their population density, even causing a population collapse (tragedy of the commons) (2) when the use of the public good is excessive, that is, there is an exploitation of the asset by cheaters. These non-cooperative individuals (mutants with the possibility of compensating for their mutation) appear spontaneously in the crop (1) and will obtain greater benefit when the population to be exploited is large; if the cheater population were too high, the population would not reach the quorum, stop producing quorum-controlled factors, and consequently stop growing (3).Although the population dynamics between cooperators and non-cooperators in P. aeruginosa have been extensively studied, the vast majority of studies have been carried out on reference strains such as PAO1 and PA14, so it is unknown if the behaviors are the same in clinical and environmental strains with a recent evolutionary past different from that of the strains studied and often with substantial changes in the regulation of their QS systems (4)(5). Therefore, in this work, its study is proposed by evaluating the frequency of population collapses of clinical strains of Pseudomonas aeruginosa, identifying which factors or conditions are involved in these population collapses of the parental strain, considering the population density and susceptibility of both the parental and cheaters in the exploitation of exoproteases.

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PROTEOLYTIC ACTIVITY OF PROTEINS SECRETED BY *ORNITHOBACTERIUM RHINOTRACHEALE*

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Abstract:

Ornithobacterium rhinotracheale (ORT) is a Gram-negative bacterium considered as an emerging pathogenic microorganism mainly affecting turkeys and chickens. This microorganism is the causal agent of ornitobacteriosis, a respiratory disease producing economical losses by affecting meat and egg production to poultry industry. The presence of ORT has been described worldwide and in Mexico was just described in 2002. Virulence factors expressed by this pathogen are scarcely known. In the present work, the proteolytic activity (PA) secreted by ORT is described. Secreted proteins obtained from cultures in agitation at 37°C show PA in casein zymogram at 30 kDa. This PA was also observed in porcine gelatin or chicken hemoglobin zymograms. PA was active in a wide range of pH but it was not observed at values above pH 8. The PA was thermo stable up to 65°C. PA secreted by a pathogen microorganism could be important to nutriment obtaining and evasion of host immune response.

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ERIC-PCR TYPING OF CLINICAL STRAINS OF SEPSIS-ASSOCIATED *ESCHERICHIA COLI*

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Abstract:

Introduction: *Escherichia coli* is an opportunistic pathogen related with extraintestinal infections such as sepsis-associated *Escherichia coli* (SEPEC), with high multidrugresistance (MDR). Strain typing and differentiation is an important tool for studying bacterial population and epidemiological surveillance of outbreaks.

Aim: To type SEPEC strains isolated from a third level hospital by ERIC-PCR, to identify their population diversity and their association with antibiotic resistance profile, virulence and phylogroups.

Material and Methods: From a collection with 30 isolates of SEPEC, were assayed susceptibility test to 17 antibiotic according with CLSI 2020 and were classified based on Magiorakos, et al (2012) criteria. Genomic DNA was extracted for amplification of nine virulence genes, the phylogroup was determined and the diversity of the strains was evaluated by ERIC-PCR. The banding patterns were analyzed according with Tenover et al. (1995) criteria.

Results: From 30 SEPEC isolates their antibiotic susceptibility profile was: 6.66% (2/30) R1, 60% (18/30) MDR, 30% (9/30) XDR and 3.33% (1/30) PDR. Virulence genes were found in the following rates: 20% (6/30) *hlyA* and *iutD*, 33.3% (10/30) *fimH*, 93.3% (28/30) *vcsgA* and *mot*B, 40% (12/30) *satA* and *fyuA*, 10% (3/30) *tosA*, 30% (9/30) *fliC*. Most strains belonged to phylogroups $B2_2$ and D1 (11/30, 36.6%) of nosocomial importance as well as $B2_1$ (3/30, 10%) and D2 (1/30, 3.33%), 2/30 (6.66%) were A1 and B1 associated with commensal strains. Typing by ERIC-PCR determined that 24/30 SEPEC strains showed <80% similarity.

Conclusion: Most of the SEPEC strains analyzed were MDR, showed virulence factors related to adherence, toxins and motility and presented medical importance. According to ERIC-PCR typing, the high diversity of the strains was determined, since 24/30 strains showed <80% similarity and therefore are not epidemiologically related.

CHARACTERIZATION OF THIOREDOXIN/THIOREDOXIN REDUCTASE SYSTEM OF CANDIDA GLABRATA

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Abstract:

Thioredoxins reductases (Trr) and thioredoxins (Trx) are present in all organisms. In the *C. glabrata* genome, there are four ORFs, which are orthologous of *Sc*Trr1 (CAGL0A02530g), *Sc*Trr2 (CAGL0I01166g), *Sc*Trx2 (CAGL0K00803g) and *Sc*Trx3 (CAGL0E00583g). These ORFs share high similarity and conserved synteny. In this work, we studied the Trr1/2 and Trx2/3 in the OSR in *C. glabrata*. Using translational fusions with fluorescent proteins, we determined that Trr1, Trr2 and Trx2 are localized in the cytoplasm; and only Trx3 is in mitochondria. This suggest that *C. glabrata* may not have a mitochondrial Trr/Trx system. Moreover, *TRR2* and *TRX2* are induced in the presence of H_2O_2 and are regulated by the transcription factors Yap1 and Skn7 and conversely *TRR1* and *TRX3* have low basal expression. *TRR1* is induced by growth medium while *TRX3* is constitutively expressed, and both *TRR1* and *TRX3* are not regulated by Yap1, Skn7, Msn2 or Msn4. We constructed single and double null mutants in Trr1/2 and Trx2/3 (*trr1*Δ, *trr2*Δ, *trx2*Δ, *trx3*Δ, *trr1*Δ *trr2*Δ and *trx2*Δ *trx3*Δ). We showed that the absence of both *TRR1* and *TRR2* delays the growth in any growth medium and the absence of *TRX2* causes methionine and cysteine auxotrophy. *trx3*Δ has no defect in growth. *trr1*Δ and *trx3*Δ are not sensitive to H_2O_2 or menadione compared to the reference strain, BG14. However, *trr2*Δ, and *trx2*Δ are very sensitive to H_2O_2 (even more sensitive than *cta1*Δ mutant). The double mutant *trr1*Δ *trr2*Δ is more sensitive to H_2O_2 than *trr2*Δ. This indicates that the resistance to oxidative stress is mediated by Trr2 and Trx2, and Trr1 and Trx3 have no role in the oxidant stress response in *C. glabrata*. Furthermore, Trr1 and Trr2 are important to respond to heat shock, protein synthesis inhibitors, and resistance to xenobiotics such as azoles and cadmium. Interestingly, in a neutrophil survival assay, we observed that each component of the Trr/Trx system is important for survival. Although *TRR1* and *TRX3* do not appear to have an important function *in vitro*, they play a non-overlapping role since *trr2*Δ and *trx2*Δ do not survive in the presence of neutrophils.

TRICHODERMA AND PLANT GROWTH-PROMOTING BACTERIA, SEARCHING FOR A SYNERGISTIC INTERACTION WITH PLANTS

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Abstract:

Plants are exposed to different biotic and abiotic factors, which can cause stress to the plants. To counteract such stresses, plants establish interactions with different beneficial microorganisms, like the fungi of the genus *Trichoderma* and plant growth-promoting bacteria (PGPB), resulting in enhanced plant growth and development, and resistance against pathogens [1]. *Trichoderma spp.* are one of the most studied microorganisms that establishes beneficial interactions with plants and are also excellent mycoparasites. These fungi uses different mechanisms during their interactions with other organisms, such as the use of effector proteins to modulate plant physiology and defense responses in order to colonize plant roots, or to attack its fungal prey [2]. In the soil, microorganisms establish different types of interactions among them, which can be synergistic or antagonistic, thus affecting their overall benefits on the plant [3]. This work aims to analyze and characterize the interaction between *T. virens* and *T. atroviride* with different PGPBs, its effect on plant growth-promotion of *Arabidopsis thaliana* plants, its ability to inhibit the growth of the pathogen *Fusarium brachygibbosum* and the expression of *Trichoderma* genes coding for effector proteins during the interactions. Our results show that the combination of *T. virens* or *T. atroviride* with *Rouxiella badensis* SER3 is better at inhibiting the pathogen growth, but the combination of *T. virens* or *T. atroviride* with *Pseudomonas fluorescens* UM270 is better at promoting *Arabidopsis* growth, improving biomass and lateral root system. To our surprise, the effector-coding genes *sm1* and *tvhydii1* from *T. virens* are downregulated during the interaction of this fungus with PGPBs and *F. brachygibbosum*, suggesting that these effector proteins may not be participating during the interaction with PGPBs and in confrontation with the pathogen. Our results show that the efficacy of biocontrol agents such as *Trichoderma spp.* could be improved in co-culture with different strains of other beneficial microorganisms, such as *R. badensis* SER3 and *P. fluorescens* UM270, and effector proteins may have different roles in interaction with other beneficial organisms.

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REGULATION OF GLYCOGEN SYNTHESIS AND DEGRADATION BY QUORUM SENSING IN PSEUDOMONAS AERUGINOSA

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Abstract:

Pseudomonas aeruginosa is an opportunistic pathogenic bacterium, which can infect hosts with a compromised immune system (1). To facilitate the establishment of infection, *P. aeruginosa* produces various virulence factors. It has been shown that expression of several of these factors, are regulated by quorum sensing (QS), which is a molecular mechanism that allows bacteria the monitoring of population densities and reprogramming the expression of genes in high cell densities (2,3).

In addition to regulating the expression of virulence factors, it is known that the QS regulates some metabolic processes such as adenosine catabolism. There are also data that indicate that the QS can positively control the transcription of enzymes involved in glycogen metabolism, for example, glycogen phosphorylase, glycogen branching enzyme and glycogen synthase (4).

Bacterial glycogen, works as a carbon warehouse, it is important to maintain the osmotic pressure of the cell and to invade new niches (5,6). Despite its importance in bacterial physiology, transcriptomic and proteomic studies that have identified changes QS-dependent in key points of their metabolism, makes it difficult to draw conclusions from the metabolic consequences of such changes in gene expression without measuring the metabolites or enzymes involved (7). So, this project intends to decipher the relationship of the QS with the regulation of glycogen concentration.

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DEGRADATION OF CHLORPYRIFOS AND LAMBDA CYALOTHRIN BY RHIZOSPHERIC FUNGI OF *TYPHA DOMINGENSIS* PLANTS FROM TURBIO RIVER

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Abstract:

Located in the state of Guanajuato, the Turbio river is one of the most polluted water bodies in Mexico due to industrial discharges. Agriculture diffusely contributes some pollutants due to the runoff of pesticides or the improper handling of their residues. However, there are natural wetlands along the Turbio river that could be removing a large amount of pollutants due their components: terrestrial or aquatic vascular plants, microorganisms and the substrate support. Therefore, this study is focused on the identification of the fungi present in the root of *Typha domingensis* from Turbio river with the capacity of degradation of chlorpyrifos and lambda cyalothrin, in order to be used as alternatives in the treatment of various environmental matrices. In this work, 12 filamentous fungi were obtained from the rhizosphere and from the surrounding water. DNA extraction, amplification, purification of the ITS2 region, and sequencing of the ITS2 region were carried out. Macroscopic and microscopic characterization and sequencing results confirmed the presence of the genera *Penicillium*, *Talaromyces*, *Trematosphaeria* and *Aspergillus*. *Penicillium* sp. RZ-1a, RZ-1b, *Penicillium* sp. RZ-5b and *Talaromyces* sp. RZ-1c, had presented the highest growth rates in medium with/without the presence of pesticides. For the degradation tests (25 and 50 ppm of chlorpyrifos and lambda cyalothrin) isolates presented high percentages of degradation for chlorpyrifos at 14 days, being 96.1%, 94.3%, 92.8% and 89.6% for *Penicillium* sp. RZ-5b, *Penicillium* sp. RZ-1a, *Talaromyces* sp. RZ-1c and RZ-1b, respectively. Meanwhile, the degradation of lambda cyalothrin was likewise high, being 94.9%, 91.5%, 91.3% and 85.5% for *Penicillium* sp. RZ-5b, *Talaromyces* sp. RZ-1c, *Penicillium* sp. RZ-1a and RZ-1b, respectively. These results indicate the ability of rhizospheric fungi to degrade pesticides in *T. domingensis* in highly polluted environment such as the Turbio river. These isolates can be a key element in remediation projects, using them as inoculants in artificial wetland systems as well as the study of their metabolism in the degradation of pesticides for future biotechnological applications as biorreactors.

PARTICIPATION OF THE ORFS PA2305 AND PA3327 IN THE VIRULENCE OF *PSEUDOMONAS AERUGINOSA* PAO1

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Abstract:

Pseudomonas aeruginosa is a gram-negative bacterium considered an opportunistic pathogen for humans, causing respiratory and soft tissue infections that are associated with hospital environments. This bacterium produce a wide arsenal of virulence factors (biofilms, pigments, elastases, proteases, lipopolysaccharides, etc.), whose factors are important for the development of infection in the host. Bacterial virulence factors are regulated by a cell-cell communication system known as Quorum Sensing [1]; however, several molecules including cyclodipeptides (CDPs) may modulate or interfere with the bacterial communication systems and thus regulate the expression of multiple virulence factors [2]. Therefore, it is of interest to investigate the participation of genes that encode for enzymes such as non-ribosomal peptide synthetases (NRPS), responsible for the synthesis of CDPs and other metabolites involved in the virulence of *Pseudomonas aeruginosa.* In this work, the ORFs PA3327 and PA2305 were studied, since both their participation in the synthesis of CDPs is unknown, likewise their role in the virulence of the *P. aeruginosa* PAO1 strain was also determined. Bioinformatic analysis revealed that the ORFs PA3327 and PA2305 encode for NRPS. Mutants of this bacterium in ORFs PA3327 and PA2305 were obtained by gene interruption using a gentamicin resistance cassette and their virulence factor production was determined. Additionally, the pathogenicity was evaluated in the PAO1 mutants in a *in vivo* model of *Caenorhabditis elegans*. The results obtained indicate that the NRPS encoded in the ORFs PA3327 and PA2305 are involved in the production of siderophores and phenazines, which synthesis depending of the quorum sensing modulation, influencing the pathogenicity of the *P. aeruginosa* PAO1 bacteria.

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ROLE OF THE PROPHAGE OF THE PSEUDOMONAS AERUGINOSA STRAIN ID4365 IN POPULATION COLLAPSES DUE TO THE EXPLOITATION OF EXOPROTEASES FROM ITS HOST

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Abstract:

Pseudomonas aeruginosa is a Gram-negative bacillus with a wide environmental distribution. Quorum sensing (QS) systems in *P. aeruginosa* control the production of public goods, such as exoproteases which are produced by individuals that are likely to be exploited by mutants in genes such as *LasR* or *rhlR* called exoprotease cheaters. These cheaters are usually selected in the population during *in vitro* evolution experiments in casein media as the only carbon source and can cause population collapse as there is a higher proportion of cheaters than producers. Bacteriophages, or phages, are viruses that infect bacteria and interact with their bacterial hosts in a continuum of infection modalities ranging from lysogenic to lytic infection. In the lysogenic state they are known as prophages, which can exert lytic development in stressful environmental conditions such as nutrient scarcity. In the *P. aeruginosa* strain ID4365, population collapses have been observed in the absence of a high proportion of exoprotease cheaters as well as spontaneous induction of prophages. In this work, the role of the prophage of the *P. aeruginosa* strain ID4365 was studied as a possible causal factor in its population collapses during its in *vitro* evolution in casein. To do this, filtrates were obtained from each initial and even pass and were dripped onto a strain of *P. aeruginosa* susceptible to phages and to quantify the bacteriophage titer (PFU/mL). The identification of individual cheaters was done by evaluating the caseinolytic activity of supernatants collected during growth in casein. In parallel, the sequence of the prophage in the genome of ID4365 was searched *in silico*. No population collapse was observed during the first 12 passages. The PFU/mL titer was low (10^0 PFU/mL to 10^2 PFU/mL) during those passages. The predicted sequence of the prophage of ID4365 was obtained, and it was a prophage with a high identity with phages of the F116-Like family such as H66 and LKA5. The frequency of collapses in casein cultures of lysogens of H66 and LKA5 in PAO1 was evaluated and an early collapse in the lysogen of LKA5 was observed. Therefore, some temperate phages such as ID4365 and LKA5 have a possible role in the collapse of their hosts during their evolution in casein médium.

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THE PLANT BENEFICIAL RHIZOBACTERIUM *ACHROMOBACTER* SP. 5B1 INFLUENCES ROOT DEVELOPMENT THROUGH AUXIN SIGNALING AND REDISTRIBUTION

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Abstract:

Roots provide physical and nutritional support to plant organs that are above ground and play critical roles for adaptation via intricate movements and growth patterns. Through screening the effects of bacterial isolates from roots of halophyte Mesquite (*Prosopis* sp.) on *Arabidopsis thaliana,* we identified *Achromobacter* sp. 5B1 as a probiotic bacterium that influences plant functional traits. Detailed genetic and architectural analyses in *Arabidopsis* grown in vitro and in soil, cell division measurements, auxin transport and response gene expression and brefeldin *A* treatments demonstrated that root colonization with *Achromobacter* sp. 5B1 changes the growth and branching patterns of roots, which were related to auxin perception and redistribution. Expression analysis of auxin transport and signaling revealed a redistribution of auxin within the primary root tip of wild-type seedlings by *Achromobacter* sp. 5B1 that is disrupted by brefeldin *A* and correlates with repression of auxin transporters PIN1 and PIN7 in root provasculature, and PIN2 in the epidermis and cortex of the root tip, whereas expression of PIN3 was enhanced in the columella. In seedlings harboring *A*UX1, EIR1, *A*XR1, *A*RF7*A*RF19, TIR1*A*FB2*A*FB3 single, double or triple loss-of-function mutations, or in a dominant (gain-of-function) mutant of SLR1, the bacterium caused primary roots to form supercoils that are devoid of lateral roots. The changes in growth and root architecture elicited by the bacterium helped *Arabidopsis* seedlings to resist salt stress better. Thus, *Achromobacter* sp. 5B1 fine tunes both root movements and the auxin response, which may be important for plant growth and environmental adaptation.

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CYTOTOXIC ACTIVITY OF ISOLATED BACTERIA FROM A MAYAN SINKHOLE LOCATED IN SISAL, YUCATAN

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Abstract:

The peninsula of Yucatán is a captivating territory of Mexico, representing 2% of the total surface of the country. It encompasses an extension of 300,000 km^2 and separates the Caribbean Sea from the Gulf of Mexico[1]. One of its most striking characteristics is the impressive number of sinkholes or "cenotes" estimated for this territory, approximately 5000 and counting, however, the real number is yet unknown[3]. Through time, surface rock (limestone) is dissolved by rainfall and other environmental factors which creates a fissure and a groundwater network. After the collapse of the limestone, a cenote is generated, creating an isolated but still connected ecological environment[2]. Cenotes are stunning places with distinctive chemical and biological characteristics, especially in terms of the microorganisms that reside in these habitats, representing a potential source of novel anti-cancer drugs[4] [5]. Cancer is one of the most serious human health problems, caused by the disproportionate increment on the number of cells due to alterations in the cell cycle[6]. The current need for new anticancer treatments is encouraging investigations focused on the exploration of marine ecosystems, such as cenotes, in the search of novel compounds useful to treat cell alterations driving cancer pathogenesis, development, and progression. In order to discover anti-cancer metabolite producer microorganisms we obtained sediment samples by scuba diving from "Pol-ac", a cenote located in Sisal, Yucatan. Sediments were inoculated in A1 marine solid media, following the serial dilution method. Liquid cultures were inoculated from single identified colonies. After 14 days obtained supernatants were extracted with ethyl acetate. Cytotoxic activity of the obtained extracts was tested employing *Saccharomyces cerevisiae.* This yeast was selected as our cancer model since it is an eukaryote expressing homologue human RAS and CDK proteins[7]. Obtained results showed a panel of extracts from "Pol-ac" isolated bacteria as promising to continue exploring its cytotoxic activity. Further work to isolate and identify the active metabolites is ongoing.

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FUNCTIONAL AND STRUCTURAL STUDIES OF TWO MODULAR ANTIMICROBIAL ENDOLYSINS: INSIGHTS INTO THE POTENTIAL APPLICATION IN CONTROLLING VIBRIOSIS IN SHRIMP FARMS

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Keywords: genome data mining; lytic activity; structural biology; *Uibrio parahaemolyticus*

Abstract:

Uibriosis is a severe bacterial disease caused by *Uibrio parahaemolyticus,* a Gram-negative (G-) bacterium that drastically affects shrimp cultures leading to high agroeconomic losses. Since the pathogen *U. parahaemolyticus* is transferred to humans through ingesting contaminated food, it also represents a human health problem. Controlling vibriosis in shrimp farms has pushed producers to use antibiotics arbitrarily, causing the development of multidrug-resistant strains. Therefore, bacteriophage endolysins have emerged as novel antimicrobial enzymes, as they catalyze the cleavage of the peptidoglycan (PG) layer, causing bacterial lysis and death. Strikingly, the endolysin KZ144 from the *Pseudomonas* bacteriophage φKZ exhibited intrinsic lytic activity against G- *U. parahaemolyticus,* but lytic activity decreased in the presence of Mg^{2+} ions from seawater. Here, a novel endolysin (OsLys) was detected by genome mining of ~229 public bacteriophages genomes from *Uibrio* spp. Structural analysis of OsLys showed a modular architecture including a Carbohydrate-Binding Domain (CBD) followed by a Catalytic Domain (CD). Structural comparisons of the crystallographic structure of KZ144 with the homology model of OsLys revealed that both share a related CDB-CD modular architecture. Nevertheless, while the active site of OsLys is consistent with lytic activity against the PG layer via a catalytic Cys^{126}, KZ144 showed lytic transglycosylase activity against MurNAc-GlcNAc via a catalytic Glu^{115}, which seems to be susceptible to inhibition by Mg^{2+} ions. Additional functional and docking studies of OsLys suggest that this endolysin is a promising antibacterial candidate for controlling *U. parahaemolyticus.*

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SEROPREVALENCE OF NEUTRALIZING ANTIBODIES AGAINST HUMAN AND SIMIAN ADENOVIRUS TYPES, INCLUDING THOSE USED IN COVID-19 VACCINES, IN HEALTHY ADULTS IN MEXICO

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Abstract:

Among the eight vaccines that were approved in Mexico to be used agasint COVID-19, five of them are based on adenoviruses (AdVs), namely Gam-COVID-Vac (Sputnik V from Gamaleya National Center), which uses human adenoviruses (HAdV) HAdV-C5 and HAdV-D26; Ad5-nCoV Covidecia (from Cansino Biologics Inc), based on HAdV-C5; Ad26.COV2-S (from Janssen-Cilag), based on HAdV-D26; and AZD1222 Covishield (from Oxford-AstraZeneca), which is based on a chimpanzee AdV. Most of the vaccines that have used AdVs have been based on HAdV-C5 and more recently HAdV-D26. AdV-based vaccines are one of the most promising platforms for the development of vaccines for use in humans, because they can induce good B- and T-cell responses. However, several studies indicate that a high percentage of the human population has been previously exposed to HAdV-C5 and has high levels of neutralizing antibodies against this virus type, while the prevalence of antibodies against HAdV-D26 are highly variable in different regions of the world, and there is not sufficent evidence that the level of long-lasting protection induced by any of the human or simian AdV-based vaccines is equally effective in all populations and regions of the world. In Mexico, there are very few and sporadic data on the seroprevalence of antibodies against AdVs, and it is not possible to anticipate whether the existing prior immunity in the Mexican population against the serotypes used in the vaccines against COVID19 may interfere with the efficacy of these vaccines, prolonged immunity or their potential use for vaccine boosters or seasonal application. In this work, we have analyzed the prevalence of antibodies against different serotypes of AdVs in the Mexican population. Pre-pandemic samples from blood donors, adults between 18 and 65 years of age. were analyzed. The presence of antibodies against HAdVs representative of each species, A to F, and simian adenoviruses (SAdV) from types SAdV-21, SAdV-25 and SAdV-31 were determined by ELISA and neutralization assays. A very high prevalence of antibodies was found against HAdV-B14 (82%), HAdV-C5 (97%), HAdV-C6 (95%), as well as for SAdV-31(81%), HAdV-F41 (82%) and SAdV-25 (80%); a lower prevalence for HAdV-A12 (40%) HAdV-D36 (55%), HAdV-E4 (40%), and very low for HAdV-D26 (3%) and SAdV-21(1%). The data obtained could contribute with the national health authorities to plan possible strategies for the application of existing vaccines during the COVID-19 pandemic and in the coming years; to plan the application of vaccines on a seasonal basis; or the potential development of new vaccines based on AdVs.

MOLECULAR EVOLUTION OF THE SPIKE PROTEIN OF SARS-COV-2: EVIDENCE OF ADAPTATION

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Abstract:

Introduction: The global scale of the COVID-19 pandemic has demonstrated the evolution of SARS-CoV-2 and the clues of adaptation. After two years and two months since the declaration of the pandemic, several variants have emerged and become fixed in the human population thanks to extrinsic selective pressures and the mutational capacity of the virus.

Objective: describe the molecular evolution of the spike (S) protein of SARS-CoV-2 by applying a neutral substitution test to reported sequences at different moments of the pandemic. Additionally, relate the probability of occurrence of the amino acids with the real functionality of the RBD.

Results: We started computing the neutral evolution of the S protein of *Betacoronavirus* and compared to the calculated neutral evolution of the S protein of SARS-CoV-2 of sequences reported at June, 2021 and at January, 2022. Specifically, Tyr and Asn have higher occurrence rates in the overall sequence of S proteins of *Betacoronavirus*, whereas His and Arg have lower occurrence rates. The *in vivo* evolutionary phenomenon of SARS-CoV-2 shows that the probability of occurrence of the emergent viral particles had more deviation than the most recent virus.

Then we carried out comparisons among the interactions between the S proteins from the VOCs (Alpha, Beta, Gamma, Delta and Omicron) and the receptor ACE2. The shared amino acids among all the ACE2 binding S proteins remain constant, indicating that these amino acids are essential for the accurate binding to the receptor. The complexes of the RBD for every variant with the receptor were used to identify the amino acids involved in the protein—protein interaction (PPI). The RBD of Omicron establishes 82 contacts, compared to the 74 of the Wuhan original viral protein. Hence, the mean number of contacts per residue is higher, making the contact thermodynamically more stable.

Our results show that most unique mutations either for SARS-CoV-2 or its variants of health concern are under selective pressures, which could be related either to the evasion of the immune system, increasing the virus' fitness or altering protein – protein interactions with host proteins. We explored the consequences of those selected mutations in the structure and protein – protein interaction with the receptor. Altogether all these forces have shaped the spike protein and the continually evolving variants.

Keywords: Spike, ACE2, SARS-CoV-2, Selective pressure, Neutrality test

SCREENING OF PHOSPHATE SOLUBILIZATION IDENTIFIES SIX *PSEUDOMONAS* SPECIES WITH CONTRASTING PHYTOSTIMULATION PROPERTIES IN *ARABIDOPSIS* SEEDLINGS

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Abstract

The interaction of plants with bacteria and the long term success of their adaptation to challenging environments depend upon critical traits that include nutrient solubilization, remodeling of root architecture, and modulation of host hormonal status. Here, we isolated and characterized ten bacterial strains based on their high capability to solubilize calcium phosphate. All strains could be grouped into six *Pseudomonas* species, namely *P. brassicae*, *P. baetica*, *P. laurylsulfatiphila*, *P. chlororaphis*, *P. lurida,* and *P. extremorientalis* via 16S rRNA molecular analyses. A *Solibacillus isronensis* strain was also identified, which remained neutral when interacting with *Arabidopsis* roots, and thus could be used as inoculation control. The interaction of *Arabidopsis* seedlings with bacterial streaks from pure cultures *in vitro* indicated that their phytostimulation properties largely differ, since *P. brassicae* and *P. laurylsulfatiphila* strongly increased shoot and root biomass, whereas the other species did not behave as probiotics. Most bacterial isolates, except *P. chlororaphis* promoted lateral root formation and *P. lurida* and *P. chlororaphis* strongly enhanced expression of the auxin inducible gene *DR5:GUS* in roots, but the most bioactive probiotic bacterium *P. brassicae* did not enhance the auxin response. Inoculation of *P. brassicae* and *P. lurida,* but not *P. chlororaphis,* improved shoot and root growth in medium supplemented with calcium phosphate as the sole Pi source. Collectively, our data indicate the high potential of *P. brassicae* to manage agriculture in a more eco -friendly manner.

PHENOTYPIC AND GENOTYPIC ANALYSIS OF SEQUENTIAL CLINICAL ISOLATES FROM *CANDIDA GLABRATA*

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Abstract:

C. glabrata is an emerging and opportunistic fungal pathogen that possesses a set of virulence attributes that allow it to survive within its host and colonize new niches within it. The objective of this study is to determine patterns of variation at the phenotypic and genotypic level in sequential clinical isolates obtained from the same patient that occur during the course of an infection. We analyzed 40 sequential clinical isolates of *C. glabrata* from 11 patients, which we initially identified with species-specific primers and genotyped with polymorphic microsatellite markers *RPM2, MT1* and *ERG3*. We have characterized the response of clinical isolates to thermal stress and also the response to oxidative stress caused by different oxidizing agents and the enzymatic activity of the catalase. We found that the clinical isolates of *C. glabrata* from each patient come from the same infection episode (they are derived from the initial isolate). These isolates can grow in a wide range of temperatures and have the ability to grow in the constant presence of different concentrations of menadione, ter-butyl hydroperoxide and H_2O_2 compared to the control strain BG14. We found that the isolates from patient 9 show higher resistance to acute exposure to H_2O_2 in stationary phase with respect to the control strain BG14 and these results correlate with the activity of the Cta1 enzyme.

KEY WORDS. *C. glabrata*, stress response, genotyping, phenotypic variation

WOLBACHIA PIPIENTIS MODIFIES PROTEIN EXPRESSION IN *AEDES AEGYPTI* CELLS TO DIMINISH THE SUSCEPTIBILITY TO DENGUE VIRUS

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Abstract:

In Mexico, control measures for reduce dengue virus human infection have not been effective, despite the great investment in anti-vector programs. The incompatible insect technique (IIT), using *Wolbachia pipientis,* which confers resistance to Arbovirus infection, seems to be an applicable and feasible measure. In this context, the objective of this work is to show evidence of the possible cellular pathways involved in strengthening the antiviral response of *Aedes aegypti* mosquitoes.

From an *Ae. aegypti* proteomics database and using the STRING software, protein-protein interaction networks of the viral entry, replication and exit pathways were constructed to explain how infection by *W. pipientis* modifies the expression of mosquito cellular proteins and antiviral response. Vesicle-mediated transport, HSP70 receptor performance, ATP synthesis, translation, histone structure, Ubiquitin signaling pathway and exocytosis were some of the cellular events affected by *W. pipientis* infection.

Based on this knowledge, it is possible to propose control alternatives to reduce the competence of mosquitoes to transmit the infection to the human population, such as the use of inhibitors of mosquito signaling pathways and to improve the IIT performance.

HUMORAL IMMUNE RESPONSE SURVEILLANCE IN A VACCINATED STUDENT POPULATION TROUGH SARS-COV-2 MPRO AND N PROTEINS

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Abstract:

Given the health contingency that the world is experiencing due to the Severe Acute Respiratory Syndrome Virus (SARS-CoV-2) that causes the COVID-19 disease and its multiple variants, the rapid development of vaccines has been promoted to make it front. In Mexico, the most widely distributed vaccines are Pfizer-Biontech, Astra Zeneca, Sputnik V, Cansino, Sinovac, Jhonson & Jhonson and Moderna. One way of knowing the effectiveness of vaccines in the immune system is by doing seroprevalence screening specifically determining antibodies against SARS-CoV-2 proteins. This is an analytical longitudinal observational study with the purpose of determining the IgG and IgM antibody titers against structural protein (protein N) and non-structural protein Main Protease (Mpro) in university students. From September to December 2021, blood samples were obtained at the School of Medicine and Biomedical Sciences of the Autonomous University of Chihuahua in a total of 83 students (34 men and 49 women). Samples from students were collected 15 days after they got the first dose and once, they obtained the second immunization were called two weeks later to get the last sample. No significant change is detected in the IgG and IgM titers against the Mpro proteins or the N protein of SARS-CoV-2 compared to the negative control, in students vaccinated with Pfizer-Biontech, Astrazeneca and Sinovac. In addition, considering gender and whether or not they had suffered COVID-19 prior to vaccination, did not detect a significant change either, except for the case that suffered from COVID-19 on dates close to the sampling and it was detected an increase in IgG.

IN-SILICO ANALYSIS OF MUTATIONS THAT ALLOW TRANSMISSION OF *AVIAN* INFLUENZA *A* VIRUSES TO HUMANS IN MEXICO

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Abstract:

Background: Gain-of-Function (GoF) are experiments in which a low pathogenic avian influenza virus is inoculated into ferrets, this allows the virus to adapt to the new host acquiring the ability to transmit between mammals. These experiments give us an insight into the mutations that an avian influenza virus needs to cross the species barrier and cause an epidemic outbreak or a new pandemic. So it is important to perform molecular surveillance to determine if these mutations could be occurring in nature. And finally, if any avian innfluenza virus is currently circulating in Mexico and contains any of these mutations.

Methodology: Mutations reported in GoF experiments published in the literature were compiled and subsequently compared in silico with sequences of HA, M1, M2, PA, PB1, PB2, NS1 and NS2/NEP proteins obtained from the Influenza Reseach Database gene bank of avian influenza viruses isolated in Mexico between 1973-2022, using Bioedit 7.2 and UGENE programs for sequence analysis.

Results: Seventy-six mutations were identified from gain-of-function studies. A total of 671 sequences of various avian influenza virus proteins isolated in Mexico were obtained, of which 400 were complete sequences and 271 partial sequences. After the analysis of these, the presence of 9 mutations (E89D, S113N and K387I in HA, D2N and V23A in NS1, D2N in NS2, R95K in M1, T81I in PB2, K26E in PA) reported (11.84%) in 177 sequences (139 for HA, 8 for NS1, 2 for NS2, 25 for M1, 2 for PB2, 1 for PA) was identified, representing 26.37% of the total sequences analyzed.

Conclusion: Although several mutations were found in several avian influenza virus proteins, these do not present, for the moment, a health risk to the population, since for the avian influenza virus to migrate from one species to another, it needs multiple mutations in different proteins simultaneously. The mutations obtained by GoF experiments may be occurring naturally in different hosts, so it is imperative to perform molecular surveillance of the different avian influenza viruses circulating in Mexico, in to prevent future Outbreaks.

STRUCTURE AND DIVERSITY OF BACTERIA AND PHAGES COMMUNITIES IN THE RHIZOSPHERE OF COMMON BEAN (*PHASEOLUS VULGARIS*)

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Abstract:

In this work we aim to study the bacterial and bacteriophages composition at the rhizosphere of common bean (*Phaseolus vulgaris*). To do this, we sampled two neighbor agriculture soils with and without previous history of cultivation. Samples were obtained before sowing the bean seeds, and 48 days after sowing (flowering stage). DNA was extracted from the soil samples and randomly sequenced with Hiseq 4000. After quality filter (Trim-Galore), we obtained an average of 80 million pair-end reads of about 150 pb per sample (17 samples in total). They were analyzed with the Kraken2 software and phyloseq R package to make taxonomic and abundance bacterial inferences. Bacteria alpha diversity in soil and rhizosphere shows H´= 7.05 and 4.02, respectively. Betha diversity showed that soil and rhizosphere bacterial communities are different with 81.9% of variance in the PCoA analysis. The soil community was dominated by *Actinobacteria*, but it decreases in presence of the plant. In the rhizosphere, the *Proteobacteria* phylum increased in abundance. To identify the viral part, the reads were assembled with MegaHit, the assembled reads were analyzed with Vibrant to predict phage sequences. Finally, we determine the similarity of the predicted phages with those known in databases, using a protein-sharing network approach with vContacT2. The viral families that predominated in the rhizosphere were *Siphoviridae*, *Myoviridae* and in less extent, *Podoviridae.* Phages related to *Proteobacteria* (*Pseudomonas*, *Rhizobium*, *Pantoea*, etc.) were found for the most part, indicating that there is a relationship between the abundance of bacterial genera and their associated viruses.

THE IRF3 AND IFI16 COMPONENTS OF INNATE IMMUNITY ARE INHIBITED IN ADENOVIRUS-INFECTED CELLS THROUGH THEIR RELOCALIZATION TO VIRAL REPLICATION COMPARTMENTS

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Abstract:

The cell responds to a viral infection through various innate antiviral mechanisms. One of the critical components of innate immunity is the activation of cellular proteins that induce the production of interferons (IFNs), which can interfere with various steps of the virus replication cycle. However, viruses have evolved mechanisms that inhibit the antiviral response of the cell. Adenoviruses (AdVs) are common infectious agents that are mainly associated with respiratory and gastrointestinal diseases, and are prominent candidates for gene and anticancer therapies, and vaccine vectors. These viruses possess a linear double-stranded DNA (dsDNA) genome, which upon entry into the cell activates the primary antiviral responses that involve sensing of dsDNA in the cytoplasm and in the nucleus, activating the cyclic GMP-AMP Synthase-Stimulator of Interferon Genes (cGAS-STING) pathway, the interferon gamma-induced cellular protein 16 (IFI16) and the interferon response factor 3 (IRF3). In turn, production of IFN also activates the Signal Transducer and Activator of Transcription (STAT-1). The antiviral response is efficiently blocked by viral proteins that repress transcription of IFN-stimulated genes allowing very efficient viral replication. Interestingly, we and others have found that in AdV-infected cells multiple cellular proteins are relocalized to virus-induced intranuclear sites where the viral genome is expressed and replicated. These sites are known as viral Replication Compartments (RC) and recent evidence from our group and others have found that they are essential for viral replication and virus-host cell interactions. In this work we have studied the reolcalization of IRF3 and IFI16 and have measured the expression of their target genes, ISG54, IFNb and IFNa, in HAdV-infected cells. Our results show that both of these key components of innate immunity were efficiently relocalized to RC, when the levels of the ISG54, IFNb and IFNa mRNA levels were reduced, indicating that IRF3 and IFI16 are inhibited

HIERARCHICAL PROTEIN SECRETION THROUGH THE INJECTISOME OF ENTEROPATHOGENIC *E. COLI*

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Abstract:

Enteropathogenic *Escherichia coli* (EPEC) is one of the main causative agents of infant diarrhea in developing countries. To accomplish the intestinal infection, EPEC relies on the Type III Secretion System (T3SS). The T3SS is a multiprotein nanomachine assembled in the bacterial cell envelope, which extends extracellularly to reach the host cell. Virulence effector proteins are translocated through this structure to hijack host signaling pathways, creating a favorable niche for the bacterium.

The T3SS is composed of several proteins that are assembled in a hierarchical order. This process is assisted by protein complexes known as molecular switches, which determine the order of secretion among three different T3-substrates, early, middle, and late substrates. The second molecular switch is a complex composed of the SepL, SepD and CesL proteins that regulates the secretion between middle and late substrates. Another protein complex that has been involved in recognizing and hierarchizing T3-substrates is the sorting platform, which is made up of the proteins EscK, EscQ and EscL. We have previously shown that the sorting platform is dispensable when T3-substrates are overproduced; however, the molecular mechanisms behind this phenomenon are poorly understood. In this work, we used a combination of biochemical and genetic approaches to describe the role of the sorting platform in T3SS biogenesis and orderly secretion. Overall, our results show a functional interconnection between the sorting platform and the second molecular switch for hierarchical secretion.

This work was supported by DGAPA/PAPIIT (IN212420) and CONACyT (284081) grants.

THE HUMAN ADENOVIRUS 36 E4ORF1 PROTEIN IS SUFFICIENT BUT IS NOT REQUIRED TO INDUCE ADIPOGENESIS IN INFECTED CELLS

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Abstract:

Adenoviruses are ubiquitous infectious agents that cause respiratory diseases, gastroenteritis, keratoconjunctivitis and have been reported as a potential factor of obesity. These viruses are one of the principal candidate vectors for gene and anticancer therapies, as well as vaccine vectors, such as those currently used for COVID-19.

Human adenovirus, species D, type 36 (HAdV-D36) can cause obesity in animal models and induces adipogenesis and increased adipocyte differentiation in cell culture. HAdV-D36 infection alters gene expression and the metabolism of the infected cells resulting in increased glucose uptake by the Glut4 glucose transporter, activation of the Ras/phosphoinositide-3-kinase (PI3K) pathway, and triglyceride accumulation by the up-regulation of Cytosine-Cytosine-Adenosine-Adenosine-Thymidine/Enhancer-binding proteins (C/EBPs) and peroxisome proliferator activated receptor γ (PPARγ). To date, the early adenoviral E4Orf1 protein has been associated with each of these effects. However, the adipogenic mechanisms altered by the E4Orf1 protein from HAdV-D36 have been evaluated in detail only in transfected cells, and it is not known whether the same activities may be affected by E4Orf1 in the context of the viral infection. Therefore, in this work we have evaluated the role of the E4Orf1 protein on adipogenesis and viral replication in HAdV-D36-infected cells, comparing the effect of the HAdV-D36 WT virus with that of a recombinant virus that does not express the E4Orf1 protein (HAdV-D36/DE4Orf1). The 3T3-L1 murine fibroblasts, which have been extensively used as an adipoctye model, were used in these experiments. HAdV-D36 infection of 3T3-L1 cells promotes proliferation and differentiation, but viral replication in these cells is abortive as indicated by undetectable expression of viral mRNA and a progressive loss of viral DNA. Therefore, we first established the conditions under which 3T3-L1 cells are permissive to infection and have found that only 3T3-L1 cells that are committed to adipocyte differentiation are permissive and support productive viral replication. Under such conditions viral mRNAs levels and viral DNA replication was measured by RT-qPCR and qPCR, respectively, and viral progeny production was determined by plaque assay in cells infected with either HAdV-D36 WT or HAdV-D36/DE4Orf1. The lipogenic effect of the E4Orf1 protein was evaluated with Oil Red O (ORO) staining; and expression of genes that control lipid metabolism was measured by RT-qPCR. The results showed that in 3T3-L1 cells that are permissive to the infection, the E4Orf1 protein is not required for expression of early or late viral mRNAs, nor for viral DNA replication or progeny production. Significantly, our data indicate that in the context of the viral infection of permissive 3T3-L1 cells the E4Orf1 protein was not required to induce the expression of the adipogenic genes C/EBPα, C/EBPβ or PPARγ, or intracellular lipid accumulation.

A NOVEL CORRELATIVE CONFOCAL FLUORESCENCE AND TRANSMISSION ELECTRON MICROSCOPY METHOD TO CHARACTERIZE EXTRACELLULAR VESICLES

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Abstract:

Extracellular vesicles (EVs) have received a great deal of attention in cell-to-cell communication studies. However, the characterization of these membranous particles remains a challenge. On the one hand, because of the size of EVs (generally < 200 nm), the spatial resolution with a conventional confocal laser scanning microscopy (CLSM) is not sufficient to resolve the nanostructures. On the other hand, in high-resolution techniques such as transmission electron microscopy (TEM), the presence of artifacts-like vesicles present in the sample can be interfering with the results. In this work, we propose a fast method to confirm the vesicular nature of EVs using a correlative light and electron microscopy approach (CLEM). To this end, the membrane selective dye FM1-43 (2 µM) was used to stain hypothetical EVs recovered from the filamentous fungus *Neurospora crassa*. For mounting the sample, red fluorescent beads were used as fiducial markers, together with stained EVs. All samples were first observed with x20/40 objective lenses under a CLSM FV1000 Olympus. After that, the samples were negatively stained for 10 min. The same regions observed with CLSM were analyzed with a TEM Hitachi H7500 (80-100 keV). CLEM results revealed that most vesicle-like structures (45.50 ± 21 nm) with membranous appearance observed in TEM overlapped with the green fluorescence signal. These results indicate that this CLEM approach is a reliable method to confirm the presence of EVs.

T6SS SECRETION MECHANISM AND NOVEL PROTEIN-PROTEIN INTERACTIONS OF TECA, A *BURKHOLDERIA CENOCEPACIA* TOXIN

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Abstract:

Burkholderia cenocepacia (Bc) is an environmental opportunistic pathogen that causes persistent, often severe, chronic lung infections in patients with cystic fibrosis and other underlying diseases.

The type VI secretion system (T6SS) is a transmembrane multiprotein nanomachine employed by many Gram-negative bacterial species to translocate, in a contact-dependent manner, effector proteins into adjacent prokaryotic or eukaryotic cells [1].

Bc employs a T6SS to survive in eukaryotic cells by disarming Rho GTPases and causing actin cytoskeletal defects. Bc protein TecA is a non-VgrG T6SS effector that is responsible for actin disruption in macrophages. TecA bear a cysteine protease-like catalytic triad, which inactivates Rho GTPases by deamidating a conserved asparagine in the GTPase switch-I region. RhoA deamidation induces Pyrin inflammasome activation [2].

Our goal is to dissect the detailed TecA secretion mechanism and the interacting partners inside the bacterial cytoplasm and the macrophages. In this study, we found that the effector protein TecA is directly translocated into macrophages by the T6SS and no chaperone or VgrG is required. By Co-IP/ MS analysis and pull-down assays, we found that TecA interacts with the T6SS tube protein Hcp, and remarkably with the sheath forming protein TssB. Our proposed model of T6SS protein recognition and secretion is discussed.

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MANNHEIMIA HAEMOLYTICA OMPH FUNCTIONS AS AN ADHESIN

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Abstract:

Mannheimia haemolytica is the causal agent of the shipping fever in bovines and in consequence a cause of high economical losses worldwide. As a pathogen, *M. haemolytica* must possess different attributes of virulence in order to get a successful infection. One of the main virulence factors that a pathogen express is adhesion molecules. Although this microorganism expresses different adhesins previously described, its participating components in this process are not totally known. In the present work, it is described the identification of a M. haemolytica 41 kDa outer membrane protein (OMP) taken part in bacterial adhesion. This protein interacts with biotin-labeled sheep fibrinogen suggesting its participation in attaching to host cells. The participation of the 41 kDa *M. haemolytica* OMP in host cell adhesion was demonstrated by interaction of this bacterium with bovine monocytes and a 45% diminishing in cell adhesion by previous incubation of *M. haemolytica* with a rabbit polyclonal serum raised against this protein. This protein was identified as OmpH by masses spectrometry. OmpH was immune recognized by a serum from bovines suffering acute or chronic pneumonia indicating its in vivo expression; also, it immune cross reacted with serum of rabbit infected with *Pasteurella multocida*, other pathogen commonly present in bovine pneumonia or shipping fever, indicating homology among proteins. Additionally, the presence of this protein in the biofilm is described, which could be an indicator of its participation during biofilm formation. *M. haemolytica* OmpH could be an important immunogen in bovine pneumoniae protection.

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ON THE ROLE OF THE ATPASE PROTEIN COMPLEX IN THE INJECTISOME OF ENTEROPATHOGENIC *ESCHERICHIA COLI*

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Abstract:

Type III secretion systems (T3SS) are essential interaction mediators between multiple bacterial pathogens (such as Salmonella, Pseudomonas, and enteropathogenic E. coli: EPEC) and host cells. Injectisomes or vT3SS, allow bacteria to inject virulence effector proteins into the cytoplasm of the host cell. EPEC injects these proteins to subvert host cell signaling pathways for its benefit. The bacterial flagellum, which is responsible for motility, is also assembled by a fT3SS, which is evolutionarily related to the vT3SS.

The injectisome and flagella share a core group of homologous proteins. Additionally, these components share sequence and structural similarities with proteins of the F-type ATPase. Some of the homologous structures in these molecular machineries are the components of the ATPase complex. In EPEC, EscN is the ATPase associated with the vT3SS, which is required to unfold and target substrates for secretion. EscN forms the ATPase complex together with EscL and EscO (FliH and FliJ in the fT3SS, respectively).

EscL negatively regulates the ATPase activity of EscN, in addition to forming a peripheral stalk. In contrast, EscO stimulates the ATPase enzymatic activity of EscN and forms a small antiparallel coiled coil structure in the center of the EscN homohexameric ring. ATP hydrolysis by the EscN-EscO complex is predicted to activate the conversion of the proton motive force into protein export, through an interaction between EscO and the export gate component EscU. However, the molecular mechanisms leading to central stalk ATPase-mediated activation of the T3SS are not fully understood.

In this work, we undertook an in-silico analysis of the T3SS ATPase C-terminal domain. Five conserved residues were identified in this domain common to all T3SS ATPases, and were substituted by site directed mutagenesis. In addition, two amino acids, that are conserved differently among vT3SS and fT3SS ATPases were also analyzed. vT3SS ATPase escN mutant was used to validate the relevance of these conserved residues. Moreover, we showed that swapping the differentially conserved residues between EscN and FliI ATPases results in impairment of the function of both proteins. Intrinsic ATPase activity of EscN was unaffected when conserved C-terminal residues were substituted. However, we revealed that nonfunctional versions of EscN could not recognize the EscO protein, resulting in impaired stimulation of EscN hydrolytic activity.

This work was supported by grants from DGAPA/PAPIIT IN212420 and CONACYT 284081.

ACTION MECHANISMS OF *ROUXIELLA BADENSIS* SER3 AGAINST POSTHARVEST FUNGAL PATHOGENS FROM A GENOMIC PERSPECTIVE

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Abstract:

Fungi are the main causal agents of postharvest diseases. As part of the microbiome of fruits and vegetables there are also beneficial microorganisms e.g., bacteria, that provide protection against the fungal pathogens, these are called biological control agents[1]. To use biological control agents and develop a product to avoid postharvest diseases, it is important to know the microorganism characteristics as well as the action mechanisms against the pathogens. Over the past decade the development of molecular techniques, like microarrays, high throughput sequencing and large-scale proteomics, have introduced new tools for the understanding of the mechanisms underlying the biocontrol properties of beneficial microorganisms[2].

In this work, bacterial strain SER3 was isolated from strawberry fruits, and it was capable to inhibit the growth of different postharvest fungi like: *Botrytis* spp., *Fusarium* spp., *Alternaria* spp., & *Penicillium* spp. *In vivo* assays on strawberry fruits showed that strain SER3 reduce the growth of *Fusarium* with a 76% and *Botrytis* with a 43%. SER3 genome sequencing revealed various features: genome size was: 5.08MB, GC content: 52.8%. Comparing 16S gene and using average nucleotide identity (ANI) & genome to genome distant calculator (GGDC) algorithms, SER3 showed closet homology to *Rouxiella badensis* with a similarity of 100%, 99% & 98% respectively. Using antiSMASH pipeline were identified gene clusters related to antibiotic and secondary metabolites production like siderophores, aryl polienes, polyketides, among others. These results show that *Rouxiella badensis* SER3 has biocontrol properties that can be used to avoid postharvest diseases.

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IMPLEMENTATION AND IMPROVEMENT OF THE CRISPR CAS 12A DETECTION SYSTEM FOR SARS-COV-2 DETECTION

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Abstract:

Coronavirus disease 2019, which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has attracted public attention. It is imperative to implement early-stage diagnostic for rapid and accurate detection of SARS-CoV-2 to contain the rapid trasmission of the ongoing COVID-19 pandemic. Methods based on CRISPR-Cas systems have been particularly promising because they can achieve a similar sensitivity and specificity compared to the golden standard RT-qPCR, especially when coupled with an isothermal pre-amplification step. We used the CRISPR/Cas12a-based collateral excision method for COVID-19 diagnosis using the Cas12a/crRNA complex for target recognition, with reverse transcription loop-mediated isothermal amplification (RT-LAMP) and the combination of crRNAs targeting SARS-CoV-2 RNA to improve the sensitivity and specificity of the method, produced the components for implementation and validated the method with clinical samples.

FROM CAP TO COLLAR-HOW THE ENDOCYTIC COLLAR IS ORIGINATED IN *NEUROSPORA CRASSA*

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Abstract:

Hyphal morphogenesis depends mainly on the establishment and maintenance of polarized growth. This is accomplished by the orderly migration and discharge of exocytic vesicles carrying cell membrane and wall components. We have been searching for evidence that endocytosis, an opposite process, could also play a role in hyphal growth, polarity maintenance and conidial germination. We analyzed proteins involved in the different stages of endocytic vesicles formation (MYO-1, ARP2/3, FIM-1, CRN-1) and their respective deletion mutants during the various stages of development in the filamentous fungus *Neurospora crassa*, utilizing laser-scanning confocal microscopy. We found that actin patches labeled with endocytic reporters accumulate in the apex of the germinating tube of conidia forming a cap. This position is maintained until the germ tube reaches about 150 microns and an elongation rate of 0.5 μm min^{-1}. Thereafter, patches begin to form a collar in the subapex, a conspicuous localization maintained in mature hyphae. Seemingly, the growing intensity of exocytosis in the apex displaces endocytic events to the subapex. This displacement may be necessary to maintain a balance between exo- and endocytosis in the course of hyphal development.

THE E1B-55KDA ONCOPROTEIN REGULATES ADENOVIRAL GENE TRANSCRIPTION

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Abstract:

Adenoviruses (AdVs) are infectious agents that cause acute respiratory infections, gastroenteritis and keratoconjunctivitis. These viruses infect numerous animal species, including humans (HAdVs), and are responsible for 5-7% of acute respiratory diseases and about 20% of gastroenteritis in children worldwide, as well as high mortality rates in immunocompromised patients. HAdVs have been used as vectors for gene therapy, vaccines, and anticancer therapies that are based on oncolytic viruses. As one of the main models of tumor virology, studies of the biology of HAdVs have led to key discoveries, including in the identification of tumor suppressors, cell cycle regulation, and regulation of gene expression. The HAdV genome encodes oncoproteins that can cooperate to induce cellular transformation and tumor formation interfering with the two main pathways that regulate cellular proliferation and apoptosis, the retinoblastoma (Rb) and p53 pathways. The HAdV E1A gene-products induce entry into the S phase of the cell cycle, activating apoptosis, which is then efficiently inhibited by the E1B-gene products, thus establishing conditions in the infected cell that are conducive to efficient viral replication or to oncogenic transformation. The E1B-55KDa (E1B) oncoprotein is one of the main candidates in the design of oncolytic viruses, as HAdVs recombinants that are null for expression of this protein have shown promising results in combined anticancer therapies. Nevertheless, the molecular activities that make the E1B-null HAdVs work as oncolytic viruses are not understood. The E1B is a multifunctional protein that is necessary for various steps of the adenoviral replication cycle, including viral DNA replication and viral gene expression, but the molecular mechanisms for each of these functions are not yet known. In this work we have studied the effect of the E1B on regulation of transcription of the HAdV gene promoters. Using a procedure that we recently established to isolate subnuclear fractions from HAdV-infected cells we measured the effect of E1B on viral gene transcription and used luciferase reporter assays to evaluate the direct effect of E1B on viral promoters. The results show that the E1B can either increase or reduce transcription by all HAdV promoters (early, intermediate and late promoters), a feature that has not been reported for any other protein encoded by a DNA virus and was only previously found for the HAdV E1A proteins. These novel findings are relevant because they help to better understand the HAdV biology and will contribute to improve the design of AdVs to develop new strategies for anticancer therapies and vaccines.

PROTEOMIC ANALYSIS REVEALS THE GLOBAL REGULATORY EFFECT OF THE BARA/SIRA AND CSRB/C SYSTEMS OF *SALMONELLA* TYPHIMURIUM IN CONDITIONS RELEVANT FOR VIRULENCE

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Abstract:

The BarA/SirA and Csr systems are present in many bacteria where control expression of genes encoding a wide diversity of cellular functions, such as carbon metabolism, motility, biofilm formation, quorum sensing, stress response, and virulence. BarA and SirA form a two-component system: BarA is the sensor kinase that autophosphorylates in response to environmental cues and then phosphorylates the response regulator SirA. Phosphorylated SirA activates the expression of the CsrB and CsrC non-coding RNAs, which have multiple binding sites for the RNA-binding protein CsrA. CsrA binds to sequences near the Shine-Dalgarno and the start codon of target mRNAs, thus blocking or favoring their translation and/or stability. Therefore, in most cases, the BarA/SirA system controls gene expression through the CsrB/C RNAs, which antagonize CsrA activity. However, some reports support that BarA/SirA can also act independently of CsrB/C and CsrA. The BarA/SirA and Csr systems positively regulate in cascade fashion the expression of the *Salmonella* pathogenicity island 1 (SPI-1), a cluster of genes required for *Salmonella* invasion of intestinal epithelial cells. BarA/SirA-CsrB/C positively regulates the expression of HilD, the master regulator of SPI-1, by antagonizing the negative effect of CsrA on *hilD* mRNA translation. To further investigate the regulatory role of BarA/SirA and Csr in *Salmonella*, we performed a LC-MS/MS label free proteomic analysis using the WT *Salmonella* Typhimurium strain and its isogenic Δ*sirA* and Δ*csrB* Δ*csrC* mutants grown in SPI-1-inducing conditions. The expression of 164 proteins was significantly upregulated or downregulated by the absence of SirA and/or CsrB/C. Most of these proteins were classified into different biological processes including virulence, motility, and metabolism; however, some of them are hypothetical. Our results show that SirA acts mainly through the CsrB/C system to control gene expression in *S*. Typhimurium. Interestingly, our analysis supports that SirA-CsrB/C simultaneously activates expression of SPI-1 genes and represses expression of genes required for the replication of *Salmonella* in the intestinal lumen (*pdu*, *eut*, and *cbi*). This inverse regulation could be involved in the generation of two *Salmonella* populations, genetically identical but phenotypically different, that cooperate to colonize the intestine of hosts.

PIGMENT-PRODUCING BACTERIA ISOLATED FROM MANGROVES LOCATED IN SISAL, YUCATAN

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Abstract:

Sisal is a picturesque small fisherman village located on the west side of Yucatán. It is surrounded by extensive and greenish Cienegas, which harbor great biological diversity. The Cienegas, the habitat of the gorgeous pink flamingos, is densely populated by four different species of mangroves[1]. Mangroves develop in the coastal plains of the tropics and subtropics, mainly around estuaries and coastal lagoons, near the mouths of rivers and streams. Latitudinal changes can have effects on different morphological attributes of plants and living organisms[2]. In the hypersaline mangroves of Sisal not only the macroscopic world is colorful, also the microscopic one since many inhabiting microorganisms have the capability to produce a plethora of vibrant pigments. However, the biotechnological potential of such microorganisms and derived pigments remains largely unexplored. Undoubtedly, pigments are molecules of high interest in food and cosmetic industry, and even in pharmacy since some natural pigments have antibiotic and UV protective properties[3-4]. Pigments can be defined as chemical substances that provide color to other materials due to the sunlight refraction[5]. Currently, most of the colorants are synthetic, posing a threat to human health, such as allergies and in some cases even cancer[6]. To avoid these dangers, current investigations are focused on natural alternatives to gradually substitute the synthetic ones with natural options, for example, at the present, microalgae and Lager type yeasts are used to produce industrial pigments[7]. In order to characterize pigment-producing bacteria we recollected sediment samples from mangrove roots in the Cienega of Sisal. Sediments were serially diluted and cultivated in A1 mangrove media and incubated at 27ºC for 14 days. Single colonies displaying pigment production were subcultured in solid media for macroscopic characterization and in liquid media for pigment production. Cultures were centrifuged, supernatants were extracted with solvents of different polarity, reduced to dryness *in vacuo*, and analyzed by thin layer chromatography. The pigment-producing bacteria library that we are generating is expanding day after day. Moreover, we are working in the chemical characterization of the pigments and analyzing their biotechnological potential.

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ANTIBIOTIC ACTIVITY OF ISOLATED BACTERIA FROM A SINKHOLE LOCATED IN SISAL, YUCATAN

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Abstract:

The Yucatan Peninsula harbors one of the largest karst aquifer networks in the world, with a surface area of 165 000 km^2 of permeable limestone [1]. Rainwater precipitation gradually dissolves the calcium carbonate, forming a groundwater network. The ongoing dissolution eventually leads to the collapse of the limestone [2]. This process generates sinkholes, locally known as cenotes, a word derived from the low-land Maya language 'tz'onot' that means cavern with water. Strikingly, there are over 2000 cenotes distributed throughout the Yucatan Peninsula. In the north, cenotes were formed by the impact of the Chicxulub asteroid creating a feature known as 'Ring of Cenotes' [3]. In the east, cenotes are associated with the Holbox fault, which formed open water bodies parallel to the coastline [4]. In these cenotes, seawater intrudes into the aquifer creating a peculiar habitat for microorganisms. Undoubtedly, sinkholes are fascinating ecosystems harboring microorganisms with different metabolic features than the terrestrial ones. In order to circumvent the global antibiotic resistance problematic, investigation efforts are focused on identifying novel metabolites with antibiotic activity in microorganism isolated from unexplored ecosystems as Sinkholes. In this sense, we performed scuba diving collection of sediment samples from a coastal sinkhole located in Sisal, Yucatan. Sediments were diluted and cultured in solid selective A1 marine media and incubated at 25ºC for two weeks. Single colonies from the recovered strains were inoculated in A1 marine broth and incubated with shaking at 150 rpm and 27ºC. The obtained supernatants were lyophilized and tested for antibacterial activity according to the M07-A10 document from the Clinical & Laboratory Standards Institute [5]. We identified two sinkhole bacterial isolates with remarkable antibiotic activity (Minimal Inhibitory Concentration = 30 µg/mL) against three different *Staphylococcus aureus* strains (ATCC 25923, 29213, and 6538). Further evaluations should be performed to determine the Minimal Bactericidal Concentration. Taxonomic assignations of the active bacterial strains will be performed *via* 16S rRNA sequencing.

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THE STRINGENT RESPONSE REGULATES THE PHB PRODUCTION IN *AZOTOBACTER VINELANDII*

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Abstract:

The stringent response is a mechanism that bacteria employ to regulate the gene expression under stress conditions such as deprivation of amino acids, phosphate or carbohydrates. The alarmone(p)ppGpp and the protein DksA are the main components of the stringent response. (p)ppGpp binds to the RNA polymerase at two different sites; the first is located between the β' and Ω subunits, and the second is on the secondary channel between β and β' subunits, being this binding site dependent on DksA protein.

Azotobacter vinelandii is a soil bacterium that synthesizes PHB, a biopolymer used to produce biodegradable plastics and biocompatible components. In this species, the PHB synthesis is positively controlled by the alternative sigma factor of general stress response RpoS, which is necessary for the transcription of the biosynthetic operon *phbBAC* and *phbR* (a specific transcriptional activator of *phbBAC*). In addition, *phbBAC* is negatively regulated at the post-transcriptional level by the RNA-binding protein RsmA (CsrA homolog). In this work, we aim to study the role of the stringent response in the PHB synthesis in *A. vinelandii*.

We constructed a mutant in the dksA gene and another strain unable to produce ppGpp (ppGpp^0) by interrupting the *relA* and *spoT* genes. The (p)ppGpp^0 and *dksA* mutants showed a reduction in the PHB content about 50 and 80 % compared to the wild-type strain, respectively. By qPCR experiments, we determined that the transcripts of *phbR*, *phbB* and *rpoS* are reduced in the *dksA* mutant. We further explored the effect of *dksA* mutation on *rpoS* expression by using transcriptional and translational reporter fusions and western-blot assays. We determined that the expression of rpoS is reduced mainly at the post-transcriptional level, which in turn, reduces the RpoS protein levels.

To confirm that the negative effect of the *dksA* mutation in the PHB synthesis is through RpoS, we complemented the dksA strain with a plasmid harboring *rpoS* gene under an inducible promoter. Unexpectedly, the complemented strain exhibited a partial restoration of the PHB levels compared to the wild-type strain, suggesting an additional regulatory pathway of the PHB synthesis by the stringent response. We identified that in the *dksA* strain, the expression of RsmZ1, a sRNA that counteracts the activity of RsmA, is also diminished.

Collectively, our results demonstrate that in *A. vinelandii*, the stringent response is necessary for the PHB synthesis, by controlling the expression of RpoS and RsmA activity.

EFFECT OF TWO MYCOBACTERIAL PROTEINS ON ALVEOLAR MACROPHAGES ACTIVATION DURING *MYCOBACTERIUM TUBERCULOSIS* INFECTION

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Abstract:

Aim of the study: During the early and progressive (late) stages of murine experimental pulmonary tuberculosis, the differential activation of macrophages contributes to disease development by controlling bacterial growth and immune regulation. Mycobacterial proteins P27 and PE_PGRS33 can target the mitochondria of macrophages. This study aims to evaluate the effect of both proteins in macrophage activation during mycobacterial infection.

Materials and methods: We assess both proteins for mitochondrial oxygen consumption, and morphological changes, as well as bactericide activity, production of metabolites, cytokines, and activation markers in infected MQs. The cell line MH-S was used for all the experiments.

Results: We show that P27 and PE_PGRS33 proteins modified mitochondrial dynamics, oxygen consumption, bacilli growth, cytokine production, and some genes that contribute to macrophage alternative activation and mycobacterial intracellular survival.

Conclusions: Our findings showed that these bacterial proteins partially contribute to promoting M2 differentiation by altering mitochondrial metabolic activity.

STUDY OF A FUNGAL ISOLATE THAT USES PLASTIC POLYMERS AS CARBON SOURCE

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Abstract:

Due to the current problem caused by the excessive consumption of single-use plastics and their poor final disposal, adverse effects on health and the environment have been observed. Within these problems, we can find the movement of invasive species using plastic as transport, production of toxic leachate, fragmentation of these plastics, and the production of microplastics and nanoplastics, which can enter the tissues. One way to avoid this problem is by biological processing of the polymer by enzymatic activities. We have a fungal consortium that has been kept in an aqueous suspension of PET, from which six different isolates were obtained. This work aims to characterize one fungal isolate and determine the possible enzymatic activities involved in using the plastic polymer as the only carbon source. The isolate was selected based on its growth in Mathur's minimal medium, using ammonium chloride as a nitrogen source and pulverized PET as a carbon source. It was incubated for two weeks (28 °C, 120 rpm). At the end of the incubation, the mycelium was recovered and inoculated on YPG-A at 28 °C for three days to verify its axenicity. Subsequently, the fungus was inoculated in different culture media to verify its radial growth and colonial morphology. Later, the fungus was inoculated in MMMs (28 °C, 120 rpm, three weeks), adding glucose or different plastic polymers (PET, PE, PP, and PS; as a carbon source at 0.03% w/v). At the end of the incubation, the cultures were centrifuged, and the cell-free supernatant was recovered. The fungal isolate grew in all the conditions tested, showing a more significant growth in the control and the medium added with PE. In the SN, the secreted protein and enzymatic activity were determined. The isolate presents morphological characteristics of *Aspergillus* and enzymatic activity mainly of b-glucosidase > esterase > lipase, depending on the culture conditions, medium with PE > PET > PS > PP. We consider it necessary to determine the proteomic profile of the isolate at different times and continue with its molecular identification.

ANTIVIRAL EFFECT OF *CHLORELLA SOROKINIANA* METABOLITES *IN VITRO*

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Abstract:

Microalgae such *Chlorella sorokiniana* are associated with benefical effects in human health. On the other hand, rotavirus is the main cause of gastroenteritis in children less than five years old worldwide. The aim of this study was to evaluate the activity of *Chlorella sorokiniana* metabolites against rotavirus *in vitro.* HT-29 cells were infected with rotavirus Wa (MOI 0.1) and treated with *Chlorella sorokiniana metabolites*; followed by viral titers determination by immunoperoxidase using specific anti-rotavirus antibodies. Results indicated that metabolites of *C. sorokiniana* reduced the rotavirus cytopathic effect in comparison with infected cells without treatment. Additionally, the viral titers in cells treated with *C. sorokiniana* metabolites were reduced significantly in 94%. Although more studies are needed, results suggest that *C. sorokiniana* might be used as an alternative treatment against rotavirus gastroenteritis.

GENETIC DIVERSITY AND MOLECULAR CHARACTERIZATION IN A SET OF CLINICAL STRAINS OF UROPATOGENIC *ESCHERICHIA COLI* PRODUCING BLEE

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Abstract:

Introduction: Urinary tract infections (UTIs) are a public health problem in Mexico and are the 3rd leading cause of morbidity in children, women of reproductive age and older adults. Approximately 50% of upEC ITUs in Mexico are multidrug-resistant (MDRs), with resistance profiles associated with the production of BLEE (β-extended spectrum lactamases).

Objective: To characterize the resistance profile, phenotypic production of BLEE, typify genes associated with virulence, phylogenetic group, presence of integrons, as well as determine the genetic diversity of a set of clinical strains of UPEC.

Material and methods: Antibiotic susceptibility was performed by the Kirby-Bauer method. Phenotypic expression of BLEE was confirmed by Hodge assay (CLSI, 2020).

Virulence potential at 17 genes, phylogenetic group, genotype O25b, presence of class 1 and 2 integrons, was performed by multiple PCR. Genetic diversity of the clinical strains was evaluated by ERIC-PCR.

Results: We included 29 clinical strains of *E. coli*, most isolated from the area of Nephrology (24%) and UTIs (100%). The antimicrobial susceptibility profile showed resistance to ampicillin, cephalotin and ciprofloxacin in 100%. Strains were sensitive in 100% to amikacin and imipenem and 89.7% to nitrofurantoin, 48.3% of the strains, showed an overall profile of MDR to 7 categories of antibiotics. Clermont's phylogroup D2 was the most prevalent in 34.5%, while 62% of the strains were identified with serogroup O25b. The genes with high frequency were, fimH in 93%, csgA, ecpA, motA and motB in 100%, intl1 in 100% and RV-intl1 in 34.5%. The analysis of the patterns by ERIC-PCR, confirmed a high genetic diversity among the UPEC strains producing BLEE, with ≥ 80% similarity. In addition, it was shown that there was a high similarity between 4 clinical strains from different areas of the HIMFG.

Conclusion: UPEC strains producing BLEE have pathogenic and resistance attributes that allow them to infect patients and persist in the hospital environment.

FUNCTIONAL CHARACTERIZATION OF A HYBRID PROTEIN METABOLIZING C-DI-GMP IN *AZOSPIRILLUM BALDANIORUM* SP245

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Abstract:

Azospirillum baldaniorum Sp245, a Plant Growth-Promoting Rhizobacteria. This bacterium promotes the growth and development of economically important crops, using several mechanisms such as phytohormone production, nitrogen fixation, phosphate solubilization, siderophores production (1).

Effective colonization of plant roots by *Azospirillum* plays an important role in growth promotion. It is now common knowledge that bacteria in natural environments persist by forming biofilms (2). Biofilms are highly structured, surface-attached communities of cells encased in a self-produced extracellular matrix, which protects bacteria from stress conditions and enhances bacteria-plant association (3). Cyclic diguanylate monophosphate (c-di-GMP) is a second messenger that regulates a variety of phenotypes, including biofilm formation, motility, and virulence in multiple bacteria. The molecule is synthesized from two molecules of GTP by diguanylate cyclases (DGC) containing a GG(D/E)EF domain; while its degradation is accomplished by phosphodiesterases (PDE) with two different EAL or HD-GYP domains (4). *A. baldaniorum* Sp245 genome encodes several GGDEF and EAL domain proteins (20 and 5, respectively), with a significant fraction (~10) predicted to be multidomain (e.g., GGDEF-EAL) enzymes containing an additional Per-Arnt Sim(PAS) sensor domain (5, 6). However, the biochemical activities and physiological functions of these multidomain enzymes remain largely unknown. Here, we present bioinformatic and biochemical analyses of a predicted PAS-GGDEF-EAL domain containing protein, AZOBR_40216, here named CdgH. For this purpose, we used the I-Tasser, UMD, and Chimera programs. We used the crystal structure of MorA and RbdA from *Pseudomonas aeruginosa* (4RNF, GXGD respectively) (7,8). In addition, we expressed, purified, and determined the PDE, and DGC activity of the recombinant protein expressed in *E. coli* BL21 with the plasmid pGEX4T-1, to measure the activities we used as substrates, bis-(p-nitrophenyl) phosphate (Bis-4pNPP) and [α-^{32}P]-GTP, respectively. Our data indicated that CdgH protein has phosphodiesterase activity only because this enzyme breaks down the phosphodiester bond from Bis-4pNPP. On the other hand, no diguanylate cyclase activity was observed in agreement with the *in silico* analyses.

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TESTOSTERONE EFFECT ON VIRULENCE FACTORS EXPRESSION OF ACTINOBACILLUS SEMINIS

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Abstract:

Actinobacillus seminis is a Gram-negative bacterium member of the Pasteurellaceae family, normal inhabitant of bovine, ovine and goat prepuces. This bacterium is also the causal agent of ovine epididymitis, orchitis and low fertility in rams worldwide. Epididymitis is mainly produced when ovines get sexual maturity and exist an increase in sexual hormones. It has been described that sex steroids interact with different pathogen microorganisms such as Escherichia coli, Pseudomonas aeruginosa and Candida albicans, modulating their virulence. This effect is unknown in *A. seminis*. In the present work, it was evaluated the effect of testosterone in the growth and expression of putative virulence factors of *A. seminis* strain ATCC 15768. The presence of testosterone (1-5 ng/mL) into the culture medium, improve the growth of *A. seminis* until a 50% with respect to medium without testosterone addition. Also, the presence of this steroid hormone induces the expression of two proteins of 23 kDa and 38 kDa and other of 25 kDa, putative adhesins, by their ability to interact with fibrinogen and fibronectin, respectively. Besides of this, testosterone induces the up expression of two proteins (75 kDa and 27 kDa) and down expression of a protein of 15 kDa in total cell extracts samples. *A. seminis* expresses a 37 kDa amyloid-like protein and its expression is affected (up or down) in the base of testosterone concentration used. This hormone does not affect neither the biofilm formation nor the quantity of formed biofilm. The effect of testosterone in the growth and expression of putative virulence factors of *A. seminist* could be important in pathogenesis of this microorganism.

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FUNGAL PUZZLE PIECE: CHARACTERIZATION OF CELL WALL PROTEIN ACW-1 IN *NEUROSPORA CRASSA*

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Abstract:

Neurospora crassa is a well-known model filamentous fungus that has been extensively used to elucidate basic eukaryotic molecular mechanisms. However, its cell wall, one of the key features that define its filamentous lifestyle, remains poorly characterized in terms of its proteome. More than 40 cell wall resident proteins (CWP) have been described so far. One of these proteins is ACW-1 (anchored cell wall protein 1, NCU08936), a glycosylphosphatidylinositol (GPI)-anchored protein that is a major component of the *N. crassa* cell wall. ACW-1 is homologous to Ecm33p (*S. cerevisiae*), which is a CWP known to be involved in the building and maintenance of the yeast cell wall. In contrast, the function of ACW-1 remains unknown. The functional characterization of CWPs is not only important to deepen the understanding of the cell wall and its role in fungal development, but it is also relevant for the implementation of biotechnological applications, like cell surface protein display technology, in these hosts. The objective of this work was to functionally characterize ACW-1. Its preliminary 3D structure prediction with AlphaFold (Jumper et al., 2021) revealed a highly ordered structure of conserved patterns of internal β-sheets. One of its bioinformatically found homologues is involved in the composition and maintenance of the cell wall in *A. flavus* (AFLA_113120). Morphologically, the absence of ACW-1 in a knock-out (*Δacw-1*) strain generated aberrant hyphal tips, even though it (2.43±0.21 mm/h) grew statistically like WT (2.60±0.19 mm/h, α=0.05). An effect was also observed under several cell wall-related stress conditions. The growth of *Δacw-1* was inhibited 80.19% in the presence of Calcofluor White (CFW, 0.45 mg/mL), a cell wall stressor that binds to cell wall chitin, as opposed to 75.71% in WT. Congo Red (CR, 0.2 mg/mL), which also binds chitin and β-1,3-glucans and disrupts chitin synthesis, also decreased 33.33% the growth of *Δacw-1* in contrast with 9.38% of WT. *Δacw-1* was otherwise more resistant to osmotic stress in NaCl 0.75 M (inhibition of growth of 79.63%) than WT (83.64%). ACW-1 was further tagged with green fluorescent protein (GFP) and imaged by laser scanning confocal fluorescence inverted microscopy. The fluorescent signal was mainly found on the most exterior section of the septa and hyphae, while no signal was detected in the Spitzenkörper. These results would suggest that ACW-1 may be an alternatively secreted CWP protein that is structurally required for cell wall integrity. Further characterization of ACW-1 is needed to expand the knowledge of the cell wall of *N. crassa,* and to be able to exploit this biotechnologically attractive fungus in an industrial manner.

Jumper, J., Evans, R., Pritzel, A. et al. Highly accurate protein structure prediction with AlphaFold. Nature 596, 583–589 (2021). https://doi.org/10.1038/s41586-021-03819-2

STUDY OF PROKARYOTIC DIVERSITY AND FUNCTIONAL MARKERS GENES INVOLVED IN THE HYDROCARBON DEGRADATION AND THE ANTIBIOTIC RESISTANCE IN SEDIMENTS OF THE COAST OF BAJA CALIFORNIA

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Abstract:

Prokaryotic diversity and the presence of functional marker genes can be used as indicators of ecosystem health and the exposure of microorganisms to various types of pollutants, respectively. The coast of Baja California (CBC) is an area with a high anthropogenic activity where different contaminants such as hydrocarbons and antibiotics can be introduced.

During the Bight 2018 campaign, 33 marine sediment samples were taken along the CBC. The environmental DNA was extracted and used as a template to amplify A) the V3-V4 region of the 16S ribosomal gene and B) functional marker genes related to the degradation of hydrocarbons and antibiotic resistance. Using the Illumina platform, a massive sequencing of the amplicons of the 16S-V3-V4 region was carried out. The sequences were processed and analyzed with the software Qiime2. Bioinformatic analysis revealed that the prokaryotic diversity (bacteria and archaea) present in the CBC comprises 68 phyla. Proteobacteria is the most abundant phylum, followed by Bacteroidetes, Crenarchaeota, and Acidobacteria. Genes encoding for alkane hydroxylase (alkB), toluene-biphenyl dioxygenase(T-B), and polyaromatic hydrocarbon ring hydroxylating dioxygenases (PAH-RHD) were used as functional marker genes involved in hydrocarbon degradation; and the genes *sul1*, *CTX,* and *qnrS* were used as antibiotic resistance marker genes. The presence of all genes was searched in the 33 marine sediment sample using end-point PCR. The amplicons of genes involved in hydrocarbon degradation were observed in 10 (*alkB*), 3 (*T-B*), and 2 (*PAH-RHD*) stations. In contrast, the genes involved in antibiotic resistance were presented in 16 (*sul1*), 22 (*CTX*), and 8 (*qnrS*) stations.

The results allowed us to know the areas where these marker genes are present and associate them with the existing microbiota, as well as to elucidate if there is a relationship between the marker genes analyzed and the areas with evidence of high anthropogenic activity.

ISOLATION AND CHARACTERIZATION OF BACTERIOPHAGES WITH THERAPEUTIC POTENTIAL TO COMBAT MULTIDRUG-RESISTANT *PSEUDOMONAS AERUGINOSA* INFECTIONS

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Abstract:

Given the alarming increase in the incidence of nosocomial infections caused by multidrug-resistant (MDR) opportunistic bacterial pathogens such as *Pseudomonas aeruginosa* and others from the group called ESKAPE, there is an urgent need to implement new effective therapies to combat them. Otherwise, it is projected that by 2050, MDR bacterial infections will be the first cause of death all over the world, setting the stage for the arrival of the *post-antibiotic* era.

In this regard, one of the most promising alternative therapies is the use of bacteriophages, also known as phages, which are viruses that infect bacteria. This proposal is based on using phages to direct a selective attack and kill the target bacteria that cause the disease, amplifying exponentially after each cycle of infection to achieve this purpose.

As part of the alternative strategies to the use of antibiotics to combat infections caused by multidrug-resistant *P. aeruginosa* strains, bacteriophage therapy is promising and has proven successful in multiple reported clinical cases. Therefore, the present work focuses on the identification and characterization of new bacteriophages with effective potential to eliminate this type of strains.

Population to study: The reference strains of *P. aeruginosa* Pa14 and PaO1 will be used, an environmental strain called PaΦ susceptible to phage infection and sensitive to the action of antibiotics, in addition to 10 clinical strains from patients with pneumonia MDR of the Hospital de Especialidades Centro Médico Nacional Siglo XXI, donated by Dr. Rosario Morales Espinosa. And bacteriophages isolated from wastewater.

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METABOLIC CAPACITY FROM *RAHNELLA* SP. TO DEGRADE XYLAN, A DOMINANT GUT SYMBIONT OF *DENDROCTONUS* SPECIES

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Abstract:

Rahnella sp. ChDrAdgB13 is the main member of the gut bacteriome core of *Dendroctonus* species, one of the most destructive pine forest bark beetles. Their high dominance and abundance, indicates that play an important role in the ecology and biology of these beetles through functions such as esters and lipids degradation, recycling uric acid and biotransform the monoterpenes present in the host trees. The aims of this study were to identify in *Rahnella* sp. ChDrAdgB13 genome the glycosyl hydrolase (GH) families involved in carbohydrate metabolism and specifically, the genes that participate in xylan degradation, to determine the functionality of a putative xylanase-ferulic acid esterase (R13 Fae) and biochemically characterize this enzyme. The carbohydrate-active enzymes prediction on the genome of *Rahnella* sp. ChDrAdgB13 revealed 25 glycoside hydrolases, 20 glycosyl transferases, four carbohydrate esterases, two auxiliary activities, one polysaccharide lyase and one carbohydrate-binding module. R13 Fae, showed amino acid identity of 67.8–99.9% to the putative esterase and glycosyl hydrolases from *Rahnella* species. The R13 Fae has 393 amino acid residue protein (43.5 kDa), with a theoretical pI of 5.94, a signal peptide of 26 amino acid residues, carbohydrate esterase (CE) catalytic domain, and carbohydrate binding module 48 (CBM48). Docking showed that R13 Fae presents a higher binding affinity to ferulic acid, α-naphthyl acetate and arabinoxylan and low binding to starch. This same affinity was observed with the R13 Fae recombinant. The purified recombinant R13 Fae enzyme showed optimal activity at pH 6.0 and 25ºC, stable at pH value from 4.5-9.0, and exhibited a half-life of 23 days at 25ºC. The enzyme was stable in the presence of metallic ions, except for Hg^{2+}. The final principal products of R13 Fae mediated hydrolysis of beechwood xylan were xylobiose and xylose, manifesting an *exo*-activity. These results suggest that *Rahnella* sp. ChDrAdgB13 hydrolyse xylan and its host and other gut microbes could assimilate its products as a nutritional source.

EXPLORING THE BACTERIAL ABILITY TO INTERACT WITH AS(III): AN AFFORDABLE SOLUTION FOR DECENTRALIZED WATER TREATMENT SYSTEMS

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Abstract:

For many years the mining tradition and the geological characteristics of Mexico, have contributed to the release and concentration of arsenic (As) in the environment. The lack of available technologies to remove As from contaminated water is one of the main factors that compromises the drinking water supply for the rural population. The rural areas and big cities' peripheries are the most affected, with around 2 and 3 million inhabitants are in risk (1, 2). The above is due to the lack of economic resources, the feeble development of environmental public policy, and the complex technification and environmental impacts of the conventional technologies to remove As from water. Physicochemical treatments are among the most efficient processes for this purpose, unfortunately, they are not affordable to decentralize water treatment systems (3, 4). The combination of biological mechanisms such as bacterial arsenite As(III) oxidation and Physico-chemical processes (adsorption) with natural materials such as pellets and bacterial biomass could represent an available option to remove As. These technologies are based on the environmental, social, and economic characteristics of the study site which are the rural areas of Xichu, Gto. Mexico. The present work focuses on the characterization of bacterial As(III) oxidation and biosorption mechanism by *Rhodococcus (R.g)*, *Exiguobacterium (E.i)* and *Microbacterium (M.h)* strains, which were able to oxidize As(IIII), corroborated by the $AgNO_3$ test and the amplification of *aox* genes. By FTIR it were identified some groups involved in the passive process of As(III) adsorption (-OH, -C=O, -NH, C-H). On the other hand, the percentage of A(III) removal by bioaccumulation in the strains was: 73% for *M.h* and *E.i* and 75% for *R.g* ($P<0.05$). The bacteria under study are the bases to develop an affordable water treatment for decentralized systems.

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GLOBAL TRANSCRIPTOMIC RESPONSE OF *ESCHERICHIA COLI* TO P-COUMARIC ACID

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Abstract:

p-Coumaric acid (p-CA) is the first intermediate of the phenylpropanoid pathway in plants, and it is a precursor of lignin monomers and other polyphenolic compounds. The aromatic acid p-CA is a precursor for compounds used in industry and it has a positive effect on human health. Due to the complex purification processes to obtain p-CA from plant material, there is an interest to produce this compound in recombinant *Escherichia coli* strains.

To determine the physiologic response of *E. coli* W3110 to p-CA, dynamic expression analysis of selected genes as well as RNA-seq and RT-qPCR experiments were performed.

To define a time response of p-CA for transcriptomic analysis, transcriptional fusions of selected genes to a fast fold GFP were used. Promoters of genes *aaeXAB* and *marR*, involved in toxic compound resistance, were induced two-fold over control at 20 minutes. Promoters of genes *clpB, clpP, dnaK* and *inaA*, encoding chaperone proteins, were induced two-fold at 40 minutes.

