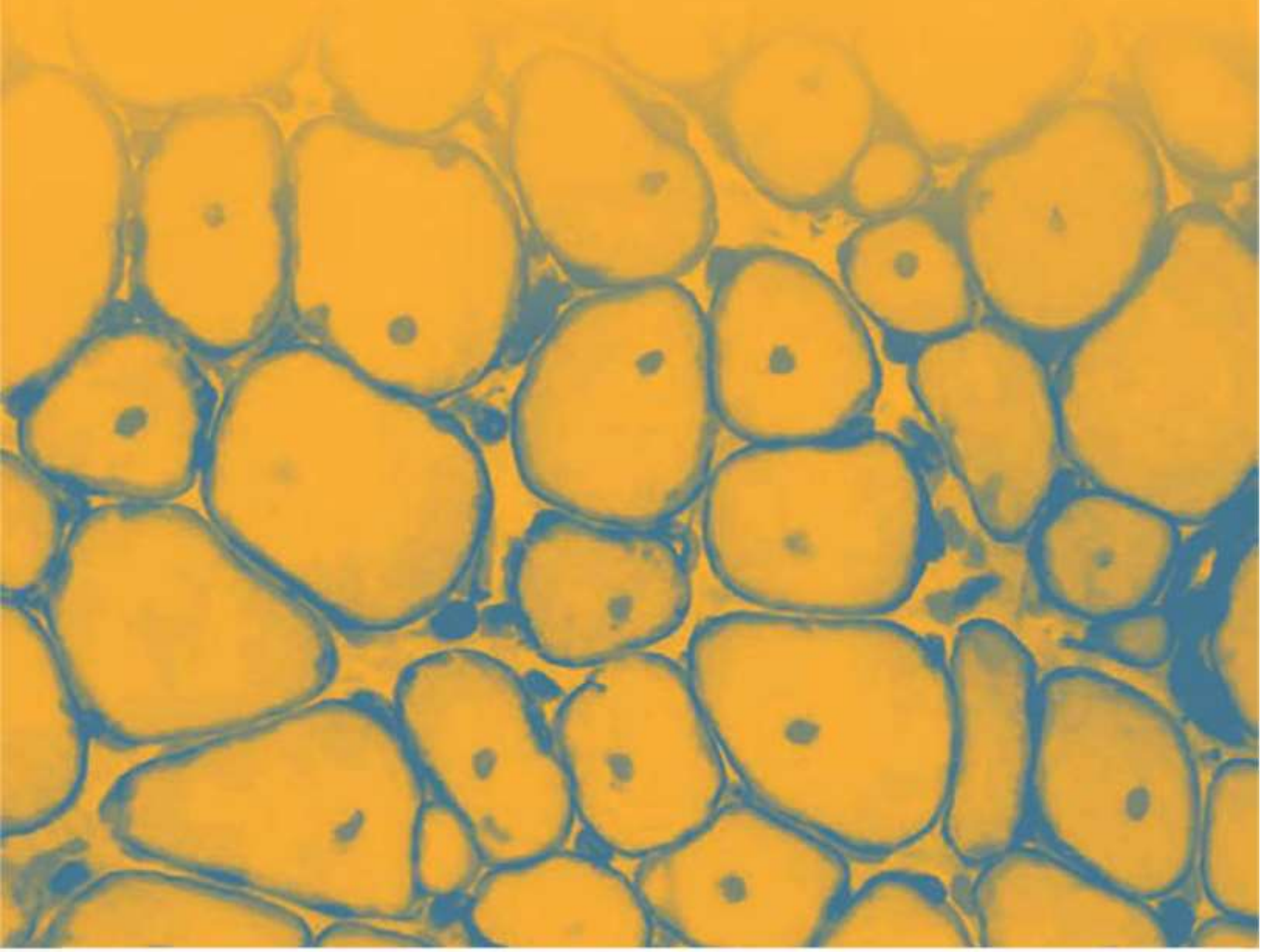
Physiological Mini Reviews

Special Issue
SAFIS + ALACF 2021 joint meeting
October 20-22, 2021

14
Volume



Vol. 14, Special Issue, October 2021
ISSN 1669-5410 (Online)
pmr.safisiol.org.ar

Physiological Mini Reviews

SAFIS
Sociedad Argentina de Fisiología

Physiological Mini-Reviews

[ISSN 1669-5410 (Online)]
Edited by **the Argentinean Physiological Society and the Latin American Association of Physiological Sciences**

Journal address: Centro de Investigaciones Cardiovasculares y Cátedra de Fisiología y Física Biológica.
Facultad de Ciencias Médicas; Universidad Nacional de La Plata;
La Plata, Buenos Aires, Argentina. Tel.-Fax: +54-211-4834833
http://pmr.safisiol.org.ar

Physiological Mini-Reviews is a scientific journal, publishing brief reviews on "hot" topics in Physiology. The scope is quite broad, going from "Molecular Physiology" to "Integrated Physiological Systems". As indicated by our title it is not our intention to publish exhaustive and complete reviews. We ask to the authors concise and updated descriptions of the "state of the art" in a specific topic. Innovative and thought-provoking ideas are welcome.

Preparation and Submission of manuscripts:

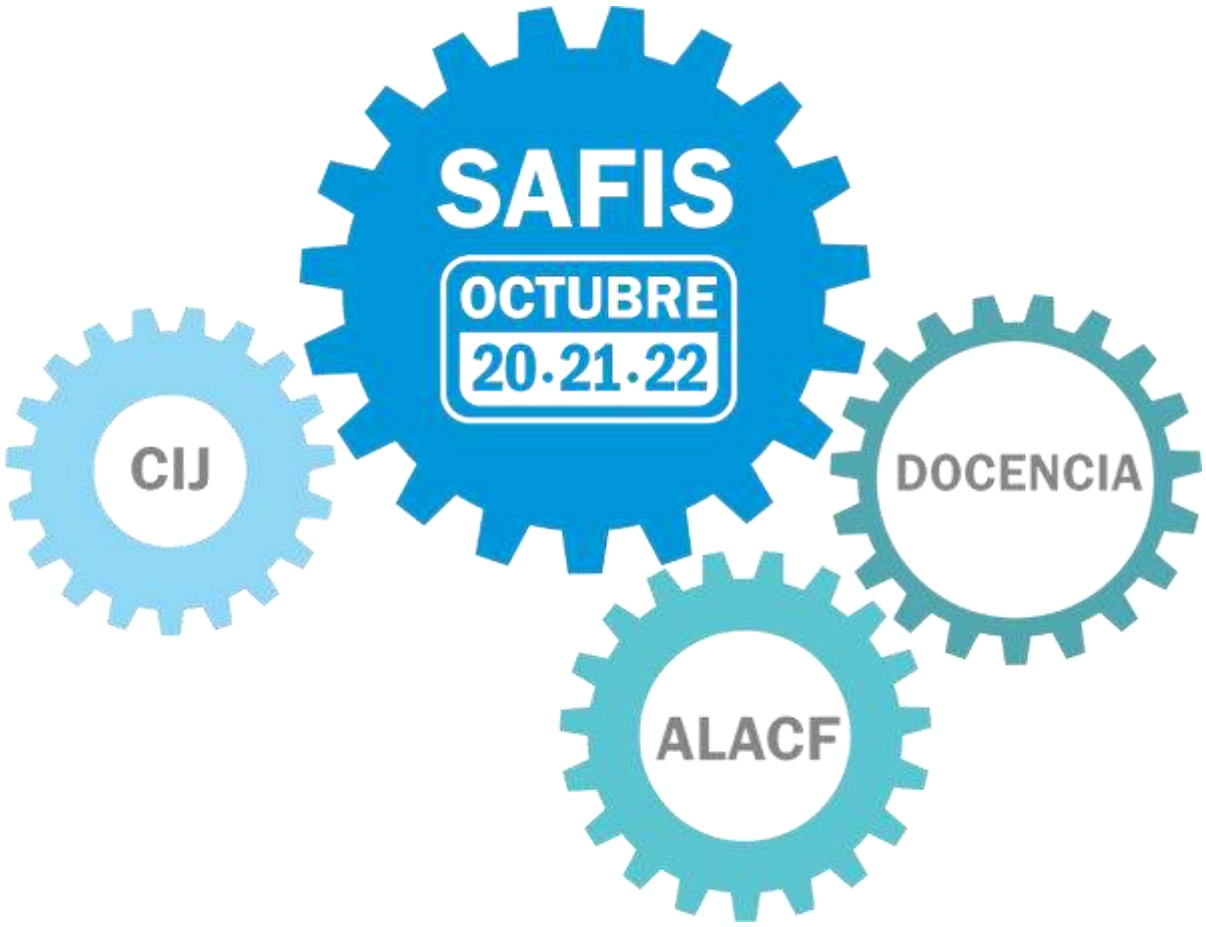
"Physiological Mini-Reviews" will have a maximum of 3000 words, 50 references and 3 figures. Material will be addressed to scientific people in general but not restricted to specialist of the field. For citations in the text please refer to Instructions in our webpage. Final format will be given at the Editorial Office. Most contributions will be invited ones, but spontaneous presentations are welcome. Send your manuscript in Word format (.doc or .docx) to: pmr@safisiol.org.ar

The “Sociedad Argentina de Fisiología” is a registered non-profit organization in Argentina. (Resol. IGJ 763-04)

Annual Meeting 2021

Discovering the physiological gears from evolution to Translation

October 20-22, 2021



CONGRESS AUTHORITIES

Sociedad Argentina de Fisiología (SAFIS)
Argentine Society of Physiology

President
Martín Vila Petroff • CIC Dr Horacio Cingolani (UNLP-CONICET)

Vice-President
Graciela Cremaschi • Facultad de Ciencias Médicas, Pontificia Universidad Católica Argentina

Secretary
Verónica De Giusti • CIC Dr Horacio Cingolani (UNLP-CONICET)

Treasurer
Luis Gonano • CIC Dr Horacio Cingolani (UNLP-CONICET)

Vocal Members
Matilde Said • CIC Dr Horacio Cingolani (UNLP-CONICET)
Alejandro Orlowski • CIC Dr Horacio Cingolani (UNLP-CONICET)
Gisela Di Giusto • IFIBIO (UBA-CONICET)
Daniel Francés • Instituto de Fisiología Experimental (UNR-CONICET)

Alternate Members
Rosana Elesgaray • Facultad de Farmacia y Bioquímica (UBA)
María Gabriela Marina Prendes • Facultad de Farmacia y Bioquímica (UBA)

Member of Norwest Region
Liliana Monasterolo • Facultad de Ciencias Bioquímicas y Farmacéuticas (UN)

Member of Cuyo Region
Emiliano Diez • Facultad de Ciencias Médicas (UNCUYO)

Member of Central Region
María del Rocío Cantero • Facultad de Ciencias Médicas (UNSE)

External members
Sergio Gradilone • The Hormel Institute, University of Minnesota (USA)
Guillermo Lehmann • Regeneron Pharmaceuticals Inc. (Tarrytown, NY, USA)

Supervisory Body
Ernesto A. Aiello • CIC Dr Horacio Cingolani (UNLP-CONICET)
Daniela Olea • Fundación Universitaria Dr. Rene G. Favaloro

Past-President
María Cecilia Larocca • IFISE (UNR – CONICET)

Asociación Latinoamericana de Ciencias Fisiológicas (ALACF)
Latin American Association of Physiological Sciences

President
Luis Sobrevía • Chilean Society of Physiological Sciences (SCHCF)

General Secretary
Alejandro Aiello • Argentinean Society of Physiology (SAFIS)

Council ALACF
Patricia Rocco • President Brasilean Physiological Society (SBFis)
Zully Pedroso • President of Chilean Society of the Physiological Sciences (SCHCF)
Martín Vila Petroff • President Argentinean Society of Physiology (SAFIS)
Henry León • President Colombian Society of Physiology (COLFISIS)
Azael Paz Aliaga • President Peruvian Society of Physiology and Physiopathology
Daniel Ortuño • President Mexican Society of Physiological Sciences (SMCF)
Mayppé González • President of the Cuban Society of Physiological Sciences (SOCCF)
Jean-Claude Dorsainvil • President of the Haitian Society of Physiology (SHF)
Paola Contreras • Delegate of the Uruguayan Society of Biosciences (SUB)
Reinaldo Marín • Venezuela Representative
Enrique Terán • Ecuador Representative
Editor in Chief Physiological Minireviews (PMR): Alicia Mattiazzi.

EDUCATION COMMITTEE SAFIS

Paula Ford • Facultad de Medicina, UBA
Fabiana García • Facultad de Ciencias Médicas, UNR
Rolando P Juarez • Facultad de Odontología, UNNE
Nicolás Enrique • Facultad de Ciencias Exactas, UNLP
María Gabriela Marina Prendes • Facultad de Farmacia y Bioquímica, UBA
Paola Boarelli • Facultad de Kinesiologia y Fisioterapia, Universidad Juan A. Maza
Silvina Villanueva • Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR
Matilde Said •Facultad de Ciencias Médicas, UNLP

Educational Advisor
Sebastián Caffera • Facultad de Medicina, UBA

YOUNG INVESTIGATORS COMMITTEE SAFIS

María Soledad Brea • Postdoctoral Fellow CONICET, Centro de Investigaciones Cardiovasculares "Dr. Horacio E.Cingolani", Universidad Nacional de La Plata-CONICET
Alejo Capiglioni • Doctoral Fellow CONICET, Instituto de Fisiología Experimental, Universidad Nacional de Rosario-CONICET
Alejandro Ciocci Pardo • Research Assistant CONICET, Centro de Investigaciones Cardiovasculares "Dr. Horacio E.Cingolani", Universidad Nacional de La Plata-CONICET
Carlos Sebastián Giménez • Postdoctoral Fellow CONICET, Instituto de Medicina Traslacional, Trasplante y Bioingeniería,Universidad Favaloro-CONICET
Ivana María Gómez • Doctoral fellow CONICET, Centro de Investigaciones Cardiovasculares "Dr. Horacio E. Cingolani", Universidad Nacional de La Plata-CONICET
Juan Ignacio Elio Mariángelo • Postdoctoral fellow CONICET, Centro de Investigaciones Cardiovasculares, Médicas "Dr. Horacio E. Cingolani", Universidad Nacional de La Plata-CONICET
Julieta Marrone • Research Assistant CONICET, Instituto de Fisiología Experimental, Universidad Nacional de Rosario-CONICET
Manuela Santalla • Postdoctoral Fellow CONICET, Centro de Investigaciones Cardiovasculares "Dr. Horacio E. Cingolani", Universidad Nacional de La Plata-CONICET

WELCOME AND OPENING REMARKS

Dear Colleagues and friends

It is a pleasure to invite you to the 2021 meeting of the Argentinean Society of Physiology (SAFIS). This year and as warm up to the Pan-American Congress of Physiological Sciences, to be held in Chile in 2023, SAFIS joins with the Latin American society of Physiological Sciences (ALACF) to host a congress of international reach with focus on the advances of physiological sciences of the region.

Due to the COVID19 pandemic we decided to organize a completely virtual meeting, taking advantage of this new form of communication and learning that we have all experienced and become familiar with during the last 2 years. To keep you glued to your monitor, we have put together an attractive, innovative and stimulating scientific program which we hope will foster new knowledge, networking, companionship and training. To achieve this ambitious goal we have organized 3 plenary conferences y 2 mini conferences, given by the most prestigious scientist in their field and 8 thematic symposiums, including new physiopathological approaches to mitigate the COVIC-19 pandemic. To relax ourselves after so much information we have organized a scientific debate in which we will discuss the balance between science for publication and science for the media. In addition this year, the Education Committee has organized a workshop on virtual learning and for the first time we have 2 symposia organized entirely by the Committee of Early Career Investigators. As a hallmark of our annual meeting the highlights will be the poster sessions and the SAFIS Prize to best work in general physiology and the Camilion de Hurtado Prize to the best study in cardiovascular physiology.

We hope you can join SAFIS and ALACF from October 20 to 21 to share cutting edge knowledge in physiology as well to interact with colleagues and friends.

For further information on the scientific program and registration please access the SAFIS website at: https://safisiol.org.ar/

Dr. Martin Vila Petroff
President SAFIS

Dear friends,

It is a pleasure to greet you in these challenging times that we have had to face. Even so, we meet again in the 2021 version of the scientific meeting of our Latin American community as members of the Latin American Association of Physiological Sciences (ALACF). ALACF activities restarted in 2020 with our virtual congress done from Chile. In the version of ALACF 2021, the ten member countries of this association proudly meet in a joint activity with the annual meeting of the Argentine Society of Physiology (SAFis), a member of ALACF.

Our Latin American community of researchers in physiology and related areas has strengthened and positioned itself firmly in recent years in the international context of the region and globally. The innovative and prolific research areas in each society member of ALACF constitute the base of the increasing interest of young physiologists to generate new interactions with peers and search for new opportunities for the development of their Academic careers. The latter has resulted in exchanges and future joint projects between ALACF member countries and with international partner Societies in the USA, the Netherlands, Spain, and Germany.

An essential aim of ALACF is to promote the development of physiological sciences in the region and the world. We believe that we will only make our growth opportunities better and better with permanent and determined participation.

ALACF receives unrestricted support from The International Union of Physiological Sciences (IUPS) as well as the largest societies in the area, i.e. The Physiological Society (United Kingdom) and American Physiological Society (APS) among others. ALACF has been positioned as a focus for the development of physiological sciences and its capacity to generate new knowledge. Thus, ALACF 2022 and 2023, and PANAM Physiological Sciences 2023 in Chile have been integrated as an activity part of The Year of Physiology program launched by IUPS in conjunction with other major societies worldwide. Likewise, publishers of specialized journals have partnered with ALACF, such as Bentham Science Publishers with its journal Current Vascular Pharmacology and Elsevier with its journal BBA General Subjects, facilitating our opportunities to disseminate the investigative work of our partners.

Participating in the ALACF 2021 in conjunction with SAFis 2021 is just one more opportunity to continue fostering these advances in recent years and envisioning new possibilities for the physiology of the future that is fast approaching us.

As president of ALACF and on behalf of the ALACF Council, I wish you very fruitful participation in the ALACF 2021 / SAFis annual meeting.

Luis Sobrevia
President ALACF

Programme at-glance SAFIS-ALACF 2021 joint meeting. 20-22 Octuber (virtual)

	Wednesday 20		Thursday 21		Friday 22
8:00-10:45	**Interactive Educational Workshop:** Hybrid Teaching. *Noelia Valle (Spain)*	**8:00-9:30**	**S3 (YIC): "Jorge Negroni":** Experimental Models for studying physiology	**8:00-9:30**	**S7:** Digestive system: an organism inside our organism.
11:00-12:30	**S1 ALACF:** ACE2 beyond Covid-19. What's new about the cardioprotective arm of RAAS?	**9:45-11:15**	**S4:** Two key moments to understand women pathophysiology: pregnancy and menopause.	**9:45-11:15**	**S8:** *Camilión de Hurtado Award*
12:45-13:15	**Opening.** Martín Vila Petroff (SAFIS)-Luis Sobrevia (ALACF)	**11:30-12:30**	**Debate in Science.** *Diego Golombek (Argentina)* .The equilibrium between the science for the paper and the science for the press.	**11:30-13:30**	**Scientific Poster Presentation**
13:30-15:00	**Poster Presentation:** Education in Physiology	**12:45-14:45**	**Scientific Poster Presentation**	**13:45-14:30**	**Conference SAFIS.** *Qinchuan Wang (EEUU).* "Evolutionary Physiology: oxidation of CaMKII a treaty between God and the devil".
15:30-17:00	**Workshop (YIC).** Professional development and Laboral continuity.	**15:00-16:30**	**S5:** Calcium signaling: impact in the physiopathology of tissues and cells.	**14:45-16:15**	**S9 SAFIS-ALACF:** Physiopathology and Covid-19 in Latino America.
17:15-18:45	**S2:** Metabolism, trafficking and cellular signaling: focusing on cellular physiology.	**16:45-18:15**	**S6:** *SAFIS Young Investigator Award*	**16:30-17:15**	**Closing Conference SAFIS:** *Gabriel Rabinovich (Argentina).* "Glycans and galectins: new therapeutic targets in cancer, autoimmunity and infections".
19:00-19:50	**Opening Conference SAFIS:** *Jack Feldman (EEUU). "Breathing Matters: preBotzinger Complex and beyond"*	**18:30-19:20**	**Mini ALACF Conferences.** News in high altitude physiology	**17:30-19:00**	**S10 ALACF:** Obesity: a systemic disease
		19:40	**ALACF Assembly**	**19:15-20:00**	**Closing ceremony**
Saturday 23 09:00: SAFIS Assembly					

CONFERENCES

OPENING CONFERENCE

Jack Feldman • UCLA, California (USA)
Breathing Matters: preBotzinger Complex and beyond

Chair: Martín Vila Petroff • Cardiovascular Research Center, La Plata (Argentina)
Co- Chair: Eduardo Luis de Vito • Alfredo Lanari Medical Research Institute, Buenos Aires (Argentina)

CLOSING CONFERENCE

Gabriel Rabinovich • IBYME (Argentina)
Glycans and galectins: new therapeutic targets in cancer, autoimmunity and infections

Chair: Maria Fernanda Troncoso • Institute of Biological Chemistry and Physic chemistry, Buenos Aires (Argentina)
Co-Chair: Graciela Cremaschi • Institute of Biomedical Research, Buenos Aires (Argentina)

SAFIS CONFERENCE

Quinchuan Wang • Johns Hopkins University (USA)
Evolution Physiology: Oxidation of CaMKII a treaty between God and the devil

Chair: Alicia Mattiazzi • Cardiovascular Research Center, La Plata (Argentina)
Co-Chair: Mark Anderson • Johns Hopkins University (USA)

MINI -ALACF CONFERENCES

News in high altitude physiology

Chair: Henry H. León Ariza • Faculty of Medicine, PROSEIM Research Group, University of La Sabana, Chía (Colombia)
Co-Chair: Gustavo Pérez • Cardiovascular Research Center, La Plata (Argentina)

Speakers:
1 - Christian Arias-Reyes • Faculty of Medicine, Université Laval, Institute Universitaire de Cardiologie et de Pneumologie de Québec (IUCPQ), Québec, Quebec City (Canada). *Decreased incidence, virus transmission capacity, and severity of COVID-19 at altitude on the American continent*

2- Laura Gochicoa-Rangel • Departamento de Fisiología Respiratoria, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas," Mexico City (Mexico). *Respiratory capacity at altitude and its relationship with sex, body surface and Christian Arias-Reyes, Laura Gochicoa-Rangel*

DEBATES IN SCIENCE

The equilibrium between the science for the paper and the science for the press

Chair: Alejandro Aiello • Cardiovascular Research Center, La Plata (Argentina)
Co-Chair: Carlos Davio • Institute of Pharmacological Research, Buenos Aires (Argentina)
Speaker:
Diego Golombek • Chronobiology Laboratory, University of Quilmes (Argentina)

WORKSHOPS AND ROUND TABLES

Interactive Educational Workshop organized by the Education Committee Hybrid Teaching

Chair: Noelia Valle • Facultad de CC Experimentales. Universidad Francisco de Vitoria UFV Madrid (Spain)
Co-Chairs: Matilde Said • Cardiovascular Research Center, La Plata (Argentina) and Sebastián Caffera • Medical University, Buenos Aires (Argentina)

R*ound Table organized by the Young Investigators Committee. Professional development and Laboral continuity*

Chair: Juan Ignacio E. Mariángelo • Cardiovascular Research Center, La Plata (Argentina)
Co-Chair: Cecilia Larocca • Institute of Experimental Physiology, Rosario (Argentina)
Speakers:
1- **Pedro Martín** • Institute of Immunological and Physiopathological Studies, La Plata (Argentina)
2- **Alicia Mattiazzi** • Cardiovascular Research Center, La Plata (Argentina)
3- **Veronica Livore** • Institute of Experimental Physiology, Rosario (Argentina)

SYMPOSIA

SYMPOSIUM # 1 ALACF
ACE2 beyond Covid-19. What's new about the cardioprotective arm of RAAS?

Chair: Mariela Gironacci • Institute of Biological Chemistry and Physic chemistry "Prof. Alejandro C. Paladini", Buenos Aires (Argentina)
Co-Chair: María Celeste Villa- Abrille • Cardiovascular Research Center, La Plata (Argentina)
Speakers:

1- **Mario Chiong** • Advanced Center for Chronic Diseases, Santiago (Chile) *"Beneficial effects of Angiotensin-(1-9) on vascular remodeling"*
2- **María José Campagnole-Santos** • Department of Biochemistry and Immunology, Biological Sciences Institute, Belo Horizonte, Brazil. *"Therapeutic actions of angiotensin-(1-7) in respiratory pathologies"*
3- **Mariela Gironacci** • Instituto de Química y Fisicoquímica Biológicas "Prof. Alejandro C. Paladini", Buenos Aires (Argentina). *"Anti-inflammatory response mediated by angiotensin-(1-7) Mas receptor activation"*
4- **Rafaela Fernandes da Silva** • Department of Physiology and Biophysics, Belo Horizonte (Brazil). *"Protective effects of alamandine on cardiac remodeling"*

SYMPOSIUM # 2
Metabolism, trafficking and cellular signaling: focusing on cellular physiology

Chair: Mariano Bisbal • Mercedes and Martin Ferreyra Medical Research Institute, Córdoba (Argentina)
Co-Chair: Daniel Francés • Institute of Experimental Physiology, Rosario (Argentina)
Speakers:

1- **Laura Gumy** • University of Otago (New Zealand) *"Local mechanisms that regulate long-distance trafficking in axons"*
2- **Eduardo Arzt** • Biomedicine Research Institute of Buenos Aires, Buenos Aires (Argentina). *"Molecular mechanisms underlying pituitary pathology"*
3- **Graciela Diaz Torga** • Institute of Biology and Experimental Medicine, Buenos Aires (Argentina). *"Advances in the knowledge of the effects of progesterone on prolactin secretion and the development of prolactinomas"*
4- **Marcelo Roma** • Instituto de Fisiología Experimental, Rosario (Argentina). *"Molecular pathways involved in the pathophysiological genesis of the non-alcoholic fat liver".*

SYMPOSIUM # 3. Organized by the Young Investigators Commission
Experimental Models for studying physiology

Chair: Manuela Santalla • Cardiovascular Research Center, La Plata (Argentina)
Co-Chair: Rocío Cantero • Instituto Multidisciplinario de Salud, Tecnología y Desarrollo, Santiago del Estero (Argentina)
Speakers:

1- **Juan Ignacio Felice** • Department of Anatomy and Histology, School of Exact Sciences, La Plata (Argentina). *"Approach to experimental problems through the use of mathematical models"*
2- **José Lombardo** • Biochemical Research Institute of La Plata, La Plata, (Argentina). *"A, B, C. elegans"*
3- **María Victoria Gavazzi** • Cátedra de Histología y Embriología Animal. Facultad de Ciencias Naturales y Museo, La Plata (Argentina). *"Analysis of Hydra as biological model in physiology"*
4- **Juan Ignacio Romero** • Laboratorio de Genética del Comportamiento Fundación Instituto Leloir, Buenos Aires, Argentina. *"Drosophila melanogaster as a model of lipid metabolism: Identification of a new human ortholog in the regulation of metabolism"*

SYMPOSIUM # 4
Two key moments to understand women pathophysiology: pregnancy and menopause

Chair: Claudia Capurro • Bernardo Houssay Institute of Physiology and Biophysics, Buenos Aires (Argentina)
Co-Chair: Verónica De Giusti • Cardiovascular Research Center, La Plata (Argentina)
Speakers:

1- **Luis Sobrevía** • Universidad Pontificia Católica de Chile, Santiago (Chile). *"Role of the insulin/adenosine axis in the placental/fetus communication in gestational diabetes"*
2- **Sarah H. Lindsey** • Department of pharmacology, Tulane University School of Medicine, New Orleans (USA). *"The role of sex, menopause and GPER in vascular remodeling"*
3- **María José Bellini** • Instituto de Investigaciones Bioquímicas de La Plata "Prof. Doctor Rodolfo R. Brenner", La Plata (Argentina). *"Role of IGF-1 in the central modulation of the female gonadal axis"*
4- **Alicia Jawerbaum** • Centro de Estudios Farmacológicos y Botánicos, Buenos Aires (Argentina). *"Oxidative and inflammatory stress in gestational diabetes"*

SYMPOSIUM # 5
Calcium signaling impact in the physiopathology of tissues and cells

Chair: Darío Krapf • Cell Signaling Cascades Laboratory, Rosario (Argentina)
Co- Chair: Luis Gonano • Cardiovascular Research Center, La Plata (Argentina)
Speakers:

1- **William E. Louch** • Institute for experimental medical research, University of Oslo (Noruega). *"Control of calcium release in healthy and sick hearts".*
2- **Juan D. Goutman** • Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres", Buenos Aires (Argentina). *"Compartmentalization of calcium signaling in ciliary cells".*
3- **Silvia Belmonte** • Instituto de Histología y Embriología de Mendoza Dr. Mario H. Burgos, Mendoza (Argentina). *"Role of ceramides in the intracellular calcium increases in human spermatozoids".*
4- **Silvina Ponce Dawson** • Institute of Physics of Buenos Aires (Argentina). *"Quantification and physiological impact of intracellular calcium flux".*

SYMPOSIUM # 6
SAFIS Young Investigator Award

Chair: Aldo Mottino • Institute of Experimental Physiology, Rosario (Argentina)
Co-Chair: Gisela Di Giusto • Bernardo Houssay Institute of Physiology and Biophysics, Buenos Aires (Argentina)
Selected abstracts

27- Availability of a rich source of sodium during the perinatal period programs the cardiovascular response after Nitroprusside infusion in adult offspring
36- Therapeutic effect of a novel truncated isoform of the human TGF-β type II receptor Fc-tag protein in a liver fibrosis rat model
89- Myocardial Hypertrophy, Fibrosis and Angiotensin II are Exacerbated in Aged Mice with Genetic Mutation of Galectin 3

SYMPOSIUM # 7
Digestive system: an organism inside our organism

Chair: Roxana Rubinstein • Institute of Biomedical Research, Buenos Aires (Argentina)
Co-Chair: Liliana Monasterolo • Faculty of Biochemical and Pharmaceutical Sciences, Rosario (Argentina)
Speakers:

1- **Guillermo Docena** • Instituto de Estudios Inmunológicos y Fisiopatológicos, La Plata (Argentina). *"The immunity of the intestinal mucosa as the starting point of its physiology"*
2- **Marcelo Choi** • Instituto Alberto C. Taquini de Investigaciones en Medicina Traslacional, Buenos Aires (Argentina). *"Intestinal Microbiota and renal function: a new dialog axis"*

3- **Darío Ramírez** • Instituto Multidisciplinario de Investigaciones Biológicas, San Luis (Argentina). *"Diet and its impact in cancer: the key role of Nrf2"*
4- **Gabriela Perdigón** • Centro de Referencia para Lactobacilos, San Miguel de Tucumán (Argentina). *"The consumption of probiotics and its benefits for the intestinal immune system"*

SYMPOSIUM # 8.
Camilión de Hurtado Award

Chair: Lascano Elena • Institute of Translational Medicine, Transplantation and Bioengineering, Buenos Aires (Argentina)
Co-Chair: Emiliano Diez • Institute of Medicine and Experimental Biology of Cuyo, Mendoza (Argentina)
Selected abstracts

39- Pacemaker Activity in Postnatal Hypothyroidism: Implications of the Nitric Oxide System and PI3K/AKT Pathway
52 - Gene therapy overexpressing Tbx20 induces cell proliferation and angiogenesis in cardiomyocyte culture
85- Beneficial consequences on myocardial mitochondrial network dynamics and function of one-month oral treatment with cannabis oil to spontaneously hypertensive rats (SHR).

SYMPOSIUM # 9. JOINT SYMPOSIUM SAFIS-ALACF
Physiopathology and Covid-19 in Latin America.

Chair: Martín Abba • Center for Immunological and Applied Research, La Plata (Argentina)
Co-Chair: Alejandro Orlowski • Cardiovascular Research Center, La Plata (Argentina)
Speakers:

1- **Patricia Rieken Macêdo Rocco** • Laboratory of Pulmonary Investigation, Carlos Chagas, Rio de Janeiro (Brazil). *"Pathogenesis of Multiple Organ Injury in COVID-19 and Potential Therapeutic Strategies"*
2- **Marcela Mercado-Reyes** • Unidad de Secuenciación y Genómica, Bogotá, Colombia. *"Substitutions in Spike and Nucleocapsid proteins of SARS-CoV-2 circulating in South America. Sequencing, clinical outcome and vaccine efficacy"*
3- **Francisco Barrantes** • Instituto de Investigaciones Biomédicas, Buenos Aires (Argentina). *"Neuropathologic manifestations of Covid-19"*
4- **Walter Manucha** • Instituto de Medicina y Biología Experimental de Cuyo, Mendoza (Argentina). *"Vitamin D and COVID-19: mechanism and efficacy"*

SYMPOSIUM # 10. ALACF
Obesity: A systemic disease

Chair: Pedro Leme • Federal University of Rio de Janeiro (Brazil)
Co-chair: Carolina Caniffi • Chemical Institute and Drug Metabolism, Buenos Aires (Argentina)
Speakers:

1- **Pedro Leme** • Federal University of Rio de Janeiro, Rio de Janeiro (Brazil). *"Lung function impairment during obesity"*
2- **Ana Paula Davel** • UNICAMP (Brazil). "Modulation of Vascular Function by Perivascular Adipose Tissue"
3- **Paola Casanello** • Pontificia Universidad Católica de Chile, Santiago (Chile). *"Early origins of obesity"*
4- **Egberto Gaspar de Moura** • State University of Rio de Janeiro, Rio de Janeiro (Brazil). *"Understanding the mechanisms of obesity related metabolic syndrome"*

VIDEO POSTERS

Section: Education-Educación 1

10

Análisis de un modelo de indagación para la Integración de las ciencias básicas en la enseñanza de la morfología-función involucrada en el registro de la presión arterial

Fages EM, Gutiérrez CE, Ponce JO, Meza Gutiérrez C, Rosende VC, Juárez RPA
Fisiología Humana. Morfofunción II. Facultad de Odontología. Universidad Nacional del Nordeste

Al integrar el contenido (conocimiento y habilidad) de la fisiología humana con otras áreas disciplinares del campo de las ciencias básicas, es necesario la implementación de diferentes estrategias de enseñanza-aprendizaje. Para abordar la interrelación morfología-función en el marco de un currículo integrado se ha propuesto la aplicación de procesos de indagación. El objetivo de este trabajo fue realizar un análisis de una propuesta educativa que responde a la indagación interdisciplinaria como metodología integradora de conocimientos de fisiología, anatomía, histología, química y física, en la enseñanza de las estructuras y procesos morfofuncionales involucrados en la toma de la presión arterial. La presente experiencia educativa se llevó a cabo en la cátedra de Fisiología Humana, módulo Morfofunción II de la Facultad de Odontología (UNNE). A partir del objetivo propuesto, se procedió a desarrollar la experiencia, como se detalla: 1) implementación de la propuesta educativa, 2) encuestas de opinión de los estudiantes sobre la integración y sobre la modalidad de enseñanza, 3) análisis cuantitativo y cualitativo (perspectiva interpretativa). El cuestionario se realizó durante el presente curso académico por 198 alumnos de forma voluntaria, con edades entre 19 y 31 años. El 92,42% de los alumnos consideró que esta modalidad de enseñanza fue adecuada y un 96,31% que permitió integrar las diferentes áreas disciplinares. De las respuestas analizadas un 62% utilizaron lenguaje adecuado y conceptos propios de las disciplinas. En un 57% las explicaciones fueron superficiales, se basaron en la observación y la experiencia personal. La indagación como estrategia de enseñanza-aprendizaje para la integración de diferentes áreas disciplinares de las ciencias básicas, en la enseñanza de la morfología-función involucrada en el registro de la presión arterial, genera procesos argumentativos que conducen a cambios conceptuales.

Palabras clave: indagación, estrategia, enseñanza, aprendizaje, integración, ciencias básicas, presión arterial.

13

Percepción de la implementación de ambientes virtuales y recursos digitales como herramientas de apoyo en la formación de estudiantes de medicina derivado COVID-19

García-Montalvo I.A.[1,2]; López-Castellanos S. L.[1]; Arjona-Pérez I.[1]
[1]Facultad de Medicina y Cirugía, Universidad Regional del Sureste, Oaxaca, México. [2]División de Estudios de Posgrado e Investigación, Tecnológico Nacional de México/Instituto Tecnológico de Oaxaca, Oaxaca, México.