Transcriptomic analyses at 20 and 60 minutes after p-CA addition were performed. The observed transcriptional profile revealed the induction of genes involved in functions related to p-CA active export by the *aaeXAB* efflux system, synthesis of cell wall and membrane components, synthesis of amino acids, detoxification of formaldehyde, phosphate limitation, acid stress, protein folding and degradation. Downregulation of genes encoding proteins involved in energy production, carbohydrate import and metabolism, as well as several outer and plasma membrane proteins was also detected. This response is indicative of cell envelope damage causing the leakage of intracellular components including amino acids and phosphate-containing compounds.

The cellular functions responding to p-CA that were identified in this study will help in defining targets for production strains improvement. The transcriptional fusion of the *aaeXAB* operon could be used as a p-CA biosensor.

EXPRESSION OF HISTONE MODIFYING ENZYMES OF *PHYTOPHTHORA CAPSICI* DURING PLANT-PATHOGEN INTERACTION

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Abstract:

Phytophthora capsici is a plant pathogen oomycete that causes root, foliar, and fruit rot in a wide range of Cucurbitaceae and Solanaceae hosts. Although this pathogen affects a broad range of crops, the molecular mechanisms underlying *P. capsici* infection are not completely understood. Recently, different epigenetic marks such as histone methylation have been reported in *Phytophthora* species regulating this pathogen's virulence (Rojas-Rojas & Vega-Arreguín, 2021). Histone methylation allows a reversible response due to regulation by histone methylases (HMT) and demethylases (HDM), and changes in these proteins could regulate the pathogen´s evasion of the plant immune response. Thus, the expression patterns of these proteins could regulate plant pathogens' virulence. Here we used assays to identify the accumulation of reactive oxygen species and cell death during the infection of *P. capsici* in *Nicotiana benthamiana* and *Cucurbita pepo*. The pathogen demonstrated a pattern of infection in both hosts inducing a hypersensitive response (HR). We also extracted RNA from host leaves during plant-pathogen interaction and by RT-qPCR we determined that genes coding for enzymes HMT and HDM, related to the epigenetic mark H3K4me3, showed changes in their expression at different post infection times in both, *N. benthamiana* and *C. pepo*. Our results suggest a putative role of the epigenetic mark H3K4me3 in the virulence of *P. capsici*.

Rojas-Rojas, F. U., & Vega-Arreguín, J. C. (2021). Epigenetic insight into regulatory role of chromatin covalent modifications in lifecycle and virulence of Phytophthora. *Environmental Microbiology Reports*, *13*(4), 445-457.

REGULATION OF PHB (POLYHYDROXYBUTYRATE) SYNTHESIS BY THE GACA-RPOS PATHWAY IN *AZOTOBACTER VINELANDII*

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Abstract:

The sensor kinase GacS and the response regulator GacA are members of a two-component system that is present in a wide variety of gram-negative bacteria. The GacS/GacA system controls the production of secondary metabolites and extracellular enzymes involved in pathogenicity to plants and animals, biocontrol of soilborne plant diseases, ecological fitness, or tolerance to stress. In *Azotobacter vinelandii* GacA activates transcription of *RsmZ* and *rsmY* sRNAs. These RNAs counteract the repressor activity that RsmA protein exerts on the translation of mRNAs involved in the synthesis of polyhydroxybutyrate (PHB) and alkylresorcinols (ARs). The synthesis of PHB and ARs is also controlled by the PTS^{Ntr} global regulatory system composed by EI^{Ntr}, Npr and $EIIA^{Ntr}$ Enzymes that participate transferring a phosphoryl-group from phosphoenolpyruvate to $EIIA^{Ntr}$. When unphosphorylated, the EIIANtr protein impairs the synthesis of PHB and ARs. The gene inactivation of both *rsmA* and *ptsN* genes (codifying for RsmA and $EIIA^{Ntr}$ proteins respectively) in the mutant *gacA-* failed to restore its capability to produce PHB and Ars.

Related to the later, this work characterized the effect of GacA on PHB synthesis in *A. vinelandii*. *GacA* inactivation reduced the stability of the protein related to the sigma factor during stationary phase, RpoS, which is necessary for the activation of the transctription of both synthesis genes PHB and Ars. The degradation of RpoS by clpP appears to be an independent effect from non-phosphorilated $EIIA^{Ntr}$.

On the other hand, the mutations performed in *clpP* restore the stability of RpoS, the transcripts of *phbR* but not the ones in *phbB* in the *gacA-* strain. Overall, these results suggest that GacA regulates the synthesis of PHB to a pos-transcriptional level in both *phbR* y *phbB* genes. This later being mainly a result of RsmA abundance, due to the lack of small RNA's transctription in a *gacA-* background.

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Mueriel-Millan, Moreno, S., Monterrosa, R. G., & Espin, and G. (2017). *Unphosphorylated EIIANtr induces ClpAp-mediated degradation of Rpos in Azotobacter vinelandii*. 1–50.

IDENTIFICATION AND CHARACTERIZATION OF BIOCONTROL AGENTS FROM AMPHIBIANS SKIN AGAINST *BOTRYTIS CINEREA*

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Abstract:

Plants are exposed to multiple organisms that can be both beneficial and pathogenic. One of the pathogens to which they are susceptible is the necrotrophic fungus *Botrytis cinerea*, which causes gray rot or gray mold disease. For many years, chemical fungicides have been used as infection control agents. However, their frequent use has been questioned because of their harmful effects on the environment and human health. This has led to the search for new ecological alternatives, such as the use of biological control agents (BCA) or biostimulants that can inhibit the growth and development of plant pathogens. Bacterial communities have been found to exist in the skin of frogs, which can protect them from infections caused by the fungus *Batrachochytrium dendrobatidis*, a pathogenic chytrid fungus implicated in worldwide amphibian declines. However, it is unclear whether these bacteria have the function of preventing and curing diseases caused by pathogenic fungi. In this work, we explored whether neotropical amphibian skin bacteria have the activity to control the development of the pathogen *Botrytis cinerea*. Through dual experiments, we identified 3 potential candidates for biocontrol activity. In addition, the compounds released by the bacteria can inhibit the germination process, and it was determined that the inhibition is dose-dependent. We also observed that the bacteria and filtrates confer a protection system in the model plant *Arabidopsis thaliana* against *B. cinerea* infection. Our results showed that bacteria from amphibian skin may have excellent potential to control diseases caused by phytopathogenic fungi affecting plants.

Keys words: bioestimulants, frogs, *Botrytis cinerea, Arabidopsis thaliana*

A NOVEL MARINE PSEUDOMONAS SPECIES WITH ANTIBACTERIAL ACTIVITY

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Abstract

Antimicrobial resistance (AMR) represents a serious threat to global health. The development of new drugs to combat infections caused by bacteria resistant to multiple or even to all available antibiotics is urgent, including those bacteria denominated by the World Health Organization as priority pathogens1. Most antibiotics used up to date have been identified from soil microorganisms. The marine environment represents an alternative source with a great potential for the identification of microorganisms that produce bioactive molecules, including antibiotics. In this study, we explored the Gulf of Mexico (GoM), the ninth largest body of water in the world, for the identification of bacterial strains showing antibacterial activity against priority pathogens. We analyzed the antibacterial activity of a collection of 82 bacterial strains isolated from marine water and sediment samples from the Southwestern GoM2. Interestingly, from this analysis we found eight Pseudomonas strains that show antibacterial activity, seven of these strains were identified as P. aeruginosa and the other one as P. sihuiensis, by phylogenetic analysis of the 16S rRNA gene sequence using the EZBioCloud database. P. aeruginosa is known to produce the molecule pyocyanin, which present antibacterial activity. The P. sihuiensis strain inhibited the growth of different pathogenic bacteria, including the priority pathogen multidrug-resistant Staphylococcus aureus. The sequencing and analysis of its genome revealed that the putative P. sihuiensis strain is in fact a novel Pseudomonas species that we denominated Pseudomonas sp. GOM7. Phenotypic and genomic analyses indicate that Pseudomonas sp. GOM7 does not produce pyocyanin and that it has a reduced pathogenicity compared with P. aeruginosa. Identification of the molecule(s) with antibacterial activity synthesized by Pseudomonas sp. GOM7 is a matter of our current investigation.

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A BACTERIAL CONSORTIUM ISOLATED FROM A MAYAN SINKHOLE PRODUCES METABOLITES WITH ANTIBACTERIAL ACTIVITY

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Abstract:

Bacterial consortiums (BCs) are amazing assemblages orchestrating a plethora of reactions in favor of the community. As result, a myriad of secondary metabolites are produced and some of them can have interesting biological activities, especially in the search of antibacterial molecules[1]. Despite BCs are ubiquitous, the interest in study them looking for antibiotics production is scarcely explored. It is even more rare when we talk about BCs inhabiting uncommon environments such as sinkholes. Sinkholes are not only breathtaking touristic attractions but also highly dynamic ecosystems harboring microorganisms with different metabolic features than the terrestrial ones[2]. In this work, we focus on characterizing in terms of metabolite profile, antibacterial activity, and taxonomic assignation a bacterial consortium isolated from the Mayan sinkhole named "Pol-ac", located in Sisal, Yucatan. Sinkhole sediments were collected by scuba diving and employed to inoculated cultures in A1 sinkhole broth selective media. After two weeks of incubation, cultures were harvested and centrifuged. The obtained pellet was employed for cryopreservation, subculturing and isolation of the strains composing the BC. The supernatant was extracted exhaustively with ethyl acetate and rotaevaporated *in vacuo* until dryness to obtain the BC crude extract. The obtained crude extract was tested for antibacterial activity, according to the M07-A10 document from the Clinical & Laboratory Standards Institute[3]. The results showed remarkable activity against *Staphylococcus aureus* ATCC 25923 (Minimal Inhibitory Concentration = 14 µg/mL). The metabolite profile of the crude extract was analyzed using a HPLC Agilent 1260 II system equipped with a C18 column (Agilent Eclipse XDB-C18, 5 µm, 4.6 × 150 mm, Santa Clara, US), operated at isothermal conditions at 30ºC, at 0.8 mL min^{-1} flow and using an elution gradient. For the taxonomic assignations of the isolated strains composing the BC, genomic DNA was isolated and employed as template for the amplification of the whole 16S rRNA gene, and further Sanger sequencing. Bacterial strains belonging to the genus *Halomonas*, *Bacillus*, and *Streptomyces* were assigned. The metabolite profile analysis is ongoing for the identification of the main compounds. Further combinatorial studies should be performed to determine synergic or additive effects, regarding the antibiotic metabolite(s) production.

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IMPROVING PRODUCTION OF THE BIODEGRADABLE PLASTIC POLYHYDROXYBUTYRATE IN *AZOTOBACTER VINELANDII*: THE ROLE OF THE PHASINS PROTEINS PHBP2 AND PHBP3

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Abstract:

Polyhydroxybutyrate (PHB) is a natural polyester synthesized by *Azotobacter vinelandii*. This polymer can be used industrially as biodegradable plastic. PHB accumulates intracellularly in the bacterium in the form of granules when the carbon source is abundant, serving as a carbon and energy reserve for the bacterium, and is degraded when the carbon source is depleted. The PHB granules are surrounded by several proteins: those involved in PHB metabolism, both in its synthesis or degradation (1), and other proteins called phasins, that constitute the major protein content on the PHB granule but do not have enzymatic activity. However, phasins can modulate the PHB synthesis or degradation enzymes in some PHB producing bacteria (2). This work focuses on determining the role of PhbP2 and PhbP3 phasins in the PHB metabolism of *A. vinelandii*.

To determine the role of PhbP2 and PhbP3, kinetics of growth and accumulation of PHB of mutants/strains with phbP2 and phbP3 genes inactivated, complemented, and overexpressed, were compared. In addition, PHB depolymerase activity assays of the wild-type strain OP and the mutant strains were performed. The results indicate that the absence of phbP2 causes a decrease in PHB degradation, which could be related with a low PHB depolymerase activity. With respect to PhbP3, the OP-PhbP3- mutant strain accumulated less PHB compared to strain OP, which would agree with increased PHB degradation due to high PHB depolymerase activity; however, the expression of PhbP3 protein in a heterologous system (E. coli), together with the PHB biosynthetic enzymes, considerably increased PHB synthesis, showing a stimulatory role on PHB synthesis instead of a control of depolymerization. With the results obtained in this work we can say that by manipulating expression of PhbP2 and PhbP3 phasins it is possible to increase the production of biodegradable bioplastics in *A. vinelandii*. The putative role of both proteins will be discussed.

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PARTICIPATION OF PROTEINS AAESEP1 AND AAESEP2 IN THE BIOGENESIS OF LIPID DROPLETS IN MOSQUITO CELLS INFECTED WITH DENGUE VIRUS

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Abstract:

Septins are a family of GTP-binding proteins that are involved in various cellular processes, including vesicular trafficking, cytokinesis, membrane remodeling, and innate immunity. In the liver derived HUH7 cell line, infected with the hepatitis C flavivirus (HCV), it has been shown that septin 9 participates in the biogenesis and transport of lipid droplets (LD), which are essential for virus replication, and the absence of septin 9 during infection affects both LD production and viral proliferation. Considering that *Aedes spp.* mosquitoes are the main vectors of flaviviruses, the objective of the present work was to study, in an *A. aegypti* mosquito cell line (Aag2), the expression of septins AaeSep1 and AaeSep2, their possible functions during LD biogenesis and their dynamics during the infection with dengue virus (DENV). To analyze septin expression during DENV infection, mosquito cells were cultured in 24-well plates until 70-80% confluence, subsequently, they were infected with DENV (MOI: 3) and cell lysates were obtained every 12 hours of infection, to measure the expression of septin AaeSep1 and AeSep2, by Western Blot, using specific, heterologous anti-septin AaeSep1 and AaeSep2 antibodies

For the analysis of the septins in lipid droplets biogenesis during DENV infection, the cells were cultured on coverslips, infected at 24 and 48 hpi, and they were processed for immunofluorescence assays, using the anti-septin AaeSep1 and AaeSep2 antibodies, red Nile stain to label lipid droplets and an antibody directed against protein C was used to monitor infection. Colocalization was indicative of interaction. To assess the role of Septins in LD biogenesis during viral proliferation, mosquito cells were grown on coverslips in 24-well plates, transfected for 24 hours with siRNAs directed against Septins AaeSep1 and AaeSep2, and then infected with DENV (MOI:3) for 48 hours. Cells were fixed and immunostained for Septins localization and with Nile red for LD quantification while the supernatants from silenced and infected cells were collected and titrated by foci formation assays in BHK21 cells. It was observed that Aag2 cells expressed the Septins AaeSep1 and AaeSep2, colocalizing with lipid droplets, but only AaeSep2 showed expression changes during infection with DENV. Furthermore, it was observed that AaeSep1 silencing affects LD biogenesis and viral proliferation, while AaeSep2 affects only viral proliferation, indicating that septin AaeSep1 and AaeSep2, have different specific functions in normal cells but both proteins are necessary for viral proliferation, possibly in virus replication.

EXTRACELLULAR VESICLES FROM *NEUROSPORA CRASSA*: VEHICLES FOR CELL WALL-RELATED PROTEINS

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Abstract:

Neurospora crassa has been used for many decades as a model organism in molecular biology and biochemistry of filamentous fungi. However, despite all the existing knowledge, there is a lack of information on the presumable biogenesis of extracellular vesicles (EVs) and their role during vegetative cell growth and development of this fungus. Thus, we set out to analyze the proteome of EVs during vegetative growth of a wild-type strain of *N. crassa* (FGSC #988). Mycelium from a 48h culture, grown in Vogel minimal medium supplemented with sucrose as carbon source and incubated at 30°C and 150 rpm, was filtered out. The EVs of the filtrate were pelleted by differential centrifugation with the last step at 100000*g* for 2h. The pellet was resuspended with lysis buffer or 20 mM Tris-HCl (pH 7.2). EVs dimensions were determined by transmission electronic microscopy (TEM) and their hydrodynamic diameter (Hd) by Dynamic Light Scattering (DLS). The proteins were separated by SDS-PAGE and analyzed by LC-MS/MS. According to the DLS, the Hd of EVs ranged from 21 to 295 nm. However, if considering the particles with >5% in the sample, the average Hd was 63.08 ± 24.97 nm; these represent the 88.64% of total particles measured in the sample. The average EVs diameter by TEM was 34.66 ± 9.96 nm. On the other hand, the identified proteome consisted of 252 proteins. Among the identified ones, a high number of proteins are related to cell wall synthesis and remodeling. Diverse proteins have transmembrane domains including some glucanosyltransferases and one cellular morphogenesis protein. Also, a set of Anchored cell wall proteins (3, 4, 5, 8, 11, and 12), cell wall protein PhiA and CCG-14 (these last are both the most abundant in the proteome of the analyzed EVs) are related to the biogenesis of cell wall (1-2). Hence, it is suggested that EVs are fundamental to transport diverse proteins that are used for the cellular growth of *N. crassa*, mainly in cell wall biogenesis-related processes.

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INSIGHTS INTO THE MECHANISM USED BY A BACTERIAL COMMUNITY TO DEGRADE LIGNOCELLULOSE

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Abstract:

In nature, lignocellulose degradation is part of the global carbon cycle making carbohydrates available for different heterotrophs. Fungi and bacteria communities efficiently deconstruct lignocellulose using carbohydrate-active enzymes (CAZy). There is a wealth of biochemical knowledge on fungi lignocellulose degradation; however, bacterial mechanisms are less studied. Consortium PM-06 is a bacterial community obtained by enrichment of the nixtamalized maize pericarp (abundant residue from the tortilla industry) native microbiota. This community degrades 80-90% of nixtamalized maize pericarp (NMP) in 192 h of culture. In this work, biochemical and multiomic approaches were used to get insight into the degradation mechanism of NMP by consortium PM-06.

PM-06 is a low diverse community where the most abundant species (86%) at the moment of maximum degradation were Aneurinibacillus migulans, Paenibacillus macerans, Bacillus coagulans, Microbacterium sp., and Bacillus thuringiensis. This consortium metabolized NMP using hemicellulases, cellulases and oxidoreductases. Metatranscriptomic profiling showed the expression of a great proportion of modular enzymes operating at the proximity of the insoluble substrate. Metascretomic analysis evidenced the presence of soluble enzymes participating in the saccharification of molecules released by modular enzymes. Lignin was consumed in the last stages of the culture; however, sequences of laccases or peroxidases were not detected. PM-06 members divided activities and established synergistic relationships to favor lignocellulose degradation. Paeanibacillus and Bacillus mainly degraded high molecular weight molecules while Microbacterium, Nocardia and Leifsonia metabolized soluble molecules and produce oxidoreductases. Degradation occurred on the surface of the substrate where microorganisms and modular enzymes were attached producing soluble molecules that were further metabolized by soluble enzymatic systems. In PM-06, oxidoreductases played key roles in degradation, one of them was to produce hydrogen peroxide a co-substrate for different enzymes, and a reactant for the formation of free radicals via Fenton reactions. In addition to enzymes, PM-06 uses free radicals to cope with polysaccharide and lignin recalcitrance This study describes a microbial tool for the utilization of a plentiful tortilla residue and provides information about mechanisms used by bacteria for the degradation of lignin and other recalcitrant molecules.

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PROPOSAL OF A SCREENING SYSTEM FOR HUMAN PAPILLOMA VIRUS (HPV) IN SEXUALLY ACTIVE MEN IN THE STATE OF VERACRUZ

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Abstract:

Human Papillomavirus (HPV) is a double-stranded, non-enveloped DNA virus with a diameter of 55 nm and a circular genome of approximately 8,000 base pairs that is divided into three main regions: The early region coding for six early proteins (E1, E2, E4, E5, E6 and E7) with regulatory functions; the late region coding for two late proteins (L1 and L2) with structural functions, and finally a long control region (LCR) which is a non-coding region where transcription factors bind and is the site of origin of replication.

It is considered the most common sexually transmitted infection worldwide and is the cause of various diseases, from benign lesions, such as anogenital warts, to precancerous lesions and different types of cancer, cervical cancer is the most representative and it is the second most common cancer in women in Mexico and worldwide. The virus initiates infection by accessing the keratinocytes of the basal layer of transitional epithelium of the ecto/endocervix, which have a high capacity for proliferation and differentiation, the women are more predisposed to the development of precancerous lesions and men act as asymptomatic vectors of infection.

Carcinogenesis is related to the process of integration of the viral genome to the host genome, this occurs when the immune system is not able to fight the infection and a persistent infection is formed. In integration occurs a loss of genetic material that compromises totally or partially the L1, L2, E1, E2, E4 and E5 genes. Molecular biology techniques such as PCR have been directed to the identification of a region of the L1 gene, which is conserved among the different HPV types, but is lost in the process of viral integration and can lead to false negatives.

This work has as aims to perform a sequence analysis by multiple sequence alignment to propose oligonucleotides that identify by PCR a region of the L1 gene and a region of the E7 gene which is not lost in the process of viral integration, and use them for the detection of HPV in samples from sexually active men, previous validation.

NEW CTPF-INHIBITORY COMPOUNDS AND THEIR EFFECT ON VIABILITY AND VIRULENCE OF *MYCOBACTERIUM TUBERCULOSIS*

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Abstract:

The emergence of multi-drug resistant (MDR) and extensively drug resistant (XDR) Mycobacterium tuberculosis (MTB) strains has driven the finding of more effective anti-TB drugs. Mycobacterial P-type ATPases could be interesting anti-TB targets due of this role in ion homeostasis across the plasma membrane and mycobacterial virulence [1]. CtpF, a calcium P-type ATPase of MTB, is activated under hypoxia and infection conditions; therefore, this pump is a potential drug target [2].

In this study, a 3D homology model of CtpF was generated for identified key pharmacophoric features of the CtpF-cyclopiazonic acid (CPA) complex. Thereupon, a pharmacophore-based virtual screening was performed using the ZINC database in order to select candidate molecules to inhibitors of CtpF [3]. The compounds selected displayed *in vitro* antimycobacterial activity, showing a minimum inhibitory concentrations (MIC) ranging from 50–100 µg/mL. Likewise, they causes inhibition of Ca^{2+}-ATPase activity in Mtb membrane vesicles (IC50) ranging from 4.1–35.8 µM. Finally, the activity of two compounds with the best biological activity was evaluated in a macrophage infection model. The compound 3134 was the best candidate by displaying 81% decrease in MTB replication within macrophage and good pharmacokinetic profile (drug-like).

Overall, the results shows the importance of CtpF for the mycobacteria survival, and as a key molecular target for the design of new antituberculous compounds.

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CELLULAR COMPONENTS OF 53BP1-FOCI ARE RELOCALIZED TO VIRAL REPLICATION COMPARTMENTS IN ADENOVIRUS 5 INFECTED CELLS

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Abstract:

Human adenoviruses (HAdV) can cause a wide range of diseases, including severe respiratory pathologies, gastroenteritis, and are potential factors of obesity. These viruses are used as vectors in anticancer and gene therapies, and as vaccine vectors, such as the ones used for SARS-CoV2. The HAdV DNA is a linear double stranded molecule that the cell recognizes as a broken DNA once it enters the nucleus, activating the DNA double-strand break repair (DSBR) mechanism, in which multiple cellular proteins participate to recognize and repair the damage. HAdV genome replication, gene transcription and mRNA processing take place in virus-induced intranuclear sites called replication compartments (RCs) where multiple cellular proteins responsible for antiviral defense, cell cycle regulation and DNA repair, among other cellular activities, are relocalized. We and others have studied the activities and composition of RCs, and have found that HAdV-RC represent fundamental hubs for virus-cell interactions; however, little is known about the mechanisms that are responsible for the intranuclear localization of the viral DNA that enters the nucleus or the initial events that lead to the formation of these structures. Interestingly, in an uninfected cell DNA damage triggers recruitment of the cellular components that detect and repair double-strand breaks leading to the formation of, so called 53BP1-foci, suggesting that these cellular proteins may associate with the HAdV DNA as it enters the nucleus. To determine whether components of DSBR relocalize to the entering viral DNA, in this study we have analyzed the intranuclear localization of major components of the 53BP1-foci, namely the Rad50, 53BP-1 and FUS proteins in HAdV-infected cells.

PARTICIPATION OF THE ORF PA4078 IN THE VIRULENCE OF *PSEUDOMONAS AERUGINOSA* PAO1

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Abstract:

Pseudomonas aeruginosa is an opportunistic pathogen responsible for multiple diseases in immunocompromised individuals, representing a serious health concern. The pathogenicity of *P. aeruginosa* strains is related to the production of virulence factors. Non-ribosomal peptide synthetases (NRPS) are involved in the production of virulence factors such as siderophores, through the regulation of the Quorum Sensing systems [1]. The NRPS have not been widely studied from the point of view of bacterial pathogenesis, being of interest to characterize the genes that encoded them and the biological function associated [2]. In this work, the ORF PA4078 whose function is unknown was studied and its role in the virulence of the *P. aeruginosa* PAO1 strain was determined. Bioinformatic analysis revealed that the ORF PA4078 encodes for a NRPS. Mutants on the ORF PA4078 were obtained by gene disruption using a gentamicin resistance cassette and their production of virulence factors was determined. Additionally, the pathogenicity was evaluated in the PAO1 mutants in an *in vivo* model of *Caenorhabditis elegans*. The results obtained indicate that the NRPS are involved in the production of siderophores and phenazines depending of the quorum sensing modulation, which influence the pathogenicity of the *P. aeruginosa* PAO1 bacteria.

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MOLECULAR CHARACTERIZATION OF THE LONG NON-CODING RNA OF PMeV-MX, A PAPAYA UMBRA-LIKE VIRUS, THROUGH THE DEVELOPMENT OF AN INFECTIOUS CLONE

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Abstract:

PMeV-Mx is a new Umbravirus-like associated with papaya meleira in Mexico, this disease causes serious economic losses in papaya cultivation. The virus has a single-stranded RNA genome of 4.3 kb, encodes two open reading frames, and has a long non-coding RNA (lncRNA). Like the umbraviruses, it does not encode a capsid protein, so it is not possible to purify viral particles to confirm the etiology of the disease. The aim of this work was to determine if the viral genome is necessary and sufficient to cause the disease, as well as to characterize the sequence of the lncRNA. An infectious clone of PMeV-Mx was generated inserting the viral genome in a binary vector using Gibson assembly. The plasmid contains the CaMV 35S promoter and a viral Ribozyme to control viral RNA expression in plants. As an approach towards the characterization of the PMeV-Mx lncRNA, regions of secondary structure putatively involved in virus replication were identified for which the design of site-directed mutants was carried out, culminating in the construction of a mutant assembled by Gibson's method. This reverse genetic aproach will allow, in the near future, the characterization of the secondary structure rich regions in plants. In addition, the construction of an infectious clone of PMeV-Mx could contribute to understatand the etiology of the disease in Mexico and facilitate to identify genetic determinants of pathogenicity.

ROLE OF RHIZOBIUM O-ANTIGEN LIPOPOLYSACCHARIDES AS RECEPTOR FOR BROAD-SPECTRUM PHAGE INFECTION AND ITS CONSEQUENCES FOR SYMBIOSIS

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In natural environments, phages coexist and interact with an ample variety of bacteria by predation, lysogeny, and resistance. These interactions involve co-evolutionary and genetic strategies that are generally unknown. The phage lytic or lysogenic interactions start with the recognition of a receptor at the surface of the bacterial cell. The molecular structure of the receptor is essential for phage specificity and host range. Therefore, the aim of this work is the identification of the receptor of broad host range phages of Rhizobium. We first characterized the host range of 29 phages in 10 strains of Rhizobium sp. The phages display a wide host range and different grades of infection, suggesting that these phages use different mechanisms to establish contact with the surface of the bacterium and to infect them. We choose the phages I4, I1.6F, I1.23, I1.9F, Y1.20, and N1.10F, which infects the CE3 strain for the next experiments. To define whether the plasmids of the strain CE3 play a role in the phage susceptibility, we evaluated CE3 strains cured of each one of the plasmids (pa, pb, pc, pd, pe, and pf). The results suggest that the genes encoded in the plasmid pb are essential for infection of the phage I4. The rest of the phages (Y1.20, I1.23, I1.9F, and N1.10F) may use other mechanism to infect since the absence of any of the CE3 plasmids is not important for the infection by these phages. To figure out that the loss of the plasmid pb correlate with the absence of phage contact with the cell we carried out adsorption experiments. In the CE3, 90% of the I4 phage was adsorbed after 40 minutes of incubation. In contrast, in the CE3 pb- the number of free unadsorbed viral particles remained constant indicating a failure in attaching to the cell. To demonstrate that the genes that codify for the O-antigen of R. etli are the receptors for the phage I4, we constructed mutant strains by cassette insertion in the three genes encoding for lps located in the plasmid pb. Phage susceptibility test carried out using these lps mutant strains will indicate the precise role of the most external moiety of the antigen-O in phage recognition. Since lps are key elements for the first stages of the symbiosis, and they could be the target for phage adsorption, we anticipate a close interplay between the evasion of phage predation and nodulation.

EFFECT OF HMGB1-INHIBITION ON THE EFFICIENCY OF HUMAN ADENOVIRUS TYPE 5 REPLICATION

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Abstract:

Human adenoviruses (HAdVs) are common infectious agents associated with acute respiratory diseases and gastroenteritis. Shortly after their discovery, HAdVs became an important model of tumor virology, leading to the elucidation of basic cellular processes, including regulation of gene expression, cell cycle control, and the activities of oncogenes and tumor suppressors. The HAdVs genome is a linear dsDNA molecule that upon entry into the cell nucleus localizes in sites where multiple cellular and viral proteins that direct viral gene trancription, RNA postranscriptional processing and DNA replication are recruited. These virus-induced intranuclear structures are called Replication Compartments (RC), and studies of their composition has shown that they are complex and dynamic compartments that interchange components with the surrounding nucleoplasm, leading to the reorganization of the cell nucleus and the control of cellular activities, ranging from regulation of gene expression to cell cycle and antiviral defense mechanisms. One of the cellular proteins that is enriched in HAdV-RC is the High Mobility Group 1 (HMGB1) protein. HMGB1 is a highly abundant DNA-binding, non-histone protein that participates in transcriptional regulation, DNA replication and repair, telomere maintenance, and nucleosome assembly, but its role in HAdV-RC is not understood. To explore the role of HMBG1 during HAdV replication, in this work we have evaluated the relocalization of HMBG1 to HAdV-RC at different times of the viral replication cycle, and have analyzed the effect of inhibition of HMBG1 on viral DNA replication and progeny production.

INTERPLAY BY *PSEUDOMONAS AERUGINOSA* AND THE KILLER TOXIN PRODUCED BY *SACCHAROMYCESCEREVISIAE*

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Abstract:

Pseudomonas aeruginosa is a gram-negative bacterium of great biomedical importance, since it presents a wide arsenal of virulence factors, thus enabling this microorganism to adapt to different environments and favoring its mechanism of infection and resistance to many antibiotics (1). In addition,it is worth mentioning that this microorganism represents, according to the WHO, a critical priority level due to the seriousness of an infection caused by this bacterium, since it causes multiple infections inthe blood, lungs, urinary tract and surgical wounds, thus being one of the greatest epidemiological concerns at the hospital level (2). To date, several virulence mechanisms of *P. aeruginosa* are known, but no effective treatment has been found for any infection caused by this bacterium inimmunocompromised patients or in hospital fomites that could be involved. It is also known that there is a variety of killer toxins produced by the yeast *Saccharomyces cerevisiae*, these toxins identified as *K1,K2, K28 and Klus*, produce an inhibitory effect on the growth of other sensitive yeasts. It has been reported that strains of *S. cerevisiae* produce these toxins while being resistant to the production of these toxins, thus being called killer strains (3). In our research group, using Kirby-Bauer experiments, we have observed that the killer toxin K1 has an inhibitory effect on the growth of *P. aeruginosa*; different growth conditions have been evaluated, such as different growth medium and pH that specifically favor both *P. aeruginosa* and *S. cerevisiae* to determine if this inhibitory effect can develop effectively even in environments that favor the development and growth of *P. aeruginosa*, in addition to determining the most optimal conditions in which the toxin has a greater inhibitory effect. The objective is to determine if the K1 toxin can be an alternative to antibiotics or a tool for the elimination of biofilms on hospital fomites, testing the toxigenic capacities of both microorganisms, the development of a possible repopulation, and structures or mechanisms of resistance to stress between them.

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STRUCTURAL CHARACTERIZATION OF A VACA VARIANT OF HELICOBACTER PYLORI (HPNUER1).

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Abstract:

Helicobacter pylori infection in humans is associated with the development of severe gastric diseases. The World Health Organization classifies *H. pylori* as a type I carcinogenic agent**.** This pathogen secretes the cytotoxin VacA, a pathogenicity factor widely studied and its product is encoded by the *vacA* gene, which has gene variants that influence the degree of cytotoxicity of the protein, considering *vacA s1i1m1* the most pathogenic. Based on the above, the main objective of this work was to structurally characterize a VacA variant of *H. pylori* from the clinical isolate HPNUER1 through homology modeling. For this purpose, the primary sequence of the *vacA* variant gene was first obtained from the genome of the isolate called HPNUER1, different modeling softwares such as I-TASSER, Phyre2 and SWISS-MODEL were used to obtain the *in silico* structure of the VacA cytotoxin. Finally, it was possible to elucidate the three-dimensional structure of the VacA variant of the HPNUER1 strain by means of SWISS-MODEL Software, obtaining the dodecameric structure that VacA adopts under physiological conditions. The model is considered to be of good quality and reliability, due to the validation parameters, for which it could be used in future research to search for inhibitors as a therapeutic alternative.

GENOME MINING OF *BACILLUS HALOTOLERANS* AF23, A THERMO- AND HALOTOLERANT STRAIN WITH PLANT GROWTH PROMOTING ACTIVITIES

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Abstract:

Plants throughout their different growth stages are exposed to different types of biotic and abiotic stress; as part of abiotic stress, salinity is considered to be highly detrimental to agriculture because of its devastating effects on productivity and food security, it is estimated that by 2050, approximately 50% of the global agricultural land will be affected by salinity[1]. The use of plant growth promoting bacteria (PGPB) is an alternative to overcome the negative effects on plants caused by saline soils[2]. In this work, a search for the activities promoting plant growth of the thermotolerant strain AF23 isolated from soils affected by underground fires was carried out through a functional genomic analysis and different bioassays. Antagonism trials performed in Petri dishes through diffusible compounds, indicated that AF23 inhibited the mycelial growth of the phytopathogenic fungi *Botrytis cinerea* and *Geotrichum candidum* with a 42% and 33%, respectively. The AF23 genome was sequenced, assembled and compared with whole genomes of other strains using the average nucleotide identity (ANI), genome-to-genome distance calculator (GGDC) and rRNA gene sequence, the strain AF23 was identified as *Bacillus halotolerans* with a similarity in these parameters of 98.9%, 97.92% and 100%, respectively. *In silico* analysis, revealed that the genome of the strain AF23 has groups of genes with high similarity to those that encode different antimicrobial compounds, genes involved in thermotolerance, genes with predicted functions in adaptation to high salinity and genes involved in plant growth promotion are also present. Other experiments showed that AF23 is able to produce siderophores, indole acetic acid, proteases and solubilize phosphate under conditions up to 200 mM of NaCl, under the same salinity concentration, in greenhouse experiments, AF23 increased the stem fresh and dry weight of tomato plants. These results suggest that *B. halotolerans* AF23 contains the genetic potential to act as PGPB under saline conditions. Additionally, it will be evaluated if AF23 modifies its membrane components as a potential protecting mechanism to maintain PGP traits under saline-soil conditions.

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ANTIMICROBIAL CAPACITY OF ETHANOLIC EXTRACTS OF PROPOLIS FROM SOUTHERN SONORA

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Abstract:

Propolis is a natural beekeeping product made by bees from different botanical sources, it has been used since ancient times by various civilizations in traditional medicine to treat various health conditions. Propolis is made up of more than 300 chemical substances, among which are terpenes, phenols and flavonoids, these have been identified that provide an antimicrobial capacity by inhibiting more than 600 microorganisms. In Mexico, it is detected the antimicrobial capacity of the propolis, however there are no researches from Southern Sonora they do not exist researches on the antimicrobial capacity, for this reason, the objective of this investigation is to evaluate the antimicrobial capacity the samples of propolis from Southern Sonora. **Methodology:** 50 g of raw propolis, collected from different hives in the South Sonora, were weighed, macerated with 100 ml of extract and 70% ethanol and filtered, the antimicrobial activity method was performed using sensidiscs and measured. the inhibition halo for each microorganism. Kanamycin was obtained as a positive control and sterile water as a negative control. **Results:** The analyzed samples (n=5) presented an inhibition halo of 11.6 mm for *E. coli*, 11.5 mm for *S. aureus* and 10.6 mm for *C. albicans,* indicating a moderately resistant capacity for the three microorganisms according to the values established by Institute for Clinical and Laboratory Standards (CLSI). **Conclusion:** Propolis from southern Sonora can be used as an alternative treatment to treat infections by *E. coli, S. aureus and C. albicans*, indicating that propolis samples from the analyzed region have an antimicrobial capacity.

Norma Oficial Mexicana NOM-003-SAG/GAN-2017, propóleos, producción y especificaciones para su procesamiento.

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A CHROMOSOMAL LOCUS FROM *STENOTROPHOMONAS MALTOPHILIA* ENCODING A T2SS AND A T5SSB, IS INVOLVED IN VIRULENCE

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Abstract:

This work is aimed at characterizing a region present in *Stenotrophomonas maltophilia* that is similar to a locus from *Pseudomonas aeruginosa*, shown in that species to be regulated by the system PUMA3 cell-surface signaling system (CSS) and involved in virulence.

S. maltophilia is a high versatile multidrug-resistant bacterium, capable of adaptation to different environments[1]. In recent years, it has shown a marked increase in the incidence of nosocomial infections, being among the top 10 global priority resistant bacteria [2]. However, very little is known about its virulence mechanisms.

The CSS is a regulatory mechanism to sense and adapt to extracellular environmental cues in bacteria[3], including starvation and other adverse conditions. The PUMA3 system (a CSS) has been described in *P. aeruginosa* in some detail. In that species, it regulates the expression of a Type II Secretion Systems (T2SS) and an autotransporter (T5SSb), which are activated under phosphate starvation[4,5]. An homologous locus was identified by our group in *S. maltophilia* and through comparative genomics analysis, revealing that the locus is only found in strains of this species in the genus *Stenotrophomonas*. Through the generation of deletions in key regulatory genes of the PUMA3 CSS, as well as in specific subunits of the T2SS and T5SSb, we are evaluating their contribution to the virulence phenotypes in *S. maltophilia* using *Galleria mellonella* larvae as an alternative infection model. We show by confocal microscopy that a transcriptional fusion to GFP using the intergenic region upstream of the first gene in the PUMA3 system is expressed in purified *G. mellonella* hemocytes.

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POTENTIAL OF SKIN BACTERIAS FROM AMPHIBIANS AS BIOCONTROL AGENT AGAINST *BOTRYTIS CINEREA*

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Abstract

The necrotrophic fungus *Botrytis cinerea* is the causal agent of is commonly known as gray mold fungus that affects wide range of crops from different plant families, both agricultural and wild members. Chemical agents are commonly used to to combat the disease causes by *B. cinerea*; however, the extensive use of chemicals entails environmental and public health issues. Therefore, biological control alternatives have been studied to inhibit the growth and development of the pathogen. The use of bacterial strains associated with amphibians have been described as possible biological control agents (BCA) as they have demonstrated inhibitory effects to control plant pathogenic fungi. Within our project, we have explored the role of bacteria from the skin of the endemic species Axolotl (*Ambystoma* sp.) against the pathogenic fungus *Botrytis cinerea*. Previous studies have published that these bacteria can protect the Axolotls from the pathogenic fungus *Batrachochytrium dendrobatidis*. Confrontation experiments revealed 5 potential candidates for biological or biocontrol activity and it is expected that the compounds released by the candidate bacteria possess biochemical properties to inhibit or slow down the development of the fungus. Thus, the candidate strains might play an important role when interacting with the candidate bacteria with the model plant *Arabidopsis thaliana* once challenged with B. cinerea infection. The outcome of the results presented help to understand on the one hand the role of amphibian skin bacteria associated with the skin of *Ambystoma* sp and on the other hand the potential role in plant-pathogen interactions or growth of pathogenic fungi of plant interest.

Keys words: biocontrol, ambystoma sp, *botrytis cinerea, arabidopsis thaliana*

COMPARATIVE METAGENOMICS OF MYCETANGIA IN THE *DENDROCTONUS FRONTALIS* COMPLEX SPECIES (CURCULIONIDAE: SCOLYTINAE) REVEALS DIVERSE AND FUNCTIONALLY REDUNDANT FUNGAL ASSEMBLAGES

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Abstract:

Dendroctonus-bark beetles (Curculionidae: Scolytinae) are associated with microbes that can detoxify terpenes, degrade complex molecules, supplement, and recycle nutrients, fix nitrogen, produce semiochemicals, and regulate ecological interactions between microbes. Females of some *Dendroctonus* species harbor microbes in specialized organs called mycetangia; yet little is known about the microbial diversity contained in these structures. Here, we use metagenomics to characterize mycetangial fungi of the *Dendroctonus frontalis* complex species. Overall fungal diversity was represented by 3 phyla, 11 classes, 19 orders, 29 families, and 35 genera, including 23 filamentous fungi and 12 yeasts. The most abundant genera were *Entomocorticum*, *Ogataea*, *Ophiostoma-Sporothrix*, *Nakazawaea, Yamadazyma* and *Ceratocystiopsis*. Analysis of α- and β-diversity indicated that fungal assemblages of *D. adjunctus*, *D. mexicanus*, *D. mesoamericanus* and *D. vitei* were more diverse than *D. barberi*, *D. brevicomis* and *D. frontalis*. A strict core mycobiome was not statistically identified; but manually only the genus *Ceratocystiopsis* was shared among seven species. The tanglegram showed evolutionary congruence between fungal assemblages and *D. frontalis* complex species. Molecular networks of mycetangia were integrated by different OTUs$^{97\%}$, some of them with different phylotypes. The presence of different phylotypes of the same genus in assemblages from *D. frontalis* complex species outlines the complexity of networks, being the most complex those from *D. mesoamericanus*, *D. mexicanus*, and *D. vitei*, and the less those *D. frontalis*, *D. adjunctus*, *D. brevicomis* and *D. barberi*. The filamentous fungi and yeasts consisted of six trophic groups including saprotrophs, pathotrophs, symbiotrophs, pathotrophs /symbiotrophs, symbiotrophs/ saprotrophs and pathotrophs/saprotrophs/symbiotrophs. These findings improve our knowledge about the diversity of mycetangial communities in species of the *D. frontalis* complex species and suggest that minimal apparently specific assemblages are maintained and regulated within mycetangia.

A YEAR-LONG STUDY OF *PERSEA AMERICANA* (AVOCADO) ASSOCIATED MICROBIOMES TO FORECAST MICROBIAL-BASED DISEASES

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Abstract

The early forecast of crops plagues and diseases can make the difference between a bad or a good harvest. The forecast of plant diseases can be achieved by modeling the behavior of plant pathogens in function of weather variables and soil properties for a particular crop and place along the time. After collection, data is analyzed to find relationships between a crop disease, a pathogen and the weather and soil physical chemical variables in a way that, after measuring the latter, we can forecast the potential of plant plagues and diseases.

The forecasting of plant pathogenic microorganisms' behavior as a function of environmental variables is less developed than those of insects. However, there are several cases of early forecasting of plant diseases produced by fungi whose apparition and strength can be forecasted in function of the infection of the previous year, the intensity of the rain season, or the winter temperature. An often-overlooked factor that influences the incidence of microorganism based-plant diseases is the composition and dynamics of the crop soil and leaves microbiomes. In order to perform more accurate plant diseases forecasting, it is necessary to add to the weather and soil assets databases, the microbial profiles of crop soils and leaves to correlate them with the incidence of plant diseases in a timeline.

In this work, the composition and dynamics of microbial communities in crop soil and leaves of avocado (*Persea americana*) were determined along a year, and related to weather (temperature, precipitation, humidity, wind velocity, solar radiation) and soil variables (temperature, humidity, electric conductivity). The relationship between soil and leaves microbial communities, weather, soil assets and avocado diseases will be shown. This work was funded by CYCASA-NORMAN Agricultura Cognitiva (Jalisco, Mexico).

THE ROLE OF YAPSINS IN THE SURVIVAL AND PATHOGENESIS OF *CANDIDA AURIS*

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Abstract:

Candida auris is an opportunistic pathogen first identified in 2009 in Japan, since then its reports have been increasing around the world and have been classified into five clades. Its main characteristic is multiresistance to first-line antifungals (azoles, polyenes and echinocandins) and its ability to generate outbreaks in the nosocomial environment. Furthermore, *C. auris* is characterized by being halotolerant and growing at 40-42ºC. The *C. auris* yapsins, a family of aspartyl proteases anchored to the cell wall and cell membrane. In other yeast species, these enzymes have been implicated in the stability and function of these ultrastructures. The CauYPS genes coding yapsins were searched and characterized to describe the main characteristics of the CauYps deduced proteins, such as their primary structure and phylogeny. The bioinformatic analysis allowed the identification of seven putative yapsin coding sequences (CauYPS1-7) in the genome of *C. auris* B11220 uploaded in GenBank at NCBI. Most of YPS genes of Candida species belonged to the CTG clade. The *CauYPS* genes are found on four of the seven chromosomes in the genome. The effect of various types of stresses that affect the wall or the membrane in the presence and absence of pepstatin at temperatures of 37°C were evaluated on the growth of *C. auris* 49 and *C. auris* 20-1498, belonging to clades III and IV, respectively. Phenotypic differences were found in the behavior of both strains, but in general the *C. auris* 20-1498 strain was more sensitive to caffeine than *C. auris* 49. Other enzymes, such as hemolysin and secreted aspartyl proteases (Sap's) have been little studied in *C. auris*. The strains of *C. auris* 49 and 20-1498 did not express hemolysin activity in blood agar medium. Inhibition by pepstatin and sensitivity to various stressors suggests a possible role of yapsins in wall and membrane function. The phenotypic difference between *C. auris* 49 and 20-1498 strains is most likely due to their belonging to different clades and are a reflection of different genomic structures, which can be verified by genome analysis and gene expression analysis.

CHARACTERIZATION OF PORCINE REPRODUCTIVE AND RESPIRATORY SYNDROME VIRUS-SPECIFIC NEUTRALIZING EPITOPES IN THE ECTODOMAIN OF THE STRUCTURAL PROTEIN GP5

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Abstract:

Infection by the porcine reproductive and respiratory syndrome virus (PRRS) represents a great concern for the pork industry, due to the affectation of the productive indexes and the associated economic losses. It has been proposed that the structural protein GP5 of the virus has epitopes capable of inducing the production of neutralizing antibodies (NAb), which constitute one of the most important antiviral mechanisms against PRRSV infection. To favor the production of NAb before a PRRSV infection, it is necessary to identify neutralizing epitopes that are also immunodominant. To that end, we selected, previously reported peptide sequences from GP5, from which we constructed three new peptides that showed high immunogenic and antigenic properties *in silico*. **Objective:** To evaluate the immunogenicity and immunodominance of three GP5 peptides (GP5B1, GP5B2, and GP5B3) in a murine model, through the detection of total and specific antibodies. **Methodology:** Using sera from mice immunized with GP5B1, GP5B2, and GP5B3, the following variables were evaluated: (i) the concentration of total IgG by direct Enzyme Linked Immunosorbent Assay (ELISA), and (ii) the concentration of antigen-specific IgG1 and IgG2 by indirect ELISA, using the peptides as capture antigens. With these results, the immunodominance and immunogenicity of the peptides were compared. **Results:** Each peptide contain two different epitopes (neutralizing epitopes PNEU1 or PNEU2, and a PANT antigenic epitope) that correspond to recognition epitopes for B lymphocytes. It was found that the three peptides were immunogenic and induced the production of specific antibodies, IgG1 and IgG2, that are largely directed against neutralizing epitopes. **Discussion and conclusion**: We present the first experimental evidence of the immunogenicity of G5B1, GP5B2 and GP5B3 in a murine model. GP5B3 turned out to be the immunodominant peptide, while PNEU1 was the immunodominant epitope. The results suggest that the immunodominance is dependent on adjacent epitopes to which they are bound. **Outlook:** Microneutralization assays are underway to determine the neutralizing potential of the antibodies. From these results, the relationship between the immunodominance of peptides and their neutralizing capacity will be determined to guide the development of a vaccine against PRRS.

Acknowledgments:
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EVIDENCE OF *IN VITRO* FORMATION OF BIOMOLECULAR CONDENSATES BY LIQUID-LIQUID PHASE SEPARATION BY THE ADENOVIRUS SSDNA BINDING PROTEIN

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Abstract:

Virus Replication compartments (RC) formed in cells infected by DNA viruses are nuclear membrane-less structures where the viral genome is replicated and expressed. Many cellular proteins that participate in viral gene transcription and posttranscriptional viral RNA processing are relocalized to RC. Interestingly, multiple cellular proteins that are components of the cellular anti-viral response, cell cycle control and double-strand DNA repair, among other cellular activities, are also recruited to these sites, indicating that RC are essential hubs for virus-host cell interactions. Although the mechanisms responsible for RC formation are incompletely understood, recent evidence suggests that they represent Biomolecular Condensates (BMCs), which display liquid properties and may form through liquid-liquid phase separation (LLPS). The proteins that can undergo LLPS are known as *scaffolds* and are commonly intrinsically disordered proteins (IDPs) or proteins with low complexity regions (LCR). Our group has studied the composition and activities of RC in human adenovirus (HAdV)-infected cells, but the available evidence on the mechanisms that lead to the formation of RC is still limited. In this study we have analyzed whether the ssDNA binding protein, DBP, one of the main components of HAdV-RC, displays properties of proteins that can drive formation of BMCs through LLPS. The DBP was predicted as a *scaffold* IDP that can drive LLPS, and we have found that this viral protein mediated the assembly of BMCs in both infected and transfected cells. In addition, we evaluated if DBP can form droplet-like BMCs *in vitro* using an enriched mCherry-DBP fusion protein fraction to evaluate the formation of droplets at various NaCl concentrations. Taken together, our results provide evidence that DBP may drive the formation of BMCs through LLPS and may act as a *scaffold* as it is sufficient to form droplets that display morphologies that recapitulate liquid droplets of previously reported BMCs that form by LLPS *in vitro.*

ABSTRACTS | Posters Neurosciences and Neurobiology

XXXIII National Congress of Biochemistry

COGNITIVE STIMULATION REDUCES ACTIVATED MICROGLIA IN MICE

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Abstract:

Neuroinflammation is a critical process implicated in AD. Microglial dysfunction is involved in almost all brain diseases and has been associated with cognitive decline processes leading to neurodegenerative diseases. In addition, recent evidence shows exercise and cognitive stimulation delay the pathogenesis of AD, improving cognitive decline and decreasing the pathognomonic hallmarks of this disease. We sought to investigate the effects of cognitive stimulation by Enrichment Environmental (EE) and Morris Water Maze (MWM) on microglia immunophenotype. Males and females 12-month-old 3xTg-AD were housed in EE that changed every 7 days and trained for 5 days every month for 3 months. At the end of the stimulation program, they were tested in a Barnes Maze paradigm and compared with 3xTg-AD of the same age and sex without stimulation. After the memory test, we obtained the brain and sixty-micrometer frozen sections were prepared as described previously and used Iba-1 antibody to identify microglia in different areas. Our results showed that cognitive stimulation improves memory and decreases activated microglia.

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COGNITIVE EVALUATION OF CHRONIC ADMINISTRATION OF GALEANA (*SPHATODEA CAMPANULATA*) IN TYPE 2 DIABETIC RATS

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Abstract:

Diabetes mellitus (DM) is becoming the epidemic of the 21st century. DM and its complications are among the chronic degenerative diseases that constitute a global health problem. Type 2 DM (DM2), caused by insulin deficiency and resistance in the body, raises glucose to harmful concentrations with a terminal prognosis if uncontrolled. Cognitive impairment is recognized as a complication of DM. DM causes cell reduction and increased neuronal death in the hippocampus, resulting in impaired memory and learning. Commercial drugs for diabetes treatment have reasonable glycemic control but can also cause adverse side effects. Therefore, supportive alternatives are sought for the treatment of patients, such as medicinal plants, among which is *S. campanulata,* belonging to the Bignoniaceae family and known as Galeana in Mexico. **Objective:** To evaluate the cognitive effects of *S. campanulata* leaf extracts in rats with DM2. **Material and methods:** Galeana leaves were collected to obtain the aqueous extract of the plant (AQESC). DM2 was induced in Wistar rats with chronic oral administration (13 weeks) of 60% fructose (6 weeks), and the extract was administered orally with a feeding tube to 200g diabetic rats. The groups of rats were healthy control, diabetic control, diabetic control treated with metformin and diabetic rats treated with the extract, with 8 rats per group. Subsequently, glycemia was assessed and behavioral tests of the elevated plus maze and novel object recognition test were performed to assess anxiety and non-spatial memory, as well as spatial recognition in the animals. Counting of whole and lesioned neurons in the CA1 segment of the hippocampus was also performed. **Results:** During 13 weeks of AQESC administration to diabetic rats, concentrations <100 mg/dL of glycemia were observed, confirming its hypoglycemic effect. Behavioral tests, as well as neuron counts, showed no significant differences between groups of healthy rats compared to diabetic rats treated with the extract. **Conclusions:** Oral administration of AQESC produces a neuroprotective effect on CA1 neurons, as well as, on memory and hippocampal-mediated learning of AQESC-treated diabetic rats.

Keywords: Diabetes mellitus, cognitive, medicinal plants, *Spathodea campanulata*.

Acknowledgments: Present work partially correspond to the Master thesis of Arias Sánchez R.A. (CONACYT: 793126). Funding was partially provided by grants to Fenton Navarro B. by CIC-UMSNH 16.2-2022.

SLEEP RESTRICTION PROMOTES THE A1 ASTROGLIAL PHENOTYPE AND INCREASES BLOOD-BRAIN BARRIER PERMEABILITY

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Abstract:

The blood-brain barrier is located at the central nervous system microvasculature. Early during development, brain endothelial cells acquire the barrier phenotype after exposure to astroglial derived factors. During adulthood, astroglia maintain the barrier phenotype by the release of diverse soluble mediators; however, during altered physiological conditions, astroglia may polarize to pro-inflammatory or anti-inflammatory phenotype. Reactive astrocytes increase the GFAP expression and present a selective pattern of gene expression depending on their phenotype. The pro-inflammatory A1 phenotype is characterized by the increased expression of the C3 complement protein and mainly exerts a neurotoxic role. While the anti-inflammatory A2 phenotype expresses the S100a10 protein and generally exerts a neuroprotective effect. Blood-brain barrier disruption occurs during neuroinflammatory conditions, especially those involving the presence of A1 astroglia. Sleep restriction promotes an inflammatory environment; however, it is unknown whether there are changes in the phenotype of reactive astrocytes and its relationship with blood-brain barrier dysfunction. To answer this question, male C57BL/6 mice were used. Mice were sleep-restricted during 5 or 10 days, using the modified platform method. Mice were sleep-restricted for 20 h daily, with 4 h of sleep opportunity each day. Thereafter, blood-brain barrier permeability assays were performed and changes in the expression of GFAP and C3 proteins were evaluated by western blot in the cerebral cortex and hippocampus. Five and ten days of sleep restriction increased blood-brain barrier permeability to sodium-fluorescein and Evans blue. Increased levels of GFAP and C3 protein were also observed after 10 days of sleep restriction, which may suggest a predominance of the A1 phenotype during chronic sleep loss.

EFFECT OF SELECTIVE INHIBITION OF NUCLEAR EXPORT WITH SELINEXOR ON AUTOPHAGY AND SENESCENCE FEATURES IN AN *IN VITRO* NEURONAL AGING MODEL

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Abstract:

Aging is a biological process characterized by a progressive loss of physiological functions and an accumulation of damage at the molecular, cellular, and tissue level over time that increases the probability of death. One hallmark of aging is the accumulation of senescent cells. *Cellular senescence* is a phenotype characterized by cell cycle arrest and a lack of response to mitotic and apoptotic stimuli. Senescence can be caused by different stressors, including autophagy failure. *Autophagy* is a catabolic process responsible for degrading intracellular components into essential biomolecules within lysosomes to maintain cellular homeostasis and prevent the accumulation of unnecessary proteins and damaged organelles. Its failure has been associated with neuronal senescence induction in aging models. For this reason, stimulating autophagy could be a promising intervention strategy to prevent neuronal senescence in brain aging. CRM1 is the main nuclear exportin in mammals, and it has been reported that its activity is enhanced in skin fibroblast from Hutchinson-Gilford progeria syndrome patients and in old healthy individuals, and its overexpression induces cellular senescence. Additionally, previous report from our lab found that CRM1 levels and its activity is also increased in the brain of aged mice. Among hundreds of proteins that CRM1 exports there is TFEB, which is a transcription factor that induces autophagy and lysosomal biogenesis genes expression. Hence, the pharmacological inhibition of CRM1 during aging could increase nuclear TFEB and revert autophagy impairment and neuronal senescence. To test this hypothesis, we analyzed if the use of a novel CRM1 inhibitor (Selinexor) could revert senescent phenotype and autophagy failure in an *in vitro* neuronal aging model. The preliminary results will be discussed in the meeting.

Key Words: Aging; Neuronal senescence; CRM1.

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KINEMATIC REPRESENTATIONS IN THE SUBSTANTIA NIGRA PARS RETICULATA ADJUST TO DIFFERENT SPATIOTEMPORAL CONTEXTS

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Abstract:

Movement execution requires coordinated activity between the sensory and motor systems and involves the integrated dynamics of several cortical and subcortical regions, including the basal ganglia (BG). The specific mechanisms of how the BG control movement remain unclear, however, one of the principal hypotheses is related to their implication in the control of movement kinematics. Here we explore this possibility by using electrophysiological recordings in freely moving rats and analyzing the neural activity of SNr (the main output nucleus of BG) during the execution of motor sequences in two behavioral contexts with different ranges of spatial and temporal content. We found that the SNr activity was correlated with kinematic parameters of the execution, especially with the position and speed. Furthermore, these kinematic representations were adjusted to different spatiotemporal movement scales. Our data suggest that position and velocity representations are maintained throughout the GB in a context-dependent manner further support their implication in movement kinematic control.

Keywords: Basal ganglia, substantia nigra reticulata, kinematics.

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AS, B-C is a PhD. student from Programa de Doctorado en Ciencias Biomédicas, UNAM and supported by fellowship 857858 from CONACyT-México.

BOROMELATONIN AMELIORATES THE COGNITIVE DEFICIT AND NEURONAL LOSS INDUCED BY ESTROGEN DEPRIVATION IN FEMALE RATS

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Abstract:

Preclinical and clinical data suggest melatonin and its analogues could have a key role as potential treatment for diseases involving cognitive deficit such as Alzheimer's disease (AD). Besides, in the last years some boron-containing compounds have shown activity in the neuronal phenomena. Using behavioral evaluation and biochemical profiles as together tools to evaluate the origin and progress of the neurodegenerative processes.

We evaluated a recently synthesized compound by our workgroup: borolatonin, a boron-containing analogue of melatonin. It was previously identified as a pharmacological agent exerting improved behavior in memory tasks, as well as limiting the accumulation of amyloid proteins in central nervous system. In the current contribution, we evaluated its ability to modulate morphological and behavioral changes in female rats with estrogen deprivation by ovariectomy. In fact, neuronal loss (estimated by determination of neurons marked with the NeuN+ antibody) was present after four weeks of hormonal deprivation, but it was limited when boromelatonin was administered during the hormonal deprivation. In agreement of this fact, amyloid-like accumulation in brain was reduced by boromelatonin administration. Moreover, also the performance in behavioral tests was improved comparatively control gonadectomized group.

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Barrón-González, M., et al. (2022) Synthesis, In Silico, and Biological Evaluation of a Borinic Tryptophan-Derivative That Induces Melatonin-like Amelioration of Cognitive Deficit in Male Rat.*Int. J. Mol. Sci.* 2022, *23*, 3229.

TIBOLONE ADMINISTRATION DECREASES OXIDATIVE STRESS IN PLASMA AND SPINAL CORD IN A TRAUMATIC SPINAL CORD INJURY ANIMAL MODEL

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Abstract:

Brackground: Traumatic spinal cord injury (TSCI) causes irreversible damage to neurological and motor function. Oxidative stress increases damage to important biomolecules that in turn impair motor activity causing progressive neurodegeneration in the spinal cord. There is currently no treatment capable of reversing the damage and promoting functional recovery of patients without generating side effects. Tibolone (Tib) is a treatment currently used for menopause and has been shown to have a neuroprotective effect by acting as an antioxidant. **Aim:** To evaluate the effect of Tib on oxidative stress in the medulla and plasma in an animal model of traumatic spinal cord injury. **Metodology:** Forty-eight male rats of the *Sprague dawley* strain were randomly distributed in 6 groups: 1) Control (water), 2) Laminectomy, 3) TSCI, 4) TSCI + 0.1 mg/kg weight of Tib, 5) TSCI + 1 mg/kg weight of Tib, 6) TSCI + 10 mg/kg weight of Tib. The administration of the different doses of Tib was performed at 30 min, 24 hours and 48 hours post-surgery and the animals were sacrificed at 72 hours. Biochemical techniques were used for the quantification of superoxide dismutase (SOD) activity and for the quantification of carbonyls, and malondialdehyde (MDA) levels in plasma and spinal cord. **Results:** It was observed that the administration of Tib at a dose of 0.1 mg/kg after TSCI increased SOD enzyme activity in spinal cord homogenates, when compared to the TSCI group without treatment. However, in plasma, SOD enzyme activity did not show significant differences. The administration of Tib at a dose of 0.1 mg/kg after TSCI significantly decreased the levels of MDA and carbonyls in plasma and in spinal cord homogenates. **Conclusions:** The results obtained in the present work show that the dose of Tib that had the best effect in decreasing oxidative stress markers in plasma and spinal cord after injury was 0.1 mg/kg, which is similar to that reported for estradiol and suggests an estrogenic effect of this synthetic hormone in the TSCI model.

Key words: oxidative stress, traumatic spinal cord injury, tibolone.

AXONAL DEGENERATION IN AN *IN VITRO* MODEL OF NEURONAL SENESCENCE

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Abstract:

As an organism age, senescent cells accumulate and are responsible of aging deleterious traits. In brain, astrocytes, microglia, oligodendrocytes and even neurons have been shown to have senescent features. Cellular senescence is a cell state characterized, among other features, by lysosomal dysfunction and the senescence associated secretory phenotype (SASP) that alters the surrounding tissue. In previous work we demonstrated that neuronal senescence is a result of macroautophagy dysfunction. Macroautophagy is a process of selective engulfment of intracellular components into double membrane vesicles that are delivered to the lysosome for degradation. As macroautophagy depends on vesicular transport and cytoskeleton integrity, in this work we wonder whether axonal degeneration could be the trigger of macroautophagy dysfunction leading to neuronal senescence.

Another feature of brain aging is the loss of neuronal axons and/or somas. Selective elimination of axons is named axonal degeneration and occurs in a cell autonomous way. This process is characterized by early cytoskeleton fragmentation. In some cases, axonal degeneration is mediated by the RIPK1-RIPK3-MLKL pathway. Our working hypothesis is that in an *in vitro* model of neuronal senescence axonal degeneration occurs via RIPK1-RIPK3-MLKL pathway, causing autophagy dysfunction and neuronal senescence. We will present our findings.

Keywords: autophagy, neuronal senescence, necroptosis

Acknowledgements: Funding was provided by UNAM-DGAPA-PAPIIT IN209221 to SCO. CONACyT fellowships were awarded to GACM (820681) and PLC (1145550). GACM is student of the "Doctorado en Ciencias Bioquímicas and PLC is student of the "Maestría en Ciencias Bioquímicas" at Universidad Nacional Autónoma de México (UNAM). We are grateful to Dra. Beatriz Aguilar Maldonado and Dr. Abraham Rosas Arellano for their technical assistance.

EFFECT OF HIGH-CARBOHYDRATE DIET CONSUMPTION ON MITOCHONDRIAL EFFICIENCY IN THE HIPPOCAMPUS AND CEREBRAL CORTEX OF WISTAR RATS

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Abstract:

Introduction: The intake of hypercaloric diets and/or reduced energy expenditure due to a sedentary lifestyle leads to a positive energy balance, promoting the development of insulin resistance (IR), metabolic syndrome (MS), obesity, diabetes, and currently, it also has been associated with neurodegenerative diseases development. In common, these abnormalities are closely related to mitochondria alterations; however, it has not been thoroughly studied. **Methodology:** Two groups of male Wistar rats (n=5; 1 month old and 100 g of weight) were fed for 120 days with a high-carbohydrate diet (Patent: MX/E/2013/047377) or standard chow (NCD; LabDiet 5001; laboratory rodent diet). At the end feeding stage, a metabolic characterization was realized. Glucose, triglycerides, cholesterol and its fractions, insulin, and insulin resistance indexes were quantified using commercial kits. From samples of the hippocampus (Hp), frontal cortex (FC), and temporal cortex (TC), mitochondrial supercomplexes by western blot or in-gel activity were analyzed; PGC-1α was evaluated by western blot, and ATP quantification was performed by a commercial kit based on glycerol phosphorylation. **Results:** Wistar rats high-carbohydrate fed developed MS shown by hyperglycemia, hyperinsulinemia, dyslipidemia, and insulin resistance. In these animals, PGC-1α expression increased in the FC and Hp but not in the TC. Also, western blot and in-gel activity assay evidenced changes in the mitochondrial metabolism from mitochondrial extracts of brain regions that showed an adaptation in the formation of respiratory complexes and supercomplexes. **Conclusion:** The MS caused by a chronic high- carbohydrate diet consumption modifies the mitochondrial energy efficiency of the Hp, FC, and TC by changing the formation of complexes and supercomplexes and the expression of PGC1- α.

PRENATAL CAFETERIA DIET EXPOSURE PROMOTES LYMPHOCYTE INFILTRATION INTO THE BRAIN AND AUTISM-LIKE BEHAVIOR IN THE OFFSPRING OF C57BL6 MICE

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Abstract:

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with an array of etiological causes, including environmental, genetic, and immunological triggers. High-energy diets activate the immune system during prenatal stages favor infiltration of peripheral immune cells and cytokines into the brain by the choroid plexus and circumventricular regions and altering microglial activity. Accumulation of immune entities and microglia activation in brain have been reported to disrupt social behavior. However, the interplay between prenatal exposure to high-energy diets, neuroinflammation and defective social behavior has not been reported. In this work, female C57BL6 mice were exposed to cafeteria diet during pregnancy and lactation. The effect of diet on social, locomotor, repetitive-stereotyped, and anxiety-like behavior was evaluated in the male offspring two-month-old. We quantified the number of infiltrating natural killer (NK1.1^{+}), dendritic (CD11c^{+}), lymphocytes (CD11b^{-}-CD45^{+}), macrophages (CD11b^{+}-CD45^{high}), and M1 (CD11b^{+}-CD45^{low}-CD86^{+}) or M2 (CD11b^{+}-CD45^{low}-CD206^{+}) microglia in the choroid plexus and cerebral cortex, hippocampus, and striatum of the male offspring by flow cytometry. Our results demonstrated that exposure to cafeteria diet during prenatal stage primed defective social interaction and repetitive-stereotyped behaviors in male offspring. Flow cytometry analysis showed lymphocyte infiltration in striatum compared to the choroid plexus in the offspring exposed to cafeteria diet. No significant changes were observed in the NK, dendritic or macrophage levels in the choroid plexus and the cerebral cortex, hippocampus, and striatum regions of those subjects. The effect of cafeteria diet exposure also did not affect microglial density or M1/M2 phenotypes. Our results indicate that exposure to a cafeteria diet during prenatal development promotes an increase of lymphocytes in brain regions of importance for ASD that could contribute to the behavioral defect in the offspring. Testing the contribution of lymphocyte infiltrates in the development of ASD-like behaviors could better explain the cellular mechanisms related to the disorder.

PRENATAL EXPOSURE TO HIGH-ENERGY DIETS AFFECTS VOLUME AND CONNECTIVITY IN THE FIMBRIA-FORNIX OF MICE OFFSPRING SHOWING ANXIETY

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Abstract:

Maternal exposure to high-energy diets primes brain alterations that increase the risk of developing behavioral and cognitive failures. Alterations in the structure and connectivity of brain regions involved in learning and memory performance are found in adult obese murine models and in humans. It is not entirely clear the contribution of prenatal exposure to high-energy diets in structural and functional modulation of brain associated with cognitive decline in the offspring. For instance, maternal exposure to high-energy diets during pregnancy primes cognitive impairment affecting learning and memory processes in the offspring after life [1–3]. We used female C57BL6 mice exposed to a Cafeteria diet (CAF) or Chow diet for 9 weeks (before, during and after pregnancy) to characterize the effect of diet on brain structural organization and its effects on learning and memory impairment in young mice. We evaluated memory and learning performance in the two-month-old offspring using the Y-maze test including forced and spontaneous alternation, Novel object recognition (NORT), Open field and Barnes maze tests. Global brain analysis included microstructural changes in white matter by diffusion tensor imaging and macrostructural changes with T1w (deformation-based morphometry). We found that the male offspring of dams exposed to CAF diet displayed no alterations on short-time or long-time spatial memory performance when compared to the control, but increased time spent in the edges resemble to anxiety-like behavior. Male offspring from dams exposed to CAF diet showed increased volume in primary somatosensory cortex and a reduced volume in fimbria-fornix, which correlate with alterations in its white matter integrity. Finally, biological modeling revealed that prenatal exposure to CAF diet predicts low volume in the fornix, which was associated with anxiety in the offspring. The findings suggest that prenatal exposure to high-energy diets prime brain structural alterations related to anxiety in the offspring.

ROLE OF NOX IN NLRP3 INFLAMMASOME REGULATION DURING CEREBELLAR GRANULE NEURONS DEATH

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Abstract:

Introduction: The NLRP3 inflammasome was first described in immune cells and plays a central role in inflammatory processes. It is known to be involved in both acute neuronal damage and neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease and multiple sclerosis. More recently, we and others showed that it is expressed in neurons. In immune cells, the induction of NLRP3 leads to the activation of caspase-1, which in turn processes pro-IL-1β generating IL-1β, that is secreted to recruit other immune cells in the site of infection to offer a timely response and restore tissue homeostasis. Some of the cellular perturbations that are able to induce NLRP3 activation include potassium efflux, lysosomal damage, reactive oxygen species (ROS) production, increased levels of the thioredoxin-interacting protein (TXNIP) and mitochondrial dysfunction. We have previously demonstrated that cell death of cerebellar granule neurons (CGN) induced by potassium deprivation triggers an early potassium efflux and an increase of ROS and TXNIP levels. Interestingly, we showed in CGN that cell death conditions induce an increase of ROS and NLRP3 levels, suggesting a possible involvement of the NLRP3 inflammasome in neuronal death. There is no much information available about NLRP3 inflammasome in neuronal death, as well as the implication of NOX activation during this process.

Objective: To evaluate the role of the NOX activation in the NLRP3 inflammasome activity and their involvement of CGN death induced by excitotoxicity and potassium deprivation.

Materials and methods: We used cultured CGN from 8-day-old Wistar rats maintained in a medium with 25mM of potassium (K25) for 7 days *in vitro*. Neuronal death was produced by culturing cells with a medium containing KCl to 5mM (K5, potassium deprivation); excitotoxic death was induced by treating CGN with 300 µM of glutamate during 20 min. Cell viability was evaluated after 24 h by the MTT reduction assay, as well as the calcein/propidium iodide incorporation; the ROS production was measured by DHE (dihidroethidium oxidation); the levels and localization of the components of the NLRP3 inflammasome were measured by Western blot analysis and immunocytochemistry, respectively; the determination of pro-cytokines and cytokines were carry out by PCR and ELISA assay.

Preliminary results: The viability of CGN in the potassium deprivation and excitotoxicity models showed a significant decrease of 50% after 24 h of treatment. The co-treatment with 1μM of the NLRP3 inhibitor MCC950, prevented cell death by 20% and 30% in the model of potassium deprivation and excitotoxicity, respectively. These results were confirmed when neural death was measured by the propidium calcein/iodide assay and the MTT reduction.

Work is underway to confirm LDH release levels, NLRP3 expression, and cytokine release.

Keywords: NLRP3 inflammasome, excitotoxicity and potassium deprivation.

Acknowledgements: This work was supported by CONACYT (285184) and DGAPA-PAPIIT, UNAM (IN216422)

HYPERGLYCEMIA DIFFERENTIALLY AFFECTS NEURONAL DIFFERENTIATION AND NESTIN, FOXO1 AND LMO3 MRNA EXPRESSION OF HUMAN UMBILICAL CORD WHARTON´S JELLY MESENCHYMAL STEM CELLS FROM NORMOGLYCEMIC AND PREGESTATIONAL DIABETES MELLITUS PREGNANCIES

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Abstract:

Diabetes mellitus (DM) during pregnancy constitutes an unfavorable environment for embryonic and fetal development, where, despite treatments, the children of mothers with Pregestational Diabetes Mellitus (PDM) have a higher risk of perinatal morbidity and mortality, with a high incidence of congenital malformations (CM). Neural tube defects are the second most common type of CM in children of diabetic mothers (CDM), who also have a high risk of undergo neurodevelopmental disorders, such as Intellectual disabilities, autism spectrum disorder and attention deficit hyperactivity disorder. The mechanisms that lead to these neuronal disorders in CDM are not yet fully understood. To analyze whether hyperglycemia differentially affects proliferation, the neuronal differentiation percentage and expression of neuronal differentiation mRNAs markers in children from normoglycemic pregnancies (NGP) and with PDM, we isolated and characterized human umbilical cord Wharton's jelly mesenchymal stem cells by flow cytometry, immunofluorescence, RT-PCR and were induced to differentiate into adipocytes, osteocytes and neurons. Proliferation assays were performed to determine the doubling time and Nestin, Tub-βIII, FOXO1, KCNK2, LMO3 and MAP2 mRNAs gene expression was assessed by semiquantitative RT-PCR. We found that hyperglycemia decreased proliferation significatively in NGP and DMP cells treated with 40mM D-glucose. The neuronal differentiation percentage significatively decreases to 74.52% and 32.02% in hyperglycemic conditions in NGP and PDM cells, respectively. In control glycemic conditions, nestin mRNA expression decreased during neuronal differentiation in both NGP and PDM cells, while FOXO1, KCNK2, LMO3 and MAP2 mRNAs expression increase during neuronal differentiation in both NGP and PDM cells. On the other hand, in hyperglycemic conditions, nestin was significantly decreased in cells from NGP, but not in cells from PDM, while mRNA expression of FOXO1 and LMO3 was significantly increased in cells from NGP, but not in cells from DMP. We found evidence that maternal PDM, with hyperglycemia in culture, affect biological properties of fetal cells.

EVALUATION OF A BORON-CONTAINING MELATONIN ANALOGUE IN THE COGNITIVE DEFICIT INDUCED BY ANDROGEN DEPRIVATION IN MALE RATS

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Abstract:

Some data from preclinical evaluation supports melatonin and its analogues as potential treatment for diseases involving cognitive deficit such as Alzheimer's disease (AD). Biochemical markers linked to origin and progress of the AD are measured as In this work, we evaluated by in silico docking studies a set of boron-containing melatonin analogues on rat MT1 and MT2 receptor models built by homology to the recent crystallized homologous human receptors. Then, we synthesized a compound (borolatonin, a boron-containing analogue of melatonin) identified as potent agonist. Its evaluation in a rat model with cognitive deficit induced by orchiectomy showed that its peritoneal administration induced ameliorative effects. Thus, the performance in behavioral tests was improved comparatively to both, control group and rat males administered with melatonin; while, by means of neuronal immunohistochemistry assays, it was demonstrated that neuronal loss due to hormonal deprivation was limited, as well as the amyloid-like accumulation in brain. Our results suggest the observed effects are by means of action on the melatonin system. Further studies are required to support or discard the proposed mechanism of action.

Farfán-García, E. D., et al. (2022). Identification and evaluation of boronic compounds ameliorating cognitive deficit in orchiectomized rats. Journal of Trace Elements in Medicine and Biology, 72, 126979.

Barrón-González, M., et al. (2022) Synthesis, In Silico, and Biological Evaluation of a Borinic Tryptophan-Derivative That Induces Melatonin-like Amelioration of Cognitive Deficit in Male Rat. *Int. J. Mol. Sci.* 2022, *23*, 3229

SLEEP RESTRICTION MODIFIES INSULIN SIGNALING IN THE HIPPOCAMPUS OF MALE RATS

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Abstract:

Sleep restriction is common problem in the modern society. In humans and rodents, sleep loss is associated to cognitive impairment and metabolic disturbances. The primary mechanism of cognitive disturbances remains unclear. However, an imbalance in molecules that altered during sleep loss such as insulin could have and important role, because it is not only essential for metabolic functioning but acts at central level regulating cognitive functions.

The aim of this study us to determinate the impact of sleep restriction on insulin signaling in brain areas related to cognition. Three-months old Wistar male rats were subjected to sleep restriction using the modified multiple platform method. Rats were placed on platforms during 20-hour (sleep loss) and were transferred to their home cage 4 hours at the end of the resting phase (sleep opportunity). On day 10, at the end of sleep restriction, restricted and control animals were sacrificed. The brain was removed, and the hippocampus was dissected. Hippocampal microvessels were isolated to evaluate the specific expression of insulin receptors in the endothelial cells of the blood-brain barrier. We determined insulin receptor expression and phosphorylated insulin receptor in total hippocampus and endothelial cells by western blot and PCR. Further, receptor localization was observed by immunofluorescence.

Sleep restriction promotes changes in the expression and phosphorylation of insulin receptors in isolated hippocampal microvessels and in whole tissue. These changes may alter insulin transport mediated by receptors expressed on endothelial cells, and thus alter insulin signaling in the hippocampus.

Our findings support the hypothesis that sleep restriction is a risk factor for the development of cognitive problems.

STUDY OF THE ENVIRONMENTAL EXPERIENCES ON BEHAVIORAL SENSITIZATION INDUCED BY TOLUENE

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Abstract:

Drug use in México have been increasing in the last years, being inhalants (toluene) among them with the highest consume. There have been identified some risk factors which predispose to drugs consumption and abuse, including the environmental factors, specially during the childhood and adolescence, where the adverse events play a critical role in triggering addictive behavior. In parallel to the risk factors, there are protection factors against the drug consuption and abuse. Thus, in the present study we evaluate the influence of different environments on the induction of behavioral sensitization induced by toluene, as an animal model of drug addiction.

Independent groups of Swiss Webster male mice were housed on: 1) standard condition, 2) stress condition (social isolation) or 3) positive environment (environmental enrichment) for 5 weeks. At the end of the first week of housing, animals were exposed to 4000 ppm of toluene or air (for control groups in each condition), this exposure went on daily during the 4 remaining weeks. Locomotor activity of mice was recorded at 1st, 5th, 10th, 15th and 20th toluene or air exposure.

Results showed that in the behavioural sensitization paradigm emerge two subpopulations, the sensitized and no sensitized ones, on the 3 housing conditions. Housing with environmental enrichment had a protective effect, demonstrated as a delay in onset of the behavioral sensitization. A tendency to exacerbate the addictive behavior was observed in the social isolation paradigm. Presents results evidence that environmental background is able to delay or exacerbate the onset of addictive behavior in subjects exposed to inhalants, stressing the idea that improving of the enviromental context can be an useful tool to increse resilience to develop addictive behavior.

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Chronic childhood adversity and stages of substance use involvement in adolescents. Drug and AlcohoLDependence. 131, 85-91., 3. Solinas, M., Thiriet, N., Chauvet, C., Jaber, M., 2010. Prevention and treatment of drug addiction by environmental enrichment. Prog. Neurobiol. 92, 572–592.

PROTEIN β-HYDROXYBUTYRYLATION IN NEURONS AND ASTROCYTES AND ITS IMPACT ON GENE EXPRESSION THROUGH H3K9BHB

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Abstract:

Metabolism impacts post-translational modifications (PTMs) in a tightly regulated and highly dynamic way. In eukaryotes, glucose is the main energy supply for most tissues, including the brain, which uptakes around 20% of total body glucose. However, when glucose availability is scarce, the ketone bodies (KBs) acetoacetate (AcAc) and b-hydroxybutyrate (BHB), act as an alternative energy fuel. BHB is the most abundant KB, constituting around 70% of the circulating KB pool. Besides serving as an alternative energy source, BHB is a versatile molecule that can bind to cell surface receptors, act as a class I histone deacetylases (HDACs) inhibitor or may directly bind to proteins as a PTM regulating thus their activity. Recently, a few proteins have been described as targets of this PTM, which has been designated as β-hydroxybutyrylation. Interestingly, this PTM has been recognized as a widespread histone mark and has been described in 38 histone lysines (Kbhb) in humans. This epigenetic mark is associated with an upregulation of gene expression, particularly of genes related to starvation in the liver.

Ample evidence shows that BHB plays a beneficial role in the nervous system homeostasis; it inhibits the inflammasome, regulates autophagy and protects from oxidative and excitotoxic damage. These functions, along with the high uptake of BHB that the brain displays under glucose-limiting conditions, highlight the importance to better understand the mechanisms that underlie these effects.

Therefore, in this work we have evaluated the presence and abundance of the β-hydroxybutyrylation in the total protein content and the H3K9bhb mark in primary cultured neurons and astrocytes. We also evaluated its abundance over time after the exposure to D- and L-BHB isomers. Histone acetylations were also analyzed, since both marks can occur at the same residues and the expression of some downstream regulated genes was evaluated. Histone acetylations and β-hydroxybutyrylation were also analyzed in the brain of mice subjected to a ketogenic diet. Results show differential effects of D and L-BHB isomers on β-hydroxybutyrylation. The detailed results and preliminary conclusions will be discussed at the meeting.

Keywords: β-hydroxybutyrylation, b-hydroxybutyrate (BHB), H3K9bhb.

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AVOCADO OIL PREVENTS NEUROLOGICAL AND OXIDATIVE DAMAGE IN A MODEL OF NEURODEGENERATION INDUCED BY QUINOLINIC ACID

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Abstract:

The intake of essential fatty acids (EFA) in both Huntington's disease (HD) patients and transgenic models has shown motor and cognitive improvement. Avocado oil contains different EFA and 60% is oleic acid, and its use through diet exerts important effects on the lipid composition of the neuronal cell membrane. The aim of this work was to study the effect of a fatty acid-rich diet included in avocado oil on the damage induced by quinolinic acid (QA). Male Wistar rats (250-280 g) were fed individually for 20 days with avocado oil (15% weight / weight). At the end of the diet, rats from the different groups were injured intrastriatally with QA (240 nmol/µL) and 2 hours after, striatal oxidative damage were measured through lipid peroxidation and the reactive oxygen species. Neurological changes were observed by counting of rotational turns in each animal after 3 days of QA lesion. We found that avocado oil diet for 20 days did not alter following parameters: the daily food intake, the body weight, and the biochemical parameters in blood. Interestingly avocado diet diminished the ipsilateral turns (89%) and recovered the GABA levels (70%) and the strital oxidative damage was prevented. Our data confirm the neuroprotective effect of a fatty acid-rich diet included in oil avocado.

CANNABINERGIC MODULATION OF PARKINSONIAN BASAL GANGLIA-CORTICO-THALAMIC NEURAL DYNAMICS

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Abstract:

Movement execution requires the control of movement amplitude, speed, direction, and timing. The basal ganglia-corticothalamic loop (BGCT) has been implicated in the encoding of such parameters. In pathological conditions such as Parkinson's Disease (PD), both movement execution and BGCT dynamics are impaired. Recently, it has been shown that the administration of cannabinoids improves motor symptoms in parkinsonian patients, suggesting that cannabinergic system manipulation could be a promising therapeutic alternative. The cannabinoid receptor type I (rCB1) is widely distributed in the central nervous system with its highest concentration in the BG output nuclei, the substantia nigra reticulata (SNr), where it regulates the release of neurotransmitters from the direct and indirect pathways. The output nuclei of the BG provide tonic GABAergic control to the motor thalamus (VL/VM), but its exact contribution to the BGCT dynamics are yet to be defined. The aim of this work is to evaluate if systemic and local (in the SNr) pharmacological manipulations of the rCB1 may provide therapeutic effects for the neural and motor symptomatology associated with PD. To accomplish this, we have developed an optogenetic-based preparation to evaluate cortico (M1)-thalamic neural interactions and their modulation by the BG output nuclei in awake/behaving mice. We found that in control animals, optogenetic M1 stimulation induced sequential neural activation in VL/VM that appears to follow and adapt to different inter-stimulus intervals. The systemic or local (SNr) rCB1 activation induced a drastic disorganization of the M1-evoked neural sequence. In hemiparkinsonian animals, the M1 stimulation failed to evoke clear sequential responses. Overall, our results demonstrate that systemic or local activation of the rCB1 in the BG output effectively modulates cortico-thalamic interactions. It remains to be determined if these changes in neural activity could be beneficial in hemiparkinsonian models, experiments that are currently being carried out in mice trained to perform forelimb movements with different durations.

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PGP is a PhD student from Programa de Doctorado en Ciencias Biomédicas (Neurobiología), UNAM and supported by fellowship 770484 from CONACyT-México.

EFFECT OF MAQUI BERRY (*ARISTOTELIA CHILENSIS*) EXTRACT ON MEMORY, OXIDATIVE STRESS AND BIOCHEMICAL COMPONENTS ASSOCIATED WITH METABOLIC SYNDROME INDUCED BY A HIGH-FAT, HIGH-FRUCTOSE DIET

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Abstract:

Metabolic syndrome (MS) is a complex condition that includes multiple metabolic and physiological alterations in various organs, mainly the liver, pancreas, skeletal muscle and adipose tissue. Recently, alterations have also been described in the brain, where most studies have focused on the impact of MS on cognition. The maqui berry has been shown to have the highest anthocyanin content when compared to other commercial berries. This is why maqui turns out to be an excellent candidate to evaluate its antioxidant and possibly neuroprotective effects, in a model of metabolic syndrome induced by a high-fat diet.

Objective:To evaluate the effect of aqueous extract of maqui berry (Aristotelia chilensis) on biochemical variables, cognitive deficit, and oxidative stress associated with metabolic syndrome induced by a high-fat, high-fructose diet in an animal model.

Methodology: Eighty female and male rats of the Sprague-Dawley strain weighing 200-250 g were used. The diets used in this study were: 1) normal rodent diet + double distilled water and 2) high fat diet + water with 30% fructose. Passive avoidance testing was performed to assess short- and long-term memory. Twenty-four hours after the memory and learning tests, the animals were sacrificed and serum and hippocampus were obtained and frozen to determine by enzymatic assays lipoperoxidation and superoxide dismutase activity. Subsequently, a statistical analysis of the data obtained was performed.

Results: In the analysis of the plasma of male and female rats, it was observed that chronic administration of maqui berry extract improved the components of metabolic syndrome, short and long term memory, as well as MDA concentration and SOD activity in the groups submitted to a high fat and fructose diet, without affecting these variables in the groups submitted to a standard diet.

In the analysis in the hippocampus of female rats, the groups treated with maqui berry extract increased glucose, total cholesterol and triglyceride levels. On the other hand, in the hippocampus of male rats treated with maqui berry extract, glucose, total cholesterol and triglyceride levels decreased.

Conclusions: These data suggest that metabolic syndrome affects differently depending on sex, that the administration of maqui berry improves the components of metabolic syndrome, improves memory and decreases oxidative stress in plasma and hippocampus of rats fed with high fat and high fructose diet and this effect also depends on sex.

PSACALIUM DECOMPOSITUM ALLEVIATES MEMORY IMPAIRMENTS IN AN ALZHEIMER'S DISEASE MOUSE MODEL

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Abstract:

Recent evidence shows that using oral hypoglycemic agents for long time improves cognitive functions in patients with Alzheimer´s disease (AD). On the other hand, *Psacalium decompositum (Pd)* is one of many Mexican plant species employed mainly for their hypoglycemic properties. Our group previously has shown that this plant has potent hypoglycemic and anti-inflammatory effects as well as antioxidant activity. Most of the identified compounds from their roots are sesquiterpenes, such as cacalol and cacalone. This study attempted to analyze the effect of the hexane extract, which is rich in sesquiterpenes, on memory in an AD mouse model with diet-induced insulin resistance.

We used 9 month old 3xTg-ADs which were divided into4 groups: 1) Normal diet (ND), 2) Normal diet plus extract (ND+E), 3) High-fat diet (FD) 34% of fat, and 4) High-fat diet plus extract (FD+E). The treatment with the hexane extract of Pd was given for one month after 2 months with high-fat diet. After treatment, animals subsequently underwent testing in a hippocampus-dependent spatial task, the Morris water maze (MWM) task and on the more cortical-dependent novel object recognition memory task.

Our data showed no significant weight changes in any treatment group. However, all high-fat diet groups showed impairment memory compared with normal diet groups in all tasks performed. Treated mice with Pd hexane extract showed improvement in training trials and probe trial of MWM. Treated mice with Pd hexane extract significantly improved the performance compared with control mice in the novel object recognition task.

Acknowledgments CONACYT, proyecto no: FOSISS-262444-Isabel Arrieta Cruz and in part to Secretaria de Ciencia, Tecnología e Innovación de la Ciudad de México, proyecto no: SECITI/042/2018 (INGER-DI-CRECITES-002-2018), RECITES.

SEARCHING HISTAMINE N METHYLTRANSFERASE INHIBITORS AND THEIR EFFECT ON HISTAMINE BRAIN LEVELS

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Abstract:

Despite the great efforts invested, the drugs available for treating Alzheimer's Disease (AD) are palliative. Therefore, the search for new therapeutics results in particular interest. In this sense, a decrease in the levels of the neurotransmitter histamine has been shown in the brains of patients with AD. Histaminergic neurotransmission becomes essential due to the enhancement of cognition and neuroplasticity, as well as neurogenesis. In addition, histamine has been shown to promote the degradation of insoluble extracellular amyloid-beta plaques and neurofibrillary tangles, histopathological findings in the AD brains. Therefore, the inhibition of the histamine catabolic enzyme, Histamine N Methyl Transferase (HNMT), represents a novel approach to the treatment of AD. For this purpose, in the present research work, molecular docking studies of 185 drugs employed for the treatment of neurological diseases with the HNMT enzyme were carried out using Autodock 4.2. Subsequently, drugs with higher affinity for the HNMT enzyme were selected to perform *in vitro* studies to corroborate HNMT inhibition and were administered to male Wistar rats to determine their effect on brain histamine levels. According to the computational studies, dihydroergotamine (-13.41 Kcal/mol), ergotamine (-13.58 Kcal/mol), and vilazodone (-12.86 Kcal/mol) were selected since they showed greater affinity for the enzyme HNMT. These compounds and the reference compounds interacted at the histamine binding site. HNMT inhibition assay and brain histamine levels of selected compounds were achieved. Selected compounds belong to drugs used to treat migraine and depression, so results are of particular interest since many patients with AD have other neurological disorders, such as depression.

Flores-Clemente C, Nicolás-Vázquez MI, Mera Jiménez E, Hernández-Rodríguez M (2021) Inhibition of Astrocytic Histamine N-Methyltransferase as a Possible Target for the Treatment of Alzheimer's Disease. Biomolecules, 11, 1408

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NEURON SPECIFIC ENOLASE AS A BIOMARKER OF DIABETIC PERIPHERAL NEUROPATHY

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Abstract:

Diabetic peripheral neuropathy (DPN) is a common complication of both type 1 and 2 diabetes. It is a leading cause of lower-limb amputation and disabling neuropathic pain. Early peripheral neuropathy may present as sensory alterations that are often progressive, including sensory loss, numbness, pain, or burning sensations in a stocking and glove distribution of the extremities. Furthermore, for its diagnostics is necessary a comprehensive metabolic profile; vitamin B12, serum protein electrophoresis with immunofixation and thyroid-stimulating hormone levels. If the evaluation is inconclusive, a neurological test such as specific antibody assays o electrodiagnostic studies, should be considered. Neuron specific enolase (NSE) is a glycolytic enzyme found in neuronal and neuroendocrine tissues that may play a dual role in promoting both neuroinflammation and neuroprotection. Thus, NSE could be a reliable, quantitative, and specific marker of neuronal injury. Depending on the injury, disease, and microenvironment. Objective: This study evaluated the plasmatic concentration of NSE in diabetics patients in the early diagnosis of DPN. Methods: Cross sectional study of 70 diabetic patients' resident in Veracruz were included. We evaluated the presence of diabetic neuropathy by quantify the loss of sensation in foots using the Semmes-Weinstein Monofilament (SWM) and NSE concentrations were determine by ELISA kit. We used logistic regression to examine the association of diabetic peripheral neuropathy with NSE, adjusting by the diabetes time and pharmacological treatment. Results: Duration of diabetes disease was above ten years in 40% and 60% of the patients was under biguanides treatment. 28.6% of diabetics were diagnostic with peripheral neuropathy. Plasma NSE levels were detected of 0.5 to 15.35 ng/mL, with higher concentration in patients with DPN ($p<0.05$). There was a significant independent association of DPN with NSE concentrations (odds ratio [OR] 1.74, 95% confidence interval [CI], 1.29-2.36) biguanide treatment (OR 0.15; 95% CI, 0.03-0.72) and diabetes time (OR 1.19; 95% CI, 1.04-2.36). Conclusion: This study indicates that development of diabetic peripheral neuropathy is related with higher plasmatic NSE concentrations and the absence of biguanides treatment.

COADMINISTRATION OF ROTENONE AND MANGANESE TO MODEL PARKINSON'S DISEASE IN RATS

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Abstract:

Introduction. Parkinson's disease (PD) result from complex interactions between genetic and environmental factors. Both rotenone and manganese are environmental stressors involved in the development of PD; determining if their interaction enhances their neurotoxicity will contribute to the knowledge regarding the interaction of environmental factors to produce PD.

Objective. To determine whether exposure to manganese (MnCl2) potentiates the ability of rotenone to model PD.

Experimental design. Male Wistar rats of 280-300 g were divided into the groups: 1) vehicle, 2) rotenone (3 mg/kg/24 h), 3) $MnCl_2$ (5 mg/kg/24 h), 4) $MnCl_2$ (10 mg/kg/24 h), 5) $MnCl_2$ (15 mg/kg/24 h), 6) $MnCl_2$ (5 mg/kg/24 h) + rotenone, 7) $MnCl_2$ (10 mg/kg/24 h) + rotenone, and 8) $MnCl_2$ (15 mg/kg/24 h) + rotenone; treatment was for eight days. After, histological (H&E stain, tyrosine hydroxylase, tubulin and a-synuclein detection) and biochemical analysis (mitochondrial function, apoptosis, oxidative stress) were performed.

Results. Rotenone reduced the rearing behavior and induced morphological damage in the striatum, globus pallidus, and substantia nigra pars compacta (SNpc). Also, it induced the dopaminergic neurons death in SNpc and reduced tyrosine hydroxylase in the striatum. Manganese treatment enhanced the effect of rotenone, mainly the morphological damage in all brain areas studied.

Conclusion. The rotenone-manganese interaction is a good tool for studying environmental interactions associated with mitochondrial defects in the progressive PD development.

Racette, B. A., Nelson, G., Dlamini, W. W., Prathibha, P., Turner, J. R., Ushe, M., Nielsen, S. S., 2021. Severity of parkinsonism associated with environmental manganese exposure. Environ Health, 20(1), 1-13. doi: 10.1186/s12940-021-00712-3.

TRPV1 IS A NOXIOUS SENSOR REGULATED BY ENDOCANNABINOIDS

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Abstract:

Pain is an unpleasant sensation that alerts us from actual or potential harm. Among the diverse proteins expressed in sensory neurons that play an essential role in signal transduction is the Transient Receptor Potential Vanilloid 1 (TRPV1). TRPV1 is a polymodal transducer of painful stimuli, functioning as an essential warning signal.

TRPV1 can be modulated by several endogenous ligands; anandamide (AEA) and 2-arachidonoylglycerol (2-AG) are endocannabinoid compounds related to arachidonic acid that are associated with analgesic effects. Currently, no experimental evidence has been reported on the influence of these endocannabinoids on the regulation of protein levels of TRPV1.

This work sought to determine if the AEA and 2-AG can modify the protein levels of TRPV1. The experiments were carried out on cultures of HEK293 cells that express transiently to the TRPV1 channel and primary cultures of dorsal root ganglion neurons (DRG), which were subjected to treatments with different concentrations of AEA. These endocannabinoids were found to modify the total protein and plasma membrane levels of TRPV1. The effect of AEA is mediated by extracellular calcium because when the cells were treated with AEA and EGTA, the protein levels of TRPV1 were not modified. In addition, we determined that AEA decreases protein TRPV1 levels through the lysosome pathway since inhibiting this degradation pathway partially rescues TRPV1 levels.

Finally, we demonstrate that AEA inhibits the acute pain response produced by the activation of TRPV1.

All these results allow us to conclude, according to the hypothesis proposed, that the AEA decreases the protein levels of TRPV1 by degradation through the lysosomal pathway.

LYSOSOMAL ALTERATIONS DURING NEURONAL SENESCENCE IN AN *IN VITRO* MODEL

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Abstract:

One of the hallmarks of aging is the accumulation of senescent cells in the organism. In old brains, and in an *in vitro* model of neuronal senescence, neurons can acquire senescent features such as lysosomal dysfunction, cytoskeleton fragmentation, and the senescence-associated secretory phenotype that alters surrounding tissue, among others senescent features. Previous work in our group established that neuronal senescence occurs as a consequence of macroautophagy dysfunction with lysosomal aberrant morphology, which could be a consequence of axonal microtubules fragmentation. On the other hand, in studies of axonal degeneration, the RIPK1-RIPK3-MLKL pathway has been found to mediate cytoskeleton fragmentation.

Macroautophagy is a conserved catabolic process that selectively digests cell components through the formation of a double-membrane vesicle around them that fuses with lysosomes to degrade engulfed components. A functional cytoskeleton and adequate function of lysosomes are essential for their fusion with autophagosomes, and consequently, for autophagy function.

We propose that neuronal senescence could be induced as a consequence of the RIPK1-RIPK3-MLKL pathway activation, which leads to axonal microtubules fragmentation, causing alterations in lysosomal morphology and transport, and hence dysfunctional autophagy. This work aims to test this hypothesis. We will present the dynamics of lysosomal morphologic alterations and microtubule fragmentations along an *in vitro* model of neuronal senescence, as well as preliminary results of the role of MLKL.

Keywords: autophagy, neuronal senescence, lysosome

Acknowledgements: Funding was provided by UNAM-DGAPA-PAPIIT IN209221 and CONACyT fellowships 1145550 to PLC and 820681 to GACM. GACM is student of the "Doctorado en Ciencias Bioquímicas and PLC is student of the "Maestría en Ciencias Bioquímicas" at Universidad Nacional Autónoma de México (UNAM). We are grateful to Dra. Beatriz Aguilar, Dr. Ruth Rincón and Dr. Abraham Arellano for their technical assistance.

PROLACTIN PREVENTS OXIDATIVE STRESS-INDUCED CELL DEATH IN HIPPOCAMPAL NEURONS

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Abstract:

Oxidative stress is related with the occurrence and progression of several neurodegenerative diseases. Efforts have been done to find neuronal antioxidant-protective factors. Prolactin (PRL) is a pituitary hormone that has been shown to be protective against oxidative stress-induced apoptosis of retinal pigment epithelial cells. Furthermore, PRL exerts a neuroprotective effect against excitotoxicity in hippocampal neurons, both *in vitro* and *in vivo* models. Using primary cultures of hippocampal neurons isolated from the brain of E16 mice, we investigated a possible protective role of PRL against oxidative stress-induced cell death. Hydrogen peroxide (H_2O_2; 100 M) induced apoptotic cell death and increased ROS generation and lipoperoxidation in hippocampal neuronal cultures as detected with MTT assay, TUNEL staining, DCFDA oxidation and TBARS assay, respectively. Preincubation with 100 nM PRL protected hippocampal neurons against H_2O_2-induced apoptotic cell death and increased oxidative damage. Furthermore, PRL-induced protection against H_2O_2 was abolished by using a prolactin receptor antagonist G129 (100 M). To assess the possible mechanism involved in these PRL actions, we evaluated the expression of both apoptosis mediators and redox enzymes by qRT-PCR. PRL downregulated H_2O_2-induced pro-apoptotic Bcl-2 family members BAX and BAD, whereas BCL2 expression was not affected either by PRL or H_2O_2. In addition, PRL downregulated H_2O_2-induced NADPH oxidase 4 (NOX4) expression and NOX enzymatic activity assessed by qRT-PCR and lucigenin assay, respectively. NADPH oxidase 2 and xanthine oxidase expression were not affected by PRL. These results demonstrate that PRL is an anti-apoptotic factor for hippocampal neurons under conditions of oxidative stress, and acts as an antioxidant at least to some extent via inhibition of NOX4 expression and activity. These findings suggest that PRL may be useful in the prevention of neurodegenerative diseases. Acknowledgments: We thank Fernando López-Barrera, Xarubet Ruiz-Herrera, Alejandra Castilla, Nydia Hernández and María Carbajo for their technical assistance.

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HISTONE DEACETYLASE 2 INHIBITION REVERSES MEMORY IMPAIRMENT INDUCED BY ACUTE STRESS IN MICE

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Abstract:

Multiple studies in animals and humans have shown that chronic stress induces learning and memory impairments, while the effects of acute stress critically depend on their temporal relationship, facilitating or preventing memory consolidation depending on whether the stress occurs during the learning event or before it, respectively. On the other hand, it has been shown that histone acetylation regulates the persistence of long-term memory. The aim of this study was to evaluate the effect of two inhibitors of class I histone deacetylase (HDAC), 4-phenylbutyrate (PB) and IN14, in mice exposed to a single 15-min acute stress session of forced swimming, 30 min before training. The study comprised three factors: 1) pharmacological treatment: Vehicle, IN14, or PB (100 mg/kg, i.p. for 2 days); 2) acute stress: present or absent; 3) memory test: present or absent. Three memory tasks were performed 1 h after the last drug injection: Novel object recognition test (NORT), Elevated T Maze (ETM), and Buried food location test (BFLT). After completion of behavioral testing, mice were sacrificed, the hippocampus removed, and samples collected to perform ELISA assays for HDAC2 expression. Acute stress induced an increase of hippocampal HDAC2 content, as well as plasma corticosterone levels, along with a poor performance in NORT, ETM, and BFLT tests. Moreover, PB and IN14 treatment prevented memory loss in stressed mice. These findings suggested that HDAC2 is involved in acute stress-induced cognitive impairment. Yet, it is worth mentioning that none of the drugs improved memory in non-stressed animals, indicating that HDACs inhibitors are not cognitive boosters, but rather potentially useful drugs for mitigating memory deficits in cognitively compromised patients. The protective effects of HDACs inhibitors on acute stress-induced amnesia observed here open the possibility of potential use of these drugs to prevent the cumulative effects of stressful events on cognitive function.

Keywords: Histone deacetylase inhibitors, epigenetic, stress; learning and memory, corticosterone, HDAC

Acknowledgments

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TNF-α RECEPTOR ANTAGONISM RESTORES PERICYTE-ENDOTHELIAL CELL INTERACTIONS AND IMPROVES BLOOD-BRAIN BARRIER FUNCTION DURING SLEEP RESTRICTION

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Abstract:

Brain pericytes stabilize blood vessels through direct contact with endothelial cells. Ten days of sleep restriction promotes pericyte detachment from the capillary wall by decreasing PDGFR-β and connexin-43 protein expression. Pericyte detachment is accompanied by a reduced expression of tight junction proteins and blood-brain barrier hyperpermeability to molecules of low and high molecular weight. These changes are associated to high concentration of pro-inflammatory mediators such as MMP-9 and A2A adenosine receptor. In this study, we describe that pericyte detachment from the capillary wall begins at short periods of sleep loss (5 days) and that the initial event seems to be a downregulation and relocation of connexin-43, with PDGFR-β being secondarily loss. We also found increased expression of MMP-9 and A2A adenosine receptor. A single dose of the TNF-α receptor antagonist R-7050 restores PDGFR-β expression in the cerebral cortex and restores the permeability of the blood-brain barrier by normalizing the permeability to Na-Fluorescein in the cerebral cortex and hippocampus. Therefore, our results suggest that the loss of gap junctions between pericytes and endothelial cells, followed by the loss of the signaling pathway regulated by PDGFR-β are the key events regulating blood-brain barrier disruption, where TNF-α plays a major role in modulating pericyte-endothelial cell junctions during short periods of sleep restriction.

THE NEUROPROTECTIVE EFFECT OF THE ENDOCANNABINOID METABOLITES OF CYTOCHROME P450 DURING THE STAUROSPORINE-INDUCED NEURONAL DEATH

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Abstract:

Cytochrome P450 (CYP) epoxygenases can metabolize the anandamide (AEA) and its products, the epoxyeicosatrienoic acid ethanolamides (EET-EAs), are biologically active and capable to activate the cannabinoid signaling pathway. The EET-EAs can be hydrolyzed by the soluble epoxide hydrolase enzyme (sEH) to form the dihydroxyeicosatrienoic acid ethanolamides (DHET-EAs), metabolites with low biological activity. It is known that the modulation of the endocannabinoid system has a therapeutic potential in the CNS diseases, since its activation has anti-inflammatory and antioxidant effects. We are, therefore, interested in studying the neuroprotective effects of EET-EAs in the neuronal death, as well as the mechanisms involved in this neuroprotection. To this purpose, we used primary cultures of cerebellar granule neurons and induced cell death with staurosporine (0.5 mM) treatment. To enrich the content of EET-EA in the cultures, we pre-treated cells during 2h with TPPU (100 mM), a specific inhibitor of soluble epoxide hydrolase (sEH) and with anandamide (20 mM). To determine the involvement of the cannabinoid signaling in the EET-EA-mediated neuroprotection, we used AM251 (1 mM), a CB1 cannabinoid receptor antagonist. Cell viability was assessed by measuring MTT reduction, as well as calcein/propidium iodide staining. Under these conditions, we found that TPPU and anandamide pre-treatment individually and in co-treatment showed a marked neuroprotective effect against staurosporine-induced neuronal death. Although we found that both anandamide and its CYP-derived metabolites resulted neuroprotective, we did not find a synergistic effect. Interestingly, we found that the observed neuroprotective effect of both conditions was reversed by the CB1 antagonist AM251. These results suggest that endocannabinoid metabolites of cytochrome P450 could play a significant role in the neuroprotection. Additionally, the observed neuroprotection could be mediated through an autocrine or paracrine mechanism.

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Cynthia Navarro-Mabarak is a CONACYT postdoctoral fellow (I1200/224/2021).

EXPLORING THE ROLE OF THE DIRECT PATHWAY OF THE BASAL GANGLIA IN SPEED CONTROL DURING THE EXECUTION OF MOTOR SEQUENCES

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Abstract:

The basal ganglia (GB) are a group of subcortical nuclei implicated in motor functions. The BG are organized in two anatomically and functionally segregated pathways, the direct and indirect pathway. While these pathways have been widely researched, there is still debate in what their exact role is. The general aim of this project is to explore the role of the direct pathway in the control of speed during sequence execution. To achieve this goal, we trained rats to perform a timed sequence of deaccelerations and accelerations while running on a motorized treadmill at different speeds. The animals learned to explicitly modulate their running speed to adjust their sequence of movements to a fixed time interval. Then we used optogenetic techniques to manipulate specifically the neuronal activity of the direct pathway. We stimulated the animals in different phases of the sequence of movements and in a "neutral" context, where no movement control or sequential behavior was required. Contrary to what was expected, we found that stimulating the neurons of the direct pathway in the dorsolateral striatum decreased speed and increased sequential time execution and percentage of correct trials. Stimulating the same animals in the neutral environment evoked a stereotypical behavioral pattern of reverse locomotion, which would explain de decreased speed during the behavioral task. This pattern was also observed in naïve animals and was exclusive to a DLS region with rich somatosensory representation of hindlimbs. Overall, our results indicate that the stimulation of the direct pathway facilitated movement but not in a general way but for specific behavioral patterns related to the anatomical organization of the structure.

Keywords: Basal ganglia, striatum, direct pathway, movement.

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ENCODING VISUAL STIMULI BY STRIATAL NEURONS

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Abstract:

Introduction. The interaction between cortical areas and basal ganglia structures is essential for perceptual integration, decision-making, and movement. The striatum is the main input of the basal ganglia, and it has been recently shown that its dorsomedial region (DMS) integrates somatosensorial, motor, auditive, and visual information. In mice, neurons from primary visual cortex (V1) send direct projections to DMS. Such cortico-striatal interaction is necessary for visual discrimination tasks. However, it is still unknown how different features of visual stimuli are represented in the striatum. For over 50 years it has been described that groups of neurons in V1 encode visual-oriented drifting-gratings. Nevertheless, it has not been reported if DMS preserves such information. We investigated if orientation information is preserved in the activity of striatal neuronal ensembles.

Objective. Characterize how visual-oriented drifting-gratings are represented in the electrical activity of DMS neurons.

Methods. Multielectrode arrays of 64 channels in tetrode configuration were used, single-unit activity from more than 400 putative neurons was isolated from C57Bl/6J awake mice (head-fixed). During neural recordings, 4 different drifting-gratings (2 directions per orientation) were shown to mice. The stimulated eye was contralateral to the DMS recorded. Mutual information was calculated in each neuron based on stimuli information. Peri-stimulus histograms evoked by different visual-oriented drifting-gratings were obtained and used to calculate the Orientation Selectivity Index (OSI) of each neuron.

Results. We found a high proportion of DMS neurons that showed responsiveness to visual stimuli. On the other hand, after stimuli onset, the mutual information was increased in the population of neurons recorded from DMS, indicating that the orientation of drifting-gratings is encoded in striatal neurons. Interestingly, only a small subpopulation of recorded neurons (~10%) showed an OSI >0.5, suggesting that a small proportion of striatal neurons are sufficient to carry on cortical information.

Conclusion. Neurons in DMS encode visual-oriented drifting-gratings. Our results suggest that the DMS has a fundamental role in the formation of visual percepts.

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CURCUMIN DECREASES THE PROTEIN OXIDATION IN BRAIN OF MICE FED A HYPERCALORIC DIET

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Abstract:

The consumption of a high-fructose diet (HFD) contributes to obesity, and systemic oxidative stress. Curcumin has been proposed that decreases the systemic oxidative stress, preventing the brain oxidative damage and neurodegenerative diseases. This study was to determine the curcumin effect on the oxidative damage in brain of mice fed a HFD. Male C57BL/6 mice of 6 weeks old were fed for a period of 15 weeks as follows: 6 mice received standard diet (SD; named group SD); 6 mice received 30% (w/v) of fructose in water (named group Fru); 6 mice received SD supplemented with 0.75% (w/w) of curcumin (named group Cur); finally, 6 mice received SD supplemented with 0.75% (w/w) of curcumin and 30% (w/v) of fructose in water (named group Fru+Cur). At the end of treatment, the mice were sacrificed and the hippocampus, frontal cortex (FC), cerebellum and striatum were isolated to determine the TBARS and carbonyls levels as markers of oxidative damage. The present study was approved by the Institutional Bioethics Committee of University of Guanajuato (CIBIUG-EX03-2020). In FC, the carbonyl levels (CL) were higher in Fru group than the SD, Cur and Fru+Cur groups (416.2±73 vs. 252.5±52.3, 309±73 and 306.7±57.8 ng of carbonyls/mg.protein, respectively; $p<0.05$); in cerebellum, CL were higher in Fru group than the SD, Cur and Fru+Cur groups (600±159 vs. 424.8±58, 345.9±81 and 398.8±140 ng of carbonyls/mg.protein, respectively; $p<0.01$); moreover, the CL were lower ($p<0.01$) in Fru+Cur group than the Fru group. With respect to striatum, fructose increased CL than the SD and Fru+Cur groups (296±44 vs. 249.7±17 and 245±17 ng of carbonyls/mg.protein, respectively; $p<0.01$); no differences were observed in Fruc and Cur groups (266±36 and 245±17 ng of carbonyls/mg.protein). In hippocampus, significant differences were observed between the SD and Fru groups (237±52 vs. 320±69 ng of carbonyls/mg.protein, $p<0.05$), and these CL were similar with respect to Cur and Fru+Cur groups (284±29 and 280±61 ng of carbonyls/mg.protein, respectively).

Conclusion: The high-fructose diet increases the oxidation to protein in the mouse brain, whereas curcumin reduces this oxidation, suggesting that fructose may induce memory deficits, and curcumin may ameliorate this deficits.

EFFECT OF KETOGENIC DIET ON MOUSE AGING

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Abstract:

Aging is a cumulative loss of physiological functions of an organism through time that increases the likelihood to die. It is the principal risk factor for several human pathologies. However, organisms age at different rates, thus a concept known as frailty has been developed to explain the differential vulnerability to adverse health outcomes of organisms of the same age. Moreover, a reduction in autophagic function has been correlated with aging. Autophagy is a catabolic mechanism for cells to selectively deliver cytosolic material into lysosomes for degradation. We have previously demonstrated that failure of autophagy during aging promotes the establishment of cellular senescence in neurons. Cellular senescence is a cell state of disturbed metabolism that leads to the acquisition of an altered gene expression and a particular secretory phenotype. Throughout lifetime, senescent cells accumulate within tissues and avoiding this accumulation has proven to be effective in mitigating several adverse effects associated with aging. Therefore, strategies focused on improving autophagy could provide a way to prevent the accumulation of senescent cells and the harmful effects associated with this. One of such strategies, that has proven to improve autophagic flux is the consumption of a ketogenic diet (KD). Consequently, we propose that a KD, by stimulating autophagy, could diminish the accumulation of senescent cells, and mitigate the adverse health outcomes associated with aging. To test this hypothesis, we assessed a 31-item frailty index and the Kondziella´s muscle strength test to evaluate the physiological aging from male and female mice (6 and 13 months old) exposed to a control diet (13.6% fat, 28.9% protein and 57.4% carbohydrates) or a KD (75.1% fat, 8.6% protein and 3.2% carbohydrates). The detailed results and preliminary conclusions will be discussed at the meeting.

Key Words: ketogenic diet, autophagy, cellular senescence, frailty

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JOINT ADMINISTRATION OF SYNTHETIC LIGANDS OF TLRS AND VINCRISTINE IN A MURINE MODEL OF MEDULLOBLASTOMA

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Abstract:

Medulloblastoma is an embryonal brain tumor that predominantly occurs in childhood. Vincristine is a chemotherapeutic drug that interferes with microtubules and causes cell cycle inhibition. Toll-like receptors (TLRs) are pattern-recognition receptors of innate immune system that are involved in recognition of exogenous molecules of microorganisms (MAMPs) and endogenous molecules considered danger signals (DAMPs). The antitumor and protumoral effects of TLR activation have been demonstrated in different types of cancer, but in the case of medulloblastoma, it is still unknown. We investigated the effects of TLR7/TLR8 and TLR9 activation with synthetic ligands (R848 for TLR7/TLR8 and ODN for TLR9) and vincristine on development and proliferation of medulloblastoma in a murine model.

Methods. Daoy cells were cultured and implanted subcutaneously in nu/nu mice. Body weight and tumor size of mice were monitored weekly, and two injections of the synthetic ligands are administered intratumorally when the tumors reached a volume of $\geq$50 mm^3. Histological sections of the tumor were made and the presence of ki67 proliferation marker was determined by means of immunohistochemistry. Results: We observed a reduction in tumor volume with joint treatment with synthetic ligands of TLR7, TLR8 and TLR9 and vincristine compared to vincristine alone. Furthermore, we found a decrease in tumor proliferation when treated with vincristine and the TLR9 ligand.

Conclusions. Vincristine decreases tumor volume but seems more effective in combination with TLR7, TLR8 and TLR9 ligands. Also, the tumor proliferation was further decreased with TLR9 activation a with ligands de TLR7, TLR8 and TLR9. Also, the tumor proliferation was further decreased with ligands on TLR9 and vincristine.

COMPARATIVE GENOMICS OF TFBSS OF LTTR TRANSCRIPTION FACTORS

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Abstract:

The large amount of knowledge related to Transcription Factor Binding Sites (TFBSs), either experimental or predictive, has driven the development and growth of several databases. However, in the case of LysR-type transcriptional regulators (LTTRs), the precise identification of the corresponding TFBSs has struggled, due to the degeneracy of their sequences. As a result, the low quality of matrices for the prediction of TFBSs in the same or orthologous organisms, will be far from reality.

In order to identify phylogenetic relationships between the variability of orthologous sequences, in this study, sequences of TFBSs for LTTR regulators were analyzed from several databases, such as: EcoCyc, RegulonDB, Prodoric, Reg Precise, RegTrans Base and Tractor DB. In this regard, 1320 sequences of TFBSs were analyzed, corresponding to 545 regulons of 75 orthologous regulators of the LysR family. To carry out the phylogenetic analyses of the TFBSs, the following characteristics were taken considered: symmetry, orientation, 15nt of length and the conservation of sub-motifs located within the BS sequence. The results show the presence of three major phylogenetic groups, with three different sub-motifs: ATC-n9-GAT, ATA-n9-TAT and TGA-n9-TCA. We also identified variants of the 3 identified sub-motifs and variations in the lengths of the TFBSs, with a range of 13, 15, 17, 17, 19, 21 and 23 nucleotides. Additionally, we also identified that the regions between the sub-motifs, or minor grooves, are A + T rich. Three different extended sub-motifs, with respect to the initial rule T-n11-A, were identified in our analysis (Schell, 1993). Our findings will allow deciphering the phylogenetic relationships of TFBSs of LTTR regulators.

Schell, M. A. (1993). Molecular biology of the LysR family of transcriptional regulators. *Annu Rev Microbiol.* 47:597-626.

ANTI-NOCICEPTIVE EFFECT OF N-ACETYLCYSTEINE IN A RAT MODEL OF TRAUMATIC SPINAL CORD INJURY

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Abstract:

Traumatic spinal cord injury (LTME) is defined as an acute, traumatic injury to nerve tissue that is located in the spinal canal. Among the most common conditions presented by patients with LTME are: partial or total loss of movement, breathing difficulties, gastrointestinal complications, incontinence or vasoconstriction, depression, loss of sensation and pain. There are studies that relate neuropathic pain with the loss of synaptic connections, which generates the loss of normal inhibitory processes mediated by opioids, y-aminobutyric acid (GABA), monoamines and glycine causing a change in the activity of glial cells mediated by oxygen free radicals. Likewise, there are studies where various antioxidants are used for the treatment of neuropathic pain such as vitamin C and E, alpha lipid acid and N-acetylcysteine (NAC), NAC exhibits a powerful antioxidant activity in the cell through the increase of intracellular glutathione (GSH), which is an important component of the pathways by which cells are protected from oxidative stress, and its activity as a free radical satracting molecule by providing hydrogen sulfide groups. The data obtained from the present work through the quantification of lipid peroxidation, the determination of the reduced glutathione concentration and the determination of fifty percent of the threshold of withdrawal of the leg and mechanical hyperalgesia, suggest that the use of NAC is able to reduce Neuropathic pain in rats induced by an LTME.

TRANSCRIPTIONAL PROFILE OF CYTOKINES EXPRESSED IN MAST CELLS STIMULATED WITH S100B, A DAMP ASOCIATED TO NEUROINFLAMMATION IN HUNTINGTON DISEASE

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Abstract:

Huntington Disease (HD) is a neurodegenerative pathology caused by a mutation in the gene encoding the protein Huntingtin (Htt). One of the hallmarks of this condition is neuroinflammation, which is triggered by damage-associated molecular patterns (DAMPs) released by damaged cells. Those molecules, in turn, activate immune cells that reside in the central nervous system (CNS). One of those DAMPs is S100B protein, a ligand of distinct pattern recognition receptors (PRRs), such as the Toll-like receptor (TLR) 4 and the receptor for advanced glycation products (RAGE). We recently reported that mast cells (MCs) participate in the manifestation of HD-associated symptoms in distinct murine models of the disease, suggesting this cell type plays a role on the neuroinflammation associated to that condition. The aim of this work was twofold: 1) to evaluate the effect of S100B protein on the cytokine profile produced by MCs; and 2) to determine the production of S100B in a murine model of HD induced by the administration of quinolinic acid (QA). Bone marrow-derived mast cells (BMMCs) from C57BL/6J mice were exposed to S100B and cytokine mRNA production was determined by RT-PCR and a multiplex qRT-PCR assay. Results shown that S100B promotes an important change on cytokine expression in MCs, inducing the production of TNF and IL-6 ad repressing the production of immune response-related genes, such as Smad7. Utilizing the TLR4 inhibitor TAK242 and the RAGE antagonist FPS-ZM1, it was found that S100B actions on MCs are dependent on both TLR4 and RAGE receptors triggering. Finally, S100B production was detected in the *in vivo* QA-induced model of HD. Our data suggest that S100B and its receptors in MCs could be a therapeutic target for neuroinflammation.

EFFECT OF CHRONIC HYPERCALORIC DIET FEEDING ON THE INFLAMMATORY STATE, AND ITS RELATION TO COGNITIVE IMPAIRMENT IN MIDDLE-AGED FEMALE WISTAR RATS

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Abstract:

Overweight and obesity are defined as abnormal or excessive fat accumulation that can be harmful to health. This condition is known to have a higher prevalence in women. Excess energy leads to adipose expansion generating hypertrophic adipocytes that produce a wide variety of pro-inflammatory molecules. The production of these molecules by adipocytes generates a chronic low-intensity inflammation, affecting the organism's functioning. Recently, it has been shown that systemic inflammation also affects the central nervous system (CNS). Saturated fat intake has been associated with memory impairment because peripheral inflammatory signals activate microglia, which then secretes more inflammatory cytokines, activating astrocytes and favoring a chronic neuroinflammatory condition that leads to neuronal damage. The objective of this study was to determine the effect of systemic inflammation produced by the chronic consumption of a hypercaloric diet on the cognitive deterioration during the animal´s middle age.

Young (6-month-old) and middle-aged (13-month-old) female Wistar rats were fed with a hypercaloric diet from weaning. The inflammatory state was measured by ELISA assay in serum, cerebral cortex, and hippocampus, and recognition memory was evaluated using the novel object recognition test (NOR).

Our data showed that obesity generates a systemic inflammation with a significant increase in IL-6, IL-1β, TNFα, and MCP-1 levels, which induces central inflammation in the cerebral cortex and hippocampus, and impairs learning and memory. This effect is more evident in middle-aged than in young rats.

Authors thank PhD. María de los Ángeles Guerrero-Aguilera from UAM-I vivarium for providing animals necessaries for this project. This work was supported by grant FORDECYT-PRONACES/263957/2020 and CONACYT Ciencia de Frontera 2019 (1783), as well as Dirección General de Asuntos del Personal Académico, UNAM, PAPIIT (IN214821). VSV, RSM and YM Rodríguez-Cortéz are CONACyT scholarship holders.

A METHOD TO INTERROGATE AND MANIPULATE PYRAMIDAL TRACT CORTICO-STRIATAL NEURONS IN RATS

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Abstract:

The motor cortex plays a main role in the generation of movements. It has been suggested that different subpopulations of motor cortical neurons are implicated in different components of the final behavioral output, such as the speed, direction or duration of movements. One of this populations are the cortico-striatal neurons of the pyramidal tract (PT). The PT neurons are known to project ipsilaterally to the striatum, the thalamus and the subthalamic nucleus and bilaterally to the brainstem and the spinal cord. The specific function PT neurons is yet to be fully understood, for which it would be useful to design and implement specific methods to interrogate/ manipulate this subpopulation in the context of behavioral execution. Therefore, this project is focused on implementing a viral-based method to express opsins for optogenetic control in PT neurons. By using a combination of complementary retrograde viruses sequentially injected in different targets of PT neurons, we found that injecting the dorsolateral region of the striatum and then ventrolateral motor thalamus, resulted in the fluorescent staining in cortical and subcortical regions consistent with PT projections. These results were confirmed with cortical and striatal extracellular electrophysiological recordings in anesthetized animals. Our results suggest that this strategy is adequate to specifically manipulate PT neurons in freely behaving animals.

Keywords: cortico-striatal neurons of the pyramidal tract, optogenetic manipulation, characterization of neuronal activity.

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OSL is a Master student from Programa de Maestría en Ciencias (Neurobiología), UNAM and supported by fellowship 1145843 from CONACyT-México.

IMMUNIZATION WITH PEPTIDE A91 INDUCES NEUROGENESIS AT THE LEVEL OF MEDULLARY HORNS IN MODERATELY INJURED RATS

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Abstract:

Post-injury neural progenitor cells (NSC) have been observed in the spinal cord in rats, it is currently unclear where they come from, whether they are medullar residents or travel from higher centers such as the hippocampal dentate gyrus and subventricular zone. The objective of the study is to identify and quantify neurogenesis in the medullary horns in moderately injured rats treated with the modified neural peptide A91.

The study was performed in Sprague-Dawley rats in a moderate blunt injury model and evaluated at 15 and 30 days. To observe neurons in early formation, double labeling with Anti-5 bromo-2'-deoxyuridine (BrdU) and doublecortin antibodies (Dcx) was used. Active neuroblast formation was found in both dorsal horns and ventral horns in rats immunized with INDP at different levels of the medulla, being much higher than what was found in rats treated with PBS.

There is a lack of studies regarding where these neuroblasts came from or if their formation at the spinal cord level is possible.

SULFORAPHANE PREVENTS OXIDATIVE DAMAGE AND COGNITIVE DECLINE IN MIDDLE-AGE FEMALE AND MALE WISTAR RATS, BUT CANNOT REVERT PREVIOUS DAMAGE IN OLD INDIVIDUALS

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Abstract:

Aging is a complex and detrimental process, which disrupts most organs and systems within the organisms. During the nervous system´s morphological and functional affections in normal aging, oxidative stress has been recognized as an age-related damaging agent, leading to cognitive decline and neurodegeneration. Some antioxidant response inducers have been tested to mitigate oxidative damage. Sulforaphane (SFN) is a molecule that improves the antioxidant and anti-inflammatory pathways. So, our aim was to evaluate if SFN was able to prevent the age-associated cognitive decline. Memory was evaluated in adult (15-month-old) and old (21-month-old) female and male Wistar rats after three months of SFN-treatment using the novel objects recognition test. Young rats (4 months-old) were used as age controls.

The antioxidant response induction, the redox state (GSH/GSSG), and oxidative damage were determined in the brain cortex (Cx) and the hippocampus (Hc). SFN increased Nrf2 and antioxidant enzymes levels and antioxidant activity in Cx and Hc, and improved redox state in adult females and males Cx and Hc, reducing the oxidative damage to proteins. Additionally, SFN decreased inflammatory cytokines suchas as IL-a, IL-b and TNF. Finally, SFN-treatment prevented memory decline in adult rats of both sexes, but not in the old animals, suggesting that that this molecule might prevent rather than revert neural damage.

Authors thank to PhD. María de los Ángeles Guerrero-Aguilera from UAM-I for providing animals necessaries for this project. This work is granted by FORDECYT-PRONACES/263957/2020. RSM, USV, RTP y PCL are CONACyT scholarship holders.

CHARACTERIZATION OF ROTENONE-INDUCED MITOCHONDRIAL AND ENDOLYSOSOMAL DYSFUNCTION IN THE CELL LINE SH-SY5Y

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Abstract:

Parkinson's disease is characterized by extensive loss of dopaminergic neurons in the substantia nigra and by the presence of Lewy bodies. A proposed mechanism for the pathogenesis of Parkinson's disease considers the alteration of the interactions between mitochondria, lysosomes, and endoplasmic reticulum. However, the molecular mechanisms through which these three organelles communicate is not well understood. It has been reported that mitochondrial dysfunction can alter the function of lysosomes and endosomes, affecting the autophagy process, vesicular trafficking and protein transport resulting in cytotoxicity due to accumulation of protein aggregates. Moreover, lysosomal dysfunction promotes the secretion of extracellular vesicles (EVs) to eliminate lysosomal waste.

There has been an increasing interest in the study of EVs which are membrane-bound vesicles that transport RNA, proteins, lipids and metabolites between cells. EVs are secreted into the extracellular space from different cell types, including neurons, astrocytes, and microglia and may play a role in the pathogenesis and development of Parkinson's disease. The biogenesis of exosomes, and EV subtype, is directly related to the endolysosomal pathway. For this reason, exosomes are proposed as potential tools for the identification of biomarkers in neurodegenerative diseases that would help in early diagnosis and disease monitoring.

Because pathogenesis of Parkinson's disease has been related to compromised mitochondrial quality control, we focused on this work to characterize the effects of mitochondrial dysfunction on endolysosomal trafficking and EV release and molecular cargo. We incubated the cell line SH-SY5Y for 24h with 400 nM of rotenone, an inhibitor of the complex I of the mitochondrial respiratory chain. We quantified through Western blot analysis the content of mitochondrial (COX IV, TOMM22), lysosomal (LAMP1), and endolysosomal proteins (annexin 2, annexin 5, Rab5c, calnexin, TSG, CD63, CD9) in total cell and EV lysates. We found increased levels of the tetraspanins CD63 and CD9 in both cell lysates and EVs. These results suggest that mitochondrial dysfunction alters endolysosomal trafficking and EV release.

ANTINEOPLASTIC EFFECT IN HUMAN GLIOMA OF *RIFTIA PACHYPTILA* EXTRACTS AND CHEMICAL PROFILE OF COMPOUNDS

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Abstract:

Secondary metabolites of animal and plant origin play an essential role in drug discovery. For some types of brain cancer, such as glioblastomas, the current treatment offers a life expectancy of 2 years. Therefore, it is necessary to continue searching for new chemotherapies. We evaluated the antineoplastic activity of extracts from the extremophile marine animal, *Riftia pachyptila*, which maintains a close symbiotic relationship with chemoautotrophic bacteria, and also studied the chemical profile of the bioactive extracts.

R. pachyptila organisms were separated into three parts (trophosome: Tr, wall: Pa, and tube: Tu), then the different extracts were obtained using solvents of varying polarity (dichloromethane-methanol and hexane). Subsequently, the extracts were evaluated in different human glioma cell lines, U373, U87, LN-18, and M059K, in treatments of 1, 10, 50, 100, and 200 µg/mL for 24h. The extracts with antineoplastic activity were analysed for p53 protein expression by western blot and immunofluorescence. In addition, a chemical analysis of the *R. pachyptila* extracts was performed by GC/MS and UHPLC/MS to determine the possible compounds present. Antineoplastic activity results were subjected to a one-way analysis of variance (ANOVA), followed by the Tukey multiple comparison tests.

The results show a differential antineoplastic effect of the extracts depending on the section of the organism and the polarity used: 1) Of the dichloromethane-methanol, the Pa extract had a cytotoxic effect on the human glioma cell lines U373 and U87, and 2) from the hexane the Tr extract presented a cytotoxic effect on LN-18 and M059K, in a concentration-dependent manner. However, these against a non-cancer cell line (BJ1) did not affect cell viability. The analysis of the biological activity revealed the stabilization of the p53 protein in the cytotoxic effect. The chemical analysis of the extracts identified more than 800 compounds, some of them with reports of antineoplastic activity.

The results suggest that *R. Pachyptila* contains secondary metabolites with antineoplastic potential on human glioblastoma and that some of the most effective metabolites come from the body and others from the symbiotic bacteria.

Protocol CONACYT No. A1-S-37634 and INNNMVS No. 147/18

PRENATAL DIET PROGRAMS THE TRANSGENERATIONAL HERITANCE OF BRAIN STRUCTURE AND ANXIETY-LIKE BEHAVIOR IN THE OFFSPRING OF RATS

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Abstract:

Accumulating evidence shows that prenatal exposure to high-energy-dense diets increases the susceptibility for metabolic and behavioral alterations in the offspring after birth. We previously found that offspring prenatally exposed to a high-energy-dense diet (cafeteria diet, CAF) exhibited brain macro and microstructural alterations which correlate with anxiety-like and depression-like behavior. We addressed whether structural brain changes and anxiety-like or depression-like behavior might be transgenerationally inherited to the offspring. We used female Wistar rat exposed to a CAF or Chow diet for 9 weeks (before, during and after pregnancy) to characterize the effect of diet on anxiety-like behavior and brain structural organization in the male offspring (F1). Anxiety-like behavior was diagnosed using the open field test, elevated maze and novelty suppressed feeding test. Deformation-based morphometry and diffusion tensor imaging was used to analyze the brain macro and microstructural alterations. Then, the F1 or F2 offspring was mated with naïve virgin female rats to provide the F2 and F3 offspring, respectively. The F2 and F3 generations were diagnosed as described for the F1. We found that the F1, F2 and F3 offspring exposed to CAF diet displayed higher anxious scores including longer stay on the edges in the open field, longer feeding latency during the suppressed feeding test, and longer time in the closed arms compared with control offspring. Deformation-based morphometry analysis identified changes in the volume of amygdala, cerebellar lobe 3, cerebellar lobe 6, frontal association cortex, hippocampus, and hypothalamus in the F1, F2 and F3 generations. Also, diffusion tensor imaging discovered greater fractional anisotropy and axial diffusivity in the amygdala, whereas greater apparent diffusion coefficient in the corpus callosum and greater axial diffusivity in the hippocampus with respect to their respective controls. Finally, biological modeling associate that macro and microstructural changes in the offspring predicts high anxiety scores. Our findings reveal that prenatal exposure to high-energy-dense diets programs the transgenerational inherited of structural brain changes and anxiety-like behavior in the offspring.

HIGH LEVELS OF CIRCULATING PROLACTIN PROTECT THE BRAIN FROM DIABETES-INDUCED OXIDATIVE STRESS DAMAGE

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Abstract:

Diabetes (DB) is a chronic metabolic disease characterized by abnormal glucose homeostasis resulting in hyperglycemia. It has been proposed that hyperglycemia leads to oxidative stress in the brain, which in turn contributes to the development and progression of neurodegeneration. Thus, factors that promote antioxidant activity in the brain could be a viable target for the treatment of DB-associated neurodegeneration. Prolactin (PRL), a hormone secreted by the anterior pituitary gland, exhibits antioxidant and cytoprotective effects on retinal pigmented epithelial cells. The aim of this study was to determine the protective effect of PRL against DB-induced oxidative damage in the brain using a murine model of type 1 DB. Wistar rats were injected i.p. with streptozotocin (60 mg/kg) and five days later blood glucose was measured to confirm DB-related hyperglycemia (levels >250 mg/dL). After 14 weeks of DB, rats were implanted subcutaneously with PRL-releasing osmotic pumps. Two weeks later, the animals were sacrificed and their brain cortices dissected. Brain cortices from diabetic rats shown a significant decrease in the total antioxidant capacity, as well as, in SOD, Gpx and Prdx activity in comparison to control rats, determinated with commercial kits. On the other hand, DB induced an increase in ROS levels measured by the reaction with DCFDA, and the oxidation of both lipids and proteins in comparison to control, determined by TBARS and Ellman and Brady assays, respectively. In contrast, hyperprolactinemia counteracted DB-induced increase in oxidative stress and stimulated the endogenous antioxidant response. These results suggest that PRL may be a protective factor against neurodegeneration induced by oxidative stress in Diabetes.

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ABSTRACTS | Posters Others

XXXIII National Congress of Biochemistry

ANALYSIS OF CERVICAL CANCER EXTRACELLULAR VESICLES AND ITS EFFECT ON MACROPHAGE POLARIZATION

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Abstract:

Background: Extracellular vesicles (EVs) are particles released naturally by cells and are delimited by a membrane formed by a lipid bilayer. Tumor-derived EVs play an important role in intercellular communication, contributing to tumor development. Some authors have shown in different types of cancer that tumor-derived EVs can be uptake by macrophages and promote macrophage polarization to an M2 phenotype. They also could contribute to the development of processes like angiogenesis or metastasis. Despite cervical cancer is one of the main causes of death due to cancer in women; the uptake and effects of cervical cancer EVs in macrophages have not been described. **Methods:** EVs were isolated from supernatants of cultures of the HeLa, C-33 A, and HaCaT cell lines by using the miRCURY exosome kit. EVs identification was performed by transmission electron microscopy and western blotting. Peripheral blood monocytes were differentiated to macrophages with M-CSF, whereas monocytes of the THP-1 cell line were differentiated with PMA. Differentiation to M0 macrophages was evaluated through the expression of the CD68 marker by flow cytometry. **Results:** EVs isolated showed a spheroidal morphology and the presence of a lipid bilayer. The EVs marker proteins Hsp90, Hsp70 and CD9 were identified in all EVs. The contamination with cell debris was ruled out due to the absence of Calnexin in EVs. Peripheral blood monocytes and THP-1 cell line monocytes after treatments changed their morphology to an amoeboid or elongated spindle-like shape, the characteristic for macrophages M0. Increased size and granularity were observed by flow cytometry, and more than 95% of cells expressed CD68 protein. The internalization of different concentrations of EVs is being corroborated. **Conclusion:** Our results indicate that EVs isolated from cervical cancer cell lines exhibit the typical markers and characteristic morphology. Peripheral blood monocytes and THP-1 cell line were differentiated to M0 macrophages with high expression of CD68. Macrophages (M0) could be able to internalize EVs at different concentrations. The effect of EVs over macrophages M0, will be evaluated after their uptake by these cells.

AUTOPHAGIC FLUX IN ATRETIC OOCYTES FROM PREPUBERTAL RATS

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Abstract:

Autophagy is an evolutionarily conserved cellular process in eukaryotic cells, it is involved in the degradation of misfolded proteins and damaged organelles. Autophagy has a fundamental role regulating the recycling of cellular components to carry out metabolic processes. This process also participates in cell elimination and is known as type II programmed cell death, which is characterized by the significant accumulation of autophagic vesicles. It is frequently observable when massive cell removal is required or when phagocytes do not have easy access to cells undergoing death (1, 2). Likewise, the autophagic flux is defined as the measurement of the autophagic activity given by the degradation throughout the autophagic process, in which the mTOR, Beclin 1, LC3, Lamp1 and p62 proteins are present. The aim of this work was to define the autophagic process during the oocytes elimination from prepubertal rats, by means immunodetection of proteins involved in the event. Rat ovaries of 19 and 28 days were processed with classical optical microscopy techniques. Ovaries were sectioned and general hematoxylin-eosin staining was performed, as well as immunodetection of the mTOR, Beclin 1, LC3, Lamp1, and p62 proteins.

Identification of irregularities on the cytoplasm of oocytes from atretic follicles suggest the presence of autophagosomes. Immunodetection of Beclin 1, LC3, and Lamp1 proteins in oocytes with clear vesicles allowed defining the presence of autophagic process. Additionally, the low levels detected of p62 protein in those oocytes with pro-autophagic proteins levels increased, allowed to define that the autophagic flux was completed during oocyte cell elimination. Our results indicate that the oocyte cell elimination in prepubertal rats is conducted by means a selective autophagy mediated by the complete degradation of the autophagosome contents.

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ONCOGENIC ROLE OF NM23-H2 IN BREAST CANCER CELLS

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Abstract:

Estrogen receptor alpha (ERα) has an established role in breast cancer biology. Transcriptional activation by ERa is a multistep process influenced by coactivator and corepressor proteins. Using yeast two-hybrid screen, we identified an ERα-associated protein, nonmetastasic protein 23 homologue 2 (NM23-H2), which consists of 152 amino acids with a molecular mass of 17 kDa.

This work shows that NM23-H2 interacts with ERα both *in vitro* and *in vivo* and regulates the transcriptional activation of ER directly through its N terminal region (AF-1) and its C-terminal (AF-2) region. Our results demonstrate that NM23-H2 acts as an ERα coactivator, increasing its transcriptional activity and target gene expression, as well as proliferation, and colony formation in breast cancer cell lines. These effects are observed in the presence and absence of ERα agonist and antagonists, suggesting a cancer estrogen independent pathway for NM23-H2. Furthermore, NM23-H2 also increases the transcriptional activity of both the androgen and progesterone receptors, suggesting a general role as coactivator for steroid receptors. Taken together these data show an important role of NM23-H2 in the development of breast cancer.

Keywords: breast cáncer, coactivators, Estrogen receptor, NM23-H2

ADAPTATION TO SUSPENSION SERUM-FREE MEDIUM OF A CHO CELL LINE PRODUCER OF RECOMBINANT HUMAN ERYTHROPOIETIN

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Abstract:

Chinese Hamster Ovary (CHO) cells are the preferred eukaryotic heterologous expression system to produce recombinant glycoproteins [1,2] such as erythropoietin (EPO). Endogenous human EPO, controls erythrocyte production and is used for the treatment of anemia and kidney disease. One of the advantages of CHO cells over other eukaryotic systems is their ability to adapt to suspension culture without animal derived components that may introduce batch-to-batch variability and adventitious pathogens [1,2]. Nevertheless, adapting cells to defined media could be challenging and time-consuming, and tend to be a cell line and medium dependent process [3]. In this work, we present the adaptation process of a CHO cell line producer of recombinant human erythropoietin (rhEPO), from an adherent cell culture with 10 % of bovine fetal serum to a suspension cell culture serum-free medium. Different media were evaluated including Biowest DMEM, Hyclone CDM4CHO, and Sartorius 4Cell-XtraCHO, with and without glutamine supplementation. The Hyclone CDM4CHO media supplemented with 8 mM of glutamine gives us better results allowing us to reach $4x10^6$ viable cells per milliliter. We present a kinetic characterization of the CHO cell line cultured in batch with Hyclone CDM4CHO 8 mM of glutamine in a 250 mL Erlenmeyer stirred at 60 rpm, including cell concentration and rhEPO production; [Thanks to PAPIIT: IN210822].

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PARCHMENT COFFEE EXTRACTS AND NOPAL MUCILAGE AN ALTERNATIVE AGAINST THE FUNGI GROWTH IN CULTURAL HERITAGE MATERIALS: STONE AND WOOD

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Abstract:

The challenge in the Conservation of Cultural Heritage against the biodeterioration of works of art is the development of alternative methods and new products that are compatible with materials, at low cost, and friendly to the environment and the health of restorers [1-3]. The objective of our study was to test aqueous extracts of parchment coffee (silverskin and parchment) and nopal mucilage [4], by-products rich in bioactive compounds, to prevent and control the growth of *Cladosporium cladosporoides*, a typical fungal species that colonizes the materials of the architectural and artistic heritage. In the test on stone specimens (marble, sandstone, travertine, basalt) and wood (pine and debarked stem of corn), coffee extracts showed a positive effect, parchment > silveskin, in inhibiting the growth of the fungus on the specimen's surface. This positive effect was synergistic in the nopal mucilage-parchment extract formulation to control the growth of the fungal strain. The characterization by DART mass spectrometry of the aqueous extracts and the parchment-mucilage formulation indicated the presence of different biomolecules and bioactive compounds of *Coffea arabica* and *Opuntia ficus-indica*. These results are a promising alternative as a natural source of bioactive compounds for The Green Conservation of Cultural Heritage [2].

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ROLE OF THE TRYPTOPHAN IN THE PROTECTION OF HUMAN GAMMA D CRYSTALLIN FROM UV RADIATION DAMAGE

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Abstract:

The lens is an intraocular and transparent structure composed mainly for a group of proteins called crystallins. The structural function of the crystallins is based on the fact that they are packed in a stable and ordered way that allows the lens to be transparent. Crystallins are divided into α-, β-, and γ- families. The γ-crystallins are the least abundant and have the lowest molecular weight, being located mainly in the nucleus of the lens in a monomeric form. γD-crystallin is the second most abundant γ-crystallin in the lens nucleus and it has four highly conserved tryptophans in positions 42, 68, 130, and 156.

Cataract is among the diseases that refer damages in the lens, and it is characterized by the loss of transparency of the lens due to the aggregation of the crystallins. There are several risk factors to the development of cataracts, such as metal ions, postraductional changes, UV radiation, etc. The lens are continually exposed to UV radiation, and absorbs radiation between 295 and 400 nm, which can lead to irreversible damages.

Tryptophans in γ-crystallins presumably absorb incoming UV radiation, suggesting that UV-induced photooxidation of tryptophan may be a critical first step initiating changes in lens proteins and thus cataract formation. In the case of γD-crystallin, its tryptophans act as an efficient UV excitation funnel by shielding the protein from UV-initiated photochemistry. However, there is also evidence of photodamage, which induces the conversion of tryptophan to kynurenine, which is a recognized marker of cataract formation and destabilization of crystallins folding. Considering all that, in this project the effect of UV radiation and the role of tryptophans is studied by spectroscopic techniques, in order to shade light into photo oxidation mechanisms that induce conformational changes and aggregation of γD-crystallin.

IN VITRO CULTURE OF THE ECTOMYCORRHIZAL FUNGUS *LACCARIA TRICHODERMOPHORA* AND ITS EFFECT ON INFECTIVITY

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Abstract:

Ectomycorrhizal fungi (EMF) have gained relevance as biofertilizers since they help in the acquisition and transport of nutrients to their hosts (1). To produce EMF vegetative inoculum in liquid culture, the C:N ratio of the culture medium is a relevant factor (2). It has been reported that many EMF are sensitive to increased N concentration, a condition that negatively affects sporome production, extraradical mycelium, and root colonization levels (3). Therefore, in this project we evaluated the effect of *in vitro* culture of the EMF *Laccaria trichodermophora* CA15-F10, subjected to different C:N ratios, on its infectivity. To achieve this objective the *in vitro* culture of EMF was performed following the methodology used by Ángeles-Argáiz (4). Five treatments were proposed, BAF-C (conventional BAF culture medium, C:N 16:1) and BAF-M (BAF culture medium modified with C:N 24:1, 20:1, 16:1 and 12:1) using urea as N source. Once the mycelium was obtained, *Pinus montezumae* plants were inoculated to determine the percentage of root colonization at 6 months. The highest percentage of colonization was observed in the BAF-C treatment (14.72 ± 4.21%) and BAF-M (16:1) (12.60 ± 4.59%). The BAF-M (20:1) and BAF-M (12:1) treatments showed root colonization percentages of 7.89 ± 4.64% and 7.10 ± 3.90%, respectively. These were not statistically different with respect to the treatment with the lowest percentage of colonization, BAF-M (24:1) with 4.92 ± 4.94% ($P < 0.05$). The percentage of mycorrhizal colonization was negatively affected in mycelium that was grown *in vitro* under C:N ratios higher and lower than 16:1. It is possible that the mycelium of EMF grown under these conditions adjusts its metabolism in a prolonged manner, demanding more photosynthates from its host or transporting fewer nutrients to the host, causing low percentages of radical colonization in its host.

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ESTABLISHMENT OF A PROTOCOL FOR A THREE-DIMENSIONAL CULTURE OF CELLS DERIVED FROM PERIODONTAL LIGAMENT

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Abstract:

Cell culture is an important and necessary process in drug discovery, cancer research, and stem cells (SCs) study. SCs are grown in two dimensions (2D), however, this form of culture has many limitations when it comes to representing *in vivo* behavior, because a 2D culture does not recreate the microenvironments and interactions present in a living organism. On the other hand, three-dimensional (3D) cultures have the advantage of emulating similar characteristics of the cell environment *in vivo*, so that aspects such as cell shape, function, and biological activity can be studied *in vitro* culture [1]. Dental stem cells (DSCs) scans have gained popularity in recent years because they are easy to obtain and do not have strong bioethical implications. In that sense, DSCs scans of the periodontal ligament (PLSCs) represent a viable SCs option due to their high rate of proliferation and their ability to differentiate into different lineages [2]. Currently there are few works that address the CTLP cultivation process in 3D. Therefore, the objective of this work is to establish the appropriate methodology for a 3D culture of PLSCs, for which growth and cell viability were evaluated.

For the establishment of the 3D culture, a commercial matrix (Matrigel®) was used at different concentrations (1, 3 and 5 mg/mL). For each concentration, PLSCs were used, which were inoculated in a 6-well plate ($2x10^4$ cells/well), with three replicates coated with Matrigel to generate the 3D culture and three replicates were cultivated conventionally (2D). The morphology was evaluated during the culture period through photomicrographs. After 6 days of culture, proliferation and viability were evaluated by the trypan blue exclusion method, obtaining that the viability was greater than 80% for all the concentrations of Matrigel® evaluated, in terms of proliferation this was increased by more than 40% in the concentrations of 1 and 3 mg / mL of Matrigel compared to the control, while for the concentration of 5 mg / mL a decrease in the speed of cell proliferation could be noticed. The results obtained in this work could provide important information on the behavior of PLSCss in a 3D environment for their subsequent use for cell therapy purposes.

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THE ROLE OF PALT$^{INK4A/B}$ IN RESISTANCE TO THE ESTABLISHMENT OF CELLULAR SENESCENCE

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Abstract:

Aging is the main risk factor for most chronic diseases and functional deficits in humans, but the fundamental mechanisms that drive it remain largely unknown. Cellular senescence is a phenotype characterized by a stable cell cycle arrest in which cells are unable to proliferate despite mitogenic stimuli and secrete a set of cytokines, metalloproteases, growth factors, etc. that alter the surrounding tissue. Senescent cells accumulate in aged tissue and contribute to aging and age-related diseases. The longest-lived rodent, the naked mole-rat (*Heterocephalus glaber*), has a healthy life of 30 years, shows no diseases associated with aging, appears to be protected from a metabolic impairment, diabetes, osteoporosis, neurodegeneration, and does not accumulate senescent cells over time. These characteristics indicate that it has developed efficient anti-aging mechanisms. However, how they resist aging processes remains largely unknown. The *Ink4a/b* locus encodes two cyclin-dependent kinase inhibitor members, p16^{Ink4a} and p15^{Ink4b}, and a protein called p19^{Arf} that inhibits ubiquitin ligase MDM2. In humans, this locus expression level increases progressively during aging, and genome-wide association studies have linked the locus to several diseases associated with aging and frailty. An alternative mRNA from this locus was identified in the naked mole-rat called pALT$^{Ink4a/b}$. We propose it contributes to avoiding cellular senescence. Our findings will be presented.

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CONTRIBUTION OF TRANSCRIPTION FACTORS MFD AND GREA IN MISMATCH (MMR)-DEPENDENT ADAPTIVE MUTAGENESIS OF *BACILLUS SUBTILIS*

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Abstract:

Stationary phase or stress-associated mutagenesis (SAM) is a phenomenon that allows non-dividing cells to acquire beneficial mutations in response to the application of a prolonged non-lethal selective pressure. This type of mutagenesis has been successfully studied in the Gram-positive microorganism *Bacillus subtilis*, using the strain YB955, which allows to evaluate the reversion frequencies to the chromosomal auxotrophies *hisC952*, *metB5*, and *leuC425*. Using this gain-of-function system, it was shown that defects in Mismatch Repair (MMR), encoded in the *mutSL* operon, promoted SAM. A further report revealed that, under conditions that saturate or inactivate the MMR system, the MutY DNA glycosylase, which processes 8-OxoG:A, G:A and C:A misspairs, promotes reversions at the *leuC425* allele in strain YB955. Of note, MutY and Mfd, a factor that couples repair with transcription, were found to work in a common pathway to generate $LeuC^+$ prototrophs. Most recent results unveiled a role for the transcription-elongation factor GreA in *B. subtilis* SAM. To further advance our knowledge regarding the mechanisms that promote bacterial genetic diversity, we investigated whether the SA mutations that are dependent on the MMR systems are modulated or not by the transcriptional factors Mfd and GreA. To address this hypothesis, *B. subtilis* strains, Δ*mutSL* Δ*mfd* and Δ*mutSL* Δ*greA* were generated and together with the parental strain YB955 tested for SAM. Our results revealed that disruption of *mfd* decreased the reversion frequencies of the *his*, *met* and *leu* mutant genes produced by the MMR-deficient strain. However, no significant effects in the reversion frequencies of these alleles were observed following disruption of *greA* in the MMR-deficient genetic background. Overall, our results suggest that the MMR-promoted mutagenic events occurring in nutritionally stressed *B. subtilis* are dependent on Mfd but do not require a functional GreA protein.

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EVALUATION OF ANTIBACTERIAL ACTIVITY OF MU-L ENDOLYSIN FROM PHIMR11 PHAGE AGAINST METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

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Abstract:

The indiscriminate use of antibiotics has caused the appearance of methicillin-resistant *Staphylococcus aureus* strains (MRSA). This microorganism is considered by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), as pathogens with high priority for the research and development of new antibacterials compounds. This due to the fact that diseases it causes increase the costs of treatment, hospitalization and the mortality rate compared to non-resistant strains. Endolysins (lytic enzymes derived from bacteriophages) have received great attention for their potent bactericidal activity, high specificity and low generation of resistance. The objective of this work is to produce by recombinant technology, MU-L endolysin from phiMR11 phage and to determine the range of conditions in which it has activity against MRSA. First, the prediction of its structure and identification of functional domains was carried out through *in silico* analysis. Subsequently, MU-L endolysin gene encoding was cloned in the expression vector pColdI. Next, genotype BL21(DE3) *E. coli* strain was used as expression system and the endolysin was subsequently purified by IMAC. Once obtained, its activity was evaluated under different biochemical conditions through optical density reduction assays against a SARM suspension. Analyzing the kinetic data, it was determined that endolysin has bactericidal activity under a wide range of pH (7-11), ionic strength (0-1 M NaCl) and temperature (20-42°C), requires Zn^{2+} for its function and Ca^{2+} to enhances it, increasing activity almost 32-fold under optimal conditions. The determination of the conditions range in which MU-L endolysin has bactericidal activity, as well as its powerful activity against MRSA, places it as a good proposal for its use in different applications.

SYMPLASTIC TRANSPORT PARTICIPATION DURING THE *ARABIDOPSIS-AZOSPIRILLUM* INTERACTION

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Abstract:

When the plant growth promoting rhizobacteria *Azospirillum brasilense* Sp245 interacts with *Arabidopsis thaliana*, it stops the growth of the primary root and increases the number of lateral roots, a phenotype attributed to bacterial auxins (Spaepen et al., 2014; Carrillo-Flores et al., 2022). Auxins, mainly indole-3-acetic acid (IAA), regulate practically all plant development processes. The synthesis of IAA takes place in the aerial part, from where it is transported to the demanding tissues by two types of transport: i) fast, which uses the phloem, and ii) cell-cell, which is carried out through of carriers and is known as polar auxin transport. It has been reported that *Azospirillum* causes an increase in auxins in the differentiation zone of the lateral roots of *Arabidopsis thaliana*, during the first days of interaction. Subsequently, was observed that the auxins are mobilized towards the meristems of the lateral roots, through the efflux carrier PGP1 (Carrillo-Flores et al., 2022). On the other hand, it is known that IAA can also be transported through plasmodesmata (PD) (intercellular channels that cross the cell wall) that connect the cytoplasm of neighboring cells, establishing a symplastic transport between them. The symplastic movement of the IAA depends on the permeability of the PD (Zambrysky, 2004), which regulated by the accumulation (CALS/GSL) or degradation (β-1,3-glucanases) of callose in the PD neck. The objective of this study is to determine the effect of bacterial IAA transport through PD on the root architecture of the gain-of-function mutants *pCRE1::icals3m* and *pCALS3::icalsm3* of *Arabidopsis*. The results showed a decrease in lateral roots of *pCALS3m::icals3m* seedlings inoculated with *Azospirillum*, suggesting that bacterial IAA is also mobilized through PD during the first days of *Azospirillum-Arabidopsis* interaction.

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SEARCH FOR INHIBITORS TO DELAY THE AGGREGATION OF CRYSTALLIN γS INDUCED BY UVB RADIATION

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Abstract:

Cataracts are defined as the partial or total opacity of the lens of the eye, wich gradually causes visión impairment. This pathology is among the leading causes of blindness worldwide and mainly affects the population over 65 years. So far, the only existing treatment is surgical removal of the lens, wich is an invasive and expensive process[1].

Crystallins constitute 90% of the total proteins in the lens and these are divided into 2 families, α and βɣ. Within the βɣ family is the human gamma S crystallin (HγS) which constitutes approximately 9% of the total crystallins. It is found in the lens cortex and its function is structural[2].

Because the lens lacks the necessary machinery for protein synthesis and repair, damage accumulates over time. Ultraviolet radiation (UV) is one of the external factors that can induce modifications in the amino acids that make up these proteins. These modifications produce a destabilization in the native conformation which, in turn, induces aggregation and cataract formation[3].

In this work we studied the effect of exposure to UVB radiation for short periods of time and the ability of 5 molecules to delay the aggregation of HγS. To characterize this effect we used turbidimetry, fluorescence and dynamic light scattering techniques.

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CLONING AND EXPRESSION OF PIGMAP PROTEIN BY RECOMBINANT SYSTEM FOR ITS POTENTIAL USE IN THE EVALUATION OF ANIMAL WELFARE IN PIGS

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Abstract:

PigMAP protein is an acute phase glycoprotein, which is secreted by pigs during a process of stress, tissue damage or infection. Biological function still unknown, however; PigMAP has important potential as a biomarker of stress in pigs. In the bloodstream during stress processes, PigMAP basal concentration increase from ten to twenty times in affected pigs (Piñeiro *et al.,* 2009; Gulhar *et al.,* 2021).

Molecular weight and secondary structure prediction of pig-MAP (access number: 7UFRB5X3016) was obtained by PyMol and DNAstar software, which estimated in 100.36 kDa with 907 amino acids. Hydrophobic region at the N-terminus of the protein was observed, the rest of the protein being highly hydrophilic. PigMAP has two delimited portions corresponding to the N-terminus and C-terminus, with the highest antigenicity index and more than 10 epitopes. PCR amplification of these two important regions (699 and 846 bp) was achieved, corresponding to two highly antigenic fragments with probability of exposure to the surface and adequate response for the development of a recombinat expression system in *E. Coli*.

N-terminus portion was cloned into the pJET1.2/blunt vector and used to amplified and cloned in frame to the pETSUMO expression vector (pETSUMO-Nterminus), finally the recombinat plasmid was corroborated by PCR and sequencing test. For production characterization, *E. coli* BL21 (DE3) strain was used for its induction by IPGT and its consequent expression of the interest protein. Finally, the production was confirmed by SDS-PAGE and Western Blot with a band at the expected molecular weight (35 kDa). Therefore, in this work we obtained for first time, one expression system for PigMAP recombinat protein with potential to development a evaluation system of the animal welfare in pigs.

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IMMUNOGENICITY OF A RECOMBINANT RHN-PORPU PRODUCED BY *E. COLI* OF *PORCINE RUBULAVIRUS* GIVES PROTECTIVE IMMUNITY OF LITTER AFTER CHALLENGE

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Abstract:

Porcine orthorubulavirus-La Piedad Michoacan Mexico virus (PRU-LPMU); belongs to the subfamily *Rubulavirinae*, is the causative agent of described as; "Blue Eye Disease" (BED) do to the corneal opacity induced lesion. The disease was first reported in the early 1980s in central Mexico around the town La Piedad in the State of Michoacán. Currently, PRU infection is endemic in the central and western-central parts of Mexico, whereas the disease remains unreported in other countries. This work aimed to evaluate the immunogenicity and protective efficacy of a recombinant rHN-PorPU on 7-day-old piglets born to previously immunized pregnant sows, after colostrum ingestion and challenge. Two challenge studies using a non-lethal (low-virulence) and lethal wild-type (2xLD50) PRU viral strain were carried out on 7-day-old piglets respectively. Three sows were immunized with rHN-PorPU formulated with a ISCOM-Matrix® adjuvant and two sows with rHN-PorPU protein alone as well as a mock-immunized pregnant sow. Quantitative ELISA detected a high concentration of anti-rHN-PorPU IgG antibodies in sow sera after the second dose of vaccine administered on day 14 until farrowing, showing viral-neutralizing and cross-neutralization activity against different variants of PRU. Sera samples from piglets of immunized sows (with or without adjuvant), showed higher concentrations of IgG antibodies of 4543 ng/mL and 2887 ng/mL respectively. A challenge study, with a wild-type PRU strain in piglets born to the rHN-PorPU-ISCOM-immunized sows (n=8) showed a survival rate of 87.5% with less severe signs of disease. Piglets of the rHN-PorPU-non-adjuvant immunized sows (n=8) showed a survival rate of 75% with a high score rate in the clinical signs. Piglets of mock-immunized sow (n=5), exhibited severe signs of disease and 100% of mortality. Our data indicate that rHN-PorPU produced in *E. coli* provide high protection to piglets after challenge exposure and induced an efficient humoral response in pregnant sows and maternally derived immunity.

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CHARACTERIZATION OF THE PRODUCTIVE CALCIUM RELEASE MODE OF THE ENDOPLASMIC RETICULUM IN HELA CELLS

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Abstract:

Calcium (Ca^{2+}) regulates a plethora of cellular processes by a transient elevation of the cytosolic Ca^{2+} concentration ($[Ca^{2+}]_i$). Cells display these transients by having a toolkit for Ca^{2+} transport that results in specific Ca^{2+} signals and requires substantial energy consumption.

There are two sources of Ca^{2+}, the external milieu, and the intracellular stores. The endoplasmic reticulum (ER) is the main intracellular Ca^{2+} source involving the activation of the inositol 1,4,5-trisphosphate receptor (IP_3R) in non-excitable cells. In HeLa cells, external ATP stimulates purinergic receptors ($P2Y_2$), activating phospholipase Cβ. This enzyme hydrolyzes the membrane phospholipid PIP_2 producing high concentrations of inositol 1,4,5-trisphosphate (IP_3) and diacylglycerol (DAG). The former engages the IP_3R resulting in Ca^{2+} release from the ER. Simultaneous recordings of the reduction in the endoplasmic reticulum calcium concentration ($[Ca^{2+}]_{ER}$) and increase in the $[Ca^{2+}]_i$ show a lack of temporal correlation, suggesting that the intraluminal Ca^{2+} regulation is more complicated than previously thought.

To study how intraluminal Ca^{2+} regulates Ca^{2+} release, we have simultaneously measured the changes in the $[Ca^{2+}]_i$ with Fura-2 and $[Ca^{2+}]_{ER}$ with G-CEPIA1er. In the absence of external $[Ca^{2+}]$, ATP induces a much smaller increase in the $[Ca^{2+}]_i$ despite the initial $[Ca^{2+}]_{ER}$ being the same as well as its reduction. This difference cannot be explained by the participation of Ca^{2+} entry channels at the plasma membrane. Phase transition analysis suggests that the productive phase is more prolonged in the presence of external Ca^{2+}.

Since the absence of external $[Ca^{2+}]$ decreased the $[Ca^{2+}]_i$, we have studied the possibility that a reduced $[Ca^{2+}]_i$ leads to a diminished SERCA pump activity, which in turn limits the time that the ER works in the productive mode. We propose then that the activity of the SERCA pump is a critical element in facilitating IP_3R-mediated Ca^{2+} release, suggesting that these two opposing toolkit members work synergistically to assure a safe role of the ER as a Ca^{2+} source.

PRESENCE OF S-RNASE IN THE POLLEN TUBE CYTOPLASM TRIGGERS PROGRAM CELL DEATH IN *NICOTIANA TABACUM*?

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Abstract:

Reproductive barriers evolved to prevent self-fertilization and its deleterious effects as well as maintain species identity, avoiding the generation of low interspecific hybrids fitness.

Two genetic barriers are recognized: self-incompatibility (SI) in intra-specific cross-pollination and unilateral incompatibility (UI) in inter-specific crosses. In both cases, the *S*-locus plays a pivotal role in the recognition and rejection of self-pollen or other pollen coming from different species.

In SI, pollen tube growth inhibition occurs in the third part of the style, while in UI, pollen tube growth stops at the stigma.

In Solanaceae, for example, the *S*-locus includes the S-RNase (female determinant) and a suite of SLFs (male determinant). Other genes known as modifier genes (MG) not linked to the *S*-locus such as *HT-B*, *NaStEP*, *120K*, and *NaTrxh* are also part of the SI response.

In interspecific pollen rejection, three mechanisms are identified: 1) Dependent on the *S*-locus and MGs, 2) Only dependent on S-RNases, and 3) Only dependent on MGs.

Nicotiana tabacum is a self-compatible (SC) species since the *S*-locus and MGs have accumulated loss of function mutations; however, when an S-RNase is expressed in transgenic plants, self-pollen is rejected. It suggests a different pollen rejection mechanism from the one that depends on the *S*-locus and MGs, which has not been described yet.

Here, we will give evidence about the final localization of S-RNase inside the pollen tube after it is taken up from the extracellular matrix of the style of *N. tabacum* transgenic plants expressing the S_{C10}-RNase. We will use transgenic *N. tabacum* pollen expressing different GFP-subcellular compartment markers. Next, we will determine whether the activity of S-RNase is solely responsible for pollen rejection by expressing an inactive mutant S-RNase in transgenic plants. Finally, we will show whether Programmed Cell Death inhibits pollen tube growth.

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HEMICELLULOLYTIC CAPACITY OF DIFFERENT PATHOTYPES OF *COLLETOTRICHUM LINDEMUTHIANUM* IN CULTURE WITH NATURAL SUBSTRATES

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Abstract:

Colletotrichum lindemuthianum is a phytopathogenic fungus that causes anthracnose in common beans (*Phaseolus vulgaris*). This species has a hemibiotrophic lifestyle or nutrition/infection strategy and presents a great diversity of pathotypes with different levels of virulence against bean varieties. The plant cell wall (PCW) is very diverse and dynamic; It is composed of cellulose, hemicellulose, pectin and lignin, so its degradation by fungi involves the secretion of a wide variety of enzymes (a-L-arabinofuranosidase, b-xylosidase, endoxylanase, cellobiohydrolases, endoglucanases, pectinases, etc.), that work in a coordinated and synergistic manner. *C. lindemuthianum* is an excellent model to study the functioning of the complex of enzymes used by its pathotypes to degrade the PCW from its host, but it also represents a potential source of enzyme production for biotechnological applications. In this study we analyzed the hemicellulases secretion profiles of one non-pathogenic (0) and three pathogenic (1088, 1472 and 2395) pathotypes of *C. lindemuthianum*. The enzymatic secretion of these fungi was determined in cultures with modified Mathur minimal medium supplemented with water hyacinth, green bean, bean hypocotyls and glucose, in an incubation kinetics of 1 to 12; 14 and 16 days. We measured arabinofuranosidase, b-xylosidase, endoxylanase, and cellobiohydrolase activities of filtered extracts of liquid medium. The results showed that the fungi grow better in cultures with natural substrates rich in hemicellulose and pectin (green beans and hypocotyls of beans, water hyacinth) than in media with glucose. Growth on natural substrates is related to increased secretion of hemicellulases, whiles glucose causes catabolic repression of enzymes. In addition, the secretion profile and levels of each enzyme are differential among the pathotypes and with each natural substrate. Pathotypes 0 and 1088 were the best arabinofuranosidase producers, pathotypes 0 and 1472 were the best xylosidase producers, and pathotypes 2395 and 1088 were the best xylanase producers. Our results revealed that among pathotypes of *C. lindemuthianum* there are different hemicellulolytic capacities.

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KIFTHERAPY: A PROPOSAL FOR CANNABIDIOL-BASED THERAPY

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Abstract:

Cannabinoids are a broad class of chemical compounds derived from the cannabis plant; among them the tetrahydrocannabinol (THC) has psychoactive effects associated with the cannabis use. On the other side, cannabidiol (CBD) is a phytocannabinoid that does not a psychoactive effect and is use for various approaches. Here in, we reported the extraction of CBD from a non-psychotropic variety of *Cannabis sativa* and its use in a vaporization device as a potential delivery manner. *Materials and Methods*. CBD was extracted using olive oil. Briefly, plant material was dried at room temperature, then it was crushed using a mortar and pestle until a homogeneous powder was formed. The biological material was then decarboxylate by heat at 90°C for 1 h. Following, olive oil was added to the sample and heated at 100°C for approximately 1 h or until a dense sample of highly concentrated CBD was formed. CBD-based oil was filtered to obtain the CBD oil, which was bottled in an amber bottle and analyzed by HPLC. CBD-based oil was diluted (1:10) and loaded into a vaporization device. We quantified the amount of CBD into the vapor. *Results.* We obtained 2.5 ng/ml ± 0.3 ng/ml of CBD. These results are comparable with previous reports which showed that the amount of CBD obtained was 3.7 ng/ml [1]. Furthermore, the HPLC analysis showed the presence of a distinct peak at 10.2 minutes which is consistent with the CBD standard. Moreover, the representative chromatogram showed two more distinct peaks at retention times of 10.6 min and 11 min, that might correspond to a minimal amount of THC and CBN, respectively. Finally, we were able to vaporize the CBD in the right device obtaining an amount of CBD around of 1 ng/ml in the vapor. *Conclusion*. We presented a novel CBD delivery by vaporization that might use as an alternative administration method.

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APPLICATION OF PRINCIPAL COMPONENT ANALYSIS IN AN ANIMAL MODEL OF METABOLIC SYNDROME INDUCTION

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Abstract:

Introduction: Metabolic syndrome (MetS) is a disease characterized by the presence of abdominal obesity, insulin resistance, high glucose serum levels, dyslipidemia, and hypertension, associated with diseases like diabetes mellitus type 2 and cardiovascular disease. The relationship between those risk factors is poorly understood due to the complex and multifactorial nature of the syndrome. MetS has a high prevalence among adult populations and represent a public health problem worldwide. It is well known that a sedentary lifestyle and an unbalanced diet play a key role in its development.

Objective: The purpose of this research is to provide statistical information using "principal component analyses" (PCA) that allows to correlate the MetS parameters along different periods of time (from 8 to 52 weeks).

Methods: Male Wistar rats (110±10 gr) were randomly divided into two groups: Control and MetS were fed with a standard diet (LabDiet 5001) and a high-fat diet (HFD 40.72% extra fat), respectively. Then, each group was randomly divided into four subgroups, 8, 18, 28, and 52 weeks (n=8 each subgroup; N = 64). The body and adipose tissue weight of the animals were measured, and the blood pressure as well, using a non-invasive method. Also, blood samples were obtained by cardiac punction and immediately centrifuged; then, the supernatant was stored at -70 °C for clinical laboratory analysis to quantify glucose, total cholesterol, triglycerides, and HDL-c. All experimental data were analyzed with PCA.

Results: The PC scores group the rats according to type of diet in different periods, while the PC loadings identify relationships between the measured parameters.

Conclusions: PCA allows 1) to group the data according to diet intake without counting previous information of the group to which they belong, and 2) to find relationships between the parameters of MetS.