Resumen: Problema de estudio: El encierro en el hogar por la amenaza del COVID-19, ha trascendido en los estudiantes (mala calidad de Internet, falta de herramientas necesarias para realizar el trabajo, miedo, estrés, falta de autorregulación, mala planificación del tiempo y distracciones), los entornos virtuales y recursos digitales se potencializaron como modelo de enseñanza para mantener la continuidad en la educación médica. Antes de este aislamiento, la educación a distancia y los entornos virtuales no figuraban en las universidades como modelo educativo, sin embargo, la autorregulación por parte de los estudiantes conlleva al fortalecimiento de su aprendizaje y memoria (explícita, dependiente de la potenciación a largo plazo en el hipocampo; implícita dependiente de AMPc-PKA-MAPK-CREB). Objetivo: Establecer la percepción que tiene la implementación de los entornos virtuales y recursos digitales en los estudiantes de primer a tercer año de Medicina de la Facultad de Medicina y Cirugía de la Universidad Regional del Sureste. Materiales y Métodos: Es un estudio descriptivo-transversal basado en un cuestionario que fue diseñado y entregado a estudiantes de primer a tercer año, el tamaño de muestra estimado (n= 318) se obtuvo a través de la calculadora de tamaño de muestra "Raosoft". Resultados: El 96,5% de los estudiantes son regulares y el 3,5% irregulares, tienen una percepción de los recursos virtuales utilizados como adecuada (84%), calidad de la tecnología percibida como satisfactoria (78,6%), recursos de aprendizaje empleados percibidos como de su agrado (84,7%), y un acompañamiento satisfactorio (74,4%) por parte de los docentes y coordinadores. Conclusión: Los estudiantes percibieron como adecuada la educación virtual y recursos digitales empleados por los docentes durante este curso escolar (2020-2021), es necesario identificar los desafíos y limitaciones para este enfoque de enseñanza-aprendizaje en pro de mejorar el aprendizaje significativo en los futuros médicos.

Palabras clave: Recursos digitales; entornos virtuales; educación médica; pandemia

16

La enseñanza de Anatomía e Histología en la FFyB afectada por la pandemia de Covid-19: De la presencialidad a la virtualidad

Cantú SM*, Lee HJ*, Rukavina Mikusic NL*, Puyo AM*, Choi MR*, Donoso AS*
*Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Anatomía e Histología. Buenos Aires, República Argentina.

Resumen: La pandemia del COVID-19 nos enfrentó a un cambio en la enseñanza de Anatomía e Histología (AeH), asignatura con un importante componente práctico presencial por la utilización del microscopio para abordar sus contenidos, surgiendo la enseñanza remota de emergencia. Objetivo: Analizar si el cambio en la metodología de enseñanza influyó en el desempeño estimado por la regularización de los alumnos en los trabajos prácticos de AeH. Metodología: Adaptamos nuestra enseñanza a un formato totalmente virtual, rediseñando por completo las clases. Propusimos una modalidad pedagógica que combinó diversos materiales didácticos generados por nuestros docentes, tanto audiovisuales (por *You-Tube*), como de guías de trabajos prácticos (TP), para escuchar y resolver de manera asincrónica y sin límite en la cantidad de reproducciones, con una videoconferencia sincrónica semanal obligatoria, para resolver dudas y actividades reforzando los conceptos más relevantes para la comprensión de los contenidos. Para andamiar el proceso de aprendizaje utilizamos también microscopios virtuales, galerías de imágenes y software de anatomía 3D. Resultados: El cambio en la metodología de enseñanza implementada no afectó el desempeño del alumnado en la regularización entre la presencialidad y la virtualidad. Conclusiones: La adaptación a la enseñanza virtual de AeH lograda por los docentes de la asignatura, capacitados en el uso de herramientas informáticas on-line para la enseñanza, contribuyó a mantener el nivel de desempeño del alumnado. A futuro, proponemos un esquema híbrido virtual-presencial, brindando acceso general a los seminarios introductorios en formato audiovisual y a las de guías de TP de manera asincrónica previo al encuentro presencial, y que éste sirva para afianzar el conocimiento adquirido empleando el microscopio y aprendiendo así la destreza para su correcta utilización. Es el inicio de un camino hacia el aula expandida donde coexistan la presencialidad y los entornos virtuales para favorecer la formación mixta bimodal.

18

Relación de estrés académico derivado del confinamiento por COVID-19 y actividad física en estudiantes de medicina, Oaxaca, México

Luis-Martínez J. M.[1]; Martínez-Martínez M. C.[1]; García-Montalvo I. A.[1,2]
[1]Facultad de Medicina y Cirugía, Universidad Regional del Sureste, Oaxaca, México. [2]División de Estudios de Posgrado e Investigación, Tecnológico Nacional de México/Instituto Tecnológico de Oaxaca, Oaxaca, México

Introducción: La pandemia derivada por el virus SARS-CoV-2, provoco un incremento en los niveles de estrés, específicamente estrés académico, el cual se manifiesta en los estudiantes universitarios, siendo mayor en los períodos de exámenes o cuando hay una sobrecarga académica. En los primeros años de la licenciatura se potencializa debido al modelo de enseñanza-aprendizaje demasiado centrado en la memorización o personalidades incompatibles con los docentes y las exigencias de algunas asignaturas. La presencia de estrés académico afecta el estado emocional, la salud física y las relaciones interpersonales de los estudiantes universitarios. Objetivo: Describir la relación presente entre la actividad física y el estrés académico percibido durante la pandemia por SARS-CoV-2 en estudiantes de la Facultad de Medicina y Cirugía de la Universidad Regional del Sureste. Materiales y métodos: Se trató de un estudio descriptivo-transversal, la muestra se determinó a conveniencia, el instrumento fue distribuido mediante la plataforma Moodle (para identificar el estrés académico se aplicó el Inventario Cognitivista Sistémico (SISCO) y el Cuestionario Internacional de Actividad Física (IPAQ)). Resultados: El 65,4% de los estudiantes considera tener estrés moderado, el 16,6% no presenta estrés, el 15,5% estrés leve y solo el 2,5% manifiesta tener estrés severo, el 84% de los sujetos realiza actividad física de manera cotidiana. Conclusiones: Con el confinamiento, hubo un incremento de los factores estresantes en los sujetos provocando con ello fatiga crónica, ansiedad y dolor de cabeza, la práctica de actividad física de manera regular durante esta pandemia influye como agente protector evitando la secreción excesiva de catecolaminas y de cortisol, de no controlarse puede conllevar a una afectación en el estado de salud de los sujetos (enfermedades cardiovasculares, estrés oxidativo e hipertensión arterial).

Palabras clave: Estudiantes de pregrado; actividad física; pandemia; estrés; COVID-19

31

Un enfoque experimental novedoso basado en citometría de flujo para evaluar la homeostasis celular y el efecto de la tonicidad en glóbulos blancos para una clase de Fisiología Animal de futuros Médicos Veterinarios

Luis Exequiel Ibarra[1, 2] y Emiliano Foresto [2, 3]
[1] Departamento de Biología Molecular, Facultad de Ciencias Exactas Físico-Químicas y Naturales, Universidad Nacional de Río Cuarto (UNRC), Río Cuarto, Argentina; [2] Instituto de Biotecnología Ambiental y Salud (INBIAS), UNRC y CONICET, Río Cuarto, Argentina;[3] Departamento de Biología Agrícola, Facultad Agronomía y Veterinaria, Universidad Nacional de Río Cuarto (UNRC), Río Cuarto, Argentina

La citometría de flujo se ha convertido en una herramienta importante en las ciencias veterinarias, médicas y biológicas. Sin embargo, en los cursos de iniciación e incluso en los cursos universitarios avanzados, los estudiantes no tienen muchas oportunidades de estar en contacto con esta herramienta de análisis celular, ya que la experimentación de laboratorio no es una práctica habitual en el plan de estudios de la carrera de Medicina Veterinaria (MV). Esta situación nos motivó a diseñar un ejercicio de laboratorio novedoso, sencillo, económico y fácilmente reproducible para estudiantes noveles de MV que cursan Fisiología Animal, pero que se puede adaptar a diferentes carreras universitarias biomédicas según necesidades específicas del currículo. El objetivo general de esta clase práctica es utilizar la citometría de flujo para analizar el efecto de la tonicidad de diferentes soluciones con distinta osmolaridad sobre el volumen celular y viabilidad en glóbulos blancos obtenidos de sangre periférica de

animales y que no se utilizan habitualmente para este tipo de experiencias. Además, implementamos el uso de un laboratorio virtual, la elaboración de un informe en formato de artículo científico y la adopción de una evaluación formativa para mejorar el aprendizaje de los estudiantes. Los ensayos permiten el desarrollo de nuevas habilidades de aprendizaje en los estudiantes de MV, que integran los conocimientos teóricos desde una perspectiva aplicada. La relevancia de este enfoque de clase para estos estudiantes radica en la estimulación de diferentes niveles de habilidades cognitivas que van desde la manipulación de materiales de laboratorio hasta el desarrollo del pensamiento científico crítico mediante la capacidad de discutir sus observaciones o resultados obtenido colaborativamente con sus pares. Además, la actividad los acerca a su futura carrera profesional en la aplicación de situaciones clínicas concretas y les brinda la oportunidad de iniciarse en el campo de la investigación.

37

Experiencia Del Taller De Microscopia Virtual En La Enseñanza De La Anatomía Y Fisiología Patológicas.

Guenzelovich, M.; Merletti, G.; Machuca Vega, A.; Alessio, V.; Iglesias, B.; Traverso, P.; Pianosky, P.; Sabella, S.
Facultad de Odontología. Universidad Nacional de Rosario. Email: marielguenz@gmail.com

Introducción: El aislamiento social obligatorio impuesto por la pandemia del Covid-19 implicó un cambio de paradigma para la educación y la formación profesional. A modo de suplir la observación microscópica de preparados histológicos se implementó el Taller de Microscopía Virtual (TMV) facilitando el acceso a los contenidos curriculares que estructuran la programación académica de la asignatura Anatomía y Fisiología Patológicas (A.yF.P.). Objetivos: Profundizar los contenidos de dicha asignatura que sustentan la práctica odontológica, generando un contexto adecuado tanto de refuerzo del aprendizaje como de evaluación de propuestas de enseñanza establecidas y establecer un espacio formal de intercambio y discusión que contribuya a la apropiación de los conocimientos básicos de la materia. Estimular el trabajo grupal de los estudiantes favoreciendo el aprendizaje cooperativo y reflexivo. Establecer nuevas estrategias didácticas que favorezcan el proceso de enseñanza - aprendizaje. Metodología: Estudio exploratorio y descriptivo. Implementación de encuestas, semiestructuradas y voluntarias, dirigida a los estudiantes de A. y F.P. (ciclos 2020/2021). Se analizaron 62 encuestas de 83 alumnos totales. Los datos preliminares se analizaron con el software Statistical Analysis Software (SAS). Resultados Preliminares: El 100% de los estudiantes considera que el taller ha favorecido el desarrollo de los contenidos temáticos de clase y les ha permitido afianzar con criterio globalizador los conocimientos de cada unidad temática. En relación a la calificación con respecto a la estrategia implementada para una mejor comprensión del contenido teórico, el 65,7% de los alumnos afirma que fue satisfactoria. Conclusiones: Estudiantes involucrados en la propuesta lúdica/ didáctica indagados hasta el momento afirman que el TMV resulta ser una herramienta motivadora y válida para el reconocimiento de estructuras histológicas, que permite articular y abordar las distintas unidades temáticas con profundidad y relacionarlas con conocimientos previos. Reconocen que dicha estrategia facilita la construcción del conocimiento, mediante la integración y discusión entre pares.

40

Nuevas ventajas para viejos recursos: estrategias renovadas en el programa de tutorías de la Cátedra de Fisiología y Física Biológica

Claudia Caldiz, Matilde Said, Juan IE Mariángelo, Eric Crocci, Alejandro Ciocci-Pardo, Julieta Vico, Agustina Sicre, Omar Vélez Rueda, Luis Gonano, Irene L Ennis.

La educación juega un papel fundamental en el desarrollo de una sociedad y es una de las actividades que se ha visto afectada con la pandemia de COVID-19. Con el fin de fortalecer a los alumnos que recursan la materia y tienen más dificultades en el aprendizaje, la Cátedra de Fisiología y Física Biológica de la Facultad de Ciencias Médicas, UNLP, intervino durante el año 2021 su programa de tutorías. El programa fue rediseñado adecuándolo a la realidad impuesta por la pandemia, obteniéndose el reconocimiento formal de la UNLP y apoyo económico del Programa para el Mejoramiento de Indicadores Académicos. Esto permitió reclutar un mayor número de tutores que redundó en la posibilidad de organizar encuentros sincrónicos semanales en grupos reducidos. Debido al aislamiento social los encuentros fueron virtuales con estudiantes dispersos en diferentes puntos del país y del extranjero. Muchos debieron no sólo aprender los contenidos formales de la asignatura sino también a desenvolverse con herramientas digitales. En estos espacios se privilegió la oportunidad de cada estudiante para practicar la exposición oral e integrar los contenidos, frente a pares y docentes; actividades que resultan limitadas en carreras con matrículas masivas como la nuestra. Los resultados indican que un 68% de los y las estudiantes que participaron de la tutoría y rindieron el primer examen parcial, aprobaron en primera instancia. Incluso, un 37% alcanzó calificaciones para aspirar a acreditar la materia por promoción, evitando la instancia de examen final. Estos resultados sugieren que el programa resulta útil para mejorar el rendimiento académico y así evitar el desgranamiento de los estudiantes. A través de estas tutorías, pretendemos no sólo brindarle a las y los estudiantes herramientas que faciliten y potencien su aprendizaje de Fisiología, sino que también los fortalezcan para enfrentar los desafíos de la carrera, y posteriormente de la profesión.

46

Reflexiones en el curso de Anatomía y Fisiología del Sistema Visual, ¿qué impacto tuvo la virtualización sobre las distintas instancias del curso para los alumnos?

Facundo Mendes Garrido, Carolina Caniffi, Rosana Elesgaray

Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Departamento de Ciencias Biológicas, Cátedra de Fisiología, Buenos Aires, Argentina. CONICET - Universidad de Buenos Aires, Instituto de Química y Metabolismo del Fármaco - CONICET (IQUIMEFA), Buenos Aires, Argentina.

Problema de estudio: Anatomía y Fisiología del Sistema Visual (AyFSV) pertenece al primer año de la Tecnicatura Universitaria en Óptica y Contactología, UBA. Hasta 2019, las clases fueron presenciales y los exámenes, escritos. Se disponía de un aula virtual (AV) en Moodle con foros y cuestionarios de autoevaluación. La pandemia impidió la presencialidad, y el equipo docente adaptó el curso a la virtualidad. Objetivos: Analizar el uso y la valoración por los alumnos de las herramientas virtuales utilizadas en 2020. Metodología: Durante 2020, los seminarios fueron grabados (YouTube) y los trabajos prácticos fueron sincrónicos (Zoom). Se sumó a los recursos existentes del AV, el material grabado. Los exámenes regulatorios se realizaron por Moodle, y los finales, fueron orales sincrónicos. Al finalizar el curso, se realizaron dos encuestas (GoogleDrive) sobre estos recursos. Resultados: Los estudiantes (100%) afirmaron que las clases sincrónicas les permitieron resolver actividades y realizar consultas. El 73% consideró que Zoom les permitió participar más activamente. Aumentó la participación en los cuestionarios de autoevaluación (Cuestionario-1: 2019-63%,82/130 vs. 2020-76%,59/78; Cuestionario-2: 2019-52%,64/130 vs. 2020-69%,54/78; $p<0,05$ test exacto Fisher) con un rendimiento similar. Los encuestados que rindieron el examen final refirieron sentirse cómodos durante la evaluación, y que el uso de Zoom mientras cursaban les dio mayor seguridad al momento de usar esta plataforma para la evaluación. El 86% prefiere la modalidad virtual frente a la presencial para los exámenes regulatorios y el 71%, para los finales.
Conclusión: La mayor participación en los encuentros sincrónicos, muestra la importancia de mantener estos espacios de interacción docente-alumno. El mayor uso de recursos digitales, impulsado por la pandemia en distintos ámbitos, puede haber facilitado su uso durante la cursada virtual de AyFSV, evidenciado por la comodidad manifestada y por la mayor participación en la autoevaluación.

51

Cambios generados por la pandemia: una comparación de las cursadas de fisiología en 2019 y 2021

Mestre Cordero, V.E.[1]; Abramovici, A.[1]; Arranz, C.[1]; Arreche, N.[1]; Balaszczuk, A.M.[1]; Caniffi, C.[1]; Cerniello, F.M.[1]; Drunday, F.[1]; Elesgaray, R.[1]; Fellet, A.[1]; Fernandez Pazos, M.d.l.M.[1]; Guil, M.J.[1]; Herbstein, F.[1]; Hermann, R.[1]; Hope, S.[1]; Marina Prendes, M.G.[1]; Mendes Garrido, F.[1]; Netti, V.[1]; Soria, D.[1]; Tomat, A.[1]; Vatta, M.[1]
[1]Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires.

La llegada de la pandemia nos ha encontrado, como docentes, con el desafío de ampliar nuestras herramientas didácticas y profundizar el uso de las TICs para mejorar nuestro acercamiento a los estudiantes. El objetivo de este trabajo fue evaluar el impacto del cambio en la modalidad de cursada, de presencial a virtual, en los alumnos de la asignatura Fisiología de la Facultad de Farmacia y Bioquímica de la UBA. Como instrumentos de análisis, se utilizaron las encuestas realizadas a los alumnos durante las cursadas 2019 (n=137) y 2021 (n=186). Se analizaron los siguientes parámetros: número de alumnos cursantes, cantidad de materias que cursan simultáneamente con la cursada de Fisiología, finales que adeudan, porcentaje de regularidad, cantidad de alumnos que trabajan y horas semanales que trabajan.
En el 2021 se observó un incremento del 14,7% en aquellos estudiantes que trabajan más de 30 horas semanales y una disminución del 22% en el número de cursantes. Se duplicó la cantidad de alumnos que cursaron solo fisiología, mientras que se observó un mayor número de finales adeudados (más de 3 finales: 25,5% en 2019 y 62,4% en el 2021). Se incrementó el número de estudiantes que quedaron regulares (regularidad: 67% en 2019 y 82% en 2021).
En conclusión, si bien el número de alumnos que trabajan aumentó, el incremento del % de regularidad que se observó durante el año 2021, podría deberse, en parte, a la disponibilidad del nuevo material de apoyo para su consulta y al cambio en la modalidad de examen regulatorio que acompañó el proceso de virtualización. No podemos descartar que al cursar menos materias, también hayan podido tener más tiempo para estudiar Fisiología. En cuanto a las materias adeudadas, en gran medida podría deberse a la falta de toma de exámenes finales durante gran parte del 2020.

54

Impacto de la virtualización en el aprendizaje de los alumnos en época de pandemia

Cámara C.A., Echarte S.M.; La Colla A.; Chisari A.N.
Departamento de Química y Bioquímica, Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata (UNMdP).

El arribo de la pandemia por COVID19 llevó a una rápida virtualización de las actividades educativas en todas las universidades del mundo, convirtiendo a las plataformas virtuales en las nuevas aulas de enseñanza y aprendizaje. Esto ha significado un reto tanto en la adaptación y virtualización del contenido por parte de los docentes, como en la adaptación de los alumnos a esta nueva modalidad. Con el objetivo de conocer las opiniones de los alumnos de la carrera de Bioquímica de la UNMdP sobre distintos aspectos de las cursadas virtuales, se realizó una encuesta anónima que consistió en responder preguntas relacionadas con sus experiencias en la virtualidad. Los alumnos encuestados (n=63) corresponden a cursantes de entre el tercer y sexto año. El 71,4% de los encuestados considera que la virtualidad perjudicó mucho el dictado de las asignaturas, el 23,8% poco y un 4,8% nada. Con respecto a los beneficios de las cursadas virtuales, la mayoría mencionó la posibilidad de administrar mejor los tiempos de estudio y acceder a clases asincrónicas en cualquier momento del día, y como inconvenientes la menor interacción con los

docentes y otros alumnos, falta de laboratorios y problemas de conectividad. Con respecto a la modalidad de las clases teóricas, los alumnos prefieren la complementación entre clases sincrónicas y asincrónicas (74,6%) para una mejor comprensión de los contenidos. En relación al aporte de los docentes y su acompañamiento durante la cursada, el 96,8% lo considera muy importante. Finalmente, un 88,9% considera que la ausencia de las actividades experimentales presenciales en el laboratorio afectó su aprendizaje, y el 82,5% prefiere exámenes presenciales. Es importante seguir avanzando en el desarrollo de la modalidad virtual, pero la presencialidad como espacio educativo sigue siendo irremplazable. Concluimos que sería recomendable optar por entornos híbridos combinando los beneficios de la presencialidad y la virtualidad.

79

En el imperio de la hiperconectividad: ¿cómo estudian los que estudian?

Valverde C.A, Gonano L.A y Ennis I.L
Cátedra de Fisiología y física biológica, facultad de Ciencias Médicas, Universidad Nacional de La Plata.

Introducción y objetivos: El término "Hiperconectividad" hace referencia a la tendencia de estar permanentemente conectados a través de diferentes entornos digitales. Considerando que el pensamiento profundo y el análisis minucioso de los mecanismos que se estudian son elementos claves para el aprendizaje significativo, nos planteamos indagar acerca de las estrategias y hábitos de estudio de las y los estudiantes de la cátedra. Pretendemos detectar si la hiperconectividad está interfiriendo en el aprendizaje. En función de los resultados que obtengamos, proponemos intervenir para fortalecer el proceso de enseñanza-aprendizaje. Métodos: conocido el porcentaje de ausentismo tras la primera evaluación parcial (de las dos programadas para acreditar el curso) y las calificaciones obtenidas por quienes fueron evaluados, realizamos una encuesta anónima y voluntaria durante la primera semana del mes de junio dirigida al total de los y las estudiantes. Resultados: Entre los resultados más significativos observamos que, de 543 encuestados, solo el 28% permanece sentado estudiando sin grandes distracciones por más de 3 horas, y solo el 8% estudia sin ningún dispositivo electrónico que lo distraiga. Estudian principalmente utilizando material digital (libros, guías, etc. en PDF). Por otra parte, el 73% no conoce el concepto de pausa activa. Conclusión: Estos resultados son el insumo sobre el que diseñaremos una propuesta piloto de intervención para aplicar en el próximo ciclo lectivo. Brevemente, pretendemos dividir a las y los estudiantes en dos grupos, control e intervención. Al grupo intervención se le propondrá estudiar en parejas y preparar un video breve sobre un tema particular de la asignatura, finalizando con una inquietud que surja del estudio. Además, se les pedirá realizar pausas activas frecuentes y evitar la hiperconectividad. Al grupo control solo se les solicitará estudiar como habitualmente lo hacen y preparar un vídeo breve en forma individual, sin otras indicaciones.

95

Estudiante, ¿Estás ahí? Pantallas vacías en una generación multipantalla.

Valverde CA, Ennis IL
Cátedra de Fisiología y Física Biológica, Facultad de Ciencias Médicas, Universidad Nacional de La Plata.

Introducción y objetivos: El 13 de diciembre de 2020 marcó un punto de inflexión abrupto en la enseñanza de la carrera de medicina de la Facultad de Ciencias Médicas de la UNLP, como en otros tantos ámbitos. En nuestra cátedra pasamos, en menos de dos semanas, de la presencialidad a la enseñanza exclusivamente a distancia. Un año y medio después, el balance respecto al rendimiento académico estudiantil es, al menos, inquietante y nos interpela para intervenir sobre nuestra actividad docente. Resultados: En el año 2020, de 1728 inscriptos, hubo un 31% de estudiantes que perdieron o abandonaron la cursada. Los resultados del segundo parcial (las 4 fechas) mostraron un porcentaje en torno al 22% de desaprobados. Una encuesta realizada online y anónima, indicó que solo el 25/26% de los estudiantes se unía siempre o muy frecuentemente a las clases sincrónicas de discusión de los trabajos prácticos/seminarios, respectivamente. Por otra parte, en 2021, de 3264 estudiantes inscriptos, abandonaron o perdieron la cursada un 50%, pero el dato más llamativo es un porcentaje de desaprobados del 43, 67 y 62% (en las tres primeras fechas de primer parcial oral a distancia). La participación de las y los estudiantes en los encuentros sincrónicos es aún menor que la registrada en 2020. Conclusión: Estos datos duros nos exigen revisar las estrategias pedagógicas adoptadas durante la virtualidad exclusiva. Creemos necesario intervenir para potenciar la interacción entre estudiantes y docentes durante el ciclo lectivo, a fin de mejorar el resultado del proceso de enseñanza-aprendizaje. Proponemos un recorte más amplio de los contenidos a desarrollar, la conformación de grupos reducidos de estudiantes con seguimiento continuo de un mismo docente que oficie también como tutor; aumentar la frecuencia de las evaluaciones periódicas autoadministradas e implementar la evaluación por pares, entre las modificaciones más relevantes.

109

Innovación y mejora en la virtualización de Fisiología: un desafío de la pandemia

Caniffi C, Abramovici A, Arranz C, Arreche N, Balaszczuk AM, Cerniello FM, Drunday F, Elesgaray R, Fellet A, Fernández Pazos MM, Guil MJ, Herbstein F, Hermann R, Hope S, Marina Prendes MG, Mendes Garrido F, Mestre Cordero V, Netti V, Soria D, Tomat A, Vatta M
Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Dpto. Ciencias Biológicas, Cátedra de Fisiología. Buenos Aires, Argentina.

Problema en estudio: Durante 2020, en el contexto de la pandemia por COVID-19, se virtualiza la cursada de Fisiología de las carreras Farmacia y Bioquímica, UBA. A partir de esta experiencia y el resultado de una encuesta dirigida a estudiantes del curso 2020, durante el 2021 se modificó el cronograma; aumentó la duración de clases sincrónicas; se redujo el número de alumnos/as

por grupo de trabajo práctico sincrónico; se actualizaron teóricos; se adecuó material de apoyo y videos de experimentos; se incorporaron reuniones docentes y se adquirió una licencia de zoom para la cátedra, además de las institucionales.
Objetivo: Comparar la valoración de los alumnos/as sobre las cursadas 2020 y 2021, teniendo en cuenta los cambios didácticos-tecnológicos introducidos. Metodología: Se realizó una encuesta (GoogleDrive) al final de la cursada 2021 y se analizó comparando con el 2020. Resultados: Ambas encuestas fueron respondidas por similar porcentaje de cursantes (2020:264 cursantes; 54% y 2021:186 cursantes; 51%). El porcentaje de alumnas/os que regularizó Fisiología fue similar (2020:86%; 2021:87%). Se encontraron diferencias en las herramientas que les permitieron mayor participación durante la cursada: Zoom (2020:91%; 2021:97%), foros en Moodle (2020:50%; 2021:5%), GoogleDrive (2020:19%; 2021:20%), mail (2020:11%; 2021:12%). En 2021, el 58% expresó que la formación de grupos pequeños favoreció la participación. La comunicación con los docentes mejoró (2020:47%; 2021:54%). Encontraron mayor utilidad en los teóricos antes de leer la bibliografía o resolver actividades (2020:46%; 2021:57%), también en las actividades propuestas y el material de apoyo (2020:49%; 2021:57%). El nivel de satisfacción general con la asignatura aumentó, y un mayor porcentaje preferiría que su formación fuera semi-presencial (2020:53%; 2021:68%). Conclusión: Los cambios didácticos-tecnológicos realizados en 2021 promovieron la participación de los alumnos/as, esto puede deberse a la planificación anticipada de las actividades y los espacios de trabajo, y mayor adecuación de los materiales diseñados para el abordaje de la asignatura.

Section: Education-Educación 2

56

Zambulléndonos en las herramientas y recursos TICs para una modificación del paradigma: de cómo la dificultad se transformó en oportunidad en la cursada de Fisiología y Biofísica UA1 de la Facultad de Medicina de la UBA

Toriano R.[1], Rivarola V.[1], Bartolomé F.[2], Blake M.[1], González Deniselle MC.[1], Capurro C.[1], Ford P.[1]
[1] Universidad de Buenos Aires, Facultad de Medicina, Departamento de Ciencias Fisiológicas, Unidad Académica 1. Paraguay 2155 4to piso. CABA. Argentina. [2] Instituto Tecnológico de Buenos Aires (ITBA), Especialización en Ciencia de Datos.

Nuestra asignatura recibe anualmente 2400 estudiantes y tiene un plantel de 200 docentes. Cualquier intento de cambio profundo debe vencer la inercia representada no solo por semejante masa de personas sino del anclaje que las formas más tradicionales de gestionar el espacio áulico implican. En los últimos 10 años la forma de enseñar la materia ha experimentado modificaciones parciales, incluyendo herramientas y recursos TICs. Sin embargo, la Pandemia de COVID19 ha acelerado el postergado cambio profundo, propiciando una transformación conceptual, permitiéndonos experimentar el "aula expandida" y allanando el camino hacia el "aula invertida". La conversión de las clases teóricas, que ocupaban el 50% del tiempo de cursada, en video-clases orientadas a la producción de "concentrados conceptuales", actualmente disponibles de manera asincrónica, es uno de los puntos fuertes de este cambio. En paralelo se organizaron Mesas sincrónicas de discusión de problemas, vía plataformas digitales, y se realizaron evaluaciones formativas y sumativas en Aulas Virtuales. Los objetivos del trabajo proponen analizar: i- los datos del canal de YouTube (171 video-clases); ii- los datos de las evaluaciones en el aula virtual; iii- las posibles correlaciones entre ambos grupos. Los datos se analizaron con Python utilizando las librerías Pandas y Seaborn. Entre los resultados obtenidos podemos señalar que los videos muestran: i- una correlación inversa entre el porcentaje de visualización media de un video y su duración; ii- de las clases divididas en varios videos, los primeros tienen mayor número de visualizaciones; iii- las variables analizadas sufren modificaciones según el cuatrimestre considerado. De las evaluaciones surge que a mayor resolución de evaluaciones formativas mayor rendimiento en las sumativas. Proponemos reducir la duración de las video-clases haciendo hincapié en los conceptos principales, así como revisar el carácter opcional de las evaluaciones formativas debido a su impacto positivo sobre las sumativas.

57

Covid-19 y el uso de herramientas virtuales: el desafío de enseñar y aprender viviendo en pandemia

Rivera MF, Majul Conte Grand MV, García CG, Marzilli Cesar FON, Di Giusto G.
Unidad Académica 1, Departamento de Fisiología y Biofísica, Facultad de Medicina, Universidad de Buenos Aires. florencia.rivera@campus.fmed.uba.ar

Debido a la emergencia sanitaria por COVID-19 la UBA suspendió las clases presenciales. Sin embargo, la UA1 del Departamento de Fisiología y Biofísica, Facultad de Medicina, garantizó, desde el comienzo de la pandemia hasta la actualidad, el dictado de clases virtuales. Transcurrido un año decidimos investigar cómo nos adaptamos al método de enseñanza virtual. El objetivo del trabajo consistió en relevar las experiencias de docentes y alumnos en torno a las herramientas virtuales utilizadas para el dictado de trabajos prácticos de Fisiología Renal y de la Sangre durante el primer cuatrimestre 2021. El relevamiento de datos se realizó mediante Google Forms. Se crearon dos encuestas anónimas, una dirigida al plantel docente (n=65) y otra dirigida a alumnos (n=1207). Del total de encuestados respondieron 40 docentes (62%) y 448 alumnos (37%). Las herramientas virtuales utilizadas en mayor porcentaje fueron: para los encuentros sincrónicos Google Meet (80%); para el seguimiento de la cursada Google Classroom (98%) y WhatsApp (50%); para la resolución de la guía de actividades Google Docs (88%), pizarras dinámicas (62%) y

encuentros adicionales (60%). El 82% de alumnos informó que las herramientas utilizadas fueron útiles para la comprensión y el seguimiento de la materia. La percepción del efecto anímico frente a la modalidad virtual fue neutra (41%), negativa (37%) y positiva (22%). El 73% de docentes reportó que invirtió más tiempo en la enseñanza virtual que en la presencial. En conclusión, aunque la enseñanza virtual implicó un mayor esfuerzo docente, los alumnos resultaron conformes con la cursada; demostrando que el uso de estas herramientas resultó beneficioso en el contexto actual. Sin embargo, una posible opción mixta (seminarios virtuales y prácticos presenciales) predomina entre los encuestados, lo que nos motiva a continuar investigando el impacto a futuro del uso de herramientas virtuales en estas nuevas modalidades de enseñanza-aprendizaje.

59

Extracción automatizada de información de publicaciones médicas mediante minería de textos: una nueva forma de revisar y seleccionar la bibliografía para actualizar temas de enseñanza.

Casal Juan José, Dorr Ricardo A, Gioia Daiana, Toriano Roxana.
Universidad de Buenos Aires. CONICET. Instituto de Fisiología y Biofísica “Bernardo Houssay” (IFIBIO Houssay). Laboratorio de Biomembranas. Facultad de Medicina, Paraguay 2155 7º (1121) Ciudad Autónoma de Buenos Aires, Argentina.

Con el auge de Internet, la cantidad de literatura médico-científica disponible para los docentes-investigadores que pretendan actualizar sus conocimientos en un tema determinado, es abrumadora. El creciente número de publicaciones mundiales hace cada vez más necesario disponer de sistemas automatizados para extraer información de ellas. El objetivo del presente trabajo fue diseñar una metodología que, utilizando la Minería de Textos (MT) como herramienta, permitiera procesar una gran base de datos científicos con el fin de obtener e integrar información sobre ciencias de la vida. Métodos: La MT se aplicó de forma accesible sobre los datos proporcionados por Europe PMC (ePMC) utilizando la plataforma KNIME. Resultados: Para cualquier tema de las ciencias de la vida, la MT permitió obtener una visión integradora sobre: i) número de publicaciones por año; ii) autores involucrados en la investigación; iii) número de trabajos publicados por cada autor; iv) análisis de filiación; v) participación cuantitativa de las revistas que publicaron los trabajos. Además, la MT de los resúmenes permitió i) la construcción de bolsas de palabras y el estudio de frecuencia uso de términos; ii) la extracción no supervisada de los temas tratados; iii) la búsqueda de relaciones entre enfermedades, prevención y tratamiento, cruzando la información con la de otras fuentes. Conclusiones: Siguiendo las instrucciones del tutorial, los docentes e investigadores sin conocimientos de programación pueden realizar con éxito la MT a partir de la literatura científica indexada. Esta metodología podría convertirse en una herramienta útil para realizar estadísticas, analizar comportamientos, seguir tendencias y hacer predicciones sobre temas de interés. Entre otras muchas ventajas, es de gran utilidad para integrar información científica y ayudar a realizar revisiones bibliográficas.

75

Una revisión sistemática del curso de fisiología en el currículum de bioquímica.

Ignacio Pasten[1], Camila Gutiérrez[1], José Luis Vega[1].
[1]Laboratorio GaPaL, Instituto Antofagasta, Universidad de Antofagasta, Antofagasta, Chile. E-mail: ignacio.pasten.ferrada@ua.cl; joseluis.vega@uantof.cl

Problema de estudio: El curso de Fisiología es obligatorio en los planes de estudio para la carrera de bioquímica. A pesar de su importancia, no existen trabajos que describan su actual aplicación en las universidades chilenas. Objetivo: Analizar el curso de Fisiología impartido para bioquímica en las universidades chilenas. Metodología: Los programas para los cursos de fisiología fueron obtenidos por solicitud a los coordinadores de cada curso y/o jefes de carrera. Resultados: En Chile, el 20% (11 de 52) de las universidades ofrecen la carrera de Bioquímica y todas ellas consideran el curso de Fisiología como obligatorio en sus planes de estudio. Sin embargo, existe una amplia diversidad en los nombres asignados, créditos transferibles y semestres que se imparten entre las universidades. El 64% lo imparte al tercer año y el 18% solicita como requisito haber cursado y aprobado la asignatura de anatomía. Se destaca que todas las universidades incluyen laboratorios y los contenidos para sistema nervioso, endocrino, digestivo, cardiovascular, renal y respiratorio, mientras que un 18% incluyen un capítulo de fisiología reproductiva. Por otra parte, en argentina el 36% de las universidades ofrecen la carrera de Bioquímica. Destacar que existe uniformidad en el nombre de la asignatura, semestre que se cursa y solicitan como requisito la asignatura de anatomía. Conclusión: Se requiere dar uniformidad al curso de Fisiología para la carrera de Bioquímica en las universidades chilenas.