ISOLATION AND IDENTIFICATION OF MICROALGAE FROM THE LEACHATE LAGOON OF THE SANITARY LANDFILL OF TUXTLA GUTIERREZ, CHIAPAS, FOR USE IN BIOREMEDIATION

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Abstract:

Because of their adaptability, microalgae are found in many industrial applications. However, the lack of studies on diversity and life cycles in different environments suggests the need for more research on new species and new ecosystems. Consequently, the present study evaluated the diversity of microalgae in the leachate lagoon of the landfill of Tuxtla Gutiérrez, Chiapas, Mexico. For its use in bioremediation, three strains were isolated and one strain was identified by a combination of morphological characteristics, classifying it taxonomically in the Chlorococcaceae family. It is intended to identify genomes, since they have not been previously studied or described. Under specific conditions during cultivation, they show pigmentation changes. These results represent a great step forward in the selection of less known media and in the discovery of new sources of bioactive compounds. The research has great technological value for bioremediation because these microorganisms found in this habitat show tolerance to high levels of contaminants.

Keywords. *Leachate, landfill, isolation, microalgae.*

BIOSYNTHESIS AND EMISSION DYNAMICS OF CAMPHENE IN *BEAUVERIA PSEUDOBASSIANA*

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Abstract:

Living organisms including plants, bacteria, and fungi, produce highly diverse and specialized metabolites. These compounds play essential roles in biological functions and have compelling applications in ecology, agriculture, and pharmaceutics. Among the compounds produced by fungi, especially by phylum Ascomycota, the terpenes play predominant roles.

Some of these metabolites, such as camphene produced by strains of *B. pseudobassiana*, have been shown to promote the development and growth of model plants, but also of economically and ecologically relevant plants such as *Agave tequilana* and *Agave salmiana*[1].

In this work we sequenced, annotated, and analyzed the genomes of two camphene producing *B. pseudobassiana* strains to identify genes involved in its biosynthesis.

Furthermore, we used the novel Modular Biological Mass Spectrometer (MoBiMS)[2], to monitor the dynamic of emission of camphene by these fungi *in vivo*.

We have now found putative Biosynthetic Gene clusters involved in terpene production, by mining the annotated genomes. We have algo elucidated the dynamics of camphene production during the development of *B. pseudobassiana*. Finally, we aim at localizing camphene within fungal tissues by employing mass spectrometry-imaging.

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STRUCTURAL AND BIOCHEMICAL CHARACTERIZATION OF COMPONENTS FROM THE SCORPION VENOM *CENTRUROIDES TECOMANUS*

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Abstract:

Centruroides tecomanus is one of the medical importance scorpion species in México, this arthropod is endemic to the states of Jalisco, Michoacán, and Colima. In *C. tecomanus* venom it has been identified the peptide Ct1a, is a beta-mammalian toxin that affects the current of voltage-gated sodium channels (Navs), especially the subtype Nav 1.6, this component is one of the most abundant, but we identified that there are other peptides with similar abundance, and they could contribute to the signs and symptoms caused by *C. tecomanus* sting. We separated the venom components by gel filtration, obtaining three fractions, where the fraction FII contains the peptides that act on the Nav channels, which were purified by cationic exchange chromatography, thirteen fractions were obtained, however, the fractions FII.11 and FII.12 were the most abundant. The Ct1a toxin was localized in the FII.11, while the peptides of the FII.12 have not been identified. The components of this fraction were isolated by one second cationic exchange chromatography and reverse-phase HPLC. The presence of six toxins were identified by electrophoretic methods and by mass spectrometry was determined the mass of 7653.633 Da of the peptide FII.12.1. This component was not identified in the transcriptome neither mass fingerprint previously reported (Valdez-Velázquez et al., 2013) and their mass is in range of scorpion toxins that affects sodium channels (Escalona, 2013). The study of these components will contribute to the identification of the peptides responsible for intoxication caused by scorpion stings and can be a tool for performing studies of the structure-function of these ionic channels

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ANALYSIS OF THE OCCUPANCY OF THE TRANSCRIPTION FACTOR MEOX2 IN THE LUNG CANCER EPIGENOME: A COMPARATIVE BIOINFORMATIC ANALYSIS

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Abstract:

The transcription factor (TF) Mesenchyme Homebox-2 (MEOX2) has been proposed as an important biomarker in non-small cell lung cancer (NSCLC), which is associated with resistance to drug-based oncology therapy, it has shown its over-expression together with imbalances in its histone code and clinical progression, both in tumor tissue and in cell lines. Likewise, by means of ChIP on chip, the ability of MEOX2 to regulate the overexpression of genetic targets at the promoter level, such as GLI-1, has been identified. However, the impact that MEOX2 may have on the regulation of the lung cancer genome and epigenome is unknown. For this reason, in order to analyze large-scale occupancy, a multi-comparative bioinformatics strategy was carried out based on data obtained by ChIP-Seq trials on the A549 cell line and public sequencing control data. Likewise, the in silico results were validated by RT-qPCR and Western Blot. The bioinformatic results demonstrated the interaction of TF in distal regions of the genome, with which it was possible to identify its possible participation in important signaling pathways for pulmonary neoplastic development, such as the Sonic Hedgehog signaling pathway; concluding that the transcription factor MEOX2 is positioned throughout the entire genome, including outside promoter regions, suggesting its participation in the epigenomic regulation involved in oncological processes. On the other hand, the multi-comparative analysis showed that the use of input controls for the ChIP-Seq analysis does not represent changes in the results of peak enrichment in the A549 lung cancer cell line, as long as the same control is used. computational model for peak calling.

ATRAC7/ROP9 SMALL GTPASE AS A NOVEL NEGATIVE REGULATOR PLAYER IN *A. THALIANA-B. CINEREA* INTERACTION

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Abstract:

Botrytis cinerea is a necrotrophic fungus that cause gray mold in more than 1400 plant species. Once it is detected by *Arabidopsis thaliana*, several plant defense responses are trigged such as Ca++ flux increase, activation of Mitogen Activated Protein Kinases (MAPKs), ROS production, cell become alkaline, callose deposition, increase of antimicrobial products and induction of phytohormone biosynthesis. Despite these responses are well known, the link between perception of the pathogens and plant defense activation is still unclear. It has been hypothesized that RAC/ROP small GTPases could be a molecular nexus in this process. In *Oryza sativa* OsRAC1, an orthologue of AtRAC7/ROP9 in *A. thaliana*, has been linked to plant response to *Magnaporte grisea.* Here we analyze its potential role during *A. thaliana-B. cinerea* interaction. We studied the response of AtRAC7-overexpressing plants infected with *B. cinerea*. RAC7 overexpression enhance *A. thaliana* susceptibility to *B. cinerea*. Characterizing plant canonical defense mechanisms such as callose deposition and ROS accumulation and performing a transcriptomic profile, we determined that RAC7 overexpression enhance *A. thaliana* susceptibility to *B. cinerea* due to the transcriptional inhibition of the plant defense responses.

PHENOTYPIC CHARACTERIZATION OF LUNG FIBROBLASTS DERIVED FROM MMP8-MMP13 DOUBLE KNOCKOUT MICE

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Abstract:

Lung fibrosis represents the final common pathway of a variety of lung injuries, and it is characterized, independently of etiology, by the expansion of the fibroblast/myofibroblast population and by the abnormal accumulation of extracellular matrix (ECM) replacing normal functional parenchyma. MMP8 and MMP13 are the principal collagenases in rodents, and the remodeling of fibrillar collagen is widely attributed to the action of these enzymes. In this study, we aimed to explore the role of these collagenases during lung fibrosis progression and resolution. Lung fibrosis was induced by intratracheal instillation of bleomycin, and inflammatory, fibrotic, and resolution stages, were evaluated in Mmp8-Mmp13 double knockout (dKO) and wild-type (WT) mice. Mmp8-Mmp13 dKO mice experienced more severe and prolonged lung fibrosis compared with WT mice. Delayed resolution and persistent fibrotic foci were observed in Mmp8-Mmp13 dKO lungs compared to WT mice. We have also evaluated the localization of Cthrc1 (collagen triple helix repeat containing 1), a marker for pathologic fibroblasts in pulmonary fibrosis, and found increased positive staining for this protein in fibrotic foci of Mmp8-Mmp13 dKO compared to WT mice. In addition, Cthrc1 co-localizes with alpha-smooth muscle (SMA) in the fibrotic foci of Mmp8-Mmp13 dKO but not in WT lungs, so we suggest that both proteins are related to a more aggressive profibrotic phenotype. To confirm these findings, we have isolated fibroblasts from the lungs of both dKO and WT mice. Mmp8-Mmp13 dKO lung fibroblasts show an increased cell migration capacity observed by wound-healing assay. We did not find a difference in cell proliferation rate under basal conditions. Additionally, to understand if there is a compensation mechanism by other MMPs, we evaluated MMP9 and MMP2 activity by gelatin zymography and found increased gelatinolytic activity in Mmp8-Mmp13 dKO compared to WT lung fibroblasts. Our results suggest that lung fibroblasts from Mmp8-Mmp13 dKO show a profibrotic phenotype, and these could be associated with a severer fibrotic response and delayed resolution of fibrosis. This work was funded by CONACYT 235891 SEP-Ciencia Básica Grant.

FTIR ANALYSIS OF THE FUNCTIONALIZATION OF ZNO NANOWIRES FOR THE IMMOBILIZATION OF ANTIBODIES

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Abstract:

The immobilization of antibodies on semiconductor materials and their study has great potential and interest for different applications in various study areas, mainly in biomedicine, because these materials can be used for the creation of biosensors based on the antigen-antibody interaction, which provides an opportunity to perform early detection for diseases or search for analytes of biological interest [1]. A fundamental step for the application of nanomaterials in biosensors is the chemical modification of the surface of nanomaterials (nanowires), its purpose is to allow the immobilization of biological recognition elements (BRE), this process is also known as functionalization. The objective of this study was to analyze the immobilization of antibodies with the silane (3-aminopropyl) trimethoxysilane (APTMS) functionalization of different morphologies of zinc oxide (ZnO) nanowires by Fourier transform infrared spectroscopy (FTIR). The nanowires were used as a platform to immobilize antibodies, by modifying the surface of the nanomaterial using potassium hydroxide (KOH)/deionized water and APTMS. In the results obtained by FTIR, bands corresponding to the correct immobilization of the antibodies on the ZnO nanowires were observed, which are the amide I signal corresponding to the C=O bond, an amide II signal (N-H), and bridges disulfide (S-S).

Salinas Domínguez, Rafael Antonio, Miguel Ángel Domínguez Jiménez, y Abdú Orduña Díaz.
«Antibody Immobilization in Zinc Oxide Thin Films as an Easy-Handle Strategy
for Escherichia coli Detection.» ACS OMEGA, 2020

STUDY OF THE REGULATION OF THE *HUMPHREYA COFFEATA* TERPENOME BY CARBON SOURCE

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Abstract:

Humphreya coffeata is a basidiomycete used in traditional medicine. Previous studies have shown that fungi produces polysaccharides (1;2) and terpenoids (3) with cytotoxic potential in leukemia cells. Terpenoids are the most abundant secondary metabolites in nature, accounting for more than 50% of secondary metabolites in fungi (4). *H. coffeata* changes the chemical profile of terpenoid acids, depending on the carbon source of the culture medium (3). Although it is not known how the regulation of terpenoid synthesis occurs by carbon source, it has been reported that in some fungi there is regulation of the expression level of terpene synthases (TPS), which carry out cyclization (terpene cyclases) and addition of functional groups (tailoring enzymes) of terpenoids (5,6). The aim of this project is to determine how the carbon source impacts the expression of terpene synthases in *H. coffeata*. Obtaining the metabolites was carried out by extraction with chloroform from the biomass and supernatants. Subsequently, their thin layer chromatographic (TLC) profiles were evaluated revealing with H_2SO_4 (10%). Through the use of preparative chromatography separation and HPLC fractionation, it will be sought to obtain differentially produced terpenoids for subsequent structural analysis. We will seek to correlate the production of differential terpenoids with the expression of the genes that code for the possible responsible TPS, using RT-qPCR.

When comparing the chemical profiles of the extracts obtained in both culture conditions, by TLC, changes in the type and amount of metabolites obtained are observed. Also, 50 sequences have been identified in the genome of *H. coffeata*, which may be putative terpene synthase genes. 45 putative tailoring enzyme sequences were found, corresponding to different cytochromes P450. Likewise, two of the sequences correspond to Δ(6)-protoilludene synthase (sesquiterpene cyclase) and one sequence to lanostane cyclase (triterpene cyclase). For this reason, it is likely that terpenoid diversification is associated to the regulation of tailoring enzymes.

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Garcia Garcia M. tesis de maestria. Pograd0 en ciencias biológicas, UNAM
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USING STANDARD OPTICAL MICROSCOPY TO VISUALIZE LABEL-FREE FUNGAL, ANIMAL TISSUE, AND PLANT SAMPLES IN 3D

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Abstract:

Three-dimensional (3D) imaging is essential in all areas of the life sciences. Standard 3D optical microscopy detects fluorescence in geometries designed for confocal discrimination or single-plane illumination. Although successful, these approaches require expensive instrumentation, specialized operation, and fluorescently labeled samples subject to phototoxicity and photodamage. Recently, bright-field (BF) microscopy has been tested for depth discrimination during evaluation of specimen morphology; however, existing methods require extensive computer modeling [1]. I address these challenges by using high-contrast BF microscopy to record the images of label-free samples at different focal planes and applying to images a set of digital filters that reject out-of-plane information [2]. From the processed image stack, a final 3D image is reconstructed using freely available software. Unlike traditional methods, in my new approach the scattered light is recorded (not fluorescence), the digital filtering is performed in real space (not in Fourier space), and the sample is label-free. By visualizing fungal, animal tissue, and plant samples and comparing with light sheet fluorescence microscopy imaging, I demonstrate the accuracy and applicability of the method. My approach is simple, robust, and inexpensive, representing an excellent opportunity to make 3D microscopy widespread and inclusive.

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INHIBITION OF *COLLETOTRICHUM GLOESPORIOIDES* WITH ETHANOLIC EXTRACT OF *LIPPIA GRAVEOLENS*

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Abstract:

Anthracnose caused by the phytopathogenic fungus *Colletotrichum gloeosporioides*, is a rotting disease that occurs during flowering, fruiting and post-harvest in economically important crops such as mango, papaya, avocado, soursop, coffee and citrus. Their control with agrochemicals generates resistant pathogens and they are contaminants for biotic and abiotic systems. The use of plant extracts for its control contributes to an alternative with great potential. Oregano is a perennial and aromatic herbaceous plant with antimicrobial effect, it contains coumeric, ferulic, caffeic, r-hydroxybenzoic and vanillic acid. The objective of this work was to determine the antimicrobial effect of *Lippia graveolens* extract on *Colletotrichum gloesporoides in vitro*. Oregano extract was evaluated at concentrations of 0.3%, 0.5%, 0.8%, 0.9%, 1%, 3% and 5%, using the poisoned medium technique. PDA and ethanol/PDA without extract were used as controls. The treatments were carried out in triplicate and incubated for 7 days at 25±2°C. The results were interpreted as percentage of inhibition, determined by the formula Pandey et. al, 1982. It was determined that oregano extract at 0.3, 0.5 and 0.8% had 44.9, 57.1 and 69.4%, respectively, inhibition of mycelial growth and from 0.9% it totally inhibited the growth of *C. gloesporoides*. *Lippia graveolens* extract at appropriate concentrations inhibits the growth of *Colletotrichum gloesporioides*, so it can be considered a biological alternative for its control.

BACTERICIDAL/PERMEABILITY INCREASING PROTEIN (BPI) EXERTS BACTERICIDAL ACTIVITY AGAINST *MYCOBACTERIUM TUBERCULOSIS*

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Abstract:

The bactericidal permeability-increasing protein (BPI) is a multifunctional cationic protein produced by neutrophils, eosinophils, fibroblasts, and macrophages with antibacterial and LPS-neutralizing properties. In the context of Gram-negative infection, BPI kills bacteria, neutralizes the endotoxic activity of LPS, and thus prohibits immune hyperactivation. Furthermore, BPI increased in patients with Gram-positive meningitis and unexpectedly showed a positive correlation between BPI and pro-inflammatory markers like TNF-alpha. BPI interacts with lipopeptides and lipoteichoic acids of Gram-positive bacteria and significantly enhances the immune response in peripheral blood mononuclear cells. We evaluate the antimycobacterial and immunoregulatory properties of BPI in infected human macrophages. Our results showed that recombinant BPI increased the phagocytosis of *M. tuberculosis* by macrophages. Recombinant BPI entered macrophages and significantly reduced the intracellular growth of *M. tuberculosis* H37 -Ra or -Rv. These results suggest that BPI has an indirect bactericidal effect potentiating the immune response in human macrophages and support that this protein is a new and broad-spectrum antibacterial peptide with the potential to apply in fighting tuberculosis

ROBUST AND VALIDATED UPLC-MS/MS METHOD FOR ASSESSMENT L-ARGININE, ADMA, AND L-CITRULINE LEVELS IN MEXICAN PREGNANT WOMEN WITH RISK OF PREECLAMPSIA

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Abstract:

Hypertensive diseases during pregnancy are the main causes of maternal mortality in Mexico. Impaired function of the placental vasculature is a key factor, where the synthesis and bioavailability of Nitric Oxide (NO) are essential for the proper development and function of the placental vascular system. Production of NO occurs under normal conditions from the reaction of L-arginine (ARG) with domains of NO-synthases, where L-citrulline (CIT) is also obtained. This process can be competitively inhibited by ARG analogs, such as asymmetric dimethylarginine (ADMA), which in normal physiological conditions are found in low concentrations, but in some pathological situations, they can become high enough to reduce NO synthesis. Circulating levels of ADMA have been reported to be significantly higher in women who subsequently developed preeclampsia, and there is great clinical interest in ADMA as a marker of cardiovascular risk. We present an UPLC-MS/MS method to simultaneously quantify L-arginine, ADMA, and L-citrulline levels in several human fluids employing a subrogate matrix (BSA, 35-mg/mL). Sample preparation (100-µL) consisted of an adaptation of the Folch method followed by a dilution with ACN. The analytes were separated using a HILIC BEH amide column (2.1 µm x 100 mm, 1.7 µm) with 10 mM ammonium formate solution, pH 3.5, and ACN as a mobile phase under isocratic conditions. The analytes were detected by positive electrospray, ESI (+). The chromatographic traces of the analytes were recorded in the multiple reaction monitoring modes (MRM), observing the fragment ions *m/z* 175.20 → 70.00 for ARG, *m/z* 176.20 → 113.00, 159.10 for CIT, *m/z* 203.25 → 46.00, 158.15 for ADMA and *m/z* 113.20 → 69.10 for D_9-choline. The fragmentation energies were 20 eV, 14 eV and 14 eV, respectively. The calibration curves were linear (r>0.99) in the ranges of 80-30000-ng/mL for L-arginine, 208-13000-ng/mL for L-citrulline and 4.8-300-ng/mL for ADMA. The method employs D_9-choline as the internal standard. Accuracy (>97.2 %) and precision (3.4-8.6 %) were according to national and international guidelines. The method showed specificity, (ADMA and its stereoisomer, SDMA) and matrix effect values of < 15%. This technique demonstrated to be effective, it requires a short preparation and analysis time and provides high specificity and sensibility for conducting studies to know the cut-off point of ADMA levels in Mexican pregnant women with a risk of preeclampsia.

Sources of support: Instituto Nacional de Perinatología (Mexico) projects 2019-1-154.

BIOINFORMATIC IDENTIFICATION OF SCNA ASSOCIATED LNCRNAS REGULATORS OF TUMORAL PHENOTYPE IN COLORECTAL CANCER

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Abstract:

Colorectal Cancer (CCR) represents the second deadliest malignancy worldwide. Around 75% of CCR patients present high levels of Chromosome Instability (CIN) that results in the accumulation of Somatic Copy Number Alterations (SCNAs). These SCNAs are associated with the amplification of oncogenes and deletion of tumor suppressor genes, and contribute to the tumoral phenotype in different malignancies. Even when this relationship is well-known, much is left to investigate if and how do SCNAs affect lncRNAs and in turn, the impact these alterations have in CCR phenotype. The present study aims to evaluate the role in CCR of differentially expressed lncRNAs as a result of being coded in regions with SCNAs in CCR patients. We downloaded RNA-seq files of the Colorectal Adenocarcinoma Project from the TCGA repository, evaluated differential expression using DESeq2, and to know which lncRNAs were coded in regions affected with SCNAs we downloaded genome sequencing data with the Affymetrix platform and the CNApp web server to map said alterations and the genes within them. We obtained 78 differentially expressed (LFC > 1 | < -1, padj < 0.05) lncRNAs coded in SCNAs, 410 miRNAs and 5028 mRNAs. We constructed a ceRNA network, predicting interactions lncRNA-miRNA-mRNA with data mining techniques and significant Pearson correlations between lncRNA and mRNA expression ($p < 0.05$), said network consisted of 30 lncRNAs, 19 miRNAs and 77 mRNAs. To understand the role that our ceRNA network plays, we performed KEGG and GO analysis and found several oncogenic and antioncogenic processes enriched by the molecular players in our network. Our results show that lncRNAs coded in regions affected by SCNAs form a complex gene expression regulatory network in CCR.

SEARCH FOR LIGAND BINDING SITES ON FABP4 PROTEIN BY X-RAY CRYSTALLOGRAPHY

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Abstract:

The FABP4 protein is responsible for the transport of fatty acids from the cell surface to peripheral tissues to be metabolized or stored, thus directly participating in fatty acid homeostasis and the lipid signaling pathway[1]. By inhibiting the protein or eliminating the gene, protection and improvement in obesity-related conditions are generated[2,3], so there is great interest in the development of an inhibitor drug. However, the great structural similarity that FABP4 has with the other members of its protein family makes it difficult to design a specific drug. One strategy that has been used to improve specificity and affinity is structure-based drug design by X-ray crystallography. This strategy has the advantage of providing information about the interactions of the protein with the ligand to find binding sites that provide high specificity and affinity[4]. Therefore, to find specific interactions in the binding site of FABP4 that provide high specificity and affinity, we evaluated several compounds isolated from *Salvia amarissima* as ligands for FABP4 by a fluorescence displacement assay. The compounds were ranked according to their inhibition constant (IC50) and the top 5 were used for co-crystallization and soaking experiments and further analyzed by X-ray crystallography. Additionally, 4-bromopyrazole and 4-iodopyrazole were included in the project as they have been used before to detect hidden binding pockets[4].

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DESIGN OF DSRNA-BASED FUNGICIDES FOR THE CONTROL OF COFFEE PATHOGEN HEMILEIA VASTATRIX

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Abstract:

Coffee is one of the major commodities in the world that is produced and exported from developing countries. Coffee is obtained from the beans of the plant *Coffea arabica*, which is generally cultivated in tropical regions where humidity is present almost all the year. These climatic conditions promote the development of diseases in the plant, such as coffee leaf rust caused by the obligate fungal pathogen *Hemileia vastatrix*, which has resulted in drops of 22% in production in Mexico in the states of Veracruz, Tabasco Chiapas and Oaxaca in the last years. Coffee farmers use resistant cultivars and conventional fungicides to treat the disease, which contaminate soil and water, and creates resistance in pathogens. A new strategy called spray-induced gene silencing (SIGS) has emerged for plant protection that does not require the application of biofungicides. This consists on the application of double-stranded RNAs (dsRNAs) in spray over the plants, that are designed to silence key genes in the pathogen, and to block virulence. In this work, we aimed to design and evaluate a dsRNA-based fungicide for the control of *H. vastatrix*. For this, the pathogen was identified by sequencing and analysis of ITS regions from *C. arabica* leaves with signs of rust disease that were collected at Cerro Mirador, Valle Nacional Oaxaca. Dicer-like (DCL) genes were selected as targets for silencing. A database search based on similarity with other DCLs in close organisms allowed the identification of a putative DCL in the *H. vastatrix* genome. A 500 bp region was selected and amplified for construction of the template for in vitro dsRNA synthesis. The fungicide activity of dsRNAs was primarily tested in planta over active leaf rust lesions. As result there was no apparent inhibition of disease symptoms. In concordance with this, the analysis of DCL expression by qPCR 24 hours after the treatment with dsRNAs showed no silencing of the transcript. These results indicate that *H. vastatrix* may not be able to take environmental RNAs efficiently, or that dsRNAs are not effective as treatment on established lesions. Ongoing experiments are directed to the dsRNAs-based fungicides on preventing the establishment of rust infection in leaves, and to explore the activity of dsRNAs designed to silence effector genes that are key for virulence of the pathogen. Finally, the results will be useful to consider SIGS as a viable alternative for the control of coffee leaf rust.

EFFECT OF PRAVASTATIN ON VASCULAR REACTIVITY TO PHENYLEPHRINE IN A RAT MODEL OF PREECLAMPSIA

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Abstract:

Preeclampsia remains one of the major causes of maternal and neonatal morbidities. Although this pathology is unique to a pregnant state, it shares biologic and pathologic features with adult cardiovascular diseases such as endothelial dysfunction. Statins, 3-hydroxy-3methyl-glutaryl-coenzyme A reductase inhibitors, are proven to be successful in primary and secondary prevention of cardiovascular mortality and other morbidities through their pleiotropic and lipid-lowering actions. On that account our objective was to estimate the effects of pravastatin on the vascular function in a hypoxic placenta model of preeclampsia.

Female wistar rats were divided into non-subrenal aortic coarctation group (non-SARC) and subrenal aortic coarctation group (SARC). Both animal groups were coupled by 3 days with male partners in a 1:1 ratio. Once pregnancy was achieved groups were assigned as control pregnant rats (P) or preeclamptic rats (PE). In order to investigate weather pravastatin excerts any differential effect on vascular reactivity as administered either in a profilactic scheme (PS) or as a treatment (TS), both (P) and (PE) animals were daily given pravastatin (5 mg/Kg) either one week before and throughout the first week of pregnancy (Prophylactic Schedule groups: PPS; n=6 and PEPS; n=6) or troughout the last two weeks of pregnancy (Treatment Schedule groups: PTS; n=6 and PETS; n=6). Systolic bloood pressure (SBP) measurements were performed in all groups at days 7, 14 and 21 of pregnancy. At day 21 of pregnancy animals were euthanized and both thoracic and abdominal aorta were removed in order to perform vascular reactivity studies with increasing concentrations of phenylephrine (Log [M] -9 to -4) in all groups.

Our results suggest that pravastatin administered in a profilactic scheme (PS) is able to prevent an increase in both (SBP) and vascular response to phenylephrine specially in PE animals. This effect seems to be mediated in a certain degree by the endothelium.

GENERATION OF SEVERAL HIGH-AFFINITY MABS ANTI-HEV B 8 TO ANALYZE CROSS-REACTIVITY AMONG PROFILIN ALLERGENS

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Abstract:

rHev b 8 is an allergen belonging to the family of profilins that are classified as panallergens and are responsible for the pollen-fruit-latex allergenic syndrome. We generated five monoclonal IgGs and one IgE from murine hybridomas against recombinant Hev b 8 and evaluated their interaction with this allergen using ELISA and biolayer interferometry (BLI). Affinity purified mAbs exhibited high binding affinities towards rHev b 8. Some of these antibodies also recognized the recombinant profilins from maize (Zea m 12), tomato (Sola l 1), and the ash tree pollen (Fra e 2). Competition ELISA demonstrated that some mAb pairs could bind simultaneously to rHev b 8. Using BLI, we detected competitive, non-competitive, and partial-competition interactions between pairs of mAbs with rHev b 8, suggesting the existence of at least two non-overlapping epitopes on the surface of this allergen. Three-dimensional models of the Fv of 1B4 and 2D10 IgGs and docking simulations of these Fvs with rHev b 8 revealed these epitopes. Furthermore, these two mAbs inhibited the interaction of polyclonal IgE and IgG4 antibodies from profilin-allergic patients with rHev b 8, indicating that the mAbs and the antibodies present in sera from allergic patients bind to overlapping epitopes on the allergen. The production of specific antibodies that recognize allergens from different sources or block interactions between allergens and antibodies mediating allergic reactions is crucial for developing successful tools for diagnostics and therapeutics.

DEVELOPMENT OF A RAPID GOLD NANOPARTICLES-BASED LATERAL FLOW IMMUNOASSAY FOR THE DETECTION OF DENGUE VIRUS

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Abstract:

Flavivirus detection in humans and mosquito reservoirs have been an important issue since they can cause a variety of illnesses and could represent a health problem in geographical zones where the vector is endemic. In this work, we designed and characterized a biosensor BASED on gold nanoparticles (AuNPs) and a commercial antibody commonly used in clinical diagnostics (4G2 antibody) that specifically recognizes domain II of protein E of the flavivirus group (including Dengue virus and other flavivirus), for the detection of Dengue virus (DENV). To prepare our biosensor, citrate-coated AuNPs of 60 nm were conjugated by adsorption with different concentrations of 4G2 antibody. First, we determined the optimal conditions for the conjugation process. For that, the pH of nanoparticle solution was adjusted (from 5 to 10) during conjugation with a final antibody concentration of 10 µg/mL (maximum concentration of antibody). The optimal pH for conjugation was determined by measuring the aggregation capability of the conjugated AuNPs by the gold aggregation test (GAT). For the 60 nm citrate-coated AuNPs used, pH 6 was the best condition for conjugation, showing a minimum aggregation value of 0.0715 compared to the other values obtained at pH 5-10. Once the best conditions for conjugation have been determined, the concentration of antibody used for conjugation was optimized using 1, 3, and 6 µg/mL. For the physicochemical characterization, we used dynamic light scattering (DLS) to determine the hydrodynamic size, ζ-potential and state of aggregation of the AuNPs and conjugates. The AuNP-4G2 conjugates at concentrations of 1, 3 and 6 µg/mL presented an increase in the average hydrodynamic diameter, compared to the naked AuNPs. Also, as part of the characterization, differences in the UV-Vis absorbance spectrum and electrophoretic migration were observed between the conjugated AuNPs (with BSA or antibody) and naked AuNPs. Additionally, we used this biosensor (AuNP-4G2 conjugate with 3 µg/mL antibody) in the assembly of a competitive lateral flow assay (LFA) for the development of an alternative test to detect the flavivirus envelope protein in isolated DENV samples. It could be used as a future tool for dengue detection (and other flavivirus) in the mosquito vector (*Aedes aegypti*) for the identification of epidemic risk regions. Functionality tests were performed using Dengue virus 2 isolated solution (LD50= $10^{-2.66}$) as a positive sample and PBS buffer as a negative control. Results showed that it is possible to detect Dengue virus *in vitro* with this gold nanoparticle-based lateral flow assay with an estimated detection limit of 5.06 x 10^2 PFU. We suggest that this biosensor could be used as an additional detection tool by coupling it to different point-of-care test (POCT) for easy detection of other flaviviruses.

LEARNING AND EVALUATION IN BIOCHEMICAL SCIENCES EDUCATION

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Abstract:

Biochemistry is a fundamental knowledge domain within the life and health sciences education, and evaluation is an inseparable aspect of the professional formative process. Evaluation in education is a process with the purpose of not only verifying the learners' achievement of course or activity objectives, but also the results analysis in terms of causes and reasons for the degree of achievement. There are different instruments and a variety of formats that can be used to assess student learning. The levels of acquired knowledge and skill must be clearly specified in the course, activity, or program objectives, so learners know what is expected of them at the end of the process, and the ways in which student development will be assessed. In addition of having evidence of the student's acquired knowledge or skill, all the instruments must be useful for feedback to promote learner development.

If an oral evaluation is considered for project advances, such as periodical evaluations for research activities within graduate studies programs, the dissertation for the "doctoral candidate" status, or thesis presentation and defense for the graduate degree, this form of evaluation must provide objective evidence of the formative process, as well as validity and reliability.

For high stakes evaluations, oral or otherwise, solid evidence of the learner's achievement obtained with the use of a standardized instrument is extremely useful, and the utilization of such instruments would also provide an oral examination with a degree of validity and reliability. Checklists and Likert Scales are structured assessment instruments where evidence of the knowledge or skill level to be accomplished is collected. The Checklist format, as the name implies, is a list of the knowledge elements and/or skills defined in the objectives, or learning outcomes, that collects whether or not these have been attained. The Likert Scale is useful by the fact that it records the extent or quality to which such knowledge elements and skills have been accomplished within the framework of the objectives.

When considering a high stakes examination in an oral fashion, such as the ones presented above, documenting the acquisition of the defined knowledge elements and skills, and the level of performance, in each is of great importance. In this work, we present an example of a Checklist and a five-point Likert Scale that can be used for such evaluation purposes.

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INHIBITION OF CU(II) INDUCED AMYLOID FIBERS FORMATION OF THE 6AJL2-R24G PROTEIN

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Abstract:

Light chain amyloidosis (AL) is one of the most common systemic amyloidosis. It is caused by the light chain variable domain over expression at the plasmatic cells. The excess of light chains induces self-association and fibrillar aggregates, which are extracellularly deposited in tissues and organs, such as liver, heart, and kidneys. The deposition of the light chains cause organ failure and eventually death. However, the fibrillar aggregation mechanism remains poorly understood.

Light chains are classified into kappa (κ) and lambda (λ) families. Recombinant light chain 6a belongs to the λ6 subgroup, it is joined to JL2 germinal gene and has been frequently found in patients with AL. In healthy individuals this protein is expressed only around 2%, in contrast, in patients is expressed in approximately 38%. Furthermore, 25% of the proteins present a substitution of Arg 24 by Gly. *In vitro* studies have shown that this mutation produce less stables light chains and higher amyloid fiber propensity.

Metal ions like Cu(II) and Zn(II) play a fundamental role in different amyloid diseases. Some studies have proposed that Cu(II) accelerate the amyloid fibril formation such as in the β-2-microglobulin (β2m) and the α-sinuclein, involved in dialysis-related amyloidosis and Parkinson disease (PD) respectively. In other cases, the Cu(II) retard the amyloid fibril formation as in the hIAPP, involved in the type 2 diabetes (T2D). On the other hand, the effect of Zn(II) in some diseases is not clear, in the hIAPP accelerate the fibril formation, however, in the amyloid beta protein (Aβ) involved in Alzheimer disease (AD), it has been observed that it is capable of accelerating or inhibiting the amyloid fibril formation. Recently, our group reported that Cu(II) accelerate the aggregation of the recombinant 6aJL2-R24G protein, nevertheless, the effect of Zn(II) is not clear yet.

In this work, the effect of Zn(II) in the 6aJL2-R24G aggregation is evaluated, as well as the effect of different fragments of the 6aJL2-R24G and SMA as inhibitors of the aggregation induced by Cu(II).

RESONANT ACOUSTIC MIXING TO ENHANCE OUTER-MEMBRANE VESICLES RELEASED BY *ESCHERICHIA COLI*

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Abstract:

Outer membrane vesicles (OMVs) are non-replicative membranous structures produced by Gram-negative bacteria and play relevant roles in bacterial survival and cell-to-cell interactions. Because of OMVs´ composition and ability to transport information to specific targets, their use in the development of next-generation therapeutics, vaccines and delivery systems has gained attention. Nevertheless, OMVs´ spontaneous release is low, limiting their commercial application. In this work, we study resonant acoustic mixing (RAM) as a strategy to increase OMVs released by *Escherichia coli*. The results were compared with OMVs released under orbital mixing (O.M). We characterized vesicle size distribution by Dynamic Light Scattering (DLS), protein profile by SDS-PAGE, and lipid profile by Thin-layer chromatography (TLC). The indirect quantification and morphology were determined by Transmission Electron Microscopy (TEM). We found that RAM increases OMVs released four-fold compared to O.M. OMVs obtained by RAM and isolated by filtration had two size distributions, while the OMVs from O.M only presented one size distribution. Also, we found different protein and lipid profiles, indicating that the mixing changes OMVs composition. We conclude that RAM is an effective strategy to improve OMVs yields by *E. coli*, possibly because this type of mixing increases mechanical and oxidative stress.

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STRUCTURAL ANALYSIS OF *CAPSICUM* DEFENSIN J1-1 AND EXPRESSION OF J1-1 K45E VARIANT IN *ESCHERICHIA COLI*

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Abstract:

Plant defensins are 45-54 amino acids, cationic, cysteine-rich antimicrobial peptides. These molecules show interesting properties as thermostability, protease or extreme pH-tolerance associated to its CSαβ 3D structure. Since their discovery in late 90´s, distinct biological activities have been described among them, antibacterial and antifungal activities have gained great attention of the international scientific community as scaffolds to develop new antibiotics. Plants are natural source of defensin variants but unfortunately, defensin recovery from tissue is difficult to achieve in high purity and quantity, in order to study their mechanisms of action. These facts limit its application as molecules to treat infectious diseases caused by bacterial or fungal pathogens. Previously, X-ray structural reports have described oligomerization in crystallized lipid-defensin complexes, this has allowed to propose putative mechanisms of action and know more about how this phenomenon take place at structural level. In our research group, previously a *Capsicum* fruit-specific defensin, J1-1, has been obtained by recombinant expression in *Escherichia coli* and has showed antibacterial activity against *Pseudomonas aeruginosa in vitro*. In this work, a set of J1-1 mutants have been designed according to a comparative analysis on structure-activity studies of lipid-defensin oligomers, with the aim to elucidate how these structural determinants affect its lipid-binding profile, lipid-dependent oligomerization and antibacterial activity. The structural analysis for mutants design and the recombinant expression and purification of J1-1_K45E is presented in this work.

MITOCHONDRIAL AND PEROXISOME DYNAMICS DURING SEXUAL DEVELOPMENT OF *PODOSPORA ANSERINA*

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Abstract:

Organelles suffice physiological requirements of the eukaryotic cell, often compartmentalizing processes like oxidative phosphorylation in mitochondria, β-oxidation in peroxisomes, or transcription in the nucleus, among many others. Organelle dynamics help to satisfy these cellular functions by organelle fusion and fission, biogenesis and degradation, and traffic. During the cell cycle, mitosis is a stage of major rearrangements in organelle distribution and morphology; therefore, organelle dynamics become utterly relevant. Although it's known how organelles behave during mitosis, much less has been described during the specialized cell division of sexual organisms, meiosis. Mitochondria and peroxisomes, closely related organelles, share several proteins involved in organelle dynamics, like the fission machinery (DNM1 and FIS1) and the GTPase Miro, a protein that serves as motor protein adaptor for mitochondria and peroxisome traffic in metazoans. In *Podospora anserina*, a model filamentous fungus, peroxisomes are dynamic during meiosis. They change in number, morphology, and localization, which relate to fusion/fission, traffic, and pexophagy. As proteins of the fission machinery and traffic between peroxisomes and mitochondria are shared, we sought to study their relation and importance for meiosis and sexual development of *P. anserina*. By generating strains deleted for *DNM1* and *MIRO1*, our results show that fission by DNM1 is necessary for mycelial growth and meiotic spore formation. Moreover, DNM1 loss causes defects in peroxisome segregation into spores and defective spindle positioning during meiosis and sexual development, underlining the relevance of mitochondrial and peroxisome fission during meiosis. On the other hand, MIRO1 is dispensable for mitochondrial or peroxisome traffic during vegetative growth but is relevant during meiotic spore germination, as germinative mycelium and peroxisome traffic show defects in absence of MIRO1. These findings show that different stages of sexual development depend on the proteins controlling peroxisome and mitochondrial dynamics and remarks the need to understand the contribution of mitochondrial and peroxisome dynamics during development in fungi and in meiosis.

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EFFECT OF CHRONIC STRESS ON EPIDIDYMAL SPERM QUALITY AND TESTICULAR HISTOLOGY

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Abstract:

Infertility has been defined as a medical and social problem that affects 15% of couples in the world, the man is considered as the sole factor of the problem in 30% of cases. Chronic stress has been reported to affect spermatogenesis causing a loss of germ cells and the initiation of an apoptotic process in adult rats. Therefore, the objective is to evaluate the effects of stress on sperm quality (viability, mobility, concentration, and morphology) as well as testosterone concentrations in young rats. Male Wistar rats of 21 days of age were randomly assigned in two groups (8/group): control group (C) and chronic stress group (CUS), which had free access to plain water and diet Chow 5001 purine. At 51 days of age, chronic stress was applied for 4 weeks, this consisted of exposing the rat to 5 different types of stress at different time spans: reduction of space with clean box (5 hours), forced swimming in hot water (28 ° C) 10 minutes, reduction of space with dirty box (5 hours), forced swimming in cold water (18 ° C) 10 minutes and restriction (3 hours). At the end of the experiment the animals were euthanized, a tissue sample was taken from the epididymal cauda for the evaluation of sperm quality, serum samples were also obtained for the measurement of testosterone by the ELISA method. The stressed animals presented a decrease in serum testosterone concentration ($p<0.02$), and low sperm concentration ($p<0.02$), mobility ($p< 0.04$), viability ($p<0.03$) and changes in morphology, in terms of histology of the seminiferous tubules in the same way there were changes in the area of the lumen and germinative epithelium of the CUS group. This study contributes to consider that stress in early life can lead to the appearance of conditions that affect fertility in adulthood.

En conclusión, el estrés crónico disminuye la concentración de testosterona, así como la calidad espermática. Este estudio contribuye a considerar que el estrés en la vida temprana puede conducir a la aparición de condiciones que afectan la fertilidad en la edad adulta.

CELLULAR SCAFFOLDS FOR BONE TISSUE OF MARINE ORIGIN

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Abstract:

Scaffolds for tissue engineering are support structures designed to facilitate the regeneration of the tissue in question; these structures can be natural, synthetic or hybrid1. In this work, scales from the Lutjanus Campechanus species are proposed as Scaffolds, which were characterized by Fourier Transform Infrared Spectroscopy (FTIR) where the presence of the amide groups characteristic of type I collagen was observed, the X-Ray Diffraction (XDR) characterization showed the presence of a phase rich in hydroxyapatite2.

Cell cultures were performed on the scales, using Human Fetal Osteoblasts (hFOB), for 1, 3, 5, 7, 14 and 21 days with a cell density of 1000 cells / mL, to test their biocompatibility, and it was shown that the scales are not cytotoxic and present a high cell viability (above 95%). Although we are still lacking tests, the above indicates that we can use them as cell Scaffolds.

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EFFECTS OF GOLD NANOPARTICLES FUNCTIONALIZED WITH POLYETHYLENEIMINE ON THE MOSS *PHYSCOMITRIUM PATENS*

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Abstract:

Polyethyleneimine (PEI) is one of the most utilized polymers for enhance the interactions between nanomaterials and biological molecules to be transported inner the cells, however their size, the linearity or not and the concentration of PEI could cause cytotoxicity. Besides, most of the research have been developed using animal cells, recently it has recovery importance in the evaluation with plant cells interactions[1].

We used different concentrations of PEI (0.025%, 0.125%, 0.625%, 0.5% and 1.5% w/v) to synthesize gold nanoparticles by chemical reduction, and then incubated them with protonemas of 10 days old of *Physcomitrium patens* (*P. patens*) for 21 days, evaluating their photosynthetical efficiency and the development of gametophore. We obtained gold nanoparticles of 15nm and monodisperse.

The concentrations of PEI at 0.5% w/v and 1.5% w/v cause the loss of the photosynthesis capability and the dead of the plants, the concentration of 0.125% cause certain stress but they are capable of recuperate the photosynthetical efficiency and, finally, the concentrations of 0.0625% and 0.025% w/v don't affect the photosynthetical efficiency but affect the size of the gametophore.

Certain polymers can cause oxidative or osmotic stress into plants, but there are no reports about the effects of the polymer or gold nanoparticles applied to protonemas of *P. patens*. That's why in this presentation we going to show you not only the standardization of the method of colloidal chemistry to synthesize gold nanoclusters using the polymer as reductant and stabilizer, but also the effects in the photosynthesis efficiency and in the development of gametophores of the moss *P. patens*.

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ANTITUMORAL ACTIVITY EVALUATION OF METHANOLIC EXTRACT OF ANNONA MACROPROPHYLLATA ON COLORECTAL CANCER

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Abstract:

Colorectal cancer is the third most incident type of cancer, and the second in mortality worldwide in both sexes, with approximately 883,200 deaths per year. Treatment for this type of cancer depends on the stage, surgery in the early stages, and chemotherapy and or radiotherapy for advanced stages. However, recurrence is common, and the 5-year survival rate is between 50% and 60%. So, the search for newer and more efficient therapies results in considerable importance (Morey, et al., 2011).

Natural products result of the secondary metabolism of different organisms such as plants, fungi, and bacteria, which have multiples uses in pharmacology, cosmetology, and nutrition, among others. Especially in oncology, reports highlight that approximately 60% of compounds used to treat cancer come from natural products (Dias, et al., 2012).

Annonaceae is a family of plants commonly known as the soursop family, used in folk medicine to treat diverse diseases, including cancer. Previous reports studied their anticancer properties, demonstrating its cytotoxicity against different tumoral cell lines. This activity has been attributed to acetogenins; secondary metabolites exclusively produced by Annonaceae species. Acetogenins can block the electron transport chain, as well as inhibit the activity of the NOX protein family, thus reducing ATP production and inducing cell death by apoptosis and autophagy. However, the molecular mechanisms underlying this effect have not been defined yet (Jacobo-Herrera et al., 2019).

In this project we evaluated the cytotoxic activity of the methanolic extract of *A. macroprophyllata* in colon cancer cells (HCT116) and its antitumor activity in vivo. Our findings indicate that the methanol extract induces autophagy by the hyper lipidation of LC3 in HCT116 cells. Furthermore, it reduces tumor growth on a xenograft model; no macroscopic toxic signals were observed in comparison to those treated with cisplatin (the reference drug used).

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INHIBITION OF TGF-βS AND THEIR RECEPTORS BY CALCITRIOL IN TROPHOBLAST CELLS

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Abstract:

Calcitriol (1a,25-dihydroxyvitamin D; active metabolite of vitamin D), is a potent secosteroid hormone synthetized in many cell types including the trophoblast cells. This hormone increases its concentration during normal pregnancy and participates in preserving a hormonal and immunological balance. In fact, previous studies have demonstrated that calcitriol regulates the biosynthesis of hormones, proteins involved in calcium transport, antimicrobial peptides and both pro- and anti-inflammatory cytokines in cultured trophoblast cells, while its deficiency has been associated to several complications of pregnancy. Contrary to calcitriol, exacerbated concentrations of TGF-bs have been reported in pathologic pregnancies such as preeclampsia; however, the role of this factor in human placental development and preeclampsia remains contradictory. **Aim:** To analyze the basal gene expression of TGF-β1, TGF-β2, TGF-β3 and their receptors TGβRI and TGβRII in primary culture of trophoblast cells. In addition, to study the effects of calcitriol upon gene expression of these ligands and their receptors as well as to evaluate the calcitriol effect upon secretion and abundance of TGF-b1 produced by syncytiotrophoblast cells. **Methodology:** We used term placentas from uncomplicated pregnancies following cesarean section. For basal gene expression, we isolated and used cultured trophoblast cells. In addition, the cells were treated with calcitriol. RNA was extracted for gene expression studies by real time PCR while TGF-b1 protein was evaluated by ELISA and western blot assays. **Results:** Overall, the results showed that basal gene expression for ligands was TGF-β1 > TGF-β2 > TGF-β3 while TGFβRII was higher expressed as compared to TGFβRI. Regarding calcitriol effects, the results showed that this secosteroid significantly inhibits the gene expression of the three isoforms of TGF-bs and their receptors. Likewise, calcitriol down regulate the protein abundance and secretion of TGF-b1. **Conclusion:** Calcitriol is a negative regulator of gene expression of the three isoforms and their receptors in cultured trophoblast cells, maybe preventing the overexpression of the signaling pathways used by TGF-βs, thus attenuating the detrimental effects that could be caused by increased and/or exacerbated concentrations of TGF-β as seen in women with preeclampsia.

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CHARACTERIZATION FUNCTIONAL OF K_{IR} CHANNELS IN TRIPLE-NEGATIVE BREAST CANCER

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Abstract:

The participation of K^+ channels is relevant in various physiological and pathophysiological processes such as migration, proliferation, and maintenance of the resting potential[1]. Increasing evidence has shown its association with several types of cancer, including breast cancer. Triple-negative breast cancer (TNBC) is considered the breast cancer with the worst prognosis. Since it lacks estrogen, progesterone, and EGF2 receptors, it is also the breast cancer with the fewest therapeutic alternatives[2]. Here we study the functional involvement of K^+ channels in the progression of TNBC. Thus, we use cell lines from different tumor stages and non-cancerous epithelial cells. Using single-channel recordings (patch-clamp) and immunocytochemical (ICC) approaches, we found that two kinds of inward rectifiers (K_{ir} channels) are associated with tumoral progression. Non-cancerous cells have a channel with properties (conductance and kinetics) similar to those described for the heterotrimeric K_{ir}4.x/5.1, which decrease their presence in TNBC. Moreover, a second inward rectifier with single-channel properties, alike the K_{ir}2.x family, appears only in cancer cells, increasing its presence in the most advanced tumor stages. These results suggest that K_{ir} 4.x/5.1 channels and K_{ir}2.x have diagnostic and therapeutic potential as molecular targets in this type of cancer.

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DHDIT2, ENCODES A CYTOCHROME P450 FROM *DEBARYOMYCES HANSENII* WHICH PARTICIPATES INTO THE DEGRADATION OF BENZO(A)PYRENE. A PROPOSAL FOR MYCO-REMEDIATION

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Abstract:

Pollutants such as polycyclic aromatic hydrocarbons (PAHs), like benzopyrene (BaP), are usually found in mixtures, they are ubiquitous and extremely toxic, contaminating soils and aquatic niches. The need for new remediation strategies using microorganisms has led researchers to look after the best ones to get rid of the pollutants without disturbing the ecosystem. We analyze the effect of benzopyrene on the physiology of various yeasts searching for a good candidate to be proposed as a myco-remediation strategy.

In this work, the BaP effect on the growth of *Candida albicans, Debaryomyces hansenii, Rhodotorula mucilaginosa and Saccharomyces cerevisiae* was evaluated. The results show that BaP degradation depends on factors such as temperature, concentration, and the probable detoxification mediated by cytochrome P450 (CYP) in the microorganisms studied. Similarly, the present study was able to identify the *DhDIT2* gene of *D. hansenii* as important for the metabolism of BaP, so we propose this yeast as a good candidate to bio-remediate BaP contaminated sites.

CYTOKINETIC FURROW FORMATION PROMOTES DNA DAMAGE AND EXPRESSION OF P53 TARGETS

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Abstract:

Mitosis is an amazing biological phenomenon in cell biology and one of the most important across the cell cycle, so it is highly regulated. Any error in the proper execution of mitosis can trigger death or the development of a disease. Chemotherapy against cancer has taken advantage of the importance of mitosis in the cell cycle, and several drugs block cell proliferation by inhibiting mitosis. Among these are antimicrotubule drugs that can promote microtubule stabilization or destabilization. Paclitaxel binds beta-tubulin and promotes microtubule stabilization. Paclitaxel is used against various types of cancer (lung, liver, ovarian, testicular, etc.). Microtubule stabilization has severe consequences during mitosis as microtubules cannot bind to all the kinetochores on chromosomes, which activates the spindle assembly checkpoint (SAC), generating an arrest in mitosis. It has been revealed that paclitaxel-treated cells can die during mitosis arrest due to the degradation of MCL1 (an anti-apoptotic protein) or exit mitosis through cyclin B degradation. This phenomenon is known as mitotic slippage. After slippage, the cells can have three fates: be arrested during interphase, re-enter a new cell cycle or enter apoptosis, the alternative death mechanism by which paclitaxel kills the cells. In our lab, we seek to address the mechanism governing cell fate following slippage exit. We propose that slippage coincides with the formation of multiple cytokinetic furrows that generate DNA damage. The damage will promote the expression of apoptosis-promoting P53 targets such as PUMA and NOXA or interphase arrest-promoting P21.

METABOLIC BIOMARKERS OF AGRONOMIC AND QUALITY PROPERTIES OF COFFEE VARIETIES

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Abstract:

Coffee is one of the most sold products worldwide and is considered the economy's engine for many countries. However, in Mexico, as in many producing countries, the quality and productivity of coffee have been undermined by widely distributed diseases such as rust (Hemileia vastratrix) and ojo de gallo (Mycena citricolor), as well as by the drought.

The organoleptic properties of this product are regulated by numerous factors, such as the genome, variety, and toast process. However, the environmental conditions also will influence them. Thus, not only will the genome contribute to the quality properties of the final coffee product. In this sense, a metabolomic approach could provide more accurate information about the coffee tree's physiological state during the coffee plant's cultivation [1]. Metabolite levels are more deeply modified depending on the agronomic characteristics and diseases during cultivation [2]. We are interested in identifying the relationship of metabolome with the coffee tree's response and resistance to plagues.

Addressing two strategies of Chromatography coupled to mass spectrometry for the analysis of plants from the Coffee Germplasm Bank of the Universidad Autónoma de Chapingo, we intend to identify marker molecules of early stages of the disease as well as molecules of resistance to drought or other types of stress. Furthermore, the metabolic phenotypes from leaf extracts will allow us to find molecules related to stress response and quality, complementing and corroborating genomic information to select or improve varieties and achieve better production.

Funding: Conacyt-DFG 2016/277850

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ELUCIDATION OF FACTORS INVOLVED IN MODULATING DISA-DEPENDENT/INDEPENDENT CHECKPOINT EVENTS DURING GERMINATION/OUTGROWTH OF *BACILLUS SUBTILIS* SPORES

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Abstract:

In response to DNA damage, cells activate mechanisms to halt cell cycle progression, allowing removal of lesions and maintenance of genome integrity. To understand these repair mechanisms, several models have been used, including *Bacillus subtilis*. Growth-limiting conditions, in this bacterium, induce the formation of spores, long-suriving, latent cell forms that are highly resistant to physical and chemical factors. When conditions are suitable for growth, dormant spores can return to vegetative growth through a germination/outgrowth process. In *B. subtilis* the DisA protein acts as a DNA damage checkpoint, during return of spores to vegetative growth, a stage at which water entry and activation of aerobic metabolism can lead to generation of oxidative DNA lesions, which can be processed by Base Excision Repair (BER) factors, including the AP endonucleases Nfo and ExoA. However, even in the absence of Nfo and ExoA, there is repair of oxidative DNA lesions during spore germination/outgrowth, suggesting the involvement of additional AP-endonuclease in the processing of these types of genetic lesions. Therefore, the current project is aimed to investigate the contribution of a third AP-endonuclease Nth to Nfo/ExoA-dependent repair transactions and the DisA-independent checkpoint events that takes place during germination/outgrowth of *B. subtilis* spores. Results from germination/outgrowth kinetics of *nth*-overexpressing, RecA- and low-fidelity polymerases-deficient, spores, and epifluorescence microscopic analysis of DNA replication suggest that Nth repair products activate a DisA-independent checkpoint mechanism in outgrowing *B. subtilis* spores lacking Nfo, ExoA and DisA.

Work supported by CONACYT (grant A-1S-27116) and UG (grant CIIC 107/2022).

THERAPEUTIC EFFECT OF LAHERRADURINE ISOLATED OF *ANNONA MACROPROPHYLATA* ON COLORECTAL CANCER

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Abstract:

Introduction: Colorectal cancer (CRC) is a significant public health problem worldwide. Currently, there are different treatments, which depend on the clinical condition of the patient. A surgical procedure is recomended for early stages, and patients in late stages and with metastases, radio and chemotherapy are used. However, the search for new treatments continues because surgeries are only successful in the first stages of the disease, and present chemotherapy has significant sequelae in patients. An alternative in the search for anti-tumor molecules is plants used in traditional medicine. Acetogenins (ACGs) have reports to be selectively toxic to several types of cancer cells, including multi-drug-resistant cell lines. Such is the case of laherradurin (LH), a cytotoxic compound against different tumor cell lines. For the above-mentioned, this work aimed to evaluate the anticancer effect of LH in an *in vivo* model of colon cancer.

Materials and methods: 1) LH was isolated, purified, and identified by chromatographic and nuclear magnetic resonance methods from the plant *Annona macroprophyllata Donn. Sm.* **2)** LD50 was determined for Balb/c and nu/nu mice. **3)** Carcinogenesis induction with azoxymethane and sodium dextran sulfate. Experimental groups: a) negative control; b) positive control; c) LH (0.5 mg/kg); d) LH (1.5 mg/kg); e) LH (3.0 mg/kg); f) LH (3.0 mg/kg) (two administrations per week); g) cisplatin (2 mg/kg). **4)** Control and supervision of weight and disease activity index (DAI) during the carcinogenesis model. **5)** Macroscopic analysis of the colon (number and size of tumors, size of the colon). **6)** Cytotoxicity evaluation in two colon tumor lines (HCT 116, SW 620) and a non-tumor cell line.

Results: The LD50 values were 11.5 and 36.5 mg/kg for Balb/c and nu/nu mice, respectively. According to the model of carcinogenesis, weight loss, increased sickness (DAI), anal prolapse, hair bristling, and lethargy in organisms were observed in the first weeks. However, the LH-treated groups showed weight recovery, decreased disease (bleeding), and a marked morphological change of the anus (prolapse) compared to the positive control. As for the macroscopic findings in the colon, there was a dose-response effect in the LH-treated groups. Also, we observed a reduction in the number and size of tumors in the groups treated with 1.5 mg and 3.0 mg/kg LH compared to the positive control, as well as in the mice treated with 2 mg/kg cisplatin. In terms of colon size, there was a decrease of about 30% for the positive

control compared to the negative control. Meanwhile, the groups treated with 3.0 mg/kg LH decreased less than 15%. The results obtained in the cytotoxicity assay show an IC50 of 5.85 and 20.35 µM for HCT 116 and SW 620, respectively. On the other hand, in the non-tumor line, the IC50 value was not reached.

Conclusions: The LH-treated groups (1.5 and 3.0 mg/kg) showed a decrease in tumor number and size, prevented colon shortening, and allowed weight recovery and disease reduction in the AOM-DSS-induced model. The HCT 116 cell line was the most sensitive to LH, while the non-tumor colon cell line did not show cell death, suggesting a selectivity for tumor cells.

CARDIAC T TUBULE SYSTEM REMODELING IN A DIABETIC BIOMODEL

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Abstract:

The main function of the heart is to pump blood to the entire body and this function is determined by the excitation-contraction coupling, of which the t-tubules, invaginations of the sarcolemma in the cardiomyocyte, are an integral part since the coupling process begins in them. This function can be altered under pathologic conditions such as diabetes.

We evaluated the changes in the t-tubule system and its conformation in the form of a network. Images of right and left ventricular cardiomyocytes from rats were used, lean zucker diabetic fatty (LZDF) as controls and zucker diabetic fatty (ZDF) as problem group or normoglycemic zucker diabetic fatty (ZDF GN) as reference.

Cardiomyocytes were isolated at 13 weeks of age and labeled with a fluorescent dye. (Di-8-ANEPPS). Images of these cells were captured under a confocal microscope. The images were analyzed with image processing and analysis software Fiji, using a dedicated plug-in, in which a 2d reconstruction of the t-tubule network was created, which allowed us to evaluate its components and characteristics.

The results obtained show changes in the number of structural components corresponding to the t-tubule network in ventricular cardiomyocytes from LZDF, ZDF and ZDF GN rats. An increase in the number of t-tubules, branches, junctions, and terminations in the network structure was found, as well as a change in the directionality of the t-tubules. The changes were evaluated both in the whole heart and in the left and right ventricle, changes in the left ventricle contribute most to the variations found in the whole heart.

We propose that the changes found could have a compensatory function, trying to supply functional alterations present in diabetic and obese models, such as the failure of intracellular calcium homeostasis.

EVALUATION OF HPV E1 TRANSCRIPT IN EXTRACELLULAR VESICLES; PRESENCE AND TRANSMISSION TO HPV-NEGATIVE KERATINOCYTES

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Abstract:

Background: Persistent infection with human papillomavirus (HPV) is one of the main risk factors associated to the development of cervical cancer (CC). The HPV genome consists into an early region (E), a late region (L) and a noncoding long control region (LCR). It has recently been proposed that, in addition to its role in the replication of the viral genome, E1 could play an important role in the progression of CC. Through massive sequencing analysis (NGS) we have identified the presence of the E1 transcript in extracellular vesicles (EVs) released by HeLa cell line. Due to EVs can establish a cellular communication system, we are interested about to confirm the presence of the transcript, assessing its integrity in EVs and evaluate its possible transmission to recipient cells. This last through the uptake of EVs by HPV-negative keratinocytes. **Materials and methods:** EVs extraction was performed using the miRCURY exosome kit. EVs were treated with nuclease S1 and amplification of the E1 transcript was performed by RT-PCR. For northern blot assay, RNA probe was designed using the pJET1.2/blunt cloning vector and competent bacteria E. coli DH5α were transformed. Plasmid extraction was performed by alkaline lysis and precipitation with polyethylene glycol. The identify of the cloned fragment was confirmed by Sanger sequencing. In vitro transcription was carried out to get the labeled probe using the Bio-16-UTP kit. To evaluate the possible effect in receptors cells, EVs uptake by HPV-negative keratinocytes is being evaluated. **Results:** The E1 transcript was identified from EVs treated with S1 nuclease. The cloned E1 fragment was successfully incorporated by *E. coli* DH5α. Plasmid sequencing validated the insertion of the sequence of interest. Dot blotting confirmed the labeling for sense and antisense probe. Northern blot assay and internalization of EVs by HPV-negative keratinocytes is being corroborated. **Conclusions:** Our results confirm the presence of E1 transcript inside EVs. We have obtained a biotin-labeled RNA probe to validate the presence and integrity of the HPV E1 transcript in extracellular vesicles released by HeLa cells.

STABILITY OF NON-SYMMETRIC *DE NOVO* TIM-BARRELS

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Abstract:

The TIM-barrel or $(\beta\alpha)_8$-barrel fold is the most common enzyme fold in nature, which consists of an eightfold repeat of (βα) units connected by loops, where the eight β-strands form a curved parallel β-sheet (the barrel) surrounded by the eight α-helices. The wide range of catalytic reactions harbored by this fold in nature, make it a promising scaffold for designing *de novo* proteins with enzyme activity. In this context, Huang et al. [1] successfully designed a *de novo* TIM-barrel through a 4-fold repeat of a βαβα unit; this protein (sTIM11) showed a large thermostability (T_m = 80°C) and relatively low thermodynamic stability (ΔG ~ 4 kcal/mol). The hydrophobic core of sTIM11 was redesigned with a modular approach, and a new TIM-barrel set of stable variants (NovoTIMs) containing mutations in three different regions of the barrel was created [2]. The three-dimensional structure of two of them (NovoTIM6 y NovoTIM13) was determined, finding that the RMSD (model vs. structure) was different in each quarter. This means that each quarter has the same sequence but a different structure. The thermal unfolding of NovoTIM13 was irreversible, this is interesting because NovoTIM13 contains the mutations designed in NovoTIM6 and NovoTIM8, both of them showing reversible thermal unfolding. In this work, we explore the thermodynamic and structural effects of symmetry breaking in the transition from NovoTIM6 to NovoTIM13. For this purpose, we are currently studying mutants where the mutations contained in NovoTIM8 were added sequentially to the NovoTIM6 framework quarter by quarter. Molecular dynamic simulations at different temperatures were carried out for all models where the number and location of each mutated quarter were modified. The preliminary physicochemical characterization of some of these proteins will be discussed.

[1] Huang, P. S. et al. (2016). De novo design of a four-fold symmetric TIM-barrel protein with atomic-level accuracy. *Nature chemical biology, 12*(1), 29-34. [2] Romero-Romero S. et al. (2021). The stability landscape of de novo TIM barrels explored by a modular design approach. *Journal of molecular biology, 433*(18), 167153.

PERILIPIN ISOFORMS EXPRESSION IS DIFFERENTIALLY REGULATED IN T4-TREATED INSULIN-RESISTANT RAT HEARTS

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Abstract:

The heart reprograms its energy metabolism during conditions of insulin resistance, which ultimately leads to the development of lipotoxicity. Lipids are stored in lipid droplets (LD) to protect the heart from lipotoxicity. Perilipins 1-5 (PLIN) are lipid droplet-associated proteins that regulate lipid storage and metabolism. On the other hand, thyroid hormones (thyroxine-T4 and triiodothyronine-T3) have beneficial effects on cardiac metabolism during insulin resistance. However, the changes in PLIN isoforms expression in response to T4-treated insulin-resistant rat hearts are not thoroughly studied. In this work, we quantified PLINs isoforms (1-5) mRNA in the heart of insulin-resistant rats (Otsuka Tokushima Long Evans Fatty, OLETF) treated with T4. The mRNA levels for PLIN1, PLIN2, and PLIN3 decreased, while PLIN4 and PLIN5 increased in OLETF rats. T4 administration in OLETF rats showed no significant changes in the mRNA levels of PLIN1, PLIN2, and PLIN3 compared to untreated OLETF. On the other hand, PLIN4 and PLIN5 mRNA levels were increased in T4-treated OLETF rats compared to untreated OLETF. The results show that PLINs are differentially expressed in the hearts of insulin-resistant rats treated with T4 and suggest that PLIN4 and PLIN5 could be participating in the regulation of lipid metabolism and storage, contributing to the proper functioning of the heart during insulin resistance.

ANALYSIS OF THE PROTEIN PROFILE OF THE FLIGHT MUSCLES OF *AEDES AEGYPTI*

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Abstract:

Aedes aegypti is an anthropophilic mosquito involved in the transmission of pathogens of medical importance such as dengue, chikungunya, yellow fever, and Zika, mainly. Even though the development of vaccines for the prevention of viral infections transmitted by mosquitoes has been a priority, mitigation strategies continue to depend on vector control, which is why for several years strategies have been designed and implemented to control the population of mosquitoes. Through flight, the females reach their host, therefore, the flight muscles become essential tools and are the ideal target for their control. In this work, we analyze the protein profile of flight muscle precursors in fourth-stage larvae. These globular structures are located at the anterior part of the thorax, named primordia. Larvae were manually dissected, characterized by mean of confocal and scanning microscopy, and proteins extracted for PAGE-SDS resolution and solubilized for mass spectrometry identification. The data obtained were compared with the database of *A. aegypti* and *A. albopictus*. All identifications in this analysis have a confidence percentage of ≥95%. In the proteomic study of the primordia, >200 proteins were identified, including muscle proteins as expected, structural proteins as paramyosin, actin, troponin, myosin heavy and light chains; and developmental-stage specific proteins expressed as “pupal specific actin”. These prepupal, therefore pre-metamorphosis tissues, express abundantly proteases and proteasome proteins. Interestingly, many immune active molecules, including phenol oxidase, PIWI, and TEP were present, which are related to preliminary reports, where a role for muscles in defense has been proposed for insects. In addition, and in agreement with transmission electron microscopy, abundant mitochondrial proteins were identified.

Knowing the protein profile of mosquitoes’ flight muscles will establish strategies and innovative methods for the biological control of vectors, avoiding non-specific and toxic insecticide spreading.

PHYTOCHEMICAL BIODIRECTED STUDY OF THE COMPONENTS WITH ANTI-NEURAMINIDASE ACTIVITY PRESENT IN LEAF AND FLOWER EXTRACTS OF ERYTHROSTEMON YUCATANENSIS (GREENM).

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Abstract:

Erythrostemon yucatanensis (Greenm) is a native species of distribution in the Yucatán Peninsula, Mexico. Previous studies carried out on inflorescences of this species showed anti-neuraminidase activity against a neuraminidase isolated from Clostridium perfringens. On the other hand, bioguided studies of antiviral activity at co-treatment (viral hemagglutinin) and post-treatment (viral neuraminidase) levels of leaf extracts of this species allowed the isolation of 5-hydroxy-7-methoxy-2-(3 ,4,5-trimethoxyphenyl)-4H-chromen-4-one, a flavone reported for the first time in the genus Erythrostemon, as one of those responsible for the activity against viral hemagglutinin, leaving the active components present at the neuraminidase level unclear in leaves and flowers of this species.

Therefore, in the present work, the main objective was a biodirected phytochemical analysis of the leaf and flower extracts of Erythrostemon yucatanensis (Greenm) distributed in the town of Sierra Papacal, Yucatán, as well as the characterization of components with anti-inflammatory activity neuraminidase. To obtain the active metabolites, a biodirected assay will be followed using an enzymatic method of inhibition of viral Neuraminidase, which is obtained from Clostridium perfringens. To obtain the chromatographic profiles of the active fractions, liquid chromatography coupled to mass and HPTLC will be used and for the identification of the pure active components Nuclear Magnetic Resonance spectroscopy (1H-NMR) will be used.

Currently, the analysis and evaluation of fractions obtained from E. yucatanensis leaves continued, selecting the active fractions. These fractions underwent gel permeation chromatography (fraction with code CYF12), obtaining the purification and obtaining a pure compound identified as Corilagin (code: CYS-N) obtaining a total of 3.6 mg, which was characterized structurally by 1H-NMR, and its comparison with parameters obtained from the literature. Likewise, the anti-neuraminidase bioassay was carried out, obtaining that, at concentrations above 400 µg/mL, this compound inhibits the activity. Subsequently, another subfraction (key: CYS-J) was purified in which the presence of a compound belonging to the flavonoid family is suspected, however, analyzes are still being carried out to confirm this last compound. On the other hand, work began with the methanolic extracts (codes: CYFB6 and CYFB7) of the inflorescences of Erythostemon yucatanensis, which underwent gel permeation chromatography, obtaining new subfractions. These nine subfractions were analyzed by CCD for the identification of less complex fractions which will be later evaluated in the anti-neuraminidase activity assay.

DESIGN OF SELF-ASSEMBLED ANTIMICROBIAL PROTEIN-BASED NANOPARTICLES

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Abstract:

The rapid increase in the resistance to conventional antimicrobial drugs (AMR) as well as the difficulty to find new small organic molecules with this activity, underscore the need to develop novel antimicrobial alternatives. Among the options to find new therapeutic options there are the antimicrobial peptides (AMPs). Although AMPs represent an opportunity to counteract the resistance of these microorganisms, their usage has been limited compared to conventional antimicrobials. However, advances in the field of nanotechnology have allowed the development of platforms to carry and display AMPs leading to increase their activity, improve their stability, and reduce toxicity.

In this project, nanoparticles (NPs) were constructed based on a rationally designed self-assembly protein (C_4-S_{10}-B_{K12}), inspired by the viral capsid proteins (Hernandez-Garcia *et al*., 2014). Three different versions of the protein were designed, each one fused with a specific AMP and expressed in *Pichia pastoris*. The proteins were purified by a salt precipitation method, and identified with techniques such as SDS-PAGE, Western-Blot and MALDI-TOF. These biomolecules were used to form nanoparticles which were characterized by Atomic Force Microscopy, demonstrating that they can self-assemble in a rod-like shape. The effect of the NPs on the growth of *E. coli* and *S. aureus* is being evaluated by the broth microdilution method and the agar diffusion method.

Hernandez-Garcia, A., Kraft, D., Janssen, A., Bomans, P., Sommerdijk, N., Schoot, P., Stuart M.C. & de Vries, R. (2014). Design and Self-Assembly of Simple Coat Proteins for Artificial Viruses. Nat. Nanotechnol., 9(9), 698–702.

3D PRINTED PAPER SPRAY IONIZATION PLATFORM COUPLED TO MASS SPECTROMETRY FOR AUTOMATED CHEMICAL ANALYSES

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Abstract:

Ambient Ionization Mass Spectrometry (AIMS) allows chemical analyses with minimal technical requirements. Paper Spray Ionization Mass Spectrometry (PS-MS) recently gained relevance for analyzing biological fluids. We designed 3D printed cartridges and adaptors for PS-MS. The system is mounted to the robotic platform "OpenLabBot"[1]. We used 3D printing to build cartridges and for coupling parts prototypes.

We modeled the PS-MS cartridges, high voltage applicator, and multiplex support for measuring ten samples per analytical run. To evaluate the chemical and ambient noise of different polymeric materials, we tested the 3D printing materials polylactic acid (PLA) and acrylonitrile butadiene styrene (ABS). In addition, we experimented with various technical parameters, such as voltage, paper type, paper tip angle, and the distance between the paper tip to the inlet of the mass spectrometer. None of the tested 3D printing polymers generated significant chemical noise. However, the PS-MS cartridges printed with PLA were more solvent-resistant than the ABS versions.

We detected caffeine, epicatechin, isoamyl acetate, furan-2-carboxaldehyde, acetaminophen, and diclofenac using the PS-MS platform. Currently, we test the PS-MS platform for different applications, such as dried blood spot (DBS) screening and quality control of agave-derived spirits.

The 3D PS-MS platform is licensed for open access; thus, it could be adapted to different uses at a low cost. Therefore, we encourage the academic community implementation of the 3D PS-MS platform for custom necessities.

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Acknowledgments: Conacyt-DFG 2016/277850 to R.W. and Conacyt postgraduate scholarships to L.D.S.R and N.S.G.R.

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SIMULTANEOUS AEROBIC-ANAEROBIC BIODEGRADATION OF AN INDUSTRIAL EFFLUENT OF POLYMERIC RESINS WITH HIGH PHENOL CONCENTRATION AT DIFFERENT ORGANIC LOADING RATES IN A NON-CONVENTIONAL UASB TYPE REACTOR

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Abstract:

The presence of phenol in the environment is a consequence of both natural actions and anthropogenic contributions, mainly of an agricultural and industrial nature. Its concentration in wastewater ranges from 0.1 to 3,900 mg/L and in some cases from 30,000 to 80,000 mg/L. Among the technologies used for its elimination, are the physicochemical, biological, adsorption, and chemical oxidation processes. For its recovery, there is adsorption, ion exchange, extraction, volatilization, polymerization, electrocoagulation, advanced oxidation and ion exchange. In this research, a new configuration Upflow Anaerobic Sludge Blanket reactor (UASB) was studied to biodegrade the phenol present in an industrial effluent of polymeric resins by varying the organic load rate in 3.2±0.6, 13.9±0.8, 33.5±1.1 and 34.6±0.9 kg COD/m^3.d, at two rates of Dissolved Oxygen (DO): 0.78±0.18 mg/L (experiments 1-3) and 1.23±0.02 mg/L (experiment 4), with a Hydraulic Retention Time (HRT) of 0.5 days at 30±0.5 ^oC. The results showed the best Chemical Oxygen Demand (COD) removal rate and phenol biodegradation (64 and 74%, respectively) at a lower organic load (experiment 1). With a gradual increase in this, during experiments 2 and 3, it decreased by 55.6 and 17%, respectively. However, by increasing the dissolved oxygen rate to 1.23±0.02 mg/L during experiment 4, the phenol biodegradation rate was slightly improved, but not the COD removal rate. With the results obtained, it is demonstrated that the strategy used for the aerobic-anaerobic biomass acclimatization was a key factor in the biodegradation of phenol present in wastewater from the polymer resin industry, which is a novel contribution in scientific research in environmental matters, given the use of real industrial wastewater, without the need to use co-substrates, biostimulation of biomass or addition of nutrients as reported in the literature. It is evidenced that with this strategy, it is possible to use anaerobic reactors of new configuration, as a novel alternative for the treatment of industrial effluents of this nature. Evidencing that the new configuration of the reactor used is a new alternative for the treatment of similar wastewater at an industrial level, significantly saving large areas of land, construction, operation and maintenance costs.

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THE EFFECT OF RESVERATROL AS A RADIOSENSITIZER IN CERVICAL CANCER CELL LINES THROUGH THE INHIBITION OF DNA DAMAGE REPAIR PATHWAYS BY HOMOLOGOUS RECOMBINATION (HR) AND NON-HOMOLOGOUS RECOMBINATION (NHEJ)

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ABSTRACT:

Cervical cancer (CC) is the second most common cancer in the world that happens in the female population. Most cases of CC are diagnosed in advanced stages. Therefore, radiotherapy is the most used therapeutic modality. The mechanism of action of ionizing radiation (IR) is to induce cell damage directly or indirectly by inducing DNA double-strand breaks or through the formation of free radicals; In response to this stimulus, the cell is able to activate DNA damage repair pathways by homologous recombination (HR) and non-homologous recombination (NHEJ) through the activation of Rad 51, Ku70 and Ku80 proteins. However, if this damage is not repaired, the cell eventually dies. New agents with radiosensitizing properties that can be directed towards these molecular targets for cancer treatment are currently being sought. A compound that we have proposed to analyze is resveratrol, a natural polyphenol, and phytoalexin, which is found mainly in peanuts, grapes, and wines. In this work, we analyze whether resveratrol (RSV) has properties as a radiosensitizer in CC, as well as the mechanism involved in this effect. To do this, SiHa, C33a, and HeLa cells were treated with RSV for 48h and IR, followed by clonogenic assays. The results demonstrated that RSV induced a significantly greater IR sensitization in the C33a cell line compared to SiHa and HeLa through a significant decrease in cell survival. On the other hand, it was also observed that the SiHa cell line was the most resistant to both RSV and RSV+ RI treatment, , while HeLa was more sensitive to RSV+ RI treatment compared to SiHa. Subsequently, in order to elucidate the repair mechanism involved in this effect, the levels of the KU80 protein were analyzed. The results demonstrated a decrease in KU80 protein expression in the HeLa cell line after treatment with ionizing radiation and RSV. Conclusions: These results could suggest that resveratrol works as a radiosensitizer in Cacu cell lines.

REAL-TIME VOC'S MEASUREMENTS EMITTED BY *NEOCHLORIS OLEOABUNDANS*

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Abstract:

Volatile compounds (VOCs) compromise a broad class of small molecules (up to ~300 g/mol) produced by biological and non-biological sources [1]. Most VOCs' roles in microalgae are still unknown. However, it is believed that they act as physiological signals affected by abiotic and abiotic factors. VOC measurements in microalgae are often destructive (vapor distillation, high temperature, extraction by solvents, etc.). A recent non-destructive method is SMPE fibers coupled with GC-MS. However, absorption and desorption are in minutes, slow for biological relevant metabolic changes. Moreover, fibers are selective to defined compounds [2]. Another on-trend VOCs assessment method is PTR-MS for real-time measurements, but not all volatiles are ionized by H3O+ reaction. Due to these constraints, it is difficult to acquire relevant information about the dynamics of VOCs in biological systems. MoBiMS is a modular real-time mass spectrometer built in our lab to study VOC dynamics in different natural models. MoBiMS is biologically compatible, a low-cost option, the data format is compatible with online databases, and it enables real-time VOC quantification [2]. Post VOC measurements, most of the MS data analysis is done using proprietary company software or using Python/R language packages. However, the license limits data analysis from other sources; moreover, despite the R and Python languages being widely used in life sciences, they are relatively slow compared to other languages used in data sciences. Julia is a novel programming language that allows quick and user-friendly data analysis [3]. The MoBiMS output format could be analyzed with Julia on VOC dynamics data. In this work, we **(1)** constructed a growth chamber adapted to MoBiMS, **(2)** measured VOCs produced by *Neochloris oleoabundans* during growth and stress conditions, and **(3)** developed an MS workflow for MS analysis in Julia. Our results indicate that light and temperature implementation at the growth chamber corroborate with previous reports of microalgae optimum growth and development. Furthermore, the complete system allowed us to continuously study the CO2 fixation cycle of *N. oleoabundans* for three days. We applied saline stress to study the dynamic VOC emissions, and we could observe some ions differentially produced during stress conditions. Finally, we compared R and Julia language workflows to determine the leading option for MS analysis. Our data showed that Julia (version 1.5.4) is 2-3 orders quicker than R (version 4.1.3). In conclusion, we have constructed a system that enables real-time monitoring of VOC measurements emitted by *N. oleoabundans* during various time ranges and conditions. We also determined that Julia is capable of MS dynamic analysis. (**Funding**: Our was funded by Conacyt-DFG 2016/277850 grant).

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METABOLIC FEATURES IN OFFSPRING OF MOUSE MOTHERS WITH HYPERANDROGENISM

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Abstract:

Polycystic Ovary Syndrome (PCOS) is characterized by hyperandrogenism and ovulatory dysfunction, which act as factors for the development of endocrine, reproductive and metabolic disturbs. Hyperandrogenism affects the foetal programming in pregnancy, increasing the probability of developing PCOS, as well as metabolic, neuroendocrine, reproductive and behavioural disorders in the daughters of these patients. In the case of sons, they have higher body weight in childhood, increased Anti-Müllerian hormone concentration in the prepubertal stage, and development of insulin resistance and metabolic syndrome. However, the data found are divergent due to the small number of subjects, the heterogeneous selection criteria and ethnicity. The aim of this work was to evaluate the role of maternal hyperandrogenism in hepatic glucose and lipid metabolism in adult males and females offspring. For this, we used 25-day-old Balb/c female mice. Experimentally induced hyperandrogenism in PCOS-like model was developed by subcutaneously injecting DHEA (6 mg/100 g body weight) once daily for 20 consecutive days. Subsequently, control and treated mice were mated with control males. As results, we found lower birth weight in the offspring of mice treated with DHEA, but higher gain weight after 3 months than control group. Interestingly, offspring of mothers treated with DHEA had greater area under the curve in the glucose tolerance test. Moreover, pyruvate and insulin tolerance test showed that pyruvate administration increased the hepatic gluconeogenesis, that altogether was associated with decrease in insulin sensitivity. In addition, results showed increase in hepatic lipid accumulation, but no changes in cholesterol or triacylglycerol serum levels. Overall, the results of present work showed that offspring of mice treated with DHEA have alterations in hepatic glucose and lipid metabolism associated to decrease in insulin sensitivity as consequence of maternal hyperandrogenism, which could favour several comorbidities such as metabolic syndrome and diabetes.

This work was carried out with the financial support PAPIIT/DGAPA/UNAM IA211020 and IN215922

RESONANT ACOUSTIC MIXING IMPROVES RECOMBINANT PROTEIN PRODUCTION IN PICHIA PASTORIS (KOMAGATAELLA PHAFFI) SHAKE FLASK CULTURES

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Abstract:

Orbital mixing (OM) is massively employed in shake flasks cultures, although significant drawbacks such as low oxygen transfer rates are well documented (1). In recent years, resonant acoustic mixing (RAM) has represented a promising tool for highly productive cells screenings and early phases of bioprocess development (2,3). Here, the performance of RAM on recombinant protein (RP) production by Pichia pastoris (Komagataella phaffi) was reported and compared to OM in shake flasks at two similar conditions of oxygen transfer, measured as two volumetric oxygen transfer coefficients (kLa) and two culture media (BMGY and BMMY). When glycerol was used as a C-source, the stoichiometric characteristics of P. pastoris X-33 growth were not affected by OM or RAM. However, when methanol was used as a C-source and inductor of RP production (rAPA, Ala-Pro-rich antigen from Mycobacterium tuberculosis (4)), significant differences were found, producing more rAPA in RAM than in OM. Limited oxygen conditions were found when glycerol and methanol were used, being lesser in RAM than OM. Because of that, P. pastoris growth was slightly higher in RAM than in OM. This work points out the essential role of the oxygen transfer rate in developing bioprocess at the shake flask level.

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EFFECT OF METFORMIN ON THE ENZYME IDO1 IN CERVICAL TISSUE OF THE MURINE MODEL K14E7

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Abstract:

Cervical cancer is a major public health problem. This disease is widely associated with human papillomavirus infection. It has been strongly related to the immunosuppressive microenvironment as an important factor in the progression, persistence, and severity of cancer.

In addition, immunomodulatory factors have been reported, such as the enzyme indoleamine 2,3 dioxygenase 1 (IDO1) in the periphery and within some tumors, for which it has been attributed to a crucial role in the microenvironment and tumor progression. In the case of cervical cancer, it has been seen that IDO1 is present in cervical intraepithelial neoplasias and that its greater expression is related to the severity of said neoplasias.

On the other hand, the murine model that uses the keratin 14 promoters for the expression of the E7 oncoprotein (K14E7) is important for the study of cervical carcinogenesis under estradiol treatment, but it is also an excellent model on its own since it has a great similarity with the natural history of the disease that occurs in women because the E7 oncoprotein has been attributed the most important role in cervical carcinogenesis. Finally, the K14E7 model has been widely used to understand the immunosuppressive mechanisms associated with HPV infection.

Metformin has been widely used as a treatment in various types of cancer, where it has been attributed that it has an effect on different metabolic pathways, and lately on pathways that modify the differentiation of T cells, for which it is attributed an effect immunomodulatory. However, to date, no studies have been conducted to see if there is an immunomodulatory effect of metformin on the IDO1 enzyme in the K14E7 murine model. Therefore, knowing if there is an effect of metformin on the enzyme IDO1 is crucial to attribute metformin as an “adjuvant” effect for therapy against Cervical Cancer.

BIOCHEMICAL CHARACTERIZATION OF COMPOUNDS FROM *HELODERMA HORRIDUM HORRIDUM* VENOM

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Abstract:

The venoms of the spiders, bees, scorpions, and snakes have been identifying diverse components with antimicrobial activity, analgesics, immunomodulators. The work of our group is focused on the characterization of compounds from the venom of the lizard *Heloderma horridum horridum*, in the transcriptomic analysis we identified 199 transcripts coding to putative defensins, exendins, natriuretics, serine proteases, phospholipases, metalloproteases, lipases, L-amino oxidase and nucleases (Lino-López et al., 2021), however, not all have been identified in the venom and characterized. The purpose of this study is to isolate the component responsible for the antimicrobial activity and characterize it. In the literature, the most common bactericidal components found in venom species may be phospholipases A_2 and low molecular weight peptides (Beck et al., 2005). Which have antimicrobial activity against various bacterial strains and bacterial strains with resistance to antibiotics (Bustillo et al., 2008; Fernandez et al., 2003; Kang et al., 2017; Krayem & Gargouri, 2020). We performed the separation of venom by molecular exclusion chromatography, obtaining seven fractions. their antimicrobial activity was evaluated on the *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 strains. The fractions VI, V, VI, and VII showed activity at minimum inhibitory concentration (MIC) of 50, 12.5, 12.5 and 3.6 µM, respectively, versus *S. aureus* and only the fractions V, VI, and VII growth inhibited of *E. coli* at concentrations of 100, 25 and 25 µM, respectively.

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THE OXYGEN TRANSFER RATE (OTR), IN SHAKE FLASKS, DETERMINES THE GROWTH AND METABOLISM OF PISCIRICKETTSIA SALMONIS

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Abstract:

Piscirickettsiosis is caused by Piscirickettsia salmonis and is the main responsible for deaths due to infectious in the salmon industry. Due to these different strategies have been developed for its control (sanitization, disinfection, antibiotics, and vaccines) [1].

Considering that antibiotics are a problem for the food industries, the formulation and preparation of anti-piscirickettsiosis vaccines is an important option, in which P. salmonis is normally used (lysed and/or inactivated biomass) [2]. This is a technology under development, and therefore the vaccines marketed to date present a great variability in terms of their effectiveness. In addition, the protective effects observed in laboratory studies have not reflected a decrease in the mortality rate, due to piscirickettsiosis [3].

Based on this background and the lack of studies on the kinetic characterization of this bacteria. This project was focused on performing a kinetic, stoichiometric and respirometric characterization of P. salmonis cultures, to study how it was affected by transfer phenomena and the stress caused by them. For this, cultures were developed in shake flasks with two configurations, conventional and with baffles, to generate two magnitude levels of mass and momentum transfer and the profiles of biomass, substrates and metabolites were measured, together with a complete respirometric characterization. Additionally, two genes (markers of virulence and immunogenicity in this pathogen) were evaluated. All this to improve the biomass for the development of quality vaccines.

Even when we obtained the same final biomass concentration, we found interesting kinetic, respirometric and metabolic differences.

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ABSTRACTS | Posters Reactive Oxygen Species

XXXIII National Congress of Biochemistry

ASSOCIATION OF SOD2 RS4880 POLYMORPHISM WITH NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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Abstract:

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world, it includes a spectrum of disorders ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which is an important cause of more serious diseases, such as liver cirrhosis and hepatocellular carcinoma. It is a disease where genetic variations and the environment interact to determine the progression of the disease. Manganese-dependent superoxide dismutase (MnSOD2), encoded by *SOD2*, plays an important role in protecting cells from oxidative stress. The rs4880 polymorphism of MnSOD2 is associated with a decrease in its enzymatic activity and consequently an increase in oxidative stress, which makes it a good candidate for developing NAFLD. In this study, we analyzed the association of the SOD2 rs4880 polymorphism in patients diagnosed with NAFLD. Sixty-one Mexicans patients diagnosed with NAFLD through the liver helastography equipment (Fibroscan) and 99 healthy subjects were included in this study. The genotyping of the polymorphism was carried out by end-point PCR, the data of the clinical variables were obtained by our work group and in previous works. Our results showed that the CC genotype could be a candidate as a protective factor for NAFLD (OR= 0.46, 95% CI = 0.24-0.86, p=0.02). Nevertheless, it is necessary to analyze a larger number of samples from this population and more studies are required in different populations.

COMPARISON OF THREE DIETS EFFECT ON OXIDANT STATUS AND ANTIOXIDANT CAPACITY IN LIVER AND HEART IN WISTAR RATS

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Abstract:

Increased ingestion of fat and carbohydrates food for a long period leads to dyslipidemia that contribute to several complications such obesity, diabetes, atherosclerosis and hypertension. These diets increase deposition of fat in adipose as well as liver and heart tissues, causing reactive oxygen species (ROS) and oxidative damage. Antioxidants within cells can be upregulated and mobilized to neutralize ROS formation. Oxidative stress (OS) produce an increased number of lipid and protein oxidation products and decreased number of antioxidant enzymes. The present study aimed to assess total oxidant status (TOS), total antioxidant status (TAS) and activities of antioxidant enzymes in liver and heart of rats fed with three different diets. Male Wistar rats were divided into four group. Control (rats were fed a normal diet), Diet 1: high fat mixture-fructose and Diet 2: high fat mixture-sucrose (fat mixture contained: lard and vegetable shortening 1:1) and Diet 3: high fat (margarine)-sucrose for 12 weeks. TOS, TAS and antioxidant enzymes were measured. Increase in TOS and decrease in TAS were observed in the liver and heart rats, in the three diets. The oxidant stress index (OSI) was significantly higher in the three diets than control group. Diet 1 and 2 presented similar patterns in biomarkers of OS meanwhile diet 3 showed different values. Finally, our results demonstrated that there is different pattern in the antioxidant systems depending of the diet type.

Keyword: Oxidative stress, Biomarkers, Antioxidant enzymes

MARKERS OF OXIDATIVE STRESS IN POSTMENOPAUSAL WOMEN WITH METABOLIC SYNDROME

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Abstract:

Background: During the postmenopausal period there are metabolic alterations that predispose to metabolic syndrome (MS), oxidative stress (OS), and the risk of developing cardiovascular diseases. Among the most important changes is the decrease in estrogen and consequently a loss of antioxidant defense and thus an increase in free radicals that favors the incidence of metabolic diseases. **Objective:** To compare the concentrations of OS markers in postmenopausal women with and without MS. In relation to oxidative damage to lipids, the concentration of one of the last products of lipoperoxidation (malondialdehyde) was evaluated; carbonyl groups were quantified for oxidative damage to proteins, and with respect to antioxidant defense, total antioxidant capacity (TAC). **Material and methods:** A cross-sectional study was carried out, including a total of 100 participating women between 50 and 60 years old. Group 1: women without MS (n=42), Group 2 women with MS (n=58). Biochemical determinations were performed using a Beckman DU 800 spectrophotometer. The results obtained were analyzed with the PRISM 6.0 program (GraphPad, USA). **Results:** Biochemical markers of glucose, insulin, HOMA IR, triglycerides, uric acid and body mass index were significantly lower in postmenopausal women without MS vs. with SM OS markers were significantly lower in Group 1 vs. 40.27 ± 17.62 pmol MDA/mg dry weight (p= 0.01), protein carbonylation 6325 ± 1551 vs 7163 ± 1029 pmol PC/mg protein (p= 0.0003) and CAT 1497 ± 297.3 vs 1619 ± 278.8 pmol Trolox equivalent/mg of protein (p= 0.041). **Conclusion:** OS markers were significantly higher in postmenopausal women with MS. Antioxidant capacity was increased in postmenopausal women with MS and this can be attributed to the body's antioxidant response to reduce free radicals.

RESPIRASOME IS MORE SUSCEPTIBLE TO HEAVY METAL INACTIVATION THAN FREE-COMPLEX I, BUT PREVENT ROS PRODUCTION

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Abstract:

It has been proposed that mitochondrial respirasome functions include a low electron leak and reactive oxygen species (ROS) formation (Jang and Javadov 2018; Maranzana *et al*. 2013). However, it has not been observed under stress conditions. To achieve that, we use seven of the most toxicological heavy metals (Blundell and Jenkins 1977) to induce a direct stress to respirasome or free-complex I (Free-CI). It is know that divalent cations like Cd^{2+}, Hg^{2+} and Cu^{2+} accumulate in mitochondria through the Ca2+ uniporter at the expense of the trans-membrane potential ($\Delta\Psi_m$) (Saris and Carafoli 2005). These metals have the capacity of substitute protein cofactors, increasing redox reactions favoring ROS production; or can oxidize catalytic residues inducing a conformational change, protein malfunction or inactivation (Hossain *et al.* 2012). Respirasome and free-CI from Ustilago maydis were isolated according to the method described by (Esparza-Perusquía *et al*. 2017). NADH:DBQ oxidoreductase activity was evaluated spectrophotometrically at 340 nm according to (Reyes-Galindo *et al*. 2019) in presence of 150 μM NADH, 600 μM DBQ and 5 μM cytochrome c. The effect of $HgCl_2$, $CuSO_4$, $NaAsO_2$, $K_2Cr_2O_7$, $FeCl_3$, $ZnSO_4$ and $CdCl_2$ was achieved with a dose-response curve (0.01 – 1000 μM). ROS production was determined using the Amplex Red probe according to manufacturer's protocol. Our results showed that Hg^{2+} was the most aggressive metal over respirasomes, while interestingly, it did not shown effect over free-CI. The same effect was observed with AsO_2^-. On the other hand, Cu^{2+} showed a stronger effect over free-CI than respirasome. The last four metals, had a lower IC_{50} on the respirasomes than the free-CI, concluding that respirasomes are more susceptible to heavy metal inactivation. Then, we determined the H_2O_2 production rate by the respirasome or free-CI in the presence of the IC_{50} of each metal. We observed that heavy metals induce the ROS production in both, respirasomes and free-CI, but while maximum H_2O_2 production obtained by the respirasomes was 0.290 nmol $H_2O_2 \cdot (min^{-1} \cdot mg\ protein^{-1})$ with Hg^{2+}, free-CI maximum production was 5.43 nmol $H_2O_2 \cdot (min^{-1} \cdot mg\ protein^{-1})$ with Zn^{2+}. We conclude that the respirasome assemble prevent electron-leak and ROS production under heavy metal stress.

This work is supported by PAPIIT (IN206320) from Universidad Nacional Autónoma de México (UNAM); CONACyT México (87160); MEXUS-CONACyT (CN-20-327). JALS is a PhD student of the Posgrado en Ciencias Biomédicas (518024299) and has a CONACyT scholarship (666472).

CATALASE GENES EXPRESSION IN RESPONSE TO H_2O_2 AND NACL IS PARTIALLY REGULATED BY HOG1 MAPK IN DEBARYOMYCES HANSENII

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Abstract:

Efficient transcriptional response in yeast plays a critical role in survival to stress conditions like exposure to oxidants and osmolytes. The expression of stress-related genes, particularly those encoding components of the antioxidant enzyme system such as catalases, is triggered to mitigate several ROS, including H_2O_2, to prevent cell damage and death.

Debaryomyces hansenii is a halotolerant yeast that shows increased tolerance to oxidative stress, attributed to the high catalase activity that results from the expression of two catalase-encoding genes (*DhCTA* and *DhCTT*). Differential expression of these genes has been studied in various carbon sources and salt concentrations, however, the key regulatory elements that coordinate their expression under oxidative stress, remain unclear.

For a better understanding of the regulation that catalase genes follow in *D. hansenii*, under oxidative and osmotic stresses, and how this response impacts in cellular survival; in this work we evaluated cell viability (spot assay), catalase specific activity, catalase genes expression profiles by RT-qPCR as well as nucleosome occupation on their promoter regions by NuSA (Nucleosome Scanning Assay), in exponentially growing cells that were subjected to a 30 mM H_2O_2 stimulus. Furthermore, to assess the role of Hog1 MAPK kinase in catalase regulation, we performed a comparative study of *D. hanseini* wild-type and hog1Δ mutant exposed to the same conditions.

Our results show that catalase activity increases after the oxidative shock. This increased catalase activity correlates with increased relative expression, as catalase transcripts follow a transient induction, but with few changes at nucleosome occupancy before and after the treatment. The comparative analysis of wild-type and hog1Δ mutant indicates that Hog1 is involved in catalase regulation upon H_2O_2 and NaCl in *D. hansenii*, as we observed diminished viability and lower expression of both genes in the mutant, and a differential expression pattern observed diminished viability and lower expression of both genes in the mutant, and a differential expression pattern, suggesting that catalase expression is important to mount an effective stress response and is partially regulated by Hog1

By understanting the main factors involved in oxidative stress response and their regulation in halotolerant yeast, it will be possible to optimize the production of secondary metabolites useful in the industry by improving cell survival upon hard conditions, which could be of main interest for biotechnology, agriculture and biomedicine in the near future.

upon H_2O_2 and NaCl in *D. hansenii*, as we observed diminished viability and lower expression of both genes in the mutant, and a differential expression pattern, suggesting that catalase expression is important to mount an effective stress response and is partially regulated by Hog1

By understanting the main factors involved in oxidative stress response and their regulation in halotolerant yeast, it will be possible to optimize the production of secondary metabolites useful in the industry by improving cell survival upon hard conditions, which could be of main interest for biotechnology, agriculture and biomedicine in the observed diminished viability and lower expression of both genes in the mutant, and a differential expression pattern.

By understanting the main factors involved in oxidative stress response and their regulation in halotolerant yeast, it will be possible to optimize the production of secondary metabolites useful in the industry by improving cell survival upon hard conditions, which could be of main interest for biotechnology, agriculture and biomedicine in the near future.

GLUCOSAMINE EFFECT ON ROS PRODUCTION EXPRESSION IN HUMAN DERMAL MICROVASCULAR ENDOTHELIAL CELLS-1

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Abstract:

Introduction: Glucosamine (GlcN) is a food supplement widely used as a nutraceutical for treating osteoarthritis 1. It is an amino sugar employed as a dietary supplement. GlcN is commercially available mainly derived from chitin in crustacean shells and is a hexosamine biosynthesis pathway substrate. Reactive oxygen species (ROS) are products of metabolic activity. They are essential regulators of cellular homeostasis, but their synthesis and storage have to be controlled to prevent ROS from eventually reaching toxic concentrations that could induce oxidative damage. These species play a dual role as both toxic and beneficial compounds. ROS exerts beneficial effects on cellular responses and immune function at low or moderate levels. At high concentrations, they generate oxidative stress, a deleterious process that can damage all cell structures[2]. The **aim** of this study was identified if GlcN induces ROS production in HMEC-1 cells. **Methods and Results:** The studies were performed in human dermal microvascular endothelial cells (HMEC-1) culture cell in MCDB131 with all supplements. Cells were treated with GlcN 5, 10 and 20 mM for 6 h. After treatment, 15 µM H2DCFDA or 10 µM DHE were incubated in MCDB131 for 20 min at 37 °C in darkness. The fluorescence was visualized and measured in a Cytation 5 Cell Image Reader (Biotek Instruments, Inc.) at an excitation wavelength 485/20 and 480/20 and 528/20 and 576/20 nm emission, respectively. It induced ROS production in a concentration-dependent manner; GlcN 20 mM induces the highest ROS production with both fluorochromes. **Conclusion:** Treatment with 20 µM GlcN induced the highest ROS production with both fluorochromes. More studies are required to determine if GlcN could induce any other cellular damage.

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FRATAXIN EXPRESSION IN PC12 AND DBTRG-05MG CELLS IN RESPONSE TO CHEMICAL HYPOXIA

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Abstract:

Introduction: The mitochondrial protein frataxin is crucial for cell life; there is no consensus about its function, but it seems to participate in mitochondrial iron homeostasis, Fe-S cluster biogenesis, and modulation of reactive oxygen species (ROS) production. Also, frataxin is up-regulated in response to hypoxia in tumors, implying that it has a critical role in tumor cell survival and/or progression. However, the HIF-1α-mediated frataxin up-regulation is apparently in contrast with the glycolytic dependence and mitochondrial metabolism reduction in hypoxic cells. As the molecular bases of this apparent paradox are still missing, we will study the frataxin expression in cancer and non-cancer cells.

Hypothesis: Chemical-induced hypoxia will increase frataxin expression and ROS production in cancer but not in non-cancer cells.

Objective: To determine the expression of frataxin after exposing PC12 and DBTRG-05MG cells to $CoCl_2$, a hypoxia mimetic agent.

Methodology: PC12 and DBTRG-05MG cells were treated with 0-1 mM $CoCl_2$. Cell viability, mitochondrial superoxide anion, ROS production, and frataxin expression were measured.

Results: $CoCl_2$ induced cell death and ROS production. Frataxin is expressed under basal conditions in PC12 and DBTRG-05MG cells and increased under hypoxic conditions.

Discussion and conclusion: Frataxin up-regulation after exposure to hypoxia is consistent with previous studies. The up-regulated expression occurred in cancer and non-cancer cell lines, indicating that frataxin has a shared role in both cell types.

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ROLE OF YWQN AND YHDA OXIDOREDUCTASES IN *BACILLUS SUBTILIS* OXIDATIVE STRESS

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Abstract:

Microorganisms are exposed to a variety of endogenous and exogenous factors that activate the synthesis of reactive oxygen species (ROS) that can inflict damages to proteins, lipids, and DNA. To counteract the genotoxic effects of ROS, bacteria count with antioxidant defenses, including the catalase/superoxide dismutase and the preventive/repair Guanine Oxidized (GO) systems. Furthermore, in addition to its wide application in bioremediation, enzymes with oxidation/reduction properties have recently been associated to cellular processes that prevent oxidative stress. The genome of *B. subtilis* possesses the genes *ywqN* and *yhdA* whose predicted products possess aminoacidic similarity to a family of proteins that employ FMN and NADP(H) to reduce Cr(VI) and Azoic dyes without generating partially reduced chemical species that promote oxidative stress. In this work, we investigated the enzymatic properties and the role of YhdA and YwqN in protecting *B. subtilis* from the cytotoxic and genotoxic effects promoted by agents that elicit oxidative stress. Results revealed that while recombinant, purified YhdA and YwqN proteins, possessed azoreductase activity, only the former was able to reduce hexavalent chromium. Furthermore, disruption of *ywqN* and/or *yhdA* increased spontaneous and H_2O_2-promoted Rif^R mutagenesis. Of note, the overexpression of *yhdA* counteracted the hypermutagenic phenotype of a *B. subtilis* strain lacking a functional GO system. Therefore, in addition to possess a bioremediation potential, YwqN and YhdA were found to be involved in counteracting the cytotoxic and genotoxic effects of intracellular and extracellular inducers of oxygen radicals, including those caused by hexavalent chromium.

Work supported by CONACYT (grant A-1S-27116) and UG (grant: CIIC 107/2022).

AUTOPHAGY ADAPTOR P62 LOCALIZATION DURING CYTOTOXIC STRESS IN LUNG EPITHELIAL CELLS

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Abstract:

Human lungs are constantly exposed to high levels of allergens, pathogens, and cytotoxic substances. In such scenarios, epithelial lung cells are subject to high stressing conditions resulting in DNA damage, increased levels of reactive oxygen species (ROS), ER stress, and apoptosis. After damage, lung epithelial cells undergo strong phenotypic changes to activate a reparative response to injury, however, this process could involve fibroblast activation and extracellular matrix remodelling, culminating in lung fibrosis. Autophagy has been involved in the pathogenesis of various lung diseases, however, the role of autophagy in Hypersensitivity Pneumonitis (HP) and Idiopathic Pulmonary Fibrosis (IPF) is not yet clear. We explored the localization of protein Sequestosome 1 (p62/SQSTM1), a classical selective autophagy receptor, in lung tissues from control subjects, HP, and IPF patients by immunohistochemistry. We observed a strong p62 positive staining in interstitial and alveolar macrophages and also in the bronchial and alveolar epithelium in HP and IPF lungs, compared to controls. Interestingly, we also found a positive nuclear localization of p62 in alveolar macrophages and some cuboidal epithelial cells in HP and IPF lungs. Nucleocytoplasmic shuttling of p62 has been previously described. To explore if cytotoxic damage induces nuclear p62 localization, we treated mouse lung epithelial cells with hydrogen peroxide or bleomycin. We observed by immunofluorescence that p62 localizes in the nucleus of some alveolar epithelial cells after cytotoxic stress induced by both, bleomycin and hydrogen peroxide, compared to control conditions. These preliminary results suggest that p62 undergoes nuclear localization in lung epithelial cells after cytotoxic damage. We still working to know if this is an autophagy-dependent or independent process. This work was funded by PAPIIT IN202221 DGAPA-UNAM.

MITOCHONDRIAL HCN3 POTASSIUM CHANNEL INVOLVEMENT IN AUTOPHAGY, OXIDATIVE STRESS AND APOPTOSIS OF RAT RENAL PROXIMAL TUBULE CELLS

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Abstract:

The family of hyperpolarization-activated cyclic nucleotide cation channels (HCN1-HCN4), known as pacemaker channels in nervous and cardiac cells, constitutes a pathway for the uptake of cations (sodium, potassium, and ammonium) in the kidney (Carrizosa *et al*. 2011; López *et al*. 2016). HCN channels are differentially distributed in the tubule segments of the nephron. Recently, we identified HCN3 in the mitochondria (mitoHCN3) of the rat and human kidney. HCN3 channel is abundant in the luminal membranes and mitochondria of the proximal tubule. HCN3 contributes to establish the membrane potential, is coupled to ATP synthesis, and regulate oxygen consumption (León *et al*. 2019; Padilla *et al*. 2020). In acidosis, HCN3 increases in lysosomes, without altering its distribution in the microvilli or mitochondria of the proximal tubule (López *et al*. 2020). Autophagy is a lysosomal pathway for cytoplasmic components degradation, and is essential for maintenance of kidney homeostasis, structure, and function. Mitophagy (autophagy of mitochondria) is preceded by a depolarization of mitochondrial membrane potential; SIMILARLY THE reactive oxygen species (ROS) production and apoptosis are voltage dependent. In this work, we study the contribution of mitoHCN3 in autophagy, ROS and apoptosis of proximal tubule cells (NRK-52E). To evaluate the effect of HCN3, it was pharmacologically inhibited with 50 uM of ZD7288 for 24h under control conditions, acidosis (inducer of autophagy) and cytotoxicity with cisplatin (inducer of apoptosis). Block of HCN3 diminished the protein abundance of Beclin 1, LC3BII and Parkin 2 in acidosis, AND increased the mitochondrial ROS levels, both in control and acidosis conditions. Long-term HCN3 inhibition depolarized the mitochondrial membrane potential in control and in apoptosis, but not in acidosis. Furthermore, inhibition of HCN3 increased the levels of early and late apoptosis in NRK-52 cells, mainly those that are physiologically compromised by cytotoxicity. Our results suggest that mitoHCN3 channels promote autophagy, protect against excess of mitochondrial ROS, and not only to regulate the mitochondrial membrane potential but also apoptosis.

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EVALUATING THE EFFECT OF CURCUMIN ON THE METACESTODE OF *TAENIA CRASSICEPS*

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Abstract:

Curcumin, a curcuminoid present in the rhizome of the plant *Curcuma longa* has multiple pharmacological effects including anticarcinogenic and anti-inflammatory properties. This work evaluates the anthelmintic effect of the curcumin molecule (98% pure) on *Taenia crassiceps* cysticerci viability *in vitro*. Cysticerci incubated in the presence of increasing concentrations of curcumin showed a dose-dependent mortality correlated with a significant increase in the production of reactive oxygen species and a partial inhibition of thioredoxin-glutathione reductase, the only disulfide reductase present in these parasites. At 500 µM curcumin, a 100% of cysticerci lethality was obtained after 2 h of treatment. Additionally, considerable damage to tegument integrity was observed at low concentrations of curcumin while at lethal concentrations of curcumin, a total loss of tegument was observed. These results suggest the curcumin-induced oxidative stress could be in the origin of the anthelminthic effect of curcumin. Mice with cysticerci were injected intraperitoneally with 20, 40, or 60 mM curcumin daily for 30 days. A decrease in the burden of cysticerci (46%) was observed with a 60 mM dose of curcumin, supporting this compound as a potential anthelmintic drug.

This work was supported by the research grant IN217920 from Dirección General de Asuntos del Personal Académico (DGAPA) UNAM at Universidad Nacional Autónoma de México

MFD-DEPENDENT PROCESSING OF 8-OXOG ACTIVATES A RECA-DEPENDENT CHECKPOINT THAT CONTROLS THE ONSET OF SPORULATION IN *BACILLUS SUBTILIS*

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Abstract:

The mechanistic aspects underlying DNA repair in sporulating cells of the Gram-positive bacterium *B. subtilis* were investigated in this report. To efficiently accomplish sporogenesis, *B. subtilis* deploy factors that prevent and/or eliminate genetic insults that compromise this process of cellular differentiation. Accordingly, *B. subtilis* sporangia, employs Mfd to couple transcription with nucleotide excision repair (NER) during processing of helix-distorting DNA lesions inflicted by ultraviolet C light and mitomycin C. Most recently, it was established that the SOS response is active during *B. subtilis* sporulation and that RecA, is required to counteract genetic lesions inflicted by physical and alkylating factors. However, two additional sporulation roles have been attributed to RecA, firstly as a factor that regulates the levels of phosphorylated Spo0A during the onset of sporulation, and secondly blocking replication and vegetative growth in further stages of this developmental pathway. Here, we report a significant decline in sporulation following Mfd disruption, which was manifested in the absence of external DNA-damage suggesting that spontaneous lesions activate the function of Mfd for an efficient sporogenesis. Accordingly, a dramatic decline in sporulation was observed following the simultaneous inactivation of Mfd and the repair/prevention guanine oxidized (GO) system (hereafter, the ΔGO system), composed by YtkD, MutM and MutY. Furthermore, the loss of Mfd and the GO system, (i) sensitized sporulating cells to H_2O_2, and (ii) elicited spontaneous and oxygen radical-induced rifampin-resistance (Rif^r) mutagenesis. Epifluorescence (EF), confocal and transmission electron (TEM) microscopy analyses, showed a decreased ability of ΔGO Δ*mfd* strain to sporulate and to develop the typical morphologies of sporulating cells. Remarkably, disruption of RecA restored the sporulation efficiency of the strain deficient for Mfd and the ΔGO system Overall, our results unveil a novel Mfd mechanism of transcription-coupled-repair (TCR) elicited by 8-OxoG which converges in the activation of a RecA-dependent checkpoint event that control the onset of sporulation in *B. subtilis.*

Work supported by the Consejo Nacional de Ciencia y Tecnología (CONACYT; Grants A-1S-27116); University of Guanajuato (CIIC-107-2022) and NIH (Grant GM131410-01). LE. M-M y VP. S-C were supported by scholarships from CONACYT.

REDOX REGULATION OF THE MITOPHAGY RECEPTOR ATG32

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Abstract:

Mitophagy is a selective form of autophagy that consists in the elimination of mitochondria. In baker´s yeast (*Saccharomyces cerevisiae*), Atg32 functions as an essential receptor for mitophagy. This protein is C-terminally anchored into the outer membrane and its N-terminus faces the cytosol. Thus, the N-terminal cytosolic domain mediates the recruitment of the autophagosome components to mitochondria. Several reports have suggested that oxidative stress is a factor, which contributes to mitophagy induction due to the observation that treatment with the antioxidant N-acetylcysteine (NAC) suppresses mitophagy in yeast cells. To further understand molecular determinants of Atg32 oxidative stress-regulation we generated variants of Atg32 where each cysteine was mutated to alanine. The C30A, C103A, C288A, C360A, C405A, C406A and C405, 406A variants of Atg32 were expressed in a *Δatg32* background and mitophagic flux was determined by Western Blot monitoring the degradation of the Idh-GFP reporter. Our results show that the absence of cysteine in position 288 triggers a severe reduction in mitophagic flux in comparison to the wild-type strain, either induced by prolonged respiratory growth or by nitrogen starvation. These results suggest that the C288 of Atg32 is necessary for complete mitophagy induction and suggests that there is indeed a redox regulation mechanism for this process.

ROLE OF NUSG/NUSA IN TRANSCRIPTIONAL MUTAGENESIS OF *BACILLUS SUBTILIS*

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Abstract:

Under conditions of nutritional stress, as those occurring during post exponential growth, bacteria deploy mutagenic processes to modify its genome and escape from growth-limiting conditions. These cellular processes commonly known as stress-associated mutagenesis (SAM) have been demonstrated to occur in distinct organisms, including the soil bacterium *Bacillus subtilis*. The contribution of transcription in modulating mutagenic processes has been demonstrated in microorganisms that actively replicate their genetic material, as well as in non-dividing bacteria.

B. subtilis possesses 7 distinct transcriptional factors, including NusA and NusG. These factors play important roles during the elongation process of RNA polymerase. Involvement of transcriptional Nus factors in SAM processes have previously been documented; accordingly, the NusA protein from *E. coli*, involved in intrinsic termination transcriptional processes, was found to be necessary to generate Lac+ colonies under starving conditions in strain *E. coli* FC40. In contrast, we recently found that disruption of nusA did not impact the reversion frequencies of the *hisC952, metB5* and *leuC427* mutant alleles in strain *B. subtilis* YB955.

In this study, *nusG* was disrupted in the strain YB955 to investigate if this transcriptional factor influences *B. subtilis* SAM. Our results revealed that, in reference to the parental strain, the null mutant *nusG* exhibited a dramatic decrease in the production of His+, Met+ and Leu+ revertants. These results support the notion that NusG promotes mutagenic events in nutritionally stressed *B. subtilis* cells. In support of this contention, overexpression of *nusG* restored the ability of the strain deficient for *nusG* to generate His+, Met+ and Leu+ prototrophs. Importantly, such effect was not observed in a double *ΔnusG ΔnusA* genetic background.

Overall, our results support the notion that under an actively transcription NusG is promutagenic in stressed *B. subtilis* YB955 cells; on the other hand, we postulate a possible joint mechanism between NusA and NusG to promote adaptive mutations in *B. subtilis*.

Work supported by CONACYT (grants: 221231 and A-1S-27116) and UG (grant: CIIC 178/2020).

S-SULFENYLATION AND S-PERSULFIDATION IN *SACCHAROMYCES CEREVISIAE* DURING CELLULAR GROWTH

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Abstract:

S-sulfenylation (PSOH) and S-persulfidation (PSSH) are post-translational modifications (PTM) in cysteine residues produced due to the reaction with oxidant species such as hydrogen peroxide (H_2O_2) and hydrogen sulfide (H_2S). Since their discovery, the number of modified proteins increase constantly in organisms of importance like mammals. However, their presence in proteins of *Saccharomyces cerevisiae* have not been elucidated, an unicellular organism implicated in industrial production of fermentative products and medical research of cellular metabolism. Besides, *S. cerevisiae* can implement fermentative and respiratory metabolism during cellular growth, a characteristic that make this organism a complete model to study both processes and the influence of redox mechanism to produce PSOH and PSSH. In this study, we compared S-sulfenylation and S-persulfidation of *S. cerevisiae* during cellular growth, between exponential (fermentation) and stationary (respiration) phases. We extracted and marked the modified proteins of *S. cerevisiae* with a specifical method for each PTM to replace them with a molecule of HPDP-Biotin to ease their identification by western blot using anti-biotin antibodies. Finally, we found that there are proteins with S-sulfenylation and S-persulfidation that are exclusive to each phase of cellular growth.

This project was financed by UNAM through the research programs PAPIIT IN209219 and IN208922.

OXIDATION OF MITOCHONDRIAL CALCIUM UNIPORTER AS A TRIGGER OF INTRACELLULAR CA^{2+} MISHANDLING AND SPONTANEOUS CONTRACTION IN CATECHOLAMINE-INDUCED ARRHYTHMIA

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Abstract:

Ventricular arrhythmias are a major cause of mortality in patients with cardiovascular diseases. Catecholamines are associated with the development of ventricular arrhythmias and no new intervention has demonstrated efficacy in reducing mortality since the use of β-blockers. Mitochondrial Ca^{2+} transport has been deemed necessary for an adequate adrenergic response; however, constant adrenergic stimulation leads to mitochondrial Ca^{2+} overload with subsequent mitochondrial dysfunction. Inhibition of the mitochondrial Ca^{2+} uniporter (MCU) has been described to reduce asynchronized contraction in cellular and animal models. In this study, we assessed the effects of MCU inhibition by administration of Ru360, a MCU inhibitor, in ventricular arrhythmia development in a model of catecholamine overload and characterized cellular and mitochondrial function to describe the subcellular mechanisms involved. The study followed the national guidelines for laboratory animal use and care. 12-15-week-old C57bl/6 male mice received Ru360 or normal saline solution via IV and a baseline ECG was recorded. Afterwards, isoproterenol (ISO) was administrated subcutaneously, and ECG recording was kept for 20 minutes. Finally, hearts were excised, and cardiomyocytes and mitochondria isolated for further characterization. Animals administered with ISO developed ventricular tachycardia and fibrillation. This was completely prevented in the group treated with Ru360. Mitochondria from the ISO group had a higher Ca^{2+} content, indicating Ca^{2+} overload, which was associated with a compromised function and membrane integrity as evidenced by a lower respiratory control ratio, Ca^{2+} retention capacity, mitochondrial membrane potential and a faster rate of mitochondrial membrane potential loss upon a Ca^{2+} insult; all of which were preserved or partially preserved in the Ru360 group. Concomitantly, we observed an elevated oxidative stress, as there was a higher peroxide production, electron leak and ROS oxidative damage in the ISO group. Remarkably, mitochondrial proteome showed an increase in ROS-driven oxidative post-translational modifications such as glutathionylation, carbonylation and s-nitrosylation. Even the MCU was target of ROS-oxidation suggesting that ROS-driven oxidative modifications increase its activity and promote mitochondrial Ca^{2+} overload.

EFFECT OF APOCYNIN ON EXPRESSION OF GENES INVOLVED IN THE ANTIOXIDANT RESPONSE IN DIABETIC SKELETAL MUSCLE

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Abstract:

NADPH oxidases (NOX) are enzymes whose only function is the production of reactive oxygen species. Skeletal muscles express two isoforms of NOX (NOX2 and NOX4), which under physiological conditions are considered important modulators of redox homeostasis. However, in pathological conditions such as diabetes mellitus (DM), it has been observed that as hyperglycemia increases, the activity and expression of NOX are also increased, which has been linked to oxidative stress and diabetic complications. Apocynin is a potent NOX inhibitor, with antioxidant and anti-inflammatory potential. It has been effective for amelioration of a variety of disorders, including diabetic complications. However, the effect of NOX inhibition in skeletal muscle during DM and its impact at the transcriptional level is unknown. Therefore, the present work aimed to evaluate the effect of apocynin on the expression of genes that participate in the antioxidant response in skeletal muscles of diabetic rats. Male Wistar rats were rendered diabetic by applying intraperitoneally a single dose of streptozotocin (45 mg/kg). Apocynin treatment (3 mg/kg/day) was administered for 8 weeks. At the beginning and at the end of the intervention, fasting blood glucose (FBG) and body weight gain was evaluated. Both slow (soleus) and fast (extensor digitorum longus, EDL) skeletal muscles were used for the quantitative analysis of the expression of the genes of interest (NOX2, NOX4, Nf-κβ, Nrf2) using RT-qPCR. Treatment with apocynin significantly reduced FBG levels. Concomitantly, in both types of muscles, apocynin also statistically downregulated NOX2, NOX4, and Nf-κβ mRNA levels, and upregulate and restore the balance in expression levels of Nrf2. In summary, our results have shown that apocynin has an impact on skeletal muscle transcriptional response during diabetes, evidenced by modulating NOXs expression and interestingly Nrf2, which is a master transcriptional factor of antioxidative defense systems.

CORRELATION BETWEEN CIRCULATING CELL-FREE MITOCHONDRIAL DNA DAMAGED LEVELS AND METABOLIC SYNDROME FACTORS IN A MEXICAN PEDIATRIC POPULATION

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Abstract:

Introduction: It has been described that lipotoxicity increases ROS generation in obese (Ob) and metabolic syndrome (SM) conditions (1).The high ROS levels oxidize easily mitochondrial DNA (mtDNA) and fragment it. To this respect, it has been reported that small fragments which correspond to MTND3 and MTCO1 genes can escape to the cytosol through the mitochondrial permeability transition pore (2) and subsequently to plasma (3) where can act as DAMP and bind to Toll-like-9 receptor on circulating leukocytes, for activating NF-κβ which promotes the synthesis of cytokines e.g. IL-1β (4). On the other hand, mtDNA can also bind to NLRP3 receptors to form the inflammasome which activates caspase-1 and, in turn, promotes the release of IL-1β, leading a chronic inflammatory response (5). **Objective:** To identify the presence of mtDNA in plasma and relationship it with pro-inflammatory cytokines levels in a cohort of children with obesity and metabolic syndrome. **Material and Methods:** 40 children with Ob and 40 children with SM were included in the study. DNA oxidized (8-OH-dG) was measured by ELISA. Whole plasmatic small mtDNA fragments (MTND3 and MTCO1) was detected by qPCR and large mtDNA fragment (intact mtDNA) by end-point PCR and quantified with Picogreen. Intact mtDNA were normalized with small fragments to evaluate its integrity. Cytokines were measured with flow cytometry. ANOVA and Spearman correlations analysis were performed in Prism software. $p<0.05$ was considered statistically significant. Approvals were obtained from the Ethics and Research Committees of the School of Medicine Tecnológico de Monterrey. All legal guardians gave their written informed consent. **Results:** A significant increase in 8-OH-dG levels was observed in the Ob and SM groups compared to the control group ($p = <0.001$). The presence of greater damage was observed in the Ob, SM 3F and SM 4-5F groups ($p = <0.0001$). A positive correlation was identified for 8-OH-dG with IL-18 ($r=0.463$, $p=0.0013$) in the Ob group. In SM 3F 8-OH-dG had a negative and significant correlation with IL-1β ($r =-0.6708$, $p= 0.007$), IL-6($r=-0.3905$, $p=0.029$), IL-33 ($r=-0.3957$, $p=0.0205$). Finally, 8-OH-dGt had a significant correlation with IL-8 ($r=-0.5149$, $p = 0.0447$) in the SM 4-5F group. **Conclusion:** Obesity and MS lead to damage and fragmentation of mtDNA, which may have directly related to the activation of the immune system.

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ABSTRACTS | Poster Signal Transduction

XXXIII National Congress of Biochemistry

ROLE OF INTRACELLULAR PHOSPHOAMINOACID MUTANTS FROM HUMAN A_{1B}-ADRENERGIC RECEPTOR

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Abstract

a1B-adrenergic receptors (α1BAR), mediate many of the actions of the natural catecholamines, adrenaline and noradrenaline. These receptors belong to the seven transmembrane domains G protein-coupled receptor superfamily and exert their actions mainly through activation of Gq proteins. These G proteins regulate phosphoinositide turnover/calcium signaling pathway and also MAP kinase (ERK1/2) cascade. Many hormones and neurotransmitters are capable of inducing α1BAR phosphorylation and desensitization, a process mediated by members of the G proteins-coupled receptor kinases (GRK) family and/or by PKC.

It is currently known the α1BAR is phosphorylated in different serines and threonines located in both intracellular loop 3 (IL3) and carboxyl terminus (Cterm). Because the role of these phospho-sites remains unknown in different down-process of the α1BAR, we have studied the role of different phospho-sites (p-sites) determined by mass spectrometry analysis. The human α1BAR wild type (WT) receptor and three receptor mutants (with nonphosphorylatable substitutions (IL3, Cterm and IL3/Cterm), all of them tagged with -GFP were expressed in HEK 293 cells.

Our results indicate that elimination of phosphorylatable residues alter calcium signalling and desensitization. Experiments are in progress to determine is receptor-β-arrestin interaction is altered in the mutant receptors, as well as to determine if the activation of the MAPK pathway is altered by these mutations.

David A. Hernández-Espinosa is a doctoral student from Programa de Doctorado en Ciencias Bioquímicas, Universidad Nacional Autónoma de México, and was the recipient of a doctoral fellowship (CVU: 706381) from Consejo Nacional de Ciencia y Tecnología (CONACyT). This work was partially supported by Grants from DGAPA UNAM (IN201221) and CONACyT (Fronteras 6676).

DIFFERENTIAL REGULATION OF HYPOXIA-INDUCIBLE FACTORS 1/2/3α OVER CANONICAL AND NON-CANONICAL WNT PATHWAYS IN COLORECTAL CANCER CELLS

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Abstract:

Canonical and non-canonical Wnt pathways are the major driving forces for the beginning and progression of colorectal cancers. Canonical Wnt pathway transduces through β-catenin stabilization, inducing cell cycle progression and proliferation, while independent β-catenin mechanisms (non-canonical Wnt pathway) are related with migration and metastasis induction. Although it is well known that co-receptors ROR1/2 are non-canonical Wnt effectors, the molecular mechanisms involved in their signaling are not well defined. Hypoxia Inducible Factors (HIFs) are master regulators of cellular adaptation to hypoxic stress which play key roles in many crucial aspects of cancer biology. We have found that colon cancer cells co-express three HIF-α isoforms under normoxic conditions. The aim of this work was to explore the interaction of each HIFα subunit (HIF 1/2/3α) on Wnt signaling pathway. First, we observed significant differences in stability of HIF-α protein subunits: while HIF-1α and HIF-2α display short half-life (<1 hr), HIF-3α protein displays much higher stability (~ 6 hrs) under normoxic conditions. The exposure to low oxygen levels (O_2 3%) induced as expected, a great increase in all HIF-α subunits levels, but while the increased HIF-1α levels were transitory, the effect over HIF-2α and HIF-3α levels were more sustained in time. The knockdown expression of each HIF-α subunit in colorectal cancer cells showed that there exists an inter-dependence expression between them. It was also found that under normoxic conditions, each HIF-α subunit positively regulates canonical Wnt pathway. However, in the case of non-canonical Wnt elements, the knockdown of HIF2/3α decreased the protein levels of ROR1/2.

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EFFECT OF HIGH-GLUCOSE IN CX30.2 EXPRESSION IN PANCREATIC β CELLS

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Abstract:

Introduction

Gap junctions are mainly formed by a family of homologous proteins named connexins (Cxs). Until today 21 genes of the Cxs have been identified in the human genome1. These channels allow intercellular diffusion of metabolites for maintaining the cellular homeostasis. In the pancreatic β cells Cx36 participates regulating the insulin secretion. In the last decade expression of Cx30.2 has been reported to co-localize with Cx36 protein in mouse pancreatic β cells. Besides, it has been shown that expression of Cx30.2 mRNA was significantly reduced in islet cultures with high-glucose 2. This was also reported in rat retinal endothelial cell cultures3. It has also been documented that autophagy is the most important regulator in β cell homeostasis and its dysregulation is involved in Type 2 Diabetes Mellitus disease 4. Moreover, it has been proposed that Cxs can regulate autophagy 5.

Objective

To investigate the effect of high-glucose in Cx30.2 expression in pancreatic β cells and its role in autophagy.

Methods

RIN-m5F pancreatic β cells were incubated for 24 hours in RPMI medium with normal glucose (5 mM) and high-glucose (30 mM). After, cells were processed for Western blot and immunofluorescence assays using polyclonal antibodies against Cx30.2, transcriptional factor EB (TFEB), LC3-I, LC3-II, Atg7, p62, actin and tubulin.

Results and discussion

RIN-m5F cells cultivated with high-glucose, showed an increased expression of Cx30.2 protein, as well as autophagy marker proteins like LC3-I, LC3-II, p62 and Atg7. This suggests an active autophagy process. Additionally, it was observed a nuclear location and an increased expression of TFEB, a lysosomal biogenesis and autophagy

regulator. Interestingly, pharmacological inhibition of TFEB correlates with decrease expression of Cx30.2. In silico analysis of Cx30.2 promoter region suggests that Cx expression is under control of TFEB and probably Cx30.2 could have participation in the process of autophagy in the pancreatic β cells.

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EFFECT OF THE NITROGEN SOURCE IN THE INDUCTION OF SOMATIC EMBRYOGENESIS OF *COFFEA CANEPHORA* PIERRE EX A. FROEHNER

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Abstract:

Somatic embryogenesis (SE) is a cell differentiation process by which a somatic cell changes its genetic program and becomes an embryonic cell. There are numerous factors involved in this process and the subsequent development of somatic embryos as plant genotype, type of explant, plant growth regulators, incubation conditions, culture medium components, among others. It is known that the nutritional composition of the culture medium, especially the macronutrients, are essential. It has been reported that both, the form and the amount of nitrogen, in the culture medium have significant effects on growth rate, morphology and cell totipotency. Five treatments with different nitrate/ammonium ratios were evaluated: 15/0, 0/15, 10/5, 5/10 and 7.5/7.5. The modifications were made to the nitrogen source of the induction medium of the protocol for the induction of SE of *C. canephora*, which consists of two phases: preconditioning and induction. For the first phase, seedlings were placed in an MS medium supplemented with 0.54 µM NAA and 2.32 µM of Kin for 14 days, after this period, five explants of 8 mm diameter were placed on Yasuda medium supplemented with 5 µM BA for the induction process. The objective of this work is to contribute to the knowledge of the mechanism by which the nitrogen source causes a change in the morphogenic response in *C. canephora* somatic embryogenesis, as an initial approach by determining the number of embryos produced in each treatment and by characterizing their morphology.

Keywords: nitrate, ammonium, direct somatic embryogenesis, development.

THE EFFECT OF ISOARBORINOL IN ADIPOGENIC MARKERS IN 3T3-L1 CELLS

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Abstract:

Introduction. Overweight and obesity are defined as an abnormal or excessive accumulation of fat that can be detrimental to health and its incidence has increased at an alarming rate in recent years, thus becoming a global health problem. Existing treatments to treat obesity have proven to be inefficient, highlighting the need to find alternative therapies, currently more attention has been paid to compounds of plant origin. Isoarborinol is a pentacyclic triterpenoid, a class of 30-carbon isoprenoid compounds, extracted from the plant *Petiveria alliacea.* To determine the anti-adipogenic potential of isoarborinol, an Oil Red O staining and a qRT-PCR were performed to measure the expression of transcription factors involved in adipogenic differentiation.

Materials and methods. 3T3-L1 preadipocytes were seeded in 12-well plates and subjected to the differentiation process. The cells were treated with isoarborinol at concentrations of 1.44 µM, 0.72 µM, 0.36 µM applying the treatment every 48 hours until day 10. To determine intracellular lipid accumulation 3T3-L1 cells were stained with Oil Red O staining, and qRT-PCR was performed to determine how isoarborinol affects the expression of transcription factors C/EBPα, PPARγ and SREBP-1c.

Results and conclusions. Isoarborinol at concentrations of 1.44 µM, 0.72 µM, 0.36 µM significantly decreased intracellular lipid concentration compared to untreated cells, with the concentration of 1.44 µM had the greatest effect and approximately reduced lipid accumulation by 30% compared to untreated cells, likewise isoarborinol treatment reduced the expression of C/EBPα, PPARγ and SREBP-1c. isoarborinol therefore inhibits differentiation and adipogenesis of 3T3-L1 cells by suppressing cellular induction of adipogenic transcription factors, PPARγ, C/EBPα and SREBP-1c.

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PAK 1 PROMOTES BREAST TUMORIGENESIS VIA PHOSPHORYLATION AND ACTIVATION OF THE CALCIUM/CALMODULIN-DEPENDENT PROTEIN KINASE II

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Abstract:

p21-Activated kinase-1 (Pak1) is frequently overexpressed and/or amplified in human breast cancer and is necessary for transformation of mammary epithelial cells. In this work, we show that Pak1-deficient breast cancer cells showed a dramatic reduction in CaMKII phosphorylation at residue T287, which is important for the activity of this kinase. In addition, using *in silico* and *in vitro* kinase assays, we showed that Pak1 interacts with and phosphorylates CaMKII not only at T287, but also at T277. Moreover, we demonstrated that both, pharmacological inhibition of Pak1 activity or reduction of Pak1 expression through siRNA-mediated assays, significantly reduced the phosphorylation of CaMKII at T287. Conversely, the expression of a rapamycin-activatable Pak1 increased its phosphorylation levels. In addition, Pak1 and CaMKII are co-expressed in breast cancer cell lines and using a human breast cancer tissue microarray (TMA), we observed a significant correlation between the expression levels of these two kinases. Next, we showed that combination of anti-Pak and anti-CaMKII agents has a synergistic inhibitory effect on cell proliferation, migration and invasion, and induced apoptosis more potently in Her2 positive and TNBC cells. Finally, we demonstrated that the combination of small molecule inhibitors targeting Pak1 and CaMKII significantly delayed the tumorigenesis of TNBC cells in a xenograft setting. These data delineate a signaling pathway from Pak1 to CaMKII that is required for efficient proliferation, migration and invasion of mammary epithelial cells, and suggest new therapeutic avenues for the treatment of TNBC.

P32 PROMOTES A MALIGNANT PHENOTYPE IN COLORECTAL CANCER CELLS

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Abstract:

p32 is a multifunctional and multicompartmental protein that has been found upregulated in numerous adenocarcinomas, including colorectal malignancy. High levels of p32 expression have been correlated with poor prognosis in colorectal cancer. However, the functions performed by p32 in colorectal cancer have not been characterized. Here we show that p32 is overexpressed in colorectal cancer cell lines compared to non-malignant colon cells. Colon cancer cells also display higher nuclear levels of p32 than nuclear levels found in non-malignant cells. Moreover, we demonstrate that p32 regulates the expression levels of genes tightly related to malignant phenotypes such as HAS-2 and PDCD4. Remarkably, we demonstrate that knockdown of p32 negatively affects Akt/ mTOR signaling activation, inhibits the migration ability of colon malignant cells, and sensitizes them to cell death induced by oxidative stress and chemotherapeutic agents, but not to cell death induced by nutritional stress. In addition, knockdown of p32 significantly decreased clonogenic capacity and in vivo tumorigenesis in a xenograft mice model. Altogether, our results demonstrate that p32 is an important promoter of malignant phenotype in colorectal cancer cells, suggesting that it could be used as a therapeutic target in colorectal cancer treatment.

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CHARACTERIZATION OF THE FUNCTION OF THE PCSNT PROTEIN AND ITS ROLE IN THE CELL SIGNALING PATHWAY MEDIATED BY HETEROTRIMERIC G PROTEINS IN PENICILLIUM CHRYSOGENUM

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Abstract:

Fungi play an important role in bio-geochemistry cycles, recycling carbon and mobilizing elements like nitrogen and phosphorus. (Naranjo-Ortiz & Gabaldón, 2019a). Fungi can produce a huge quantity of low molecular weight products, called secondary metabolites. These molecules are used by human beings because some of them have high added value such as antibiotics. (Keller, 2019)

Penicillium chrysogenum is a filamentous fungus that has been used as an industrial producer of penicillin and considered as a model organism of secondary metabolism. PcSNT is a multidomain protein of P. chrysogenum, that is probably an effector of the heterotrimeric G proteins pathway mediated by αPga1 subuinit, It´s well known that G proteins regulates secondary metabolism, toxicity and development process as conidiation.

The domains of PcSNT includes protein-protein (BHA), interaction and protein-DNA interaction (SANT, -Ada2-, -N-CoR- TFIIIB and PHD). As a first strategy of PcSNT characterization making Knockdown mutants by RNAi silencing strategy where obtained. We observed two different phenotypes, the first one not too different from the parental and the second one with a fluffy phenotype. The phenotype was characterized by measuring conidiation, radial extension and micro-cultures. In the first case, with the second phenotype we observed differences in conidiation in two or more magnitude orders. In both cases during the rate of radial extension wasn't significative comparing three different media. We observed changes in septation, thickness and ramification a long the hyphae in three different media, suggesting us a carbon source as a regulator too. Using mass spectrometry, phosphorylated sites were identified in solid media using mutants with different genetic backgrounds Wis 54-1255 (Wild type pga1, normal Pga1 functionl), Δpga1 y pga1Q204L. S903 and S738 are present in the different strains, but T1531 is just present in Wis 54-1255.

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CHARACTERIZATION OF TGF-B-LOADED EXTRACELLULAR VESICLES FROM COLORECTAL CANCER CELLS

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Abstract:

Extracellular vesicles (EVs) are membranous bodies secreted by different cell types, functioning as mediators of intercellular communication and involved in both physiological and pathological processes. The EVs molecular cargo includes a wide variety of bioactive molecules, such as proteins, lipids and nucleic acids; such molecular cargo depends on the cell type and also on the physiological and pathological conditions occurring at the time of packaging and secretion of EVs. Cancer cells secrete EVs that may contain molecules able of modifying the phenotype of target cells, as they may mediate intercellular communication and may also promote a cancerous phenotype. The oncogenic activity of these EVs might be due to their molecular cargo, being TGF-β1 one of the potential molecules that might have such activity [1].

Transforming growth factor β (TGF-β) is a cytokine with pleiotropic activity in homeostasis and in certain pathologies, including cancer. Activation of the TGF-β signaling pathway causes cell cycle arrest in healthy cells and in early stages of cancer, suggesting that this pathway has a key role in tumor suppression. On the other hand, TGF-β is upregulated in various types of cancers in advanced stages, where acts as tumor promoter; an example is the case of colorectal cancer (CRC) [2]. Some reports show that cancer cells may secrete EVs loaded with TGF-β1, which promotes the epithelial-mesenchymal transition (EMT) of cancer cells and favor their migratory and invasive capacities [3]; here, we have isolated and characterized EVs from CRC cell line SW620, cultured on monolayer, and looked for the presence of TGF-β1, latent and active.

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EFFECT OF IL-2 IN STAT1 PHOSPHORYLATION IN CERVICAL CARCINOMA LINES

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Abstract:

Cancer is a process of uncontrolled growth and spread of abnormal cells, cervical cancer is a type of cancer that originates in the cells that line the cervix, cervical cancer was reported in 2020 as number 4 in incidence in women from all over the world and the third in death, and as the number 2 in Mexico.

IL-2 has been used as an effective immunotherapy against melanoma for approximately 20 years, through the activation of the JAK/STAT pathway. The JAK/STAT pathway is involved in numerous physiological cellular processes, such as proliferation, differentiation, apoptosis, and regulation of the immune system; however, aberrant regulation of STAT can lead to pathological events, including malignant cell transformation and metastasis. STAT1 plays important roles in cytokine-induced signaling pathways and can act as an antiviral and antibacterial mediator, growth inhibitor, and inducer of apoptosis.

Some authors suggest that HPV16 E6 protein mediates STAT1 transcription by activating STAT3 in cervical cancer or STAT1 and STAT3 may compete for the same receptor docking sites.

On that basis, an assay was carried out to observe the phosphorylation of STAT1 in which a greater phosphorylation of STAT1 was observed at 35 minutes of treatment with 100U/mL of IL-2 and in the case of treatment with 10U/mL of IL -2 does not increase STAT1 phosphorylation.

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UROCORTIN 2/CRF2R MEDIATES AKT AND ERK 1/2 ACTIVATION IN 3T3-L1 ADIPOCYTES

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Abstract:

Urocortin 2 (Ucn2) is a neuropeptide expressed in adipose tissue, and it has been associated with obesity and impaired insulin sensitivity in metabolic tissues such as skeletal muscle. Ucn2 is part of the corticotropin-releasing factor family that it plays a fundamental role in regulating the hypothalamic-pituitary-adrenal axis. Alterations in this axis have been related to emotional, behavioral, alimentary, and metabolic disorders. Ucn2 and Ucn3 are considered selective CRF2R ligands. In the periphery, this system has been found in various tissues, particularly in skeletal muscle and pancreas, where important functions related to glucose homeostasis have been described. Adipose tissue is historically known as fat storage and a crucial element in energy homeostasis; this important endocrine organ synthesizes and releases several hormones like adiponectin, leptin, resistin, and angiotensinogen, among others. However, several studies have reported that Ucn2, Ucn3, and the CRF2Rs are highly expressed in adipose cells, and their actions under physiological conditions are not fully described. It is known that CRF2Rs activate AMPc/PKA, PLC/IP3/Ca2+, PI3K/Akt, and the mitogen-activated protein kinases (MAPKs) signaling pathways. Besides, depending on the cellular model, MAPKs and Akt activation may involve several signaling molecules and receptor tyrosine kinases (RTKs) transactivation. Nevertheless, ERK 1/2 and Akt activation by CRF2R and the molecular mechanisms involved in these two kinases activation had not been described until this work, which is crucial to understanding the CRF system in adipose cells. In this study, we describe ERK1/2 and Akt activation in response to Ucn2 stimulus in 3T3-L1 adipocytes, as well as the molecular mechanisms involved in this activation. It was found that ERK1/2 and Akt activation exhibited a different time-course response, and both were dependent on ligand concentration. Additionally, stimulus with Ucn3 also induced ERK1/2 and Akt activation. Using specific inhibitors for specific signaling molecules demonstrated that ERK1/2 and Akt activation in response to Ucn2 was dependent on Gi/o, Src, PI3K, and EGFRs transactivation. On the other hand, insulin is an important hormone that leads the main biological functions of adipose tissue through insulin receptor activation. Abnormalities in this signaling pathway are associated with pathologies such as metabolic syndrome, diabetes mellitus, and insulin resistance. In the last decades, urocortins have emerged as critical modulators of energy homeostasis; however, the role that urocortins play in adipose cells remains unclear, so we are interested in elucidating the effects of Ucn2 on the insulin signaling pathway in this tissue. In this context, preliminary data from our laboratory indicate that, in 3T3-L1 adipocytes, the Ucn2 exerts regulatory actions in the insulin signaling pathway.

EFFECT OF CORTICOTROPIN-RELEASING FACTOR (CRF) ON ERK 1/2 ACTIVATION INDUCED BY INSULIN-LIKE GROWTH FACTOR-1 (IGF-1) IN CHO-K1 CELLS

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Abstract:

Corticotropin-releasing factor (CRF) is the major physiological activator of the hypothalamic-pituitary-adrenal (HPA) axis and coordinates the neuroendocrine response to stress. CRF actions are mediated by the CRF receptor type 1 (CRF1R), a member of the G protein-coupled receptors (GPCRs). However, an excessive increase in CRF levels induces alterations in the duration and intensity of signals mediated by CRF1R. Additionally, the chronic stimulation of GPCRs could desensitize members of the receptors tyrosine kinase (RTKs) family, such as the insulin-like growth factor-1 receptor (IGF-1R), through heterologous desensitization mechanisms. IGF-1R stimulates essential cellular processes, including proliferation, differentiation, survival, and metabolism, and thereby is essential for normal growth and development. Interestingly, a reduction in the levels and effects of IGF-1 in psychiatric disorders such as depression and anxiety has been reported. Similarly, in these pathological states, CRF levels are elevated; however, the molecular mechanisms in this relationship have not been explored.

In this work, we determine the molecular mechanisms involved in the regulatory role of CRF in the IGF-1 actions, particularly in ERK 1/2 activation, an important kinase in the MAPK pathway. For this, CHO-K1 (Chinese Hamster Ovary) cells were transfected with the HA-CRF1R receptor using the lipofectamine method. Transfected cells were pre-incubated with CRF (time-course and concentration-response assays) and stimulated with IGF-1. The results showed that CRF through the CRF1R reduces ERK 1/2 phosphorylation induced by IGF-1. Similarly, we found a reduction in the phosphorylation of IGF-1R and in the scaffold protein Shc. We also examine the role of serine/threonine kinases using specific inhibitors. We observed that rapamycin and SP600125, both inhibitors for mTOR and JNK, respectively, prevent the reduction of ERK 1/2 phosphorylation induced by pre-incubation with CRF. These results suggest the participation of mTOR and JNK in a desensitization mechanism induced by CRF; these kinases could act at the level of IGF-1R and/or Shc, increasing phosphorylation in serine/threonine residues and reducing phosphorylation in tyrosine residues and impaired MAPK pathway activation. Currently, we are elucidating the role of other proteins involved in the CRF1R and IGF-1R pathways, such as β-arrestins, an important scaffold protein in desensitization mechanisms.

Financing: This work was supported by CINVESTAV-IPN, CDJQ held a CONACYT graduated scholarship (CVU: 1002001).

IDENTIFICATION AND EVALUATION OF THE INTERACTION BETWEEN BIOMOLECULES PRESENT AT THE "MANILKARA ZAPOTA" SEEDS VERSUS THE OF P53, P21, Δ-LACTOFERRIN AND β-CATENIN CRYSTALOGRAPHIC STRUCTURES

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Abstract:

The chicozapote (Manilkara zapota) is a tree of the sapotacea family. This species is commonly found in the flora of southern Mexico, with a wide wealth of medicinal plants. The cultivation of Manilkara zapota has been limited mainly to the production of the fruit as food, as well as to the obtaining of the latex, the utilization of this species has been neglected, considering that all parts of the tree present a great amount of chemical-biological compounds of interest. Therefore, the main objective of our work is the identification and evaluation of the interaction of biomolecules of the seed of "Manilkara zapota" versus the crystallographic structures of the transcription factor, Delta-lactoferrin, β-catenin, p53 and p21; by means of analytical techniques LC/MS, Molecular docking and Molecular dynamics. Considering preubs antiproliferative results on cancer cell lines HCT116 and Du 145, we hypotesed that Manilkara zapota contains secondary metabolites, with antiproliferative properties, which can interact with transcription factors and have effect on sumoylation pathway having consequences on cell cycle regulation. The improved interaction of the transcription factor alone or sumoylated with the selected Manilkara zapota metabolite could be used in the future as a less aggressive alternative treatment in chemical therapy in cancer patients, since current treatments, which include radiotherapy, chemotherapy and immunotherapy, although beneficial, present concomitant side effects and long-term sequelae. The p53 protein is involved in cell cycle regulation, acts at the level of the G1 to S step and when activated induces apoptosis in response to DNA alteration. p53 mediates its effect in part through p21 and therefore they are usually studied together. p21 has both p53-dependent and p53-independent effects, and the latter in turn inhibits cyclin-dependent kinases (CDKs), arresting the cell cycle by inhibiting DNA replication. Delta-lactoferrin (ΔLf) is a transcription factor whose expression is down-regulated in cancer, ΔLf possesses anti-proliferative properties and induces cell cycle arrest, it is also modified by SUMOylation, therefore, cooperation and (or) competition between SUMOylation, may contribute to the establishment of fine regulation of ΔLf transcriptional activity according to target gene type and cellular homeostasis. The β-catenin

signaling pathway facilitates cancer stem cell renewal, cell proliferation and differentiation, thus playing crucial roles in tumorigenesis and response to therapy.

In the present work, 9 secondary metabolites and 6 peptides were selected, using the mass HPLC equipment, after a defragmentation analysis was readned using the “ChemDraw®” program and subsequently molecular docking and molecular dynamics of the selected molecular structures from Manilkara zapota versus the Delta-lactoferrin, β-catenin, p53 and p21 crystallographic structures was assayed.

EFFECTS OF CBFB INHIBITION BY CRISPR-CAS IN BREAST CANCER

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Abstract:

Core binding factor (CBF) is a DNA-binding transcription factor of genes related to development, mainly in embryogenesis, hematopoiesis, and bone development. CBF is composed of a DNA binding RUNX subunit (RUNX1-3) and a non-DNA binding CBFB subunit, which regulates RUNX protein activity by modulating the auto-inhibition of the RUNX subunits.

Furthermore, as for many genes critical for development, CBF-regulated genes are also involved in carcinogenesis. Alterations in CBFB expression and significant mutations have been reported in different types of cancer, such as liver, cervical and breast cancer. Recently, in whole exome and genome sequence analysis with 100 breast cancer samples, including mexicans samples, we found mutations in CBFB gene.These findings strongly suggest that there might be a relation between CBFB and tumor development. Nevertheless, the biological roles of CBFB in carcinogenesis have not been fully elucidated.

Therefore, to test whether CBFB is required for a malignant phenotype of breast cancer, we used CRISPR-Cas9 gene editing system to knock out the *CBFB* gene in MCF-7 breast cancer cell line. CBFB knocked expression resulted in increased proliferation, enhanced multicellular spheroid size and a slight increased in clonogenic capacity. Remarkably, using an *in vivo* Zebrafish xenograph model, we observed enhanced cell migration upon CBFB inhibition. Moreover, microarray analysis showed that signaling pathways related to cell migration, invasion and proliferation, among others, are modulated when CBFB is knocked out.

In conclusion, this report provides evidence that CBFB is involved in breast cancer cells functions during carcinogenesis.

REGULATION OF FFA1 RECEPTOR INTERACTION WITH B-ARRESTIN 2

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Abstract:

Free Fatty Acids Receptor 1 (FFA1) is a G protein-coupled receptor (GPCR) that is activated by medium and long-chain fatty acids such as a-linoleic and docosahexaenoic acid (DHA).

G proteins as well as b-arrestins are the principal intracellular transducers of GPCR signaling. In the case of FFA1, b-arrestin 2 promotes clathrin-mediated FFA1 internalization and MAP-kinase ERK1/2 activation which exerts transcriptional regulation. Therefore, b-arrestin 2 can disrupt the G protein signaling, promote intracellular trafficking of FFA1 and induce its own signaling pathways. It is well known that phosphorylation of intracellular regions of GPCRs is crucial for b-arrestins recruitment, and that different specific combinations of phosphorylated serine and threonine residues generate differences in how arrestins interacts with receptors and its downstream signaling partners, which is traduced in different effects. This conception is called the “barcode hypothesis”.

We aimed to elucidate if serine and threonine residues in FFA1 previously identified as putative sites for receptor phosphorylation and regulation, have a role in FFA1-b-arrestin 2 interaction. By performing FRET imaging and co-immunoprecipitation, we found that T215 (at intracellular loop 3 of FFA1), T287, T293, and S298 (at carboxy-terminal region) are important for b-arrestin 2 interaction with FFA1 in response to DHA (agonist) and phorbol 12-myristate 13-acetate (PMA, a PKC activator). Our results are consistent with a previous study from our laboratory which found that these residues participate in DHA and PMA induced FFA1 internalization and ERK1/2 activation. Thus, we identified a group of serine and threonine residues at FFA1 that regulates its interaction with b-arrestin 2, which could be useful to decode the phosphorylation codes that regulate the b-arrestin 2 related effects of this receptor.

ROLE OF TOR SIGNALING PATHWAY IN THE RESPONSE TO HEAT STRESS IN CORN (ZEA MAYS)

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Abstract:

Corn is a crop of great economic importance, whose production has been affected in recent years by climate change. Heat stress is one of the conditions that has increased. Its adverse effects include increases in oxidative stress, protein denaturation, pigment degradation and up to 45% decrease in the number of corn grains. One of the signaling pathways in plants that is modified in response to heat stress is that of TOR (Target of Rapamycin), a Ser/Thr kinase that regulates cell growth and proliferation (*Salazar-Díaz et al., 2021*). Recent data indicate that this pathway regulates the translation of mRNAs of enzymes that participate in the polyamine metabolism. Polyamines are involved in germination, early growth, and stress response in plants; its exogenous application decreases the damage caused by heat stress.

This project aims to evaluate the role of TOR signaling and the effect of polyamines in the heat stress response in two varieties of Mexican corn: Chalqueño from highlands with mild climate and Tuxpeño, synthetic variety 536 (VS-536), from tropical climate. To determine phenotypic changes in response to stress and the effect of polyamines, the growth of primary root, mesocotyl and coleoptile was measured. To evaluate TOR signaling, the levels of total and phosphorylated ribosomal protein S6 were determined. For the response to heat stress, the levels of heat shock proteins, Hsp101 and Hsp70, were measured. So far, it was observed that application of heat shock at 42 °C for 2h to 72h-imbibed seeds, significantly reduced the length of primary root by 65.3% for Chalqueño and 60.3% for VS-536 in relation to plants kept at 25°C. A greater reduction of the mesocotyl was observed for VS-536 (82.1%) than for Chalqueño (60.8%), while the length of stem and coleoptile was reduced by 49.2% and 38.3% for Chalqueño and VS-536, respectively. These results indicate that heat shock reduces the growth of different organs in the young maize seedling, to different extent for the analyzed varieties. The analysis of TOR pathway activity, heat shock proteins, as well as the effect of polyamine application is in progress.

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Salazar-Díaz et al. (2021). iScience, 24(11), 103260.
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TRANSCRIPTIONAL ANALYSIS OF THE GAC/RSM PATHWAY IN *AZOTOBACTER VINELANDII* UNDER NITROGEN FIXATION /NON NITROGEN FIXATION CONDITION

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Abstract:

Azotobacter vinelandii is a soil bacterium that produces compounds of biotechnological interest: Alginate, polyhidroxybutyrate (PHB) and alkylresorcinols (AR). The synthesis of these metabolites is controlled by GacS/Rsm signal transduction pathway. GacS/A is a two-component signal transduction system (TCS) that regulates the activity of the post-transcriptional control system Rsm.

The Rsm system includes eight small non-coding RNAs (RsmZ1-7 and RsmY) and the translational repressor protein RsmA. In *Pseudomonas aeruginosa,* The signal transduction of the GacS/GacA pathway has been shown to be influenced by the histidine kinases (HK) RetS and LadS. In this work we take the information produced in a previous work that analyzed the RNA expression in *A. vinelandii* in two conditions: in the medium without nitrogen, where the bacteria enter in the biological nitrogen fixation process; in contrast, a medium supplemented with ammonium where the nitrogen fixation is not produced (Barney et al. 2017). Since in *A. vinelandii*, the synthesis of the mentioned compounds occurs under conditions of nitrogen fixation, it is interesting to analyze the expression of the HKs related to the GacS/A-Rsm pathway and the expression of the genes of the Rsm system.

Barney BM, Plunkett MH, Natarajan V, Mus F, Knutson CM, Peters JW. Transcriptional Analysis of an Ammonium-Excreting Strain of *Azotobacter vinelandii* Deregulated for Nitrogen Fixation. Appl Environ Microbiol. 2017 Sep 29;83(20):e01534-17. doi: 10.1128/AEM.01534-17. PMID: 28802272; PMCID: PMC5626987.

ADENOSINE DERIVATIVE TREATMENT INDUCES TRANSCRIPTOMIC CHANGES OF HEPATOCELLULAR CARCINOMA BY REGULATING WNT/β-CATENIN SIGNALING

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Abstract:

Introduction. Carcinoma hepatocellular (HCC) is estimated to be the 7th cancer in incidence and 4rd in mortality in 2020. Nowadays there is not an effective treatment against this pathology; therefore the study of new therapeutic agents becomes relevant. It has been described that Wnt/β-catenin pathway is involved in the pathogenesis of HCC; Aberrant activation of the pathway induces changes in the localization of β-catenin, increasing it in the nucleus, inducing the expression of genes involved in cell proliferation and maintenance of the tumor environment. Our research group has been developed an adenosine derivative compound, IFC-305, which is shown that has a clear hepatoprotective effect, preventing and reversing carbon tetrachloride-induced liver fibrosis in rats and also showed chemoprevention of HCC in a sequential model of cirrhosis-HCC in rats.

Aims. To determine the transcriptomic changes mediated by IFC-305 in hepatocelular carcinoma and whether it modifies the regulation of Wnt/β-catenin signaling pathway.

Methods. HepG2, Huh7 and SNU449 human hepatocellular carcinoma cell lines, and HepaRG, human hepatic like cell line, were exposed to IFC-305 to determine the cytotoxicity and β-catenin transcriptional activity was detected. Transcriptomic analysis was performed in HepG2 by sequencing using Illumina Hiseq technology.

Results. The transcriptomic analysis showed us that 78 genes are differentially expressed by the effect of IFC-305, while the functional enrichment analysis shows that the methylation and glycolysis pathways are mainly represented, as well as signaling pathways involved in carcinogenesis such as Wnt/Beta-catenin pathway. IFC-305 reduces cell survival of tumoral cell lines but is not cytotoxic for HepaRG, non tumoral cell line. Also IFC-305 increased Dkk1, the principal inhibitor of the Wnt/β-catenin signaling pathway. The transcriptional activity of β-catenin is reduced by effect of IFC-305in tumoral cell lines exposed to IFC-305 compared with non-treated cells. Currently we are evaluating expression and quantity of signaling pathway components.

Discussion. The IFC-305 modulates Wnt/B-catenin pathway increased Dkk1 and reduces cell survival in HCC cell line. Considering IFC-305 is able to ameliorate cirrhosis and its differential effects on tumor and non-tumoral cell lines, this open the door to novel strategies for cancer treatments.

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GLYCINE MODULATION OF PRO- AND ANTI-INFLAMMATORY CYTOKINES AND THEIR GPR-6 GENE EXPRESSION IN ADIPOGENESIS

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Abstract

Introduction The glycine level in plasma is generally observed to be reduced in patients with obesity and diabetes mellitus as compared to control subjects. These kinds of diseases show low grade inflammation, some studies have reported that the glycine modifies this state. Cytokines are key modulators of acute and chronic inflammation through a complex network of interactions. It has been inferred that GPR-6 could be associated in adenylate cyclase-activating G protein-coupled receptor signalling pathway and regulation of metabolic process as adipogenesis. **Objective** Analyse the modulation of cytokines and the roll of the orphan receptor GPR6 in a chronic inflammatory by TNF stimulus. **Methods** For differentiation, the cells were cultured to confluence (8 x 104 cells), the cell culture of 3T3-L1 was made in 6 wells plate (4 x10^5 cell per well) in DMEM/F12 medium. The 3T3-L1 cell were stimulated with TNF-α (10mM) during 30 minutes as an inflammatory model in the cells. The gene expression was measured by RT-qPCR. **Results** Our results showed that TNF stimulus decreased the orphan gene expression in vitro and glycine reverts the gene expression of GPR6 **Conclusion** Our conclusion the GPR-6 modulate inflammatory environment by glycine treatment.

EFFECT OF THE IFC-305 IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINES ON THE PI3K/AKT/MTOR PATHWAY

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Abstract:

B-cell acute lymphoblastic leukemia (B-ALL) is a hematological cancer caused by the malignant transformation of progenitor B cells that proliferate uncontrollably in bone marrow, peripheral blood, and extramedullary sites. The PI3K/Akt/mTOR pathway in B-ALL is hyperactivated, promoting the proliferation of leukemic cells and resistance to treatment. Among the new alternatives for the treatment of cancer is IFC-305, an adenosine derivative that has been studied in hepatocellular carcinoma (HCC). It prevents and reverses cirrhosis in animal models, it has an anticarcinogenic effect and it induces autophagy *in vivo* and *in vitro*. While in hepatic stellate cells it decreases the levels of phosphorylated proteins AKT and P70S6K.

The objective of this project is to evaluate the effect of IFC-305 on the activation of the PI3K/Akt/mTOR pathway, autophagy, and apoptosis in B-ALL cell lines. Cytotoxic effect of IFC-305 on B-ALL cell lines: REH (low risk), Nalm6 (intermediate risk) and SUP-B15 (high risk) was determined by MTT assay. It will be determined whether there is a synergistic effect between IFC-305 and the mTORC1 inhibitors Everolimus and Gedatolisib to evaluate apoptosis by flow cytometry and activation of the PI3K/Akt/mTOR signaling pathway and autophagy measuring levels of proteins.

Our results indicate that IFC-305 has a cytotoxic effect on the three B-ALL cell lines at an inhibitory concentration 50 (IC50) of 4.4 mM for REH, 2.4 mM for Nalm6 and 25 mM for SUP-B15. This suggests that IFC-305 will have a greater effect on the regulation of PI3K/Akt/mTOR pathway activation in B-ALL types classified as low and intermediate risk, as observed in a previous trial where cells were treated for 24 h with IFC-305 at 1 mM, 3 mM, 5 mM, and 10 mM and decreased p-P70SK6 protein in a dose-dependent manner. These results suggest that IFC-305 influences the regulation of the activation of the PI3K/Akt/mTOR signaling pathway and could reduce the proliferation of leukemic cells in B-ALL.

LISOPHOSPHATIDYLINOSITOL (LPI) BLOCKS TOLL-LIKE RECEPTOR (TLR)4-DEPENDENT PRO-INFLAMMATORY AND PRO-ANGIOGENIC CYTOKINE PRODUCTION IN MAST CELLS

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Abstract:

Toll-like receptor (TLR)4 receptor is importantly involved in innate immunity responses against Gramm-negative bacteria lipopolysaccharide (LPS) and other pathogen and damage-associated molecular patterns (PAMPs and DAMPs, respectively). Its signaling system leads to the activation of IRAK and MAPKs that, in concert, modulate the nuclear translocation of NFκB transcription factor in a number of immune cells. TLR4 triggering causes the generation of reactive oxygen species (ROS) and the production of pro-inflammatory, regulatory, and pro-angiogenic cytokines, such as the tumor necrosis factor (TNF)α, interleukin (IL)-6, IL-4, IL-2, the transforming growth factor (TGF)-β, chemokines such as CCL-2 and the vascular-endothelial growth factor (VEGF). Together, those mediators mediate not only protective but also deleterious innate immunity reactions, such as defense against pathogens or tumor angiogenesis. Due to the role of this receptor on the initiation of inflammation, research on compounds and signaling pathways leading to its inhibition and/or modulation is an active field of research. In this work we tested the effect of the bioactive lipid lisophosphatidylinositol (LPI) on the TLR4-mediated MC activation. Cultures of bone marrow-derived mast cells (BMMCs) were generated in the presence of IL-3 and sensitized with monomeric IgE before to be stimulated with LPS for distinct times. After that, total RNA was isolated and the production of selected cytokine mRNA was analyzed by RT-PCR. In another set of experiments, the effect of a pre-incubation with LPI (100nM) on LPS-induced cytokine mRNA accumulation was evaluated. Our results showed that LPI importantly inhibits the production of IL-6, TNFα, IL-4, TGF-β, CCL-2 and VEGF mRNAs induced by LPS in MCs. Finally, we found that the specific GPR55 antagonist ML-193 prevents the inhibitory effect of LPI, suggesting that this lipid and its GPCR-coupled receptors participate in a negative control loop that downregulates TLR-4 activation in those innate immune cells and, potentially, could diminish MC-dependent inflammation *in vivo*.

SEA SNAILS CONOTOXINS MODULATE BONE CELL ACTIVITY

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Abstract:

The skeletal system is a dynamic tissue, constantly changing to fulfill its diverse functions. The adaptation of the skeletal microarchitecture to the environment is controlled by a process known as bone remodeling, which is the resorption and formation of small units of bone and repeated throughout life to maintain the skeleton's integrity. Bone resorption is carried out by osteoclast and formation by osteoblasts. A close balance between bone remodeling cycles is necessary to maintain bone mass. When the balance is disturbed, it can lead to pathological conditions, and these diseases have in common the necessity for new treatments to correct bone mass. The venom of the *Conus* marine snails can contain up to 200 pharmacologically active peptides, named conotoxins, that target several receptors, including ion channel receptors present on bone cells. The properties of four synthetic conotoxins were characterized *in vitro* and *ex vivo* using cell proliferation and bone cell differentiation and activity assays. Bone marrow cells of Balb/c mice were treated with different concentrations of conotoxins, demonstrating a dose-dependent proliferation inhibitory effect. Then, we cultured isolated mouse bone marrow cells in osteoblastogenic conditions in the presence of conotoxins (100 ng/ml). After 21 days of culture, the conotoxins decreased the osteoblast mineralization activity. In contrast, conotoxins at a concentration of 100 ng/ml promoted osteoclast differentiation of mouse bone marrow cells induced by RANKL and M-CSF. The effects on osteoclastogenesis were RANKL-dependent. The conotoxins (100 ng/mL) consistently had a pro-osteoclastic effect when using human peripheral blood mononuclear cells. Conotoxins increased the resorption activity of mouse osteoclast as well. RT-qPCR analysis showed a modulation in the expression of marker genes involved in osteoblastic and osteoclastic cell differentiation (*Nfatc1, Rankl, Runx2, Opg*). Our results indicated that the conotoxins tested can modulate bone cell differentiation and activity and could be used to correct bone remodeling in diseases characterized by excessive bone formation.

USE OF DINO-SL TO IMPROVE A CDNA LIBRARY FOR Y2HS IN *Symbiodinium microadriaticum* CassKB8

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Abstract:

Symbiodiniaceae belongs to a family of photosynthetic dinoflagellate protists, which establish endosymbiosis with cnidarians including corals. The coral reef health thus, depends heavily on this association, and in the last decades large reef areas have been lost due to global warming and environmental stresses that destabilize such cnidarian-Symbiodiniaceae symbiosis. This has prompted us to generate approaches to study this important symbiosis in the *Cassiopea xamachana-Symbiodinium microadriaticum* CassKB8 model system. Consecuently, we developed a strategy to improve the performance and yield of a cDNA library to be used in the Yeast-Two Hybrid System (Y2HS) to find RACK1 ligands from *S. microadriaticum* CassKB8 (smicRACK1). Construction of cDNA libraries takes advantage of the characteristic poly(A) tail at the 3' end of transcripts; however, this is not the case for the 5' end, which leads to under-represented 5' ends. Some strategies such as SMART (Switching Mechanism at 5' end of RNA Transcript) have been developed to improve the performance of the cDNA libraries. Nevertheless, there are some organisms that present transcripts with a conserved 5´-end sequence. In dinoflagellates, this corresponds to a 22-nt conserved sequence called Dino Spliced Leader (Dino-SL), which is post-transcriptionally added to the 5' end of all their nuclear mRNAs (Islas-Flores et al., 2021). We took advantage of the Dino-SL to generate a cDNA library from the dinoflagellate *S. microadriaticum* CassKB8. To confirm that this strategy in fact improves the performance of the library, we also generated a SMART-based library. Comparison of sequences from both cDNA libraries, showed a significantly higher yield, length of sequences, number of transcripts, and better 5' representation from the Dino-SL-based than from the SMART library. In addition, we confirmed that the cDNAs from the Dino-SL library were adequately expressed in the yeast cells when the Y2HS was developed. This also resulted in successful screening and identification of seven putative SmicRACK1 ligands.

This work is supported by grant 285802 from CONACYT.
Islas-Flores, T.; Galán-Vásquez, E.; Villanueva, M.A. Screening a Spliced Leader-Based *Symbiodinium microadriaticum* cDNA Library Using the Yeast-Two Hybrid System Reveals a Hemerythrin-Like Protein as a Putative SmicRACK1 Ligand. Microorganisms 2021, 9, 791. https://doi.org/10.3390/ microorganisms9040791

CHRONIC LEPTIN TREATMENT INDUCES EPITHELIAL-MESENCHYMAL TRANSITION IN MCF10A MAMMARY EPITHELIAL CELLS

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Abstract:

Background: Leptin is a cytokine-like hormone that functions as a link between obesity and breast cancer [1]. Leptin treatment induces Epithelial to Mesenchymal Transition (EMT) in BC cell lines [2]. In non-tumoral breast epithelial MCF10A cells, acute leptin treatment induces partial EMT [3]. However, the effect of chronic leptin treatment on EMT in non-tumorigenic breast cells has not been fully explored. **Objectives:** This study aimed to evaluate the effect of chronic leptin treatment on the induction of EMT in MCF10A cells. **Results:** We found that chronic leptin treatment induces a switch from an epithelial to a mesenchymal morphology, partial loss of E-cadherin and gain of vimentin expression. Immunolocalization experiments showed a partial loss of E-cadherin at cell junctions and increased cytoplasmic localization of Vimentin in leptin-treated cells. Moreover, chronic leptin treatment increased collective cell migration and invasion. Furthermore, when cultured in non-adherent conditions (hanging drop) leptin treated cells exhibited reduced cell aggregation, increased survival, and decreased apoptosis, which correlates with increased FAK and Akt phosphorylation. Finally, bioinformatic analysis in two publicly available RNAseq datasets from normal breast tissue shows that high levels of leptin mRNA correlate positively with the expression of mesenchymal markers and leptin signaling, and negatively with epithelial markers. **Conclusions:** Thus, our results demonstrate that chronic leptin treatment induces EMT in non-tumorigenic MCF10A cells and suggest that high leptin expression in normal breast tissue may induce EMT and contribute to increased risk of breast cancer.

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MODULATION OF BONE CELL ACTIVITY AND BONE REMODELING BY SULFATED POLYSACCHARIDES DERIVED FROM BROWN ALGAE

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Abstract:

Bone remodeling is essential for bone homeostasis and occurs throughout our life. Bone cells like osteoblasts and osteoclasts orchestrate this remodeling consisting in two phases: bone resorption followed by bone matrix formation and mineralization. When an imbalance between these phases occurs during pathologies such as osteoporosis, bone mass is lost, increasing bone fragility and the risk of fracture.

We characterized the anabolic and antiresorptive effect of sulfated polysaccharides, called fucoidan, isolated from three marine brown macroalgae: *Macrocystis pyrifera, Sargassum muticum* and *Undaria pinnatifida*. Algae samples were collected in Todos Santos Island, Baja California, and compounds extracted using the acid hydrolysis method. Sulfated polysaccharides were obtained using NaCl precipitation and successive ethanol washings. Chemical characterization of the extracts confirmed that the content in total carbohydrates, fucose, uronic acids and sulfates corresponded to sulfated polysaccharides.

In vitro cell proliferation assays were performed on MC3T3-E1 osteoblast precursor cells and extracted fucoidan all caused a concentration-dependent inhibition of cell proliferation after 24 hours of culture. In mineralization assays using MC3T3-E1 or mouse bone marrow cells, the sulfated polysaccharides increased the mineralization as measured with alizarin red staining. These results demonstrated the capacity of fucoidan to modulate the proliferation and mineralization of osteoblastic cells. In contrast, in osteoclastogenesis assays, fucoidan extracts inhibited the formation of osteoclasts induced by RANKL and M-CSF *in vitro*. Finally, the effect of fucoidan on bone remodeling was assessed *ex vivo* using calvaria from 4-6 day-old mice. After 7 days of culture, histomorphometrical analysis indicated that the fucoidan extract from *M. pyrifera* increased the bone area compared to control-treated calvaria.

We demonstrated that fucoidan from different brown algae have a dual role in the bone remodeling process by promoting mineralization and inhibiting osteoclast formation in a dose-dependent manner *in vitro*. Thus, fucoidan are potent molecules that could be used to treat bone related diseases.