78

FisioMed, una aplicación para teléfono inteligente, para aprender fisiología resolviendo problemas clínicos.

García Tello V[1]., Rivera López, C. A. [1], Mireles Ramos, D. L. [1], Mendoza Ángeles K. [1], Campos Castolo, E. M. [2], Camacho Morales, J. A.[2], Hernández Falcón, J. [1]
[1] Departamento de Fisiología, Facultad de Medicina, UNAM. [2] Departamento de Informática Biomédica, Facultad de Medicina, UNAM.

El aprendizaje de la Fisiología suele ser un reto para los estudiantes de diversas ciencias biológicas, pero es muy conspicuo en el caso de los estudiantes de Medicina. El estudio de la Fisiología “pura” suele parecer árido y sin aplicaciones para la práctica médica. El uso de matemáticas, física y química lo vuelve aún más difícil. Ante este panorama y, a sugerencia de un grupo de estudiantes, desarrollamos una aplicación de tipo videojuego inmersivo para equipos inteligentes (teléfono, tableta,

computadora) en formato Android® e IOS®. Ella consiste en una serie de simulaciones (y videos) de un médico de base y un estudiante de internado rotatorio que es cuestionado sobre los aspectos fisiológicos básicos de diversos casos clínicos.
Las preguntas de cada caso clínico son presentadas al jugador, quien debe contestar correctamente. Si acierta, avanza en el juego y obtiene diversos premios. Si falla, se le ofrece retroalimentación. El programa cubre las tres unidades didácticas de la asignatura del programa académico de la licenciatura en Médico Cirujano (Fisiología Celular y del Sistema Nervioso, Fisiología Cardiorrespiratoria y Renal, Fisiología Endocrina y Digestiva). Sin embargo, está diseñada de tal manera que sea útil para otros estudiantes que cursan fisiología como son, odontólogos, biólogos, ingenieros biomédicos, químicos farmacobiólogos, etc.
La aplicación cuenta con una base de casos clínicos, otra de respuestas una más de referencias bibliográficas actualizadas y un glosario. Permite identificar al estudiante, mediante un nombre de usuario y su correo, proveerle de retroalimentación y hacer un seguimiento puntual de su proceso de aprendizaje . De acuerdo con las políticas de la UNAM, el acceso a la aplicación es gratuito. Actualmente se encuentra en fase de prueba.
Proyecto desarrollado con financiamiento del programa UNAM-DGAPA-PAPIME, Clave PE211317.

88

Comparación del rendimiento de los estudiantes entre la modalidad virtual y la presencial utilizando debate guiado en grupos pequeños y evaluación cuantitativa y cualitativa continua

Giorgi Gisela, Fernández Delias María Florencia, Chrestia Juan Facundo, Vera Marcela, Stupniki Sofía, Facchinetti María Marta.
Cátedra de Fisiología Humana, Departamento de Biología Bioquímica y Farmacia, Universidad Nacional del Sur

Problema de estudio: El aislamiento social nos desafió a encontrar una nueva forma de desarrollar el "rol docente". Nuestro objetivo fue evaluar la eficacia de la metodología empleada en la modalidad virtual comparando el desempeño de los estudiantes en el año 2020(virtual) y 2019(presencial). Metodología: Las clases teóricas fueron sincrónicas o grabadas previamente. Además, se fomentó la realización de trabajos sobre temas de interés social. En las actividades prácticas virtuales, desarrolladas sincrónicamente, los alumnos se dividieron en pequeños grupos y se evaluaron continuamente mediante cuestionarios y rúbricas cualitativas. Se implementó el Aprendizaje Basado en Problemas (ABP) a través del debate de casos clínicos y del empleo de simuladores (metaneuron,PhysioEx). Se realizaron exámenes parciales y de promoción virtuales. La comunicación docente-alumnos se realizó mediante la plataforma Moodle y Whatsapp. Resultados: Primero analizamos el desempeño cualitativo, clasificado como altamente satisfactorio, satisfactorio o insatisfactorio, en base a la participación en los encuentros virtuales y al rendimiento en los cuestionarios. Se observó que el 39% de los estudiantes obtuvieron un desempeño altamente satisfactorio en virtualidad, similar al observado en presencialidad (38%). Sin embargo, sólo el 30% obtuvieron una evaluación satisfactoria en virtualidad, mientras que en presencialidad fue del 39%. Respecto del desempeño cuantitativo vimos que en 2019 el 26% estudiantes aprobaron con promoción, 70% aprobaron sin promoción y 4% desaprobaron. En 2020 detectamos reducción de los estudiantes que aprobaron con promoción (16%), aumento de los aprobados sin promoción (81%) y sin cambios de los desaprobados (3%). Conclusiones: Las diferencias en el desempeño cualitativo satisfactorio de los estudiantes entre ambas modalidades podrían deberse a problemas de conectividad. Sin embargo, no se vieron diferencias en la cantidad de alumnos aprobados, demostrando que el sistema ABP, la evaluación continua, las clases teóricas grabadas y la fluida comunicación docente-alumno aseguran la adquisición de los contenidos mínimos de la asignatura.

90

Experiencias en educación a distancia en la atención primaria de salud

Suárez N[1], Cépedes E.M.[1], Guerrero A[1], Carrión E[1], Rodríguez R[2], Reinoso S.M. [1]
[1] Universidad de Ciencias Médica de la Habana, Facultad Calixto García, Departamento de Ciencias Básicas Biomédicas, Cuba. [2] Policlínico Universitario Primero de Enero, Cuba.

Introducción: Actualmente la humanidad se enfrenta a la pandemia de la COVID-19 que presenta alta tasas de trasmisión y letalidad. Cuba no escapa a este fenómeno, lo que impone retos para la Educación Superior. Se fomenta la Educación a Distancia en la Atención Primaria de Salud en las carreras de Ciencias de la Salud.
Objetivo: Identificar los factores negativos que influyeron en la Educación a Distancia y la satisfacción de los estudiantes encuestados con esta modalidad en la Atención Primaria de Salud. Método: Se realizó una investigación descriptiva de corte transversal a los 84 estudiantes de Ciencias Médicas que se encontraban en el Policlínico Gregorio Valdés de Cojímar, del municipio Habana del Este, desde marzo a julio del 2020. La totalidad brindó su consentimiento para participar en esta investigación. Se les aplicó un cuestionario de lo positivo, negativo, interesante y las sugerencias que permitió identificar los factores negativos que influyeron en la Educación a Distancia y la satisfacción de los mismos con esta modalidad en el área de salud. Resultados: Entre los factores que influyeron negativamente estaban: la inconformidad con la retroalimentación de los profesores (72,6 %) y la poca disponibilidad de recursos tecnológicos (54,8%). Sin embargo, los estudiantes estuvieron satisfecho con esa modalidad de enseñanza (80,9%). Conclusiones: en el Policlínico Gregorio la Educación a Distancia se desarrolló con satisfacción de la mayoría de los estudiantes, a pesar de las limitaciones con la tecnología y restricciones en retroalimentación con los profesores.
Palabras clave: Educación a Distancia, estudiantes, COVID, Policlínico.

98

El "arte" de tomar decisiones en torno a la Evaluación del aprendizaje en tiempos del covid-19

Reyes MP[1]; Quiñones M[2]; Bonatti P[2], Reyes Toso C F[1].

[1] UBA. Fmed.Dpto Ciencias Fisiológicas, UA2; [2] UBA Fce cátedra de Administración general y Seminario de integración y aplicación

La evaluación del aprendizaje es un tema sensible y se deben considerar una serie de variables que son diversas y su definición no es sencilla. Estas están vinculadas a: 1) la disciplina, currícula, tipo de materia; 2) modelo educativo y sus niveles de desempeño, 3) los mecanismos de evaluación 4) en esta situación de pandemia a las regulaciones institucionales.

¿Cómo afecta el cambio de modalidad presencial a virtual en evaluación del aprendizaje? Se tuvo en cuenta que este escenario sumó no solo el aislamiento, sino la falta de herramientas tecnológicas y espacio adecuado, la conectividad necesaria y en los estudiantes extranjeros, el hecho de estar en su país de origen de habla no hispana tuvieron dificultades con el idioma por falta de estímulo. Se realizó un relevamiento a través de un cuestionario semi-estructurado sobre las herramientas empleadas en la modalidad virtual. Participaron 41 docentes (21 de Facultad de Medicina -FMed- y 16 de la Facultad de Ciencias Económicas -FCe-). Algunas de las herramientas utilizadas con más frecuencia fueron: paddlet para síntesis; talleres de discusión, pizarra virtual, Menti, Quizizz y kahoot. Las evaluaciones parciales se realizaron mediante google docs o forms. En las cátedras de FMed y FCe (Fisiología UAII, Administración general y Seminario de integración y aplicación) la posibilidad de contar con un campus dotado de herramientas al alcance de los docentes y estudiantes facilitó la posibilidad de realizar la evaluación de modo sincrónico. Ante esta situación de pandemia, la educación virtual cobró relevancia para garantizar la continuidad académica. Revisar los procesos de evaluación en esta circunstancia se vuelve un proceso reflexivo e indispensable. Adecuar dichas herramientas es un arte que facilitó la comprensión y el aprendizaje de los contenidos como el seguimiento del proceso de aprendizaje por esta razón tomamos este desafío que relevamos en el presente trabajo.

100

Ciencias básicas biomédicas: una retrospectiva de enseñanza híbrida en tiempos de Covid 19

González-Jardinez, M. [1], Alonso-Pupo, N. [2]

[1] Doctora en Medicina. Especialista de primero y segundo grado en fisiología normal y patológica. Profesora Auxiliar de la Universidad de Ciencias Médicas de La Habana. [2] Doctora en Medicina. Especialista de primero grado en anatomía humana. Máster en Neurociencia y Biología del Comportamiento. Profesora Auxiliar de la Universidad de Ciencias Médicas de La Habana.

Introducción: La irrupción de la COVID-19 en Cuba dio inicio a suspensión de clases presenciales. La docencia universitaria migró a una modalidad a distancia, con soporte en las tecnologías de la información y las comunicaciones. El principal desafío fue diseñar un sistema de enseñanza orientado al aprendizaje, que considerase las ventajas y desventajas del espacio virtual, respondiera a enfoque integrados y mantuviera la calidad del proceso. Objetivos: Describir la experiencia del proceso enseñanza aprendizaje híbrido, aplicado en la asignatura sistemas nervioso, endocrino y reproductor.

Comparar el rendimiento académico de los estudiantes de medicina que cursaron la modalidad híbrida, curso 2020-2021, con el año anterior. Métodos: Se realizó un estudio cualitativo, de carácter descriptivo, sobre el diseño y la aplicación del modelo híbrido para estudiantes de primer año de Medicina, en la asignatura sistema nervioso, endocrino y reproductor, en la Facultad Manuel Fajardo de la Universidad de Ciencias Médicas de la Habana. Se realizó la comparación del porciento de promoción e índice de calidad de la asignatura con el curso anterior. Resultados: Se aplicó un modelo educativo híbrido, que incluyó en su etapa virtual actividades de orientación al estudio independiente y autoevaluación. En la etapa presencial se trabajó la clase taller con modalidad de aula invertida. La evaluación se realizó mediante seminarios integradores con aprendizaje basado en problemas y al final con un examen escrito. Los resultados de la asignatura mostraron un aumento en la promoción (84,9 %) con respecto al curso anterior (63,3 %); al igual que el índice de calidad, que de 19,7 % ascendió a 51,9 %. Conclusiones: Se ratificó la importancia del trabajo metodológico en la selección de un modelo educativo híbrido acorde a circunstancias extraordinarias. Lo más complejo fue la implementación del sistema de evaluación. Se garantizó la adquisición de las habilidades en los estudiantes, expresados en mejores resultados académicos.

102

Impacto de un Curso de Actualización en Fisiología Humana en el Pregrado de Ciencias de la Salud, durante la Pandemia

Vila DT[1]; Stacchiotti MN[1]; Traverso LL[1]; Ulfeldt NA[1]; Verduna CM[1]; Urbina FG[1]; Bianchi MEV[1]

[1]Cátedra II de Fisiología Humana Normal. Facultad de Medicina. Universidad Nacional del Nordeste. Corrientes, Corrientes, Argentina. Mariano Moreno 1240. fisiologiahumana2@med.unne.edu.ar

Problema de estudio: La oferta de Cursos de actualización de Fisiología es escasa en la educación de pregrado en las carreras de Ciencias de la Salud. La internacionalización del Curriculum de Fisiología, en pregrado de Ciencias de la Salud es un área a ser sistematizada en la educación de pregrado. Objetivos: Describir los resultados de un Curso de actualización de Fisiología Humana, aprobado por Res. Nº458/19 C.D., auspiciado por la SAFIS, desarrollado en pandemia, desde la asignatura Fisiología Humana II, de la Facultad de Medicina de la UNNE (FDMUNNE). Metodología: La planificación consistió en generar un aula virtual con 10 módulos dictados durante tres meses (80 horas totales). Los 11 docentes fueron ex-becarios o ayudantes alumnos rentados de la asignatura, que se encontraban ejerciendo la profesión de medicina o kinesiología, en sus respectivas áreas. La evaluación era formativa en cada

módulo, con un examen final, permitiendo acceder a un certificado emitido por Secretaría Académica, FDMUNNE. La estrategia didáctica consistía en tratar por cada docente especialista un contenido de Fisiología y cómo lo evaluaba en la práctica profesional. El acceso era gratuito por reglamentaciones vigentes. Resultados: Se inscribieron 1044 alumnos de 29 universidades, 22 (75,9%) nacionales y 7 (24,1%) internacionales. Aprobaron 619 (59,3%), siendo el desgranamiento 31,5%, pertenecientes a 12 carreras relacionadas a las Ciencias de la Salud. Mediante una encuesta de satisfacción, las fortalezas del curso fueron: calidad del material de estudio, contenidos claros y específicos. Las debilidades fueron: calidad de video/audio y ciertas explicaciones. Conclusión: Los cursos de Pregrado de Actualización de Fisiología en Ciencias de la salud, tienen una gran demanda en estudiantes de carreras de ciencias de la Salud nacionales e internacionales. Probablemente este curso representó una oportunidad al estudiante para reflexionar acerca de la importancia de conocer fisiología y cómo se lleva a la práctica profesional.

107

Desafíos de la evaluación en el contexto de la virtualidad: análisis de las ventajas y desventajas de uso de cuestionarios Moodle desde una aproximación estadística

Speranza ED [1, 2]., Ferreira AC[1], Nieto E [1, 2]

[1] Cátedra de Fisiología Animal, Facultad de Ciencias Naturales y Museo, Universidad Nacional de La Plata, Av. 122 y 60 s/n, 1900, La Plata, Buenos Aires, Argentina. [2] Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Godoy Cruz 2290, Ciudad Autónoma de Buenos Aires (C1425FQB), Argentina

Ante la virtualización de las clases en el 2020, la Cátedra de Fisiología Animal (FCNyM, UNLP) comenzó a utilizar la plataforma Moodle tanto como repositorio de clases teóricas asincrónicas, material de lectura y guías de actividades como para la evaluación. Esta última, previamente oral, se realizó de manera continua, mediante cuestionarios de autoevaluación (no acreditables) luego de cada unidad y dos exámenes parciales (acreditables). Para ambos tipos de evaluación se utilizaron cuestionarios Moodle con preguntas aleatorias a partir de un banco de preguntas común (~350 preguntas de 4 tipos diferentes). El desempeño de los estudiantes (nota) vario significativamente según la unidad temática y según tipo de pregunta ($p<0,01$; ANOVA), pero no según el docente a cargo del estudiante. La duración de cada examen fue cercana al límite y determino significativamente la cantidad de respuestas sin responder ($p<0.01$, test t). La nota de autoevaluación estuvo correlacionada con la nota de la unidad correspondiente del primer parcial, ($r = 0,8$, $p<0,0001$) pero no del segundo, probablemente debido a la circulación de un banco de preguntas "copiadas" generado por los estudiantes mediante capturas de pantalla de los cuestionarios de autoevaluación que contenía >90% de las preguntas de las ultimas 5 unidades. Los ajustes de los cuestionarios en 2021 (ej. disminución del tiempo límite, inclusión de nuevos tipos de preguntas, agregado preguntas nuevas al parcial, etc.) resultaron en un descenso de la nota promedio de parcial (4,7±1,9 vs. 6,9±1,6, $p<0,0001$, test t) con una distribución de asimetría opuesta (0,16 vs -0,74 en 2020). Los cuestionarios Moodle ofrecen numerosas ventajas (autocorrección, diversidad de formato, flexibilidad horaria, etc.), aunque son susceptibles a fraude y no siempre reflejan la apropiación de conceptos y procesos fisiológicos. El análisis estadístico contribuye a la optimización dinámica necesaria para el uso eficaz de los mismos.

111

Generando espacios sincrónicos de colaboración entre pares, en la asignatura de Fisiopatología-I 2021 de 3° año de Medicina, de la Universidad de Chile.

Emilia M. Sanhueza Reinoso[1] y Pedro P. Figueroa Navarro[2].

[1] Programa de Fisiopatología-ICBM. Facultad de Medicina, Universidad de Chile. [2] Escuela de Medicina. Facultad de Medicina, Universidad de Chile.

Introducción: Dado que la experiencia 2020 totalmente asincrónica, nos dejó la inquietud respecto del nivel de logro del razonamiento fisiopatológico, nos propusimos para la asignatura Fisiopatología I-2021 rediseñar la metodología de las actividades prácticas de Análisis de Casos Clínicos (ACC) n=9, haciéndolas online, sincrónicas y en grupo pequeño, con la metodología que hemos denominado ACC-VAR ("Vamos, Analizamos y Regresamos") y promoviendo el trabajo colaborativo mediante Evaluación entre pares (EEP) n=4. Objetivo: Promover la activa participación de estudiantes e interacción entre pares, en actividades sincrónicas ACC-VAR online, para contribuir al desarrollo de la capacidad de análisis crítico fisiopatológico. Metodología: Curso de 250 estudiantes, dividido en 2 secciones, distribuidos al azar en 28 subgrupos/sección (4-5integrantes/grupo pequeño). Previo estudio de contenidos teóricos, ingresaron a una sesión Zoom mediante un link común, vía plataforma institucional "U-curso". Participaron 7 docentes, a cargo de 4 subgrupos c/u, tiempo asignado: 1h 50min. En los ACC-VAR los estudiantes reciben en el momento, los antecedentes clínicos, "van" a su sala pequeña a interactuar, "analizan" respondiendo consensuadamente un Google forms, luego "regresan" a la sala general del docente, a compartir con los otros 3 subgrupos sus conclusiones. El docente modera, retroalimenta y entrega nueva información para la siguiente fase, repitiéndose la secuencia y progresando el análisis fisiopatológico del caso planteado. Finalizada cada unidad temática, evaluaron anónimamente en base a una pauta, la participación de sus pares con nota de 1 a 7. Fueron redistribuidos para cada unidad. Resultados: El rango de notas promedio de las EEP1-4, fue 6.83-6.99 y el de notas mínimas individuales 2.50-6.70. La mayoría de los estudiantes opinó favorablemente acerca de la actividad (me gusta+ me gusta mucho=80%), el 100% de los docentes destacó el nivel de participación de los estudiantes.
Conclusión: La metodología utilizada propicia la participación y el análisis crítico colaborativo de los estudiantes contribuyendo al aprendizaje.

114

"Fisio-Box": Experiencia de la Cátedra de Fisiología del Departamento de Bioquímica de la Universidad Nacional de la Patagonia San Juan Bosco.

Nickels N[1]; Temporelli MB[1]; Pujana M[1], Góngora P [1],Miranda A[1]

[1] Universidad Nacional de la Patagonia San Juan Bosco, Facultad de Ciencias Naturales y Ciencias de la Salud, Departamento de Bioquímica, Cátedra de Fisiología fisiologiafarbiotul@gmail.com

Introducción: Las medidas implementadas desde la Universidad Nacional de la Patagonia San Juan Bosco (UNPSJB) para disminuir el número de contagios durante la pandemia incluían: evitar ingreso de personas con comorbilidades al edificio universitario, disminuir el aforo en los espacios cerrados, mantener la distancia social. En el Laboratorio de Bioquímica, se evitó el procesamiento muestras clínicas, disminuyendo el tiempo de permanencia en dicho espacio. Eso nos demandó, como equipo de cátedra, a implementar alternativas para la realización de las valiosas experiencias para el entendimiento de la Fisiología. Objetivo: Compartir la innovación realizada para la realización de experimentos en la Cátedra de Fisiología del Departamento de Bioquímica de la UNPSJB durante la pandemia. Desarrollo de la experiencia: Se prepararon en cajas denominadas "FisioBox" el material de laboratorio, reactivos, instructivos correspondientes a los experimentos de Laboratorio de: Neurofisiología, Fisiología Renal, Digestiva, Respiratoria y Cardiovascular. El reparto de las cajas fue coordinado a través de nuestras redes sociales en diferentes puntos de la ciudad e incluso a otras localidades. Para acreditar la experiencia, cada grupo debió preparar contenido audiovisual fundamentando los resultados de la experiencia. Se evalúo a través de rúbricas, ponderando diferentes habilidades creativas, dominio del tema, entrega en tiempo, etc. Posteriormente se subió el contenido a nuestra aula virtual para que ser utilizada como material de estudio. Conclusiones: Las "Fisio-box" fueron una alternativa inclusiva e incentivadora, permitiendo la realización de experimentos a todos los estudiantes, independientemente de su condición de salud, siendo un punto de encuentro entre ellos para poder sostener el ritmo de estudio en la situación actual. Por otra parte, como equipo de cátedra, la pandemia nos permitió ser más creativos generando propuestas que incluyen desde la incorporación de tecnología hasta la realización ubicua de la experiencia, todo pensado para el beneficio del proceso de aprendizaje de nuestros estudiantes.

115

Innovaciones pedagógicas en Fisiología de la Universidad Nacional de la Patagonia San Juan Bosco

Nickels N[1]; Temporelli MB[1]; Pujana M[1], Góngora P[1], Miranda A[1]

[1] Universidad Nacional de la Patagonia San Juan Bosco, Facultad de Ciencias Naturales y Ciencias de la Salud, Departamento de Bioquímica, Cátedra de Fisiología. fisiologiafarbiotul@gmail.com

Introducción: Los modelos pedagógicos actuales proponen combinar contenidos tecnológicos, pedagógicos y disciplinares. Desde la Cátedra de Fisiología para Farmacia y Bioquímica (FFYB) de la Universidad Nacional de la Patagonia San Juan Bosco (UNPSJB), intentamos incorporar y combinar estos contenidos para adecuar y potenciar las actividades teórico-prácticas durante la pandemia favoreciendo el proceso de enseñanza-aprendizaje. Objetivo: Compartir la experiencia adaptativa del equipo docente de la FFYB de UNPSJB. Desarrollo de la experiencia: Las innovaciones se realizaron sobre contenidos: Teóricos (T), Seminarios (S), Experiencias de Laboratorio (L), Evaluaciones (E) y Redes Sociales (RS): T: Incorporación de un canal audiovisual (Youtube) para disponer de forma asincrónica del contenido teórico favoreciendo el aprendizaje ubicuo. Realización de un encuentro sincrónico semanal con resolución de casos clínicos través de la metodología de aprendizaje basado en problemas (APB). S: Utilización del simulador Physioex 10.0 (on line) y cuestionario on line del tema semanal (con metodología de retroalimentación y devolución inmediata de la nota) L: Incorporación de cajas con material de laboratorio para que algunas experiencias prácticas se realicen desde un ámbito extrauniversitario con el objetivo de crear contenido audiovisual para ser compartido a sus pares. E: Realización de un trabajo colaborativo y defensa oral sincrónica de un caso clínico, con posterior espacio para preguntas, evaluándose a través de rúbricas. RS: Comunicación instantánea por RS, con incentivo audiovisual a través de reeles, y cuestionarios. Conclusiones: Desde el presente espacio curricular, tomamos el momento presente como una oportunidad para innovar, generando propuestas que integran la tecnología, la pedagogía y la Fisiología. Nos queda pendiente, medir a través de alguna herramienta, el grado de satisfacción de los estudiantes con las innovaciones incorporadas y si éstas fueron efectivas para que incorporen el conocimiento y sean protagonistas de su propio aprendizaje.

Section 1: Inmunity – Inflamation - Cancer 1

2

Analysis of the expression of protein kinase C alpha (PKCα) as a possible predictive marker in thyroid cancer.

Campos Haedo M.N.[1], Díaz Albuja, J.A.[1], Diaz Flaqué M.C.[1], Cayrol M.F.[1], Debernardi M.M., Sterle[1], H.A., Perona M.[2,3], Juvenal G.J.[2,3], Cremaschi G.A.[1], Rosemblit C.[1].

[1] BIOMED UCA-CONICET, Buenos Aires, Argentina. [2] Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina. [3]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Buenos Aires, Argentina.

Introduction: Thyroid cancer (TC) incidence has been increasing within last decades. Numerous studies established that PKCα overexpression correlates with cancer aggressiveness and therapy resistance. However, its role in TC remains poorly studied. We have previously demonstrated that PKCα is overexpressed in TC cells and mediates hormones-induced proliferation through MAPK and AKT. Objectives: To analyze the relationship between PKCα expression levels with clinical and tumor parameters in TC patients. Methods: R2 Genomics Analysis and Visualization Platform (http://r2.amc.nl) analyses were performed on the GSE126729 dataset (n=28); for analyses on the Kaplan-Meier plotter (https://kmplot.com/), cBioPortal (https://cbioportal.org/) and Metascape (https://metascape.org/) platforms, mRNA sequencing data from the PanCancer Atlas TC dataset (n=504) were used.
Results: Analysis of PKC family members expression through R2 indicates that PKCα expression is the highest in TC and in anaplastic TC patients. cBioPortal analysis showed a positive correlation between PKCα and MAPK4 (S=0.46, p<0.001), PIK3CG (S=0.35, p<0.001) and VEGFD (S=0.35, p<0.001). Enrichment analysis through Metascape platform showed activation of MAPK (p<0.001) and PI3K (p<0.001) programs in samples where PKCα is overexpressed. In the Kaplan-Meier TC database, higher PKCα expression is associated with poor overall survival in men (HR: 19.7, p<0.001), and low tumor mutational burden (HR: 13.21, p<0.01) . These results indicate that PKCα expression could have a role in reducing patients' survival. Bioinformatical analyses in TC patients confirm our previous in vitro results demonstrating PKCα is the predominant PKC isoform with a leading role in TC proliferation.
Conclusion: Our findings could improve diagnosis, provide new therapeutic target and alternatives to treatments for this disease. Despite its increasing incidence and mortality in many cases, TC constitutes a poorly studied area.

9

Thyroid hormone-mediated regulation on intracellular glutathione concentration and antioxidant enzyme activity in lymphoid tissue of Balb/c mice

Contin M.[1]; Macri Delbono R.[2]; Costilla M.[2]; Romeo H.[2]; Klecha A.[2]; Cremaschi G.[2]; Tripodi V.[1]; Barreiro Arcos M.L.[2]

[1] Department of Analytical Chemistry and Physical Chemistry, School of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina. [2] Institute of Biomedical Research (BIOMED-CONICET), Argentine Catholic University (UCA), Buenos Aires, Argentina.

Introduction: Thyroid hormones (TH) regulate metabolism and redox status in most tissues. We previously demonstrated that TH increase reactive oxygen species (ROS) in lymphoid cells. However, the antioxidant defense mechanisms involved in ROS clearance have not yet been elucidated. Objectives: To analyze the intracellular glutathione content, the GSH/GSSG ratio and the activity or expression of antioxidant enzymes in lymphoid tissue from euthyroid and hyperthyroid mice. Methods: Hyperthyroidism was induced in Balb/c mice by treatment with thyroxine in drinking water (12 mg/ml) for 40 days. Lymphoid cells from lymph nodes (LN) and spleen (S) were purified for biological assays. Assessment of GSH and GSSG was performed by liquid chromatography and tandem mass spectrometry (HPLC-MS/MS). Catalase (CAT) and Glutathione peroxidase-1 (GPx-1) expression was quantified by real-time PCR and western blot. The conversion of H_2O_2 to molecular oxygen by CAT was determined by spectrophotometry. ROS were evaluated by DCFH-DA staining and flow cytometry. Results: We found that GSH and GSSG were increased in LN and S from hyperthyroid mice, and the GSH/GSSG ratio was similar to euthyroid mice (% increase- GSH_{LN}:30.2±2.1, GSH_S:29.6±1.8; $GSSG_{LN}$:32.4±2.9, $GSSG_S$:31.7±2.7; n=5; p<0.05). The total intracellular glutathione content was increased in both tissues. *In vitro* treatment of lymphoid cells from hyperthyroid mice with a glutathione synthesis precursor (N-acetyl-cysteine, 2mM) increased GSH content and decreased ROS production. CAT activity was increased in LN and S from hyperthyroid mice as well as its genomic and protein expression (% increase- $Activity_{LN}$:93.4±7.1, $Activity_S$:82.3±6.7; $mRNA_{LN}$:85.1±6.2, $mRNA_S$:147.2±9.7; $Protein_{LN}$:154.3±9.7, $Protein_S$:165.7±10.1; n=6; p<0.05). GPx-1 expression was increased in hyperthyroid mice (% increase- $mRNA_{LN}$:43.7±3.1, $mRNA_S$:39.8±4.7; $Protein_{LN}$:47.6±5.1, $Protein_S$:71.1±6.6; n=6; p<0.05). *In vitro* treatment of lymphoid cells from euthyroid mice with an oxidative stress inducer (H_2O_2, 250µM) increased the genomic expression of antioxidant enzymes. Conclusions: TH induce oxidative stress and regulate the antioxidant system in lymphoid tissue cells.

17

Evaluation analysis between IL-6 levels and COVID-19 symptoms in Mexicans with psychiatric disorders

[1]Ramos-Méndez MA, [1,4]Juárez-Rojop IE, [2] González-Castro TB, [3]Tovilla-Zárate CA, [4]Villar-Soto M, [1]Alberto Nolasco G, [4]Villar-Juárez GE

[1] Universidad Juárez Autónoma de Tabasco, División Académica de Ciencias de la Salud. [2]Universidad Juárez Autónoma de Tabasco, División Académica Multidisciplinaria de Jalpa de Mendez. [3] Universidad Juárez Autónoma de Tabasco, División

Académica Multidisciplinaria de Comalcalco. [4] Hospital de Alta Especialidad de Salud Mental de Villahermosa, Tabasco.[4] Sociedad Mexicana de Ciencias Fisiológicas.
Introduction: Patients with psychiatric disorders are a high-risk group; which their clinical features could have an impact in the typical symptomatology of COVID-19. Due to, we evaluated the differences of IL-6 levels between in psychiatric disorder patients with COVID-19 and general population with COVID-19 in a Mexican population. Objective: compare IL-6 levels in COVID-19 positive psychiatric patients with different population groups. Methods: 156 subjects were divided into four groups: i- 31 patients with psychiatric disorder with COVID-19 (PD-C), ii- 57 patients with psychiatric disorder without COVID-19 (PD-WC), iii- 31 subjects without psychiatric disorder and with COVID -19 (WPD-C) and iv- 31 subjects without psychiatric disorder and without COVID-19 (WPD-WC). IL-6 was determined using serum in a commercial kit test. Statistical analyzes will be performed with version 20.0 of the SPSS statistical software. The level of significance will be $p < 0.05$. The values will be presented as an average plus standard deviation, (151 samples analyzed). Results: PD-C group remained asymptomatic during the two months of clinical monitoring. Otherwise, in WPD-C group the principal symptoms were: headache (80%), arthralgia (44%), fever (45%), cough (35%), myalgia (32%), and diarrhea (22%). Regarding to IL-6 serum levels, the mean in the groups was: i- 4.44±13.65 in PD-C group, ii- 1.49±1.58 in PD-WC group, iii- 1.52±4.94 in WPD-C group and iv- 1.21 ±0.63 in WPD-WC group. Conclusions: psychiatric groups (PD-C and PD-WC) either with or without COVID-19 present higher levels than the subjects without psychiatric disorders (WPD-C and WPD-WC). The clinical features behind the psychiatric diagnosis play an important role in IL-6 levels in the Mexican population. Therefore, it is necessary to carry out experimental studies to addresses the implication in the COVID-19 symptomatology.

19

Identification of intracellular LFA-1 vesicles that polarize to the IS during NK cell activation

Pariani AP[1], Marin LM[1], Hidalgo F[1], Fussi F[2,3], Borini-Etichetti C[1], Favre C[1], Larocca MC[1]
[1] Instituto de Fisiología Experimental, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario (UNR), Rosario, Argentina. [2] Área Farmacología, Facultad de Cs. Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. [3] CONICET
Introduction: NK cells are cytotoxic cells from the innate immune system. They form a specialized junction with their target cells called immune synapse (IS). IS formation is highly dependent on NK receptors such as the integrin LFA-1. The mechanisms involved in LFA-1 localization at the IS remains unclear. AKAP350 is a centrosome and Golgi apparatus (GA)-scaffold protein that participates in LFA-1 recruitment to the IS, thus conditioning NK cytolytic activity. Objective: The aim of this work was to elucidate the mechanisms underlying LFA-1 organization during NK cell activation. Methods: YTS (NK) cells, YTS cells with decreased expression of AKAP350 (AKAP350KD) and YTS cells expressing AKAP350 Golgi-binding domain (AKAP350GBD), were exposed to sensible target cells for 30 minutes. LFA-1 distribution in YTS cells was analyzed by immunofluorescence confocal microscopy. Relative distance to the IS (RD) was estimated as the difference between the distance from each LFA-1 vesicle to the IS and the distance from the cell centroid to the IS, related to the latter. Results are expressed as media±standard error. Results: Analysis of activated YTS cells revealed the presence of an intracellular pool of LFA-1 vesicles, which partially colocalized with RAB11 (recycling endosomes) and with GM130 (GA). The assessment of LFA-1 vesicles localization indicated that they polarized to the IS in activated YTS cells, and that this polarization was impaired in AKAP350 KD cells (RD: CONTROL: -0.14±0.01, KD: 0.05±0.02, n=30, p=0.001). Interestingly, the specific displacement of AKAP350 from the GA, which inhibits LFA-1 localization at NK-IS, also impaired LFA-1 polarization towards the IS (RD: Control: -0.22±0.03, AKAP350GBD: 0.03±0.02, n=30, p=0.03). Conclusion: Our results reveal the presence of an intracellular pool of LFA-1 which associates with the GA and might be relevant for NK-lytic IS maturation.

20

Regulation of CDC42 Interacting Protein 4 (CIP4) association with microtubules during the establishment of the immune synapse in natural killer (NK) cells

Marin L.M.[1], Pariani A.P.[1], Hidalgo F.[1], Larocca M.C.[1]
[1] Instituto de Fisiología Experimental, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario (UNR), Rosario, Argentina.
Introduction: NK cell cytotoxicity requires extensive actin and microtubule remodeling and reorganization of membrane receptors at the NK-target cell immune synapse (IS). CIP4 is a CDC42 effector that scaffolds proteins involved in actin remodelling, which has a prominent role in NK-IS maturation. CIP4 contains an amino-terminal domain that allows CIP4 interaction with microtubules. Objective: Our aim was to characterize CIP4 subcellular localization and specifically CIP4 interaction with microtubules during NK cell activation. Methods: CIP4 subcellular localization was analyzed by immunofluorescence confocal microscopy and CIP4 interacción with microtubules was additional assessed by western blot in microtubule extracts of resting (attached to IgG coated coverslips) and activated (attached to ICAM-1 and anti-CD28 coated coverslips) YTS-NK cells. Results are expressed as media ± standard error. Results: Immunofluorescence studies showed that ICAM-1/anti-CD28 activation of NK cells induced CIP4 translocation to the centrosome (Centrosomal CIP4 (%): IgG: 7 ± 3, n: 33 cells; ICAM-1/anti-CD28: 11 ± 4, n: 23 cells; p= 0,02) and to the activated cell surface (AS) (AS-CIP4 (%): IgG: 10 ± 3, n: 33 cells; ICAM-1/anti-CD28: 14 ± 5, n: 23 cells, p= 0,01). Western blot analysis of microtubule-rich cell extracts showed a decrease of microtubules associated CIP4 in ICAM-1/anti-CD28 activated cells (microtubule-CIP4 (%), IgG: 50 ± 5; ICAM-1/anti-CD28: 22 ± 7, n: 3; p= 0,01). Similarly, immunofluorescence studies

showed that CIP4 localization at microtubules was reduced in ICAM-1/anti-CD28 activated cells (microtubule-CIP4 (%): IgG: 50 ± 6, n: 33 cells; ICAM-1/anti-CD28: 41 ± 4, n: 23 cells; p= 0,001). Conclusion: NK cell activation induces significant changes in CIP4 localization, eliciting a prominent decrease in CIP4 interaction with microtubules. The mechanisms underlying CIP4 relocalization or the relevance of CIP4 relocalization on NK-IS maturation will be a matter of future studies.