COMPARISON OF TOTAL PHOSPHORYLATION IN CERVICAL CANCER CELLS CULTURED IN MONOLAYER AND IN A THREE-DIMENSIONAL SYSTEM

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Abstract:

Monolayer cell cultures have been the standard for cancer biology research, however their ability to accurately reflect the molecular mechanisms of tumors occurring in vivo is limited. Three-dimensional culture systems are becoming increasingly popular due to their ability to mimic tissue-like structures more effectively than monolayer cultures, facilitate the possibility to better recapitulate several of the biological and molecular characteristics of tumors *in vivo*, such as cancer cells heterogeneity, cell-extracellular matrix interactions, development of a hypoxic microenvironment, signaling pathway activities depending on contacts with extracellular matrix, differential growth kinetics, more accurate drugs response, and specific gene expression and epigenetic patterns.

On that basis, the comparison of total protein phosphorylation in cervical cancer cells cultured in monolayer and in a three-dimensional system was performed.

It was observed that in cells cultured in a three-dimensional system there is a general increase in the presence of tyrosine phosphorylated proteins and possibly one of the most evident is a member of the EGFR family, however it is still necessary to verify which proteins it is.

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BORIC ACID ORCHESTRATES SHOOT AND ROOT DEVELOPMENT IN *ARABIDOPSIS* SEEDLINGS AND IMPROVES MERISTEM VIABILITY IN *MEDIATOR18* MUTANTS

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Abstract:

Boron (B) has been considered either as a nutrient or as a toxic non-essential element for plants and considerable debate arose recently regarding its functions and mechanisms of action. To gain further detail on the roles of boron in growth, development and viability of meristems, *Arabidopsis* wild-type and *mediator18* mutants, these later showing genetically fixed cell death in the pro-vasculature of roots, were germinated and grown side by side in agar-solidified plates with a standard nutrient solution supplemented with increasing concentrations (0.25-8 mM) of boric acid (BA). In the WT and *med18-1* mutants, BA exerted a dose-dependent inhibition of leaf formation, but in contrast, low (0.25-1 mM BA) concentrations recovered primary root growth in *med18-1* mutants. BA promoted root branching in WT seedlings but not in *med18-1* mutants, which manifest an enhanced lateral root formation capacity under a wide range of BA concentrations. The growth response of the primary roots in the mutants was related to protection of meristems from cell death and reduced expression of the ERF115 transcription factor, which is induced in inner tissues upon damage, and normalization of auxin-inducible gene expression within the root tip. Irrespective of the overall growth repressing effects in the shoot and root system, it seems clear that important protective functions are orchestrated by BA, which supports the viability of root meristems in *Arabidopsis*.

EFFECT OF HYPERGLYCEMIA AND INFLAMMATION ON THE MACROPHAGE POLARIZATION MEDIATED BY RESVERATROL AND D3T

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Abstract:

Currently, there is an important area of research for the identification of stimuli that can promote the phenotype exchange or polarization of macrophages from pro-inflammatory M1-type to anti-inflammatory M2-type, which would contribute to ameliorate inflammatory-mediated diseases, such as metabolic syndrome and obesity. However, the effect of different bioactive compounds under oxidative stress-induced hyperglycemia on polarization has been scarcely investigated. RAW 264.7 macrophages were incubated in medium with glucose 5 (standard) or 25 mM (high) and stimulated with LPS (10, 60 and 100 ng/mL), as a pro-inflammatory inducer, in order to evaluate the macrophage polarization after resveratrol (RSV) or D3T (2.5, 5, 10 and 20 µM) supplementation. At standard glucose (SG) condition without LPS, D3T did not negatively affect macrophage viability; however, RSV significantly decreased viability in a dose-dependent manner up to 21%. LPS stimulation at 60 and 100 ng/mL significantly increased macrophage viability; whereas both bioactive compounds maintained macrophage viability similar to that of SG condition. Furthermore, RSV and D3T decreased nitric oxide (NO) in a dose-dependent manner, and GSH levels up to 34%. Under high glucose (HG) conditions, both bioactive compounds with 10, 60 and 100 ng/mL of LPS also increased macrophage viability up to 34, 53 and 74% respectively. As expected, NO production was significantly higher in LPS-stimulated macrophages at 60 and 100 ng/m, which was further decreased by RSV and D3T supplementation up to 36 and 39% respectively in a dose-dependent manner, whereas only D3T supplementation increased GSH levels at 100 ng/mL and normalized MDA values at 60 ng/mL of LPS. Under LPS-stimulation with 60 ng/mL, pro-inflammatory (IL-1 and IL-6) interleukin gene expression (by qPCR) was higher under HG condition. Interestingly, RSV decreased mRNA relative expression of pro-inflammatory interleukins, while D3T increased the anti-inflammatory (IL-10) interleukins. In addition, we observed a positive correlation between viability, MDA and IL-10 under the evaluated conditions, which indicates that in a context of obesity, hyperglycemia plays a fundamental role in the elements that influence inflammation by modifying the proliferation rate of resident macrophages. Overall, macrophage phenotype after polarization depends on the bioactive compound applied, which suggest that their effector role can be differentially mediated through the diet.

EFFECT OF *TOLL-LIKE RECEPTOR 4* (TLR-4) ACTIVATION BY LPS ON THE MIGRATORY AND PROLIFERATIVE CAPACITY OF PROSTATE CANCER TUMOR CELLS, PC-3

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Abstract:

Prostate cancer (PCa) is the most common malignancy in men, with most PCa-related deaths due to metastases. Inflammation as a promoter of tumor growth is a characteristic that allows cells to acquire capacities that contribute to the development and progression of cancer, through the production of inflammatory molecules, growth factors, angiogenic factors, as well as signals that favor the transition epithelium-mesenchyme.Stimulation of TLR-4 by exogenous ligands (LPS), as well as endogenous ligands (HSP, fibrinogen, and HMGB1), induces the production of proinflammatory cytokines.

Long-term activation of the TLR-4 signaling pathway in prostate epithelial cells can promote cell activation, proliferation, migration, survival, and tumor transformation. However, the effect of LPS on PCa metastasis has not been investigated in detail. Thus, the objective of this study was to determine whether the presence of LPS affects the migratory and proliferative capacity of PC-3 cells.

Cells were cultured in standard culture medium in the presence and absence of LPS. To evaluate the migratory capacity, tests were performed in transwell chambers and for the proliferative capacity, the cells were counted. The presence of LPS significantly increases the migratory and proliferative capacity of PC-3 cells. This effect is dependent on the concentration of LPS used.

DIFFERENTIAL EFFECTS OF FENTANYL AND METHADONE ON MAST CELLS

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Abstract:

Opioids, like morphine, fentanyl, and methadone, are the first line in the treatment of pain; nevertheless, opioids also are immunosuppressors. Opioids act by binding to the opioid receptors, within which is the μ-opioid receptor. The μ-opioid receptor is a G-protein-coupled-receptor (GPCR) that activities G_i-proteins. Morphine, fentanyl, and methadone, even though they are μ-opioid receptor agonist, are also biased agonists. Morphine and methadone have biased agonism for Gi-protein signaling, while fentanyl has it for β-arrestin. Due to this property, they have different effects on immune cells. Mast cells (MCs) are elements of the innate immune system with the capacity of release inflammatory mediators, such as the tumor necrosis factor (TNF)-α. Due to their location (close to blood vessels and peripheral nerve terminals), MCs constitute one of the first cell types to respond to pathogen invasion and tissue damage. Previously we reported that morphine inhibits the secretion of TNF-α induced by lipopolysaccharide (LPS) on murine bone marrow-derived mast cells (BMMCs). In that effect, μ and Δ opioid receptors were found to play an important role. However, the effect of fentanyl and methadone on MCs is unknown. The aim of this study was to determine the immunomodulatory effects of fentanyl and methadone on MCs. BMMCs were stimulated with increasing concentrations (0.01, 0.1, and 1 mM) of fentanyl or methadone for 30 min, before to LPS (500 ng/μL) stimulation. TNF-α production was determined by ELISA. 1 mM of fentanyl or methadone inhibited the secretion of TNF. Interestingly, the inhibitory effects seemed to be associated to the capacity of methadone to induce the formation of extracellular DNA traps in BMMCs, and this effect was not prevented with 10 μM of naloxone, an antagonist of opioid receptors. On the other hand, inhibition generated for 1 mM of fentanyl on LPS-triggered TNF production is not prevented by naloxone (10 μM). These findings suggest that morphine, fentanyl, and methadone, although they are μ-opioid agonists, have different mechanisms of signaling, although the participation of distinct opioid receptors cannot be ruled out.

INTERACTION BETWEEN WNT AND LYSOPHOSPHATIDIC ACID (LPA) RECEPTOR SIGNALING PATHWAYS IN COLON CANCER

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Abstract:

Colorectal cancer is the third cause of death from cancer worldwide. Aberrant canonical Wnt signaling is a hallmark of this type of cancer. It has been reported that LPA is a "bioactive lipid" and its G-protein -coupled receptors may play different roles in colon cancer inducing cell proliferation, migration, survival, and angiogenesis.

LPA receptors expression changes under malignant conditions: we found that while $LPAR_1$ and $LPAR_2$ are expressed at low levels in non-malignant 112CoN cells, RKO malignant cells overexpress $LPAR_1$ and $LPAR_2$ and SW480 cancer cell line only overexpress $LPAR_1$. We also found that LPA and Wnt3A induce a strong ERK activation in all colon cell lines that were not additive. LPA and Wnt3a were both able to stimulate β-catenin transcriptional activity and the b-catenin phosphorylation at S552 and S675 residues, again in an apparently non- additive manner. In addition, we found that $LPAR_1$ and the Wnt effector Dvl3 interact in RKO cells, and we are currently investigating if this interaction occurs via PDZ-interacting motifs located in both proteins.

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EFFECT OF THE IGF-2/IGF-1R COMPLEX ON THE MIGRATION CAPACITY OF THE MDA-MB 231 CELLS: ROLE OF ERβ ACTIVATION

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Abstract:

Triple negative breast cancer (TNBC), is characterized by being highly invasive and it has a high rate of mortality, with an overexpress the estrogen receptor β (ERβ). By activating the ERβ of MDA-MB 23 cells (a representative line of TNBC), with a specific agonist (DPN), their migratory capacity is stimulated. Furthermore, emerging information suggests that there is an intersection between, estrogens and the insulin-like growth factor (IGF) system.

It was interesting for us to investigate whether ERβ activation induces changes in the elements of the IGF system, affecting the migratory capacity of MDA-MB 231 cells.

Our results indicate that the activation of ERβ by the chronic presence of DPN for 72 hours induces an increase in the expression of IGF-2, both at the mRNA and protein levels. In addition, we observed that the chronic presence of IGF-2 exacerbates the migratory capacity of MDA-MB 231 cells, positively associated with an increase in the level of expression of the transcription factor *Zeb1* and a reduction in the expression of E-Cadherin. Another molecular element involved in its migratory capacity is the functional expression of the Na_v 1.5 channel. MDA-MB 231 cells exposed to IGF-2 increase the expression level of this channel.

MDA-MB 231 cells express mRNA for IGF-1R, which can activate two signaling pathways: a) PI3K/AKT and b) MAPK's, to discriminate which of the two intracellular pathways is involved in the migratory capacity stimulated by IGF-2, we used specific antagonists for each of the pathways. The results obtained show that blocking either of the two pathways has a negative impact not only on the migratory capacity of MDA MB 231 cells, but also on their proliferative capacity.

With the results obtained, ERβ and the IGF-2/IGF-1R complex could be proposed as new pharmacological targets for the treatment of triple negative breast cancer.

AUTOPHAGY SIGNALING DURING GERMINAL CELL DEATH IN OVARIES FROM PREPUBERTAL RATS

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Abstract:

Autophagy is present in oocyte elimination during prepubertal stages of rats during sexual maturation. Although important advances in autophagic process have been made, the fine mechanism of autophagy during oocyte elimination have not been completely deciphered. In this work, the participation of diverse proteins involved in the autophagy progression during germinal cells in rat ovaries were analyzed. The proteins mTOR, mTORp, Beclin 1, LC3A, and Lamp1 were immunodetected in oocytes undergoing autophagic cell death. Additionally, expression of the same proteins and MAPK/ERK pathway were evaluated in isolated oocyte populations. Our observations revealed an increased labeling of the Beclin1, LC3A and Lamp1 and a significant decrease in labeling of mTOR and p-mTOR, indicating activation of the autophagy process. We also found the possible influence of ERK1/2 in downregulation of p-AKT in the oocytes, this could indicate the influence of the energetic stress to induce the autophagic cell death in oocytes. These results suggest that downregulation of mTOR could be mediated by low energy levels and sustained starvation involving the phosphoinositide 3-kinase (PI3K)/AKT/mTOR and MAPK/ERK pathways.

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ROLE OF HYDROPHOBINS IN ASEXUAL SPORE DEVELOPMENT IN *NEUROSPORA CRASSA*

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Abstract:

Hydrophobins are small amphiphilic proteins of fungi that have the peculiar physicochemical property of polymerizing at the interface of a hydrophobic/hydrophilic environment. In filamentous fungi, these proteins are secreted and assembled at the cell wall of asexual spores (conidia) and, presumably, at the aerial hyphae from which the spore bearing structures (conidiophores) originate. Hydrophobins are needed for the efficient dispersal of asexual spores and for the adhesion to plant tissues. Our general work hypothesis states that each morphogenetic transition in *Neurospora crassa* is a response to the intracellular ROS formation. We hypothesize that hydrophobins serve as barriers for the entrance of O_2 to the fungal spore. As such, hydrophobins appear at specific stages through development. The *N. crassa* genome contains two hydrophobin genes: *eas* and *nc2*. We have characterized the mutant phenotype of strains lacking *eas* and *nc2* across all stages of morphogenesis: germination, growth of trophic hyphae, adhered mycelium, emergence of aerial mycelium and production of conidiophores and conidia. Additionally, we have cloned the *eas* and *nc2* genes and fused them with a fluorescent tag to track the expression of each hydrophobin through all stages of development.

MLBIG1 CONTROLS ARF2 ACTIVATION DURING *MUCOR LUSITANICUS* YEAST DEVELOPMENT THROUGH THE PKA PATHWAY

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Abstract:

M. lusitanicus (previously *M. circinelloides f. lusitanicus*) is a dimorphic mucoral fungus and opportunistic pathogen, the virulent being the mycelial form. It is a study model to understand cell differentiation and fungal virulence. The Arf family proteins are monomeric G proteins involved in the regulation of vesicular trafficking in eukaryotes, and they depend on ArfGEF-type proteins (guanine nucleotide exchange factor) for their activation by exchanging GDP for GTP. The central role of ArfGEF proteins is the regulation of vesicle transport between the endoplasmic reticulum, the Golgi apparatus and the plasma membrane. Previously, our group reported the role of the Arf2 protein in the yeast development of *M. lusitanicus*. *arf2* transcript accumulates mainly in the yeast stage and the Δ*arf2* mutant showed an inability to generate yeast compared to the wild strain. On the other hand, *M. lusitanicus* has six genes in its genome that code for ArfGEF proteins. Through a genetic-molecular approach, it was shown that MlBig1 physically interacts with Arf2, in addition that the mutation of the *mlbig1* gene generated the same phenotype as Δ*arf2*, and that the mutation of the codon that encodes threonine 871 (residue phosphorylatable by protein kinase A, PKA) of MlBig1 abolishes its activation as a guanine nucleotide exchanger, demonstrating the role of this MlBig1 amino acid residue in yeast development. With this research, it is possible to propose new molecular targets for the treatment of mucormycosis and/or the control of yeast morphology (avirulent), as well as in the optimization of processes based on fermentation.

Patiño-Medina, J.A., Maldonado-Herrera, G., Pérez-Arques, C., Alejandre-Castañeda, V., Reyes-Mares, N.Y., Valle-Maldonado, M.I., Campos-García, J., Ortiz-Alvarado, R., Jácome-Galarza, I.E., Ramírez-Díaz, M.I., Garre, V., Meza-Carmen, V. (2018) Control of morphology and virulence by ADP-ribosylation factors (Arf) in *Mucor circinelloides*. *Curr Genet.* 64(4):853-869.

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ISOLATION AND CHARACTERIZATION OF ARABIDOPSIS MUTANTS WITH ENHANCED TOLERANCE TO SEROTONIN

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Abstract:

Serotonin (5-hydroxytryptamine) is a bioactive indoleamine widely distributed in plants in which regulates a diversity of plant growth and developmental processes. We previously showed that serotonin regulates primary root growth inhibition, lateral and adventitious roots formation, as well as hairs root development in Arabidopsis (Arabidopsis thaliana) seedlings[1], effects in which serotonin interacts with ROS, jasmonic acid and ethylene signaling pathways[2]. To gain more insight into the growth and developmental process as well as regulatory mechanisms by which serotonin modulates plant development, we performed a genetic screen for identifying Arabidopsis mutants with impaired serotonin response. Two mutants with enhanced tolerance to the primary root growth inhibition induced by serotonin were isolated and named them serotonin resistant1 and serotonin response2 (*ser1* and *ser2*). Genetic analysis indicated that in both cases the serotonin tolerance was caused by a monogenic recessive mutation. Phenotypic analysis showed that the mutants *ser1* and *ser2* were reduced in size compared with the wild-type Col-0. Furthermore, serotonin double mutant (*ser1/ser2*) showed accelerated flowering and senescence as well as impaired flower, siliques and seed development. Additionally, serotonin mutants also were related in mediates the jasmonic acid and ethylene responses. Taken together, our results provide genetic evidence of the functional role of serotonin in plants modulating root architecture and plant growth by interacting with jasmonic acid and ethylene signaling. Our results suggest that *ser1* and *ser2* are two novel genetic elements in serotonin signaling in Arabidopsis.

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EFFECT OF *O*-GLCNACYLATION ON AKT PHOSPHORYLATION IN ORAL CANCER CELLS

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Abstract:

Alteration of signaling pathways is a typical feature during tumor transformation/progression, how is the case of the PI3-kinase/AKT pathway in oral squamous cell carcinoma (OSCC). AKT phosphorylation is crucial to trigger different cellular processes as proliferation, survival, growth, metabolism, angiogenesis and metastasis. Recently, it has been reported that O-GlcNAcylation, which is a dynamic and reversible post-translational modification where a GlcNAc residue is added to a Ser and Thr residues of proteins, is able to regulate the functions of different signaling proteins. However, it is still unknown whether the O-GlcNAcylation has a role in AKT phosphorylation when the PI3-kinase/AKT pathway is activated by the Epidermal Growth Factor (EGF). To study the effect of O-GlcNAcylation on AKT phosphorylation through activation of the PI3-kinase/Akt pathway by EGF. Cultured oral cancer cells were subjected to different treatments to favor the O-GlcNAcylation and PI3-kinase/AKT pathway activation. The AKT phosphorylation was verified by immunocytochemistry and western blot. It was observed that in treatments favoring O-GlcNAcylation, AKT phosphorylation was increased compared to control cells. Interestingly, O-GlcNAc was increased in the same cells. This result was corroborated by western blot. Our results are in agreement with those reported in other carcinomas in which increased phosphorylation of AKT by O-GlcNAc was observed, suggesting that O-GlcNAcylation could be important in the PI3-kinase/Akt pathway to impact different cancer-associated cellular processes.

Victoria Jiménez-Castillo, Daniela Illescas-Barbosa, Edgar Zenteno, Beatriz XóchitlÁvila-Curiel, Maria Cristina Castañeda-Patlán, Martha Robles-Flores, Daniel Montante-Montes De Oca, Eduardo Pérez-Campos, AnayetzinTorres-Rivera, Abdelouhab Bouaboud, Patrick Pagesy, Carlos Josué Solórzano-Mata & Tarik Issad. Increased O-GlcNAcylation promotes IGF-1 receptor/Phosphatidyl Inositol-3 kinase/Akt pathway in cervical cancer cells. Sci Reports 2022 121.2022 Mar 16. https://www.nature.com/articles/s41598-022-08445-0.

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PROTEOMIC AND MOLECULAR STUDY OF SOMATIC EMBRYOGENESIS IN *COFFEA SPP.*

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Abstract:

The genus *Coffea* includes more than 127 species, of which *C. arabica* and *C. canephora* are the most economically important worldwide. Tissue culture is a tool that allows studying and understanding the mechanism of cell differentiation of different biological models. Among plant tissue culture, somatic embryogenesis (SE) allows the study of biochemical and molecular processes carried out during the development of various plant species. This process consists on that somatic cells, when cultivated under the right conditions, give rise to embryogenic cells that, when they go through morpho-physiological processes, produce somatic embryos and subsequently complete plants. In our laboratory, a protocol is being optimized to induce indirect SE in *Coffea arabica*, that is, from callus and cell suspensions; while for *Coffea canephora*, the standardized process for SE induction is performed directly on leaf explants. SE induction consists of two crucial stages: preconditioning and induction. In both biological systems, plant growth regulators (PGR) play an important role for the induction of SE, especially auxins. Genetic analyzes of the biology of auxin have revealed that its synthesis, as well as its transport, signaling and response to, are essential for SE to be carried out. Thus, the aim of this work is to study the proteome and identify the proteins that accumulate differentially throughout the induction process and, based on the results, to analyze their possible participation during cell differentiation and SE induction in *Coffea spp*.

IDENTIFICATION OF SIGNALING PROTEINS INVOLVED IN CD13-MEDIATED CELL ADHESION AND PHAGOCYTOSIS

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Abstract:

CD13 is a membrane-bound ectopeptidase expressed on various cell types and highly expressed on myeloid cells. CD13 is involved in various functions, such as proteolytic regulation of bioactive peptides, viral receptor, angiogenesis, and tumor metastasis. CD13 has also been implicated in cell adhesion and phagocytosis, as cross-linking of CD13 by certain CD13-specific antibodies induces these processes. Unfortunately, the CD13-interacting proteins involved in cell adhesion signal transduction and phagocytosis are still unknown.

We combined immunoprecipitation and liquid chromatography coupled to mass spectrometry methods and identified 12 CD13-interacting proteins by cross-linking CD13 on the cell membrane with antibodies. Considering the subcellular location, the list was reduced to 8 proteins corresponding to cytoplasmic and membrane proteins.

Interestingly, 2 of the 8 selected proteins, CAP1 and HSPB1, are found in focal and anchorage adhesions, which are specialized cellular structures formed in the processes of cell-matrix adhesion and cell-cell adhesion, respectively.

Encouragingly, among the 8 proteins identified we found the membrane protein FCGR1A, which we previously demonstrated colocalization with CD13 on phagosomes formed through FCGR1A-mediated phagocytosis, suggesting that the interaction between these receptors could have a functional implication in both FCGR1- and CD13-mediated phagocytosis.

In summary, CAP1, HSPB1 and FCGR1A were identified as CD13-interacting proteins that could be functionally involved in the CD13-mediated signaling pathway of cell adhesion and phagocytosis.

MEDIATOR18 REGULATES ARABIDOPSIS ROOT SYSTEM ARCHITECTURE, AUXIN SIGNALING AND IS A CRITICAL FACTOR FOR CELL VIABILITY IN ROOT MERISTEMS

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Abstract:

The Mediator (MED) complex plays a key role in the recruitment and assembly of the transcription machinery for the control of gene expression. Here, we report on the role of MEDIATOR18 (MED18) subunit in root development, auxin signaling and meristem cell viability in Arabidopsis thaliana seedlings. Loss-of-function mutations in MED18 reduce primary root growth, but increase lateral root formation and root hair development. This phenotype correlates with alterations in cell division and elongation likely caused by an increased auxin response and transport at the root tip, as evidenced by *DR5:GFP*, *pPIN1::PIN1-GFP*, *pPIN2::PIN2-GFP* and *pPIN3::PIN3-GFP* auxin-related gene expression. Noteworthy, *med18* seedlings manifest cell death in the root meristem, which exacerbates with age and/or exposition to DNA-damaging agents, and display high expression of the cell regeneration factor *ERF115*. Cell death in the root tip was reduced in *med18* seedlings grown in darkness, but remained when only the shoot was exposed to light, suggesting that *MED18* acts to protect root meristem cells from local cell death, and/or in response to root-acting signal(s) emitted by the shoot in response to light stimuli. These data point to MED18 as an important component for auxin-regulated root development, cell death and cell regeneration in root meristems.

SIMULTANEOUS EVALUATION OF CHANGES IN INTRACELLULAR CALCIUM, MEMBRANE POTENTIAL, AND INTRACELLULAR PH DURING CAPACITATION IN HUMAN SPERMATOZOA

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Abstract:

Capacitation is defined as a series of physiological changes that occur in mammalian sperm during their journey through the female reproductive tract to acquire the ability to fertilize an oocyte (Chang, 1951). Among the changes that the sperm develops is the increase in the amplitude of the flagellar beat called hyperactivation, (Ritagliati et al., 2018); and the acrosomal reaction, an exocytosis process that releases enzymes facilitating the penetration of the sperm and the subsequent fusion of the pronuclei (Gervasi & Visconti, 2016).

Particularly, three molecular parameters that occur during capacitation have been proposed: a) increased intracellular calcium levels, b) alkalization of the cytoplasm, and c) hyperpolarization of the plasma membrane. These changes are closely related to each other since at a functional level: they act as positive regulators in cell metabolism and swimming, producing hyperactivated motility and the development of the acrosomal reaction. Therefore, such changes are considered markers of the training process and have even been proposed as fertility predictors (Matamoros-Volante et al., 2021). However, these changes have not been determined simultaneously in sperm during capacitation.

Using flow cytometry coupled to imaging, and florescent dyes that allow determination of these capacitation markers, we simultaneously analyzed these three parameters in the subcellular segments of sperm, at different capacitation times.

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EFFECT OF NOBILETIN ON THE SCC-9 CELL LINE IN THE INDUCTION OF APOPTOSIS AND CELL MIGRATION

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Abstract:

Squamous cell carcinoma of the tongue (TSCC) has increased its incidence in Mexico from 1 to 5% in recent decades. It is a pathology of epithelial origin, which has been related to alcohol consumption, tobacco use and papillomavirus infections. It is an aggressive cancer, characterized by inhibition of apoptosis, self-sufficiency to growth signals, tissue invasion, metastasis, unlimited division and angiogenesis. Its late diagnosis requires multidisciplinary management such as surgery, chemotherapy, radiotherapy and/or immunotherapy and sometimes glossectomy is used. The treatment scheme is invasive and affects the quality of life and limits the survival of patients, in addition to affecting healthy cells. For this reason, various research groups have devoted themselves to the search for alternative treatments. Flavonoids have been widely studied in recent decades, they belong to the group of polyphenolic compounds and are secondary metabolites of plants. Its anticancer activity acts on various molecular and biochemical targets, which are related to its molecular structure, concentration and type of cancer. Nobiletin belongs to the group of methoxylated flavones, lipophilic and permeable, which is extracted from the peel of citrus fruits, which has shown chemopreventive activities in breast, gastric, colon, ovarian, pancreas and nasopharyngeal carcinoma. Currently, its effect on TSCC has not been characterized with certainty, so in the present study we evaluated the effect of nobiletin on the Scc-9 cell line, derived from TSCC9, on the induction of apoptosis and cell migration. Our results show that nobiletin has an anticancer effect because it promoted viability and migration inhibition, induction in the formation of apoptotic bodies, decreased phosphorylation of kinases, including those involved in the PI3K/AKT and ERK/p38 pathways. Similarly, it induces a change in the ratio of the expression of pro-apoptotic and anti-apoptotic proteins, as well as the regulation of caspase -9 and -3, in addition to PTEN. These data suggest that flavone could act as a chemoprotective agent against TSCC. Potential therapeutic agent for future research in in vivo models. Keywords: Squamous cell carcinoma, nobiletin, flavonoids and apoptosis.

Keywords: Squamous cell carcinoma, nobiletin, flavonoids, apoptosis.

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NOBILETIN REGULATES INVASION, MIGRATION AND METASTASIS IN SQUAMOUS CELL CARCINOMA OF THE HYPOPHARYNX

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Abstract:

Squamous cell carcinomas of the head and neck are very aggressive and are diagnosed in late stages, metastases. In Mexico, it represents 90% of oral neoplasms and with a 5-year survival rate. Three treatments are used for hypopharyngeal cancer: radiation therapy, chemotherapy, and surgery; its side effects include nausea, fatigue, sores in the mouth and throat, difficulty opening the mouth, and dental problems. For these reasons, the search for new treatments of natural origin is intended. Nobiletin 5, 6, 7, 8, 3´, 4´-hexamethoxyflavone is a polymethoxyflavone that inhibits proliferation and migration in different types of cancer. Its effect on squamous cell carcinoma of the hypopharynx has not currently been evaluated. For these reasons, it is intended to evaluate the effect of nobiletin on the invasion, migration and metastasis in the FaDu cell line, derived from squamous cell carcinoma of the hypopharynx. An experimental and longitudinal study was carried out on the FaDu cell line, treated with nobiletin at different concentrations in each of the experiments. We determined cell viability with the MTT (3-2-5-diphenyl-tetrazolium) assay, migration by the transwell and Wound-healing assay, formation of apoptotic bodies with the TUNEL assay, cell morphology with thiazole orange, phosphorylation of protein kinase by Western Blot and ELISA assays to evaluate vascular endothelial growth factor. Our results showed that nobiletin inhibited proliferation, induced apoptotic body formation and changes in cell morphology in a dose-dependent manner. Cell migration and invasion at 50 µM negatively regulated Bcl-2/Bax expression; these data suggest that cell viability is reduced by inducing apoptosis. In addition, it regulated the phosphorylation of the ERK/JNK and PI3K/AKT pathways; PTEN expression and MMP 2 and 9 activity. These results suggest that nobiletin inhibits cell metastasis. MAPK inhibitors. PI3K and MEK reversed nobiletin processes on VEGF viability and expression in FaDu cells. Nobiletin presented anticancer properties, a possible treatment alternative in future research for oral squamous cell carcinoma of the hypopharynx, since it inhibited cell proliferation by 40%, decreased migration and induced apoptosis by regulating kinase B and phosphoinositol 3 kinase.

Key words: oral squamous cell carcinoma, flavonoids, nobiletin, apoptosis.

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DISSECTING THE ACTIVATION OF GROUP I PAK KINASES BY USING A FRET BASED BIOSENSOR

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Abstract:

PAK kinases are important regulators of a variety of cellular processes, including cell motility, cell division, gene transcription and apoptosis. Its aberrant activity leads to the development of several pathologies, including cancer and neurodegenerative diseases. Due to this strong implication in human health, the signaling patways regulated by PAKs are a subject of intensive reserach. However, the fine control of localization and activation of PAKs remains elusive. Here, we report the design of a Group I PAK genetically-encodable FRET-based biosensor, which is phosphorylated in vitro by PAK1 but not by the closely related Group II PAK family member PAK4 nor by another protein kinases, and it is activated in cells by EGF stimulation or by co-expression of constitutively active PAK1, Rac1 and Cdc42, but not by RhoA. As these kinases participate in regulating diverse fundamental cellular functions, a number of which require translocation into different cellular compartments, it is important to understand how PAKs activity is specifically regulated in these locations. To this end, we targeted our FRET-based biosensor to the cell membrane and to the cytoplasm to examine PAK activity dynamics in these cellular compartments. Our results showed that membrane-targeted Group I PAKs activity differs from that in the cytoplasm, indicating differential regulation of PAK activity at different subcellular locations.

CONTRIBUTION OF THE MITOGEN-ACTIVATED PROTEIN KINASE HOG1 TO THE HALOTOLERANCE OF THE MARINE YEAST *DEBARYOMYCES HANSENII*

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Abstract:

Halotolerant species are adapted to dealing continually with hyperosmotic environments, having evolved strategies that are uncommon in other organisms. The HOG pathway is the master system that regulates the cellular adaptation under these conditions; nevertheless, apart from the importance of *Debaryomyces hansenii* as an organism representative of the halotolerant class, its HOG1 pathway has been poorly studied, due to the difficulty of applying conventional recombinant DNA technology. In our publication, we described for the first time the phenotypic characterisation of a null *HOG1* mutant of *D. hansenii*. *Dhhog1Δ* strain was found moderately resistant to 1 M NaCl and sensitive to higher concentrations. Under hyperosmotic shock, DhHog1 fully upregulated transcription of *DhSTL1* and partially upregulated that of *DhGPD1*. High osmotic stress lead to long-term inner glycerol accumulation that was partially dependent on DhHog1. These observations indicated that the HOG pathway is required for survival under high external osmolarity but dispensable under low and mid-osmotic conditions. It was also found that DhHog1 can regulate response to alkali stress during hyperosmotic conditions and that it plays a role in oxidative and endoplasmic reticulum stress. Taken together, these results provide new insight into the contribution of this MAPK in halotolerance of this yeast.

Sánchez, N. S. et al. Current Genetics (2020) 66:1135–1153
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CHARACTERIZATION OF NON-CANONICAL WNT SIGNALING IN CANCER STEM CELLS OF COLORECTAL CANCER

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Abstract:

Colorectal cancer (CRC) is one of the types of cancer with the highest incidence and mortality worldwide. CRC is considered as an aberrant Wnt pathway disease, because mutations in APC, antagonist of Wnt pathway, are recognized 70-80% of CRC cases and they are the first genetic alterations detected within the process that will progress to CRC. Specifically, APC is involved in degradation of β-catenin, transcriptional coactivator responsive to Wnt ligands (1). Wnt pathway, where β-catenin participates, being the first and the most described, has been given the name of canonical. Furthermore, Wnt ligands are capable of activate β-catenin-independent transduction so these molecular mechanisms downstream of Wnt signal are categorized as non-canonical. For many years, it was thought that the activation of Wnt pathways, both canonical and non-canonical, occurred in a linear manner and even in an antagonistic form between them. However, current evidence begins to establish that this does not necessarily happen in all cases. In our laboratory, it was previously shown that in RKO cells, a cell line from CRC, Wnt/ β-catenin (canonical) and Wnt/ calcium (non-canonical) are activated simultaneously, affecting cellular migration (2). Wnt/ β-catenin is also related to maintenance of normal and cancer stem cells (CSC), the latter cellular subpopulation being crucial in tumors, due to their characteristics such as chemoresistance and self-renewal. In contrast, evidence is scant regarding the involvement of non-canonical Wnt pathway in CSC. Therefore, the objective of the present work is to know whether non-canonical Wnt pathway participates in functions of CSC. The results show that β-catenin-independent Wnt pathways promote self-renewal and proliferation of CSC in RKO and SW480, a cell line that has the truncated form of APC, and therefore, representative of the majority of cancer cases.

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INCREASED *O*-GLCNACYLATION PROMOTES IGF-1 RECEPTOR/PHOSPHATIDYI INOSITOL-3 KINASE/AKT PATHWAY IN CERVICAL CANCER CELLS

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Abstract:

O-GlcNAcylation is a reversible post-translational modification on serine and threonine residues of cytosolic, nuclear and mitochondrial proteins. O-GlcNAcylation level is regulated by OGT, which adds GlcNAc on proteins, and OGA, which removes it. Abnormal level of protein *O*-GlcNAcylation has been observed in numerous cancer cell types, including cervical cancer cells. In the present study, we have evaluated the effect of increasing protein *O*-GlcNAcylation on cervical cancer-derived CaSki cells. We observed that pharmacological enhancement of protein *O*-GlcNAcylation by Thiamet G (an inhibitor of OGA) and glucosamine (which provides UDP-GlcNAc substrate to OGT) increases CaSki cells proliferation, migration and survival. Moreover, we showed that increased *O*-GlcNAcylation promotes IGF-1 receptor (IGF1R) autophosphorylation, possibly through inhibition of protein tyrosine-phosphatase 1B activity. This was associated with increased IGF-1-induced phosphatidyl-Inositol 3-phosphate production at the plasma membrane and increased Akt activation in CaSki cells. Finally, we showed that protein *O*-GlcNAcylation and Akt phosphorylation levels were higher in human cervical cancer samples compared to healthy cervix tissues, and a highly positive correlation was observed between *O*-GlcNAcylation level and Akt phosphorylation in theses tissues. Together, our results indicate that increased *O*-GlcNAcylation, by activating IGF1R/ Phosphatidyl inositol 3-Kinase (PI-3K)/Akt signaling, may participate in cervical cancer cell growth and proliferation.

Jiménez-Castillo, *V.*, Illescas-Barbosa, D., Zenteno, E. *et al.* Increased *O*-GlcNAcylation promotes IGF-1 receptor/Phosphatidyl Inositol-3 kinase/Akt pathway in cervical cancer cells. *Sci Rep* 12**,** 4464 (2022). https://doi.org/10.1038/s41598-022-08445-0

TGF-β/SMAD CANONICAL PATHWAY INDUCES THE EXPRESSION OF TAZ (WWTR1) TRANSCRIPTIONAL COFACTOR IN LIVER CANCER CELLS

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Abstract:

In the liver, the TGF-β and Hippo pathways are critical for organ size control, tissue regeneration, and cancer progression. The transcriptional cofactor TAZ, also named WWTR1, is a downstream effector of Hippo pathway that plays a key role in the maintenance of liver physiological functions. However, the upregulation of *TAZ* expression has been associated with the progression of liver cancer. Recent evidence shows crosstalk of TGF-β and Hippo pathways since TGF-β modulates *TAZ* expression through different molecular mechanisms in a cellular context-dependent manner. Here, we evaluate the molecular interplay between the TGF-beta/Smad canonical pathway and *TAZ* expression. We analyzed the *TAZ* gene promoter sequence, identifying SMAD binding elements. Our results suggest that TGF-β/SMAD canonical pathway induces the activity of the *TAZ* gene promoter, increasing its mRNA levels and, subsequently, its protein levels in HepG2 cells. In addition, TGF-b signaling promotes TAZ protein nuclear localization. Thus, this work provides evidence that the TGF-β/SMAD canonical pathway exerts crosstalk with the Hippo pathway by enhancing TAZ levels and its nuclear accumulation in liver cancer cells.

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ACTIVATING THE CD95/CD95L PATHWAY INDUCES PROLIFERATION IN HPV+ CERVICAL CANCER CELLS

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Abstract:

Cervical cancer is the fourth most common cancer in women. In Mexico, it represents the second cause of women's death and continues to be a significant public health problem. Therefore, it is necessary to study new molecules that can promote the elimination of tumour cells and serve as therapeutic targets that affect the immune system. Cancer cells have different ways of escaping from apoptosis. Like, modification of the expression of pro- and anti-apoptotic proteins, as well as the expression of CD95 at the cell membrane. Several studies have shown that CD95 signalling cascades are often altered in malignant tumours, leading to non-apoptotic signaling that contributes to tumour growth, invasion and pro-inflammatory roles. However, the role of the CD95 pathway is not fully elucidated in cervical cancer. For this purpose, we determined the presence of CD95, its cognate ligand CD95L and its role in the cell proliferation of cervical cancer cells. Extracellular and intracellular staining of CD95 and CD95L in HeLa (HPV18+), INBL (HPV18+), Caski (HPV16+) and C33A (HPV-) was determined by flow cytometry. Cell lines were incubated in the presence of different concentrations of recombinant CD95L to determine its effect on cell proliferation which was evaluated by the cristal violet technique. HPV-positive cells express CD95 extracellularly in more than 90% of the cells. However, the C33A cell line, negative for HPV, expresses a very low percentage of CD95 extracellularly. CD95L is present in the cytoplasm of the cervical cell lines. Stimulating the CD95 pathway with low concentrations of CD95L in cervical cancer cells induce cell proliferation. On the contrary, high concentrations of CD95L inhibit cell proliferation and induce apoptosis. The activation of the CD95 pathway can induce proliferation and apoptosis in a dose-dependent manner. Our results suggest that cervical cancer cells use the CD95 pathway to promote cell proliferation and survival. The presence of both the CD95 receptor and the ligand confers apoptosis resistance to cervical cancer cells.

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ROLE OF THE GPR30 RECEPTOR IN THE EPITHELIAL-MESENCHYMAL TRANSITION INDUCED BY IL-6 IN LUMINAL BREAST CANCER CELLS

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Abstract:

Breast cancer is the leading death caused by malignant neoplasm worldwide. The luminal subtype responds to the stimulus of 17-β-estradiol (E2), allowing the activation of receptor ER-α and the transcription of genes that promote carcinogenic characteristics. Likewise, the enzyme phosphatase with homology to Src protein domain 2 (SHP2) is a target gene of ER-α, and its expression is critical for the epithelial-mesenchymal transition (EMT). IL-6 secretion by cancer-associated fibroblasts promotes the proteasomal degradation of ER-α as well as drug resistance and metastasis[1]. However, the IL-6-induced EMT underlaying mechanisms are unknown. Also, the GPR30 receptor is an alternative receptor for E2, which could regulate ER-α target genes and the activation of SHP2 pathway. This work aims to elucidate the role of GPR30 in the IL-6-induced EMT in luminal breast cancer cells. We observed that E2 promotes the proliferation of the luminal breast cancer cells MCF-7; however, IL-6 inhibited this effect. Besides, cells treated with the MG132 proteasomal inhibitor reverted this effect, supporting the role of IL-6 in the ER-α proteasomal degradation. Also, these treatments have no effect on normal (MCF-12) mammary epithelial cells or triple-negative cancer cells (MDA-MB-231). Besides, E2 does not affect migration or invasion of MCF-7. In spite of that, IL-6 or the co-treatment with E2 inhibited both events in luminal and triple-negative breast cancer cells. In addition, these effects were inhibited by G15, an antagonist of GPR30, suggesting that IL-6 induces the TEM in MCF-7 cells through GPR30.

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EVALUATION OF THE ANTI-ADIPOGENIC EFFECT OF NOVEL ESTROGEN RECEPTOR BETA LIGANDS

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Abstract:

One of the strategies used in the search for new treatments against obesity, the pandemic of the 21st century, is the *in silico* design and *in vitro* characterization of new ligands of the estrogen receptor beta (ERβ), because its activation has been associated with the inhibition of adipogenesis and promotion of browning. Therefore, in this work we carried out molecular dynamics studies and ADME-Tox analysis of six molecules (A-F) found by molecular docking by the group of Dr. Gildardo Rivera. The analysis of the RMSD and RMSF values indicated that molecules A, B and D allowed the formation of a stable complex with ERβ, in addition to maintaining the six mobile regions of the protein. Furthermore, all six molecules presented a safe ADME-Tox profile. On the other hand, treatment of 3T3-L1 cells with 10 μM of molecules A and B during the first three days of the adipogenesis protocol inhibited the formation of lipid droplets until the seventh day of culture. Using the ORO stain, a reduction in lipid accumulation of approximately 40% was observed. Likewise, real-time RT-PCR assays showed, that molecule A reduced the expression of the pro-adipogenic markers PPARγ and C/EBPα by 50% and 82%, respectively, while molecule B, decreased the expression of the same transcription factors by 83% and 59%. In contrast, molecule D did not show any significant effect on the 3T3-L1 line. These results show the potential of molecules A and B for the control of adipogenesis, however, it is necessary to confirm whether their mechanism of action involves binding to ERβ.

BIOCHEMICAL AND MOLECULAR CHARACTERIZATION OF A 29 KDA PROTEIN FROM *SYMBIODINIUM MICROADRIATICUM* CASSKB8 THAT IS PHOSPHORYLATED ON THREONINE IN RESPONSE TO LIGHT

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Abstract:

Symbiodinium microadriaticum is a photosynthetic dinoflagellate that can exist as a free-living organism or in symbiosis with *Cassiopea xamachana*. Due to their photosynthetic nature, dinoflagellates require mechanisms to respond to light stimuli, which are sensed by specific receptors. Such receptors can respond to specific wavelengths, and include the phytochromes, cryptochromes, melanopsis and phototropins. The stimuli result in a signaling cascade, where phosphorylation/dephosphorylation events are fundamental to activate physiological responses in the cell. In *S. microadriaticum* CassKB8, information of the light sensing mechanisms and the signaling pathways that occur downstream are not known in detail. We have previously characterized SBiP1, a 75 kDa protein that was highly phosphorylated on Thr under darkness, but upon light stimulation, significantly decreased its phosphorylation level in three different species of Symbiodiniaceae including *S. microadriaticum* CassKB8[1, 2]. In parallel, we observed a protein with an apparent molecular weight of 29 kDa (p29), which displayed the opposite behavior; that is, it became significantly phosphorylated on Thr upon the light stimulus in dark-adapted cells from two different species of Symbiodiniaceae. This phosphorylation occurred very fast since it was observed after a stimulus of as short as 30 sec of light. This suggests a signaling cascade with an upstream fast-responding photoreceptor. Therefore, identification of p29 will be fundamental to dissect the pathway. We are currently isolating p29 by 2D electrophoresis for that purpose.

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1.Castillo-Medina, R. E., Islas-Flores, T. & Villanueva, M. A. (2019). PeerJ, 7, e7406.
2.Castillo-Medina, R. E., Islas-Flores, T. & Villanueva, M. A. (2022).
Acta Biochimica Polonica, 69(1), 155-164

A PTP1B-CDK3 SIGNALING PATHWAY REGULATES CELL CYCLE PROGRESSION THROUGH RB-E2F ACTIVATION IN HUMAN GLIOBLASTOMA CELLS

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ABSTRACT:

Glioblastoma (GB) is the most frequent and aggressive malignant primary tumors in the Central Nervous System (CNS), and represents an important health problem due to its high rate of mortality and the lack of an effective therapy. Therefore, the identification of new potential drug targets may provide novel therapeutic strategies for the treatment of these brain tumors. Recent evidence indicates that Protein Tyrosine Phosphatase 1B (PTP1B) is overexpressed in different types of cancer. However, the role of this enzyme in GB development remains elusive.

Using a SILAC-based phosphoproteomic approach we identified the Cyclin-dependent kinase 3 (Cdk3) as a novel PTP1B substrate. Local docking and molecular dynamics studies revealed stable interactions between PTP1B's catalytic domain and Cdk3. In addition, an *in vitro* phosphatase assay confirmed that PTP1B dephosphorylates Cdk3 at Tyr15. Interestingly, these two proteins interact in the nuclear envelope of HEK293-T cells, as well as in the nucleus and cytoplasm of human GB cell lines. Finally, our results showed that pharmacological inhibition of PTP1B promotes a delay in cell cycle progression. PTP1B inhibition significantly reduces Cdk3 activity, with the consequent repression of E2F transcriptional activity in an Rb dependent-manner, and the down-regulation of E2F target genes Cdk1, Cyclin A, and Cyclin E1. These findings delineate a new signaling pathway from PTP1B to Cdk3, needed for efficient cell cycle progression in an Rb-E2F dependent manner in human GB cells, and suggest new therapeutic strategies for the treatment of this type of tumors.

Keywords: Protein Tyrosine Phosphatase 1B, Cell Cycle, CDK3, Cancer, Glioblastoma.

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SBIP1 IS A CHAPERONE FROM SYMBIODINIACEAE THAT IS ACTIVATED BY LIGHT AND TEMPERATURE

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Abstract:

Symbiodiniaceae are photosynthetic microalgae that establish endosymbiosis with reef-building corals and provide them with an important energy input for their growth and support. The prolonged and increasingly intense temperatures due to global warming compromise the physiology of these microalgae and thereby, the coral ecosystems that depend on it. Thus, it is important to study the molecular mechanisms involved in the responses to temperature changes in these cells. In a previous study in Symbiodiniaceae using dark-to-light transition assays, we detected an endoplasmic reticulum HSP70 family chaperone that we named SBiP1, and whose level of Thr phosphorylation is modulated by light (Castillo-Medina et al. 2019). This protein is activated by light via its dephosphorylation, presumably to assist newly synthesized light-dependent proteins. In general, HSP70 proteins are recognized for their assistance in the correct folding of proteins, which includes misfolded proteins during heat stress events. Here, we determined whether SBiP1, in addition to acting as a chaperone for newly synthesized proteins, also acts as a chaperone for such misfolded proteins by stress in *Symbiodinium microadriaticum* CassKB8. We found that exposing cells for 30 min at 32 ºC in dark conditions caused Thr dephosphorylation of the protein. Likewise, when the cells were exposed to 32 ºC for a prolonged period of 12 h in the dark, the highly phosphorylated SBiP1 was converted into a protein with a low level of phosphorylation. Both results were similar to those on the response to the light stimulus at a control temperature of 26 ºC. These data indicate that SBiP1 activation is not light-dependent and suggest that its chaperone function may occur both under conditions of homeostasis during protein synthesis, and also triggered by heat stress events.

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EVALUATION OF AKT AND NF-κB SIGNALING IN MCF-7 CELLS EXPOSED TO SERA FROM OBESE WOMEN TREATED WITH METFORMIN

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Abstract:

Breast cancer is a public health problem worldwide, accounting for 46.3% of all neoplasms in women and 15 % of deaths from the neoplastic disease. Breast cancer is a multifactorial disease, but obesity has been associated with a 26% increase in the probability of developing a neoplasm in the breast tissue of postmenopausal women. Within the therapies for treating breast cancer, Metformin has shown a protective effect against the development of this neoplasm in 30% of users. However, in vitro studies have reported the use of high concentrations of the drug that exceed the bioavailable concentration in blood. Using human breast cancer cells MCF-7 for the evaluation of the IR/Akt/p70S6K pathway and the proliferation response, we compared human sera with different metabolic and hormonal characteristics. Our results showed an increase in Akt phosphorylation that had a direct effect on cell viability under stimulation with sera from obese women. In particular, sera from obese postmenopausal women induced higher proliferation rates associated with increased Akt phosphorylation, which was reversed by short-term Metformin treatment in women with insulin resistance. Contrary to what was observed in women without insulin resistance who presented the negative regulation of the NF-kB pathway.

ABSTRACTS | Posters Systems Biology & Bioinformatics

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MEMORY IN TRANSCRIPTIONAL REGULATORY DYNAMICS OF *ESCHERICHIA COLI* IN STRESSFUL ENVIRONMENTS

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Abstract:

Bacteria live in dangerous environments that alternate between the presence and absence of stressful conditions. To 'remember' exposure to previous hostile environments, microbes often keep information obtained while they were in the presence of the stimulus, for example, through epigenetic modifications or by inheriting proteins and transcription factors from their ancestors(Govers et al. 2018). Previous studies have shown that transcriptional regulatory dynamics in response to stress are transitory and reversible, and can modify global patterns of gene expression that are stably maintained even in the absence of the stimulus that triggered the stress response(Bheda 2020). In this work, we focus on evaluating the role of hysteresis in the transcriptional regulatory dynamics of *Escherichia coli* in response to fluctuating environments that alternate between the presence or absence of a semi-lethal concentration of a beta-lactam antibiotic. We quantified gene expression dynamics using transcriptomics and a library of fluorescent reporters, allowing us to identify genes that stably maintain their differential expression upon removal of the antibiotic. Using high-throughput experimental assays, we also evaluated how these genes can modify the survival probability of bacteria to subsequent exposure to different antimicrobial substances. Interestingly, we found that genes that maintain their differential expression are mostly implicated in core metabolic functions, suggesting a link between bacterial metabolism and drug tolerance. We conclude by arguing that identifying genes implicated in maintaining a memory of previous stressful environments can be used for the design of rational treatment strategies that are effective at suppressing pathogenic bacterial populations.

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IN SILICO CHARACTERIZATION OF BGC´S OF LANTHIPEPTIDES II LOCATED BY GENOME MINING IN CLOSTRIDIALS

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Abstract:

The growing antimicrobial resistance (AMR) is an urgent problem that puts medical advances and our current way of life at risk. The development of new antibiotics classes has slowed since the 1980s despite constituting an important approach to addressing AMR. Our workgroup is focused on secondary metabolites as a source to develop new antibiotics. Among these, lanthipeptides are RIPPS (ribosomally synthesized and post-translationally modified peptides) with structure and biological activities that have been under research. This class of peptides shows little resistance, as reported with nisin A, a common food preserver. The activity of different Lantipeptide has also been tested to combat problematic strains, including Clostridiodes difficile. The genome mining strategy was used to discover biosynthetic gene clusters (BGC´s) of lanthipeptides II. LanM sequences (biosynthetic enzymes for post-translational modification of the precursor peptide) from the MIBiG database were analyzed with BLAST resulting in the identification of around 300 genes that synthesize new LanM. Subsequently, a LanM phylogenetic analysis found 39 homologs belonging to 28 bacterial genomes of the Clostridiodes order, this order has been extensively studied, but not for their metabolic machinery. The genomes associated with the selected LanM were analyzed with the antiSMASH platform to identify BGCs. After a manual characterization, based on a verification of the presence of all the essential genes, enzyme domains, phylogenetic background, peptide structure, and physicochemical qualities, 10 BGC's were selected as complete and capable to have a biosynthetic pathway to producing class II lantibiotics. The strategy allowed us to identify 23 lantibiotics associated with the BGC's selected. The BGC NC_014393-R18 from *Clostridium cellulovorans* 743B, associated with 2 lantibiotics, was selected as a candidate for an *in silico* characterization of its essential genes associated with studies based on phylogeny, conserved domains, and structural folding of its products, these studies suggest a high probability of activity *in vivo*, so the construction of a biological system based on vectors for the heterologous expression of lanthipeptides would allow testing their antibiotic activity against resistant bacteria, as well as their structural and chemical characterization in future works. The present work demonstrated the capacity of genome mining and bioinformatics for the exploration of genetic and chemical spaces of class II lanthipeptides, which allowed the identification of possible new members of this type of natural product in clostridial.

HORMONE SIGNALING CROSSTALK IN THE ARABIDOPSIS INTERACTOME

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Abstract:

Phytohormones regulate every aspect of a plant's life. The participation of auxins and cytokinins in promoting apical growth in the shoot and the root, respectively; the importance of ethylene in fruit ripening; and the involvement of gibberellins in the activation of seed germination are some examples of the critical role of phytohormones. The physiological responses to hormones usually start with the perception of the molecule; then, a signal is transduced (involving activators, repressors, or phosphorylation) to trigger a transcriptional response via transcription factors. Several of the steps mentioned above rely on protein-protein interactions (PPIs). Additionally, the physical contact between proteins often alters their 3D conformation and can also block or enhance their functions.

This work explored the crosstalk between phytohormone signaling pathways established via physical contact to find interactors of well-known proteins that mediate hormone responses. First, we retrieved information about PPI in Arabidopsis and built a protein-protein interaction network containing 57 937 interactions. Then, we highlighted proteins involved in hormone signaling pathways; our work focused on seven pathways: auxins, cytokinins, gibberellins, brassinosteroids, abscisic acid, ethylene, and jasmonic acid. We identified 340 interactions between 170 proteins participating in 3 key steps of signaling: reception, signal transduction, and transcriptional responses. We observed a high interconnection between proteins involved in the different signaling pathways. Then, to find potential regulators of the signaling pathways, we focused on the first neighbors of the hormone-related network and identified 1100 proteins that interact with them.

Interestingly, we detected several proteins that interact with proteins from different pathways. We are now assessing the functional relevance of the identified hubs. The latest results will be presented.

Keywords: Plant development, Plant hormones, Protein-protein interactions, transcription factors

STRUCTURAL BASIS AND FUNCTIONAL SPECIFICITY OF A CYCLO/MALTODEXTRIN ABC IMPORTER SYSTEM FROM THERMOANEROBACTERALES

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Abstract:

Carbohydrate metabolism via cyclo/maltodextrins (CM-C/D) is an uncommon pathway for starch assimilation that includes the formation of heat-resistant cyclodextrins (CDs) and linear dextrins using extracellular cyclomaltodextrin glucanotransferases (CGTases). The CM-C/D pathway is essential for hyperthermophilic microorganisms (>70°C) living in starch-poor environments since CDs are related to resource competition in microbial communities, such as monopolizing substrate availability or mitigating the toxicity of surrounding organic substrates and volatiles, as well as carrying antimicrobial and signaling molecules. This work revealed a putative C/D ABC importer system (MdxEFG-MsmX) from hyperthermophilic bacteria by database mining ~246 public genomes from Thermoanaerobacterales. Sequence analysis also revealed that the *mdx*EFG importer cassette belongs to a gene cluster for the CM-C/D pathway, which is conserved in 22 genomes from 3 different species (*Caldanaerobacter*, *Thermonaerobacter*, and *Thermoanaerobacterium*). Structural analysis of the MdxEFG importer system from *Thermoanaerobacter mathranii* showed that MdxE binding protein includes a sugar-binding site for C/D molecules, which CGTases synthesize. Subsequently, MdxE releases the C/D molecules into the MdxFG permease subunits, which internalize them into the cytoplasm using a promiscuous MsmX ATPase. Structural analysis, docking simulations, homology modeling, and biochemical studies revealed that the recombinant MdxE binding protein could recognize, bind, and deliver C/D molecules to the MdxFG system, providing new insights into a nonclassical pathway for starch metabolism in hyperthermophilic bacteria.

Keywords: *cyclodextrins; hyperthermophilic bacteria; starch metabolism; structural biology*

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METABOLIC RESPONSES OF BACTERIAL COMMUNITIES TO DISCHARGED XENOBIOTICS BY THE CHICXULUB RING OF CENOTES

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Abstract:

The development of high throughput sequencing technologies and bioinformatic tools have led to expand the knowledge of microbial diversity, as well as its metabolism and community relationships. Recently, there is a consensus regarding the potential of the Yucatán Coast on producing new knowledge about microbial communities. By processing georeferenced information concerning both local geohydrology and agricultural activities, two zones were determined as potential sites where pollutants are discharging by groundwater fluxes (Sisal-Palmar in the west, and Dzilam-Bocas in the east). We sampled wetland sediments from two locations in each zone: one conserved and another perturbed. The taxonomic composition of microbial communities was determined by using 16S rRNA amplicon sequencing and Quantitative Insights Into Microbial Ecology (QIIME2). Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt 2) was also performed to investigate xenobiotic-associated pathways. We discovered that differences in bacterial communities were significant at the zone (east-west) and not with the conservation status of each site, following a similar spatial pattern as that for groundwater fluxed of the Chicxulub Ring of Cenotes. We also found that *Dehaloccodia* was highly present in the eastern zone, which was reported to reductively dehalogenate organochlorides. Additionally, the metabolic pathway of Nitrotoluene degradation has also higher rates in the east zone. Conversely, this phylum and this pathway showed lower rates in the west zone. This spatial pattern was consistent with the geographical distribution of regional agricultural activities.

QUEST FOR BACTERIOPHAGES IN SOILS AND RHIZOSPHERES FROM MEXICO

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Abstract:

Bacteriophages are biological entities that can regulate host population size, maintain diversity, and mediate horizontal gene transfer. Phage ecology has been extensively explored in aquatic environments. However, the role of bacterial viruses in terrestrial ecosystems remains unexplored, even though soils represent a wide taxonomic diversity of microorganisms. Moreover, phage-bacteria interactions are essential in the ecology and evolution of these soil microbial communities. Here, we searched for bacteriophages in soil and rhizospheres metagenomes to determine their taxonomic diversity in these environments. We created a unique database of bacterial viruses with which we could determine a profile of the present taxa, the phylum Uroviricota the most abundant in all samples. Of the 278 viral genera found in samples associated with soils and rhizospheres, eight belonged exclusively to soils and 256 to rhizospheres. Soil phages such as *Friunavirus, Pahsextavirus, Rogunavirus,* and *Uedamuthuvirus* have been associated with phyla Proteobacteria and Firmicutes hosts. On the other hand, *Shapirovirus, Unahavirus, Asteriusvirus,* and *Shamshuipovirus* in rhizospheres have been associated with hosts of phyla such as Proteobacteria and Bacteroidetes. Finally, the diversity indices calculated for soils and rhizospheres show that phage diversity increases from soil to rhizosphere, indicating that these systems are very diverse. So far, we have recovered phages in terrestrial environments using our unique bacterial virus database, demonstrating that it is possible to identify genera of these microorganisms in soils and rhizospheres compared to the NCBI viral databases.

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IN SILICO AND *IN VITRO* STUDY OF ANTI PROLIFERATIVE COMPOUNDS IN BREAST CANCER FOR PKM2 AND HDAC8

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Abstract:

Cancer is a disease with a high rate of morbidity and mortality worldwide; in our country its control and treatment are still uncertain. It is a topic of interest in research in the medical and pharmaceutical chemical area; The development of new techniques by computational methods, aims to design and propose new therapeutic agents through molecular coupling that allows a series of predictions to be made in the most probable orientation and position between a molecule. Previous studies have shown that proteins such as PKM2 and HDAC8 are targets of interest in cancer development; likewise, the study of compounds directed to them have had favorable but inconclusive results, which has motivated to continue investigating the chemical structure and its modifications, in order to improve and observe a better antineoplastic effect. The research work presented is currently in progress and is based on the molecular coupling between compounds with promising anti proliferative activity (derivatives of quinazolines, imidazolines, DASA 58 and C9) with proteins highly expressed in cancer such as PKM2 and HDAC8. The results obtained so far reflect good binding energy (compound NM6 ΔG -7.2, N2A ΔG -7.67, 20N ΔG -7.3, 14N ΔG -7.22, 4N ΔG -7.33). The amino acids (LEU218, LEU211, PHE244, PRO117, ALA214,) and the participating interaction links are coincident, giving stability to the compounds.

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REGULATION OF TRANSCRIPTOME OF TROPHOBLAST CELLS BY CALCITRIOL AND TGF-β1

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Abstract:

Calcitriol and transforming growth factor beta (TGF-β1) are molecules whose effects on cells could be similar or opposite. Currently, there are several reports of independent effects of calcitriol and TGF-β1, however, there is no information regarding the combinatory effects of these compounds in placental cells. **Aim:** To study the effects of calcitriol, TGF-β1 and their combination upon the transcriptome of trophoblast cells using a whole genome microarray. **Methodology**: We used cultured syncytiotrophoblast cells to identify distinct transcriptional landscapes after each treatment. Total RNA samples were processed on Clariom D human microarray to assess global gene expression, followed by bioinformatics analysis. **Results:** Microarray analyses revealed a set of differentially expressed genes (DEG) by the treatments. Venn diagrams showed that most of the DEG were exclusive for each treatment, although 149 up-regulated DEG and 71 down-regulated genes overlapped among the different conditions. In addition, there were only 21 up- and 4 down-regulated common DEG. Enrichment pathway analysis identified that calcitriol modulates several genes involved in metabolic process of vitamins and steroids as well as in antimicrobial and immune responses. In relation to TGF-b1, this factor showed poor regulation in these cells, which was associated with immune response while the co-treatment up-regulated genes involved in neutrophil mediated immunity, biosynthesis process of unsaturated fatty acid and eicosanoids. In contrast, co-treatment down-regulated genes that are implicated in digestion, mobilization and transport of lipids and PPAR signaling pathway. **Conclusion:** Overall, the results showed DEG by each treatment that were associated with different transcriptional landscapes. In particular, the combinatory treatment showed that might regulate the development, defense, transport and lipids metabolism of placenta during pregnancy.

This work was supported by CONACyT, México [grant number 282770].

URINE AND PLASMA METABOLOMICS REVEALED ENDOTHELIAL DAMAGE IN SUBJECTS WITH THE CORONAVIRUS DISEASE (COVID-19)

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Abstract:

Introduction: Coronavirus disease (COVID-19) is the infectious pathology caused by the SARS-CoV-2 (1). Despite vaccination and treatment with antivirals, some subjects still develop mild to severe symptoms or ultimately die (2,3). Some studies suggest that the host's response to the virus may cause such health problems (4). However, available evidence regarding the molecular perturbations linked to COVID-19 is scarce.

Methods: Here, we performed a pilot study involving fourteen hospitalized subjects with COVID-19 (5 requiring mechanical ventilation, positive to a nasopharyngeal swab RT-PCR) and ten control subjects (medical professionals with no symptomatology). Urine and plasma were collected for mass spectrometry-based untargeted metabolomics and comprehensive chemoinformatics analyses. Multivariate and univariate analyses were applied to assess for grouping patterns and metabolites abundance differences among cohorts. Appropriate statistical tests also determined clinical and demographic differences.

Results: No differences in demographic parameters were found between COVID-19 and control cohorts. Ventilated subjects tend to be ten years older than non-ventilated COVID-19 subjects. Principal component analysis revealed a better differentiation of COVID-19 subjects when analyzing the urine metabolome, while the plasma metabolome better differentiated ventilated vs. non-ventilated COVID-19 individuals. More metabolites were found down-modulated in plasma, while more metabolites were up-regulated in urine when comparing COVID-19 vs. control subjects. We noted an array of novel dysregulated vasoactive peptides involved in the kinin family in COVID-19 subjects, including bradykinin, neurokinin A, and substance P metabolites.

Conclusion: We suggest that COVID-19 subjects experience a dysregulation in the kinin- kallikrein and tachykinin systems that may contribute to vascular endothelial dysfunction and cardiovascular disease development.

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COMPARATIVE MOLECULAR DYNAMICS SIMULATIONS OF ANTI-APOPTOTIC BCL2 PROTEIN IN APO AND HOLO FORMS

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Abstract:

Apoptosis is a natural process required for the removal of redundant cells during development, potentially dangerous cells and those in senescence. Cell death dysregulation has been implicated in a variety of human diseases such as cancer, neurodegenerative disorders, and autoimmunity. This process is regulated by several proteins among them, those belonging to the Bcl-2 family. Members of this family are grouped according to their participation in the apoptotic mitochondrial pathway in pro- and anti-apoptotic proteins. The members of this family are characterized by the Bcl-2 homology (BH) domains, BH1, BH2, BH3, BH4, as well as an intrinsically disordered region (IDR) depicted as “flexible loop domain” (FLD), and a transmembranal (TM) region that anchors mitochondrial outer membrane (MOM). The interaction between pro-apoptotic and pro-survival proteins of Bcl-2 family exquisitely regulate cell death.

We built models by homology of Bcl-2 full-sequence length in monomeric form (apo-Bcl-2) and in complex with the BH3 domain of Bax (holo-Bcl-2). The Bcl-2 protein was analyzed with its transmembrane domain anchored to a lipidic bilayer of DPPC, imitating physiological conditions. We performed molecular dynamics (MD) simulations using the GROMACS program and OPLS-AA force field. The simulations were performed under NPT conditions for 1 μs for each Bcl-2 (apo/holo) model). Here we show the result of simulations performed at 323.15 K.

Here we performed a comparative analysis between apo-Bcl2 and holo-Bcl2. We used essential dynamics to identify global collective movements of proteins which are crucial for the regulation of biological activity. Our results show that in both systems conformational changes in the FLD which upon MD simulation go from an extended conformation far away from the main core of the protein to a more compact structure, folded on itself and got closer to the globular head, forming new interactions between FLD and the hydrophobic groove of Bcl-2. Furthermore, in holo-Bcl2 form the peptide BH3 binding to the hydrophobic groove Bcl-2 has an allosteric effect on FLD’s flexibility, which favors the appearance of new interactions between FLD and different regions of the main core of Bcl2, which contributes to the stability of the structure. This demonstrated that the FLD and the hydrophobic groove might be essential regulators of Bcl-2 activity.

STRUCTURAL BLOCKADE OF OMICRON'S SPIKE PROTEIN BY POLYPHENOLIC COMPOUNDS

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Abstract:

SARS-CoV-2 is responsible for the Covid-19 disease. Spike protein (S protein) is one of the most important of the infective process of the virus. infection process begins with structural changes in the S protein to bind to ACE2 receptor and mediate fusion with the host cell. There are several variants of the original virus; these variants have a greater number of mutations in the S protein. Flavonoids are secondary metabolites with antimicrobial, antiviral and anti-inflammatory activity and are known to improve the body's defenses against diseases including coronaviruses.

In this work, the molecular docking technique on the S protein is used in order to analyze the effect of the mutations that SARS-CoV-2 Omicron variant has on the union of flavonoids in open and closed conformation.

Interaction analysis and binding energies yielded an energy difference of -0.173 kcal.mol-1 for the wild S protein with respect to the H1-coupled omicron variant; whereas, with the N1 molecule a difference of -0.336 kcal.mol-1 was found on the same proteins. Affinity increment on the closed structure is believed to be due to the contribution of 6 Omicron mutations that are interacting non-covalently with the ligands, stabilizing the binding.

These interactions are located in the RBD area near the ACE2 binding site (Image1). In open conformation, interactions that are in the center of the protein that could be interrupting inter-protomer electrostatic contacts between S2 and S1 subunits. We are working on the cloning and heterologous expression of the S protein to do in vitro experiments and check these present interactions and possible blockages in S protein by polyphenolic compounds.

Image 1 Interactions of closed and open S. In green interactions in chain A, yellow in chain B and Orange mutations of Omicron that come into contact with N1 and H1

IDENTIFICATION OF A CONJUGATIVE PLASMID IN *GALLIBACTERIUM ANATIS* ISOLATED FROM BACKYARD BIRDS

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Abstract:

Gallibacterium anatis is a Gram-negative bacterium of the *Pasteurellaceae* family and is the cause of salpingitis and peritonitis in laying hens, causing a decrease in egg production throughout the world.

In our laboratory several bird pathogens have been isolated recently. Molecular comparison between these bacterial field isolates lets to find bacteria containing plasmids. One of these strains of *Gallibacterium anatis* named HCJ1.4.1 was analyzed at genomic level: total DNA was extracted with high-quality and was sequenced with PacBio technology. The HCJ1.4.1 genome assembly and gene annotation were performed, obtaining a 2,718,991 bp, distributed in 2.683 Mbp for the chromosome and 35,249 bp for the plasmid pGA_heco.

Nowadays bacterial genetics of plasmid has shown a dark scenario in medical microbiology, although little is known into microorganisms of veterinary interest. We search in the pGA_heco plasmid for metabolic activities encoded to improve the environmental persistence of bacteria, but we do not found genes for antibiotic resistance. The genetic analysis of pGA_heco, shows that it is a typical conjugative plasmid of a wide range of hosts. Similar conjugative plasmids can spread to other strains or species; for example, between members of the *Pasturellaceae* family such as *Avibacterium paragallinarum*, *Pasteurella multocida* and *Aggregatibacter actinomycetemcomitans*, and *Haemophilus influenzae*. The genes that make up pGA_heco plasmid belongs to TSS4: *tra*L, *tra*C, *vir*D4, *vir*B1 to *vir*B11 genes and a type III toxin-antitoxin system. In silico analysis shows that similar plasmids, could play an important role in the pathogenic potential of the bacterium.

DIVERSITY OF SECONDARY METABOLITE BIOSYNTHETIC GENE CLUSTERS PRESENT IN METAGENOMES OF SEDIMENTS FROM ONE SINKHOLE OF YUCATAN

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Abstract:

Natural products are an important source of bioactive compounds produced by the secondary metabolism in organisms such as bacteria, plants, and fungi, and these are used in pharmaceuticals and agriculture.

For a long time, traditional biotechnological techniques such as phenotypic screening, extracts, and biosynthesis have been used to search for bioactive compounds. However, in the last decade, omics sciences and bioinformatics have emerged as important tools and new techniques for mining genomes. The metagenomics era has allowed access to the genomic content of non-culturable organisms that are estimated to be 99% of the organisms in an environmental sample.

In bacterial genomes, the genes involved in the secondary metabolite biosynthesis pathway are arranged in groups called biosynthetic gene clusters.

In this work, we characterize three metagenomes that were sampled from one sinkhole of aquatic sediments at different depths to identify novel biosynthetic gene clusters.

Leonard Katz, Richard H Baltz, Natural product discovery: past, present, and future, Journal of Industrial Microbiology and Biotechnology, Volume 43, Issue 2-3, 1 March 2016, Pages 155–176, https://doi.org/10.1007/s10295-015-1723-5

IN SILICO PREDICTION OF BM*VDAC* ISOFORMS AND THEIR INTERACTION WITH *BOS TAURUS* PLASMINOGEN.

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Abstract:

Rhipicephalus microplus is an ectoparasite distributed worldwide that causes economic losses in the livestock industry. In Mexico, *R. microplus* is one of the most relevant ticks in the field of veterinary healthcare and livestock industry. *R. microplus* mainly feeds on cattle and transmits diverse pathogens such as *Babesia bigemina*, an apicomplexan protozoa parasite. The current research on the control of ticks is focused on integrated tick control programmes, including vaccination. In previous work we have reported the identification of Bm*VDAC*, a mitochondrial porin which is expressed in ticks and it is modulated by *B. bigemina* infection. Recently we reported the efficacy of recombinant Bm*VDAC* as a vaccine to control *R. microplus*.

In order to explore the possible function of Bm*VDAC* in the invasion of tick midgut cells by *B. bigemina* we investigated the proteins with which it interacts during the *B. bigemina* infection process, the results have shown that Bm*VDAC* interacts with the bovine plasminogen at 72 h post-repletion time, besides at the same experimental conditions, an anti-Bm*VDAC* specific antibody recognized three protein spots with the same molecular weight in a 2D western blotting. These data suggest that different Bm*VDAC* isoforms could be expressed in midgut cells as a consequence of *B. bigemina* infection. We hypothesize that Bm*VDAC* activates plasminogen in plasmin, facilitating the invasion of the parasite to the tick midgut cells and this mechanism is regulated by the expression of Bm*VDAC* isoforms.

The aim of this work was to predict the role of Bm*VDAC* isoforms in the activation of bovine plasminogen performed by bioinformatic approaches. A genomic BLAST search, showed a single copy of *vdac* in the genomes of *R. microplus* and *I. scapularis*, ruling out the possibility of the expression of multiple *Bmvdac* gene copies. Additionally, twelve unique amino acid residues susceptible to phosphorylation and acetylation located at non-transmembrane protein regions and molecular pockets were predicted. Bm*VDAC* homology-based model was post-translationally modified in silico with the predicted CPRs located in the pocket and non-transmembrane regions using the Vienna-PTM web server tool. In the first protocol, 100 predictions were run with every receptor-ligand combination using the Hex 8.0.0 software. In the second protocol 100 results were obtained for each receptor-ligand combination using PatchDock Software, after that, the 10 models with the lower ΔG were processed with FireDock Software. Models in which the plasminogen interacted with non-accessible Bm*VDAC* regions were excluded. By Molecular Docking analyses we found three amino acid phosphorylated residues were consistently implicated in the stabilization of the Bm*VDAC*/Plasminogen interaction.

Our data suggested that the Bm*VDAC* phosphorylation may play an important role during the infection process of *B. bigemina* in the midgut tick cells.

SEQUENCING OF THE *COFFEA ARABICA* GENOME AND DETERMINATION OF SOME OF ITS EVOLUTIONARY CHARACTERISTICS

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Abstract:

Coffee is one of the most worldwide consumed beverages, with consumption of over 3 billion cups of coffee daily. *Coffea arabica* represents more than 60% of world coffee production, characterized by its low bitterness, better aromatic properties, and low caffeine content. *C. arabica* is an allotetraploid species (2n=4x=44) derived from a hybridization event of two diploid species: *C. canephora* (2n=2×=22) and *C. eugenioides* (2n=2×=22).

Coffee rust, caused by the fungus *Hemileia vastatrix*, is one of the diseases that has had the most significant impact on world coffee production. The development of resistant varieties has been the most ecological and economical method to combat rust. However, most of these varieties have been obtained by introgression from closely related species of the *Coffea* genus, which reduces the quality of the drink. Furthermore, the search for sources of resistance in wild *C. arabica* plants has not been an option due to the low variability within the species.

This work aims to assemble and analyze an individual's genome derived from seeds of a plant of *C. arabica* variety Bourbon (highly susceptible to rust) and to identify differences and conserved genomic elements between different *C. arabica* cultivars and between *Coffea* spp. sequenced genomes.

THE ROLE OF NON-CODING SNPS ASSOCIATED WITH ALZHEIMER'S DISEASE IN NEURONAL SUBPOPULATIONS OF FRONTAL AND ENTORHINAL CORTEX

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Abstract:

Alzheimer's disease (AD) is the major cause of dementia worldwide; it is estimated that by 2050 the incidence will triple worldwide. Three phases of the disease have been reported: the cellular phase, mild cognitive impairment and dementia. The first is of relevance as it precedes the onset of beta-amyloid protein aggregate formation and Tau phosphorylation, the most relevant cell types in this phase are glia and neurons. On the other hand, it is estimated that between 60% and 80% of the disease is due to genotype. Single nucleotide polymorphisms (SNPs) are the most common type of genetic variation at the population level. Through genome-wide association studies (GWAS), the association between SNPs and phenotype is studied, and about 90% of AD-associated SNPs are found in non-coding regions.

In 2019 Mathys et al. released the first single cell RNA sequencing data from AD patients, thereafter, at least 4 more studies have been published. These data allow us to learn about the heterogeneity of cell types in a specific tissue, and to compare a pathological state in terms of their expression.

For this work, in the systems biology and translational medicine laboratory we have developed workflows to use different omics data to integrate expression and regulatory information, and thus characterize the role of non-coding SNPs in neuronal heterogeneity.

ASSEMBLY PATTERNS AND DYNAMICS OF SYNTHETIC MICROBIAL COMMUNITIES BASED ON COMPETITIVE INTERACTIONS

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Abstract:

Bacteria rarely live in isolation, but rather, they associate with other organisms of their same or different species, forming communities. Despite all the studies about life of bacteria within their communities, little is known about how those communities came into existence, and how different initial conditions may affect their assembly. In this work, we will analyze such environmental variations trying to assess which variables are fundamental to establishing the community as we know it, and the multiple changes that may arise. With the use of microfluidics, we will closely monitor our community's responses to subtle changes in their environment, which we will also introduce in a controlled manner. To do this, we will use a Bacillus community, in which each of its members shows a different ecological role, and their coexistence is based on antagonistic interactions. With this, we expect to improve our understanding of how different conditions generate changes in community assembly, hoping to find the principles of utmost importance.

DETECTING RECOMBINATION IN SARS-COV BY USING INFORMATION THEORY IN A BAYESIAN CONTEXT

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Abstract:

Recombination is an important source of novelty in the evolution of coronaviruses. For instance, there is evidence that SARS-CoV-2 acquired part of its genome by recombining with pangolin infecting coronaviruses (Zhang *et al*. 2020). Thus, accurately identifying recombination events is paramount to reconstruct the evolutionary history of coronavirus in general and the origin of SARS-CoV-2 in particular. Here we apply a novel approach to identify recombination events to a diverse set of coronavirus genomes. This approach uses recent developments on the use of information theory in Bayesian phylogenetic analyses (Lewis *et al*. 2016). In brief, this approach finds recombination events by identifying segments of the genome that show dissonant phylogenetic histories. Dissonant phylogenetic histories are in turn identified by measuring the drop in information content of merged tree files (resulted from Monte Carlo Markov Chains in Bayesian phylogenetic analysis) from different genomic segments. Statistical significance of identified dissonant segments is evaluated by using Bayes factors (Neupane *et al*. 2019). By this approach, we were able to identify statistically significant recombination events in the evolution of coronaviruses. We are preparing scripts in Perl and R to facilitate detection of recombination by using the approach described here.

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Zhang T, Wu Q and Zhang Z. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. Curr Biol. 2020 Apr 6;30(7):1346-1351.e2. doi: 10.1016/j.cub.2020.03.022.

ABERRANT *CLDN6* EXPRESSION IN GASTRIC CANCER IS ASSOCIATED WITH ENHANCED CHOLESTEROL METABOLISM AND REDUCED CYTOTOXIC ACTIVITY

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Abstract:

Differentially expressed Claudin-6 (*CLDN6*) in Gastric Cancer (GC) is associated with poor prognosis and survival of patients. Since, GC is very heterogeneous, finding specific molecular subtypes and novel prognostic and drug targets is essential for early diagnosis and precise treatment. In the current study, we investigated genes and pathways associated with aberrant *CLDN6* expression in The Cancer Genome Atlas (TCGA) Stomach Adenocarcinoma Pan-Cancer Atlas Data (STAD) by using tools like CBioPortal**,** and Bioconductor's- clusterProfiler, Pathview, and DoRothEA- R (version 4.1.3) packages. We found that 96.88% of *CLDN6* high GC samples have Chromosomal instable (CIN) molecular subtype. High *CLDN6* expression in GC samples concurs with higher mutations in *TP53, MIEN1, STARD3, PGAP3,* and *CCNE1* genes. Several MAGEA genes *(MAGEA6, MAGEA3, MAGEA4, MAGEA2, MAGEA9B, and MAGEA12),* Apolipoproteins (APOA2, APOH, APOC3, APOA1, APOC2) and transcription factors- HNF-4α and HNF-1α express highly in *CLDN6* high GC. Integrated pathway analysis reveals that upregulated APOs expand to enhanced cholesterol metabolism, which contributes significantly to several aspects of cancer progression including diminished infiltration of immune cells and suppression of NK and T cell cytotoxic activity. Downregulation of several important receptors related to the activation of cytotoxic cells like NKG2D, NKp44, NKp46, CD244, DNAM1, CD28, CD69, CD38, TRAIL, and perforin validates that GC with aberrant *CLDN6* expression procures reduced cytotoxic activity. **Conclusion-** Aberrant *CLDN6* expression in GC gains enhanced cholesterol metabolism and reduced cytotoxic activity. Upregulated genes like APOA-2 and MAGEA9b along with HNF4α can be explored as novel prognostic and drug targets for *CLDN6* high GC.

CONGENITAL ABSENCE OF UTERUS AND VAGINA: A GENE INTERACTIONS ANALYSIS BASED ON PPI NETWORKS

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Abstract:

Congenital absence of uterus and vagina is a rare condition affecting 1:5000 women. It is clinically recognised as the Mayer-Rokitansky-Küster-Hauser syndrome (MRKH, ORPHA:3109), in which the affected females are otherwise phenotypically normal, and usually display a balanced 46,XX chromosomal complement. The aetiology of this condition remains unexplained, as mutations in heterogeneous candidate genes display a low frequency among cases; therefore, recent research suggests that a polygenic mechanism may be involved. To explore putative gene circuits underlying this condition, we performed a genome-level mutational analysis using chromosomal microarrays and whole exome sequencing in four type-1 MRKH women. Genes harbouring potentially pathogenic variants, as determined by population frequencies, clinical databases and computational predictors of protein impact, were prioritized and collected as patients' gene datasets. Protein structural analysis for the most prominent variants was performed by homology modelling. Then we performed a gene-interaction analysis approach, based on STRING protein-protein interaction networks (PPI), using previously identified candidate genes and further integrating the patients' genes. The results revealed the enrichment of functional modules, mainly related to RNA-processing and morphogenesis of reproductive structures, as well as the Notch and WNT/b-catenin signalling pathways and epithelial morphogenesis. Using centrality measures (CentiScaPe), we identified genes which may function as major regulators of such network, including *ESR1*, *STAG2* and *EXOSC2*. Our results add evidence on the role of the WNT signalling pathway and oestrogen receptor activity in the development of MRKH, however, larger groups of patients will be required to fully uncover the mechanisms of this complex condition.

IN SILICO STUDY OF NEW INHIBITORS OF THE HUMAN ORNITHINE DECARBOXYLASE

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Abstract:

Polyamines (PA) are ubiquitous aliphatic polycations. These are involved in cellular processes such as transcription, stress response, cell proliferation, etc. [1]. Therefore, PAs have been associated with neurodegenerative diseases, metabolic disorders, and cancer. The ornithine decarboxylase (ODC) is the first enzyme of the PAs synthesis pathway and catalyzes the decarboxylation of ornithine forming putrescine (Put) [1]. An accumulation of PAs has been found in various tumor cells, that could be associated to an increase in the ODC. Thus, ODC has been considered as a therapeutic target to decrease tumor growth. In some organisms, lysine decarboxylase (LDC) catalyzes the decarboxylation of lysine (Lys), forming the PA cadaverine (Cad). However, this enzyme is not present in fungi and animal cells [1]. Interestingly, ODC from *Saccharomyces cerevisiae* and *Rattus norvegicus* can decarboxylate Lys [2,3]. However, this feature has not been reported for human ODC. Considering that the latter could also use Lys as a substrate, in this work we search, by *in silico* assays, for molecules with chemical similarities with Lys, which can inhibit the activity of this enzyme. This screening was performed using the crystallographic structure of the human ODC (PDB:2OO0), where the cofactor of the enzyme (Pyridoxal phosphate, PLP), a competitive inhibitor (1-amino-oxy-3-aminopropane, APA) and Cad are bound. It is important to mention that Cad was found in a different place from the active site, suggesting the presence of an allosteric binding site for this molecule [4]. We started with a total of 369 molecules, which were docked in both, the active site, and the possible allosteric site. We obtained around 30 molecules with high affinity towards one or both sites. Thus, these results allowed us to computationally observe that Lys can probably bind the human ODC and thus can interact with compounds structurally analogous to this amino acid and with some diamines. As a perspective, these ligands will be experimentally validated by thermal shift assays that will allow to identify new inhibitors for human ODC.

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IMPLICATIONS OF THE CRYSTAL STRUCTURES TOPOLOGY OF SARS-COV-2 MAIN PROTEASE (MPRO) IN MOLECULAR DOCKING

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Abstract:

Development of pharmacological treatments against SARS-CoV-2 infection is essential since there are no drugs with global distribution and those currently authorized do not have the desired effectiveness. Through molecular docking, molecules capable of inhibiting the activity of one of the proteins essential for the viral replicative cycle, can be proposed, specifically the Mpro protease (also known as 3CL). The crystal structures resolved by X-ray diffraction represent a specific conformation of the protein, and not considering the flexibility of the active site1, so it is necessary to determine the characteristics that influence the docking models. Mpro structures of three medically important coronaviruses: SARS-CoV (3F9H, 6XHN, 7K0H), MERS-CoV (4YLU, 5WKJ, 7TQ7) and SARS-CoV-2 (5RL5, 6M03, 6ZRU, 7KPH, 7TOB) were used. Between the different structures, the catalytic residues (His 41 y Cys 145) maintain the same structural conformation, both between structures of the same virus and between distinct species, in the same way as the hydrophobic character of the electron density. On the contrary, the electrostatic potential changes, being structures with a neutral catalytic cavity and others with a negative electrostatic potential. Molecular docking was performed with well-known inhibitory molecules. The blind docking indicated that using the crystal structures with an inhibitor in the catalytic site more feasible models are obtained to predict interactions in this region. In docking directed to the catalytic cavity using molecules such as boceprevir or nirmatrelvir, the same structure can result in models with different ΔG values of up to 7 kcal/mol. Structures with the most negative ΔG are usually those with the most negative electrostatic potential at the active site. All the above, added to the preference of certain functional groups for certain regions of the catalytic cavity1, highlight the importance of the characterization of the catalytic cavity and the use of more than one crystallized structure in molecular docking.

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CONSTRUCTION AND ANALYSIS OF GENE CO-EXPRESSION NETWORKS OF *USTILAGO MAYDIS*

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Abstract:

Through gene interactions, biological systems respond to a range of compounds and environmental perturbations, and these genetic components combine to form complex networks. In recent years, a number of gene co-expression networks have been built due to the large expansion in experimental data obtained utilizing methods like microarrays and RNA sequencing. These networks enable the identification of gene clusters that are co-expressed and may function in the same process. These networks may then be connected to biological processes of relevance to industry, medicine, and academia. At this study, we constructed the *Ustilago maydis* genetic co-expression network from the expression data of 168 samples from 19 series that are related to the GPL3681 platform deposited in the NCBI. This network was examined to find clustering of co-expressed genes, which were analyzed using Gene Ontology analysis, as well as hubs. Finally, we use a hypergeometric analysis to select important modules based on a predicted collection of transcription factors and virulence genes.

PREDICTION OF PROTEIN-PROTEIN INTERACTIONS AND MOLECULAR DOCKING OF THE PUTATIVE PROTEIN ERMP1 FROM THE YEAST *S. POMBE*

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Abstract:

Endoplasmic reticulum metalloprotease 1 (Ermp1) is a putative 91.8 kDa zinc-dependent protein, a novel member of the M28 family of metalloproteases. Ermp1 is located to the endoplasmic reticulum (ER) instead of the cell membrane of the fission yeast *S. pombe*. The predicted topology is composed for the aminopeptidase domain located toward the N-terminus cytosolic region, 9 transmembrane helices and a C-terminal cytosolic region, but the function is unknown. Although, its orthologs in human and rat are related to the response to stress in ER[1] and the maturation of ovarian follicles[2], respectively. To identify the possible function of Ermp1 in yeast, we performed a prediction of protein-protein interactions (PPI) using the human ERMP1 interaction network as template, which one reported in BioGRID database. By ortholog analysis, we identified 36 homologous proteins in *S. pombe*. Because of the difficulty for obtaining a possible biological 3D model of the complete structure of Ermp1, we decided to work with the proteolytic domain for modeling by homology in Phyre2 and the docking protein-protein in ClusPro 2.0 and PathDock-FireDock. Also, we selected 7 proteins from the PPI prediction with a high ortholog evidence for modeling the 3D structures in Phyre2 and AlphaFold. The amino acid sequences of Amk2, Gsk3, Pmc1, Oca8, Ypt5, Fis1 and Pex12 were analyzed in PROSPER for the cleavage sites prediction. Only Amk2, Pmc1 and Oca8 had potential hydrolysis sites by metalloproteases at their N-terminus. Moreover, the Ser168 and Ser279 phosphorylation sites close to the catalytic pocket of Ermp1 were predicted by homology analysis with human ERMP1 and the using webserver NetPhos 3.1, therefore is possible that it can be modulated by kinases. The docking results showed that Ermp1 has affinity for the N-terminal lysine and leucine residues of Amk2, Pmc1 and Oca8. Additionally, the kinase site of Gsk3 showed interactions with Ermp1, around the phosphorylation sites predicted. We propose that Ermp1 can contributed to the recycling of amino acids for the protein synthesis[3] and/or post-translational modification by proteolysis.

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ANALYSIS OF ECCD3, ESX3 SECRETION SYSTEM COMPONENT AS *MYCOBACTERIUM TUBERCULOSIS* DRUG TARGET

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Abstract:

Drug-resistant tuberculosis (DR-TB) is a global health problem that needs the development of new drugs and the identification of novel therapeutic targets. The ESX3 secretion system is essential to *Mycobacterium tuberculosis* survival and virulence. This system is comprised of EccB3, EccC3, EccD3, and EccE3 proteins. The aim of this study was to evaluate EccD3 protein as drug target. The 3D structure of *M. tuberculosis* EccD3 protein was predicted by homology modeling using *Mycolicibacterium smegmatis* structures as templates in SwissModel. We selected 34 antituberculosis drugs and obtained their 3D structures from PubChem. Protein-drug interactions were evaluated by molecular docking using AutoDock Vina. Biological activities, ADME properties and toxicity were obtained by online webservers. EccD3 structure of *M. tuberculosis* was obtained with high quality. Two potential sites predicted to destabilize EccD3 structure present in the interfaces were identified and selected as drug targets. The best bindings with the EccD3 dimer interfaces were against moxidectin and selamectin with -8.4 and -7.4 kcal/mol of binding energy free, respectively. We found interactions of moxidectin and selamectin with EccD3 interfaces *in silico* and these interactions may alter the dimer structure of EccD3. EccD3 protein have a potential as moxidectin and selamectin target.

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INSIGHTS INTO THE COASTAL MICROBIAL ANTIBIOTIC RESISTANCE THROUGH A META-TRANSCRIPTOMIC APPROACH IN YUCATAN

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Abstract

Antibiotic resistance (AR) is one of the greatest human and clinical challenges associated with different pathogenic organisms. However, in recent years it has also become an environmental problem due to the widespread use of antibiotics in humans and in livestock activities. The ability to resistance to antibiotics comes from antibiotic resistance genes (ARGs) and our understanding of their presence in coastal environments is still limited. Thus, we assessed the composition and abundance of ARGs through an analysis of high-throughput meta-transcriptomic sequences to explore the microbial resistome of four sites of the Yucatan coast. In total, 6952 ARGs were uncovered, which participate in the resistance to tetracycline, macrolide, rifamycin, fluoroquinolone, phenicol, aminoglycoside, cephalosporin and other antibiotics. The action mechanisms of these ARGs were mainly efflux pump, antibiotic target alteration and antibiotic target replacement. Similar ARGs were detected in the samples but show dissimilar enrichment levels. With respect to the sampling sites, the ARGs were present in all the samples collected, either from preserved or contaminated areas. Important to note, sediments of the preserved area of Dzilam presented the second highest level of ARGs detected, probably because of the antibiotics dragged to the coast by submarine groundwater discharge. In general, the resistance to a single antibiotic was greater than multi-resistance, both at the level of gene and species; and multi-resistance in organisms is acquired mainly by recruiting different mono-resistance genes. To our knowledge, this is the first study that describes and compares the resistome of different samples of the Yucatan coast. This study contributes to generating information about the current state of antibiotic resistance on the Yucatan coasts for a better understanding of ARGs dissemination and could facilitate the management of ARGs pollution in the environment.

DOCKING ANALYSIS ON MOLECULAR TARGETS AND MECHANISMS OF TAU PROTEIN IN THE TREATMENT OF FRONTOTEMPORAL DEMENTIA

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Abstract:

Tau protein is the main microtubule-associated protein of a mature neuron, and its function is related to the formation of neurofibrillary tangles (NFT) [1]. Activation of various protein kinases and phosphatases results in tau phosphorylation and suspension. In abnormal tau phosphorylation [2], hyperphosphorylated tau is the main cause of neurodegenerative pathologies, known as tauopathies. [3]. One way to treatment tauopathies such as fronto-temporal dementia is with the use of quinine, which has been reported to prevent to TAU hyperphosphorylation, however, it was classified as a toxic compound that causes eye problems [4].The objective of the present work was to find some molecules that present better biological activity and with less cytotoxic damage, we implement a Virtual Screening on a molecular database, in which a group of compounds with a functional similarity to the quinine. With the hits compounds obtained a Molecular Docking were developed on the VQIINK target site of the TAU protein, described as the site where the inhibition of hyperphosphorylation in TAU effect. [5] The structural differences are reported, their conformations more stable and their intramolecular interactions between the TAU protein and the hits proposed as better therapeutic agents, same as could combat the problems related to neurodegenerative diseases. For the development of the docking, we divide the procedures into the following phases:

1) Selection and preparation of the protein with the Chimera program
2) Selection and preparation of the ligands with the Avogadro program
3) Tests with the ligands and the protein in the Autodock program to find the leading compounds

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COMPUTATIONAL STUDY OF THE T-TYPE VOLTAGE-DEPENDENT CALCIUM CHANNEL (CACNA1G)

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Abstract:

Epilepsy is a disorder of the central nervous system, which affects approximately 70 million people worldwide and is one of the most common neurological diseases in the world. Currently, there are more than 25 drugs approved for its treatment, however, about one third of patients do not respond to it. The development of seizures is mainly generated by an uncontrolled release of neurotransmitters at the nerve endings, accompanied by an increase in T-type calcium channel currents (presumably due to CACNA1G). In silico studies are useful for the analysis of molecules of biological interest and drug discovery. Among these computational tools are homology modeling, which allows obtaining a three-dimensional conformation of a protein whose structure has not yet been reported, and molecular dynamics (MD), which allows analyzing the behavior or evolution of a system under constant conditions over time. Due to the scarce information on the mechanism of action of drugs targeting the calcium channel, computational techniques can provide us with information on the interactions, affinity and conformational changes produced by our ligands to CACNA1G, which will generate useful information for the design of new molecules with pharmacological potential.

In this work, a homology model based on the reported crystallography (PDB: 6KZO) was built by dividing the protein into 4 segments in the public webserver I-TASSER. Subsequently, they were joined using the Schrödinger-Maestro module, by means of an alignment with 6KZO. Once the complete model was obtained, it was subjected to relaxation using all-atom molecular dynamics (AA-MD) simulations to validate the quality of the model. The systems for the AA-MDs were built in the CHARMM-GUI web server, adding the post-translational modifications, a three-point model (TIP3) was used for the water molecules, phosphatidylcholine (POPC) for the lipid membrane and the corresponding ions were added using NaCl at 0.15 M. The 3 MD simulations were performed in the Gromacs program using an isothermal-isobaric (NPT) assembly at 1 atm pressure and 310.15 K. The systems were subjected to 5000 minimization steps followed by 6 equilibrium steps prior to the production simulations. The CHARMM36 force field was used in all systems. A quality evaluation process of the CACNA1G structure was performed in the MolProbity public server. The initial model obtained 65.77% of favored residues in the Ramachandran diagram, once the MDs were performed, the representative structure of the simulations was evaluated and 82.75% of favored residues were obtained in the Ramachandran diagram, a substantial improvement in the quality of the model for further molecular docking studies and ligand-protein molecular dynamics simulations.

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CHRONIC EXPOSURE TO PETROLEUM-DERIVED HYDROCARBONS ALTERS THE SKIN BACTERIAL COMMUNITIES AND METABOLITE PROFILES

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Abstract:

Introduction: Petroleum hydrocarbons (PH) are ubiquitous molecules in the environment and the skin is constantly exposed to them. Aging, skin pigmentation, wrinkles, and cancer are common disorders associated with chronic exposure to PH1. Toxic intermediate metabolites derived from PH degradation2 and changes in the composition of the skin bacterial communities3 are possible contributors. However, the evidence supporting such hypotheses is derived from epidemiological, in-vitro, and in-vivo studies. We, therefore, performed a pilot study evaluating the in-situ bacterial communities and metabolite profile in the skin of subjects chronically exposed (EX) and non-exposed to PH (NEX).

Methods: Two cohorts were included, five workers from auto repair and tire shops (EX) and five random subjects with no history of PH chronic exposure (NEX). Surficial skin samples of the arm and middle finger (dominant hand) were collected by a moistened cotton swab for mass spectrometry-based untargeted metabolomics/chemoinformatics and 16S rRNA sequencing analyses. Multivariate and univariate statistical analyses were applied to assess grouping patterns and abundance differences among groups, respectively. The CICESE's Bioethics Committee approved the study and informed consent was obtained from all participants.

Results: Globally, EX subjects presented an increased bacterial diversity (Shannon index) and a distinct bacterial community structure vs. NEX individuals. Select oil-degrading bacteria (ODB, e.g., family Dietziaceae, Nocardiaceae, Aeromonadaceae) were more abundant in EX subjects and functional metabolic profiling by PICRUST suggested an increase in PH degradation. Such differences were more pronounced in hand (anatomic site with more exposure to PH) vs. arm on EX subjects compared to NEX individuals. An array of chemically more diverse metabolites were identified in EX subjects, some associated with PH degradation.

Conclusions: We suggest that chronic dermal exposure to PH alters the skin bacterial community structure leading to an increased abundance of bacteria capable of degrading PH. Our findings contribute to understanding the potential adverse effects of PH on our health.

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CDK-KINASE ACTIVITY INHIBITION IMPACTS THE CARBON METABOLISM IN MAIZE GERMINATION

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Abstract:

CDK/Cyclin complexes are the main cell cycle regulators by phosphorylating diverse targets inside the nucleus. Its nuclear kinase activity is recognized as a driving force that triggers the molecular events through the cell cycle phases to generate two daughter cells with identical genetic material.

Additional to their nuclear function, recent evidence indicates that cyclins and CDKs may be located outside the nucleus: cytosol, mitochondria, or endoplasmic reticulum, for example. There, cell cycle regulators, as single proteins or forming a complex, may play a relevant role in key metabolic targets.

This work explored the specific function of Cyclin/CDKs kinase activity on the global metabolism of maize embryo axes during germination.

The approach was to isolate and imbibe maize embryo axes in the presence of glucose (an important proliferation inducer) and the CDK kinase-specific inhibitor RO-3306.

Results showed that embryo axes on glucose are prone to gain size and weight after 48 h of germination. In contrast, embryo axes with both glucose and RO-3306 are unable to grow and remain with similar characteristics as embryos axes without glucose.

A metabolomic analysis at 24 h indicated that carboxylic acid metabolites related to the Krebs cycle such as succinic, citric, and malic acid were reduced on kinase inhibitor treatment, while some amino acids derived from the carboxylic acid cycle, in contrast, were increased, among them are serin, valine, leucine, and phenylalanine.

Sugar metabolism was also altered: RO-3306 impaired the galactose and fructose accumulation. Finally, fatty acid precursors levels were also modified, resulting in 3-hydroxybutanoic and 4-hydroxybutyric acids build up.

Maize is one of the most important crops in the world and Mexico. Successfulhe carbon mobilization and partition during germination, and the possible influence of the cell cycle regulation may

MOLECULAR AND BIOCHEMICAL ANALYSIS OF GLUTAMATE RECEPTORS FAMILY (GLR) IN SOLANACEAE, USING THE HABANERO PEPPER (*CAPSICUM CHINENSE* JACQ.) AS A MODEL

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Abstract:

Glutamate-like receptors (GLRs) of plants are non-selective cation channels (NSCC) that, upon binding to a ligand, produce a conformational change, activating a signaling cascade that leads to physiological events related to root development, defense responses, abiotic stress, among other processes. GLR genes have been found in species such as *Arabidopsis*, *Oryza sativa*, *Medicago truncatula*, woody species and *Solanum lycopersicum*. With the release of the habanero pepper genome, this work identified 17 *GLR* sequences (*CcGLRs*) that share a typical GLR structure, with four transmembrane domains (M1-M4), two ligand-binding domains (LBD), an amino-terminal domain (ATD) and a carboxy-terminal domain (CTD). Phylogenetic analyses classified the 17 CcGLRs into three clades; clade I is shared with tomato members and is placed in a separate clade from *Arabidopsis*; clade II and III are shared with members of tomato, *Arabidopsis*, rice, and woody species. From molecular docking analysis, it is suggested that D-Ser, Glu and Gly may be ligands of the CcGLRs, with Glu likely to bind preferentially to most of the CcGLRs of the three families. By performing possible protein-protein interaction analyses, it is suggested that CcGLRs could interact with a variety of proteins that appear to be involved in various signaling events, transport, defense, etc. The results presented in this work provide insight into the structure and possible function of plant GLRs and discuss the main differences between these proteins between Solanaceae and the model plant *Arabidopsis*.

EXPLORING THE UNFOLDING FREE ENERGY LANDSCAPE OF THE THERMOPHILIC β-ATPASE SUBUNIT BY MOLECULAR DYNAMICS SIMULATIONS

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Abstract:

ATPase is a very important enzyme, since it is responsible for synthesizing adenosine triphosphate (ATP) for most of cellular reactions. This enzyme works as a rotational motor where the β subunits function cooperatively through hinge/scissoring motions. Various studies have shown that the β subunit isolated from the thermophilic bacterium *Bacillus PS3* (Tβ), maintains its structural nature similar to that found in the ATPase complex. [1] This characteristic makes it an effective model to study the relationship that keeps its flexibility, structural stability and its hinge/scissoring conformational changes.

Free energy landscapes (FEL) generated from molecular dynamics (MD) data have been successful in explaining kinetic barriers in conformational space both in the native state and in the folding process. [2] To evaluate the stability of Tβ, MD simulations at different temperatures were performed in this work. From the MD results, Tβ unfolding free energy landscapes were constructed considering the variables: Accessible Surface Area (ASA) (polar and non-polar) and Secondary Structure (SS) (α-helix, β-sheet and unordered). From the FEL analysis it is possible to observe that the stability of SS is lost as the temperature increases, however, the exposure of ASA doesn't increase considerably, as expected for a completely unfolded structure.

An inspection of the Tβ topology showed that the unfolded structure behaves as a molten globule and maintains residual structure in the N-terminal domain, mainly due to the hydrophobic β-sheet structure, which better tolerate thermal vibrations. In addition, the exposure to water of this type of structure is unfavorable, which allows Tβ to be more thermostable.

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ANALYSIS OF GENETIC BIOMARKERS FOR ATHEROSCLEROSIS IN ENDOTHELIAL CELLS

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Abstract:

Atherosclerosis (At) is the main cause of worldwide. According to the World Health Organization (WHO) in 2018, 17.9 million deaths were associated with atherosclerosis-related diseases such as myocardial infarction or stroke. In Mexico ischemic diseases represent 17.3% of annual deaths.

The physiopathological process initiates with damage in endothelial cells and continues with a Low-Density Lipoproteins (LDL) aggregate in the intimate of medium and large-sized arteries.

The atheroma plaque growth and may cause unstable states and eventually the fragments scatter. Have been reported several factors that contribute to the development of At, such as Diabetes Mellitus, Hypertension, Obesity, Hypertriglyceridemia, Insulin Resistance, and elevated LDL levels. The disease progression takes from a few years to several decades, the process breakthrough is silent and difficult to detect, which eventually leads to sudden lethal thrombotic events.Currently, the clinical detection of this pathology takes place in the late stages.

Hence, new alternatives for prediction in the early stages of the disease, such as the generation of Machine Learning (ML) models based on Single Nucleotide Polymorphism (SNPs) and the development of risk scores are primordial. The principal aim of this work is to validate early stages biomarkers related to At identified by ML on related cell systems. For the identification of putative SNPs associated with At we used genomic data sets from GWAS Catalog, 1000 genomes project phase 3, and the Human Genome Diversity Project. The data pre-processing involved data mining and genetic attributes selection. Subsequently, we built and evaluated Artificial Neuronal Networks (multilayer perceptron) and decision tree algorithms. The results revealed the putative SNPs associated with At in a specific cellular type. Also, a polygenic risk score (PRS) function was generated from AI models and genetic attributes. This PRS was assigned to different populations, and the SNPs with the highest value were selected and evaluated in the Amerindian native population from Mexico.

Genes associated with the identified SNPs were related to lipid metabolism, and it is possible suggest a regulation of the atherosclerosis progression. In conclusion, the strategy used in the present work allowance the identification and selection of putative biomarkers involved early diagnosis of atherosclerosis.

CHARACTERIZATION OF THE DOCKING MECHANISM OF DOPAMINE AGONIST ON THE DOPAMINE RECEPTOR 2

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Abstract:

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of ovarian stimulation in assisted reproduction technology. At present, the etiology of OHSS is not fully understood. Though, vascular endothelial growth factor (VEGF) is a crucial mediator for the pathophysiology of OHSS. Clinical data suggest that dopamine agonists could be a promising option for the treatment of ovarian hyperstimulation syndrome in women at high risk in *in vitro* fertilization treatment or Intracytoplasmic sperm injection cycles, dopamine agonists decrease the phosphorylation of the VEGF receptor 2 (VEGFR2) and reduce the incidence and severity of OHSS. Quinagolide, a non-ergot-derived dopamine agonist, is most effective than cabergoline in the prevention of OHSS though quinagolide administered in high doses is associated with poor tolerability. Previous studies have shown dopamine receptor 2 (DAR2) colocalizes with VEGFR2 at the cell surface of endothelial cells. Dopamine pretreatment increased the translocation and colocalization of VEGFR2 with DAR2 and increased VEGF-induced phosphorylation of Src-homology-2-domain-containing protein tyrosine phosphatase (SHP-2), and subsequently increased the phosphatase activity of SHP-2. Lastly, active SHP-2 then dephosphorylates VEGFR-2. Our main purpose was to analyze *in silico* the possible activation of the DAR2/ VEGFR2 receptor with a dopamine agonist. *In silico* analysis was used molecular docking using three different proteins of DAR2 from PDB. Molecular docking studies revealed stable interactions between dopaminergic agonists and the DAR2 targets. The data showed that agonists made hydrogen bond interactions and other interactions with vital catalytic residues such as 114 Asp and 389 Phe of the receptor. The binding affinity energy between cabergoline and DAR2 is different in the three proteins analyzed meanwhile that of quinagolide is the same in all cases. Quinagolide interaction with the receptor is stable even in the absence of the Gi protein or in the DAR2/VEGFR2 complex. These results could explain the differences observed in clinical trials shown by the treatment of OHSS with dopaminergic agonists.

IDENTIFICATION OF CRISPR-CAS SYSTEMS IN GENOMES OF *ACINETOBACTER CALCOACETICUS-ACINETOBACTER BAUMANNII* COMPLEX

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Abstract:

The *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex or Acb complex is conformed by six species: *A. baumannii*, *A. calcoaceticus*, *A. nosocomialis*, *A. pittii*, *A. seifertii* and *A. dijkshoorniae*. *A. baumannii* is the specie of most clinical importance, involved with health care associated infections (HAIs). Clustered regularly interspaced short palindromic repeat (CRISPR) arrays and CRISPRassociated genes (cas) constitute bacterial adaptive immune systems and function as avariable genetic element. The aim of this study was to perform a genomic analysis of Acb complex strains, available in database to describe and characterize CRISPR systems and *cas* genes. The genomes were extracted in database of the National Center for Biotechnology Information (NCBI) and Pathosystems Resource Integration Center (PATRIC). The analysis was carried out using different bioinformatics programs. A total of 292 sequences of chromosomes and plasmids were included [*A.baumannii* (149), *A. nosocomialis* (42), *A. pittii* (76), *A.calcoaceticus* (12), *A.lactucae/A. dijkshoorniae* (2) and *A. seifertii* (11)]; associating with samples of blood (n=55/292), sputum (n=27/292), wound (n=13/292), urine (n=11/292), and respiratory tract (n=10/292) of patient. The Sequences Typing (ST) was determined using Ribosomal multilocus sequence typing (rMLST), where the genomes were mainly associated with 29 rSTs: rST8482 (n=25/ 292), rST8237 (n=10/292), rST8274, rST8863(n=7/292), rST8770(n=6/292) and rST31297 (n=5/292), for the other genomes was not possible to determine. The CRISPR arrays were identified by CRISPRCasFinder, CRISPRDetect and CRISRPRminer, defining 78 confirmed arrangements in 26% (n = 76/292) of the Acb complex sequences. The *cas* genes associated were found in 9.5%(n=28/292). The 51% (n = 149/292) of the arrays were identified in *A. baumannii* sequences (55 arrays confirmed and 94 probable); in the case of *A. nosocomialis*, *A. pittii, A. calcoaceticus*, *A. dijkshoorniae* and *A. seiferttii*, 106 arrays were recognized (21 confirmed and of remainder as probable). The arrays were characterized by the presence of between three and 158 Repeat Sequences (SR) and up to 157 Spacer Sequences (SS), main associated with a consensus SR: GTTCTTCATCGCATAGATGATTTAGAAA. Interestingly, the CRISPRCasFinder tool detected 178 questionable arrays, associated with 41 consensus RS, 91% (n=163/178) of them were conformed of two RS and one SE, with lengths between 18-36 bp. The SEs of the arrays were related with sequences of prophages and plasmids of different species of genus Acinetobacter. The plasmid sequences analyzed showed the presence of small arrays, composed of three SR and two SS, linked with type I-F systems CRISPR-Cas; however, they lack *cas* genes. The implementation of different bioinformatic tools made it possible to define CRISPR-Cas systems type are characteristic of *A.baumannii* and other species that belong to the Acb complex, demonstrating their presence in chromosomal and plasmid sequences.

ESTIMATION OF INTERACTION STRENGTHS IN THE *E. COLI* REGULATORY NETWORK

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Abstract:

Network models of gene regulation have been successful in the identification of relevant motifs and modules. These substructures are the basis for some of the observed complex behavior in biology. Nonetheless, these findings are based on network models that are purely binary in nature, leaving out any information about the intensity of the regulatory event. The integration of quantitative information into regulatory network models may provide further insight into the organization principles that govern these systems, allowing us to better partition the network into strongly connected submodules that can be modeled independently, or to study the dynamic stability of the system and its attractors.

We propose two methods for the inference of regulatory strengths (i.e., the intensity with which regulator A affects the expression of target gene B): 1. A sequence-based approach in which the strengths are derived from estimates of the binding affinity of regulators with the upstream region of their targets, and 2. A transcriptomic-based approach in which the strengths are derived from the regression coefficients of linear feature selection algorithms. We used these estimated regulatory strengths to analyze how they are organized in the network: how the strengths vary depending on the class of the regulator (local or global), on the nature of the interaction (activation or repression), or on its position within certain network motifs. We finally discuss the possible implications of our observations and future perspectives.

Acknowledgements: This work was supported by grant IN202421 from PAPIIT-UNAM to JAF-G.

CHARACTERIZATION OF THE COUPLING MECHANISM OF SCORPION β-NEUROTOXINS ON THE VOLTAGE-GATED SODIUM CHANNEL HNAV1.6

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Abstract:

Voltage-gated sodium channels (Nav's) are complexes of transmembrane proteins that are key to cellular functions, mainly in the generation and propagation of action potentials. Knowing the mechanisms that control and affect the behavior of these channels is crucial for understand the diferents channelopathies related to their malfunction, and thereby favoring the development and design of molecules with modulatory potential. Among the most efficient modulators are the beta neurotoxins present in scorpion venoms, these have the particularity of having an active surface that allows them to interact with a specific site of the Nav's. Despite knowing, through the use of in vitro techniques, the effect of beta neurotoxins on Nav channels, the molecular mechanism by which modulation is carried out is still unknown. In order to elucidate these mechanisms, computational methods have been used, mainly based on in silico simulations of these biological systems in order to mimic conditions as close to the experimental ones. This project aims to elucidate the mechanism of interaction at the molecular level by two scorpion β-neurotoxins nCssII and rCssII with the human sodium channel Nav1.6 using computational techniques such as: homology modeling, molecular coupling and simulations. by molecular dynamics to elucidate important residues in the toxin-channel interaction.

GENOMIC ANALYSIS OF DIFFERENT PATHOTYPES OF *COLLETOTRICHUM LINDEMUTHIANUM*

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Abstract:

In plant-pathogen interactions, phytopathogens confront the complex structure of the plant cell wall (PCW). In this interaction, there is a close co-evolution, where the plant evolves to counteract infection by pathogens, and these in turn evolve to evade plant resistance. The degradation of the main of PCW components by phytopathogens requires the combined and synergistic action of several enzymes belonging to the group of CAZymes. *Colletotrichum lindemuthianum* is the main pathogen of common bean (*Phaseolus vulgaris*), whose nutrition and infection strategy includes the secretion of a set of CAZymes. In addition, this pathogen presents a great diversity of pathotypes with different degrees of virulence against bean varieties. In this study we analyze genomes and the repertoire of genes encoding CAZymes in four pathotypes of *C. lindemuthianum* isolated from bean crops from different regions of México. Fungal genomes were sequenced using the Illumina NovaSeq6000 platform. De novo assemblies were performed using SPAdes v.3.15.4, the Funannotate tool was used for functional annotation, and a genomic comparison of the four genomes was performed using Venn diagrams. Functional annotation focused on identification of conserved domains proteins, transcription sites, tRNAs, gene identification, and determination of biological function. The sizes of the genomes obtained were 89.3 to 92.4 Mb. In general, the pathotypes differed in the number of unique genes (11,859 to 12,225 genes), and the number of orthologous genes for the four pathotypes amounts to more than 11,000. Venn diagrams revealed 12852 shared annotations among the four pathotypes and own annotation for each of them. Regarding the genes encoding CAZymes, differences were detected mainly in the number of genes from the AA7 and CE10 families. However, the genomes of the pathotypes also showed differences in the number of genes encoding transcription factors of the Zn_2Cys_6 family involved in the regulation of CAZymes transcription.

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IN SILICO ANALYSIS OF PROMOTERS OF PUTATIVE GENES ENCODING CHONDROITIN LYASES IN *AVIBACTERIUM PARAGALLINARUM*

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Abstract:

Infectious coryza is a disease of the respiratory tract of birds caused by a gram-negative bacterium called *Avibacterium paragallinarum*. This disease is cause of high economical losses to the poultry industry due to medical treatment, the death of birds, ant the drop in egg production. To get a better knowledge how the bacterium produces the disease, it has been investigated at the genomic level what type of virulence factors it contains. In the present work, an *in-silico* analysis was carried out to identify the encoding genes of the RNA polymerase sigma factors and the associated transcriptional regulators harbored in the genome of AVPG2015 (CP058307.1). This information was used to propose the mechanism that controls the expression of two genes encoding putative chondroitin lyases (*chl*1 and *chl*2). For this, the synteny of the genes that constitute the probable transcriptional units was analyzed and the possible upstream promoters of the genes were predicted. We found three genes encoding sigma factors (σ70, σ32 and σ24) and twenty-seven genes encoding transcriptional regulatory proteins within the AVPG2015 genome. For the case of *chl*1, in an upstream 500 bp sequence were predicted two putative promoters, one recognition site for Sigma 70 and five recognition sites for the TyrR, ArcA, Ihf and Fnr. Within upstream 3000 pb, were predicted seven promoter sequences as well as their potential recognition sites for transcriptional regulators. For *chl*2 gene, two possible promoter sequences were predicted into 500 bp region, but only one recognition site for the Lrp protein were found. In upstream 3000 pb region of *chl*2, there were predicted six possible promoter sequences with their respective binding sites for sigma factors (σ70) and transcriptional regulators. These *in-silico* observations suggest a higher possibility of chondroitin lyases expression mediated by Sigma 70, although several regulators could modulate changes in the expression of both enzymes.

TOWARDS THE CREATION OF A METABOLOMICS DATABASE OF TERRESTRIAL AND MARINE SPECIES IN MÉXICO

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Abstract:

Introduction: México harbors great biodiversity of species and small studies have evidenced their capability of potential to synthesize metabolites with biomedical and biotechnological applications. To expand the chemical knowledge of terrestrial and marine species, we initiated a nationwide effort (METxico Project) to characterize the metabolomes of select species and provide data access to the community by creating a web platform. This work shows preliminary results of the metabolomes and web platform (under a beta version).

Methodology: We collected 109 species (90 and 19 of terrestrial and marine origin, respectively), and metabolites were extracted with a mixture of methanol:acetonitrile: ethyl acetate, and data acquired by liquid chromatography-high resolution tandem mass spectrometry. Data were analyzed by an array of chemoinformatic and web-based tools (GNPS, SIRIUS, Moldiscovery) to identify the metabolite's chemical classes and molecular structures. Results were incorporated into a web platform (soon to be released) created by React (JavaScript library) and various plug-ins for data visualization (e.g., plotly, leaflet).

Results: A total of ~53k potential metabolites were detected (~24k with MS2 associated) to 1970 Da of which ~800 were identified at the molecular structure. In-silico advanced annotation expanded the identification to ~6,700 metabolites. 85 and 154 distinct chemical classes and subclasses were identified, respectively. Lipid metabolites were more present across all species. In some cases, chemotaxonomy analysis revealed a tight clustering of samples assigned to similar taxa. The web platform, aided by visualization plug-ins, shows the results from a global perspective to an individual point of view.

Conclusion: The METxico project will provide invaluable chemical knowledge of the species inhabiting the country that we hope could permanently be available to the community.

REPOSITIONING OF MOLECULES WITH POTENTIAL SENOLYTIC ACTIVITY USING VIRTUAL SCREENING

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Abstract:

Background: Cellular senescence (CS) is a state of irreversible cell cycle arrest that is achieved in response to various stressors that cause multiple alterations at the morphological and molecular levels. An important feature of CS is the activation of signaling pathways that promote survival and antiapoptotic resistance (SCAPs). During aging, senescent cells (SC) accumulate in organs and tissues, promoting the appearance and progression of chronic and degenerative diseases. Several authors have shown that SC elimination helps to stop or reverse disease progression while increasing life expectancy. The use of small molecules capable of selectively inducing death has been proposed to eliminate SC. These molecules are called senolytics.

Objective: To identify and reposition drugs that, through a multitarget mechanism, induce the selective death of human prostate epithelial cells (HPEC) induced to senescence by oxidative stress (SIPS).

Materials and methods: Microarrays were used to determine the differentially expressed genes in an HPEC-SIPS model. A gene regulatory network (GRN) was built and analyzed to identify the possible SCAPs. Subsequently, the three-dimensional structure of the proteins encoded by these genes was used to target senolytic drugs and molecules, using various computational approaches such as structural similarity search, docking, molecular dynamics, chemoinformatic analysis, and network pharmacology.

Results: Through the GRN analysis 4 SCAPs (SERPINE1, PDGFB, EFNB1, and PIK3CD) were selected as pharmacological targets, in addition to 11 leading molecules (4 drugs approved by the FDA, 3 in the experimental phase, and 4 molecules synthesized in our laboratory), that potentially inhibit more than one SCAP.

Conclusion: Eleven leading molecules were found that will be tested due to their high structural similarity and physicochemical properties. The selected molecules share multiple targets with known senolytics, so we expect that a multitarget mechanism might mediate their activity by inhibiting more than one SCAP, targeting proteins, thus eliminating HPEC senescent cells.

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TRANSCRIPTOMICAL ANALYSIS OF FLORAL DEVELOPMENT OF CIRICOTE (*CORDIA SEBESTENA*).

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Abstract:

Anacahuita (*Cordia sebestena*) is a distylous trees, presenting two morphs based on the length of the pystil: long and short. The stigma in one morph is at the same height as the anthers in the other morph, this condition is known as reciprocal herkogamy. Genetic mechanisms governing the development of distyly are still unknown in this species. Using RNA-seq approach, this study is trying to identify the expressed genes involved in the development of both floral morphs in *C. sebestena*. Composite samples of stamens and of pistils per stage/morph combinations at three developmental stages: early (closed buds), mid (popcorn) and late (flower in anthesis) of long and short morphs were collected by triplicate, and for each one total RNA was isolated. 30 transcriptomes and their replicates were sequenced using Illumina platform in paired-end mode to obtain 719 million reads of 150 bp length for each sequenced sample. A total of 342, 933, 866 million reads were obtained and assembled into 102, 459 unigenes. *C. sebestana* unigenes were annotated by function and differentially expressed genes between long- and short-styled wer identified.

Key words: ciricote, distyly, transcriptomics.

A MIRNA-BASED DEEP LEARNING MODEL TO BOOST THE PREDICTIVE POWER OF OBESITY CLINICAL/METABOLICALLY MARKERS

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Abstract:

Obesity is a major risk factor for metabolic disease. However, there are people with obesity who present metabolic health [1-2]. There exist several studies that compared control and obese groups measuring and quantifying microRNA from tissue samples (blood, muscle, gingiva, etc.) or exosomes from humans. The microRNAs (miRNAs) are small RNAs of ~22nt. The miRNAs are related to different responses to diseases and environmental stresses. In obesity, miRNAs are related to the regulation of metabolic and cellular processes, lipid metabolism, insulin signaling, inflammation, cell growth, and even neurogenesis. Furthermore, there is evidence that miRNAs directly correlate with clinical and metabolic variables like total cholesterol, triglycerides, glucose, insulin, and high-density lipoprotein cholesterol. Given this, some miRNAs have been proposed as biomarkers to detect obesity, healthy (HO) or unhealthy (UO) [2].

Despite this evidence, there are no reported studies that incorporate information from different public datasets, from different ethnic backgrounds, with samples from different tissues, and from lean, obese healthy, or obese unhealthy groups. For this reason, I have developed a deep learning model, that uses miRNA expression from public datasets, that not only detects obesity but identifies a minimum set of relevant miRNAs (proposed biomarkers) [3]. This model is a causal model that helps to better understand non-linear relations between miRNAs and clinical variables. The model, when using the proposed biomarkers and clinical variables, improves the HO/UO detection accuracy, sensitivity, and specificity. New or existing data from different regions, environments, ethnic backgrounds, or countries can be incorporated into this model to make it specific to a determined social context.

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STUDY OF CHANGES IN THE GASTROINTESTINAL ARCHAEOME AND ITS RELATIONSHIP WITH CARDIOVASCULAR RISK

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Abstract:

The composition of the gastrointestinal microbiota (GITm) is related to health and disease, despite the broad work reporting the abundance and diversity of bacteria in this human ecosystem, there are few studies focused on identifying the archaea present in the GITm.

From the intestinal archaeome, the methanogenic archaea stand out with the capacity to metabolize trimethylamine (TMA), which is produced mainly by the bacteria of the GITm; the accumulation of TMA is a precursor of atherosclerotic plaque andis related to an increased risk of cardiovascular events. Therefore, we identify the diversity and functionality of archaea present in the GITm and we propose the possibility of using archaea as identifiers of health and cardiovascular risk.

For the study used of sequences of fecal samples from 218 patients with atherosclerotic disease and 187 control individuals. Through the use of computational tools, the archaeome was identified in the GITm of healthy patients and those with atherosclerosis.

The results can be used for the development of new methods of detecting cardiovascular risk, as well as the evaluation of correct intestinal health. This will be subsequently allow reverse genomics analysis to be carried out, which consists in designing strategies allowing the cultivation of archaea in laboratory conditions through analysis of genomic potential and to favor their use as archaeobiotics that protect cardiovascular health, similar to what is made with intestinal probiotics. This strategy that can help reduce lethal cardiovascular events in the Mexican population.

PARAMETRIZATION OF THE FVCB BIOCHEMICAL MODEL FOR C3 PHOTOSYNTHESIS USING BAYESIAN INFERENCE

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Abstract:

Producing enough food for 9,700 million people in 2050 demands crops with higher yields. In wheat, plant breeding has increased yield by optimizing light interception and harvest index. In recent years, however, yield increases using these strategies are slowing down. Increasing photosynthesis is suggested as an untap strategy to further yield increase. Despite its potential, genetically improving photosynthesis has not been achieved because it is a difficult-to-measure, multigenic trait with strong interactions with the environment. To improve photosynthesis, therefore, we need to measure, or at least estimate, the individual biochemical processes that collectively contribute to the leaf photosynthesis rate. A numeric estimation of each component is known as photosynthesis parameter. Traditionally, photosynthesis parameters are estimated by fitting photosynthesis measurements to the Farquhar, Von Caemmerer and Berry (FvCB) biochemical model. There are at least three limitations with this strategy. First, it requires at least a gas exchange analyzer, but better parameter estimation additionally requires chlorophyll fluorometers and equipment to control oxygen concentration. Few laboratories have all three devices. Second, it is time and work consuming; the full measurement set could take up to three hours. The third limitation is that the parameters are estimated by consecutive least squares regressions. This stepwise optimization, with each step conditional on previous optimizations, could result in suboptimal or completely biased results. Here, we present a strategy to develop a better mathematical method to estimate the parameters by using Bayesian inference and a full model posterior sampling resorting to Markov Chain Monte Carlo algorithms. Our working hypothesis is that the use of Bayesian inference in the full FvCB model could potentially decrease the number of measurements and/or decrease the number of devices needed to properly fit the model and prevent suboptimal solutions. We test this hypothesis by estimating the full set of photosynthesis parameters with the traditional and our new Bayesian inference-based approach. We used 12 CIMMYT wheat lines with contrasting Radiation Use Efficiency, which potentially have genetic variability in photosynthesis parameters. The preliminary results are presented here.

Acknowledgments: The authors thank to UNAM for PAPIIT grant IA207021, CONACYT for scholarship to UGPG and Matthew Reynolds from CIMMYT for kindly supplying the wheat lines.

GENE CO-EXPRESSION NETWORK AND THE REGULATION BY THE RNAI MACHINERY DURING MYCOPARASITISM IN *TRICHODERMA ATROVIRIDE*

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Abstract:

Trichoderma atroviride is a filamentous fungus widely used in agriculture, among its applications it stands out as a biological control agent against different phytopathogenic fungi of agricultural importance. The process in which some of the *Trichoderma* strains exert biocontrol is called mycoparasitism [1]. Therefore, different genes that participate in this process have been described by expression analysis and loss of function experiments [1], but one of the challenges is to be able to understand the relationships that genes have with each other during this process. In this work, a weighted gene co-expression network was elaborated from 90 RNA-seq libraries of the wild-type strain of *T. atroviride* and mutants in the RNAi machinery in confrontation with *Alternaria alternata, Rhizoctonia solani* AG2, and *Rhizoctonia solani* AG5, in three different stages of mycoparasitism: before contact, during contact and after contact. We chose these fungi because they cause severe symptoms in plants, but they are also efficiently controlled by the *T. atroviride* wild-type strain. However, knockout mutants of the *dcr2* and *ago3* genes are unable to control the growth of any of these species. In this work we show the first network of gene co-expression during mycoparasitism in *Trichoderma*, which gave us information on different modules of genes that are associated with particular biological functions during mycoparasitism in the WT strain and in the *T. atroviride* RNAi mutants, in addition, we identified the hub genes of each of the modules, which gives us information to know how these genes are related and how the RNAi machinery plays an important role in this process.

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LEA-LIKE PROTEINS IN DESICCATION-TOLERANT ORGANISMS

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Abstract

All life forms on the planet need water to survive. There are organisms that can tolerate losing more than 90% of their water content, called desiccation tolerant organisms. Examples of desiccation tolerant organisms are most of the plant seeds. In order to tolerate desiccation, seeds accumulate a group of proteins called late embryogenesis abundant (LEA) proteins. The consensus idea of how LEA proteins confer desiccation tolerance is by acting as non-classical chaperons that protect proteins and membranes during water loss. A characteristic that separates LEA proteins from other proteins, and could be of great importance to perform their roles during desiccation is their intrinsic structural disorder. Since LEA proteins lack a stable tridimensional structure, it has been hypothesized that the physicochemical properties encoded in their sequence are crucial to perform their functions. Using this premise, we compared the sequence parameters values of four plant LEA proteins and their respective proteomes in search of the parameters that best differentiate LEA proteins from other proteins. We found that LEA proteins have a high fraction of disorder promoting amino acids (≥ 0.76), low hydropathy (≤ 0.46) and low mean net charge (≤ 0.035). Using these parameters, we were able to separate the disordered and hydrophilic LEA proteins (about half of them) from the rest of the respective plant proteomes (~99%). We defined all the proteins with such properties as LEA-like. We search for LEA-like proteins in the proteomes of two desiccation tolerant organisms: the tardigrade *Hypsibius dujardini* and the aquatic larvae of the sleeping chironomid, *Polypedilum vanderplanki.* Using the publicly available RNA-seq data from hydrated and desiccated samples of these organisms, we obtained the transcript accumulation levels of the LEA-like genes. We found that some transcripts accumulate during desiccation, just like the canonical LEA proteins from plants. Based on these similarities with LEA proteins, we hypothesized that LEA-like proteins with accumulation of their transcripts in desiccation will have a chaperone-like function *in vitro.* On the whole, the physicochemical properties and accumulation levels during desiccation represent an innovative way to find proteins with possible relevant roles during desiccation in tolerant organisms.

BIOINFORMATIC ANALYSIS OF THE INTERACTION BETWEEN THE HUMAN HEAT SHOCK PROTEIN 70 (HSP70) WITH ITS TARGET PROTEINS

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Abstract:

Proteins are involved in all biological processes, to properly carry out their functions they must fold and maintain a specific 3-D structure, however, stressful conditions can affect their structure. The molecular chaperones, named heat shock proteins (Hsp´s) are responsible for maintaining protein homeostasis. The Hsp70 are well conserved among species, whose activity has been related to the folding, refolding, and protection against protein aggregation. Among the Hsp70 target, proteins include the intrinsically disordered proteins (IDPs), which have more than one possible 3-D structure and each of these conformations can play a different function. Under some conditions, IDPs tend to form nonspecific interactions and aggregates that are often associated with the development of different pathologies. In this work by bioinformatics tools, we analyzed the prediction of protein-protein interaction between the human Hsp70 with diverse target proteins. From the sequence of the different target proteins, we predicted possible binding sites to interact with Hsp70. We also identified and modeled the intrinsically disordered protein regions (IDPR) in the structure of targets. The evaluation of the protein-protein interaction by molecular docking showed the coupling of the Hsp70 with different protein targets, identifying loops or poorly structured regions. In addition, we found that the type of charged amino acids and therefore the electrostatic interactions are determinants in the interaction of Hsp70 with its different substrates. From this data, we conclude that electrostatic interactions lead to the interaction of Hsp70 with its different clients.

CHARACTERIZATION OF A *VACCINIA VIRUS* ISOLATE FROM AN IMMUNOCOMPROMISED PATIENT WITH PROGRESSIVE *VACCINIA* IN COLOMBIA

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Abstract:

Introduction: Vaccinia virus (VACV) is a member of the genus Orthopoxvirus was successfully used for the first immunizations and is currently used as a vector for vaccine development. VACV is a double-stranded DNA genome of 194,711 bp. Although genomic information is available for vaccine strains, a considerable knowledge gap exists regarding the genetic diversity of zoonotic VACV in aspects related to the infection, ecology, and epidemiology. Although the World Health Organization (WHO) declared global smallpox eradication in 1980, concerns over emerging poxvirus infections have increased as Monkeypox virus (MPXV) continues actively circulating in endemic regions. In recent years, several strains of VACV have been isolated in Colombia. Methodology: To evaluate the evolutionary history of the VACV isolate from an immunocompromised patient developing progressive vaccinia (VACCO). We compared 29 complete genome sequences of Orthopoxviruses available from the GenBank. DNA sequencing was performed using the library prepared with MGIEasy Universal DNA Library prep kit (MGI, China) in the instrument MGISP100 (MGI, China). Raw reads were trimmed using trim_galore (v. 0.6.6) with a quality threshold of ≥ 30. Filtered reads were then mapped using bowtie2 (v.2.4.5) against VACV genome from the NCBI database (assembly GCF_000860085.1, NC_006998.1). The genome assembly was performed using the mapped viral reads by SPAdes (v3.13.1). The integrity of the genome assembly was confirmed using QUAST (v5.2.0). To have the same annotation procedure, all the 30 genomes were annotated with Prokka (v.1.12). Additionally, the homologous groups were identified using Roary (v.3.13.0), and a phylogenetic tree was constructed with the core genome using IQ-TREE. Result and discussion: Genome assembly yielded eight contigs with contiguity of assembly, measured by the N50 of 148345 and a total number of bases assembled of 183,819 bp. VACCO genome encodes for 203 proteins. We obtained 126 homologous groups (core genes) and 61 groups in only one genome or <10% occurrence. Among the core gene of genomes, we evidenced genes with role in virus assembly and morphogenesis, such as A4L, D9R, F4L, G5R, G7L, G9R and proteins that might provide virion attachment to target cells as H1L, H3L, H5R, H7R; among other genes with essential functions in the interaction of VAVC. In the phylogenetic analysis VACV was closely related to others isolated from Canada, the USA, and Brazil. Conclusion: In this study, we characterize the core genome of VACV, which allows a better understanding of the evolutionary history of the zoonotic VACV in Colombia.

3'-UTR OF THE SARS-COV-2 GENOME AS A POSSIBLE SOURCE OF PIRNAS

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Abstract:

P-element-induced wimpy testis-interacting RNAs (piRNAs) are ncRNAs sequences that bind transposons and interfere with the translation of new genes. We searched for 28 nt sequences in the 3' UTR of SARS-CoV-2 (Wuhan patient genome, GenBank: MN908947.3), containing a conserved region of at least 10 nt homology to previously reported piRNAs in databases. We found 6 sequences that were verified for the 2L-piRNA server as piRNAs (1). Taking into account that piRNAs are involved in several diseases, such as different kinds of cancers, we suggest that more research must be done in this regard.

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EXPLORING THE DIVERSITY, ECOLOGY, AND EVOLUTION OF CYCLOMALTODEXTRIN GLUCANOTRANSFERASES IN DOMAINS BACTERIA AND ARCHAEA

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Abstract:

Cyclomaltodextrin glucanotransferase (CGTase; EC 2.4.1.19) is the key enzyme of Carbohydrate Metabolism via Cyclo/maltodextrins (CM-C/D), an unusual starch-transforming pathway. The CM-C/D is a convenient adaptation since cyclo/maltodextrins include amphipathic cyclic oligosaccharides capable of monopolizing substrate availability, encapsulating toxicity substrates, or carrying antimicrobial and signaling molecules. According to the Carbohydrate-Active enZymes (CAZy; www.CAZy.org) database, there are only 48 characterized CGTases isolated from bacteria and archaea, of which ~80% comes from the overexplored mesophilic Bacilli Class bacteria. Here, we explored the diversity, ecology, and evolution of CGTases by data mining alongside comparative genomics and predictive function analysis. As a result, we identified 334 hypothetical CGTases by exhaustively filtering 7,551,351 proteins from bacteria and archaea keep in the GenBank using a customized algorithm. The phylogenetic analysis confirms that CGTases (including both characterized and hypothetical CGTases) are grouped in three different clades separated by the well-characterized α-amylases (outgroup) and include CGTases from microbial genera that have never been reported as C/D producers. Surprisingly, CGTases from G+ (Bacilli and Clostridia) conserve 5 domains ABCDE$_{CBM20}$ classic architecture, while G- (Gammaproteobacteria) and Archaea (Thermoccoci, Haloarchaea, Thermoprotei) include three different architectures, four (ABC-E$_{CBM20}$), three (ABC), and five domains ABCDE$_{CBM20}$/ ABCDE$_{arch}$. Additionally, the phylogenetic tree shows that CGTases from G- diverged from the same ancestor of CGTases from G+ and archaea, suggesting an unknown common ancestor with an ABC architecture. The analysis also suggests that CGTases from Haloarchaea acquired CGTases by a possible horizontal transference from halophilic Bacilli. ~19% of CGTases come from thermophilic ecological niches, while 81% comes from mesophilic bacteria. Additional analyses revealed that genes related to transport, degradation, or metabolic assimilation are frequently located in the vicinity of a *cgt*ase gene except for a few Thermococci. Finally, the rational exploration of genome data allowed exploration of CGTase diversity related to producing microorganisms, multidomain distribution, and genomic context.

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TRANSCRIPTOMIC ANALYSIS OF THE *CM-334/P. CAPSICI/N. ABERRANS* PATHOSYSTEM REVEALS MOLECULAR MODULATION DURING RESISTANCE-BREAKING RESPONSE

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Abstract:

Phytophthora capsici is an important pathogen worldwide because its spread affects pepper production worldwide. This pathogen causes foliar blight, root rot, fruit rot, and crown rot syndromes, resulting in total crop losses. Although current control strategies rely on chemical fungicides, crop rotation, and soil-water management, the use of resistant varieties like CM-334 is the best option. The "Criollo de Morelos" pepper 334 (CM-334) is highly resistant to *P. capsici* strains, regardless of the aggressiveness of the strain or the environmental conditions. However, when the nematode *Nacobbus aberrans* infects peppers, they lose this resistance by a process defined as "Resistance-breaking". Breakdown of resistance results from a transcriptomic reconfiguration of the pepper that induces some defense genes, such as WRKY-a, POX, and EAS. The interest in identifying and describing the resistance process to *P. capsici*, and the breakdown that occurs by *N. aberrans*, has allowed us to establish a model in which we can analyze the modulation process in both scenarios and identify this transcriptomic modulation. The objective of the present work was to carry out a transcriptomic analysis that allowed us to describe the resistance-breaking process in the early (12 h) and late (24 h) stages. Our findings demonstrate that modulation of resistance and resistance-breaking are independent processes that depend on the presence of both pathogens and that their timing modulation is dynamic. We also identified that light-regulated plant defense pathways play an important role during resistance-breaking. This study demonstrates that resistance-breaking is a dynamic process that modifies molecular resistance profile in pepper, is dependent on the presence of both pathogens, and that the light-regulated pathway is a crucial network during this process

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THE SPATIAL STRUCTURE IN BACTERIA COMMUNITIES WITH METABOLIC INTERACTIONS BECAUSE OF SELECTION PRESSURES

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Abstract:

All living organisms have networks with other organisms via dynamic interplays which hold the ecosystems' functionality. Especially in microbial ecosystems, most of the interactions are mediated by metabolic exchange, in particular, the cross-feeding interactions, determined like byproducts exchange with directionality, that is known to produce shifts in the population's dynamic and composition (Reyes-González, 2022). These shifts are powered by the cost-benefit of the production of the metabolites to exchange, an example of that is the synthesis and exchange of amino acids (Mee et. al, 2014). In recent studies, it has been found that added to consortium conformation the environmental variability produces a continuum of interactions (Harcombe et. al, 2014; Hoek et. al, 2016). Another factor is the spatial structure, which has demonstrated an advantage to cooperation behaviors (Kovács, 2014) thus increasing the reciprocity of metabolites exchange. So in this work, the main objective is to comprise the biotic microbial interactions role in spatially explicit environments in a consortium conformation with two Escherichia coli K12 auxotrophic mutant strains to tyrosine and leucine respectively, which on minimal media without amino acids show obligate mutualism. Through our experimental model, we studied the spatial-temporal effects on different agar culture media (M9 medium without amino acids, M9 supplemented with amino acids, and LB medium) to observe how the consortium responds to a selection pressure applied by a bacteriostatic antibiotic (chloramphenicol) and, along with our computational model based on individual agents, that we developed for view the interaction behavior, our results reiterate that the spatial structure on M9 media without amino acids stimulates cooperation and present a low antibiotic sensibility; while as enrich is the environment with amino acids decrease cooperation and all the consortium has high antibiotic sensibility. We hypothesize that this phenomenon is due to the metabolism involved in each media culture that generates different growth velocities as observed on enriched media where consortium grows too fast, in contrast to a medium without supplementation where the growth is slow. These results suggest that cooperation is favored by the spatial structure and, therefore, grants an advantage in face of high chloramphenicol concentrations.

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TRANSCRIPTIONAL HETEROGENEITY OF STATIONARY-PHASE BUDDING YEAST CELLS

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Abstract:

The budding yeast *Saccharomyces cerevisiae* is a well-characterized biological model, frequently used to study complex cellular mechanisms such as aging. The chronological lifespan of yeast is defined as the survival of a non-dividing population during the stationary phase. While assays of the chronological lifespan of mutant strains have shed light into mechanisms of aging in yeast and other organisms, population heterogeneity during the stationary phase limits the potential of this aging model. Here, we hypothesize that aging populations of yeast display different genetic expression profiles leading to a set of cells that can live longer or shorter than others within the same population. To gain insight into the complex aging-associated cellular heterogeneity of yeast, we will use a single-cell RNA sequencing strategy to describe the gene-expression profiles of thousands of individual cells, allowing to identify and accurately quantify cellular subpopulations during the stationary phase and pinpoint genes that are active in specific processes. This would contribute to our understanding of the mechanisms of chronological aging in heterogeneous cell populations. In addition, we will characterize the single-cell expression profile of the long-lived *swr1* deletion strain, impaired in nucleosome exchange and chromatin remodeling. This will contribute to our understanding of the mechanism about cellular heterogeneity in aging cultures and aging-associated transcriptional profiling changes induced changes in chromatin remodeling leading to extended cellular lifespan.

ANALYSIS OF A POLYGENETIC RISK FUNCTION FOR OSTEOSARCOMA

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Abstract:

Osteosarcoma (OS) is the most prevalent primary bone neoplasm worldwide, characterized by the formation of immature bone tissue and osteoid tissue. This cellular imbalance that gives rise to abnormal growth occurs predominantly in adolescents and young adults with a peak incidence between 15 and 19 years old. The etiology of OS is poorly understood, however individual susceptibility encompasses environmental, genetic and lifestyle factors that impact the appearance of this pathology. One of the drawbacks of this disease is that the diagnosis is made at a late stage. The 5 to 20 year survival rate is estimated to be less than approximately 60% with surgical and pharmaceutical intervention in patients with localized disease. While it worsens to less than 20% in the presence of metastases. This highlights the need to generate better early diagnosis strategies. In this sense, strategies are being developed that employ the use of genetic biomarkers such as single nucleotide polymorphisms (SNPs) in conjunction with artificial intelligence (AI) tools such as machine learning and data mining. It has been shown that the generation of a function that calculates the polygenetic risk value (PRV) has a relevant role in the diagnosis of complex diseases. However, some disadvantages are observed when assigning this score, one of them is the limited number of genome wide association studies (GWAS) that indicate the polygenic influence in the development of this disease. In addition to the fact that the genetic diversity in these studies is limited to the European population and most of the sex chromosomes are excluded. In this work, the VRP used in different neoplasms will be evaluated, taking into account the work previously carried out in the laboratory where the genetic factor is considered when using expression data in OS cell lines with which machine learning models were generated in set. Which is that each model produces an independent prediction. The predictions of the different models are combined to obtain a single prediction. With which it is intended to build a specific VRP function for OS. The genotypic information associated with the phenotype must be taken into account. Which will be applied to different populations where specificity and accuracy will be taken as an advantage. In conclusion, the generation of a function that calculates specific VPR for OS will function as an important pillar in the genetic diagnosis of this disease.

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UNVEILING METABOLIC TRAITS OF *ARGEMONE MEXICANA* L. RHIZOBIOME

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Abstract:

The Mexican prickly poppy (*Argemone mexicana* L.) is a plant from the Papaveraceae family which produces over 30 different benzylisoquinoline alkaloids (BIA), including sanguinarine and berberine [1]. It has been used since ancient times in traditional medicine in Mesoamerica and other parts of the world [2].

Interestingly, sanguinarine is detected in root exudates from this plant, and radicles form developing seedling display the ability to secrete sanguinarine [3]. Recently, a B-type ATP Binding Cassette transporter (ABCB) involved in sanguinarine and berberine mobilization, has been described in *Argemone* seeds and roots [4].

Employing a metagenomic approach, in here we report the taxonomic composition of the microbiota associated to roots from mature *A. mexicana* plants (rhizobiome). Description is presented in terms of beta diversity, as well as richness and evenness, compared to bulk soil. Significant differences in the dominant microbial populations were observed in samples from the rhizosphere, suggesting a possible effect of the root excreted alkaloids.

Metabolic traits regarding nutrient solubilization and plant grow promotion were strongly represented across rhizobiome genes. Among them, nifA and nifZ, involved in nitrogen fixation, as well as ipdC, dhaS, IaaM and IaaH, corresponding to indole-3-acetic acid biosynthesis pathway were particularly noteworthy. Carbon, nitrogen, and energy metabolisms were markedly influenced by the differential taxa distribution, both at phyla and family levels. This is the first metagenome-wide association study of the *A. mexicana* rhizobiome.

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IN SILICO IDENTIFICATION OF RIBOSWITCH MOTIFS WITHIN PROKARYOTIC GENOME CODIFYING SEQUENCES REVEALS RECURRENT ANNOTATION ERRORS

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Abstract:

As a novel regulatory element of gene expression, the study of RNA has contributed to the elucidation of new molecular regulatory mechanisms in organisms from all kingdoms of life. Among them, riboswitches have a special place since they can recognize their target molecules with great specificity and high affinity, without the need of any protein component. Throughout searching for these elements in bacterial and archaeal genomes, we found recurrent annotation errors within codifying regions. Our evidence is based on the ability to identify riboswitch motifs with great precision in genomic sequences due to the high degree of conservation of their primary sequences and secondary structures, information that is used to build covariance models, available at the Rfam database. We used these models for each of the 50 riboswitch classes described until now in this database, to find the location of riboswitches within the genomic sequences. Then, we compared these positions with the beginnings and ends of genomic regions annotated as genes or ORFs. The results of this comparison and subsequent analysis, provide us with essential information on the prevalence of annotation errors and evidence on the feasibility of using our computational approach based on the genomic identification of riboswitches to prevent such seemingly recurrent annotation mistakes.

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BIOLOGICAL ACTIVITY ESTIMATION OF PEPTIDES DERIVED FROM GRAIN THROUGH COMPUTATIONAL PREDICTION ALGORITHMS IN METABOLIC DISEASES

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Abstract:

Introduction.Metabolic diseases such as obesity, diabetes, and cardiovascular disease are considered a global health problem, associated with high mortality and a low quality of life. Plant-derived bioactive peptides have been associated with a number of health benefits; several peptides with antidiabetic potential have been identified in grain that could lower blood glucose levels, improve insulin absorption, and inhibit key enzymes involved in the development and progression of diabetes. An understanding of the molecular mechanisms of these peptides will contribute to the development of new peptide-based therapies.

Aims. Identify and characterize molecular targets of plant-derived bioactive peptides, isolated from the soybean (*Glycine max*), bean (*Phaseolus vulgaris*), and quinoa (*Chenopodium quinoa)* proteins, through bioinformatics tools.

Materials and Methods. Nine peptides with antidiabetic activity from plants such as soybeans, beans, and quinoa were selected. Sequences of each peptide were obtained from NCBI and subsequently converted to SMILES sequences in BIOPEP. SwissTargetPrediction was used to compare the 2D and 3D homology of peptides with their targets and were analyzed to predict their molecular pathways using DAVID Bioinformatics tools. For each peptide, the physicochemical properties were determined (isoelectric point, molecular weight, estimated T1/2, instability index, +/- charges, aliphatic index, GRAVY index) using ProtParamTool.

Results. Most of the targets identified for the nine peptides are molecularly classified as Family A G protein-coupled receptors, proteases, and oxidoreductases. The most importantly modulated signaling pathways were associated to lipid and atherosclerosis pathway, renin-angiotensin system, AGE-RAGE signaling pathways in diabetic complications, endocrine resistance and TNF signaling pathway. In addition, one of the peptides from quinoa showed a strong regulation of neurological signaling pathways.

Conclusions. The analyzed peptides have numerous biological effects with the potential to regulate metabolic signaling pathways in chronic-degenerative diseases.

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STUDY OF CROSS-RESISTANCE AND COLLATERAL SENSITIVITY TO BETA-LACTAM ANTIBIOTICS IN AN *ESCHERICHIA COLI* SYSTEM WITH DIFFERENT ANTIBIOTIC RESISTANCE GENES TEM

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Abstract:

Beta-lactam antibiotics are the most prescribed due to their high efficacy and low toxicity to the human body (Suarez *et al.* 2009), which is why they are found in the environment at sublethal concentrations that favor the development of microbial communities that are highly resistant to antibiotics. These bacteria can produce enzymes, such as beta-lactamases, which hydrolyze and deactivate the beta-lactam ring of antibiotics and thus reduce the effectiveness of treatments. Therefore, it is vital to understand the effect of previous exposures to these antimicrobials in different genetic backgrounds. To study this problem, we characterized and performed experimental evolution experiments consisting of an antibiotic ramp for eight days, increasing different beta-lactam antibiotic concentrations. We performed this experiment using a family of Escherichia coli that already contained five different TEM-resistant genes (Goulart *et.al* 2013) introduced by a non-conjugative plasmid. After the evolutionary experiment is complete, we test this final population for cross-resistance with the remaining b-lactam antibiotics. To further understand the effect of the previous resistance, we extracted the plasmid before and after the cross-resistance experiment. We sequenced it to observe if there were changes in the TEM gene already contained. Or if other mechanisms give the resistance. We aim to identify collateral sensitivity or cross-resistance and propose the most effective antibiotic combinations.

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RELATIONSHIP BETWEEN GENES INVOLVED IN GLYCEROL AND TRIACYLGLYCEROL BIOSYNTHESIS UNDER NITROGEN STARVATION IN *CHLAMYDOMONAS REINHARDTII*: A BIOINFORMATIC ANALYSIS

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Abstract:

The production and accumulation of lipids under abiotic stress has been identified in *Chlamydomonas reinhardtii,* a model green microalga. Several studies have shown that in the absence of nitrogen *C. reinhardtii* increases the production of triacylglycerols (TAGs). Previous studies have focused on the function of genes that allow the formation of triacylglycerol from diacylglycerol, while genes responsible for the synthesis of key precursors, such as glycerol, have received less attention.

The aim of this study is to identify the transcriptional relation between genes involved in the production and accumulation of glycerol and TAGs in nitrogen starvation. For this analysis, 85 genes involved in the synthesis of these metabolites were selected from transcriptomic data generated by Boyle et al (2012). Expression patterns were analyzed over a period from 0 to 48 h in nitrogen starvation. The results suggest that glycerol-3-phosphate dehydrogenase 2 (an enzyme coded by *CrGPDH2*) and glycerol kinase (an enzyme coded by *GK*) may play an important role in the relationship of the production of both glycerol and TAGs. RT-qPCR experiments are ongoing to further investigate this subject.

Boyle, N. R., Page, M. D., Liu, B., Blaby, I. K., Casero, D., Kropat, J., Cokus, S. J., Hong-Hermesdorf, A., Shaw, J., Karpowicz, S. J., Gallaher, S. D., Johnson, S., Benning, C., Pellegrini, M., Grossman, A., & Merchant, S. S. (2012). Three acyltransferases and nitrogen-responsive regulator are implicated in nitrogen starvation-induced triacylglycerol accumulation in Chlamydomonas. *Journal of Biological Chemistry*, *287*(19), 15811–15825. https://doi.org/10.1074/jbc.M111.334052

BIOGEOCHEMICAL FUNCTIONS OF BACTERIAL COMMUNITIES INHABITING WETLAND SEDIMENTS OF THE YUCATÁN COAST

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Abstract:

Coastal sediments provide a complex mixture of nutrients because of organic matter deposition from the upper water column, making suitable habitats for bacterial communities. Thus, bacteria play key roles in the uptake and release of nutrients through these ecosystems, as well as in the regulation of global biogeochemical cycles. Four wetland sites were selected based on georeferenced information for land uses and geohydrological conditions. The sites were grouped into two zones, each one with a perturbed site and another conserved: a west zone (Sisal and El Palmar Reserve) and an east one (Dzilam and Bocas de Dzilam Reserve), where groundwater of the Chicxulub Ring of Cenotes discharges. We collected sediment samples from each site to analyze by using 16S rRNA amplicon sequencing. Quantitative Insights Into Microbial Ecology (QIIME2) was performed for taxonomic characterization. Phylogenetic Investigation of Communities by Reconstruction of Unobserved States (PICRUSt2) was also used to investigate metabolic functions and genes associated with the biogeochemical cycles of carbon, nitrogen, sulfur, and phosphorus. 14 phyla were found in total. *Acidobacteria* was found ubiquitously. *Proteobacteria* and CK.2C2.2 were the most abundant phyla in the west, while *Nanoarchaeota* and *Crenarchaeota* dominated in the east. *Epsilonbacteraeota*, *Actinobacteria* and *Zixibacteria* were found exclusively in the west, whereas *Diapherotrites*, *Euryarchaeota*, *Patescibacteria*, *Nitrospirae* and *Cyanobacteria* were in the east only. Spatial patterns in the rates of metabolic functions were also found. Methane and sulfur metabolisms, as well as carbon fixation by prokaryotes and phosphorus transporters showed higher rates towards the east. In contrast, nitrogen metabolism, regulation of phosphorus starvation, photosynthesis and carbon fixation by photosynthetic organisms had higher rates in the west. Taxonomical contributions to these metabolic functions were also explored. This study aims to set baselines in both local diversity and biogeochemical functions of bacterial communities for a region whose economy is growing rapidly.

INFERRING CO-EXPRESSION NETWORKS OF *ARABIDOPSIS THALIANA* GENES DURING THEIR INTERACTION WITH *TRICHODERMA* SPP

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Abstract:

In nature, plants cohabit with a wide variety of microorganisms including bacteria, fungi, protists, and archaea, where they form communities that constantly interact. These interactions can be beneficial or deleterious for plants, having serious implications for crop yields and food security. Although the mechanisms of interaction are complex, molecular mechanisms can be predicted from gene expression data and co-expression network analysis from the organisms involved. It allows identifying genes with an important role in the phenomenon under study. In this study we propose a comprehensive bioinformatic approach to generate co-expression networks from mutualistic interactions based on high-throughput data (transcriptomics), to elucidate the molecular mechanisms of gene expression during plant-fungus interaction using the model plant *Arabidopsis thaliana* co-cultured with the mutualistic fungi *T. atroviride,* and *T. virens*. Our results indicated a high similarity of response triggering a transcriptional reprogramming in *A. thaliana*, identifying conserved mechanisms between fungi with a mutualistic lifestyle. In addition, our method identified the induction of specific genes in the plant, observing contrast differences at 72 hours of co-cultured. Gene co-expression networks of *A. thaliana* showed that beneficial mutualistic fungi triggered an hypoxic response, defense mechanism and toxin metabolic process in the plant. These observations suggest that hypoxia could be related to plant defense mechanisms, owing to genes related to defense and hypoxia were positioned in the same community for both fungi.

Keywords: Gene co-expression network, beneficial mutualists, transcriptomics, differential network analysis, hypoxia.

LIGAND TRANSPORT ANALYSIS OF MALONATE PRODRUGS THROUGH SUCCINATE DEHYDROGENASE BY CAVER WEB AND CICLOP

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Abstract:

Protein tunnels are pathways for ligands to active sites found in the core of proteins with complex three-dimensional structures (1). Succinate dehydrogenase (SDH) is a mitochondrial complex conformed by four subunits that contains various prosthetic groups (2). Malonate ester prodrugs such as Diethyl and Dimethyl-Malonate (DEM/DMM) are permeable substances capable of inhibiting SDH, however, their effect at mitochondrial level has not been reported (3). In this study was shown that both DEM and DMM act as non-essential activators of succinate reductase activity. Using molecular dynamics and molecular docking it was demostrated that both compounds binding to the quinone sites Q_P (SDHB) and distant Q_D (SDHD) with different affinity. However, the enzyme-ligand complexes were not stable on the Q_p and Q_D sites. Therefore, the Caver Web server was used to perform trajectory assays of these ligands through tunnels 2 and 8, which form a network that connects the prosthetic groups (Heme and FeS) with the Q_D. In this case, the significant differences were in length: 11.3 Å and 37.5 Å; and the bottleneck radius: 3.1 Å and 1.8 Å, respectively. The results of the trajectory analysis from the surface to the active site indicated that the two ligands were capable of being transported according to the negative values of Esurface, Emax and Ebound. In addition, the parameters of Ea and Ebs; did not show a difference in the tunnel 2 trajectories (Ea=0.4, 0.5; Ebs=0.5, 0.4), in the case of tunnel 8, the DMM values (Ea= 0.3; Ebs=-0.4) showed a slight difference compared to DEM (Ea= 0.5; Ebs= 0.2). Finally, the CICLOP server supported the interaction of tunnels 2 and 8 as a natural hydrophobic cavity able to connect SDHA-D, with pore volume = 18404 $Å^3$, 444 amino acid residues were detected on the inner surface based on a single atom, of these 154 are completely inside, 83 are charged (53 positive and 30 negative), 196 are hydrophobic and 248 hydrophilic. In conclusion, DMM and DEM initially bind to the Q_D site and subsequently internalize into an internal cavity that forms a tunnel that positively affects the flow of electrons between the prosthetic groups of SDH.

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PREDICTING TRANSCRIPTION FACTOR CANDIDATES THAT REGULATE GENES OF THE CAROTENOID BIOSYNTHETIC PATHWAY IN FRUITS OF *CAPSICUM* SPP.

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Abstract:

Chili pepper (*Capsicum* spp.) fruits are good sources of bioactive compounds, such as carotenoids, capsaicinoids, vitamins, flavonoids, and phenolic compounds. During the ripening process, the pericarp of *Capsicum* fruits accumulates high amounts of carotenoids. Although the carotenoid biosynthesis pathway in the *Capsicum* genus has been widely studied from different perspectives, the transcriptional regulation of genes encoding carotenoid biosynthetic enzymes has not been elucidated in this nonclimacteric fruit. In this work, we analyzed RNA-Seq transcriptomic data from the fruits of 12 accessions of *Capsicum* spp (four wild, six domesticated, and two reciprocal crosses between domesticated and wild-type accessions) during the ripening process [0, 10, 20, 30, 40, 50, and 60 days after anthesis (DAA)] using the R package Salsa. With this package, we performed coexpression analyses between the standardized expression of genes encoding carotenoid biosynthetic enzymes [target genes (TGs)] and genes of all expressed transcription factors [TFs], hypothesizing that both TF and TG genes should show highly similar expression profiles. We selected the best candidates (highest *P* values) that might regulate the expression of genes encoding the carotenoid biosynthetic enzymes. Additionally, we analyzed the promoter region of each biosynthetic gene to identify putative binding sequences for each selected TF candidate as a complementary criterion for selection. These results are the base for further gene functional studies to corroborate their participation in the regulation of this biosynthetic pathway in *Capsicum* spp. Project CB280755 (Conacyt).

A NOVEL MOTIF (Nβ) THAT LEADS SECRETION OF LACKING SIGNAL PEPTIDE PROTEINS

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Abstract:

Post-translational events are essential for an accurate cell physiology. This includes protein localization within or out of the cell. Protein secretion includes several cellular delivery systems in which molecular labels are recognized in the protein sequences themselves. One of these signals is widely known as signal peptide.

NaTrxh is a protein recently characterized as essential for pollen rejection response in the S-RNase self-incompatibility system in *Nicotiana alata* [1]. An important feature of NaTrxh is that despite lacking a signal peptide, it possesses the information to lead its secretion [2]. A motif called Nβ (Ala-17 to Pro-27) has been identified as the sequence that leads the extracellular localization of NaTrxh [3].

From a BLAST analysis, Nβ or Nβ-like sequences were found within different proteins of all biological domains. Consensus sequence analysis has allowed us to experimentally determine that the positions 4 to 11 of the Nβ sequence are essential for its role as a secretion signal. Furthermore, we have identified three positions (5, 8 and 9), which appear to be essential for this function and experimental analysis are being carried out for their assessment.

Another critical feature Nβ motif must possess to act as a secretion signal is the position it occupies within the primary structure of the protein. All Nβ-containing proteins whose secretion is confident (*UniProtKB*) has this motif towards the N-terminal and our experimental data confirmed this hypothesis.

The characterization of the Nβ motif as a novel signal sequence will be useful to propose this sequence to predict an extracellular localization of any protein that contains it and that lacks a typical signal peptide.

PAPIIT-UNAM IN230920; CONACyT fellowship to AZ-G
PAPIIT-UNAM IN230920; CONACyT 240927

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ABSTRACTS | Poster Toxicology & Pharmacology

XXXIII National Congress of Biochemistry

THE MOBIMS: A MINIATURE MASS SPECTROMETER FOR MONITORING VOLATILES IN BIOLOGICAL SYSTEMS

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Abstract:

Volatile Organic Compounds (VOC) are a large and diverse group of molecules that serve as long-distance infochemicals in specific contexts, playing essential roles in many ecological interactions. Volatiles also represent a characteristic phenotype of an organism under different environmental conditions. Understanding the dynamics of VOCs in biological systems helps establish their ecological roles. This field, however, remains poorly understood, mainly because of technological limitations.

We assembled a Modular Biological Mass Spectrometer (MoBiMS) for the real-time monitoring of volatiles [1]. The MoBiMS is based on a residual gas analyzer and adapted to a closed chamber that allows experiments under controlled conditions. A gas-dose valve highly regulates the inlet of the system. The ion source operates at 70eV, making it compatible with volatile reference databases (such as the NIST DB). The analyzer is a quadrupole mass spectrometer coupled to a continuous secondary electron multiplier detector (C-SEM) that improves the detection. The MoBiMS system can monitor up to 300 ions simultaneously. In the performed tests with standards, we could detect different chemical classes of both inorganic and organic volatiles, such as alcohols, ketones, and esters. We also analyzed the behavior of some volatiles directly from their biological source. The online monitoring of VOCs for several days with high temporal resolution (~500 ms) is also possible. The analytical performance of the MoBiMS demonstrates great utility for research on volatile-mediated interactions in biological systems under ambient conditions. In addition, the modular design of this system allows modifications according to the research needs.

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5-FU AND TAMOXIFEN MODIFY MCRP EXPRESSION AND CSC PERCENTAGE IN SW480 CELLS

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Abstract:

Colorectal cancer (CRC) ranks third in terms of incidence and second in terms of mortality worldwide, and it is the first leading cause of death related to gastrointestinal cancer. Its comprehensive treatment with monoclonal antibodies (mAbs) and cytotoxic drugs has increased the survival of patients with CRC. However, its efficacy may be limited by the presence of the membrane-bound complement regulatory proteins (mCRP): CD46, CD55 and CD59, which can inhibit complement-dependent cytotoxicity (CDC) and regulate intracellular signaling pathways to promote the tumoral progression. The effect of the expression of mCRP on mAbs efficacy is well-known, but its relationship with cytotoxic therapy and cancer stem cells (CSC) has not been established yet. Thus, we decided to analyze the impact of cytotoxic therapy on mCRP expression in colon cancer cells (SW480), and in CSC, transduced with a reporter system based on SOX2/OCT4 activity and GFP expression (1). The drugs used were 5-fluorouracil (5-FU), a cytotoxic drug that has been used in CRC therapy for more than 40 years, and tamoxifen (Tam), whose administration has decreased CD55 levels in breast cancer cell lines (2).

Cell viability of cells exposed to the drugs was determined by a MTT assay (72h). Both 5-FU (IC50= 75.6 µM) and Tam (IC50= 9.5 µM) have a cytotoxic effect on SW-480; Tam is more potent than 5-FU and 5-FU plus Tam combination has a synergic effect (IC50= 17.5 µM). Flow cytometry analysis showed that 72h exposition to 5-FU induces the expression of CD55 and CD59 and reduces the CSC population, showing no effects on CD46 expression. In contrast, Tam enriches CSC population, although it also induces CD55 and CD59 expression. Exposing SW-480 cells to 5-FU and Tam modifies mCRP expression and the percentage of CSC, which could be directly affecting therapeutic mAbs efficacy and patient survival. It would be relevant to elucidate whether mCRP can regulate CSC, an intrinsically resistant population that causes cancer relapses.
Supported by UNAM-PAPIIT IN219719 and CONACyT A1-S-18285.

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ABERRANT CYTOKINESIS AS AN ALTERNATIVE MECHANISM OF PACLITAXEL TOXICITY IN CANCER TREATMENT

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Abstract:

Mitosis is a fundamental process in the cell cycle. Anti-cancer therapy uses drugs that target microtubules and prevent the correct formation of the mitotic spindle, causing a mitotic arrest. Paclitaxel is one of the most widely used antimicrotubule drugs in chemotherapy. It has been proposed that prolonged mitotic arrest causes cell death and is the primary mechanism by which antimicrotubule drugs cause cancer cell death. However, it has been shown that some cells can slip out from the arrest and may continue in the cell cycle or die in the subsequent G1 phase. Results from our group and other laboratories have shown that released cells have DNA damage. In addition, we have observed the formation of aberrant and incomplete cytokinesis during slippage. We propose that the appearance of contractile rings towards the end of prolonged mitosis causes DNA damage, which is associated with interphase death. In the HCT116 cell line, inhibition of contractile ring formation decreases the percentage of cells positive for the gamma-H2AX mark (DNA damage marker) and reduces the number of DNA damage positive foci. Moreover, inhibition of cytokinesis increases the viability of paclitaxel-treated cells after cell release. Protein analysis confirmed that caspase 3 activation is lower in cells where cytokinesis is inhibited, as well as gamma-H2AX and Bax levels. The expression of p53 targets such as p21 and Bad is also lower when cytokinesis is inhibited in paclitaxel-treated cells. These results demonstrate that the formation of contractile rings at the end of prolonged mitosis is one of the factors promoting the formation of DNA damage. Furthermore, they present an alternative mechanism of paclitaxel activity that is post-mitosis and is dependent on the response to DNA damage. This finding is relevant for determining the factors associated with paclitaxel resistance since the involvement of the DNA damage response was not considered in the treatment with taxanes and other antimicrotubule drugs.

EXPRESSION OF PRORENIN/RENIN RECEPTOR AND ITS FUNCTION ON CARDIOVASCULAR SYSTEM IN THE OFFSPRING OF PREECLAMPTIC RATS

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Abstract:

Preeclampsia is a characteristic disease of pregnancy, OMS reports a prevalence of 10% in all pregnancies worldwide. Preeclampsia (PE) is characterized by hypertension and proteinuria beginning on the twentieth week of gestation, it can progress to a multi-organ ill with variable clinical characteristics. PE conditions problems in the women who suffer it, and also influences the health of the products. It has been observed that offspring from pregnancies complicated by preeclampsia develop cardio-metabolic diseases in adult life. Barker proposed the theory that diseases that manifest during adult life are programmed during intrauterine life. The renin angiotensin system is a key system for regulation of blood pressure and could be involved in the manifestation of these diseases. Within the components of the renin-angiotensin system, the prorenin receptor (PRR) induces profibrotic signaling events that are independent of angiotensin production. We used a subrenal aortic coarctation which resembles a clinical preeclampsia in rats. The offspring was analyzed at 4, 8 and 12 weeks of life, measuring weight, height, blood pressure and expression of PRR in cardiac tissue using the Western Blot technique. We observed restriction of intrauterine development and decrease in the number of litters in pregnancy with PE compared to healthy pregnancy, in terms of blood pressure, a progressive increase is observed in males at 4, 8 and 12 weeks, likewise increase in the expression of PRR. As for females from a pregnancy with PE, an increase in blood pressure and PRR expression is observed at 4 weeks, but this normalizes at 8 and 12 weeks. We attribute this effect to female sex hormones. With the results obtained, we conclude that offspring from a pregnancy complicated by preeclampsia have predispositions to cardiovascular diseases such as hypertension and the expression of PRR is proportional to the manifestation of the disease, suggesting that the elevation of blood pressure is mediated by these receptors.

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NON-DESCRIBED ITRACONAZOLE EFFECT ON IMMUNITY CELLS IN A MURINE-EUMYCETOMA TREATMENT

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Abstract:

Eumycetoma is a neglected disease caused by fungi, characterized by the formation of subcutaneous grains which generally appear in extremities, after a traumatic implantation of the etiological agent. The clinical aspects of eumycetoma consist of swelling of the inoculated arms or legs due to subcutaneous granulomas that contains sinuses which drain seropurulent material and grains, generally black-colored. *Madurella mycetomatis* is the most common etiological agent of black grain eumycetoma.

Since actinomycetoma incidence is bigger than eumycetoma in Mexico, the study of the last has suffered a lag. The disease is related with some geographical and socioeconomic aspects, hence is important to continue providing data about eumycetoma from various perspectives. In this work, we used an eumycetoma murine model adapted to the conditions of our laboratory at Facultad de Estudios Profesionales Zona Huasteca, UASLP, with the aim of evaluate the progression of the disease, macroscopically and in an histopathological level, during the course of an itraconazole treatment. This antifungal has been extensively used and has demonstrated to be effective when used along with surgical intervention to treat eumycetoma. After 50 days developing eumycetoma, the mice start with an itraconazole treatment for 4 weeks. Interestingly, macroscopically bigger grains were observed in the itraconazole-treated group compared to those found in the untreated control group. In contrast, microscopically the fungal grain was notably reduced at the end of treatment in the itraconazole-treated group. However, what we observed as a bigger grain resulted as an increased inflammatory reaction, unspecifically extended among tissue. Although the effect that azoles exert on fungal pathogens is well known, there may be other mechanisms poorly explored for these drugs. Thus, itraconazole may play a role as an immunity stimulator, an undescribed mechanism for this antifungal.