21

Melatonin prevents tumor growth through of genes implicated in processes like circadian rhythms, cell cycle and angiogenesis

Cárdenas-Romero S[1], Salgado-Delgado R[1], Ramírez-Plascencia O.D[3,4], Baez-Ruiz A[1], Flores-Sandoval O[1], Azuara-Alvarez L.E[1], Escobar C[2] and Saderi N[1].
[1] Laboratorio de Neuroanatomía Funcional y Ritmos Biológicos, Facultad de Ciencias, Universidad Autónoma de San Luis Potosí, San Luis Potosí, México. [2] Laboratorio de Ritmos Biológicos y Metabolismo, Facultad de Medicina, Departamento de Anatomía, Universidad Nacional Autónoma de México, México. [3] Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA, USA. [4] Neurology, Harvard Medical School, Boston, MA, USA.

The hypothalamic suprachiasmatic nucleus (SCN) regulates the circadian rhythms to keep body physiology synchronized to the light-dark cycle (LD). Circadian Desynchronization (CD) has been associated to cancer and local angiogenesis. Previous studies from our laboratory showed that the CD by constant light (LL) promotes the tumor growth and vascularization in rats inoculated with glioblastoma cells, an effect that is counterbalanced by melatonin. To investigate the integrative role of this hormone, we explored the melatonin effects over the expression of clock, cell cycle and pro-angiogenic genes in the tumor tissue and the liver of rats assigned to 5 different groups: 2 of them in LD; the other 3 were kept in a LL. One of LD and 2 of LL groups were injected with glioblastoma cells; moreover, a group of the LL with cancer received a daily dose of melatonin. We registered the locomotor activity and body temperature of the animals, also analyzed the mRNA of liver and tumor tissue through RT-PCR. We performed a 2W-ANOVA plus Turkey´s test to data that are presented as mean ± standard error of the mean. We observed that melatonin modified the rhythm of p53 and Tnfα in tumor tissue (n = 3-4), and of Per2, p21, Cyclin E, VEGF-A, PDGF and Tnfα in the liver (n = 3-6), as well as the daily amount of mRNA (Per2, Rorα, p53, VEGF-A, Tnfα and Ang in tumor tissue, n = 3-4; p21, VEGF-A, PDGF, Tnfα, MT1R and MT2R in the liver, n = 3-6). These results indicate that melatonin could protect from CD and its pathological consequences by promoting the expression of suppressor genes (e.g., Rorα). Interestingly, the hepatic expression of p21, Cyclin E, VEGF-A, Tnfα, MT1R and Rev-erbα under LL with cancer occurred rhythmically, suggesting cancer as a synchronizer under LL. Supported by Conacyt 243298, FAI 2020, CA-UASLP 254. Acknowledgment to Biomedical Science Postgrad, Faculty of Medicine, UASLP. Keywords: Circadian Desynchronization, cancer, angiogenesis, melatonin, clock genes, cell cycle genes and pro-angiogenic genes.

28

Effects of interferon alpha 2b combined with vitamin K2 on liver carcinogenesis in mice

Vera M.C.[1], Lucci A.[1,2], Lorenzetti F.[1], Comanzo C.G.[1], Heit Barbini F.J.[3], Álvarez M.L.[1,2,3], Quiroga A.D.[1,2,3], Carrillo M.C.[1,2]
[1]Instituto de Fisiología Experimental (IFISE), Facultad de Cs. Bioquímicas y Farmacéuticas, CONICET, UNR. [2]Área Morfología, Facultad de Cs. Bioquímicas y Farmacéuticas, UNR. [3]CAECIHS, Universidad Abierta Interamericana, Rosario, Argentina.

Vitamin K2, which is present in dairy products, and it has been recommended as a micronutrient supplement in humans, holds strong anticancer properties. Interferon (IFN)-α-2b administered during development of hepatic preneoplasia decreased both number and volume percentage of altered hepatic foci by increasing apoptosis within the foci. Objective: to evaluate whether the therapy of IFN-α-2b with vitamin K2 has a synergistic inhibitory action on DEN-induced hepatocarcinogenesis in mice. Methods and Results: 14-day-old mice were injected intraperitoneally (ip) with 25 mg/kg DEN (control group with tumor, CT). After 10 months mice were divided in groups: CT; IFN: CT mice treated with IFN-α-2b $6.5x10^5$ U/kg ip 5 times/week/3 weeks; VK2: CT mice that received vitamin K2 5 mg/kg ip 5 times/week/3 weeks; and IFN+VK2: CT mice which received both drugs. Animals were euthanized after treatments and livers were excised. We previously found that CT mice treated with IFN-α-2b had fewer tumors/liver and a trend to be smaller in size (compared to CT livers). Also, immunoblotting analysis showed increase proapoptotic Bax protein in IFN group respect to the CT group. In this study, cytochrome c levels (immunoblotting) increased in IFN group compared to CT animals (+125%*); the other groups did not show any differences respect to CT. The antiapoptotic protein Bcl-2 showed an increase expression in VK2 and IFN+VK2 groups (+64%* and +75%*, respectively). Finally, we found that levels of antiapoptotic protein Bcl-X_L were increased in IFN+VK2 group (+142%*) (*p<0.05 vs CT, n=5). Conclusion: Our findings indicate that IFN-α-2b contributes to reducing liver tumor development in mice treated with DEN. Interestingly, vitamin K2 seems to block the positive proapoptotic effect of IFN-α-2b. This is in agreement with our in vitro studies in SK-HEP-1 cells as well as with our studies performed in in the early stages of liver cancer development in rats.

43

Involvement of Insulin-like growth factor 2 mRNA-binding protein 1 (IGF2BP1) in ABC transporters modulation by Sorafenib in Hepatocarcinoma (HCC) cell lines.

Bucci Muñoz M[1], Semeniuk M[1], Livore V.I[1], Banchio C[2], Mottino A.D[1], Ceballos M.P[1], Ruiz M.L[1].
[1] Instituto de Fisiología Experimental (IFISE-CONICET), Fac. de Cs. Bioq y Farm. Universidad Nacional de Rosario. [2] Instituto de Biología Molecular y Celular de Rosario (IBR-CONICET), Fac. de Cs. Bioq y Farm. Universidad Nacional de Rosario.

IGF2BP1 is an RNA-binding protein highly expressed in various types of solid tumors. Its exp ression was found to promote HCC cell proliferation, migration, invasion and correlate with poor survival and prognosis. Sorafenib (Sfb) is the standard systemic therapy used for advanced HCC. Resistance to Sfb still remains one of the major causes of treatment failure and often involves the upregulation of ABC transporters, like ABCB1 and ABCC3. We aim to evaluate whether IGF2BP1 is involved in ABCB1 and ABCC3 modulation by Sfb in HCC cell lines. HepG2 and HuH7 cells were incubated with Sfb 2µM for 48h and 72h; DMSO was added to control cells (C). IGF2BP1 was transiently knocked down with shRNA targeting human IGF2BP1 mRNA (sh-IGF2BP1) or scrambled (sh-SCR) as control in HepG2 cells. Twenty-four h after transfection, cells were treated with Sfb 2µM for 48h. IGF2BP1, ABCC3, ABCB1 protein expression were determined by western blotting. Data was presented as mean±S.D, n=3-6, *p<0.05 vs. C, #p<0.05 vs sh-SCR. Statistical analysis was performed using the Student's t test or One-Way ANOVA followed by Newman-Keuls test. Sfb treatment induced IGF2BP1, ABCB1 and ABCC3 protein expression at 48h (128±3*%,121±3*%, 142±3*%; respectively) and 72h (167±10*%, 138±4*%, 180±14*%; respectively). HuH7 cells behaved in a similar fashion. The knockdown procedure resulted in decreasing IGF2BP1 protein expression by 48% and leaded to ABCB1 and ABCC3 down-regulation (58±4#%, 64±16#%; respectively). As expected, Sfb increased IGF2BP1, ABCB1 and ABCC3 expression (128±6#%, 122±3#%, 142±3#%; respectively). The knockdown of IGF2BP1 prevented IGF2BP1 and ABCB1 induction by Sfb (69±10#%, 85±13#%; respectively). ABCC3 protein levels remained increased in sh-IGF2BP1 cells treated with Sfb. These results suggest that the induction of IGF2BP1 is responsible for ABCB1 upregulation by Sfb. Targeting IGF2BP1 could be a useful tool to modulate multidrug associated resistance proteins, in order to minimize the resistance to Sfb in HCC.

60

The influence of the lipid environment on human AQP1: an *in silico* study

Casal JJ[1], Dorr RA[1], Gioia DS[1] Toriano RM[1]

[1] Universidad de Buenos Aires. CONICET. Instituto de Fisiología y Biofísica "Bernardo Houssay" (IFIBIO "Houssay"), Laboratorio de Biomembranas. Facultad de Medicina. Paraguay 2155 7mo piso. CABA. Argentina

Aquaporins (AQP) are channels that ensure a rapid and reversible control of water permeability (Pf). In the case of hAQP1 (hAQP1), it has been described that they can transit from a high to a lower Pf state, depending on membrane tension. The aim of this work was to study the influence of the lipid environment on the hAQP1 tetramer by molecular dynamics simulations (MDS). Two heterogeneous lipid bilayers, representative of mammalian (M) and cancer (C) cells, and another one only of DPPC, were generated around hAQP1. CHARMM-GUI was used to construct the three systems from the crystallographic structure of hAQP1 (PDB 4CSK) that was embedded in 70×70Å lipid bilayers, with TIP3P water molecules, neutralizing ions (0.15M KCl), and a temperature set at 310K. CHARMM36m force field was used to run a 100ns MDS. GROMACS, MDAnalysis and VMD were used to evaluate RMSD (MDS stability); membrane density; protomeric pore profile; electron density; protein self-diffusion coefficient; distances between ar/R residues and water molecules near them; pore length in the narrow zone; and protein flexibility (local bending angle of alpha helices). Mean, SD and ANOVA test were used for statistics.

Our results show that: i) the constriction at the ar/R site varies from a narrow to a wide conformation: a narrow state coincides with the absence of water molecules at the site; ii) there are differences in membrane electron density among M and C systems; iii) protein diffusion is DPPC>M>C; iv) the pore is longer in M; v) differences in protein flexibility are observed, especially in helices 1, 2 and 4. In conclusion, we present quantitative evidence that membrane composition subtly but significantly affects AQP1 dynamics. Our findings confirm the need for further progress in the regulation studies of the aquaporins by their lipid environment, avoiding generalized conclusions from a particular MDS system.

Section 2: Cardiovascular 1

3

P-wave dispersion in the electrocardiogram, its origin clarified

Carmona Puerta R [1], Lorenzo Martínez E [2], Chávez González E [1], Rabassa López-Calleja M.A [3], Castro Torres Y [4], Cruz Elizundia J.M [1], Padrón Peña G [1], Rodríguez González F [1]

[1]Servicio de Electrofisiología y Arritmología. Hospital Universitario Cardiocentro "Ernesto Guevara". Villa Clara, Cuba. [2]Departamento de Fisiología. Universidad de Ciencias Médicas de Villa Clara, Cuba. [3]Jefa del Comité Académico de Cardiología. Hospital Universitario Cardiocentro "Ernesto Guevara". Villa Clara, Cuba. [4]Unidad Coronaria. Hospital San Juan de Dios. Santiago de Chile, Chile.

Introduction: Local theory and the vectorial theory are used to explain the origin of P-wave dispersion (PWD). There are no previous studies that analyze both at the same time. Objectives: We set out to determine the implication of local and vectorial theories in the origin of PWD. Methods: Cross-sectional study in 153 randomly selected patients aged 18-70 years, undergoing electrophysiological study. Inhomogeneous atrial conduction was evaluated by atrial electrogram dispersion in terms of duration (EGM_{dur}dis) and morphology (EGM_{morph} dis). P-distal coronary sinus interval (P-DCS) was also measured. P-wave was measured twice, firstly at a calibration of 20 mm/mV and a sweep speed of 50 mm/s, enhancement 10x (basic measurement [BM]), and second time at sweep speed of 150 mm/s, enhancement 80-160x (high precision measurement [HPM]). The values are presented as median [interquartile range]. Results: PWD with BM was 48 ms [36-54 ms] while with HPM it was 4ms [0-10 ms], p<0.001. With BM, maximum and minimum P- wave duration presented a moderate correlation (r=0.342; p <0.001), using HPM it becomes strong (r = 0.750; p <0.001). In cases with P-DCS<80 ms (r = 0.965; p <0.001), but not with P-DCS≥80 ms (r = 0.649; p <0.001), the previous correlation became almost perfect with HPM. EGM_{dur}dis and EGM_{morph}dis were weak but significantly correlated with PWD. This correlation became moderate in patients with P- P-DCS≥80 ms and disappeared in those with P-DCS<80ms, using BM and HPM. Conclusion: Vectorial theory explains almost entirely the PWD phenomenon. Inhomogeneous conduction could be an additional mechanism to explain PWD, but its contribution is small.

4

The specific inhibition of the cardiac electrogenic sodium/bicarbonate cotransporter leads to cardiac hypertrophy.

Di Mattia RA[1], Blanco PG[2], Portiansky EL[3], Jaquenod De Giusti C[1], Diaz Zegarra LA[1], Valverde CA[1], Gonano LA[1], Aiello EA[1], Orlowski A[1]

[1]Centro de Investigaciones Cardiovasculares "Dr. Horacio Cingolani", Facultad de Ciencias Médicas, Universidad Nacional de La Plata-CONICET. La Plata, Argentina. [2]Servicio de Cardiología, Facultad de Veterinaria, Universidad Nacional de La Plata. La Plata, Argentina. [3]Laboratorio de Análisis de Imágenes, Facultad de Veterinaria, Universidad Nacional de La Plata-CONICET. La Plata, Argentina.

Introduction: The Na^+/HCO_3^- cotransporter (NBC) is one of the main alkalinizing transporters on cardiomyocytes. There are two isoforms of NBC: the electrogenic NBCe1 and the electroneutral NBCn1. Although both isoforms enters Na^+ into the cell, NBCe1 contributes with half of Na^+ per HCO_3^-, so it has a major efficiency. We have previously found a reduction of NBCe1 activity together with an increased NBCn1 activity in cardiac hypertrophy (CH) models.

Aims: We developed an interference RNA cloned in a cardiotropic adeno-associated vector (AAV9-shNBCe1) to study the effect of the specific inhibition of NBCe1 in CH. Methodology: We delivered the virus through a lateral tail vein injection in male 3 months old Wistar rats and then performed a series of studies to assess CH, using an AAV9-shControl as control. Data is expressed as means±S.E.M. and is compared with Student's t-test or two-way ANOVA test as needed. Results: After 30 days of injection, we confirm a significant reduction on NBCe1 ventricular expression and activity. In addition, we found an increase in left ventricular mass index obtained by echocardiography on hearts injected with AAV9-shNBCe1 (AAV9-shControl: 1.01±0.1; n=11; AAV9-shNBCe1*: 1.46±0.11, n=11; *p<0.05 vs AAV9-shControl). This result was consistent with cardiomyocytes' cross-sectional area analysis and an increase in ANP mRNA was found. There were no differences found in blood pressure. Furthermore, we discovered a compensatory increase in NBCn1 and Na^+/H^+ exchanger expression. Conclusion: Overall, these results suggest that the CH is developed, at least in part, by the decrease in NBCe1 expression. We propose that this reduction triggers a compensatory response involving the increase of the expression of the remaining alkalinizing transporters. This mechanism would in turn induce the enhancement of intracellular Na^+ levels, leading to Ca^{+2} overload trough Na^+/ Ca^{+2} exchanger acting through its reverse mode. Such increase of Ca^{+2} could lead to CH.

29

Cardiac Performance in a Familial Parkinson's disease Model

Santalla M[1, 2] Gómez IM[2], del Valle S[1], Ciocci Pardo A[2], Valverde CA[2], Ferrero P[1, 2].

[1] Departamento de Ciencias Básicas y Experimentales. UNNOBA. [2] Centro de Investigaciones Cardiovasculares "Dr. Horacio E. Cingolani" FCM, UNLP-CONICET

Introduction: Mutations in *PARK7*, which encodes DJ-1 protein, are associated with familial Parkinson´s disease (FPD). DJ-1 plays a key role in the maintenance of redox state and mitochondrial performance in cardiac tissue. Loss of DJ-1 function induced by mutations involved in FPD might affect cardiac performance. Objective: The objective was to investigate if the systemic deletion

of the DJ-1β gene (*Park* flies), the *Drosophila* ortholog of human DJ-1, affects the cardiac function in a *Drosophila melanogaster* genetic model of FPD. Methods: *Park* flies and wild-type flies were studied at 7 and 40 days after emerging from the puparium. Locomotor activity was evaluated by climbing assays. Cardiac performance was studied in semi-intact heart preparations tracking the movement of the heart by microscopy. Mitochondrial membrane potential was assessed using Rodamine-123 assay. Results: 7-day-old *Park* flies showed a reduced climbing ability consisted with a PD phenotype. Compared to control, young *Park* flies exhibited reduced heart rate (HR: beats/min) 136,1 ± 13,48 n=14 vs 100,2 ± 6,75 n=17; and contractility (µM) (23,19 ± 2,7 N=11 vs 15,31 ± 1,33 N=15). Diastolic interval (sec) was augmented (0,4 ± 0,04 N=14 vs 0,56 ± 0,04 N=17). Forty-day-old flies showed an accentuated reduction of HR (105 ± 9,03 N=12 vs 80,35 ± 6,7 N=15), a lengthening rate (µM/sec) of contraction (0.48 ± 0.07 N=9 vs 0.3 ± 0.04 N=15) and relaxation (0.47 ± 0.06 N=9 vs 0.25 ± 0.03 N=15). *Park* flies did not expressed changes in the mitochondrial state at 7 or 40 days. Data are mean ± SE. P-values were determined using Student's test. Conclusion: Our results show that systemic deletion of DJ-1β impairs the cardiac performance without changes in the mitochondrial state. These effects were observed in young flies, even before a motor impairment had been manifested, indicating that cardiac effects precede motor impairment.

30

Calcium/Calmodulin dependent Kinase II and Ca^{2+} alternans in cardiac myocytes: induction, prevention, or lack of effect?

Racioppi MF, Agüero R, Rizzardi F, Mattiazzi A, Vila Petroff M y Gonano LA. Centro de Investigaciones Cardiovasculares Horacio Cingolani. UNLP-CONICET.

Introduction: The Ca^{2+}/calmodulin dependent kinase II (CaMKII) phosphorylates multiple targets involved in cardiomyocytes Ca^{2+} cycling and its activity increases in response to high pacing frequencies. The role of CaMKII in the genesis of arrhythmogenic Ca^{2+} alternans has not been extensively studied and the available data results controversial showing both prevention and promotion of Ca^{2+} alternans.

Objectives: To determine if the activation of CaMKII impacts on the magnitude of Ca^{2+} alternans in nonfailing ventricular myocytes when these are paced at crescent frequencies. Materials and methods: Ventricular cardiomyocytes were obtained from wistar rats (8-12 weeks old) and from WT and S2814A mice after heart excision and enzymatic digestion. Cells were loaded with Fluo-4 and line-scanned in a confocal microscope to detect cytosolic Ca^{2+}. Pharmacological inhibition of CaMKII was tested with 2.5 µM of KN93. Cells were field stimulated at 1, 3, 4 and 5 Hz. Statistical analysis was performed by T test, data is presented as mean±SEM, n= number of cells. Results: In rat cardiomyocytes treated with vehicle (DMSO) and KN93 the average alternans ratio (the difference in amplitude between consecutive transients divided by the amplitude of the larger transient) elicited at 5 Hz was not significantly different (p=0.27, n= 20 and 12 respectively). Indeed, when comparing the AR of WT versus S2814A myocytes we did not find significant differences (p=0.69, n=18 per group). Conclusions: The pharmacological inhibition of CaMKII activity and the specific prevention of RyR2 phosphorylation at S2814 does not lead to changes in alternans magnitude. The physiological context in which alternans are evaluated could determine the relevance of CaMKII activity for alternans development and deserves further study given the clinical interest to use CaMKII inhibition as a cardiovascular therapy.

34

Effects of gallic acid on myocardial ischemia-reperfusion injury: involved mechanisms

González Arbelaez LF[1], Schinella GR[2], Mosca SM[1]
[1] Centro de Investigaciones Cardiovasculares ¨Dr Horacio E Cingolani¨ CCT-CONICET, [2]Facultad de Ciencias Médicas, Universidad Nacional de La Plata, La Plata, Buenos Aires, Argentina.

Introduction: It was previously demonstrated that gallic acid, a natural phenolic compound found in several fruits and medicinal plants, have several health-promoting effects. Objectives: To determine the effects of gallic acid on ischemia-reperfusion injury analyzing the involved mechanisms. Methods: Isolated rat hearts perfused by Langendorff system were assigned to the following groups:1)Non ischemic control (NIC):110 min of perfusion; Ischemic control (IC): 30 min of normothermic global ischemia and 60 min of reperfusion (R); GA group: 0.25, 0.5 and 1µM gallic acid was administered during the first 10 min of R. Infarct size (IS) was determined by TTC staining. Systolic and diastolic function were assessed by left ventricular developed pressure (LVDP) and left ventricular end diastolic pressure (LVEDP), respectively. Left ventricle of other hearts (n=3), submitted to the same protocols, were used to determine the expression of phosphorylated forms of Akt, eNOS, GSK-3β and PKCε by western blot. Data are given as means ± SE and analyzed using repeated measures of two-way analysis of variance (ANOVA) with Turkey´s post-test for multiple comparisons among groups. A p value <0.05 was considered significant. Results: 0,25 and 1 µM of GA did not modify the IS and post-ischemic myocardial function detected in IC group. 0,5 µM of GA decreased the IS [8±2% (n=6) vs 31±2% (n=9) in IC] and improved the post-ischemic recovery of myocardial function. At the end of R, LVDP and LVEDP were 61±4% and 27±3 mmHg vs 15±3% and 51±5 mmHg in IC, respectively). The expression of all kinases decreased approximately 50% of NIC value (considered as 100%) in IC and increased the same percentage in GA-treated hearts. Conclusion: The data show that acute treatment with gallic acid only at the onset of reperfusion decreased the infarct size and attenuated the post-ischemic myocardial contractility dysfunction through the Akt/GSK-3β/eNOS/PKCε dependent pathways.

50

Effects of meis1 overexpression in murine cardiomyocytes.

López AE1, Bauzá MDR1, Simonin JA2, Halek JM1, Crottogini A1, Belaich MN2, Olea FD1, Locatelli P1
1 INSTITUTO DE MEDICINA TRASLACIONAL, TRASPLANTE Y BIOINGENIERIA (IMETTYB- UNIVERSIDAD FAVALORO- CONICET), 2 Universidad Nacional de Quilmes.

Introduction: As ischemic heart disease is the main cause of death worldwide there is particular interest in developing gene therapies to induce adult cardiomyocyte (CM) mitosis, an approach that would warrant efficient electromechanical coupling of new cells to the myocardial sincitium. The transcription factor Meis1 was proposed as a CM cell cycle inhibitor in mice, as its expression level increases from postnatal day 1 to P7, when CMs proliferative window is closed.
Objectives: To transduce neonatal rat CMs with a baculoviral vector overexpressing meis1 (Bv.Meis1) and assess the effects on proliferation rate and the expression of angiogenic genes. Methods: Rat neonatal CMs were transduced with Bv.Meis1 at MOI 200. The effect of meis1 overexpression on cell proliferation was evaluated by cell count and MTS assay at 48 hours and 5 days post-transduction (PT). Angiogenic gene expression was assessed by RT-qPCR. Proliferation MTS assay was performed incubating HMEC cells with the supernatant of meis1 transfected CMs at the same time points. For statistical analysis we used t test (significance: $p < 0.05$). Results: Cell count and MTS proliferation assay revealed a decrease in cell division rate at 5 days PT. Number of cells: 359,156±27,278 Bv.Meis1 vs. 387,000 ±15,846 Bv.Null, $p<0.05$. Cell proliferation (MTS assay): 76.96±12.78% Bv. Meis1 vs. 100±13.41% Bv.Null, $p<0.01$. Proliferation evaluation by MTS assay on HMEC revealed increased cell division at 5 days PT. Cell proliferation: 118.7±20.99% Bv.Meis1 vs. 100±12.91% Bv.Null, $p<0.05$. vegf and angiogenin expression were increased in CMs transduced with Bv.Meis1 at 48 hours PT (vegf fold increase: 1.269±0,1946 Bv.Meis1 vs. 1.004±0,1079 Bv.Null, $p<0.05$, and angiogenin fold increase: 1.190±0.1398 Bv.Meis1 vs. 1±0.0153 Bv.Null, $p<0.05$). Conclusion: The transduction of neonatal rat cardiomyocytes with a baculovirus encoding meis1 confirmed the cell cycle inhibitor role in CMs. However, the overexpression of the angiogenic factors angiogenin and vegf suggest that Meis1 could exert an angiogenic role which needs to be confirmed with further experiments.

58

Post-ischemic mitochondrial and myocardial improvement by a non-alcoholic extract of Argentinian red wine in mice

Fantinelli JC, Ciocci Pardo A, Said M, Mosca SM
Centro de Investigaciones Cardiovasculares ¨Dr Horacio E Cingolani¨, Universidad Nacional de La Plata, La Plata, Buenos Aires, Argentina.

Introduction: We previously reported that the treatment of a non-alcoholic extract of Cabernet-Sauvignon red wine (RWE) was able to attenuate the myocardial stunning. Objectives: To assess the effects of RWE on myocardium and mitochondria submitted to severe ischemia leading to irreversible injury. Methods: Isovolumic perfused mice hearts were exposed after stabilization to a 30-min global ischemic period (GI) followed by 2 hours of reperfusion (R) in absence (ischemic control hearts: IC) and presence of RWE infused prior to ischemia and early during reperfusion. Infarct size (IS) and lactate dehydrogenase (LDH) release were measured. Left ventricular developed pressure (LVDP), left ventricular end diastolic pressure (LVEDP) and $-dP/dt_{max}$ were used to assess myocardial systolic function, diastolic stiffness and myocardial relaxation, respectively. In isolated mitochondria from hearts submitted to 30-min of GI and 10 min of R, untreated and treated with RWE, the permeability transition pore (mPTP) resistance to opening Ca^{2+}-mediatedand membrane potential were assessed. Data are given as means ± SE and the analysis was performed using repeated measures of two-way analysis of variance (ANOVA) with Turkey´s post-test for multiple comparisons among groups. A p value <0.05 was considered significant. Results: RWE significantly decreased the IS (23±3% vs 41±4% in IC, n = 8) and LDH level (199±76U/L vs 519±88U/L in IC, n=8). At the end of R, LVDP and $-dP/dt_{max}$ were 32±6 % and 30 ±4% vs 16±5 % and 11± 4% in IC, respectively, n=8). LVEDP was not modify by RWE. Mitochondria from RWE treated hearts (n=4) showed a greater mPTP resistance to opening Ca^{2+}-mediated and a lesser depolarization than untreated hearts mitochondria (n=4). Conclusion: These data demonstrated that RWE decreased the cell death, reduced the post-ischemic myocardial contractility and relaxation dysfunction and improved the mitochondrial state at reperfusion.

80

Mechanism of Calcium Cardiac alternans: Insights from a human myocyte mathematical model.

Cely-Ortiz CA[1], Gonano LA[1], Valverde CA[1], Lascano EC[2], Mattiazzi A[1]
[1] Centro de Investigaciones Cardiovasculares “Dr. Horacio Cingolani”, Facultad de Ciencias Médicas, UNLP, Conicet La Plata. [2] Universidad Favaloro, Buenos Aires.

Introduction: Cardiac calcium (Ca) transients can alternate in a large-small sequence from one beat to the next, a condition called Ca alternans (CaA), that usually occurs during rapid pacing or in some pathological conditions.
The mechanisms of CaA remain controversial. The two main mechanisms under dispute are 1. Ca release refractoriness and 2. Inability of the sarcoplasmic reticulum (SR) Ca-ATPase (SERCA2a) to cope with the increased velocity of SR Ca uptake imposed by tachycardia. Aims and Methods: Using the Lascano-Negroni human cardiac myocyte mathematical model, known to accurately reproduce intracellular Ca handling, we explored these two possibilities.
Results: In myocytes mimicking the behavior of WT mice myocytes, increasing stimulation frequency (from 70 to 182 bpm) at 1.2 mM external Ca, evoked an immediate alternation of the action potential (AP) and peak Ca current (ICaL) associated to CaA. After

a few beats, AP and ICaL alternans stabilized whereas SR Ca content, SR Ca release and Ca transient increased until they reached a plateau. Although SR Ca content remained high and constant, SR Ca release began to fluctuate (alternate). These results indicate that SERCA2a is not the limiting factor for Ca release and that CaA are reflecting an increased refractoriness at the level of the mechanisms that release Ca. To further test this idea, similar simulations were performed in myocytes mimicking a RyR2 or a SERCA2a gain-of-function. While the RyR2 gain-of-function completely avoids CaA, SERCA2a gain-of-function increased SR Ca uptake (showing again that SERCA2a function was not limited), but exacerbates CaA, confirming alterations in Ca release refractoriness. Conclusions: The model suggest that Ca release refractoriness and not SERCA2a function, governs the onset of intracellular CaA.

84

Characterization of single nucleotide polymorphism variants in genes associated with autonomic modulation due to heart rate variability in a group of weightlifting athletes

Mina-Paz Y [1 3], Jordan K[2], Matta-Miramar A.J[1 3], Zambrano-Ríos D.C [1 3], García-Vallejo F[1]

[1] Laboratory of Molecular Biology. Department of Physiological Sciences, School of Basic Sciences, Faculty of Health, Universidad del Valle, Cali, Colombia. [2] Department of Biology, Georgia Institute of Technology, Atlanta USA. [3] Faculty of Education and Sports Sciences, Escuela Nacional del Deporte, Cali, Colombia. Corresponding author email: Yecid.mina@endeporte.edu.co

Introduction: During a training process, there may be marked physiological differences in the behavior of the heart rate (HR) which is determined by the autonomic nervous system modulation that includes the sympathetic or parasympathetic influence. Such influence affects the variability between HR, and the recovery rate, even in aerobically healthy individuals. Associated with this, the genetic variability in the behavior of the autonomic modulation between R-R intervals measured by HR variation, before, during, and after training, turns out to be different allowing a differential sports development.

Objective: To identify the differential presence of Single Nucleotide Polymorphisms (SNPs) in genes which are associated with autonomic modulation in a group of weightlifting athletes. Methods: To participate in the present study, we randomly selected a weightlifting athlete's group between 14 and 25 years old. A search of SNPs variants associated in ACHE, CHMR2 genes was performed to full genome through Next-Generation Sequencing and later we performed a bioinformatic analysis. Results: The most representative results in the five genes studied were for the M2-type muscarinic acetylcholine receptor gene -CHMR2- in the polymorphisms rs17168815, [G>C/G>T] intron variant (40. 50 sec); rs6943656 [A>G] (0, 20, 30 sec) and rs324640 [G>A / G>T] (no sec); however, the rs8191992 [T>A] SNP was not significant. Moreover, by coexpression networks analysis, we found a variable degree of association of SNPs in CHMR2 with other genes including to BCTA1, ALG10B, BCL11A, CLPB, GNG11, CAV1, ADRA1V, CCDC141. Conclusion: In the present study, athletes group exhibited significant statistics differences of CHRM2 SNP variation that allow them improving adaptations on HR decreasing during sports practice. Identifying of these SNPs by the first time in a Colombian group of weightlifting athletes, shall allow us to optimize changes in HR variability during sports preparation, since currently only the physiological condition is used as a tool to enhance training and obtain a sporting achievement.

Keywords: heart rate variability, autonomic modulation, anaerobic exercise

112

Salt-loaded pregnant rats as an animal model of preeclampsia: is it a valid model?

Rojas D[1], Abad C[2], Piñero S[1], Chiarello DI[3], Proverbio F[1], Marín R[1]

[1] Center for Biophysics and Biochemistry (CBB), Venezuelan Institute for Scientific Research (IVIC), AP 21827, Caracas 1020A, Venezuela. [2] Department of Pharmacology and Toxicology, Faculty of Pharmacy in Hradec Kralove, Charles University, Akademika Heyrovskeho 1203, Hradec Kralove 500 05, Czech. [3] Cellular Signaling and Differentiation Laboratory (CSDL), School of Medical Technology, Health Sciences Faculty, Universidad San Sebastián, Santiago 7510157, Chile.

Introduction: Preeclampsia is a pregnancy-specific syndrome with multisystem involvement which leads to fetal, neonatal, and maternal morbidity and mortality. To try to unveil the pathophysiological mechanisms involved in the development of preeclampsia, animal models have been investigated. In this regard, a model of salt-loaded pregnant rats has been studied, showing to share several pathological characteristics of the preeclamptic women. In this study, it was compared several physiological measurements, fetal and placental parameters between preeclamptic pregnant women and salt-loaded pregnant rats. It was also compared biochemical measurements of red blood cell ghosts and placental homogenates from both preeclamptic pregnant women and salt-loaded pregnant rats. A comparison of the effects of the treatment with magnesium sulfate ($MgSO_4$) on several of these parameters was also included in the current study. Methods: Salt-loaded pregnant rats received 1.8% NaCl solution ad libitum as a beverage for seven days, starting on 15th day of pregnancy. Red blood cells and placenta were obtained from both preeclamptic pregnant women and salt-loaded pregnant rats. Results: Salt-loaded pregnant rats showed, similar to preeclamptic women, showed an increased level of lipid peroxidation and a lowered Ca^{2+}-ATPase activity in placental and red blood cell ghosts, as well as an increased osmotic fragility of the red blood cells. $MgSO_4$ treatment of preeclamptic pregnant women modifies both the Ca^{2+}-ATPase activity and the level of lipid peroxidation of their red blood cell membranes, reaching values similar to those of normotensive pregnant women. The diminution of the level of lipid peroxidation by $MgSO_4$, can account for the increase in Ca-ATPase activity. Similar results were obtained for the effect of $MgSO_4$ in salt-loaded pregnant rats. Conclusion: Salt-loaded pregnant rats represent a valid model for the study of preeclampsia.

Section 3: Vascular – Renal - Respiratory

22

Effect of *Spirulina maxima* on vascular reactivity in aortic rings from rats fed a diet enriched with reheated vegetable oil.

López-Canales OA[1], Ubaldo-Reyes LM[2], Juárez-Oropeza MA[3], Paredes-Carbajal MC[1].
[1] Department of Physiology, Faculty of Medicine, Universidad Nacional Autónoma de México. [2] Department of Anatomy, Faculty of Medicine, Universidad Nacional Autónoma de México. [3]Department of Biochemistry, Faculty of Medicine, Universidad Nacional Autónoma de México.

Introduction. It has been shown that reheating oil is able to produce trans fatty acids that have been linked to impaired vascular function. Supplementation of *Spirulina maxima* in the diet has been shown to have cardioprotective effects, however, it is not yet described if it can improve the vascular response of animals subjected to a diet rich in reheated vegetable oil. Objective. Determine the effect of Spirulina maxima on the vascular response of rats fed reheated vegetable oil at 7.5%. Methods. Adult male Wistar rats were divided into 3 groups: Group A. Control diet; Group B. Diet enriched with reheated corn oil at 7.5% and group C. Group B diet plus 5% of Spirulina maxima. After 7 weeks, *in vitro* studies were performed in aortic rings with and without endothelium to evaluate vasomotor responses induced by phenylephrine and carbachol. Results are shown as concentration-response curves where each point represents the mean ± S.D. (n=6). Results. The addition of *Spirulina maxima* to the diet had no significant effect on the contractile responses to phenylephrine (2.59±0.38 vs 2.52±0.21 g). The C-R curve to carbachol in aortic rings with endothelium from animals with diet B showed an increase in pD2 (-5.32) and decrease in relaxation (34.81±12.37% of contraction) compared to group A (-6.32 and 5.10±5.27 % respectively), while group C, reestablished vascular function by decreasing pD2 (-6.10) and increasing vasorelaxation (16.62±14.78 of contraction). The addition of indomethacin or L-NAME showed a significant change in the carbachol-induced response in both groups B and C. Conclusion. The diet with 7.5% reheated oil causes a decrease in muscarinic receptor-dependent nitric oxide synthesis/release and an increase in a COX-dependent vasoconstrictor metabolite. Furthermore, the results suggest that *Spirulina maxima* prevents these impairments and could be used to counteract the deleterious effects of reheated vegetable oil diet.

26

Analysis of the spatial correlation between NK1 receptor and glycine transporters immunolabelling in preBötzinger complex cells.

Diaz-Escarcega R[1]; Miranda-Arango M[2]; Olmos-Pastoresa Carol A[1]; López-Meraz ML[1]; Beltran-Parrazal L[1]; Morgado-Valle C[1].
[1] Instituto de Investigaciones Cerebrales, Universidad Veracruzana, Xalapa, Veracruz. Mexico. [2] Department of Biological Sciences, The University of Texas at El Paso, El Paso, TX. USA

Introduction: The preBötzinger complex p(reBötC) is a heterogeneous interneuronal network that generates the inspiratory phase of the respiratory rhythm. It contains excitatory glutamatergic and inhibitory glycinergic and gabaergic neurons. Immunoreactivity to neurokinin-1 receptor (NK1R), whose endogenous ligand is substance P, is an anatomical marker for preBötC neurons. Efforts to characterize the profile of the cells coexisting in the preBötC include immunohistochemistry, mRNA hybridization and single-cell mRNA analysis. Aim: Here, we aimed to quantified the coexpression of tyrosine hydroxylase (TH), or glycine transporters (GlyT) GlyT1 or GlyT2, with NK1R in cells in the preBötC area. Methods: We used the Protein proximity index (PPI) as a measure of colocalization of two immunofluorescent signals in confocal images from mouse preBötC. We quantified the number of DAPI labelled nuclei, and the number of NK1R, GlyT1, GlyT2 and, TH immunolabelled cells. We quantified the PPI and cross-correlation of images containing double immunolabelling for NK1R-GlyT1, NK1R-GlyT2 and NK1R-TH combinations.
Results: We found that ~14.4% of nuclei do not colocalized with any immunolabel, suggesting that they correspond to glial cells. We found higher than expected PPI and cross-correlation of NK1R label with TH label, and of NK1R label with GlyT1 label. Conclusions: We discuss the functional meaning of our findings.

33

Decreased expression of CB_2 receptors in atherosclerosis is associated to a vasorelaxing effect of HU308 on aortic rings

Álvarez-Valadez, M.d.R.[1]; Virgen-Ortiz, A.[1]; Rodríguez-Hernández, A.[2]; CeballosGutiérrez, A.[2]; Figueroa-Gutiérrez, A.[2]; Andrade, F.[3] and Sánchez-Pastor, E.A.[1].
[1]Centro Universitario de Investigaciones Biomédicas, Universidad de Colima, Colima 28045, México. [2]Facultad de Medicina, Universidad de Colima, Colima 28040, México. [3]Tecnológico Nacional de México/Instituto Tecnológico de Colima, Villa de Álvarez 28976, México.

Introduction: It has been suggested that dysregulation of the endocannabinoid system is involved in the pathophysiology of atherosclerosis. Some studies have associated activation of CB_2 receptors (CB_2R) to reduced atherogenic effect. However, there are no studies that demonstrate the relationship between CB_2R 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 CB_2R 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. CB_2R expression and localization in aortic rings

was evaluated by immunohistochemical staining and confocal microscopy. Also, the role of CB_2R on vascular tension was determined in isometric tension recordings using HU308 (CB_2R agonist). Blood pressure (BP) was monitored using a sphygmomanometric method, for 90 min after intravenous administration of HU308. The data were analyzed by one-way ANOVA and showed as mean ± SEM (n = 8). Results: CB_2R expression in smooth muscle of rat aorta decreased in severe lesions compared with control (0.66±0.08 vs 1 UA, p = 0.0003). Moreover, while CB_2R activation elicited vasoconstriction in healthy rats (118.57±3.72 %; p < 0.0001), it caused vasorelaxation in aortic rings with mild (92.89±2.19 %; p < 0.0292) and severe lesions (94.06±1.83 %; p = 0.0057). BP at 90 min, increased in mild lesions compared to control (Systolic pressure = 149.87±6.62 vs 110.87±6.71 mmHg, p = 0.0002; Diastolic pressure = 115.91±7.88 vs 73.35±4.55 mmHg, p < 0.0001), while in severe lesions it was not modified. Conclusions: Expression of CB_2R 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.

41

P-selectin and vWF mediates platelet adhesion to endothelial cells induced by oxidized high-density lipoprotein through LOX-1/NOX-2/ROS pathway.

Prado Y[1, 2], Pérez L[1], Simon F[1, 2].
[1] Laboratorio de Fisiopatología integrativa, Departamento de Ciencias Biológicas, Facultad Ciencias de la Vida, Universidad Andrés Bello, Chile. [2] Instituto Milenio en Inmunología e Inmunoterapia, Chile

Introduction: The low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are the main members of bloodstream-circulating lipoproteins. LDL is associated with increased risk of vascular diseases, while HDL is quite recognized as an atheroprotective factor by prevents vascular diseases such as atherosclerosis and coronary artery disease. HDL signaling preserve vascular endothelial function including hemostasis regulation, due exhibits strong antithrombotic activity, improving fibrinolytic capacity and supporting antiinflammatory actions. Systemic inflammatory conditions, including sepsis, hypertension and diabetes are characterized by a prominent oxidative environment promoting oxidative modifications to several macromolecules. Consequently, circulating lipoproteins are oxidized through modifications mediated by oxidative enzymes and non-enzymatic attacks produced by ROS. Noteworthy, it has been shown that HDL is more susceptible than LDL to oxidation, and importantly, the oxidized form of HDL (oxHDL), has shown reduced atheroprotective properties due its pro-inflammatory and pro-thrombotic activity. Aim: To evaluate platelet adhesion to endothelial cells (ECs) induced by oxHDL and elucidate the underlying mechanisms involved in this process. Methodology: Platelets isolated from healthy volunteers were co-cultured with human ECs stimulated with native HDL and oxHDL and platelet adhesion to ECs was measured in the presence of P-selectin, vWF, LOX-1 and NOX inhibitors and antioxidant and reducing agents. Results are presented as mean ± SD (n = 6 - 11). Significant differences were assessed by one-way ANOVA and Dunnett's post hoc test. The experimental protocols were approved by the Committee of Bioethics and Biosafety from Universidad Andres Bello. Results: Inhibition of P-selectin and vWF expression decreased oxHDL-induced platelet adhesion to ECs. Furthermore, oxHDL-induced platelet adhesion to ECs was inhibited by the LOX-1/NOX-2/ROS pathway inhibitors. Finally, P-selectin and vWF expression was decreased by LOX-1/NOX-2/ROS pathway inhibitors. Conclusion: P-selectin and vWF mediates platelet adhesion to ECs induced by oxHDL through LOX-1/NOX-2/ROS pathway. Acknowledgments. Fondecyt Regular 1201039.

45

Role of calcium channel TRPV4 in the Acuaporin 2-dependent renal cell migration

Rivera M.F., Beltramone N., Rivarola V., Ford P., Capurro C., Di Giusto G.
Laboratorio de Biomembranas, IFIBIO-HOUSSAY (UBA-CONICET), Facultad de Medicina, UBA.

We have previously shown that Aquaporin 2 (AQP2), in addition to its canonical role as a water channel, promotes renal cell migration. This promigratory effect is due, at least in part, to the modulation of Na+/H+ exchanger (NHE1) activity. Since NHE1 activity is highly modulated by calcium and we showed a physical and functional interaction between AQP2 and calcium channel TRPV4, we propose to further investigate TRPV4 contribution in AQP2-dependent renal cell migration. For experimental procedures, we used a renal cell line stably transfected with AQP2: AQP2-RCCD1. We evaluated TRPV4 participation in collective and individual cell migration through wound healing and cell tracking assays in presence of the potent specific agonist GSK1016790A (GSK, 10nM) and the selective inhibitor HC-067047 (HC, 10µM). Cell viability was checked with trypan blue staining. Finally, TRPV4 localization was analyzed with immunofluorescence assays. Our results showed that, both inhibition and activation of TRPV4, reduce collective cell migration (Control: 30.44±0.59%, n=39; HC: 24.72±0.92%, n=20; GSK: 15.65±1.79%, n=9; p<0,001) and directionally index (D, Control: 0.921±0.007, n=54; HC: 0.804±0.017, n=5; GSK: 0.666±0.028, n=63; p<0.001). Viability assays demonstrated that decreased cell migration is not due to an increment in percentage of cell death (Control: 1.04±0.23%, n=7; HC: 1.21±0.30%, n=3, ns; GSK: 1.79±0.40%, n=4, ns). We have already shown that lamellipodia of AQP2-expressing cells have high TRPV4 expression but after GSK treatment its localization changes and disappears from lamellipodia (AU, Control: 1371±79, n=74; GSK: 492±82, n=15, p<0.001), perhaps explaining the decreased migration when GSK is used. Our results demonstrated that, in the presence of AQP2, the mechanosensitive TRPV4 is active during lamellipodia protrusion, but additional stimulation leads to its endocytosis preserving cells of calcium damage. AQP2/TRPV4 interplay contributes to mechanisms governing migratory AQP2-dependent behavior, supporting the idea that transport proteins do not act isolatedly but in networks of functionally cooperating units.

47

Vascular endothelium modifications in a high-fat diet-induced obesity model

Ubaldo-Reyes LM[1], López-Canales OA[2], Ángeles-Castellanos AM[1], Paredes-Carbajal MC[2]

[1]Department of Anatomy, Faculty of Medicine, Universidad Nacional Autónoma de México. [2]Department of Physiology, Faculty of Medicine, Universidad Nacional Autónoma de México.

Introduction: Obesity-induced by a high-fat diet causes metabolic and cardiovascular alterations. When describing diets, the effects on weight, adiposity, and glucose are usually included. However, functional modifications undergone by the vascular endothelium remain unclear. Objective: Analyze the effects of a fatty acids-rich diet on *in vivo* blood pressure and vasomotor responses of rat aortic rings to phenylephrine and carbachol. Methods: Adult male Wistar rats were randomly assigned to one of two conditions: an *ad-libitum* control group (CTRL) or a high-fat-diet 60% group (HFD). In both groups, blood pressure (indirect method), food, and water consumption were quantified daily throughout the experimental period. After eight weeks of diet, *in vitro* studies were performed in aortic rings with and without endothelium to evaluate vasomotor responses induced by phenylephrine and carbachol. Results are shown as the mean ± S.D. (n=6). Results. In the HFD group, since the sixth week, an increase in both systolic and diastolic blood pressure was found, respect to the CTRL group (99.79±7.79 vs 126.1±5.85 mmHg) and (69.65±5.95 vs 95.61±3.05 mmHg), respectively. No changes in heart rate were observed. In aortic rings with and without endothelium, no significant effects were observed on the response to phenylephrine (10^{-5} M) between HFD and CTRL groups (2.08±0.39 vs 2.55±0.60g). However, in the HFD group, a decrease in the maximal vasodilator response to carbachol (10^{-5} M) regarding the CTRL group was observed (5.10±5.27 vs 19.7±27.09 %, respectively). Indomethacin (10^{-6} M) in the HFD group, decreased the maximal relaxation induced by carbachol, respect the CTRL group (4.35±5.54 vs 25.24±11, respectively). Conclusion:. The results show that *in vivo*, a fat-enriched diet causes hypertension. While *in vitro*, the endothelium decreased the synthesis/release of nitric oxide activated by muscarinic receptors and increased the synthesis of prostanoids dependent on the cyclooxygenase pathway.

Grant Support PAPIIT-UNAM IA207321

49

L-NAME arterial hypertension induces ocular hypertension and morphological and molecular changes in the cornea

Santana-Garrido Á [1,2], Reyes-Goya C[1], André H[3], Vázquez CM[1,2] and Mate A[1,2]

[1] Departamento de Fisiología, Facultad de Farmacia, Universidad de Sevilla, 41012 Sevilla, Spain [2] Epidemiología Clínica y Riesgo Cardiovascular, Instituto de Biomedicina de Sevilla (IBIS), Hospital Universitario Virgen del Rocío/Consejo Superior de Investigaciones Científicas/Universidad de Sevilla, 41013 Sevilla, Spain. [3] Department of Clinical Neuroscience, St. Erik Eye Hospital, Karolinska Institutet, 11282 Stockholm, Sweden.

Introduction: Oxidative stress, inflammation and fibrosis have crucial interplay in the pathophysiology of ocular pathologies being able to produce vision loss, for example in corneal diseases. Arterial hypertension (AH) leads to oxidative and inflammatory imbalance contributing to the development of fibrogenic progress in many hypertensive target organs. Objective: Despite the harmful impact of AH on the retina, its effects on the cornea have been studying scarcely. Here we aimed to design the highlighted effects of severe AH in the cornea. Methods: To this end, AH was induced by the administration of NG-nitro-L-argininemethyl-ester (L-NAME) in 10-12-week-old male C57B/6J mice, monitoring weekly blood and intraocular pressure (IOP) by rebound tonometry. Morphological changes and ROSgeneration by NAPDH oxidase were analyzed, as well as the localization/expression of NOX isoforms (NOX1, NOX2 and NOX4) and inflammatory biomarkers (PPARα-γ, IL-1β, IL-6, IL-10, TNF-α and COX-2). Furthermore, Masson trichrome and Sirius red staining were carried out to explore the fibrotic status of the cornea, and the expression of collagen isoforms and MMPs/TIMPs ratio were performed in order to evaluate the participation of collagen metabolism. Data are presented as means±SEM of at least n=6, and were subjected to unpaired Student's t-test or ANOVA. Results: Hypertensive animals showed an increase in IOP values together with a thinner cornea when compared with normotensive animals. Moreover, AH increased NADPH oxidase activity and ROS-generation in the cornea, accompanied by transcriptional upregulation of NOX isoforms and inflammatory biomarkers. Besides L-NAME-treated animals presented a fibrotic cornea, with overexpression of collagen isoforms and a reduction of the agents implicated in its degradation. Conclusion: We report structural changes in the cornea and high IOP values in LNAME-hypertensive animals and we strengthen the importance of NADPH oxidase as a major ROS-generating enzyme system involved in oxidative, inflammatory and fibrotic events in the cornea.

70

Angio-arteriogenesis: Purinergic receptors P2Y1 and P2Y2 are downregulated in critical limb ischemia

Nuñez Pedrozo C.N.[1]; Peralta T.[1]; Crottogini A.J.[1]; Cuniberti L.[1]; Olea FD.[1]

[1] Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTYB-Universidad Favaloro-CONICET).

Introduction: Angiogenic stimulation has been the main experimental strategy for the treatment of peripheral artery disease (PAD). In recent years, P2Y receptors have been implicated in several angio-arteriogenic functions. In particular, P2RY1 and P2RY2 are associated with endothelial sprouting, transactivation of KDR and ERK1/2, neointima formation, angiogenesis and arteriogenesis.

Objectives: Based on recently published transcriptomes on the progression of PAD, we compared gene expression of P2RY receptors, and its associated biological processes in patients with ischemic claudicating PAD (IC), critical limb ischemia (CLI), and healthy adults (HA). Methods: Muscle biopsy data were obtained from the GEO (GSE120642) and processed in the UseGalaxy platform. Transcriptomic analyses were performed employing the EdgeR package with an adjusted p-value (FDR) ≤0.05 and fold change (FC) < 1 or > 1. The raw counts were normalized with the TMM method and the differential gene expression was analyzed with ExactTest. The results were subjected to GO enrichment analysis. Results: Comparing IC (n=4) vs HA (n=4) groups, 42 genes were differentially expressed, while in CLI (n=4) vs HA groups 2123 genes were significantly altered (FDR ≤0.05, logFC < 1 or > 1). We observed a differential expression of P2RY1 (FDR ≤ 0.05) and P2RY2 (FDR ≤ 0.05) only between CLI and HA groups. GO analysis showed a negative regulation of vascular smooth muscle cell proliferation (p <0.05), a positive regulation of ERK1 and ERK2 cascade (p <0.05) and a positive regulation of sprouting angiogenesis (p <0.05). Conclusion: The observed down-regulation of P2RY1 and P2RY2 in the most severe stage of PAD, added to the alteration of biological processes related to angio-arteriogenesis, suggest that those receptors would be strong candidates for future trials of gene therapy. Further research on the role of each receptor in vascular pathologies would help to develop new strategies for PAD.

92

Effects of renal ischemia and Angiotensin II type 2 receptor (AT2R) agonism on end-binding protein 1 (EB1) expression

Fussi MF[1]; Hidalgo F[2]; Pariani A[2]; Rivabella Maknis T[2]; Girardini JE[3].; Monasterolo LA[1,4,5]; Larocca MC[2]; Molinas SM[1,5]
[1]Área Farmacología. Facultad de Cs. Bioquímicas y Farmacéuticas. Universidad Nacional de Rosario. [2]IFISE-CONICET. [3]IDICER–CONICET. [4]CIUNR. [5]CONICET. E-mail: sara_molinas@yahoo.com.ar

Introduction: Ischemic injury is one of the main causes of acute kidney injury (AKI). Tubular remodeling in response to AKI involves the dedifferentiation and regeneration of the remaining epithelial tubular cells. Microtubule dynamic instability plays a central role in renal repair after AKI. EB1 is a central regulator of microtubule dynamic instability that participates in tubulogenesis. We demonstrated that AT2R activation by its agonist C21, prevented tubular epithelial cell damage induced by ischemic injury in a rat model and in MDCK cells. Objective: To evaluate if the renoprotective effects of C21 were associated with changes in EB1 expression. Methods: Male Wistar rats (n=6) underwent 40 min unilateral renal ischemia + 1 day of reperfusion (IR). C21, 0.3mg/Kg/d i.p. (Vicore Pharma), was administered for two days prior to IR or sham operation. MDCK cells were grown in conditions that assure well-defined epithelial polarity (n=3).To simulate ischemia by ATP depletion, cells were exposed to antimycin A (10 uM) and 2-deoxyglucose (10 mM) during 90 min followed by 24 h reoxigenation. Cells were pretreated with C21 1mM or its vehicle during 24 h. EB1 protein abundance was evaluated in renal cortex or in MDCK lysates by western blot. Data are expressed as mean±SEM. Statistics: ANOVA followed by Newman-Keuls test. Results: In rats, IR damage reduced EB1 expression (-50%*). C21 increased EB1 expression in sham (+230%*) and IR (+83%*,#) animals. Similarly, MDCK cells submitted to IR showed a decrease in EB1 expression (-72%*) that was partially prevented by C21(-25%*,#). C21 increased EB1 expression in control (+45%*). *p 0.05 vs C, #p<0.5 vs IR. Conclusion: we demonstrated that IR induced a decrease in EB1 expression in renal tubular cells. AT2R activation by C21 promoted an increase in EB1 expression which could mediate C21 renoprotective effects by modulating microtubule dynamic instability.

105

Chronic treatment with Zn-Telmisartan improves cardiac function and the protective renin-angiotensin-system axis in ovariectomized spontaneously hypertensive rats

Martínez VR[1]. Díaz RG[1], Pérez NG[1], Vélez Rueda JO[1], Lofeudo JM[1], Silva MG[2], Gironacci MM[2], Williams PAM[3], De Giusti VC[1].
[1]Centro de Investigaciones Cardiovasculares (CIC-CONICET-UNLP). [2]Instituto de Química y Fisicoquímica Biológicas (IQUIFIB-CONICET-UBA). [3]Centro de Química Inorgánica (CEQUINOR-CONICET-UNLP)

During menopause, an imbalance between the pressor Angiotensin II (AngII) and the protective (Ang 1-7) arms of the renin-angiotensin-system (RAS) exists, which leads to oxidative stress, hypertension and cardiac dysfunction. Restoring RAS balance would prevent cardiovascular diseases in menopausal women. We have previously modified the structure of the AngII receptor blocker telmisartan (Telm) with Zinc (ZnTelm), demonstrating higher drug effectiveness. In this work, we examined whether chronic ZnTelm treatment is a better alternative to prevent cardiovascular damage during menopause than Telm alone. We used 16-week-old spontaneously hypertensive rats (SHR) which were sham-operated or bilateral ovariectomized (OVX-SHR). OVX-SHR rats were randomly divided into 3 groups: non-treated (control), treated with Telm or ZnTelm (10 or 11 mg/kg/day, respectively, through drinking water for 8 weeks). Results (n=6 per group) were analyzed by ANOVA. * p <0.05 vs control and # p<0.05 vs Telm. ZnTelm promoted higher reduction in blood pressure (in mmHg, control: 185±3, Telm: 128±6*, ZnTelm: 107±5*#) and cardiac hypertrophy (echocardiographic determination) than Telm. Isolated papillary muscles exhibited less myocardial stiffness than control in both treatment groups (in g/mm^2, control: 1.35±0.24, Telm: 0.69±0.05*, ZnTelm: 0.67±0.04*). ZnTelmtreatment markedly decreased myocardial reactive oxygen species (in % of control: Telm:93.6±4.7, ZnTelm: 55.5±3.4*#) and lipid peroxidation (in % of control: Telm: 98.8±3.4 and ZnTelm: 55±5.3*#). Radioimmunoassay measurement of cardiac Angiotensins demonstrated that ZnTelm induced a decrease in AngII level (in pg/mg, control: 0.87±0.02, Telm: 0.34±0.05, ZnTelm: 0.24±0.04*#), and an increase in Ang 1-7 (in pg/mg, control: 8.6±0.1, Telm: 22,01±0.3, ZnTelm: 24.2±0.8*#). Our results suggest that addition of zinc to an antihypertensive drug improves its activity, stimulating the protective RAS axis, thereby strengthening its cardioprotective benefits such as reducing oxidative stress and improving diastolic cardiac function. Further experiments are needed to elucidate its mechanism of action.

Section 4: Endocrine and Digestive 1

5

Hemeoxygenase 1 inhibition exacerbates cholestatic injury in bile duct ligated rats

[1]Martín PL, [1]Taurizano D, [1]Razori MV, [2]Massa EM, [3]Roma S, [1]Roma MG, [1, 2]Basiglio CL
[1]Instituto de Fisiología Experimental (IFISE - CONICET), [2]Area Bioquímica Clínica; Fac. Ciencias Bioquímicas y Farmacéuticas, UNR. [3]Area Histología, Fac. Ciencias Médicas, UNR. Rosario, Argentina

Introduction: We showed that hemeoxygenase-1 (HO1) induction, and consequent bilirubin (BR) elevation, protects the liver from oxidative-stress (OS)-induced cholestasis *in vivo*. Aim: To further characterize the protective role of BR, by evaluating the effect of HO1 inhibition at early stages of obstructive cholestasis. Methodology: Male Wistar rats were subjected to a 7-day bile-duct ligation (BDL, *n*=6) or sham surgery (Sh, *n*=5). HO1 was inhibited with Zn (II) protoporphyrin IX (PP, 25 mg/Kg b.w., i.p., 24h before BDL (PP+BDL, *n*=6) or Sh (PP+Sh, *n*=5). Blood samples were obtained before surgery (BS1) and before euthanasia (BS2), and BR, alanine-aminotransferase (ALT), alkaline phosphatase (ALP) and pseudocholinesterase (CHE) were determined. Liver was removed to assess lipid peroxidation and histological damage. Results (media±SD for BS1/BS2 in Sh; PP+Sh; BDL; PP+BDL) were, respectively: BR (mg/dL) N.D./0.11±0.04; N.D./0.17±0.05; N.D./8.60±0.15[a]; N.D./0.50±0.08[a,b]. ALT(U/L) 49±6/40±4; 72±18/52±21; 153±35/206±39[a]; 169±24/211±35[a]. ALP(U/L) 447±94/731±80; 469±77/740±107; 423±96/1430±184[a]; 487±90/1931±220[a,b]; CHE(U/L) 311±70/337±71; 274±40/315±29; 417±60/363±70; 296±51/253±48; [(a)]p<0.05 *vs* BS1/Sh; [(b)]p<0.05 *vs* BDL (Kruskal-Wallis' test followed by Dunn's multiple-comparison test, when applicable). After BDL, BR levels increased far more in BDL than in PP+BDL, confirming HO1 inhibition. ALP elevations (indicative of bile-acid-accumulation-induced hepatocellular damage) confirmed the cholestasis establishment in BDL and PP+BDL groups. Hepatic-lipid peroxidation (nmol MDA/mg prot, media±SEM) was higher in PP+BDL than in BDL (7.0±0.6 *vs.* 5.4±0.3, p<0.05), showing that, under cholestatic conditions, oxidative damage is worse when BR production is impaired. Hematoxylin/eosin-stained liver samples revealed obstructive injury (bile-duct proliferation/dilatation, inflammatory infiltrates, fibrosis) that were more noticeable in PP+BDL than in BDL, indicating that BR-generation impairment worsens obstructive injury. Conclusion: BR ameliorates BDL-induced OS damage, thus contributing to limit the inflammation-driven progression of chronic cholestatic diseases. This was not still reflected in biochemical markers of hepatocyte integrity, suggesting that acute hepatocellular damage by BLD is more related to the direct effect of retained bile acids than to OS-mediated injury.

6

Intestinal Microbiological Profile and Tgr5 Expression in an Animal Model of Cholecystectomy

Cortés Pastrana RC[1], Lindo Pérez DA[2], Caamal Ley A[2], Vargas González A[2], Yáñez Pérez V[1], Pacheco Pantoja EL[1]* *Autor correspondiente
[1] Escuela de Medicina, Universidad Anáhuac Mayab, MÉXICO. [2] CIR Hideyo Noguchi, UADY, MÉXICO

Introduction: Intestinal microbiota plays an important role in bile acids regulation and the intestinal balance, which is very sensitive to extrinsic factors. The microbiome consists of a delicate balance of Bacteroidetes (gram-negative) and Firmicutes (gram-positive), which is altered after cholecystectomy, leading to disorders like long-lasting diarrheas to malabsortion syndromes. Also, gene expression can be altered, like Tgr5 (Gpbar1). Objectives: To determine the differences between the intestinal microbiome and the expression of Tgr5 in a cholecystectomy animal model. Methods: Nine New Zealand rabbits divided into 3 groups: cholecystectomy (COL), simulated surgery (SHAM) and no surgery (Control). In COL the gallbladder was extracted whereas in SHAM only intestinal manipulation was done without any extraction The DNA was obtained from faeces collected on day 0 and 30 days after the interventions. The microbiota was analyzed by New Generation Sequencing, creating16S gene libraries. RNA was extracted from liver, gut, pancreas and adrenal gland, reverse transcribed, and analyzed with qPCR for Tgr5 gene. Results: After the surgeries, COL showed the highest amount of absolute genes ($7.9x10^7$), followed by SHAM ($2.3x10^7$) and Control ($3.8x10^7$). Regarding the Phylum, COL showed a greater proportion of Bacteroidetes (21.7%) and lower of Firmicutes (63.5%), compared to SHAM (17.1% and 68.1% respectively). Regarding the gene expression, Tgr5 demonstrated the lowest expression for liver in the Control group compared to both COL and SHAM, and greater expression for adrenal gland in the Control compared with the others. The greater expression for the gut was seen in SHAM. Conclusions: The change in COL bacterial population compared to SHAM, suggests that the cholecystectomy itself, could be the cause for the disbiosis suffered by the post cholecystectomy patients. As for Tgr5 gene expression, the findings might imply a change in regulation of bile acids absorption due to the change of this receptor in cholecystectomized subjects.

32

Study of Mrp2 impairment induced by fructose in primary culture of hepatocytes. Preliminary data

Barosso[1] IR, Medeot[1] AC, Schuck[1] VS, Andermatten[1] RB, Ciriaci[1] N, Sánchez Pozzi[1] EJ
[1] Instituto de Fisiología Experimental, IFISE, CONICET

The increment consumption of fructose in the world diet contributes to the rise in total calorie intake and is related to an increase in the incidence of the Metabolic Syndrome (MS). Previously, we demonstrated that administration of 10% fructose in drinking water over 8 weeks to normal rats, a model of MS, reduced bile flow and decreased the expression of the canalicular transporters Mrp2 (Multidrug resistance associated protein 2) and Bsep (bile salt export pump). To study the signaling pathways involved in fructose actions, we develop a cellular model to evaluate its effects on Mrp2. Methods: The study was carried out in sandwich-cultured rat hepatocytes. Cells were treated with fructose (1-10-24 mM) for 3 days. LDH (lactate dehydrogenase) release in the media was measured by a detention kit (Wienner Lab). Mrp2 activity was evaluated by secretion of fluorescent methylfluorescein (GMF) using the index BEI (biliary excretion index). For that, treatments were performed duplicated, in one the experiment was performed with standard buffer whereas in the other a Ca^{2+}/Mg^{2+} free buffer was used. The BEI of GMF was calculated as: BEI = ($fluorescence_{Ca^{2+}/Mg^{2+}}$ - $fluorescence_{Ca^{2+}/Mg^{2+}\text{-free}}$)/$fluorescence_{Ca^{2+}/Mg^{2+}}$x100%. Results: The release of LDH to the medium (%Control) was increased after cells treatment with Fructose 10 mM (357*±32) and Fructose 24 mM (574*±32) increased the release of LDH to the medium. n=4 (*p<0.05 vs Control) and were considered toxic to the cells. Fructose 1 mM did not affect LDH (92±3) and produced a tendency to decrease the BEI by 40% with respect to the Control (there was no statistically significant difference). (Average ± Standard Error; n=4). Conclusions: Though the decrease in Mrp2 transport induced by Fructose 1mM was not statistically significant, these preliminary results suggest that is possible to develop an *in vitro* model to study cellular effects of fructose related to canalicular transport.

35

Role of TNF-α receptor 1 signaling on downregulation of intestinal P-glycoprotein by high-fat diet in mice

Barranco MM[1,2], Perdomo VG[2,3], Zecchinati F[4], Manarin R[3], Massuh G[1], Sigal N[1], Vignaduzzo S[5], Mottino AD[4], Villanueva SSM[4], García F[1,2]

[1]Laboratorio de Fisiología Metabólica, Facultad de Ciencias Médicas, Universidad Nacional de Rosario. Rosario, Santa Fe, Argentina. [2]CONICET. Rosario, Santa Fe, Argentina. [3]Área Parasitología, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. Rosario, Santa Fe, Argentina. [4]Instituto de Fisiología Experimental-CONICET. Rosario, Santa Fe, Argentina. [5]Área Análisis de Medicamentos, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. Rosario, Santa Fe, Argentina.

Obesity is characterized by a proinflammatory state with increased cytokines levels as well as metabolic disorders, where the signaling pathway mediated by tumor necrosis factor alpha (TNF-α) through its receptor 1 (TNFR1) is involved in these alterations. Patients with this metabolic disorder take medicaments that are initially subjected to intestinal metabolism and disposition. P-glycoprotein (P-gp), expressed predominantly at the ileum, is a relevant component of the intestinal transcellular barrier by decreasing the absorption of toxic xenobióticos and therapeutic drugs orally incorporated, thus modulating their bioavailability. The aim of this study was to evaluate the effect of a high-fat diet (HFD, 40% fat for 16 weeks) on intestinal P-gp mRNA expression and activity in wild-type male C57BL/6 (C57, 5 weeks old, n: 20) mice and knockout mice for TNFR1 (R1KO, 5 weeks old, n: 20) to delineate a possible role of TNF-α signaling. The statistical comparisons were done by *t*-student or one-way ANOVA followed by the post hoc Tukey test. Results were expressed as % of C57-Control group. All mice fed with HFD increased their weight and adipose mass, in addition to showed higher cholesterolemia and triglyceridemia levels respect to controls. Only the C57-HFD group presented increased glycemia levels and insulin resistance. Ileal mRNA expression of P-gp was 62% lower in C57-HFD than in control animals. This result correlated well with a 48% decrease in the apical transport rate of the P-gp substrate, Rhodamine 123, in everted intestinal sacs. In contrast, HFD did neither modify the intestinal P-gp expression or activity in R1KO mice. Besides, C57-HFD mice showed elevated TNF-α mRNA levels, whereas in R1KO mice this cytokine was not detectable with either diet. Herein, we demonstrate an impairment of the P-gp barrier function induced by HFD in mice, with the inflammatory response mediated by TNF-α receptor 1 signaling likely involved.

38

Prolactin modulation of hepatic ABC transporters in a murine model of obesity. Study of Signal transducer and activator of transcription 5 (STAT5) role

Sedlmeier MG[1], Ceré LI[1], Marinochi MV[1], Catania VA[1], Ronco MT[1], Francés DEA[1]

[1] Instituto de Fisiología Experimental (IFISE-CONICET), Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR, Suipacha 570, Rosario, Argentina.

Obesity is a metabolic disease characterized by alterations in serum levels of different hormones such as prolactin (PRL). Previously, we reported that mice fed with 40% High-Fat Diet (HFD) displayed elevated plasma levels of PRL that were associated with an increased canalicular expression of the ABC transporters Breast Cancer Resistance Protein (Bcrp) and P-glycoprotein (P-gp), since using bromocriptine (Brc, inhibitor of PRL release) protein expression of transporters were decreased. Also, previous studies have shown that PRL was able to induce transcription of basolateral hepatic transporters and its cognate receptor (*Prlr*) through activation of STAT5. We aimed to evaluate the mechanism involved in PRL modulation of canalicular transporters *in vivo* and *in vitro*. Five-week-old C57BL/6 mice were fed with regular chow diet (CHOW, n=8) or a HFD (n=8) for 16 weeks. Another set of animals were injected with Brc (4 mg/kg, n=4 each group) or vehicle (n=4) during three days. Data were expressed as

means±s.e.m. Significance was determined by Student's t-test. Nuclear STAT5 protein expression was increased in HFD (+150%; p<0.05), as its targets: Bcl-xL (protein expression, +130%; p<0.05) and *Prlr* (mRNA levels, +80%, p<0.05). Brc treatment was able to abolish the increases above mentioned (p<0.05). To go in deep in the study, hepatocytes were isolated from livers (n=2-4) by collagenase perfusion and stimulated with PRL 0.1μg/mL. Protein expression of Bcrp and P-gp was induced by PRL (+45% and +80% respectively; p<0.05). mRNA levels of *Abcg2* were also increased (+50%; p<0.05), suggesting a transcriptional induction. Similarly, mRNA levels of *Prlr* augmented after PRL treatment (+60%, p<0.05). These results indicate that STAT5 could be involved in PRL induction of canalicular transporters and that isolated hepatocytes constitute a good model to continue the study of underlying mechanisms, since it mimicked the expression pattern of transporters and targets genes found *in vivo*.

48

Rational design of potential Shiga toxin type 2 inhibitors by virtual screening

Gioia D.S.[1], Casal J.J.[1], Dorr R.A.[1], Toriano R.[1]
[1] Universidad de Buenos Aires. CONICET. Instituto de Fisiología y Biofísica “Bernardo Houssay” (IFIBIO “Houssay”), Laboratorio de Biomembranas. Facultad de Medicina. Paraguay 2155 7mo piso. CABA. Argentina

Shiga toxin (Stx) is known as one of the most potent bacterial toxins. It is present in the group of "Shiga toxin-producing *E. coli*" (STEC) which contains the genes for Stx1 and Stx2. STEC is one of the most important emerging pathogens of foodborne infections. Human STEC infection reveals in a broad clinical spectrum whose most severe manifestation is Hemolytic Uremic Syndrome (HUS) which is associated with Stx2 and which still has no specific treatment. Stxs are AB5 toxin type consisting of a monomeric, enzymatically active A subunit non-covalently linked to a pentameric B subunit responsible for binding to the globotriaosylceramide (Gb3), a specific receptor on the cell surface. The A subunit enters the target cell where it injures the eukaryotic ribosome, arresting protein synthesis. The aim of this work is to identify small molecules that block the RNA-N-glycosidase activity of subunit A and thus prevent ribo-toxic activity. The strategy used and the preliminary results were: i) starting from the structure of the crystallized protein (PDB Stx2-1R4P) and through FPOCKET software, one "druggable pocket" was selected from 20 detected; ii) using FDA and Maybridge Hitfinder compound libraries (20000 compounds), virtual screening (VS) was performed; iii) using molecular docking techniques, an affinity study between those compounds and crystallized Stx2 was carried out and 10 compounds (hits) were selected; iv) the complexes with the best scoring and favorable interactions were selected and regrouped in clusters considering both lipophilic properties and structural diversity; v) using molecular dynamics (MD) calculations, the temporal stability of the ligand-Stx2 complexes and their binding energy were studied. In conclusion, from the combination of VS and MD techniques, a series of structurally diverse compounds with potential anti-Stx2A activity was identified. In the future, structural modification of the hits will allow us to improve their pharmacodynamic and pharmacokinetic profiles.