HYDROGEN SULFIDE IMPROVES VASCULAR DYSFUNCTION INDUCED BY CHRONIC STRESS RESTRAINT IN RATS

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Abstract:

Several lines of evidence have shown that chronic stress decreases the levels of hydrogen sulfide (H_2S) in the hypothalamus. Furthermore, chronic stress induces cardiovascular alterations such as vascular dysfunction, and H_2S is implicated in regulating the cardiovascular system. H_2S has a potential pharmacological effect on vascular dysfunction induced by several pathologies. However, up to date, the effect of NaHS (sodium hydrosulfide; H_2S donor) on chronic stress restraint-induced vascular dysfunction has not been evaluated. Thus, this study aimed to determine the effect of NaHS on chronic stress restraint-induced vascular dysfunction in the aorta and mesenteric artery. For this purpose, 24 male Wistar rats were divided into four groups. The first group (n=6) was the control group without chronic stress restraint. The other three groups (n=18) were subjected to restraint stress for 2 h per day for eight weeks in a transparent acrylic tube. At week four of the stress protocol, the animals were divided into three groups that received daily i.p. administration for four weeks with: (1) nothing; (2) phosphate buffer saline (PBS; 1 ml/kg); and (3) NaHS (5.6 mg/kg). Aortas and mesenteric arteries were cut into rings and horizontally mounted with nichrome wire in an organ bath. Then, cumulative concentration-response curves of carbachol (CCh, $1x10^{-9}$ M - $1x10^{-5}$ M), sodium nitroprusside (SNP, $1x10^{-9}$ M - $1x10^{-5}$ M), or noradrenaline (NA, $1x10^{-9}$ M - $1x10^{-4}$ M) were determined and the vascular response was recorded. Chronic stress restraint: (1) increased the vasoconstriction induced by NA, (2) decreased the vasorelaxation induced by CCh, and (3) failed to modify the vasorelaxation induced by SNP in the aorta and mesenteric artery. Remarkably, the treatment with NaHS improved the vasorelaxation induced by CCh and decreased vasoconstriction induced by NA in the aorta. On the other hand, NaHS improved the vasorelaxation induced by CCh and SNP in the mesenteric artery. These findings suggest that NaHS reverted the chronic stress restraint-induced vascular dysfunction and may be used as a therapeutic option for the treatment of the cardiovascular alterations induced by chronic stress.

EXPOSURE TO BIS (2-ETHYLHEXYL) PHTHALATE (DEHP) INDUCES OXIDATIVE STRESS IN HUMAN SKELETAL MUSCLE CELLS

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Abstract:

The plasticizer bis (2-ethylhexyl) phthalate (DEHP) dysregulates the balance between reactive oxygen species (ROS) production and antioxidant defenses. Despite the available information on DEHP's hazardous effects in mammals, its potential impact in cells remains unclear. The objective of this study was to assess changes in redox metabolism induced by DEHP in human skeletal muscle cells in primary culture. After obtaining informed consent, rectus abdominis muscle samples were collected from healthy women undergoing programed cesarean surgery at term. Skeletal muscle cells were isolated and grown under standard cell culture conditions. Cells were exposed to 1 mM of DEHP (treated group) for 13 days (n = 25); cells maintained without DEHP were considered as the control group (n = 25). Superoxide radical ($O_2^{\bullet-}$) production, thiobarbituric acid reactive substances (TBARS) and protein carbonyl (PC) levels, as well as superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx) and glutathione S-transferase (GST) and activity were quantified using spectrophotometric methods; transcript levels of antioxidant enzymes, peroxisome proliferator-activated receptor (PPAR)-alpha, caspase-3 (cASP3), nuclear factor erythroid 2-related factor 2 (NRF2) and peroxiredoxins (PRXS) were quantified through reverse transcription quantitative polymerase chain reaction (RT-qPCR). Exposure to DEHP increased $O_2^{\bullet-}$ production, SOD and GST activities, as well as TBARS and PC levels ($p<0.05$). In addition, transcripts of all genes were altered under DEHP treated condition. These results suggest that DEHP induces oxidative stress in human skeletal muscle cells in primary culture. Overproduction of $O_2^{\bullet-}$ and increased lipid peroxidation could exacerbate degenerative processes and over-production of peroxisomes in skeletal muscle leading to an increase in cell death.

Keywords: apoptosis, cytotoxicity, human, oxidative stress, phthalates

TESTOSTERONE ENHANCES, VIA A GENOMIC PATHWAY, AIRWAY SMOOTH MUSCLE RELAXATION INDUCED BY SALBUTAMOL AND THEOPHYLLINE, TWO DRUGS USEFUL IN THE TREATMENT OF ASTHMA

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Abstract:

Androgens are related to the severity of asthma symptoms. In childhood, asthma symptoms are more common in boys than in girls. This phenomenon reverses at puberty when symptoms decrease and plasma concentrations of testosterone (TES) increase in young men. Plasma levels of TES vary between 5-50 nM in men throughout their lives. Androgens are known to exert their physiological effects via genomic and non-genomic pathways. Genomic effects depend on the androgen receptor (AR) to modulate transcription and protein synthesis, whereas nongenomic effects occur over a short period of time and are independent of AR activity. β_2-adrenergic agonists such as salbutamol (Sal) and theophylline (Theo, a methylxanthine) are reliable options for the pharmacological treatment of asthma. These drugs increase cyclic adenosine monophosphate (cAMP) concentrations and promote protein kinase A (PKA) activation. This enzyme triggers the opening of K^+ channels, leading to the relaxation of airway smooth muscle (ASM). Chronic incubation of guinea pig trachea with TES (40 nM for 48 hours) enhanced Sal- and Theo-induced relaxation. The Sal Sal e was abolished by flutamide (an AR antagonist). In tracheal myocytes, chronic incubation with TES increased Sal- and Theo-elicited K^+ currents (IK^+), which were also abolished by flutamide. The Sal- and Theo-induced increase in IK^+ was blocked by 4-aminopyridine and iberiotoxin, suggesting that delayed rectifier voltage-gated K^+ channels (K_V) and high-conductance Ca^{2+}-activated K^+ channels ($K_{Ca}1.1$) are involved in the TES potentiation effect. Immunofluorescence studies demonstrated that chronic exposure to TES increased β_2-adrenergic receptor and $K_V1.2$ expression in ASM. In conclusion, chronic exposure to physiological levels of TES in guinea pig ASM promotes β_2-adrenergic receptor and $K_V1.2$ upregulation, favoring Sal and Theo responses, and likely limits the severity of asthmatic exacerbations in teenage boys and men.

RELATED-THYROID HORMONE GENES ARE ALTERED BY ACUTE EXPOSURE TO 2,4-DICHLOROPHENOXYACETIC IN RAT TESTES

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Abstract:

Thyroid hormones (TH) exhibit pleiotropic regulatory effects on growth, development, and metabolism. Available evidence indicates that the presence of HT transporters, deiodinases, and thyroid receptors in the testes is critical for normal testicular and reproductive function[1]. Recently, several animal studies have been conducted to understand the effects of some chemicals as endocrine disruptors, including thyroid disturbances. There is a wide range of environmental contaminants, including pesticides, and the damage it suffers can cause alterations in testicular development and function.[2,3,4]. Here, we study the effects of exposure to 2,4-dichlorophenoxyacetic acid on the gene expression of HT transporters, deiodinases, and thyroid receptors in rat testes. **Methods:** Adult male rats (250-300 g) were used and randomly divided into two groups. The control group (CNT, n=6) received saline solution; acute exposition was induced with three intraperitoneal injections in one week of 100 mg/ kg of 2,4-dichlorophenoxyacetic acid group (2,4-D group, n=6). After, the rats were weighed and euthanized. The gene expression of mct8, mct10, oatp1c1, Dio 2-3, Trα and PPIA (housekeeping gene) on testis was analyzed by RT-PCR. Statistical analyzes were performed using GraphPad Prism 8 software. Data were analyzed using ANOVA or the Kruskal-Wallis test (P<0.05 was considered significant). All procedures were performed in accordance with the Standard Mexican (NOM-062-ZOO-1999), under the approval and supervision of the Ethics Committee of the Autonomous University of Tlaxcala. **Results:** The relative expression of mct8 was significantly lower in 2,4-D group. In contrast, the relative expression of mct10 and oatp1c1 did not have significant differences. The relative expression of Dio2 was significantly lower in 2,4-D group. Interestingly, the relative expression of Dio3 and Trα did not have significant differences. **Conclusion:** This study showed that the acute administration of the commercial herbicides 2,4-D presented varying degrees of alteration in the expression of genes associated with HT in the rat testis, so it could be considered an endocrine disruptor. Further studies are required to elucidate both mechanisms of toxicity.

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CYTOTOXIC EFFECT OF ETHANOL EXTRACTS OF BRAZILIAN PROPOLIS ON HUMAN COLORECTAL ADENOCARCINOMA CELLS

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Abstract:

Introduction: Propolis is a plant resin produced by bees from botanical sources. Among the biological and therapeutic properties that propolis have been reported to have are antioxidant, anti-inflammato, antimicrobial, hepatoprotective and modulation of the immune response, their biological properties will depend on their chemical composition. Brazilian propolis has identified different chemical compounds among which are flavonoids (acacetin, biocanine, pinobanksin, pinocembrin, quercitin). Research has shown that propolis has cytotoxic activity against various cancer cell lines. For this reason, the objective of this research is to evaluate the effect of Brazilian propolis extracts on the HT-29 cell line for further analysis in various therapeutic uses as an antiviral agent.

Methodology: Culture and subculture of the HT-29 cell line was carried out in RPMI medium, for the identification of the cytotoxic effect of Ethanolic Extracts of Propolis (EEP) by means of the MTT method evaluating the following concentrations of EEP 400, 200, 100, 50 and 25 µg/mL and the absorbance was measured at 570 nm, the % of cell viability and the level of cytotoxicity was identified according to the criteria of ISO-10993-5 and IC50 using mathematical models.

Results: The 5 EEP were prepared from 5 samples of raw propolis of brazilian origin and their cytotoxic effect on the HT-29 cell line was analyzed, an n=9 of each of the concentrations analyzed was obtained. The concentrations of 50 and 25 µg/mL were the concentrations that were not cytotoxic to the cells having a percentage of cell viability of 92 and 89 respectively for each concentration.

Conclusion: The EEP samples analyzed demonstrated that at concentrations of 50 and 25 µg/mL they did not present a cytotoxic effect on the HT-29 cell line, which allows us to perform antiviral activity analysis using the HT-29 cell line as a host of the viruses and the EEP as treatments through in-vitro assays.

DNA DAMAGE DURING MITOTIC SLIPPAGE AS A NEW MECHANISM OF PACLITAXEL TOXICITY

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Abstract:

Cell division is regarded as an important therapeutic target for cancer treatment. Paclitaxel (PTX) is an anti mitotic drug which avoids the mitotic exit inhibiting microtubule dynamic. As a result of PTX action, the cell could die during mitosis or escape from mitotic arrest through a process called «*mitotic slippage*». The cells which were liberated from mitotic arrest also could be detained in G1 phase, progress through cell cycle or die of apoptosis. We know PTX provokes DNA damage and toxicity in cells that went out of mitotic arrest. On the other hand, our investigation group has demonstrated that during mitotic slippage numerous cells have drastic movements in the cell membrane like-failure cytokinesis. Due to PTX promotes the formation of cytokinetic furrows (CF), we suggest that these movements of the membrane during mitotic slippage are due to the formation of this type of furrows and they are the cause of cytotoxicity and death cell observed later. The aim of this project is to determine the relationship between the formation of CF and the cell death in HCT116 cells treated with PTX that were released from a prolonged arrest in mitosis.

COMPARISON OF *LACHESIS ACROCHORDA* VENOM COMPOSITION ORGANISM OF DIFFERENT BIOGEOGRAPHIC ZONES FROM COLOMBIA

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Abstract:

Aim: This work aims to compare protein composition of *Lachesis acrochorda* venoms from Colombia.

Methods: To characterize the samples, venom was sourced from 10 individuals of different biogeographic zones in Colombia and grouped for venom compounds monitoring. Binary dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-Page) and reverse phase high performance liquid chromatography (RP-HPLC) were performed. A slightly modified version of [1] was used in the chromatographic characterization in a Shimadzu SPD-10A HPLC system with a C18 column Zorbax Eclipse XDB (4.6 x 250 mm, 5µm). EnzChek™ assay kits were used to determine protease and phospholipase A_2 activity. Finally, specific action of venoms on bovine fibrinogen was determined following the method described by [2].

Results: The samples showed a high percentage similarity in their chromatographic profiles. Four zones were delimitated in the chromatogram (peptides, small, medium and large protein) according to [1]. Zones 2 and 3 appear to have the highest conservation grade, whereas zone 1 shows two different types of peptide composition and zone 4 has a unique peak for one biogeographic zone. Electrophoretic content showed 11-12 bands with the characteristic pattern for viperids according to [3]. Finally, the enzymatic activities showed a high diversity between samples and zones, highlighting the phospholipase A2 activity from Caldas sample, which doubles the activity compared to the venoms from the other zones and the pro-thrombin activity (fibrinogen clot formation) from all samples.

Main Conclusion: The results show a similar venom profile among the samples studied, with specific differences in peptide composition, which, in addition to the enzymatic activities, represent a starting point to explain the pathophysiological results observed in human envenomation and, moreover, to study the activity of different antivenoms against venoms from several biogeographic zones.

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KYNURENINE ATTENUATES MITOCHONDRIAL DEPOLARIZATION AND NEURONAL CELL DEATH AHR-INDEPENDENT WAY IN A PARKINSONIAN MODEL INDUCED BY ROTENONE EXPOSURE

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Abstract:

Parkinson's disease (PD) is the second most prevalent neurodegenerative disease characterized by progressive motor decline due to dopaminergic neurons deficit. Although the exact etiology of the disease is unknown, however, an important role of mitochondrial damage in the development of the disease has been discovered. On the other hand, tryptophan metabolism along the kynurenine pathway has been implicated in many pathological processes, in fact, multiple imbalances of the kynurenine pathway have been shown to be involved in PD pathogenesis.

Nowadays it is known that kynurenine is an endogenous ligand of the aryl hydrocarbon receptor (AhR) a ligand-dependent transcription factor. Numerous publications have reported that AhR activation play a critical role in the central nervous system. Recent evidence in a mouse model has shown that AhR can regulate the expression of Parkin protein, an E3 ubiquitin ligase enzyme that plays an important role in neuroprotection through promoting the selective degradation of damaged mitochondria in a process called mitophagy. In fact, mutations on Parkin protein are direct associated with PD development. Due to the above, we proposed to evaluate whether the overexpression of Parkin, through the AHR activation with kynurenine can attenuate the neuronal death induced by rotenone a pesticide strongly associated with PD. This compound inhibits complex 1 of the electron transport chain promoting loss of the mitochondrial membrane potential and cell death. To achieve this goal, SH-SY5Y neuroblastoma cells were differentiated with 50 ng/mL of brain neurotrophic factor and 10 µM of retinoic acid for 18 days and exposed to rotenone (50 nM) to evaluate the effect of the AHR agonist on Parkin levels, mitochondrial membrane potential and cell viability. Our results show that AHR is distributed homogeneously in the cytoplasm of differentiated cells and its activation with 200 µM of kynurenine treatment induces Parkin protein levels. This induction is counteracted when a pretreatment with CH223191(10µM), an AhR antagonist, is added. Moreover, through the use of annexin V-IP staining, we showed that 8 h kynurenine pre-treatment attenuates in around 16% rotenone-induced neuronal cell apoptosis. Additionally, using TMRE cationic dye we show that this type of death was preceded by a collapse of mitochondrial membrane potential and this effect decreased proximally 30% with kynurenine pretreatment simultaneously to the decrease of mitophagy

process. However, none of these effects were depleted by CH223191 pretreatment, so it is assumed that they are AhR-independent phenomenon possibly attributed to other properties described of kynurenine metabolites, such as antioxidant potential or its ability to reduce excitotoxicity due to its antagonistic effect on NMDA receptors on neurons. In conclusion, this investigation introduces the possibilities of kynurenine and its metabolites as valuable adjuncts or alternative therapies for neurodegenerative disorders such as Parkinson's disease.

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PUNICA GRANATUM PEEL EXTRACT AFFECTS *GIARDIA LAMBLIA* TROPHOZOITES CYTOSKELETON

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Abstract:

Giardiasis is a worldwide infection caused by protozoan parasite *Giardia lamblia*. New treatment alternatives are necessary due to emergence of resistant strains and treatment failure[1]. The identification of antiparasitic molecules form agro-industrial waste, like pomegranate peel (PP) is a sustainable alternative[2]. Several phytochemicals have demonstrated their effects through the alteration of molecular targets essential for parasite survival[3]. *Giardia* cytoskeleton is a unique structure involved in cell motility, division, adhesion and differentiation[4]. Due to their importance, said disturbance is related to cellular damage and cytotoxicity.

In this work the antigiardial effect of PP polyphenolic extract was evaluated on *Giardia lamblia* trophozoites *in vitro*. Parasite kinetics were performed to evaluate growth and adhesion capacity, morphological changes were evaluated by SEM, alteration of a-tubulin expression and distribution were analyzed via western blot and immunofluorescence assay respectively.

As a result, *Punica granatum* extract caused inhibition on growth and adhesion capacity. The most important finding was the alteration of a-tubulin expression and distribution in a concentration-independent manner. In addition, the extract caused elongation, alteration of normal cell shape, and flagella abnormalities.

This work showcases the first evidence of the effect *Punica granatum* peel extract has on *Giardia* cytoskeleton, due to polyphenols presence that interact with microtubules and a-tubulin as potential molecular targets. The study of identified molecules is a promising alternative for their use as potential antigiardiasic agents.

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NON-CONTACT CO-CULTURE FOR IN VITRO CYTOTOXICITY ASSESSMENT OF THE RECOMBINANT ANTICANCER PROTEINS TAT-PTEN-LTV AND KLA-PTEN-LTV

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Abstract:

Currently, Breast cancer is the one with the highest incidence in the female population worldwide and stands out as the leading cause of death from malignant tumors in Mexico, causing nearly eight thousand deaths in 2020. About 20% of Breast cancers overexpress the human epidermal growth factor receptor 2 (HER2), therefore they tend to be more aggressive due to cell cycle control and survival dysregulation. Pharmacotherapy is widely used for Breast cancer treatment; however, drug resistance, inappropriate delivery, low selectivity and poor tumor penetration are some associated disadvantages. To solve these problems, the implementation of cell penetrating peptides (CPP), can enhance the effectiveness of current therapies. Similarly, the coupling of tumor-homing peptides would improve selectivity, reducing adverse effects. Therefore, the proteins targeting HER2-positive Breast cancer were developed: TAT-PTEN-LTV and KLA-PTEN-LTV. Made up of a CPP (TAT or KLA), the tumor-homing peptide LTV (specific for HER2) and the tumor suppressor protein, PTEN, capable of inhibiting the PI3K-AKT-mTOR signaling pathway.

The coding gene sequences for the chimeric proteins were confirmed by DNA sequencing and inserted into the eukaryotic expression vector pCEFL, HEK293T cells were transfected using the Xfect™ polymer and cultured in a non-contact co-culture with Breast cancer cells. Non-contact co-culture is a strategy in which cells are co-cultured in two different compartments (insert membrane and well); allowing indirect cell-cell interaction through the pore of the membrane. Using this method followed by the WST-1 assay, it was possible to evaluate the anticancer effect of the TAT-PTEN-LTV and KLA-PTEN-LTV proteins on the HCC1954 and MCF7 cell lines, obtaining a significant inhibition result on the HER2-positive Breast cancer cell line HCC1954 with 12.25% (SD= 1.29%) and 25.95% (SD= 0.9%) respectively, inferring the preferential anticancer activity of these proteins against HER2-positive Breast cancer cells. In this way, the non-contact co-culture method allows to obtain biological results of recombinant proteins quickly, since it is possible to perform it without producing and purifying large amounts of protein, allowing optimization of resources in the development of recombinant anticancer proteins *de novo*.

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UVB AND UVC INHIBITS CELLULAR PROCESSES RELATED TO CARCINOGENESIS IN CERVICAL CANCER CELL LINES

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Abstract:

The interaction of UV and cell generates free radicals producing cell death, senescence and proliferation alteration among other cell processes changes. UVB and UVC potentially could be used in therapy as an alternative for common radio and chemotherapy. In this work we where interested in seeking the quantity of UV necessary to inhibit cell proliferation and induce cell death. Therefore we make a dose-response and temporal time experiment at different doses of UVB and UVC. Interestingly we find that UVB and UVC present almost the same effect at a similar energy in SiHa, HeLa, C4.1, C33A and Calo cell proliferation. UVB treatment arrest SiHa cells in S phase in a dose-response shape. Cell migration and invasion shows inhibition since 15 sec of UV exposition showing a profound effect at 25 sec of UV treatment. These UVB cell effects seams protein p53 dependent because it has been shown an increase dependent of UVB doses. These results show that UV can be used for inhibit cellular processes related to carcinogenesis in cervical cancer cell lines opening the possibility to cancer patients.

DESIGN, PRODUCTION, AND EVALUATION OF THE RECOMBINANT PROTEIN E4ORF4 LINKED TO THE CELL PENETRATING PEPTIDE MAP AS A NEW AGENT AGAINST CANCER

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Abstract:

There were 19.3 million cancer cases reported and almost 10 million deaths registered in 2020. Plenty of proteins with activity against cancer have been isolated from viruses such as the Anemia Chicken Virus (Apoptin) and Human Adenovirus (E4orf4). E4orf4 demonstrated in early studies the capacity to elicit cell death specifically in cancer cells. Interactions with phosphatase PP2A and Src kinase are the main collaborators by which E4orf4 possess its anticancer activity. Using proteins is attractive towards development of targeted cancer therapies, however, one of the most important hurdles to tackle is the delivery into cells. Cell-Penetrating Peptides (CPP) are peptides used as vehicles for the delivery of biomolecules. In the present study, a CPP and a poly-histidine sequence were fused with E4orf4 as a potential therapeutic anticancer protein. The CPP fused was Model Amphipatic Peptide (MAP), which has demonstrated one of the highest internalization rates. Firstly, we designed the sequence of MAP-Hisx6-Glyx4-E4orf4, referred simply as MAP-E4orf4, and codon optimization was done for the chosen expression system *Escherichia coli* BL21. Predictions of the tertiary structure of native E4orf4 and MAP-E4orf4 were carried in the Robetta Server to confirm the conservation of the folding compared to E4orf4 by itself. Subsequently, protein-protein dockings were run on the ClusPro Server to see the interactions between MAP-E4orf4 with PP2A and Src. Results demonstrated the maintenance of the 3D structure of the fusion protein and the conservation of its interactions with PP2A and Src, important for its activity. With this, molecular cloning was conducted in *E. coli* DH5a of MAP-E4orf4 inside the plasmid pET30a(+) and expression was carried on the BL21 strain. Expression levels were visualized with the induction of 5 mL of BL21 culture and extraction of soluble proteins using Sample Buffer. The extraction was analyzed in an SDS-PAGE electrophoresis gel where a strong band below the 26 kDa mark could be seen, corresponding to the recombinant protein size of 21.3 kDa. Further purification will be carried on using IMAC chromatography. Anticancer activity will be evaluated with different cancer cell lines and the Vero cell line as a control, and internalization of MAP-E4orf4 will be evaluated by confocal microscopy.

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ROLE OF GTPASES IN THE CYTOSKELETON RE-ARRANGEMENT AND CELL MIGRATION OF MURINE MACROPHAGES AS A TARGET OF ORGANOPHOSPHATE PESTICIDE RESIDUES

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Abstract:

Organophosphate (OP) pesticides are widely distributed chemicals with toxic effects, including immunotoxicity. Previous reports showed that methyl OP, both parent compounds and their metabolites, exhibit immunotoxicity through reducing cytokines secretion such as interleukin (IL)-2, in human peripheral blood mononuclear cells. Secretion pathways are closely related to the cytoskeleton assembly and function, such as other cellular activities as maintaining cell morphology or supporting vesicular traffic that can be affected by exposure to OP compounds. However, no complete relationship between the immunotoxic effects of OP exposure and the modification of the cytoskeleton has been described. Here, we explore the effects of methyl OP compounds on cytoskeletal elements and their regulation in murine macrophages. We tested malathion and its dialkylphosphate (DAPs) metabolites: dimethyl dithiophosphate (DMDTP), dimethylthiophosphate (DMTP) and dimethylphosphate (DMP) in both cytoskeleton acellular assays and in the RAW264.7 macrophages cell line. We found that malathion and its DAPs reduced actin and tubulin polymerization rates and total polymerized actin at 0.01 µM and retard the tubulin elongation phase at 1 µM treatment. In RAW264.7 cells, DAPs induced spindle like cell morphology, in particular with DMTP and DMP (0.01 µM), which also induced cell polarization, pseudopod formation and an increase in filopodia, with no visible modification of tubulin cytoskeleton after 2 h of treatment. Additionally, we tested a cytoskeleton-dependent activity such as cell migration through the wound healing assay, where we observed that DMTP and DMP increased RAW cells migration at 0.01 µM. Further, we examined the effect of DAPs on the activation of GTPase Rho family proteins (RhoA, Rac1 and Cdc42) as these are related to the regulation of the cytoskeleton re-arrangement. We found that DMP slightly reduced RhoA activity but increased Rac1 and Cdc42 activities at 5 min of exposure and up to at least 2 h. To verify the role of Rac1 and Cdc42 activation in the DMP-induced effects, we chemically inhibited Rac1 and Cdc42 activity in RAW264.7 cells. We observed that inhibition of Rac1 reduces the cell polarization and the cell migration induced by DMP, but Cdc42 inhibition resulted in a complete inhibition of DMP effects. All together these results suggest that methyl OP compounds, particularly DMP, can modify macrophage cytoskeleton activities through the activation of Cdc42, which may represent a potential molecular target for OP compounds. The disruption of cytoskeleton of immune cells such as macrophages can also be related to immunotoxic effects reported in OP exposure.

Financing: CONACyT grant number 153468.

STRUCTURAL AND ANTIMICROBIAL CHARACTERIZATION OF THE MOST ABUNDANT COMPONENTS FROM THE VENOM OF THE SCORPION *THORELLIUS INTREPIDUS*

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Abstract:

The Scorpions are a feared group of arthropods because their sting is painful and can compromise people life. Up today there have been described more than 2700 scorpion species around the world and just close to 4% of this species are medical important, most of the scorpion species don´t produce any serious sign or symptoms in humans.

Scorpion venoms possess a wide diversity of molecules with different pharmacological activities: antibacterial, antifungal, antiviral, antiparasitic, immunosuppressive, analgesic, anticancer, anti-insect activities and so on.

In our project we analyzed the scorpion venom of *Thorellius intrepidus* an endemic scorpion from Jalisco and Colima, this scorpion is not considered of medical importance. We separated the venom in four fractions (FI-FIV) according to their molecular size using gel filtration chromatography, the fraction IV was the most abundant with the smallest molecules, it represented close to 95% of the area under the curve in the chromatogram at 280 nm. The contained of this fraction was separated by chromatography in RP-HPLC and we identified 3 abundant components, which their antimicrobial activity against *Staphylococcus aureus* ATCC 25923 and *E. coli* ATCC 25922 were evaluated at concentration between 15-160 µg/mL, showing only activity in *S. aureus*. In the last part of the project, we will fully characterize the antimicrobial activity and identify the structure of this molecules using different spectroscopic methods: 1H NMR, 13C-NMR, Infrared and Mass spectrometry.

With this project we try to face the bacterial resistance phenomenon, obtaining new molecules that could be used in the treatment of infections caused by resistant bacteria.

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CHARACTERIZATION OF *IBERVILLAE SONOROE* ROOT EXTRACTS OBTAINED WITH DIFFERENT SOLVENTS AND THEIR CYTOTOXIC ACTIVITY ON GLIOMA CELL LINE

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Abstract:

Gliomas are primary brain tumors formed when glial cells grow out of control and are very malignant cancer especially the glioblastoma subtype. The treatment of choice is surgery followed by adjuvant radiotherapy and/or chemotherapy, despite this, the survival is very low. Phytochemical compounds from medicinal plants provide unlimited opportunities for new drugs in cancer therapies. In this study, the potential cytotoxic extracts of *Ibervillae sonoroe* in glioma cells was evaluated. The extracts were obtained from infusion of maceration dry root of *Ibervillae sonoroe,* using different solvents such as acetone, acetonitrile, acetoethyl, ethanol, methanol, hexane, ter-butanol, chloroform, dichloromethane, and water. The extract characterization was analyzed by infrared spectroscopy and thin-layer chromatography. The *in vitro* cytotoxic tests of the extracts at different concentrations were realized using the glioblastoma cell line LN18 through the red neutral and MTT assays to determine cell viability, as well morphology cell changes were observed at 48h.

THE ANTIPSYCOTIC DRUG, PENFLURIDOL, INHIBITS KV10.1 CHANNELS

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Abstract:

In the last decades, there has been an increased research interest surrounding new drug targets to find new cancer diagnostics and therapies. One of these potential drug targets is the Kv10.1, which is expressed in 70% of cancer varieties[1]. Pharmacological inhibition of Kv10.1 has shown promising results, decreasing some hallmarks of cancer[2]. However, finding specific Kv10.1 modulators has been challenging, with most of the molecules being promiscuous, due to the similarity of Kv10.1 with other K^+ channels. Therefore, research on the Kv10.1 channel has focused on searching for new and selective modulators.

Here, we run a primary fluorescent screening assay to detect new Kv10.1-modulators measured through changes in membrane potential in HEK-WT and HEK-Kv10.1 cells. We found that responses in HEK-Kv10.1 were statistically more prominent in amplitude with respect to the HEK-WT. HEK-Kv10.1 responses were inhibited with loperamide, a new Kv10.1 blocker discovered for our group. We tested 26 compounds, and interestingly the fluorescent responses mediated by Kv10.1 channels were inhibited by the antipsychotic drug, penfluridol.

Whole-cell patch-clamp experiments confirmed fluorescent results. We observed penfluridol (300 nm) inhibits 98% Kv10.1 currents, from 7.86 ± 4.62 nA in control versus 0.13 ± 0.04 nA in presence of penfluridol (n = 4). The inhibitory effect of penfluridol was dose-dependent, with an IC50 of 40 nM ± 3.

Penfluridol has been described as a drug with different targets, including ion channels and receptors, such as dopamine receptors (D1) and T-type calcium channels. Here we found that penfluridol also can inhibit Kv10.1 channels. Penfluridol has been described as a molecule with anti-cancerous activity, which would be explained through its inhibitory effect on Kv10.1 channels.

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LEUKOCYTE MTNF-α AS A MECHANISM OF ADAPTATION TO INFLAMMATORY PROCESSES IN LEAD-EXPOSED WORKERS: NADPH OXIDASE AS A MEDIATOR OF OXIDATIVE STRESS

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Abstract:

In Mexico, lead exposure is a health problem because workers in the metallurgical and battery recycling industries have poor safety conditions and poorly controlled processes [1]. Lead intoxication causes detrimental effects at the biochemical, physiological, and behavioral levels [2]. At the molecular level, lead involves covalent bonds to proteins, interaction with stereospecific sites of divalent cations (Ca++) and toxic metabolites production. Lead exposure might generate a pro-inflammatory state that could be associated with cellular damage and oxidative stress. TNF-α is an essential pleiotropic cytokine in host defense, inflammation, and apoptosis induction [3]. We found that lead exposed workers present higher frequency of infections, higher leukocyte apoptosis and low basal concentration of TNF-α compared to non-lead exposed workers, implying a dysfunction in the immune response [4]. The aim of this work is to study in leukocytes incubated with lead (*in vitro*) and in leukocytes from lead-intoxicated patients (*in vivo*), the oxidative stress associated with TNF-α release, apoptosis and necrosis induction and the increase of membrane TNF-α positive leukocytes with NADPH oxidase as a mediator of these effects.

No statistically significant difference in necrosis, apoptosis (by flow cytometry), and lipid peroxidation (by spectrophotometry) was found in leukocytes after incubation of whole blood with lead (5 µM), n=3. Two populations were studied: 1) non-lead exposed (n=17) and 2) lead exposed (n=17) workers from a battery recycler in León, Guanajuato. We found high blood lead concentrations (= 45.7 µg/dL), low Δ-ALAD enzyme activity, high lipid peroxidation and superoxide dismutase activity in leukocytes from lead exposed workers, which could indicate that these cells show oxidative damage when there is a high blood lead concentration. No significant statistical differences were found in the necrosis and apoptosis values of leukocytes of lead exposed workers compared with those of non-lead exposed workers. However, NADPH oxidase activity at baseline and after stimulation with lipopolysaccharide was lower in lead exposed than in non-lead exposed workers; in addition, no statistical difference between baseline and stimulation in lead exposed workers was found, which could suggest that workers have leukocyte dysfunction with a lower inflammatory response due to chronic exposure to high lead concentrations.

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BIOLOGICAL EFFECT OF 4*H*-BENZO[*D*][1,3]OXAZINES IN BREAST CANCER CELLS

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Abstract:

The precursors and 4*H*-benzo[*d*][1,3]oxazines recently synthetized were studied in cell lines of breast cancer (BC) MCF-7 (ER+, PR+, HER2-) ductal, CAMA1 (ER+, PR+/-, HER2-) lobular and HCC1954 (ER -, PR-, HER2+) lobular and SKBR-3 (ER-, PR-, HER2+) ductal. The precursors and the synthesized 4*H*-benzo[*d*][1,3]oxazine compounds showed various degrees of inhibition of cell proliferation with a notable effect for those compounds that had an aryl substituted at C-2 of the molecules. 4*H*-benzo[*d*][1,3]oxazines showed an IC50 rating of 1.035 to 157.4 μM in MCF-7, 1.98 to 139 in CAMA1, 1.27 to 93.08 in SKBR-3, and 1.032 to 157.2 in HCC1954 cells. Of 20 compounds tested, interestingly, compounds 9, 5, and 5 showed inhibition of cell proliferation in CAMA1, SKBR-3 and HCC1954 at concentrations of 15, 50 and 160 μM, respectively, while compound 17 had no effect on MCF-7 cells. In CAMA1 cells, compounds 6, 2 and 8 had an effect at 15, 50 and 160 μM, respectively, while compounds 5, 6, 10 and 17 did not inhibit cell proliferation. Interestingly, compounds 14, 3 and 3 elicited an effect at 15, 50 and 160 μM, respectively, in SKBR-3 cells. Finally, in HCC1954, compounds 6, 1 and 7 had an effect at 15, 50 and 160 μM, respectively, while compounds 3, 7, 9, 12, 13 and 17 did not show inhibition of cell proliferation. Cell phenotype and biomarker differences are not associated with the effect of precursors and benzoxazines on cell proliferation. However, all four cell lines responded to benzoxazines while surprisingly, the SKBR-3 cell line responded to precursors and benzoxazines. These compounds represent possible drug candidates for the treatment of breast cancer. However, further trials are needed to elucidate its full effect on cellular and molecular features of cancer.

TOXICOLOGICAL EFFECTS OF ACUTE ADMINISTRATION OF *SPATHODEA CAMPANULATA* IN WISTAR RATS

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Abstract:

In 2018, the World Health Organization (WHO) reported that 170 countries use traditional medicine, including medicinal plants, which have properties that exert a beneficial therapeutic effect on the human body, representing a pharmacological alternative for many diseases. However, these are used without knowing the adverse side effects in the short or long term. The scientific validation of medicinal plants is essential for clinical use, allowing information about their safety, using acute, sub chronic, and chronic toxicological analysis. *Spathodea campanulata*, commonly known as Galeana, has many uses in traditional medicine (renal diseases, gastric ulcers, malaria, antioxidant, anti-inflammatory, antibacterial, and hypoglycemic properties). Despite its widespread use, there are only two toxicological reports, which are incomplete. **Objective**: To determine the acute toxicity of aqueous extracts of galena leaves (Spathodea campanulata). **Methodology**: The acute toxicity study was carried out according to OECD guide No. 420, "Fixed Dose Procedure," using Wistar rats (n=6). For Toxicity resolution, clinical signs, weight, and body temperature were measured. A general urinalysis was performed. At the end of the test time established in guide No. 420, they were euthanized, and a necropsy was practiced. Blood was collected for hematic biometry and blood chemistry. The organs were processed for histopathological study. **Results**: In the administration of doses of 300 and 2000 mg/kg, 100% survival was observed, and there were no alterations in clinical signs (Piloerection, eyes half shut, secretions, changes in motor activity or sickness behavior). No significant differences in weight, temperature, urinalysis, hematology, and blood chemistry were found. A histological study showed no damage to the organs analyzed (liver, kidneys, heart, lungs, brain, pancreas, and spleen. **Conclusion**: *Spathodea campanulata* aqueous extract has no acute toxicity.

Keywords: Toxicity, medicinal plants, *Spathodea campanulata*.

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POTENTIAL ROLE OF TNF-α AND TNFRS IN CSCS ENRICHMENT INDUCED BY DOXORUBICIN IN TRIPLE NEGATIVE BREAST CANCER

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Abstract:

Doxorubicin (Dox) is widely used in the treatment of triple-negative breast cancer (TNBC). However, resistance development by cancer cells limits its efficacy. Tumor necrosis factor-alpha (TNF-α) is a pro-inflammatory cytokine upregulated in TNBC microenvironment, and it has pro-tumoral effects1. In addition, the presence of tumor subpopulations with intrinsic resistance to therapy, such as cancer stem cells (CSCs), impairs therapy outcome. A CSC-like phenotype may be induced by continuous exposure to chemotherapeutics2, or by TNF-α, yet the relationship between these factors remains unknown. This study aims to analyze the role of TNF-α and its receptors (TNFRs) in the induction of a CSC-like phenotype driven by exposure to Dox and their contribution to phenotype maintenance.

For CSCs identification in the TNBC cell line MDA-MB-231, we employed the reporter system SORE6-GFP, which is responsive to the stem cell transcription factors SOX2 and OCT4 and produces a fluorescent signal3 detected by flow cytometry. The cytotoxic effect of Dox was evaluated by the MTT assay, and the expression levels of TNF-α and TNFR1/2 were measured by flow cytometry analysis. Under continuous treatment with a non-cytotoxic concentration of Dox, a significative enrichment of CSCs was observed. Additionally, treated cells displayed a 2-fold increase in the IC50 of Dox. Moreover, in non-treated cells, TNF-α showed a similar expression in CSCs and non-CSCs, meanwhile, TNFR1 and TNFR2 displayed differential expression between these subpopulations. However, after continuous treatment with Dox, alterations in the expression of TNF-α and TNFRs were detected.

Taken together, our results indicate that Dox induces the enrichment of CSCs. This could be driven by drug-induced stemness or by CSCs selection, and to elucidate the mechanism further experiments are required. However, TNF-α and TNFRs may be related to the phenotypic changes observed. These molecules regulate survival and apoptosis pathways, and changes in their expression observed after Dox treatment, suggest their involvement in the survival of CSCs, or the induction of a CSCs-like phenotype.

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TARGETED INHIBITION OF ONCOGENE ERBB2 AND RELATED GENES OF INTEREST IN HER2 POSITIVE BREAST CANCER CELLS IGF-1R AND ITGB1 DUE TO SIRNA ACTIVITY

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Abstract:

Breast cancer is the second highest occurring cancer and fifth deadliest in both men and women worldwide while in Mexico it is the highest cause of death within cancer deaths in women as well as the most diagnosed. Current treatments have developed several inconveniences and issues including acquired resistance by the tumor while monoclonal antibodies rose as an alternative to cytotoxic drugs, they too have appeared not as effective in the more aggressive HER2 positive cancer types due to several mutations resulting in the deletion of the targeted receptors or activation of alternative cell growth paths as well as the immune system not targeting the tagged cells. The eRbB2 oncogene encodes a member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases, the HER2 receptor, which due to association of its abhorrent overexpression with some adenocarcinomas has risen to clinical importance, including highly aggressive breast cancer. While HER2 receptor has been often described as having a major role if not the main one in the survival of cancer cells, there have been other receptors identified as enhancers of cell survival. Some of these identified receptors are IGF1R —insulin like growth factor 1 receptor— while not an oncogene it is highly overexpressed in most malignant tissues where it functions as an anti-apoptotic agent by enhancing cell survival, together with regulating tumor cell motility and adhesion; and ITGB1 — integrin subunit beta 1—which is also involved in cell adhesion and recognition in a variety of processes including immune response and metastatic diffusion, proliferation and inflammation of tumor cells, both have been implicated in the therapeutic resistance of multiple solid cancers. The silencing or inhibition of targeted gene expression using siRNAs to induce apoptosis and inhibition of both cell growth together with oncogene transcription could allow for novel therapies in given cancer patients. In this work the test cell growth inhibition was measured through a WST1 assay on HER2 positive breast cancer cells> SK-BR-2 and HCC1954 against MCF-7 and Chang cells as negative controls after being exposed with liposomes carrying siRNAs eRbB2, IGF-1R, ITGB1, and an additional test carrying a mix of the RNAs to test synergic activity among the tested RNAs. After which a qPCR assay was carried out to determine if at a transcription level the oncogene had been silenced in the cell line-RNA combination which had the highest growth inhibition (SK-Br-3 + eRbB2). The assays conducted on HER2 positive breast cancer cells using siRNA eRbB2 provide evidence of cell growth inhibition and reduced targeted gene expression and transcription however no significant synergic activity was noticed nor supported by the results given through these assays.

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DETERMINATION OF THE EFFECT OF PRENYLATED CHALCONES ON THE MEMBRANE POTENTIAL, APOPTOSIS AND METABOLOME OF CASTRATION-RESISTANT CELLS IN PROSTATE CANCER

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Abstract:

Prostate cancer is the most frequently diagnosed cancer in men after skin cancer and the second leading cause of cancer-related death worldwide, it is also a heterogeneous disease. In Mexico, according to data from the National Cancer Institute (INcan), prostate cancer has an incidence of 16% with a mortality rate of 13 per 100,000 men. The most common treatment for patients with advanced prostate cancer is an androgen ablation by castration therapy, however many patients treated through androgen deprivation have developed castration resistance and it is related to the mutant and splice variants of the androgen receptor. For this, is very important to search for alternatives for the treatment of prostate cancer. The aim of this study was to determine the effect of prenylated chalcones on the morphology, viability, and apoptosis of cell lines such as PC3 and DU145 and to obtain knowledge about the possible alternative pharmacological in the castration-resistant prostate cancer. First, the cells interacted with different concentrations of prenylated chalcones and we analyzed the viability through the MTT assays and different times, then we select the chalcones with effect on the viability cell and determine the IC50. After we analyzed the membrane potential of the cells treated with the chalcones and we determined cell apoptosis by flow cytometry, and we analyzed the metabolites of these cells. The data indicated that the compounds PVONA/3F and PVINA/2CL affected both cell lines tested, reducing their viability up to 46.6% and 26.56%, respectively, on the PC3 line. In the same way, the compounds PVONA/3F and PVINA/2CL reduced the viability up to 48.94% and 28.29% respectively, at a time of 48h. Treatment of DU145 and PC3 cells with the chalcones PVONA/3F and PVINA/2Cl (IC50 µM) increased the number of cells in the early and late stages of apoptosis. These results indicate that apoptosis plays an important role in the death machinery on DU145 and PC3 cells treated with both chalcones. After treatment with PVONA/3F and PVINA/2CL chalcones, impaired mitochondrial function characterized by knockdown of PMM in comparison with untreated cells. Finally, we found differences between the metabolites of the cells treated with the chalcones, whit respect the untreated cells. These results indicate that PVONA/3F and PVINA/2Cl are promising lead compounds and deserve further investigation for the prevention and treatment of human prostate cancer.

This work was supported by UACM and the grant for the project CCyT-2022-1 of the Colegio de Ciencia y Tecnología and the support of CONACYT for the student CVU number 1103353.

ENVIRONMENTAL CD EXPOSURE AS A FACTOR RISK TO INSULIN RESISTANCE DEVELOPMENT: A PEEP TO INSULIN SECRETION MECHANISMS

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Abstract:

Insulin resistance (IR) is a pathology associated with hypercaloric diet consumption and, recently, environmental cadmium (Cd) exposure. To maintain overgeneration and insulin secretion, β-cells require great energy production, and thereby mitochondrial bioenergetics plays a crucial role. This work aimed to evaluate the mitochondrial bioenergetics in insulin synthesis-release processes in insulin resistance models by Cd exposure in environmental concentration. Male Wistar rats were divided into two groups, 1) control group (Cnt) and 2) Cd-15 ppm group. Cadmium was administered in drinking water for 3-months. At the end of exposure time, insulin biosynthesis transcriptional factors (PDX-1, MafA, NeuroD1, Insulin) and mitochondrial life cycle (Fis1, Drp1, Mfn1, Pink1, and Parkin) were evaluated by western blot. In addition, *in vitro* insulin secretion was stimulated by glucose and palmitic acid, and calcium analysis and ATP synthesis were performed. The results showed increased insulin, MafA, and NeuroD1 in the Cd group. Likewise, increased Mfn-1, Fis-1, Drp1, Pink1, and Parkin. In vitro, glucose stimulation observed overexpansion of insulin secretion second phase, while palmitic acid and glucose showed an additive effect in both secretion phases. Finally, in vitro calcium and ATP analysis after glucose or palmitic acid stimuli had different adaptations in dependence on time. The results allow us to conclude that in Cd-IR models, insulin biosynthesis is modulated by MafA and NeuroD1. In turn, it increases the insulin granule pool necessary for secretion's first and second phases. Second phase overexpansion suggests that Cd interplays with glucose canonical pathway coupled to calcium fluxes generating major exocytosis and thus hyperinsulinemia. Finally, the results indicate that Cd induces mitochondrial fission and possible mitophagy on islets, conditioning the mitochondrial efficiency and the ATP synthesis, which is a limiting step in insulin release.

ANTI-INFLAMMATORY EFFECTS OF POLYPHENOLIC EXTRACT OF *VITIS VINIFERA* POMACE ON CARRAGEENAN INDUCED PAW EDEMA

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Abstract:

Inflammation is the immune system's response to harmful stimuli, such as pathogens, damaged cells, toxic compounds, or irradiation. Carrageenan-induced paw edema represents the classic model of acute inflammation, which is widely used to evaluate the anti-inflammatory potential of pharmacological substances (1). In the search for anti-inflammatory molecules, it has been shown that phytochemicals can be modulators of the inflammatory process. The grape (*Vitis vinifera*) is widely used in the wine and juice industries, which can lead to massive amounts of waste, including grape skins, pulp, stems and seeds. Grape pomace contains a variety of phytochemicals, especially polyphenols such as resveratrol and quercetin (2). In this study, the anti-inflammatory effects of polyphenolic extract from grape pomace were evaluated.

Thirty-six male BALB/c mice (n=6 per group) were used. Six groups were employed: intact group, carrageenan group, indomethacin group (10 mg/kg i.p.) and three grape pomace groups (doses of 10, 20 and 40 mg/kg i.p.). The variables analyzed were edema, inflammatory cytokines (IL-1β and IL-6), lipid peroxidation, and expression of ciclooxyenase-2 (COX-2) and myeloperoxidase (MPO).

The results of the study showed that the administration of carrageenan in the subplantar region caused edema and an increased in the levels of cytokines (IL-1β and IL-6) and proinflammatory enzymes (COX-2 and MPO), as well as lipid peroxidation. The administration of the polyphenolic extract from grape pomace inhibited the increase in edema, lipid peroxidation as well as the release of the cytokines IL-1β and IL-6; in addition, the expression of proinflammatory enzymes COX-2 and MPO was decreased. This effect was dose-dependent; thus, the most effective dose was 40 mg/kg, achieving similar results to the indomethacin group.

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MORPHOLOGICAL CHARACTERIZATION AND PHYTOCHEMICAL EVALUATION OF *CALLISTEMON CITRINUS* LEAF PHYTOSOMES

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Abstract:

Advances in phytomedicine and its applications in clinical research show the value of herbal medicine in the treatment and prevention of diseases. Phytosome are one of the novel colloidal drug delivery systems to standardize plant extracts or phytoconstituents with phospholipids. Bioavailability is an important factor to be considered to improve a compound reaches it systemic circulation as intact compound. *Callistemon citrinus* leaf extract (CCLE) has demonstrated its potential effect as an antiobesogenic agent due to the presence of phenolic and terpenoid compounds. **Aim**: In this study *C. citrinus* leaf phytosomes (CCLP) were prepared and characterized based on physical and chemical properties. **Methods**: CCLE and soybean phospholipids (1:1 v/v ratio) were used to preparer the phytosome (200 mg/kg). Phytosome vesicles was reduced using ultrasonication in hydration medium (PBS pH 7.4) with NaCl (150 mM). The phospholipid complexes (CCLP) were lyophilized to realize an analysis with scanning electron microscopy. Finally, the phytochemical compounds of CCPL and CCLE were determined by GC-MS and the high-performance liquid chromatography (HPLC). **Results**: The particle size of *C. citrinus* phytosome was 130 ± 18.30 nm with a roughly spherical form and high encapsulation efficiency (80.84%). The most abundant terpenes compounds detected in CCLH and CCLP were 1,8-cineole, l-pinocarveol, pinocarvone, borneol, globulol, phytol, β-amyrin, betulin and lupeol. Results of HPLC showed three phenols compounds present in both CCLH and CCLP. 4-hydroxybenzoic acid, p-coumaric acid and gallic acid. **Conclusion**: *C. citrinus* phytosomes presented a better solubility and improved permeability as the *C. citrinus* extract. In addition, the majority compounds remain.

SUCROSE AND ARSENIC INDUCE MUSCULAR INSULIN RESISTANCE THROUGH DIFFERENT PATHWAYS WHICH ARE MUSCLE-DEPENDENT

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Abstract:

Introduction: Skeletal muscle is responsible for up to 80 % of postprandial glucose disposal. Insulin stimulates glucose uptake by translocating GLUT4 to the sarcolemma. Several pathways regulate the trafficking of GLUT4, including sorting it into the storage vesicles (GSV), the proteolytic processing of the Tether containing an Ubx domain for GLUT4 (TUG) and Akt phosphorylation. Muscle insulin resistance can originate from a sedentary lifestyle, hypercaloric diets or, the exposure to endocrine-disrupting pollutants such as arsenic.

Aim: To evaluate the alterations induced by sucrose and arsenic exposure on the pathways involved in insulin-stimulated GLUT4 translocation in quadriceps and gastrocnemius muscles.

Methods: Male Wistar rats were treated with 20 % sucrose (S), 50 mg/L sodium arsenite (A) or both (A+S) in drinking water for 8 weeks. Body weight was monitored weekly. Intraperitoneal insulin tolerance (ITT) test was on the 7th week of treatment. Quadriceps and gastrocnemius muscles were obtained after 12 h fasting or after 30 min intraperitoneal insulin injection. We analyzed GLUT4 translocation to the sarcolemma by a sarcolemma membrane-fractionation followed by Western blot. We assessed the protein abundance of the proteins involved in GLUT4 translocation by quantitative Western blot.

Results: Male rats treated with S and A+S gained more weight and had a higher body mass index than control, and A treated animals. Compared with controls, S, A, and A+S treated animals had higher plasmatic glucose levels at 60 min during the ITT. Thus, indicating that all treatments induced insulin resistance. In quadriceps, S-treated rats had higher insulin-induced sarcolemma GLUT4 levels, Akt phosphorylation levels and decreased insulin-stimulated TUG proteolysis. Conversely, A and A+S inhibited GLUT4 translocation to the sarcolemma and reduced insulin-stimulated Akt phosphorylation and TUG proteolysis. All treatments reduced this muscle's protein levels of the GSV marker VAMP2. All treatments in gastrocnemius increased basal GLUT4 levels in the sarcolemma while inhibiting insulin-induced GLUT4 translocation. These effects correlated with lower basal levels of TUG and impaired insulin-stimulated TUG proteolysis. Moreover, S reduced calpain-10 protein levels in this muscle, while A and A+S inhibited insulin-induced Akt phosphorylation.

Conclusion: Our results indicate that arsenic and sucrose act through different pathways to impair GLUT4 trafficking, correlated with Akt phosphorylation in the quadriceps, while in gastrocnemius the proteolytic pathway had a higher role in insulin resistance.

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OBTAINING AND EVALUATING THE TOXICITY OF PLANT EXTRACTS OF SOLANUM CERVANTESII AND OTHER SPECIES OF THE SOLANACEAE FAMILY FROM HUIXQUILUCAN, STATE OF MEXICO

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Abstract:

The Solanaceae family are herbaceous or woody plants, erect or climbing, annual or perennial, fruiting or fruitless, varying greatly in size and shape. This family is one of the most diverse on the planet and in Mexico there are 34 genera with 381 species, approximately. Solanaceae have a great economic value since there are species that are edible or for pharmaceutical application, but there are also those for psychotropic use or that represent a risk to public health due to their toxicity.

The knowledge of Solanaceae in Mexico is heterogeneous, since there are areas with recent records and adequate collections, while in others they are underrepresented, likewise this lack of knowledge in the community can be detrimental because some of these species can be poisonous because they present highly harmful alkaloids such as solanine, scopolamine, atropine, hyoscyamine and nicotine that can cause acute or immediate intoxication in people who come into contact with them.

For this reason, it is important to know the danger that some species present for the communities that coexist with these plants that grow in the wild, so analyzing the type and amount of toxins in extracts of these plants through methods such as chromatography and general bioassay of Lethality in Artemia salina will allow us to determine and compare the level of toxicity they have.

The procedures that are carried out to obtain and determine these chemical compounds start from the collection of individuals of the Solanaceae family in the municipality of Huixquilucan, carrying out drying, maceration with the use of various solvents (hexane, ethyl acetate, methyl alcohol and acidified water) obtaining the extract by means of rotary evaporation and the fractionation of some of them in column and plate chromatography.

Obtaining these plant extracts allows us to generate the lethality bioassay in *A.* salina, which consisted of exposing *A. salina* nauplii for 24 hours with 20, 50 and 100 uL of the plant extract and then counting the survivors. The corresponding negative controls were used for each experiment and were performed in triplicate.

The initial results with the total extracts show us that Solanum cervantesii has highly toxic compounds since even at low doses of the extract, no brine shrimp could survive. Experimentation with the fractionation of soluble extracts and establishing the type of substances that exist in these extracts is still to be done to determine if the population of the municipality of Huixquilucan is at risk for manipulating or using this type of plant.

MICROPLASTICS IN TROPICAL GAR´S DIET (*ATRACTOSTEUS TROPICUS*): EFFECTS ON ENZYME ACTIVITIES

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Abstract:

The poor management of plastic waste has caused these materials to reach the most remote aquatic environments on the planet directly or indirectly. Plastic particles < 5 mm are called microplastics (MPs). These particles are formed by the wear or fragmentation of larger particles or manufactured on that scale for commercial use. The presence of MPs in aquatic environments causes them to be ingested by the organisms that inhabit there, among which are fish of nutritional importance for humans. Among the polymers ingested by fish are acrylic (polymethylmethacrylate - PMMA), a polymer commonly used in facial masks, food packaging, cosmetology, pharmacology, medicine, and others.

In this sense, the present work evaluated five different percentages of Mps-PMMA (0.0, 0.25, 0.50, 0.75 and 1.0 %) incorporated in the food for tropical gar (*Atractosteus tropicus*) for 60 days. The exposed fish's parameters and rates of growth, survival, and digestive enzymatic activity were evaluated.

The fish's weight and length were not significant differences among treatments. The fish's growth indices (AWG, SGR and CF) were not statistically different among treatments. Fish survival was not statistically different. In general, the evaluated population obtained a survival rate of 94%.

In the case of digestive enzymes, alkaline proteases decreased significantly with increasing percentage of MP-PMMA in the diet, as did trypsin and chymotrypsin ($p=0.018$, 0.012, 0.002, respectively). Leucine aminopeptidase and alpha-amylase activities were significantly different among treatments ($p=0.011$, 0.004, respectively). Lipase activity did not significantly differ among treatments.

These preliminary results reveal that the percentages of PMMA MPs incorporated in the food, under our experimental conditions, did not affect fish growth and survival. However, changes in enzyme activity are observed, particularly in alkaline proteases trypsin and chymotrypsin, which could imply a reduction in protein digestion.

Keywords: Microplastic, polymethylmethacrylate, tropical gar (*Atractosteus tropicus*)

OXIDATIVE STRESS IN LITHOBATES CATESBEIANUS BY TEST EXPOSURE TO CHLOROTHALONIL

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Abstract:

In the world the use of pesticides is important and unavoidable, these chemical compounds are applied for different purposes and each of them very important. However, this has caused adverse effects on the ecosystem, the adverse effects have been described in various organisms, among which are amphibians, these organisms due to their life cycle are strongly affected by the presence of pesticides, both in the water as in the ground.

Objective of the study was to demonstrate whether exposure for 48 h to the fungicide Chlorothalonil generates oxidative stress in Lithobates catesbeianus larvae.

Methodology. The mean lethal concentration (LC50) of Chlorothalonil was determined at 48 hours of exposure in bullfrog tadpoles, using the modified Lorke method (Garrido-Acosta et al, 2014), to use the least number of test organisms. Oxidative stress was determined using one tenth of the median lethal concentration and lipid peroxidation and the activity of the enzymes super oxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) were determined with exposure times 6, 12, 24 and 48 hours in tadpoles.

Results. When doing the literature review, no antecedents of chlorothalonil and bullfrog tadpoles were found, so the determination of the median lethal concentration was re-performed after 48 hours of exposure, the result was 0.1754 mg /mL. With this result, the tests were carried out to determine the oxidative stress; lipoperoxidation increased significantly after 6 hours of exposure, and up to 24 hours, the same result was observed with the enzymes SOD and CAT; On the other hand, the activity of GPx increased significantly after 24 h.

Conclusion. Exposure of tadpoles to chlorothalonil for 48 hours induces oxidative stress.

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METAL COMPLEXES FORMED WITH EDTA, MELATONIN, AND ITS MAIN METABOLITES: COMPUTATIONAL DFT STUDY AND IMPLICATIONS FOR A LEAD INTOXICATION ALTERNATIVE TREATMENT

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Abstract:

In this computational work, we report a study of 45 possible complexes that we suggest may be formed between Pb and other metals with melatonin, melatonin metabolites, and EDTA, analyzing the stability and viability of these through the Gibbs free energy of complexation (ΔΔG), molecular orbitals, and energy decomposition analysis at the PBE/TZ2P DFT level of theory. We show that most complexes present exergonic energies of reaction, and thus spontaneous complex formation. In addition, we show that the AMK and 3OHM melatonin metabolites possess electronic and thermodynamic properties adequate to act as lead trapping molecules due to the lower Pauli repulsion energies involved in the complexes they form and their large ΔΔG negative values. Therefore, it is shown that both melatonin and some of its metabolites may be employed in a potential treatment for lead intoxication through transport by stable Pb-complexes, as an alternative to the usage of EDTA[1-8].

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THE DRUG COMBINATION DOXORUBICIN, METFORMIN AND SODIUM OXAMATE INHIBIT CELL PROLIFERATION THROUGH β-CATENIN INACTIVATION IN SARCOMA CELL LINES

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Abstract:

Sarcomas are a rare and heterogeneous group of tumors with high rates for distant metastases and mortality. They are grouped according to the site of origin into soft tissue sarcoma (STS) and bone tissue sarcoma (BTS) which represent 80% and 20% of total cases, respectively. The therapeutic aims for sarcoma are to reduce recurrence and minimize morbidity and mortality. Despite previous efforts to introduce new therapeutic approaches, the standard treatment for sarcomas has remained unchanged for nearly 40 years. First-line treatments are currently led by anthracyclines as doxorubicin, alkylating agents, and taxanes. However, these compounds are not histologically driven or specific to any biomolecular pathways, therefore inducing high toxicity levels and low response rates. Recently, it was demonstrated an antineoplastic effect of the drug combination doxorubicin, metformin and sodium oxamate through apoptosis and autophagy induction as well as cell proliferation inhibition in breast and colon cancer. However, the mechanisms affected by this therapy to inhibit cell proliferation remains unclear. The protein β-catenin have been stablished as a central regulator of cancer cell proliferation. When the protein is translocated to the nucleus, it activates the expression of gene targets as cyclin D1, c-myc and snail to promote cell cycle progression. In this work we demonstrated that β-catenin signaling pathway is differentially activated between osteosarcoma and liposarcoma cell lines. Constitutive nuclear location and transcriptional activity of β-catenin was observed in osteosarcoma cell lines. Moreover, under doxorubicin, metformin and sodium oxamate combined treatment β-catenin activity decrease and cell proliferation is diminished. Finally, liposarcoma cells showed sensitivity to multidrug treatment despite to signaling pathway inactivity. All together these findings support the addition of metformin and sodium oxamate to doxorubicin as an alternative treatment for sarcomas.

EVALUATION OF THE TOXIC ACTIVITY OF HEXANIC EXTRACT OF *SEDUM MORGANIANUM*

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Abstract:

There is a large number of secondary metabolites that have been identified, their biological effects and interactions have been studied in the last century, highlighting their uses as antimicrobials, antifungals, cytotoxic and anticancer activity[1]. Mexico is a country with an enormous biodiversity in plants, so it is important to study endemic species with possible therapeutic effects, in recent years have been studied species of the *Crassulaceae* family that have proved to have positive therapeutic effects[2]; *Sedum morganianum* is a species belonging to this family and its endemic to Mexico, this plant has not been investigated for its possible therapeutic effects. To study the toxic effects of *S. morganianum* we use the dry extract, for this purpose, the maceration of the dry plant in pure hexane was carried out, then the solvent was separated using a rotatory evaporator. We have evaluated the toxicity of the hexanic extract of *Sedum morganianum* in cancer cell lines and in *Artemia* spp. model. The extract was dissolved in dimethylsulfoxide (DMSO) and an aliquot was made for the assays in both models. The results of the tests performed suggest a high level of toxicity in brine shrimp model and effects in the cancer cell line. The findings in this research suggest that *Sedum morganianum* has metabolites with biological activity that may be pharmacologically useful.

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APOPTOTIC AND AUTOPHAGIC EFFECT OF LITHIUM SALTS IN AN *IN VITRO* MODEL OF CERVICAL CANCER

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Abstract:

Cervical cancer (CC) is the fourth most common cancer among women, with more than 500,000 new cases per year and about 250,000 deaths (Fowler, *et al.* 2022). Therefore, the importance of the research on the employment of new therapeutic strategies such as lithium salts (lithium chloride (LiCl) and lithium carbonate (Li2CO3)), which have been used for the treatment of bipolar disorder and depression (Aronson, 2016). Nevertheless, in recent years the use of LiCl and Li2CO3 has been focused on as antitumoral agents, due to their effects on different signaling pathways related to cell proliferation, autophagy, and apoptosis in different types of cancers, like prostate, ovarian, colorectal, neuroblastoma, and medulloblastoma, but lacking information in CC (Ge, *et al.* 2010; Petrovich, *et al.* 2019; Sarkar, *et al.* 2005). Therefore, the present work aims to study the antitumoral activity of LiCl y LI2CO3 in CC cell lines, through the determination of the antiproliferative activity, expressed by the concentration required to induce a 50% decrease in the cell number (IC50), assessed by crystal violet tinction, as well as the determination of activation of apoptosis and autophagy through the identification of the related proteins in those signaling pathways by western blot technique.

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A-LINOLENIC ACID, AN OMEGA-3 POLYUNSATURETED ACID PROTECTS AGAINST INDOMETHACIN-INDUCED GASTRIC INJURY IN THE RAT

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Abstract:

Non-steroidal anti-inflammatory drugs (NSAIDs) are a group of drugs worldwide used, however, their use generates gastrointestinal damage in patients who consume them. Therefore, natural alternatives are sought to reduce gastric damage caused by NSAIDs, such as omega-3 polyunsaturated fatty acids (w-3 PUFA), which induce anti-inflammatory and antioxidant effect. Among the omega-3 PUFAs, docosahexaenoic acid (DHA) has recently demonstrated gastroprotective effect, however the effect of a-linolenic acid (ALA), which is mainly found in seeds such as chia has not been studied so far. The objective of this work was to evaluate the gastroprotective effect of ALA in a murine model of gastric damage induced by indomethacin in female Wistar rats. ALA was administered orally acutely (300 mg/kg, p.o.) or for 10 days (20 mg/kg, p.o.), two hours later indomethacin (INDO) was administered orally to induce acute gastric damage (30 m/kg, p.o.). Three hours after the INDO administration, the rats were euthanized, and the gastric lesions were evaluated to obtain the total area of damage. Gastric tissue was collected to quantify levels of leukotriene B4 (LTB4) by enzyme-linked immunosorbent assay, and reduced glutathione (GSH) by colorimetric assay. ALA exhibits gastroprotective effect both macroscopically and microscopically due to a single oral administration and 10 days oral administration against acute gastric damage caused by indomethacin. LTB4 levels decrease significantly with ALA treatment, while GSH levels increase with both treatments. ALA has a gastroprotective effect against indomethacin, being one of the first reports in this model of gastric damage. Our results suggest that ALA induces gastroprotective effect throw the antioxidant pathway activation.

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COLLECTION AND PHYSICOCHEMICAL CHARACTERIZATION OF EXPIRED ACETAMINOPHEN

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Abstract:

Worldwide, more than one million tons of medicines are produced, of which approximately 3% will reach their useful life and will be considered expired medicines. In Mexico, the Secretaría de Medio Ambiente y Recursos Naturales (SEMARNAT) classifies expired drugs as hazardous waste and therefore they cannot be distributed, stored, marketed or administered legally within the national territory due to the consequences caused by their presence in the environment (NOM-052-SEMARNAT-2005). According to the Ministry of Health, more than 200 million units of expired medicines are generated annually in Mexico, of which only 30% are properly disposed of and are delivered to agencies that regulate this waste, such as the National System for the Management of Packaging and Medicine Waste (SINGREM). In Tabasco, landfills are limited (only two in the entire state) and SINGREM has not been operating in that region since its creation in 2007, which maintains significant delays in the management and final disposal of medicine waste and its containers in the state with diverse effects, both in public spaces and in diverse ecosystems. This work is part of a research that aims to measure the ecotoxicological effects caused by some expired medicines, such as paracetamol, since it is one of the most prescribed by the medical community and also one of the most self-administered by people. Initially, two campaigns for the collection of expired medicines were organized and carried out in two higher education institutions. In the first stage, all the medicines recovered were classified by pharmaceutical form, therapeutic group and year of expiration, obtaining results similar to those reported in the literature, with a greater frequency of the different pharmaceutical forms of paracetamol (granules, suspension, solution, syrup, capsules or tablets). In a second stage, due to their relevance and high frequency (72%), the expired paracetamol tablets will be pulverized and subjected to different physicochemical characterization processes such as thin layer chromatography, continuous extraction methods (Baltierra-Hernández, 2019), UV-Vis spectrophotometry scans and Fourier transform infrared techniques. The results will allow us to identify the presence and purity of the active substance (Acetaminophen) and the characteristics of its other components.

EFFECT OF DHA ON OXIDATIVE STRESS AND MICROBIOTA IN A MURINE MODEL OF INDOMETHACIN-INDUCED INTESTINAL DAMAGE

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Abstract:

Non-steroidal anti-inflammatory drugs (NSAIDs) are used highly prescribed drugs due to their antipyretic, analgesic and anti-inflammatory properties. However, this group of drugs exhibits important gastrointestinal side effects. Therefore, a better alternative is necessary, docosahexaenoic acid (DHA), a PUFA (poly-unsaturated fatty acid) w-3, is emerging as an option of treatment because it induces gastro protective effect against damage induced by NSAIDs[1,2] however, the intestinal protection has not been evaluated. For this reason, this research aims to study the enteroprotection of DHA against intestinal damage induced by indomethacin (INDO). Methods: Female Wistar rats were administered whit DHA (3 mg/kg, p.o.) in a model of intestinal damage induced by INDO (3 mg/kg, p.o.). The macroscopic intestinal damage was measured and expressed as % enteroprotection, in addition, a histological study was performed to observe intestinal the ulcers; and indicators of antioxidant activity were measured in tissue (SOD, GSH, MDA and MPO). Subsequently, the relative abundance of Enterobacteriaceae, *Bacteroides, Clostridium, Akkermansia* and *Lactobacillus* was evaluated in feces by qRT-PCR; and the LPS component was determine in serum by ELISA kit. As a result, we found that DHA significantly decreased the intestinal damage generated by the NSAID. In addition, DHA prevented the reduction in GSH levels and SOD activity induced by intestinal damage. Furthermore, DHA pretreatment decreases MPO activity and MDA levels that are elevated after NSAID treatment. Likewise, DHA prevents the increase in serum LPS caused by INDO. Finally, the administration of INDO significantly increases the abundance of *Akkermansia* while it decreases *Lactobacillus*; in contrast, these changes are prevented when DHA is co-administered. Therefore, our results suggest that DHA prevents intestinal damage by activating the antioxidant pathway, preventing oxidative stress markers and DHA also prevents the alteration in *Akkermansia* and *Lactobacillus* abundance caused by NSAIDs. Which outlines DHA as an option for treatment of NSAIDs-induced intestinal damage.

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TREATMENT OF PREECLAMPSIA WITH METFORMIN: EFFECTS IN REVERTING FETAL PROGRAMMING OF BREEDING

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Abstract:

Preeclampsia (PE) is a complication of pregnancy with a high incidence in our country. There is evidence of the association between PE and the risk of suffering metabolic syndrome (MS) in both mothers and their children. On the other hand, fetal programming refers to the adaptations to an microenvironment with insufficient provision of nutrients or oxygen during fetal life that induce changes in postnatal metabolism and susceptibility to chronic diseases in adulthood. Metformin is a drug capable of reducing metabolic disturbances such as insulin resistance. It is unknown whether metformin treatment during preeclampsia can prevent cardiovascular and metabolic damage of the offspring. To investigate this issue, female Wistar rats were divided into 4 experimental groups: a) Healthy pregnant b) Healthy pregnant treated with metformin c) PE d) PE treated with metformin. The PE model was achieved using the subrenal coarctation of the aorta (CARS) procedure. 5 mg/Kg of metformin was administered along all pregnancy. The pups were measured for weight and height, blood pressure (BP), blood glucose, cholesterol, and triglycerides at birth and at 4 and 8 weeks of age. Metformin treatment reduced the weight of healthy pregnant rats, but did not change the weight of PE rats. PE decreased the number of pups per litter and treatment with metformin reverted this effect. PE increased BP in late pregnancy, that was reduced in the group treated with metformin. The blood pressure of the breeding of mothers with PE, both females and males, showed higher levels of SBP compared to the other groups. Offspring of metformin-treated preeclamptic mothers showed lower BP levels compared to thoseof untreated PE rats. The results suggest that metformin treatment of the mother with PE contributes to prevent the development of arterial hypertension in the offspring.

CHIMERA DESIGNED WITH HYPOTHETICAL ACTIVITY AGAINST TRICHOMONAS VAGINALIS

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Abstract:

Introduction: Trichomoniasis is a sexually transmitted disease caused by the protozoan parasite *Trichomonas vaginalis*. This parasite affects 3.9% of the world's population. *T. vaginalis* has developed resistance to metronidazole, which is a drug used for the treatment of this infection. The reduced form of metronidazole causes breaks in the parasite's DNA strand, inhibiting its synthesis and thus its viability. The parasite has shown resistance to metronidazole, therefore, is a need to search for new compounds with trichomonicide activity. **Objective**: This work aimed to perform an approach to the computer-assisted drug design, searching for small molecules (< 500 Da) that can act as a drug against trichomoniasis. **Methods**: For this, first, we performed a search for molecules with therapeutic potential against *T. vaginalis*, using as a target a metalloproteinase, TvMP50, which is a virulence factor of the parasite involved in its cytotoxicity toward the host cell. Subsequently, a high-throughput screening based on molecular descriptor analysis was developed; the resulting molecules were processed by molecular docking analysis to identify the molecules with better interaction with the active site of TvMP50. Finally, fragments of the most active molecules were generated and assembled into new molecular entities, which were re-evaluated against the target protein. **Results:** We found 34 compounds with trichomonacidal activity by bibliographic analysis. Of them, 21/34 compounds accomplished Lipinski's rules and were evaluated by molecular docking against TvMP50. The compounds that interacted with the active site were fragmented and reassembled in chimeras. We obtained that the Emodine-Lucidin isopropyl chimera had the optimal binding into TvMP50. **Conclusion**: The chemoinformatic allowed us to obtain Emodin-Lucidin isopropyl ether, a new chimeric molecular entity with a hypothetical activity against TvMP50 of *Trichomonas vaginalis*.

This work was supported by UACM and the grant for the project CCyT-2021-1of the Colegio de Ciencia y Tecnología and the support of CONACYT for the student CVU number 1082640.

PARTICULATE MATTER PM_{10} AFFECTS THE MISMATCH REPAIR (MMR) PATHWAY THROUGH SETD2 DOWNREGULATION

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Abstract:

Air pollution represents an environmental problem, impacting negatively in human health. Particulate matter of 10 micrometers or less in diameter (PM_{10}) is related to pulmonary diseases, including lung cancer. Mismatch repair (MMR) is a postreplication process that preserves DNA homeostasis and guarantees genomic stability. The goal fo MMR is to correct spontaneous base–base mispairs and small insertions–deletion loops (indels) that are mainly generated during DNA replication. When MMR is deficient it fails to correct these errors, causing microsatellite instability (MSI), a type of genomic instability that is characteristic for tumor cells. SETD2 is a histone methyltransferase responsible for histone H3 lysine 36 trimethylation (H3K36me3) of chromatin, an epigenetic mark associated with gene transcription, and has been linked with the induction of some MMR components. In this study, we evaluated the effect of PM_{10} in the expression levels of SETD2, as well as the effect in the expression levels of MMR components MLH1, MSH2 and MSH6, using the A549 lung cancer cell line. A549 cell cultures were exposed to PM_{10} (10 μg/cm^2) for 24 h to evaluate the expression and protein levels of *SETD2*, *MLH1*, *MSH2*, and *MSH6*. We observed that PM_{10} decreases the expression levels of *SETD2*, *MLH1*, *MSH2*, and *MSH6* in A549 cells, compared with non-treated cells. Co-localization of SETD2/H3K36me3 was lower in PM_{10}-treated cells in comparison with non-treated cells. Finally, micronuclei (MN) frequency was higher in PM_{10}-treated cells in contrast with non-treated cells. Our results suggest that PM_{10} causes defects in MMR pathway through downregulation of SETD2 and MMR components MLH1, MSH2 and MSH6, predisposing cells to the generation of microsatellite instability in transformed cells.

Keywords: PM_{10}, SETD2, A549, mismatch repair, micronuclei, microsatellite instability

THE ANTIDEPRESSANT DRUG SERTRALINE INHIBITS KV4.2 CHANNELS

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Abstract:

Kv4.2 is a voltage-gated K^+ channel that underlies the fast-inactivating, transient outward K^+ current (I_{tof}) in the heart. This current modulates the duration and/or shape of the action potential and plays a prominent role in cardiac repolarization, since its inhibition has been associated to the development of arrhythmias. Sertraline is a selective serotonin reuptake inhibitor antidepressant drug that can induce cardiac toxicity, even at therapeutic doses (~ 8 μM), leading to ventricular arrhythmias and sudden cardiac death. However, it is not well understood how this antidepressant drug can produce such cardiac effects. In the present work we show that sertraline inhibits Kv4.2 channels in a concentration-dependent (IC_{50} = 3.9 μM) but voltage-independent manner. Sertraline did not affect the voltage dependence of channel activation, although this drug accelerated both the channel activation and inactivation kinetics and produced a slowing of the recovery from inactivation. In addition, sertraline induced a tonic block of the current and, when Kv4.2 channels were maintained at the closed-state, the current was inhibited by approximately 50%. Our findings suggest that sertraline inhibits Kv4.2 channels in the closed-state, although it could also affect channel inactivation.

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EFFECT OF HYDROGEN SULFIDE ON VASCULAR DYSFUNCTION INDUCED BY TYPE 2 DIABETES MELLITUS IN RAT THORACIC AORTA

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Abstract:

Hydrogen sulfide (H_2S) is a gasotransmitter that has been involved in the regulation of the cardiovascular system. H_2S is synthesized from L-Cysteine by three enzymatic pathways, but cystathionine- γ-lyase (CSE) predominates in the cardiovascular system, especially the myocardium and vascular smooth muscle cells. This study aimed to determine the effect of chronic administration of sodium hydrosulfide (NaHS; inorganic H_2S donor) and DL-Propargylglycine (DL-PAG; CSE inhibitor) on the vascular dysfunction in thoracic aorta obtained from male diabetic Wistar rats. For that purpose, neonatal rats were divided into two main sets that received: (1) citrate buffer (n=6) and (2) a single dose of STZ (70 mg/kg/i.p., n=6) on the third day of birth to induce diabetes. After 12 weeks, the diabetic animals were divided into 4 subgroups (n=6 each) which received daily i.p. injections during 4 weeks of: (1) nothing; (2) vehicle (PBS, 1 ml/kg); (3) NaHS (5.6 mg/kg); and (4) DL-PAG (10 mg/kg). After treatments (16 weeks), vascular function by *in vitro* experiments (organ bath) was determined. We observed that type 2 Diabetes Mellitus induced by streptozotocin leads to: (1) an increase in glucose levels; (2) a decrease in vasorelaxation to angiotensin 1-7 (Ang-1-7) and vasoconstriction induced by angiotensin II (Ang II) compared to control group. Interestingly, after of treatment, NaHS increased vasorelaxation and vasoconstriction to Ang 1-7 and Ang II, respectively, when compared to vehicle. On the other hand, the treatment with DL-PAG did not affect the responses. These results suggest that chronic treatment with NaHS improved vascular dysfunction produced by streptozotocin-induced type 2 Diabetes Mellitus and may have a potential therapeutic application.

C-PHYCOCYANIN PREVENTS IMPAIRED AT1, AT2, AND MAS RECEPTORS EXPRESSION, ENDOTHELIAL DYSFUNCTION, AND HYPERTENSION CAUSED BY CHRONIC KIDNEY DISEASE

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Abstract:

Introduction: C-phycocyanin (CPC) is a nutraceutical pigment found in the cyanobacteria A. maxima (Spirulina) with a nephroprotective and antihypertensive activity that can prevent the development of hemodynamic and molecular alterations caused by chronic kidney disease (CKD).

Objective: This study aims to determine if the anti-hypertensive effect of CPC is associated with preventing the impairment of: (1) hemodynamic variables, (2) renal function, and (3) the endothelial function in the aorta caused by alterations in the expression of AT1, AT2, and Mas receptors in rats with CKD.

Materials and methods: Thirty-two normotensive (blood pressure ≤ 120/80 mmHg) male Wistar rats were divided into four groups (n=8): (1) sham + 1 ml/kg/d vehicle (100 mM of phosphate buffer, PBS, pH 7.4) administered by oral gavage (og), (2) sham + 100 mg/kg/d og of CPC, (3) CKD induced by 5/6 nephrectomy (NFx) + 1 ml/kg/d og vehicle (PBS 100 mM), (4) NFx + 100 mg/kg/d og of CPC. One week after surgery, the CPC treatment began and was administrated for four weeks. At the end of treatment, the hemodynamic variables and renal function were evaluated by a non-invasive method coupled to the tail rat by a CODA system (Kent Scientific) and colorimetric assays kits (Spinreact), respectively. Then animals were euthanized, and their thoracic aorta was used to determine the endothelial function as well as expression of AT1, AT2, and Mas receptors.

Results: The 5/6 NFx caused hypertension four weeks after the surgical procedure. In addition, the serum creatinine, blood urea nitrogen, and uric acid were increased. CKD caused endothelial dysfunction reducing the vasorelaxant response to cumulative concentrations of angiotensin 1-7 (1x10-4M-1x10-2M) and increasing the contractile response to cumulative concentrations of angiotensin II (1x10-4 M-1x10-2M). The expression of the AT1 and AT2 receptors increased, and the Mas receptor's expression was reduced by CKD. Remarkably, the treatment with CPC prevented hypertension, renal function impairment, and endothelial dysfunction in the angiotensin system mediated by AT1, AT2, and Mas receptors caused by CKD.

EPICATECHIN EFFECT IN AN EXPERIMENTAL PRE-ECLAMPSIA MODEL

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Abstract:

Preclampsia (PE) is a pregnancy specific disorder characterized by de novo development of hypertension and proteinuria. Both the pathophysiology and the treatment of this disease are not clearly established. Epicatechin is a natural product that has shown beneficial effects in several conditions including hypertensive as well as having recognized antioxidant capacity. The objective of this work was to evaluate if the Epicatechin can reduce blood pressure in an experimental model of preclampsia and observe the effect that conductance vessels (thoracic and abdominal aorta) have on reactivity. For this, 250g female Wistar rats were used divided into groups of pregnant control and pregnant women with subrenal aortic coarctation, divided into three treatments: a) Vehicle, b) Epicatechin (10 mg/Kg/day) during the first two weeks or last two weeks of gestation. Blood pressure and weight were recorded, and a glucose tolerance curve was performed, Then, the animals were sacrificed to assess vascular contractility in aortic rings using a conventional preparation for isolated organ. The results showed that rats with PE have an increase in systolic blood pressure, blood glucose and vascular contractility (abdominal aorta) compared to rats with normal pregnancy. While treatment with Epicatechin decrease systolic blood pressure, and the contractility to phenylephrine and angiotensin II in abdominal portion of preclamptic rats treated in the 1st and 2nd week. We conclude that Epicatechin is a substance capable of preventing a significant increase in systolic blood pressure in the preclampsia model, however, this is not directly associated with the contractile response of conductance vessels, therefore, it is suggested that epicatechin effect is on resistance vessels.

POLYPHENOLS INHIBIT TUMOR GROWTH AND COULD BE USED AS AN ALTERNATIVE FOR CHEMO-SENSITIZATION IN ORAL CAVITY AND OROPHARYNGEAL CARCINOMA

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Abstract:

Polyphenols such as Curcumin (CUR) and Resveratrol (RES) have shown pharmacological activity in different medical areas, including oncology. In in vivo models, polyphenols have reduced the growth of xenografts of some types of carcinomas; however, there is little evidence on the effect of these compounds on oral cavity and oropharyngeal carcinoma (OCOC). Likewise, the influence of oncogenic viruses such as the human papillomavirus (HPV) is still under review.

The aim of the work was to demonstrate the effect of the compounds CUR and RES, alone or in combination with Cisplatin (CDDP) in vitro on the viability of cell lines of OCOC positive or negative to HPV, to demonstrate their potential as inhibitors or growth reducers of OCOC cell line xenografts in an in vivo model in immunodeficient mice, as well as testing their ability to chemo-sensitize xenografts in the in vivo model.

The CUR and RES compounds affected the viability of the cell lines SCC152, SCC090, SCC025 and FaDu from 100 uM concentration, in the case of CDDP from 20 uM an effect is observed. The SCC152 and SCC025 cell lines were inoculated into NOD-SCID mice subcutaneously for the generation of a xenograft tumor on the back of each mouse; 7 doses of CUR, RES, CDDP and their combinations were administered. Tumor volume was reduced at the doses administered, the CUR-CDDP combination greatly inhibited tumor growth in xenografts generated by the SCC152 cell line.

At the end of treatment, the remaining tumors were removed and divided to be fixed with paraformaldehyde or frozen at -80°C. Subsequently, histology and immunohistochemistry assays will be carried out, as well as some PCR tests to deduce the participation of a particular signaling pathway.

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EFFECTS OF RESVERATROL AGAINST *GIARDIA LAMBLIA* TROPHOZOITES THROUGH *IN SILICO* AND *IN VITRO* APPROACHES

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Abstract:

Giardia lamblia is a protozoa that causes giardiasis, an intestinal disease with global distribution. Infection is managed with antimicrobials, although side effects, drug resistance and treatment failures are a clinical challenge[1]. The search for new therapeutic drugs that interrupts molecular targets essential for parasite survival is a valuable approach[2]. In this sense, the cytoskeleton of *Giardia* is a complex and distinctive structure implicated in their pathogenesis and proliferation[3]. Resveratrol (RSV) is a polyphenolic compound found in the skin of red grapes, peanuts and various fruits. Recently, synthetized derivatives of RSV have demonstrated antiproliferative, cell cycle arrest and apoptotic events on cancer cell lines by tubulin polymerization inhibition[4]

In this work the antigiardial effects of RSV were evaluated on *Giardia lamblia* trophozoites. *In silico* approaches were used to identify the potential RSV interaction with *Giardia* tubulin. To evaluate proliferation and adhesion effects, growth kinetics were performed. Morphological alterations and tubulin expression were analyzed by SEM and Western blot, respectively. Apoptotic-like events were also identified using annexin-V and propidium iodide.

By docking assay we identified the binding site of RSV to *Giardia* tubulin suggesting their microtubule interaction and antigiardiasic potential. *In vitro* experiments results confirmed that RSV causes growth and adherence inhibition, decreased cell viability and tubulin expression in a concentration-dependent way. Alterations on morphology trophozoites treated with RSV was also demonstrated. Our findings propose that RSV could be an alternative for giardiasis treatment.

[1]Santos, Helena Lucia Carneiro, and Karina M Rebello. "An Overview of Mucosa-Associated Protozoa: Challenges in Chemotherapy and Future Perspectives." *Frontiers in cellular and infection microbiology* vol. 12 860442. 25 Apr. 2022.

[2]Vázquez-Jiménez, Lenci K et al. "Recent Advances in the Development of Triose Phosphate Isomerase Inhibitors as Antiprotozoal Agents." *Current medicinal chemistry* vol. 29,14 (2022): 2504-2529.

[3]Lagunas-Rangel, Francisco Alejandro et al. "An update on cell division of Giardia duodenalis trophozoites." *Microbiological research* vol. 250 (2021): 126807.

[4]Thomas, Elizabeth et al. "A Novel Resveratrol Based Tubulin Inhibitor Induces Mitotic Arrest and Activates Apoptosis in Cancer Cells." *Scientific reports* vol. 6 34653. 17 Oct. 2016.

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