83

Hyperglycemia in murine model of type 2 diabetes impairs differentially blood-brain barrier permeability in various brain regions

Posadas-Ramiro N.A.[1], López-Pérez S.J.[1] and Ureña-Guerrero M.E[1]
[1] Departamento de Biología Celular y Molecular, CUCBA, Universidad de Guadalajara, México.

Type 2 diabetes mellitus (T2DM) is a highly prevalent degenerative metabolic disease, characterized mainly by hyperglycemia and vascular endothelial dysfunction. Vascular endothelial cells ensure the functioning of the blood-brain barrier (BBB) and homeostasis of the brain. In this study, BBB permeability was evaluated in a murine model of T2DM.

Six-week-old C57BL/6 male mice randomly distributed into two groups: 1) control: treated with Nicotinamide (NA) + vehicle; and 2) experimental: treated with NA+streptozotocin (STZ). NA (120 mg/kg) was applied 15 min before vehicle (0.1 M $Na_3C_6H_5O_7$, pH 4.5) or STZ (100 mg/kg dissolved in vehicle). Treatments were applied intraperitoneally (i.p.) on days 0 and 2. Blood glucose levels were measured at 4 h of fasting, before the treatments, and every week for 16 weeks after treatment. BBB permeability was evaluated at 2, 4, 8, 12 and 16 weeks after treatment, through fluorescein extravasation to the brain. After 10 min of systemic diffusion of 10% fluorescein (5 mL/kg, i.p.) the animals were anesthetized and perfused transcardially. Fluorescein concentration in ng/mg of tissue was measured in frontal cortex, striatum, hippocampus, entorhinal cortex, and hypothalamus. Data were represented as median ± 95% CI and analyzed using the Mann-Whitney U test to establish the significant differences at p≤0.05; from n=46 mice for the control group and n=56 mice for the experimental group, which were distributed in the study time points, with at least one n=6 in each point. Treatment with NA+STZ increased significantly the blood glucose levels from week 4 to 12 (≈180 mg/dL) relative to the control group (≈130 mg/dL). Hyperglycemia increased fluorescein extravasation to the brain parenchyma, mainly at 12 weeks after treatment, with a different regional susceptibility. We conclude that the hyperglycemia compromises the functionality of the BBB, which could be related to the neuronal alterations find in patients with T2DM.

93

Higher expression of NADPH oxidase 4 (Nox4) in placenta from pregnant women with severe COVID-19.

González M[1], Loyola M[2], Campos C[1, 3], Palma P[1, 3]

[1]Laboratorio de Investigación Materno-Fetal (LIMaF), Departamento de Obstetricia y Ginecología, Facultad de Medicina, Universidad de Concepción, Concepción, Chile. [2]Escuela de Tecnología Médica, Facultad de Ciencias de la Salud, Universidad San Sebastián, Concepción, Chile. [3]Servicio de Obstetricia y Ginecología, Hospital Clínico Regional Guillermo Grant Benavente, Concepción, Chile.

Introduction: Severe COVID-19 in pregnancy is associated with premature birth, and histopathologic description of the placenta reveal signs of maternal and foetal malperfusion. Placental dysfunction could be generated due to hyper-inflammatory and oxidative state, mechanisms in which the catalytic subunits of NADPH oxidase, Nox2 and Nox4, could play an essential role in placental pathology in response to SARS-CoV-2 infection. Objectives: This study aimed to determine changes in the expression of Nox2 and Nox4 in the placenta of pregnant women who suffered from severe COVID19, compared to asymptomatic cases and controls. Methods: Placentas were obtained from pregnancies with a confirmed result of PCR for COVID-19 (after signing the informed consent and approval of the ethics-scientific committee of the Concepción Health Service). Tissues were extracted from the placenta, stored in 4% paraformaldehyde (4°C, 6-12 h), and later preserved in 70% ethanol (4 °C). The samples were dehydrated, clarified in Xylol and embedded in histological paraffin. The inclusions were cut (4 µm thick) and adhered to silanized glass slides, finally being dried (in the oven, 24 h). For immunohistochemistry (IHC) were used, anti-Nox2/gp91phox and anti-Nox4 antibodies (Abcam) (dilution 1:2000 v/v) and secondary antibodies conjugated to HRP. From 20x images (4-6 for each sample) was calculated the IHC optical density score (ImageJ). Means±SD were compared by nonparametric Mann-Whitney test. *Results:* There are no differences in Nox2 expression between severe and asymptomatic cases. In severe COVID-19 cases (n=4), there is a higher expression of Nox4 ($p<0.05$), with a remarkable location in syncytiotrophoblast and endothelium of chorionic villi, which is very low in asymptomatic cases. Conclusion: Severe COVID-19 in the third trimester of gestation is associated with higher expression of Nox4 in the placenta, which could be a mechanism to induce oxidative stress and placenta dysfunction in response to the systemic disease caused by SARS-CoV-2 in pregnant women.

108

Acute exposure to Paraquat and 2,4-D on the expression of genes related to thyroid hormones and biochemical parameters in male rat

Conde-Maldonado V[1,2], Morales-Juárez C[1,2], García-Nieto E[1], Juárez-Santacruz L[1], Alvarado-Olivares M[3], Luis E[4,5], Anaya-Hernández A[1,*]

[1] Centro de Investigación en Genética y Ambiente, Universidad Autónoma de Tlaxcala, Tlaxcala, México. [2] Maestría en Ciencias en Sistemas del Ambiente, Universidad Autónoma de Tlaxcala, Tlaxcala, México. [3] Instituto de Neuroetología, Universidad Veracruzana, Veracruz, México. [4] Cátedras CONACyT - Instituto de Fisiología Celular, Universidad Nacional Autónoma de México, CDMX, México. [5] Laboratorio Nacional de Canalopatías, Instituto de Fisiología Celular, Universidad Nacional Autónoma de México, CDMX, México* arely.anayahernandez@uatx.mx

Introduction: Paraquat and 2,4-dichlorophenoxyacetic acid (2,4-D) are the most widely used commercial herbicides in Mexican agriculture. Endocrine alterations have been related to chronic exposure (occupational or environmental) to these herbicides. However, acute exposure is scarcely studied, so in the present work, we evaluate the effects of acute exposure to Paraquat- and 2,4-D-based commercial herbicides on biochemical and hematological parameters, and the expression of genes related to thyroid hormones in testis. Methods: Eighteen healthy male albino Wistar rats weighing (180–250 g) were used. The rats were divided into 3 groups, namely: control (CNT, n=6), Paraquat (PQT, 10 mg/kg; n=6) and 2,4-D (100 mg/kg; n=6). In PQT and 2,4-D groups, the acute exposition was induced by an i.p. injection of the respective herbicides which were dissolved in 100 µl of saline solution; whereas the CNT group received an i.p. injection of vehicle (saline solution). Three groups were kept for 1 week and euthanized with pentobarbital overdose. All animal procedures and the protocols of the present investigation were approved by our Institutional Ethics Committee (NOM-062-ZOO-1999). The biochemical and hematological parameters were analyzed in plasma and blood, respectively. The genes expression of the thyroid hormone receptors (TRa, TRb), and deiodinases (Dio2-3) in the testis are semi-quantitatively evaluated with RT-PCR. Data obtained (mean ± SEM) from exposed groups were compared with data from the control group using Student test (GraphPad Prism 5.01). Results: Acute exposition of PQT or 2,4-D had no effect on testis's relative expression of thyroid hormone-related genes. PQT group had higher serum concentrations of glucose and creatinine. 2,4-D group had higher serum levels of glucose and triglycerides; lower serum concentrations of urea and urea nitrogen. Besides, acute exposure to PQT and 2,4-D did not alter any hematological parameters. Conclusion: Acute exposure to PQT primarily affects carbohydrate metabolism, while 2,4-D exposure affects carbohydrate, lipid, and protein metabolism.

110

Effects of superior ovarian nerve section on proestrus and estrus day on spontaneous ovulation and estrous cyclicity in the rat.

Gutiérrez S.[1], López X.[1], Ramírez D.A.[1] 1Laboratorio de Biología de la FES Zaragoza, Campus III, Tlaxcala. UNAM.

In the adult rat, the ovulation is modulated by the superior ovarian nerve (SON) in a stimulatory and lateralized way, however there is little evidence that considered such response depending on the day of the estrous cycle. For this purpose, we analyzed the effects of the unilateral section of the SON on proestrus and estrus day on the ovulatory response and estrous cyclicity. Cyclic rats of the CII-ZV strain (n = 5 rats per group) at 13.00 h on proestrus or estrus were submitted to a section of the left or right SON (L-SON or R-SON), or left or right sham surgery (L-Sham or R-Sham). The animals were sacrificed one estrous cycle after surgery (on estrus), the ovulatory response and estrous cyclicity were analyzed. The results are expressed as the mean ± standard errors of the mean. Differences in ovulatory response were analyzed using the Mann-Whitney U test, the percentages of estrous cyclicity were analyzed using Fisher exact probability test. A *p* value less than 0.05 was considered statistically significant. On proestrus, L-SON did not modify ovulation compared to the L-Sham. The R-SON yielded higher number of ova shed only by the left ovary. On estrus, L-SON did not modify the ovulatory response compared to the L-Sham. The R-SON resulted in a higher ovulation only in the right ovary. The estrous cyclicity of the animals with a unilateral section of the SON performed did not modify in comparison to sham surgery groups. Results suggest that the participation of SON on the ovulatory response is depending on the severed nerve and the day of the estrous cycle. The left SON does not appear to be essential in such effects, while the right SON play an inhibitory role. Research supported by UNAM-DGAPA-PAPIIT IA-206321.

Section 1: Inmunity – Inflamation - Cancer 2

61

Establishment of multicellular tumor spheroids (MCTS) as an *in vitro* model for studying sorafenib resistance in hepatocellular carcinoma (HCC)

Palma NF[1], Chares LG[1], Livore VI[1], Ferretti AC[2], Lucci A[1,2], Comanzo CG[1], Vera MC[1], Alvarez ML[1,2], Mottino AD[1], Carrillo MC[1,2], Quiroga AD[1,2], Ceballos MP[1].

[1] Instituto de Fisiología Experimental (IFISE), Facultad de Ciencias Bioquímicas y Farmacéuticas, CONICET, UNR, Rosario.

[2] Área Morfología, Facultad de Ciencias Bioquímicas y Farmacéuticas, UNR, Rosario.

Multidrug resistance counteracts the efficiency of sorafenib (Sfb), an important first-line therapy for HCC, and effective chemotherapy strategies are still missing and under research. Spheroids provide more reliable results than standard 2D *in vitro* cell cultures since they mimic features of *in vivo* tumors. We have shown that EX-527 (EX), a sirtuin 1/2 inhibitor, enhances the inhibitory effect of Sfb in spheroids of HCC cells (HCC-S). Stromal cells in solid tumors contribute to cancer progression and chemoresistance. Aim: to generate MCTS composed of HCC and stroma cells. Methods: MCTS of HCC (HepG2 or Huh7), endothelial (EA.hy926) and hepatic stellate (LX-2) cells were obtained at different ratios (A)1:1:1, B)1:0.6:0.4, C)1:0.3:0.3, D)1:0.1:0.1) by liquid overlay technique and, once generated, morphology (microscopy) and volume (diameter) were evaluated. EA.hy926 and LX-2 were labeled with the CFSE and DiI probes, respectively, to examine their distribution inside MCTS (fluorescent microscopy). Proliferation rate was calculated at 72h (volume 72/0h). Viability (APH assay) and proliferation were determined in Huh7 treated with Sfb 8µM or EX 40µM for 72h. HCC-S were used as control. Results: While HepG2 cells formed loose aggregates, HepG2-MCTS formed highly compact and more spherical cell aggregates (50%* less volume than HepG2-S). Huh7-MCTS were similar in shape and compactness to Huh7-S, but presented with higher volumes (A)+66%*, B)+47%*, C)+49%*), except for D). Cell tracker dyes confirmed the presence of cancer and stromal cells inside the MCTS. Proliferation rate was similar between MCTS and HCC-S from both cell lines, except for A) that grew more slowly (-30%*). Compared with Huh7-S, Huh7-MCTS exhibited stronger resistance to Sfb (viability: A)+68%*, B)+38%*, C)+42%*); similar volume and EX (viability: A)+218%*, B)+150%*, C)+127%*; volume: (A)+145%*, B)+112%*, C)+91%*), except for D). *p<0.05 vs. HCC-S. Conclusion: MCTS seem to be a better 3D model for studying drug response in the context of cancer-stroma interactions.

63

Thyroid hormones (THs) induce oncogenic signaling pathways involved in T cell lymphoma (TCL) progression

Debernardi MM[1], Diaz Albuja JA [1], Sterle HA[1], Paulazo A[1], Díaz Flaqué MC[1], Rosemblit C[1], Cremaschi GA[1], Cayrol F[1].

[1]Laboratorio de Neuroinmunomodulación y Oncología Molecular, Instituto de Investigaciones Biomédicas (BIOMED-UCA-CONICET), Buenos Aires, Argentina.

THs influences tumor progression by direct actions on cancer cells, tumor microenvironment and the antitumor immunity. Our most recent results indicate that THs, acting via integrin αVβ3, promotes cell proliferation, survival and induces an angiogenic program in TCL cells. These lymphoproliferative disorders are very aggressive, and the available therapeutic regimens have poor results, with a high rate of relapses and few effective options for rescue therapy. The understanding of the molecular mechanisms of THs actions in malignant cells could lead to the identification of new therapeutic targets.

The main aim of this work was to evaluate the effect of THs on the oncogenic intracellular pathways that influence lymphoma progression and were found dysregulated in most of TCL patients. For this propose we analyzed TCL cell lines corresponding to immature (CUTLL1) and mature (OCI-Ly12, OCI-Ly13.2) human subtypes after 10, 15 and 30 minutes THs treatment. We found that physiological concentrations of THs significantly increase STAT1, 3 and 5 phosphorylation in both CUTLL1 and LY13.2 ($p<0.05$, $n=3$) TCL cells. Moreover, cilengitide, a specific inhibitor of integrin αVβ3, significantly decreases not only the total effect of THs on STAT1 and 3 phosphorylation but also reduce the basal activation of these transcription factors ($p<0.05$, $n=3$) in TCL cells. On the other hand, it was found that the genetic program related to GATA3 transcription factor was associated with a poor clinical response in TCL patients. We thus, evaluate GATA3 expression after 48 hours treatment with THs and found a significant increase in the TCL cells evaluated ($p<0.05$, $n=3$). All data are shown as mean ± SD.

Our results provide the rational basis to continue studying the molecular mechanisms of THs actions in malignant cells that could lead to the identification of new therapeutic targets, like integrin αVβ3, to improve current treatment outcomes in TCL patients.

66

Presence of Tumor Necrosis Factor Alpha in Pulpal Inflammatory Processes

Guenzelovich M.I.[1], Pisterna G.V.[1], D'arrigo M.[2], Diviani R.[2], Spoleti P.[1]

[1]Facultad de Odontología. [2]Facultad de Ciencias Bioquímicas y Farmacéuticas -Universidad Nacional de Rosario.

Introduction: The dental pulp is a specialized connective tissue that undergoes an inflammatory process (pulpitis) when injured. Tumor necrosis factor alpha (TNFα) is a cytokine secreted by cells of the immune system and plays an important role in promoting and developing this process. Objectives: to determine the presence of TNFα in inflamed pulps. Methodology: the biological material was obtained from patients who attended the Endodontics Chair at the Rosario School of Dentistry. Pulpitis diagnoses

were taken into account according to the AAE classification (2008): Symptomatic Irreversible Pulpitis (n = 30) and Asymptomatic Irreversible Pulpitis (n = 30). Controls: healthy pulps of teeth extracted for orthodontic reasons (n = 15). All samples were stored until processing in 4 drops of physiological solution in Eppendorf tubes and frozen at -20 ° C. To expose the cytokine, a thaw, crush, freeze process was performed. TNF detection: ELISA test (BD OptEIA TM). Results The Mann-Whitney test was applied to compare the TNF-α medians of the evaluated groups. Asymptomatic group: median: 12.5, IQR: 24.4. Symptomatic group; median; 20, IQR: 25.65. (P-value = 0.53) Conclusion: TNFα intervenes in inflammatory events that trigger irreversible pulp pathology. Irreversible pulpitis diagnoses are based on clinical analysis based on subjective and objective findings. In this study, no significant difference was found between the medians of TNFα alpha in the groups evaluated. It can be inferred that tumor necrosis factor alpha plays a fundamental role in both acute pulp inflammatory processes and those that are in the process of chronic evolution, such as asymptomatic irreversible pulpitis.

74

Rac function modulates the effect alkaline gradient on clear renal cell carcinoma mortality: role of isoform 1 of Na^+/H^+ exchanger function.

Cabral B.[1], Mechali A. [1], Di Giusto G. [1], Beltramone N. [1], Capurro C. [1], Ford P. [1], Rivarola V[1].
[1]Universidad de Buenos Aires. Facultad de Medicina. Departamento de Fisiología. Laboratorio de Biomembranas. Buenos Aires, Argentina. CONICET-Universidad de Buenos Aires. Instituto de Fisiología y Biofísica "Bernardo Houssay" IFIBIO-HOUSSAY. Buenos Aires, Argentina. mariv@fmed.uba.ar

The association between proliferation and intracellular pH elicits the possibility that extracellular pH (pHe) may modify cell survival. Moreover, as tumor extracellular acidity is a hallmark of cancer, is probable that pHe affects differently cancer or normal cells. Our previous studies showed that cells derived from renal cell carcinoma (RCC) were more sensible to cell death after 72h exposition to 9.6 mM NaOH (mild alkalosis) than normal cells. Moreover, the combination of alkali plus inhibition of Na+/H+ exchanger isoform 1 (NHE1) improved normal tissue damage induced by alkali. The aim of this study was to investigate if this process were dependent on the Rho GTPases Rac1. We use three renal cell models: HK2, derived from normal human proximal epithelial cells, 786-O and Caki-1, both derived from human RCC. We exposed cells to Rac1 inhibitor IA116 alone or in combination with alkaline media or HOE 1uM, an NHE1 inhibitor. Then, we estimated cell survival by acrydin orange–ethidium bromide experiments. Our results show that after 72h inhibition of Rac induced cell dead in all cell lines. Alkaline-induced cell death was potentiated with Rac inhibition in HK2 and 786 O cells (% of alkaline-induced apoptosis: HK2 vehicle 25±5 vs 58±6, $p<0.01$ n=10; 786-O vehicle 31±6 vs 70±12, $p<0.05$ n=10). Rac inhibition blocked the apoptotic effect of NHE1 on HK2 cell exposed to alkaline media death (% of NHE1-induced apoptosis: vehicle 3.5±0.5 vs 0.25±0.5, $p<0.01$ n=10). In summary, while NHE1-induced cell death is dependent on Rac function, alkaline-induced cell death does not need Rac but it is attenuated by a Rac pathway. Future experiments are needed to evaluate the mechanism of this Rac-mediated attenuation.

Keywords: kidney, pH, cancer, NHE1

76

Two new ion transport mechanisms in human erythrocytes and a new senescence hypothesis: Effect of oxidation on the Mechano-Activated K^+ Channel.

Mendible, M.E.[1], Zambrano-Arnone, A.[2], Aguilar, V.H.[3] and Romero, J.G.[1,2]
[1]Escuela de Biología. [2] Instituto de Biología Experimental, Facultad de ciencias. [3] Instituto de Geografía, Facultad de Humanidades y Educación, Universidad Central de Venezuela.

The human red blood cell (hRBC), an enucleated cell, cannot go through a classical apoptosis, although its half-life-span is 120 days. It is accepted that hRBC $[Ca]_i$ increases over time and this change is related to senescence. However, the molecular mechanisms for counting time remains unknown. We have described for the first time two new ion-transport-mechanisms in hRBC, a Mechano-Activated-K^+-Channel (HEMKCA) and a voltage-dependent K^+/Ca^{2+}-exchanger. With these mechanisms, we have proposed a new hypothesis for hRBC senescence, in brief: mechanical stress within capillaries produces HEMKCA transient activation, depolarizing the membrane and consequently activating the exchanger, producing a Ca^{2+} inflow, which will activate proteases, producing a decrease in the capacity of Ca^{2+} transport, among other effects; These will accumulate over time, leading to a stiffer and denser cell, which will, consequently, produce its withdrawal from circulation. Here we present the effect of oxidative stress on HEMKCA activity. hRBC were taken by epidermal puncture and measured HEMKCA activity with Patch Clamp (inside-out), oxidizing the membrane with H_2O_2 (inner-side) and t-BHP (both-sides). Internal oxidation with 25, 50 and 100uM produced a decrease in Po from 0.115 to 0.023, 0.123 to 0.043 and 0.115 to 0.048($p<0.05$,$n\geq15$), at expense of a decrease in the dwell time(ms) 3.582 to 1.485, 3.345 to 2.437 and 4.825 to 2.398($p< 0.05$,$n\geq16$) and an increase in the closed time(ms) 86.64 to 1138.20, 95.86 to 966.90 and 91.150 to 715.82($p< 0.05$,$n\geq15$), respectively. Interestingly, oxidizing the outer side of the membrane did not produce significant differences. No effect on conductance was observed, and the time course of the effect was clearly dependent on oxidants concentration. Thus, oxidation affects HEMKCA directly and the molecular target is exposed to the cell interior. Here, we present oxidation as a damping mechanism for aging and it is discussed within the framework of our new senescence hypothesis.

82

Integrin αvβ3 a potential prognostic biomarker OF chemotherapy response in breast cancer

[1]Neuroimmunomodulation and Molecular Oncology Laboratory, Institute for Biomedical Research (BIOMED), School of Medical Sciences, Pontifical Catholic University of Argentina (UCA), and the National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

Diaz Albuja J.A.[1], Sterle H.A[.1] , Cayrol F.[1] , Paulazo M.A.[1] , Campos Haedo M.[1] , Debernardi M.[1] , Rosemblit C.,[1] Graciela A Cremaschi[1] , Díaz Flaqué M.C.[1]

Despite the development of novel therapies, breast cancer (BC) tumors are treated with conventional therapy sooner or later. Due to tumor heterogeneity, it is necessary to define new biomarkers to identify groups with different molecular characteristic to improve the correct treatment decision. The impact of thyroid status in BC growth has previously been studied. It has been found alterations of thyroid function during chemotherapy BC treatment and demonstrated that T3 induces chemosensitization of BC cells. However, the relationship between thyroid hormones (THs) membrane receptor, integrin αvβ3 and BC response to chemotherapy remains unclear. The aim of this study is to evaluate the relationship between THs and integrin αvβ3 expression as prognostic value in BC patients. The mRNA expression of ITGB3 in TCGA-PanCancer Atlas, BC dataset (1084 patients) were correlated with ABCB1 and ABCG2, (Pearson, R score >0.3 and p<0,05). The diagnostic role of ITGB3 in BRCA was assessed by receptor operating characteristic (ROC) curve analysis. ITGB3 mRNA levels was higher in non-responder patients treated with anthracycline (AUC=0,673, p=1.8e-10) and taxanes (AUC=0.675, p=1.9e-07) respectively. To confirm the association between integrin and MDR1 transporter, we conducted in vitro assays of BC MDA-MB_231 cells treated with TH and evaluated their action on MDR1 protein levels and Rho efflux in the absence or presence of the integrin selective inhibitor cilengitide. Data are shown as mean ± SD. **p<0.01 respect to untreated cells, n=3. We found that integrin β3 is correlated with worse overall survival and response to anthracyclines and taxanes pointing out its role as a cancer biomarker with potential clinical utility. In patients with high integrin β3 mRNA expression we found significant correlation with proteins involved in drug transport such as P-gp and BCRP. We also demonstrated that THs through integrin αvβ3 modulate the activity of drug transporters. These results point out the role of THs and their membrane receptor, in BC response to treatments and introduce a new biomarker with potential clinical significance.

106

The expression of insulin-like growth factors in A549 cells with induced neuroendocrine-like phenotype

Soto J.E. *, Mendieta I., Escobar-Cabrera J.E., García-Alcocer G., Berumen L. C.

Posgrado en Ciencias Químico Biológicas, Facultad de Química, Universidad Autónoma de Querétaro

Lung cancer is one of the most common types of cancer and the leading cause of cancer-related mortality worldwide. Neuroendocrine-like (NE-like) phenotype is present in lung cancer which is more aggressive; the main characteristic of NE-like is the presence of granules that contain neuroendocrine markers and neuropeptides like growth factors, which could promote proliferation, migration, inhibition of apoptosis, and resistance to therapies. Moreover, studies have shown that NE -like can be induced from epithelial cell cancer, due to changes in the cancer microenvironment that could generate neuroendocrine differentiation (NED); therefore, NED has been replicated in vitro by exposure to agents that elevate intracellular cAMP such as forskolin (FSK) and isobutylmethylxanthine (IBMX). In the present study, the expression of IGF-1, IGF-2 and IGF-1R in A549 cells was studied. Neuroendocrine differentiation was induced in A549 cells; the cells were seeded in 24-well plates and then treated with 0.025 mM FSK + 0.025 mM IBMX for 120 h. Cells were taken to extract RNA, then the RT-PCR was performed to synthesize cDNA. The experiments were carried out in triplicate and differences between the treated group and control group were analyzed using Student's t-test. Differences with P<0.05 were considered statistically significant. To evaluate whether the transdifferentiation of A549 cells was carried out, the expression of the synaptophysin as the neuroendocrine marker was analyzed, showing a significant difference with a p=0.036. Furthermore, the expression of the IGF-2 was less than the control meanwhile the expression of IGF-1R and IGF- 2R were not different compared to the control group. This model let us confirm that IGFs can be produced by specialized cell types such as neuroendocrine cells and may interact through paracrine and autocrine mechanisms with neighboring cancer cells. This work was financed by FOFI-UAQ and CONACYT.

Section 2: Cardiovascular 2

42

Effects of LRE1, an inhibitor of soluble adenylyl cyclase, on ischemia-reperfusion injury in isolated rat heart

Ciocci Pardo A, Mariángelo JIE, Aiello EA, MOSCA SM
Centro de Investigaciones Cardiovasculares ¨Dr. Horacio E. Cingolani¨, CCT-CONICET, Facultad de Ciencias Médicas, Universidad Nacional de La Plata, La Plata, Argentina.

Introduction: The role of soluble adenylyl cyclase (sAC, one of the sources of cAMP) in cell signaling has been widely studied, its participation in ischemia-reperfusion is not clear. Objective: To examine the effects of LRE1, a sAC inhibitor, on myocardial post-ischemic alterations. Methods: Isolated perfused rat hearts were assigned, after 20 min of stabilization, to the following groups: 1) Non-ischemic control (NIC): 90 min of perfusion; 2) Ischemic control (IC): 30 min of global ischemia (GI) and 60 min of reperfusion (R), 3) LRE1: 10 µM LRE1 was administered during the initial 10 min of R. Infarct size (IS) was measured by TTC staining. Left ventricular developed pressure (LVDP) and left ventricle end-diastolic pressure (LVEDP) were used to assess systolic and diastolic function, respectively. Other hearts (n =3) were submitted to 30 min of GI and 10 min of R, in absence and in presence of LRE1. The lactate dehydrogenase (LDH) release during 10 min of R was measured. In isolated mitochondria, mitochondrial state was assessed through the Ca^{2+} retention capacity (CRC, Calcium Green 5N). Data were given as means ± SEM and analyzed using ANOVA followed by Turkey´s test. A $p<0.05$ was considered significant. Results: LRE1 decreased IS [(16 ± 2 % (n=4) vs 32 ± 2 % in IC (n=6)] and improved the post-ischemic recovery of myocardial function. At the end of R, LVDP was 74 ± 5 % vs 18 ± 3 % and LVEDP was 19 ± 4 vs. 55 ± 7 mmHg in IC, respectively. LRE1 increased CRC (150 ± 21 vs 67 ± 14 nmol/mg protein) and reduced LDH release (155 ± 19 vs 290 ± 61 U/L). Conclusion: These data demonstrate that LRE1 cardioprotects the myocardium against ischemia-reperfusion injury. This effect could be attributed to an improved mitochondrial state mediated by sAC inhibition.

65

Ca^{2+} efflux through the translocon contributes to endoplasmic reticulum stress and Ca^{2+} mishandling in stunned myocardium

Mariángelo JIE[1], Valverde CA[1], Vittone L[1], Said M[1], Mundiña-Weilenmann C[1]
[1]Centro de Investigaciones Cardiovasculares- CCT-CONICET La Plata - Facultad de Ciencias Médicas- Universidad Nacional de La Plata.

Aims: The function of endoplasmic reticulum (ER), a Ca^{2+} storage compartment and site of protein folding, is altered by disruption of intracellular homeostasis. Misfolded proteins accumulated in the ER lead to ER stress, unfolded protein response (UPR) activation and ER Ca^{2+} loss. ER stress is present in myocardial stunning, a temporary contractile dysfunction occurring after brief periods of ischemia which is proposed to be triggered by oxidative stress and Ca^{2+} overload. We explored whether ER Ca^{2+} efflux through the translocon, a major Ca^{2+} leak channel activated during ER stress, contributes to Ca^{2+} mishandling and the consequent contractile abnormalities of the stunned myocardium. Methods: Mechanical performance, cytosolic Ca^{2+}, UPR markers and oxidative state were evaluated in perfused rat/mouse hearts subjected to a brief ischemia followed by reperfusion in absence (I/R) or presence of the translocon inhibitor, emetine (I/R+E, 1 µM). Data are expressed as mean ± SEM. Statistical significance was determined by Student's test and ANOVA, as appropriate. Results: Emetine precluded the I/R-induced increase levels of three UPR signaling markers: GRP78, sXBP1 and phospho-eIF2α. Translocon inhibition improved the post-ischemic contractile recovery together with a remarkable attenuation in myocardial stiffness when compared to I/R without treatment (+dp/dt I/R 1187.7±124.7 vs I/R+E 2704.2±321.0 mmHg/sec; LVEDP I/R 48.4±1.87 vs I/R+E 17.63±5.66 mmHg, $p<0.05$, n=5-7) The diastolic Ca^{+2} overload occurring at the first minutes of reperfusion was significantly blunted by emetine treatment (I/R 218.4±33.1 vs I/R+E 117.4±13.0 % pre-ischemic diastolic values, $p<0.05$, n=7), with a partial recovery of the I/R-induced oxidative stress (reduced glutathione levels I/R 7.89± 0.34 vs I/R+E 10.46±0.38 µg GSH/mg prot, $p<0.05$, n=5). Conclusion: Blocking ER Ca^{2+} store depletion via translocon suppressed ER stress and improved mechanical performance and diastolic Ca^{2+} handling of stunned myocardium. Modulation of translocon permeability emerges as a therapeutic approach to face dysfunctional consequences of the I /R injury.

67

Analysis of cardiac looping morphogenesis in the zebrafish model

Lombardo VA[1, 2], Armesto R[1], Heise M[3], Abdelilah-Seyfried S[3,4]
[1]Instituto de Biología Molecular y Celular de Rosario (IBR-CONICET-UNR). [2]Centro de Estudios Interdisciplinarios (CEI-UNR).
[3]Institute of Molecular Biology, Hannover Medical School, Germany. [4]Institute of Biochemistry and Biology, Potsdam University, Germany. lombardo@ibr-conicet.gov.ar

Cardiac looping is a morphogenetic process during vertebrate heart development which brings the developing heart chambers into an approximation of their definitive topographical relationships. Abnormalities in this process result in human congenital heart defects. The aim of this work was to investigate cardiac looping morphogenesis and analyze the role of Bone morphogenetic protein (Bmp) signaling pathway during this process using zebrafish as animal model. We used the myocardial zebrafish reported line [Tg(myl7:eGFP)^{twu34}] to analyze heart morphogenesis during cardiac looping and combine fluorescence and confocal microscopy techniques with cell signaling pathways inhibition assays. We describe the process of cardiac S-looping

morphogenesis in the zebrafish embryo [from 30 to 54 hour post fertilization (hpf)] and establish two parameters for measuring their extension, named: looping angle (α) and looping overlap (index a/b). During cardiac looping, Bmp signaling pathway has a regional patterning which correlates with bending of the nascent heart tube. Upon its pharmacological inhibition (LDN193189 & K02288, both 20 μM from 30 to 54hpf), myocardial cells maintain cuboidal cell shapes and S-shaped bending is impaired showing an increase in the looping angle (LDN193189, α=105±20°, n=18, P<0.001; K02288, α=98±16°, n=27, P<0.001) and index a/b (LDN193189, a/b=4.3±2.6, n=18, P<0.001; K02288, a/b=3.3±1.7, n=27, P<0.05) compared with control hearts (control: DMSO 0.2%v/v, α=77±12°, n=24; a/b=2.2±0.7, n=24). Values are shown as mean ± s.d.. One Way ANOVA - Holm-Sidak method was used for all statistical analysis. These results provide novel insights into the molecular control of cardiac looping morphogenesis in the zebrafish with relevance for a more comprehensive understanding of human congenital heart defects.

81

Critical lysine demethylase regulation in heart regeneration

Peralta T.M[1]; Nuñez Pedrozo C.N[1]; Locatelli P[1], Crottogini A[1], Olea D[1], Cuniberti L[1].
Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTYB-Universidad Favaloro-CONICET).

Introduction: Heart failure and cardiac injury leads to an irrecoverable loss of cardiomyocytes that significantly reduces heart function and life span in mammalian species. Up to date, the research community has focused on achieving heart regeneration mainly through cardiomyocyte proliferation. Recent publications reveal cardiomyocytes dedifferentiation as the first step in cardiac regeneration. Objective: To analyze the heart expression profile of epigenetic genes related to cell dedifferentiation in a cross-species design. Methods: The RNA-Seq sample data of each specie was obtained from BioProject database and was further processed on the UseGalaxy platform. Transcriptome analysis was performed employing the EdgeR package with the *exact* statistical method and the generalized linear model method. The transcriptome collection included the following ones: human (fetal, healthy adult and MI adult samples), sheep (fetal, healthy adult and MI adult samples), mouse (post-natal regenerative window (P1-P7) and non-regenerative (P8-P15)) and lastly, zebrafish (heart samples post cardiac injury (days post injury 1, 3, 7, 14, 21)). Results: The gene KDM1A had higher expression in the human and sheep fetal condition in comparison to their MI adult counterpart (FDR: <0.001 and <0.001). Mouse transcriptomes showed that KDM1A had not significant expression between the healthy and MI condition in the regenerative window; moreover, KDM1A became downregulated in the MI samples of the non-regenerative window (FDR: <0.05). Finally, KDM1A expression did not change in the zebrafish transcriptomes for each day post injury. Conclusion: Transcriptome analysis revealed a pattern in KDM1A expression profile across all species. Analysis of KDM1A expression showed no change in the regenerative hearts of mice and zebrafish. However, KDM1A was downregulated in the non-regenerative injured hearts belonging to human, sheep and mouse. These results support the notion of the KDM1A gene as a key regulator of cell dedifferentiation and emerges as a potential target for future heart regeneration therapies.

91

Isolation, characterization and transduction efficiency of ovine Muse cells for traslational research in cardiac regeneration

Castillo M.G.[1], Bauza MDR.[1], Locatelli P[1], Crottogini A.[1], Olea D.[1], Cuniberti L.[1]
[1] Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTYB-Universidad Favaloro-CONICET), Buenos Aires, Argentina.

Introduction: Multilineage differentiating stress-enduring (Muse) cells are non-tumorigenic endogenous pluripotent-like stem cells identified as SSEA+ cells. However, their features in large mammals needed for translational cardiac regeneration researches have not been described. Objective: Since ovine models of cardiac diseases are being increasingly used, we aimed at isolating Muse cells from ovine adipose tissue and characterize them. In addition, we tested the transduction efficiency of a baculoviral vector to genetically modify these cells. Methods: Ovine Muse cells were isolated from abdominal adipose tissue under a stress procure and cultured in suspension for 5 days and then expanded in adherence until passage 4. Mesenchymal stem cells (ASC) were also isolated. Muse cells were labeled with an antibody against the embryonic marker SSEA3. Gene expression of pluripotency markers (Nanog and Oct4) and S1P receptor 2 (S1PR2) was measured by RTqPCR in Muse cells and ASC. Ovine Muse cells were then transduced at different multiplicity of infection (MOI) with a baculoviral vector expressing the green fluorescent protein (Bv.CMV-GFP). The optimal transduction efficiency (TE) was determined by flow cytometry. Data were analyzed using Student-test and expressed as mean±SD. Results: Muse cells were 99.81% positive for the SSEA3 compared with 14,60% in ASC. TE was MOI 100: 75,86%; 200: 84,30% and 400: 87,21%. Relative gene expression in Muse cells was for S1PR2 (2.7± 1.1 vs.1.0±0.2, p<0.05), Nanog (2.5± 0.4 vs. 1.0±0.1, p<0.05) and Oct4 (7.2± 1.3 vs.1.23±0.7, p<0.05) compared to ASC. Conclusion: The ovine Muse cells were positive for SSEA3, Nanog and Oct4 demonstrating their characteristic of pluripotent cells, in addition they were positive for S1PR2. Additionally, they showed high ability to be genetically modified, suggesting their potential use in preclinical myocardial regeneration assays. Keywords: Muse cells; Baculovirus; sheep; pluripotency.

96

Effect of membrane domains in the Na^+/H^+ exchanger localization and function

Zavala M.R.[1], Godoy Coto J. [1], Longarzo L. [2], Bernasconi A. [2], Maté S.M. [2], Villa Abrille M.C. [1]
[1] Centro de Investigaciones Cardiovasculares “Dr. Horacio E. Cingolani”; [2] Instituto de Investigaciones Bioquímicas de La Plata “Profesor Doctor Rodolfo R. Brenner”

The plasma membranes of eukaryotic cells contain specific domains (MD) –e.g., caveolae- in which key signal transduction proteins are localized. The Na^+/H^+ exchanger (NHE1), an integral membrane protein, is involved in the maintenance of intracellular pH. We postulate here that a preferential membrane partition of NHE1-into/out of MD- is critical for their function. Objective: Evaluate the organization of plasma membranes and the role of MD in the regulation of NHE1 activity. Methods: In cardiomyocytes isolated from normotensive, Wistar, and spontaneously hypertensive rats, SHR, it was determined: the structure of the membranes; NHE1 activity (ammonium pre-pulse method); expression of MD marker proteins, flotilin1 (F1) and caveolin3 (C3); the treatment with 2.5mM methyl-β-cyclodextrin (MβCD) was used for evaluating the effect of MD disruption). The data are expressed as mean ± SEM. Either an unpaired Student's t-test or One-Way ANOVA were used to compare groups. A $p < 0.05$ was considered statistical significance. Results: Localization of F1 and C3 in light fractions of the sucrose gradient was used as MD markers. NHE1 was only found in the MD of Wistar´ cardiomyocytes. MβCD destabilized MD in cardiomyocytes of both rat strains (shifting both F1 and C3 to the bottom of the gradient), promoting, in Wistar, the translocation of NHE1 out of MD and increased maximal NHE1-mediated proton efflux [JH+ (mmol/L/min): 2.88±0.27, n=6; vs control 1.80±0.18, n=6, *p<0.05). On the other hand, the disruption of MD in SHR by MβCD not modify neither the location nor the activity of NHE1 [JH+: 3.56±0.22, n=5 vs control 3.819±0.55, n=5, ns). Conclusions: In Wistar a fraction of NHE1 is in MD while in SHR this exchanger is exclusively located outside these domains, showing greater activity. We propose that a preferential partition of NHE1 in MD could constitute a new regulatory mechanism of its activity.

99

Extracellular mitochondria as a potential biomarker of pathological cardiac hypertrophy development

Cavalli F[1] and Godoy Coto J[1]; Velez Rueda O[1]; Valverde C[1]; Ennis IL[1].
[1] Centro de Investigaciones Cardiovasculares "Horacio E. Cingolani", Facultad de Ciencias Médicas, Universidad Nacional de La Plata (UNLP) – CONICET. Argentina

Introduction: several tissues are capable of releasing mitochondria into the bloodstream as a communication mechanism, increasing the release of dysfunctional mitochondria in some diseases. In pathological cardiac hypertrophy (PCH) development, the main organ affected is the heart, so it would be expected that most dysfunctional mitochondria in blood derive from it.
Objective: to study extracellular mitochondria as a biomarker for the development of PCH induced by arterial hypertension.
Methods: 9 and 12-month-old male spontaneously hypertensive rats were used. Cardiac function was evaluated by echo- and electrocardiogram. Mitochondria were isolated from the left ventricle and plasma to study the mitochondrial membrane potential with rhodamine-123. Western blots were conducted as isolation purity control. Transmission electron microscopy was performed in cardiac tissue. Results are expressed as mean±SEM (n) and compared by T-test, considering $p < 0.05$ as statistically significant, otherwise is stated. The animal protocols were approved by the Care and Use of Laboratory Animals of our institution.
Results: We found a decrease in the thickness of the septum in diastole [9m: 1,20±0,10 (4) vs 12m: 0,90±0,048 (4)] and systole [9m: 2.22±0.14 (4) vs 12m: 1.74±0.10 (4)] with preserved mid-ventricular shortening [9m: 30.23±1.55 (4) vs 12m: 26,89±.3,23 (4), p=0,387]. Additionally, a trend to decrease the QT interval duration and the amplitude of the QRS was observed. Mitochondrial membrane potential trended to be lower in the elder group in both heart [9m: 2.93±0.17 (4) vs 12m: 2.60±0.11 (4) p=0.158] and plasma [9m: 0.095 ± 0.008 (4) vs 12m: 0.084 ±0.011 (4) p=0.457]. Accompanying the previous results, conserved extracellular mitochondria were found in left ventricular micrographs, suggesting that myocytes release mitochondria into the interstitium.
Conclusion: Using a simple method, we were able to isolate extracellular mitochondria from peripheral blood, which status seems to worsen with age and can be potentially used as a biomarker for PCH.

103

Pharmacological and non pharmacological therapies to prevent NBCe1 impaired activity in ovariectomized cardiomyocytes

Ibañez AM; Godoy Coto J; Yeves A; Ennis IL; Lofeudo JM; Aiello EA; De Giusti VC.
Centro de Investigaciones Cardiovasculares, UNLP-CONICET, La Plata

During menopause women are exposed to an increase in cardiovascular risk, typically associated with lack of estrogens. Classic hormone replacement therapy (HRT) has not been as successful as expected in preventing such pathologies, therefore it would be of great importance to describe alternative therapies to prevent cardiovascular risk in menopause. Many of the beneficials effects that estradiol exert on the cardiovascular system are mediated by GPER (G- coupled-estrogen receptor). Sodium/bicarbonate cotransporter (NBC) is an important intracellular pH regulator. Impaired activity of the electrogenic isoform NBCe1 is correlated with increased cardiovascular risk. Objective: explore chronic activation of GPER and aerobic exercise as potential therapies to address intracellular cardiac alterations in OVX hearts. Methods: Bilateral ovariectomy was performed in 10 weeks old female Wistar rats (OVX). The animals were randomly assigned to a sedentary group (OVXsed) or to an aerobic swimming routine (8 weeks/5days a week) (OVXex). Another group of animals underwent a treatment during one month with either G1 (specific agonist of GPER) or vehicle (OVXvh). Data is expressed as mean±SEM, and was analyzed using a one way ANOVA with Tukey postest for multiple comparisons. Results. NBCe1 activity was diminished in OVX and aerobic training was able to prevent it parcially. (Change of pH after activation of NBCe1 with high K+: SHAM 0,249±0,019, n=4; OVXsed 0,090±0,015 n=7*; OVXex 0,144±0,014 n=12) Chronic GPER activation with G1 completely restored NBCe1 activity to sham levels (SHAM 0,149±0,018, n=9; OVXvh 0,065±0,008 n=7*; OVXG1 0,148±0,045 n=4). Conclusion: NBCe1 activity is impaired in OVX cardiac

myocytes, and it can be modulated using both pharmacological and non pharmacological therapies. Future experiments will help to further describe the effect of these therapies in cardiac alterations after OVX.

104

Antiarrhythmic action of chronic melatonin in hypertensive female rats

Diez E.R. [1,2], Libanti B. [3], Carrión A. M. [1], Miatello R.M. [2,3], Renna N.F. [2,3], Prado N.J. [1,2]

[1] Instituto de Fisiología, Facultad de Ciencias Médicas, Universidad Nacional de Cuyo. [2] Instituto de Medicina y Biología Experimental de Cuyo, UNCuyo-CONICET. [3] Fisiología Patológica, Facultad de Ciencias Médicas, Universidad Nacional de Cuyo.

Arrhythmias are complications during reperfusion of the ischemic myocardium and hypertension increase the arrhythmic risk. Acute melatonin is antiarrhythmic, but there is less information about females' animals with cardiovascular risk factors receiving chronic melatonin treatment. The objective of this work was to determine if the chronic administration of melatonin in drinking water was able to reduce blood pressure and if the effect persisted in isolated rat hearts to confer protection against reperfusion arrhythmias in female hypertensive and normotensive rats. Female spontaneously hypertensive rats (SHR) and Wistar Kyoto rats (WKY), ten weeks old, received melatonin dissolved in water (3-5 mg/kg/day, MEL) for 15 days. Blood pressure was determined every 5 days by plethysmography in the animals' tail. After this period, we evaluated the electrocardiogram in isolated hearts undergoing a 10 min regional ischemia, followed by reperfusion of 10 min. Melatonin reduced systolic pressure in hypertensive rats from 186.8 ± 2.4 to 159.2 ± 3.7 mmHg (mean ± SEM, $P < 0.01$ by repeated measurements ANOVA) but not in normotensive rats (treated 118.8 ± 4.6 and not treated 119.8 ± 4.1 mmHg). Melatonin did not prevent ventricular hypertrophy of hypertensive rats (confirmed by cardiac weight / body weight). The hypertensive rats suffered more ventricular fibrillation during reperfusion and melatonin reduced it in hypertensive and normotensive hearts (hypertensive 9/10, treated hypertensive 2/10, $P = 0.0055$; WKY untreated 5/12, treated normotensive 0/10, $P = 0.031$). Our results confirmed the antihypertensive effects of oral melatonin administration in female rats and a reduction in reperfusion arrhythmias.

Section 3: Endocrine and Digestive 2

11

Relationship Between Salivary Alpha-Amylase and Body Mass Index in Young Adults

Juárez RPA, Mendoza M, Celia AC

Grupo de Investigación y Desarrollo: Saliva como Fluido Diagnóstico. Facultad de Odontología. Universidad Nacional del Nordeste.

Available evidence suggests possible link between body mass index (BMI) and salivary alpha-amylase (sAA), although the direction of association is controversial in adult population. Therefore, the study aimed to establish the existence and direction of any associations between sAA and BMI among young adults. This cross-sectional study included a sample of 50 undergraduate dental students between the ages of 19 and 34 (21.10 ± 2,99 years), 42% men and 58% women (χ^2=1,28, p=0,2579). The study involved measuring sAA and assessing BMI. Unstimulated whole saliva samples were collected in the morning (6:30-7:30 am) and afternoon (4:00-6:00 pm). Analysis of sAA was achieved by a kinetic method at 405 nm (CNPG3 substrate). All analyses were undertaken in duplicate. Values were expressed as mean ± standard deviation. Paired samples *t*-test and Pearson's correlation test were performed. The mean BMI of participants was 23.85 ± 3.30 kg/m^2, 66% presented a normal weight (BMI ≤ 25 kg/m^2), 28% overweight (BMI 25-29.9 kg/m^2), 4% underweight (< 18,5 kg/m^2) and 2% obesity II (35-39.9 kg/m^2). Morning sAA levels (190,84 ± 61,80 U/ml) were lower than those in the afternoon (282.74 ± 59.60 U/ml) with differences statistically significant (t = 16.51, p < 0.0001). The morning and evening values of sAA did not correlate with age. Men showed higher sAA levels (am: 250.38 ± 41.32 U/ml; pm: 340.76 ± 36.22 U/ml) than women (am: 147.72 ± 29.67 U/ml; pm: 240.72 ± 30.44 U/ml), with significant differences (am: t= 9.17, pm: t=11.87, p < 0.0001). BMI and sAA levels showed a significant positive correlation (am: r=0.35, p=0.0121; pm: r= 0.40, p=0.0036). Thus, sAA may be a promising salivary marker for evaluating overweight risk in young adults. Further larger-scale study is needed to confirm the present findings. Key words: salivary alpha-amylase, body mass index, young adults, overweight risk

12

Maternal and fetal p110α deficiency induces sex-specific changes in feto-placental growth and placental mitochondrial function

Salazar-Petres ER, Carvalho D, Lopez-Tello J, Sferruzzi-Perri AN

Centre for Trophoblast Research, Department of Physiology, Development and Neuroscience, University of Cambridge.

The placenta is vital for the transport of nutrients from mother to the fetus for growth. The phosphoinositol 3-kinase (PI3K) pathway regulates growth in relation to nutrient supply. Previous work have demonstrated that loss of the PI3K-p110α isoform in either the fetus or mother alters placental morphology and transport capacity in line with fetal growth outcomes. Previous data also suggests that placental growth and functional capacity are fueled by energy provided by mitochondria and influenced by fetal sex. Here we determined whether loss of PI3K-p110α in the mother versus the fetus affects placental mitochondrial function and feto-placental growth on each fetal sex. Virgin 4-months-old C57BL/6 wildtype (WT) and heterozygous PI3K-p110α deficient (α/+) female mice were mated to α/+ and WT males, respectively, to generate litters of mixed genotype (WT and α/+). On day 18 of pregnancy, dams (WT, n=5 and α/+ n=7) were killed and each fetus and placenta were weighed. The transport labyrinth zone of the placenta (LZ) was micro-dissected, weighed and subjected to high resolution respirometry to analyze mitochondrial function. Data are presented as mean ± SEM and analyzed using two-way ANOVA followed by Tukey's test. In female fetuses, there was an overall effect of maternal and fetal genotype to reduce fetal and LZ weight without a significant change in placental weight. In contrast, α/+ male fetuses were lighter than WT male littermates and on each parental cross, and both placental and LZ weights were less for male α/+ than WT littermates, an effect significant in α/+ dams, but not WT dams. Interestingly, male fetuses also showed an interaction effect between maternal and fetal genotype on spare respiratory capacity, which results greater in α/+ LZs from α/+ dams. Our results indicate that maternal and fetal α/+ genotype affect feto-placental growth and placental mitochondrial function in a sex-specific manner.

14

Intestinal multidrug resistance-associated protein 2 (MRP2) is downregulated by oxidative stress (OS) via proteosomal pathway in caco-2 cells.

Zecchinati F[1], Tocchetti GN[1], Domínguez CJ[1], Barranco MM[2, 4], Arana MR[1], Perdomo VG[3,4], Mottino AD[1], Ricardi L[1], García F[2,4], Villanueva SSM[1]

[1] Instituto de Fisiología Experimental, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. [2] Laboratorio de Fisiología Metabólica, Facultad de Ciencias Médicas, Universidad Nacional de Rosario. [3] Cátedra de Parasitología, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario. [4] CONICET-Rosario

Oxidative stress (OS) produced by continuous exposure to dietary contaminants, is a key factor in the development of gastrointestinal disorders, in which the intestinal barrier is altered. However, the information concerning the influence of OS on the expression of intestinal MRP2, an essential component of the intestinal transcellular barrier exhibiting pharmaco-toxicological relevance by limiting the orally ingested toxicants and drugs absorption, is actually scarce. We recently demonstrated a negative

posttranslational regulation of rat intestinal Mrp2 after acute exposition to OS. The aim of this work was to evaluate the long-term effect of OS on intestinal MRP2 expression by treatment of Caco-2 cells, a model of human intestinal epithelium, with tert-butyl hydroperoxide (TBH) for 24 h. Statistical analyses were performed using one-way ANOVA followed by the post hoc Tukey-test for multiple comparisons and results expressed as a percentage difference with respect to control. We first confirmed that TBH did not have a cytotoxic effect at concentrations below 1000 µM by MTT assay. However, when cells were exposed to TBH 1000 µM, the cellular metabolic activity was significantly decreased respect to C (-76%, $p<0.05$, n=6). Next, TBH treatment (250 and 500 µM) increased lipid peroxidation end products (+140 and +159%, respectively) and reduced SOD activity (-29 and -35%, respectively) compared to control group ($p<0.05$, n=6), indicating the induction of OS in this cell line. Assessment of MRP2 expression in total cell membranes (TCM) fraction by western blotting, showed that MRP2 protein significantly decreased (-41%) after treatment with TBH 250 compared to C ($p<0.05$, n=6). Significantly, treatment with the proteasome inhibitor MG132, was able to completely block the decrease in MRP2 protein expression in TCM induced by TBH. Conclusion: we demonstrated a proteosomal degradation of intestinal MRP2 by long-term exposition to OS.

25

Preliminary relationship between dental indicators, stress perceived and injuries in high-performance athletes

Testoni DN[1], Borgatello CG[2], Viani MS[1], Palomino J[1], Mateu Gagliardi J[1], Muñoz R[3], Gongora L[3], Molinas AK[1-4], Masia HD[1].
[1]School of Odontology, National University of Rosario, Argentina. [2]PROFISIO, National University of Rosario, Argentina. [3]Club Newell's Old Boys, Rosario, Argentina. [4]CIC-UNR.

Introduction: One of the risk factors for periodontal disease is chronic psycho-physical stress, which is capable of modulating the immune response and oral microbiota. Chronic periodontal disease causes elevated blood levels of cytokines, and both conditions have been related to injuries in high performance athletes. Objective: Evaluate the relationship between periodontal disease, perceived stress and the incidence of injuries in professional male soccer players. Methodology: Project was approved by the Odontology Bioethics Committee, including informed assent. Twenty professional male soccer players aged 18 - 22 year-old were evaluated. Dental evaluations were carried out by Green Vermillion Index (GVI), and periodontogram. In addition, acidification velocity (AV) by Snyder test was evaluated using a saliva sample. Then the Levenstein Perceived Stress Test was applied, and reports of total injuries in the last season were collected, as well as the average time of return to the sport. The statistics was carried out with the software SPSS by t student method (mean±SE). Results: The results showed that GVI was 0-1 in eight players (group 1), 2 in eight players (group 2) and 3 in four players (group 3). GVI showed a statistically significant correlation for all injuries ($p<0.05$; p=0.0146) between group 1 and 2; and differences in days to recovery (37±20 vs 59±25). Snyder test at 72 h showed in group 1 two players with moderate AV, while in group 2 four players showed moderate-severe VA. Levenstein test coefficient was highest in the group 2 than group 1 in both last two years (0.353 vs 0.341) and last month (0.346 vs 0.32) but no statistical significant correlations were observed. Conclusion: These findings suggest that the chronic inflammation of low grade from the oral illnesses and perceived stress, show relationship with potential risk for sports injuries and time to return to sport.

71

Spatial memory in hyperglycemic rats treated whit an anthocyanin extract from *Hibiscus sabdariffa*

López-Pérez S.J., Acosta-Nungaray A.A., Cervantes-Gómez A., Ureña-Guerrero M.E., Cuéllar-Pérez J.R., Posadas-Ramiro N.A.
Departamento de Biología Celular y Molecular, CUCBA, Universidad de Guadalajara.

Hyperglycemia characterizes diabetes mellitus (DM), and diabetics have poorer memory performance than non-diabetic patients. Spatial memory, a memory modality involving the hippocampus, can be explored in rats through the Barnes maze. Given the high worldwide prevalence of DM, the search for new therapies for glycemic control is pertinent, and plant bioactive compounds represent an interesting option, especially those that have a wide popular acceptance, such as *Hibiscus sabdariffa* flowers rich in anti-inflammatory and antioxidant anthocyanins. Whit this context, the goal of this study was to analyze whether the consumption of an anthocyanins extract from hibiscus flower prevents the spatial memory decline associated with hyperglycemia. A single dose of streptozotocin (STZ; 55 mg/kg) was intraperitoneally injected to adult male Wistar rats (n=12) under fasting conditions (n=11), including intact (n=11) and vehicle-treated rats (n=11) as experimental controls. Blood glucose level ≥ 200 mg/dl at 72 h after STZ injection were considered hyperglycemic. After that, a group of rats received the anthocyanin extract dissolved in drinking water (n=13) for the next 30 days. Blood glucose level were taken every 10 days. Then, animals were exposed to a Barnes maze, under the following scheme: two-days acquisition period (days 1 and 2, three 5-min sessions/day, 60 min apart; a consolidation period (day 3, without sessions) and a retrieval period (day 4, two 5-min sessions, 60 min apart). Mean ± standard deviation of total escape latency, in seconds, was measured for each experimental group, and one-way ANOVA with Tukey *post-hoc* test was applied to verify significant differences between groups at $p<0.05$. STZ-treated animals that received the anthocyanins extract showed lower blood glucose levels and shorter escape latencies than those without extract, most of them with values like controls, pointing a palliative effect of the extract and highlighting its potential therapeutic use.

73

Effect of vagotomy on fertility in rats with polycystic ovary syndrome

Chaparro A[1], Martínez E[1], Espinoza J A[1], Linares R[1, 2] y Morales L[1]

[1] Physiology of Reproduction Laboratory, Biology of Reproduction Research Unit, Facultad de Estudios Superiores Zaragoza, UNAM, Mexico City, Mexico. [2] Laboratorio de Endocrinologia, Biology of Reproduction Research Unit, Facultad de Estudios Superiores Zaragoza, UNAM.

Polycystic ovary syndrome (PCOS) affects about 15 to 18% of women of reproductive age. It is characterized by hyperandrogenism, cysts, and oligo-anovulation. In rats, one of the models that reproduces these characteristics is the administration of a dose of estradiol valerate (EV). Previous studies show that the information carried by the vagus nerve (VN) participates in the regulation of ovarian functions and in the development and maintenance of PCOS. In female rats with PCOS, unilateral or bilateral sectioning of VN reestablish ovulation; thus, the objective of the present study was to analyze whether these oocytes can be fertilized. For this, 10-day-old female rats of the CII-ZV strain were injected with 2mg of EV, 50 days later, left (LSVN; n=9), right (RSVN; n=8) or bilateral sectioning of the VN (BSVN; n=8) was performed. At 10 days post-surgery, the animals that presented a proestrus were placed with a male of proven fertility; the next day the presence of the sperm plug was searched. Results represent the mean ± SEM, the fertility data were analyzed by Fisher's test and the organ weights by ANOVA, followed by Tukey-Kramer. Those values whose p was ≤0.05 were considered different. The sperm plug was observed in 72% of the animals with LSVN, 63% with RSVN and 40% with BSVN. Only one female from each group with LSVN or RSVN became pregnant. The weight of the uterus and ovaries was not modified by vagotomies. Ovarian morphology showed cysts, but also corpora lutea, indicative of ovulation. These results allow us to suggest that in the rat with PCOS, the elimination of the information that travels through the VN restores the signals that facilitate ovulation, however, the lack of pregnancy indicates an alteration in the quality of the oocyte or of the mechanisms that regulate fertilization and maintain pregnancy.

Research supported by the programs: UNAM-DGAPA-PAPIIT IN216519 and the “Programa de Becas Posdoctorales, UNAM”.

Section 4: Neurology

15

Glyphosate exposure affects motor behavior and β-catenin expression in development rats

Forneris P, Luna SA, Borgatello CG, Rosso SB
Laboratorio de Toxicología Experimental, Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario.

Introduction: Glyphosate (Glyph) is a broad-spectrum herbicide for agricultural weed control, and due to many Glyph-resistant crops, usage has increased significantly. Even though perinatal exposure of Glyph might affect brain development, the impairment on cytoarchitecture and behavioral manifestation are still unclear. β-catenin is a key component of the Wnt-canonical pathway regulating the formation and function of neuronal circuits. Objective: the aim of this study was to examine the effects of Glyph exposure on brain development and maturation in rats by in vivo tests and in vitro assays. Methodology: male Wistar rats, postnatal day 7, were treated subcutaneously with a Glyph solution (without adjuvants) in saline phosphate buffer (PBS). A dose of 70 mg/kg was tested every 48 h for 14 days (n=14). PBS injections were used as controls (n=14). After sacrifice and brains dissection, we analyzed β-catenin expression in different brain regions such as: prefrontal cortex, dorsal striatum and cerebellum using Western blot technique. To evaluate the motor skills, behavioral tests were performed: open field (motility time), rotarod (time spent on the rod) and pole test (time to descend). The statistical analyze was carried out by t-test and two-way ANOVA method (mean ± SE, n=28). Results showed that Glyph exposure led to changes in β-catenin expression pattern in prefrontal cortex ($p=0.0418$). Furthermore, studies in mature cultured neurons exposed to the herbicide also showed alterations in the β-catenin pathway during synaptogenesis. In addition, Glyph treatment caused a deficiency in rotarod in a day 3, compared to control groups ($p<0.05$). Conclusion: taken together, these findings suggest that the exposure to glyphosate induces motor dysfunctions in developmental rats probably accompanied by a down regulation of the Wnt-β-catenin pathway. In future experiments, we will try to identify new effectors of Wnt canonical pathway involving in the Glyph neurotoxicity.

23

Brain vascular alterations during the postnatal period in a rat model of intrauterine growth restriction.

Asensio JA*, García RD* & Seltzer, AM. **These authors contributed equally to this work.*

Introduction: Spontaneously hypertensive rats (SHR) endure pregnancy with placental insufficiency, resulting in chronic fetal hypoxia and postnatal neurodevelopmental delay. SHR pups have been proposed as a model for intrauterine growth restriction (IUGR). Impaired cerebrovascular development is strongly related to alterations in the neurovascular unit (NVU). Caveolin-1 (CAV-1) is associated with microvessels, astrocytes and pericytes, the main components of the NVU and it is associated with the tissue response to hypoxic injuries. Objectives: To evaluate brain vascular development during the postnatal period in SHR pups. Methods: SHR and Wistar Kyoto (WKY) pups at P7 and P14 were used to obtain cerebral cortex and cerebellum histological slices. Masson's trichrome (MT) was performed to detect arterioles; and CAV-1 / IB4 double fluorescent-staining for NVU. We used Image J and AngioTool software to determine the following variables: total number of junctions (TNJ), total number of endpoints (TNEp), vessels area (VA), average vessels length (AVL), lacunarity index (LAC) and ratios IB4/CAV-1. Unpaired Student t-test used for Statistical analysis, the results were reported as Mean ± SEM. Results: Cerebral cortex and cerebellum from SHR P14 presented a significant increase in the number of arterioles. WKY cortex from P7 to P14 manifested a significant increase in TNJ, TNE, and VA; and a decrease in LAC. Only TNE and VPA increased significantly in SHR from P7 to P14. In SHR cortex P14, TVL, and TNEp there were significant differences between ratio CAV-1/IB4, where IB4 had higher expression. In LAC, the situation was reversed. Cerebellum P7 and P14, there were no significant differences in CAV-1 and IB4. Conclusions: The microvascular development of the SHR brain was characterized by an increased number of arterioles, high lacunarity index and poor capillary network. These data together with the altered CAV-1/IB4 ratio suggest a probable delay in NVU consolidation.

55

L-alliin modulates inflammatory markers expression in the cerebral cortex of mice with diet-induced obesity.

Davalos-Vazquez A[3], Sánchez-Sánchez M[1], Sánchez-Orozco N[3], López-Roa R.I[2], Ortuño-Sahagún D[1], Carrera-Quintanar L[3].
[1]Centro Universitario de Ciencias de la Salud, Instituto de Investigación en Ciencias Biomédicas. [2]Centro Universitario de Ciencias Exactas e Ingenierías, Laboratorio de Investigación y Desarrollo Farmacéutico. [3]Centro Universitario de Ciencias de la Salud, Laboratorio de Ciencias de los Alimentos.

The energy imbalance and alterations in the metabolism observed in diet-induced obesity (DIO) lead to increased secretion of pro-inflammatory cytokines and metainflammation, which may represent a threat to the central nervous system. Neuroinflammation has been associated with many neurodegenerative diseases and is considered a critical promoter of cognitive decline. L-alliin (S-allyll-L-cysteine sulfoxide) is a compound in garlic that has been attributed with antioxidant and anti-inflammatory properties. Previously, our group has described that L-alliin is able to immunomodulate the inflammatory response *in vivo* in the C56BL/6J mouse model of obesity. Objective: to evaluate the anti-inflammatory effect of L-alliin in the cerebral cortex of mice with diet-induced obesity. Methodology: Two groups of male C57BL/6J mice were fed different diets: Standard diet (STD) & High-Fat Diet (HFD) for 8 weeks. The groups were then subdivided into four groups: STD (n=4) and OBS (n=4) control

groups and DIO+1 (n=5) and DIO+2 (n=5) as experimental groups which were administered 1 mg/kg and 5mg/kg of L-alliin daily for 5 weeks. At week 13 mice were stimulated with LPS, then sacrificed and their cerebral cortex was dissected. Gene expression of pro-inflammatory cytokines was determined by RT-qPCR and analyzed by $2^{-\Delta\Delta CT}$ method. Results: After L-alliin treatment we observed that there were no significant differences between OBS and HFD+1mg groups. However, a decreased in relative gene expression of IL-6, IL-1β and TNFα was observed between OBS and HFD+5mg. Conclusion: 5 mg/kg doses of L-alliin modulate IL-6, IL-1β and TNFα expression in DIO mice. This improvement could reflect a beneficial and protective effect against neuroinflammation caused by obesity. Despite the results, a detailed study of the possible mechanisms involved will need to be conducted.

64

Temporal Dynamics of Spike Trains in the Raphe Nuclei During Urethane Sub-states in Rats

Ruiz J.[1], Mateos D.M.[2], Rodriguez A.[3], Devera A.[3], Rivas M.[3], Gonzalez J.[3], Torterolo P. [3] and Pascovich C.[3, 4]

[1] Facultad de Ingeniería. Universidad Nacional de Entre Ríos, Carrera de Bioingeniería, Oro Verde-Argentina. [2] Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina. [3] Laboratorio de Neurobiología del Sueño, Departamento de Fisiología, Facultad de Medicina, Universidad de la República, Montevideo-Uruguay. [4] Consciousness and Cognition Laboratory, Department of Psychology, University of Cambridge, UK.

Neurons of the dorsal and median raphe nuclei (DRN and MnR, respectively) play a key role in the regulation of the sleep-wake cycle; nevertheless, the dependence of their neuronal dynamic on the state remains uncharacterized. The present study aims to estimate the entropy rate using binary Lempel-Ziv complexity (LZC) for spike trains (LZC ST) and for interspike intervals (LZC ISI bin), as well as to determine the firing rate (FR), coefficient of variation (CV) and Lempel-Ziv complexity for interspike intervals discretized by ordinal patterns (LZC ISI OP), of raphe neurons in two different urethane-induced brain sub-states in rats (n = 64): active or “REM-like” and slow wave or “SWS-like” (SW). Our hypothesis was that the complexity at the neuronal level would be lower during SW state. For statistical analysis, multilevel linear models were built using the nucleus as a random effect and the state as a fixed effect. The different variables were tested comparing active and SW state groups. As predicted, the LZC ISI bin was significantly higher in the active state compared with the SW state ($1.05 \pm 7.8x10^{-3}$ vs $1.03 \pm 9.7x10^{-3}$ mean ± SD; n = 91/156; $p < 0.05$). The FR of the neurons was also significantly higher during the active state (15.51 ± 1.98 vs 10.06 ± 1.98; $p < 0.01$). However, LZC ISI OP, LZC ST and CV, were not significantly different between both groups ($0.70 \pm 3.52x10^{-3}$ vs $0.70 \pm 4.12x10^{-3}$, $p = 0.18$; $4.3x10^{-3} \pm 4.53x10^{-4}$ vs $4.4x10^{-3} \pm 4.82x10^{-4}$; $p = 0.79$; 0.57 ± 0.08 vs 0.66 ± 0.05; $p = 0.12$, respectively). We conclude that a lower complexity during SW state is only captured when using LZC ISI bin.

72

The Concept of a Central Brain Oscillator. Honeybee Brain Electrical Oscillations by Microtubules

Gutierrez BC[1], Cantiello HF, and Cantero MR

[1] Laboratorio de Canales Iónicos, Instituto Multidisciplinario de Salud, Tecnología y Desarrollo (IMSaTeD, CONICET-UNSE), Santiago del Estero, Argentina.

Brain waves are coherent patterns of synchronized electrical oscillations thought to represent the activity of neurons that is evidenced by electroencephalogram (EEG) and local field potential (LFP) recordings. However, oscillatory electrical activities in the mammalian brain have also been observed across phyla. Insect brains generate oscillatory activity patterns that resemble their vertebrate counterparts. Microtubules (MTs) are highly charged polymers, and important structures of the cytoskeleton in neurons. Recent studies (Cantero et al, 2016; 2018; 2019) demonstrated that different assemblies of brain MTs, including the isolated polymers generate spontaneous and self-sustained electrical oscillations. To gain insight into the electrical oscillatory activity of MTs in the brain of an animal model, we isolated brains and MT sheets from the honeybee (*Apis mellifera*). The patch clamp technique was applied to MT sheets of purified honeybee brain MTs. High resistance seal patches showed electrical oscillations that linearly depended on the holding potential between ±200 mV and had a mean conductance ± SEM of 9.2 ± 0.3 nS (n = 14). To place these oscillations in the context of the brain, we also explored LFP recordings from the Triton X-permeabilized whole brain of worker honeybees that unmasked spontaneous oscillations after, but not before tissue permeabilization. There is no evidence of a particular region producing robust electrical activity; however, the mushroom bodies could be related to it. Frequency domain spectral analysis of time records indicated at least two major peaks at approximately ~38 Hz and ~93 Hz in both preparations. These oscillations were partially similar to those observed in similar preparations of mammalian MTs, and represented low and high gamma brain waves, usually reported in humans and other animals. The present data provide evidence that MT electrical oscillations are a novel signaling mechanism implicated in brain wave activity, associated with cognitive function in other animal models. The study was funded by FONCyT, PICT 2016 N°3739, PICT 2018 N°3337, and Universidad Nacional de Santiago del Estero, PI UNSE N°23/E004.

87

Sleep Deprivation in Crayfish: Study of Brain and Cardiorespiratory Electrical Activity

Osorio-Palacios M, Oliver-Domínguez I, Aguayo-Solís R, Hernández-Falcón J and Mendoza-Ángeles K

Departamento de Fisiología, Facultad de Medicina, UNAM, México

In vertebrate and invertebrate animals, sleep is essential for the maintenance of life itself. For example, in complex organisms, sleep deprivation in mammals elicits changes in the structure of EEG and dysregulation of cardiorespiratory activity. In rats, after

two to three weeks of sleep deprivation, animals loss weight despite a great increase in food intake. If deprivation continues, they finally die. In invertebrates as crayfish, 24 hours of sleep deprivation are enough to cause death, however, we do not know if sleep deprivation in this animal elicits changes in the structures of electroencephalogram and dysregulation of cardiorespiratory activity. The main goal of this work was to analyze brain and cardiorespiratory electrical activity of adult crayfish *Procambarus clarkii* to compare the dynamics of these variables in control condition and after sleep deprivation by using time-frequency analysis. We used male animals in intermolt, synchronized to light-dark cycles 12:12. In cold anesthetized animals we implanted electrodes on deutocerebrum, both gills chambers and cardiac sinus. After two days of recovery, we recorded, simultaneously, behavioral and electrical activity. For behavioral records, we defined two body positions of the animal: walking and lying on one side and associated each one with the time of recording. We found that EEG from control sleeping animals showed a decrease in power at 30 Hz, as compared to walking animals that had high power in the frequency band analyzed, 0-60 Hz. Sleep deprived animals presented even lower power in all EEG frequencies even when they were allowed to sleep. After sleep deprivation, we found that walking crayfish presented low power EEG like sleeping animals. Both conditions are accompanied by oscillations in cardiorespiratory frequency. In conclusion, sleep deprivation modifies the dynamic of brain electrical activity and cardiorespiratory regulation in crayfish. This work was supported by the program UNAM-DGAPA-PAPIIT IN231620.

97

Mental health and cortisol response to traumatic and violent images: comparison between urban and suburban citizens in Mexico City

Cerda-Molina AL[1], Mayagoitia-Novales L[1], Mendoza-Mojica SA[2], Borráz JI [1]
[1] Departamento de Etología, Dirección de Investigaciones en Neurociencias, Instituto Nacional de Psiquiatría "Ramón de la Fuente Muñiz". [2] Unidad Académica Profesional Tejupilco, Universidad Autónoma del Estado de México

There is evidence that living in suburban communities provides some advantages over living in big urban cities, mainly in terms of mental health. However in countries such as Mexico, insecurity and violence are one of the main problems that suburban citizens face, affecting the well-being of people and probably altering the hypothalamus-pituitary-adrenal (HPA) axis and cortisol secretion. The goal of this study was to compare symptoms of mental health and cortisol in response to traumatic and violent images between people living in a big urban city (Mexico City) and in small suburban cities (Estado de México). We exposed 122 adults (67 women, 55 men) to traumatic and violent images (from the Affective Picture System IAPS, CSEA-NIMH, 1999), and took four saliva samples to measure cortisol (basal, 15, 30, and 45 min post-images) and applied the Symptom Checklist-90-R. We used a Generalized Equation Model with cortisol as dependent variable and cities (Urban *vs*. Suburban), time of samples and sex as independent. Symptom Checklist-90-R was analyzed with a MANOVA. Results showed that overall cortisol levels of suburban citizens were higher than the urban ($F = 4.38$; $P = 0.03$). However cortisol response was different between cities (X^2 Wald = 14.48, d.f. = 3, 122; $P = 0.002$); suburban citizens had a flattened cortisol profile whereas urban citizens showed a rise of cortisol 15 min after the images ($P < 0.05$). Besides, suburban participants had more symptoms of the Checklist-90-R than urban ($F = 3.610$, d.f. = 8, 11, $\eta^2 = 0.20$, $P < 0.001$) mainly for somatization ($P < 0.001$). No sex differences were found. These results suggest that people in small suburban areas had an altered HPA axis probably resulting from the habituation to living under the stress of insecurity and violent scenarios, consequently affecting their mental health.

101

Can the brain be taken as a whole when choosing housekeeping genes for studding sex differences?

Dadam F.[1,3], Vivas L.[1,2], Caeiro XE[1]
[1]Instituto de Investigación Médica Mercedes y Martin Ferreyra-INIMEC-CONICET-UNC. [2]Facultad de Ciencias Exactas Físicas y Naturales- UNC. [3]Facultad de Psicología - UNC

Expression of sexual dimorphic genes in differente brain areas are been extensively studied. But can the brain be taken as a whole when chossing housekeeping genes (HKG) for studing sex differences? This study aimed to define whether sex chromosome complement (SCC) and/or the organizational hormonal effects may differentially modulate relative gene expression of three common used HKG, glyceraldehyde-3-phosphate dehydrogenase (*Gapdh*), Ciclophylin (*Cyc*) and ribosomal subunit 18S (*18s*) in different brain areas. For this purpose, we used mice of the "four core genotypes" mouse model, in which the effect of gonadal sex (testes/ovaries) and SCC (XX/XY) are uncoupled. Brains were collected from gonadectomized mice and relative gene expression of basal *Gapdh, Cyc and 18s* genes at fore/hindbrain nuclei were assessed using quantitative real time-PCR. Data were subjected to a 2-way mixed ANOVA with gonadal sex (male/female) and SCC (XY/XX) as independent factors. Furthermore, to identify the HKG with the most stable expression; HKGs stability test- geNorm and Normfinder- were used. Sex-dependent expressions of commonly used housekeeping genes at the SFO and AP brain levels were observed. At SFO *Gapdh* and *Cyc* genes showed a female phenotype. Furthermore, statistical data demonstrated a SCC effect on *Cyc* gene expression in the SFO as well as for *18s* at the AP. At the NTS, OVLT and PVN no differences in gene expression were observed. Besides, the analysis of the M-value for each HKG demonstrated not only the importance of taking into account sex as a factor (since the stability values were always much higher when males and females worked together) but also studying each area independently (obtaining in this way lower M-values than working all the brain tissue together). Our findings underscore the importance of empirical determination of reference genes to effectively and accurately normalize RT-PCR data before quantifying target genes.

Section 5: ALACF Best Work Award Poster Modality

Jury:

Cecilia Larocca • Institute of Experimental Physiology, Rosario (Argentina)
Patricia Rocco • Laboratory of Pulmonary Investigation, Carlos Chagas, Rio de Janeiro (Brasil)
Ma. Del Carmen Cortés • Institute of Physiology Benemérita Universidad Autónoma de Puebla (México)

7

Involvement of the P2X3 receptor in neuronal hyperexcitability in a colitis model in C57BL6 mice

Sánchez-Navarro CA[1], Valdez-Morales EE[2], Barragán-Iglesias P[3], Barrios-García T[3], Guerrero-Alba R[3]

[1] Master's Student in Biomedical Research, Department of Medicine, Health Sciences Center, Autonomous University of Aguascalientes, Ciudad Universitaria, Aguascalientes, Mexico. [2] Cátedras CONACYT. Autonomous University "Benito Juarez" of Oaxaca, Department of Medicine and Surgery. [3] Department of Physiology and Pharmacology, Basic Sciences Center, Autonomous University of Aguascalientes, Ciudad Universitaria, Aguascalientes, Mexico.

Introduction: Previous studies have been shown that acute colitis enhances the excitability of colonic nociceptive dorsal root ganglia (DRG) neurons[1]. However, the molecular mechanisms involved in this hyperexcitability are not fully understood. Extracellular adenosine 5'-triphosphate (eATP) has been established as a key sensory signaling molecule in inflammatory pain through activation of P2X3 receptors[2], which are highly expressed in nociceptive DRG neurons[3]. Aim: To determine if P2X3 receptors participate in neuronal hyperexcitability during an inflammatory process. Methods: Colitis was induced by intrarectal administration of Dinitrobenzene sulfonic acid (DNBS) 200 mg/kg in ethanol 50% in C57BL/6 mice. The severity of colitis was assessed by weight loss and macroscopic and microscopic scores of damaged colonic tissues. The neuronal excitability of T8-L2 Dorsal Root Ganglia (DRG) neurons was evaluated by measure changes in rheobase and action potential firing using the perforated patch clamp technique. The role of the P2X3 receptor was studied using a selective P2X3 antagonist, A-31749, and its expression was evaluated by western blot and immunofluorescence. Results: Colonic sections collected 4 days post-DNBS treatment showed focal ulceration, crypt destruction, goblet cell depletion, and mucosal infiltration of immune cells. DRG neurons from DNBS-treated mice showed increased P2X3 expression and hyperexcitability (rheobase decreased 51%, $P < 0.05$, unpaired *t*-student test, n = 7). TNF-α expression levels are significantly higher in the colonic tissues of DNBS-treated mice compared to the control samples ($P < 0.05$, unpaired *t*-student test, $n = 8$) and the incubation of DRG neurons with TNF-α recapitulated the hyperexcitability effect of DNBS- treated mice on rheobase and this effect was blocked with the selective P2X3 antagonist receptor (A-31749). Conclusions: These results suggest that the release of proinflammatory mediators during colitis, such as TNF-α, enhanced excitability of sensory DRG neurons innervating the colon through modulation of activity P2X3 receptors.

[1]Stemkowski, P.L., et al. J Physiol, 2015. 593(16): p. 3739-55. [2]Deiteren, A., van der Linden, L., de Wit, A., Ceuleers, H., Buckinx, R., Timmermans, J.-P., De Winter, B. Y. (2015). *PLoS ONE*, *10*(4), e0123810. http://doi.org/10.1371/journal.pone.0123810
[3]Burnstock, G., P2X receptors in sensory neurones. Br J Anaesth, 2000. 84(4): p. 476-88.

24

Effect of doxycycline and propranolol on human pterygium cell viability.

Delgado-Alvarado I[1], Barrios-García T[4], Valdez-Morales EE[2], Barba-Gallardo LF[3], Guerrero-Alba R[4]

[1] Master's Student in Biomedical Research, Department of Medicine, Health Sciences Center, Autonomous University of Aguascalientes, Ciudad Universitaria, Aguascalientes, Mexico. [2] Cátedras CONACYT. Autonomous University "Benito Juarez" of Oaxaca, Department of Medicine and Surgery. [3] Department of Physiology and Pharmacology, Basic Sciences Center, Autonomous University of Aguascalientes, Ciudad Universitaria, Aguascalientes, Mexico. [4] Department of Medicine, Health Sciences Center, Autonomous University of Aguascalientes, Ciudad Universitaria, Aguascalientes, Mexico.

Introduction: Pterygium is a fibrovascular tissue of a triangular shape that grows from the peribulbar conjunctiva toward the cornea[1]. The current treatment is the incision of the sclera supplemented with medications. However, it has a high recurrence rate of approximately 50% to 90%[2]. For this reason, the need arises to look for new non-invasive alternatives that help prevent or reduce the pterygium's recurrence. Doxycycline and propranolol could be a potential alternative because both drugs have been shown to have anti-angiogenic and anti-proliferative effects on other tissues[3, 4]. Aim: To evaluate the effects of doxycycline and propranolol on human pterygium cell viability. Methods: Pterygium samples were obtained from 4 male and 3 female patients, age 52 ± 5. The fresh pterygium tissue from the surgical excision patients was cut into small pieces and placed in a culture dish. The culture dish was placed in an incubator with 95% O_2 and 5% CO_2 at 37°C. The cells were cultured in DMEM plus F12 medium and passaged for 3 to 7 generations. The stable cells were treated with doxycycline (1, 10, 20, 20, 40 µg/ml) or propranolol (1, 5, 10, 25, 50, 100 µmol/ml) e incubated for 24 hrs. The activity cytotoxic of doxycycline and propranolol was measured by MTT assays. Results: Doxycycline and propranolol showed potent cytotoxic activity in cultured human pterygium cells with an IC50 = 16.31 ± 1.21 µg/ml for doxycycline and IC50 = 24.58 ± 1.39 µM for propranolol. This cytotoxic activity was dose-dependent manner. Both treatments at maximum

concentration induced 90% of mortality of human pterygium cells compared to the blank control ($P < 0.05$). Conclusion: These results demonstrated that doxycycline and propranolol suppressed the cell survival of cultured human pterygium cells, which suggests that they could represent novel therapies. However, additional studies are necessary to determine and understand the mechanisms.
[1]Shahraki, T., Arabi, A., & Feizi, S. (2021). Pterygium: an update on pathophysiology, clinical features, and management. *Therapeutic Advances in Ophthalmology*, *13*, 251584142110201. https://doi.org/10.1177/25158414211020152. [2]Malozhen, S. A., Trufanov, S. V., & Krakhmaleva, D. A. (2017). Pterygium: Etiology, pathogenesis, treatment. In *Vestnik Oftalmologii* (Vol. 133, Issue 5, pp. 76–83). Media Sfera. https://doi.org/10.17116/oftalma2017133576-83. [3]Wang, S. Q., Zhao, B. X., Liu, Y., Wang, Y. T., Liang, Q. Y., Cai, Y., Zhang, Y. Q., Yang, J. H., Song, Z. H., & Li, G. F. (2016). A new application of an old drug: Antitumor activity and mechanisms of doxycycline in small cell lung cancer. *International Journal of Oncology*, *48*(4), 1353–1360. https://doi.org/10.3892/ijo.2016.3375. [4]Xu, T., Xiao, X., Zheng, S., Zheng, J., Zhu, H., Ji, Y., & Yang, S. (2013). Anti-angiogenic effect of propranolol on the growth of the neuroblastoma xenografts in nude mice. *Journal of Pediatric Surgery*, *48*(12), 2460–2465. https://doi.org/10.1016/j.jpedsurg.2013.08.022

62

The receptor protein tyrosine phosphatase z: a possible prognostic biomarker for medulloblastoma.

Santana Bejarano MB[1], Grosso Martínez PR[1], Godínez Rubí JM[1], Ortuño Sahagún D[2]
[1] Laboratorio de Patología Diagnóstica e Inmunohistoquímica, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara. Guadalajara, Jalisco, México. [2] Instituto de Investigación en Ciencias Biomédicas, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara. Guadalajara, Jalisco, México.

Introduction: Medulloblastomas (MB) are aggressive CNS neoplasms of embryonic origin. Four distinct molecular subgroups have been described: Wingless (WNT), Sonic Hedgehog (SHH), Groups 3 and 4. The MB-WNT group has the best prognosis. Recently, elevated ALK expression in this group has been described as a good prognosis indicator for MB patients. ALK is activated when PTPRZ is inhibited. PTPRZ is a receptor protein tyrosine phosphatase; it is expressed by glia cells and neurons in injured areas of the brain. A direct relationship between PTPRZ and MB has not been demonstrated before**.**
Objective: To identify PTPRZ as a possible prognostic biomarker in MB. Methods: This is a cross-sectional analytical study. It includes 22 MB samples. PTPRZ expression in MB tissue samples was immunohistochemically examined and analyzed for mark, intensity, and distribution. Results were correlated with MB clinical and histopathological variables. Qualitative variables are expressed as frequencies and percentages followed by x2 or F-fisher. Correlation between variables was determined by Spearman´s coefficient. Results: PTPRZ intensity expression was associated with tumor stage ($p= 0.043$), showing a correlation between high PTPRZ expression and low tumor stage ($p=0.014$, $rho= -0.54$). Likewise, PTPRZ intensity correlated with the variable of necrosis in MB cases ($p=0.02$, $rho=-0.47$). PTPRZ distribution was associated with histological variants of MB ($p=0.002$), where diffuse distribution tends to be in the less aggressive presentation of MB and focal distribution tends to be in the extensive nodularity variants, which have variable outcomes. Conclusions: PTPRZ expression has an association with low tumor stratification and low necrosis percentages in patients with MB. This analysis provides new evidence for PTPRZ expression in MB. Higher intensity correlates with good prognosis. We propose PTPRZ expression as a possible prognostic biomarker for MB.

77

Effect of time-restricted eating on high-fat diet-induced metabolic dysfunction in a Drosophila melanogaster obesity model

Salgado-Canales D.J[1,2], Quenti D.S[1], Lourido M.F [1], Cifuentes M.[2], L. Tobar N.A[1]
[1] Laboratory of Obesity and Energy Metabolism in Geriatrics and Adults (OMEGA), INTA, University of Chile. [2] Laboratory of Cellular and Molecular Biology, INTA, University of Chile.

Introduction: Molecular clocks regulate metabolism according to signals such as light/dark and fasting/eating cycles. In obesity, these clocks are altered, and time-restricted eating (TRE) has been proposed as a therapeutic tool.
Drosophila melanogaster is a validated model for studying chronic diseases. We established an obesity phenotype with hyperglycemia, insulin resistance and elevated fat after 14 days of high-fat diet (HFD). Objective: To determine the impact of TRF on metabolic parameters and altered peripheral molecular clock components in flies fed a HFD. Methods: Male flies were fed a HFD for 10 days (HFD_{10}), then randomly distributed into 4 groups according to diet (control (CD) or HFD [CD + coconut oil 5%]), and regimen (ad libitum (AL) or TRF [food available 12h/day)] for the following 7 days. We measured hemolymph glucose, total triglycerides (TT), food intake and the expression of clock genes and the insulin resistance marker Nlaz, before and after the intervention. U-Mann Whitney or Kruskal Wallis Test plus Dunn's multiple comparisons and Cosinor analysis were used to evaluate clock gene rhythms. Data are expressed as mean ± SD (30-50 flies/measure-point, 3-6 independent experiments/points). Results: A HFD_{10} increased glucose, TT, and Nlaz. At the end of the intervention, TRF prevented glucose elevation in HFD and CD, as well as a greater adipose accumulation observed in HFD-AL, which was not attributable to lower intake. Additionally, we observed changes in Clk, Tim, and Per´s expression peak, showing that diet and regimen affected the expression pattern. Moreover, HFD increased Clk´s amplitude and shortened Tim´s period. Conclusion: TRF prevents glucose and TT increase in an obese fly model fed a CD or HFD, regardless of intake. A HFD alters clock genes rhythm, and the regimen affects the expression peak. The metabolic changes related to molecular clock alterations support TRF as a potential therapeutic tool.

94

Impaired rate-dependent depression of the Hoffman reflex in type-2 diabetes with clinical signs for peripheral neuropathy

Salinas LF[1], Trujillo VE[1], Cuellar CA[2]

[1] Faculty of Medicine, Universidad Autónoma del Estado de México. [2] School of Sport Sciences, Universidad Anáhuac México

Type-2 diabetes (T2D) is a chronic and metabolic disease characterized by hyperglycemias resulting from deficits in insulin secretion or insulin resistance. An estimated of 463 million people suffered this condition in 2019 according to the International Diabetes Federation, having a rapid increasing impact in low and middle-income countries. Among T2D complications, peripheral neuropathy (PN) is being one of the main, causing sensory symptoms including pain, numbness, contributes to foot ulceration and limb amputation.

There are several tests that will be use to diagnose peripheral nerve damage as clinical examination, nerve conduction studies, sensory tests, and biopsies. However, recently the loss rate-dependent depression (RDD) of the H reflex elicited with 2-3 electrical pulses in lower limbs has been used to evaluate alterations in sensory processing. In this study the RDD was performed in 17 T2D subjects (DE48.0±15.3 years) vs. 30 controls (DE 29.3±6.7 years) in different frequencies (0.2, 1.0, 2.0, 5.0 and 10.0 Hz) with a total of 10 pulses for each one.The Shapiro-Wilk test was performed and if it passed ($p > 0.05$), the Student's t-test was used to compare two groups, if not, the Mann-Whitney rank sum test was used instead. P values <0.05 were considered significant. It was observed a significant decrease of the RDD of the H reflex in T2D subjects at 1 Hz ($p < 0.001$), 2 Hz ($p < 0.001$), 5 Hz ($p < 0.001$)10 Hz ($p < 0.001$) but not at 0.2 Hz ($p > 0.05$), especially in overweight and obese patients. Therefore, this test will be to use as a tool in combination with the clinical examination for diagnosis and assessment of this disease, even in the early stages.

113

The Adenosine receptor A2B regulates the cytoskeletal remodeling of podocytes.

Mendoza-Soto P[1], Torres A[1], Jara C[1], Cappelli C[1], Tellez A[1], San-Martín R[1]

(1) Laboratorio de Patología Molecular, Instituto de Bioquímica, Facultad de Ciencias, Universidad Austral de Chile, Valdivia, Chile.

Abstract: Homeostasis in multisystemic vertebrates is strictly dependent on proper renal function. The structure responsible for blood filtering and albumin retention is the glomerular filtration barrier, where podocytes enwrap and compress the glomerular capillaries with highly branched actin cytoskeletal projections called foot processes. Simplification of this structure leads to nephrotic syndrome and proteinuria, which is the primary cause of chronic kidney disease. The nucleoside adenosine has modulatory actions in the kidney and its increased abundance is involved in the pathogenesis of diabetic nephropathy. Thus, we aimed to study the participation of the podocyte adenosine A2B receptor in rearrangements of their actin cytoskeleton.

Materials and methods: Streptozotocin-induced diabetic rats were treated with MRS1754 (A2B-selective antagonist) and monitored for glycemia and proteinuria. After 15 days of treatment kidneys were analyzed by electron microscopy while glomerular enriched fractions were analyzed by qPCR and Western blot. Human Immortalized Podocytes treated with adenosine, TGF-beta and MRS1754 were seeded onto laminin-521 coated cover slides and recorded by time lapse microscopy during spreading. GTP-bound Rho-GTPases were detected by G-LISA and affinity precipitations. mRNA and protein relative abundance of selected targets were detected by qRT-PCR and Western blot respectively.

Results: The antagonism of the A2B receptor with MRS1754 protects the glomerular filtration barrier *in-vivo* against foot process effacement and proteinuria. Treatment of human immortalized podocytes with MRS1754 prevents the remodeling of the actin network and reduces their spreading capacity. Conclusion: Antagonism of the A2B adenosine receptor reduces podocyte motility and rearrangements of the actin cytoskeleton.

Funding**:** This work was supported by FONDECYT grant 1211613 (R.S.M.), CONICYT 21192272 (P.M.) and Vicerrectoría de Investigación, Desarrollo y Creación Artística, UACh. (VIDCA).

Section 6: SAFIS Young Investigator Award

Chair: Aldo Mottino • . Institute of Experimental Physiology, Rosario (Argentina)
Co-Chair: Gisela Di Giusto • Bernardo Houssay Institute of Physiology and Biophysics, Buenos Aires (Argentina)
Jury:
Horacio Cantiello • Instituto Multidisciplinario de salud, tecnología y desarrollo, Santiago del Estero (Argentina)
Cristian Favre • Instituto de Fisiología Experimental, Rosario (Argentina)
María Inés Vaccaro • Instituto de Bioquímica y Medicina Molecular, Buenos Aires (Argentina)

27

Availability of a rich source of sodium during the perinatal period programs the cardiovascular response after Nitroprusside infusion in adult offspring

Porcari C.Y[1], Macagno A[1], Caeiro X[1], Vivas L[1; 2], Godino A[1; 3]
[1] Instituto de Investigación Médica Mercedes y Martín Ferreyra (INIMEC-CONICET-UNC), Córdoba, Argentina. [2] Facultad de Ciencias Exactas Físicas y Naturales, Universidad Nacional de Córdoba, Córdoba, Argentina. [3] Facultad de Psicología, Universidad Nacional de Córdoba, Córdoba, Argentina.

Osmoregulatory mechanisms may be vulnerable to environmental electrolyte and / or endocrine changes during the perinatal period, differentially programming developing-offspring and affecting them even in adulthood. Our previous results have shown that voluntary sodium intake during pregnancy and lactation induces a long-term effect on the adult offspring osmoregulatory response to osmotic challenges. The aim of this study was to evaluate whether the free access to hypertonic NaCl solution (HipNaCl) during the perinatal period can induce a differential programming of the cardiovascular response induced by a vasodilator agent “sodium nitroprusside” in adult offspring. With this purpose, we studied Wistar rats, which manipulation (M) period covered dams from 1 week before conception until offspring turned 1-month old. The experimental group (M-NaCl) had free access to HipNaCl (0.45M NaCl), food and water; and control group (M-Ctrol) had free access to food and water only. We evaluated in male and female offspring (2-month-old) the changes(Δ), in the Mean Arterial Pressure (MAP), the Heart Rate (HR), the Pulse Pressure, the Diastolic and Systolic Arterial Pressure (DAP,SAP) induced by Sodium Nitroprusside iv infusion (1mg/ml). The data were expressed as M±SE; n = 10.The repeated measures ANOVA indicated that in male and female Nitroprusside decreased the ΔMAP (male: F_{treat}=36.79; p<0.001. Female: F_{treat}=60.25; p<0.001) and ΔSAP (male: F_{treat}=13.14; p<0.001. Female: F_{treat}=64.71; p<0.001) in M-NaCl and M-Ctrol groups. However, male M-NaCl group kept ΔMAP and ΔSAP significantly higher than the M-Ctrol after infusion (ΔMAP F_{int}=3.33; p<0.001; ΔSAP F_{int}=2.05; p=0.004). In M-NaCl groups of both sexes, we observed an increase in ΔHR after infusion of Nitroprusside (male: F_{int}=1.66; p=0.035. Female: F_{int}=1.77; p=0.018) compared to M-Ctrol groups. The data indicate that the availability of a rich source of sodium during the pre/postnatal period induces a long-term effect on the adult offspring baroreflex response with some dimorphic characteristics.

Support by:PUE CONICET;FONCYT,SECYT,Fundación Roemmers

36

Therapeutic effect of a novel truncated isoform of the human TGF-β type II receptor Fc-tag protein in a liver fibrosis rat model

La Colla A[1]; Cámara CA[1]; Bertolio MS[2]; Rodríguez TM[2]; Echarte SM[1]; Dewey RA[2,3,4]; Chisari AN[1]
[1] Departamento de Química y Bioquímica, Facultad de Ciencias Exactas y Naturales, Universidad Nacional de Mar del Plata. [2] Laboratorio de Terapia Génica y Células Madre, Instituto Tecnológico de Chascomús (INTECH)-CONICET/UNSAM. [3] Centro de Medicina Traslacional (CEMET) Hospital de Alta Complejidad en Red “El Cruce” Nestor Carlos Kirchner, Florencio Varela. [4] Rad Bio S.A.S.

Liver fibrosis is a hallmark feature of liver diseases. Current therapeutic options for these patients are limited. It is well established that transforming growth factor beta (TGF-β) promotes liver fibrosis. As a result, the development of agents with a high potential for achieving a specific and long-lasting block of TGF-β action, is clinically relevant. We have recently described the presence in human cells of a new splicing variant of TGF-β type II receptor that renders a truncated mature protein of 57 amino acids known as TβRII-SE. Previously, we showed that lentiviral-mediated overexpression of this truncated endogen isoform of the human TGF-β type II receptor Fc-tagged protein (Lv.TβRII-SE/Fc) had a strong prophylactic effect in preventing liver injury, inflammation and fibrosis. In this line, the aim of this work was to study, in a carbon tetrachloride (CCl_4)-induced liver fibrosis rat model, the therapeutic effect of Lv.TβRII-SE/Fc. Experimental groups were designed as follows: The control group received CCl_4 vehicle; the CCl_4 group received CCl_4 for 10 weeks; and the Lv.TβRII-SE/Fc + CCl_4 group received CCl_4 for 10 weeks and Lv.TβRII-SE/Fc at week 4 (n=4-5). Two-way ANOVA was employed; data was shown as mean ± SD. Compared to the CCl_4 group, Lv.TβRII-SE/Fc treated

animals showed decreased liver to body weight (BW) ratio, spleen to BW ratio, and alleviation of the irregular shape and shrinkage of the liver. Administration of Lv.TβRII-SE/Fc also significantly diminished CCl_4-induced liver enzyme elevation (Aspartate transaminase and Alanine transaminase). Histological analysis of liver sections revealed that liver architecture, liver injury, inflammation and fibrosis were attenuated in Lv.TβRII-SE/Fc + CCl_4 animals. These results suggest that lentiviral delivery of TβRII-SE/Fc regulates liver injury and fibrosis to exert its therapeutic effect against CCl_4-induced liver fibrosis in rats. All in all, TβRII-SE/Fc represents a good candidate for further development of a novel antifibrotic liver treatment.

89

Myocardial Hypertrophy, Fibrosis and Angiotensin II are Exacerbated in Aged Mice with Genetic Mutation of Galectin 3

Fontana Estévez FS[1.a]*, Betazza MC[1]*, Touceda V[1.a, 2], Silva MG[3], Penas F[4], Seropian I[1], Selser C[1], Villaverde A[1], Cianciulli T[5], Morales C[6], Gironacci MM[3], Miksztowicz V[1, 2, b], González GE [1, 7, b].

[1] Universidad Católica Argentina. Facultad de Medicina, Instituto de Investigaciones Biomédicas UCA-CONICET. Buenos Aires, Argentina. [2] Universidad de Buenos Aires. Facultad de Odontología. Cátedra de Bioquímica General y Bucal. Buenos Aires, Argentina. [3] Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica, Dpto. Química Biológica, IQUIFIB (UBA-CONICET), Buenos Aires, Argentina. [4] Instituto de Investigaciones Biomédicas en Retrovirus y SIDA (INBIRS), Facultad de Farmacia y Bioquímica. [5] División Cardiología, Hospital de Agudos "Dr. Cosme Argerich". [6] Universidad de Buenos Aires, Facultad de Medicina-CONICET, Departamento de Patología Instituto de Fisiopatología Cardiovascular (IBIMOL), Buenos Aires, Argentina. [7] Universidad de Buenos Aires, Facultad de Odontología. Cátedra de Anatomía Patológica, Buenos Aires, Argentina. [a] Fellow from the National Council of Scientific and Technical Research (CONICET), Argentina. [b] Member of the Investigator Career from the National Council of Scientific and Technical Research (CONICET), Argentina. Both authors contributed equally. Dr. Germán E. González, MD, PhD. Alicia Moreau de Justo 1600- Piso 3- (C1107AFF), Buenos Aires – Argentina. E-mail: germangonzalez@uca.edu.ar

Background: Galectin 3 (Gal3) is increased in cardiac remodeling and heart failure under pathological conditions. However, the role of Gal3 on ventricular remodeling in aging is unknown.

Objective: We aimed to study if genetic deletion of Gal3 (Gal3KO) modifies the aged related cardiovascular changes in mice.

Methods: Male C57 and Gal3KO mice were followed up for 24 months. After 2 years, non-invasive systolic blood pressure (SBP, mmHg) was measured and echocardiography was performed. Myocyte cross-sectional area (MCSA) and Interstitial fibrosis were quantified in H&E and Picrosirius red-stained sections. SIRT-7, MMP-2, and MMP-9 mRNA levels were measured by RT-qPCR. Cardiac Angiotensin II (ANGII) levels were quantified by radioimmunoassay. Results: (Media±SEM). At 24 months SBP (mmHg) was: 116±4 *vs* 116±4 and the shortening fraction (%) 61±1 *vs* 60±4 in C57 in Gal3KO respectively (p=NS). The lack of Gal3KO increased cardiac hypertrophy as measure by: 1) cardiac mass/tibia length (mg/mm) (9.7±1.3 vs 7.9±1.4, p<0.05); 2) septum thickness (mm) 2±0.02 *vs* 1±0.02 (p<0,05); 3) posterior wall thickness 2±0.04 *vs* 1.4±0.05 (p<0.0001), and 4) MCSA (um2) 159±10 vs 103±6 (p<0.05) in Gal3KO *vs* C57 respectively. Myocardial fibrosis was also increased in Gal3KO mice (8±1 %) *vs* C57 (5±1 %; p<0.05). Those findings were also associated with increased levels of cardiac ANGII (7±1.5 ng/g *vs* 3±0.5, p<0.05) and MMP-9 (0.9±0.2 *vs* 2.2±0.3 AU, p<0.01) at the same time that SIRT-7 mRNA levels were reduced (1.2±0.1 *vs* 0.6±0.1, p<0.05) in C57 and Gal3KO mice respectively.

Conclusion: Gal3 is a critical regulator of myocardial remodeling in aging. The lack of Gal3 exacerbated the cardiac hypertrophy and fibrosis independently of hypertension. This data strongly suggests that cardiac ANGII, MMP-9 and SIRT-7 are mechanisms associated with our findings.

Keywords: Aging, Galectin-3, Angiotensin II, Cardiac Remodeling, Hypertrophy, Fibrosis, Hypertension.

Section 8: Camilión de Hurtado Award

Chair: Lascano Elena • Institute of Translational Medicine, Transplantation and Bioengineering, Buenos Aires (Argentina)
Co-Chair: Emiliano Diez • Institute of Medicine and Experimental Biology of Cuyo, Mendoza (Argentina)
Jury:

Gerardo Garcia Rivas • Tecnológico de Monterrey, ITESM (México)
Cristina Arranz • Instituto Química y Metabolismo del Fármaco, Facultad de Farmacia y Bioquímica, UBA (Argentina)
Santiago Miriuka • Laboratorio de Investigación Aplicada a las Neurociencias (LIAN) de la Fundación FLENI, Buenos Aires (Argentina)

39

Pacemaker Activity in Postnatal Hypothyroidism: Implications of the Nitric Oxide System and PI3K/AKT Pathway.

D'Angelo V.[1], Martinez C.[1], Duca M.[1], Hope S.[1], Tavernise R.[1], Abramovici Blasco A.[1], Arreche N.[1], Fellet A.L.[1]
[1] Department of Physiology, School of Pharmacy and Biochemistry, University of Buenos Aires. IQUIMEFA, CONICET.

Thyroid axes and nitric oxide (NO) system modulate cardiovascular function. We previously demonstrated that thyroid hormone regulates NO bioavailability affecting mean arterial pressure (MAP) and heart rate (HR) in denervated heart. The aim of this study was to evaluate the involvement of NO system in the regulation of pacemaker activity in postnatal hypothyroidism. Male Sprague–Dawley rats weighing approximately 50 g were used in this study and were randomly assigned to one of the groups: euthyroid rats (eut, received SC injections of 0.9 NaCl (0.1 ml/100 g body weight)) and hypothyroid rats (hypo, received 0.02% methimazole in drinking water). Methimazole treatment was for 60 days. Measurements of MAP, HR, NO synthase (NOS) activity (citrulline method) and western blot analysis of NOS, caveolins1-3 and Akt were performed in the right atrium. Hypo group showed a decreased MAP (*mmHg*, *hypo: 58±1 vs eut:90±1, n=6, p<0,05)* and HR values *(bpm, hypo:211±1 vs eut:346±1, n=6, p<0,05).* Hypothyroidism decreased NOS activity *(UA, hypo:287±16 vs. eut:18358±3495, n=13, p<0,001), e*ndothelial NOS (eNOS) protein levels *(hypo: 1,76±0,09 vs eut:2,04±0,17, n=6, p<0,01)*. No differences in inducible and neuronal NOS as well as caveolin-1 protein levels were observed. Hypo rats showed increased caveolin-3 *(hypo:0,90±0,09 vs eut:0,81±0,08, n=8, p<0,05)*, total-AKT *(hypo:3,20±0,07 vs eut:2,38±0,36, n=6, p<0,05)* and phosphorylated-AKT *(hypo:2,11±0,21 vs eut:0,92±0,20, n=6, p<0,001)* protein levels. Results are mean ± SEM, unpaired t-test was used as statistical analysis (SPSS 23 version). Our findings suggest that decreased HR of hypothyroid rats was associated with decreased NO production in right atrium. This reduction of atria NOS activity may be due to a decreased eNOS protein level as well as an increase of negative regulator of the enzyme, caveolin-3. The PI3K/AKT-pathway seems not to be involved in this mechanism.

52

Gene therapy overexpressing Tbx20 induces cell proliferation and angiogenesis in cardiomyocyte culture.

Bauzá MDR[1], López AE[1], Simonin JA[2], Belaich MN[2], Cimbaro FS[1], Cuniberti LA[1], Crottogini AJ[1] Locatelli P[1], Olea FD[1].
[1] Instituto de Medicina Traslacional, Trasplante y Bioingeniería (IMETTyB)-Universidad Favaloro-CONICET. [2] Universidad Nacional de Quilmes.

Introduction: transcription factor Tbx20 has been described as an inductor of cell proliferation and angiogenesis. We hypothesized that gene therapy overexpressing Tbx20, would promote myocardial regeneration after myocardial infarction. Objectives: to design baculovirus encoding Tbx20 gene (Bv-Tbx20) to be used as gene therapy vector and evaluate its functionality on the increase in cell proliferation, cell cycle gene expression, and angiogenesis in neonatal rat cardiomyocytes (CM). Methods: in culture of CM transduced with BvTbx20 and BvNull (placebo) at 2 and 5 days post transduction we measured CM proliferation by cell counting and MTS assay, angiogenesis by HMEC cells proliferation cultured with supernatants and gene expression of angiogenic (vegf, angiopoietin, angiogenin, and prokr2) and cell cycle genes (Cyclin D1, MEF2C, p21) by RT-qPCR. Data were analyzed statically using Student's t Test to compare means between groups and expressed as mean±SD. Results: at 2 days post-transduction, CM-BvTbx20 showed higher percentage of cell proliferation (CM-BvTbx20: 113±6.7 vs. CM-BvNull: 100±8.4%, p<0.01), cell counting (621250±35778 vs 584500±31597cells, p<0.05), and mRNA relative expression of vegf (1.7±0.6 vs 0.4±0.4, p<0.05), angiogenin (1.8±0.5 vs 0.7±0.6, p<0.05) and prokR2 (7.9±3.8 vs 1.9±2.9, p<0.05). At 5 days post-transduction, CM-BvTbx20 showed higher percentage of endothelial proliferation (CM-BvTbx20: 115.2±8.4 vs CM-BvNull: 100±10.4, p<0.05) and mRNA relative expression of vegf (CM-BvTbx20: 5±4.2; CM-BvNull: 0.9±0.9, p<0.05), angiopoietin (CM-BvTbx20: 3.1±1.7; CM-BvNull:1±0.5, p<0.05), angiogenin (CM-BvTbx20: 3.5±2.5; CM-BvNull: 0.6±0.4, p<0.05), mef2C (CM-BvTbx20: 7.7±10 vs CM-BvNull:0.8±0.7, p<0.05) and lower p21 (CM-BvTbx20: 0.6±0.5 vs CM-BvNull: 7.7±7.2, p<0.05). Conclusion: Tbx20 overexpression in CM increased cell proliferation and induced angiogenesis in vitro. These results suggest that Tbx20 may be potentially useful as a therapeutic factor to stimulate myocardial regeneration.

85

Beneficial consequences on myocardial mitochondrial network dynamics and function of one-month oral treatment with cannabis oil to spontaneously hypertensive rats (SHR).

Pereyra E[1]; Godoy Coto J[1]; Cavalli F[1]; González Arbelaez L[1]; Fantinelli J. C[1].; Aranda O[2]; Colman Lerner E[3]; Velez Rueda O. [1]; Mosca S[1]; Ennis I[1].

[1]Centro de Investigaciones Cardiovasculares "Horacio E. Cingolani", Facultad de Ciencias Médicas, Universidad Nacional de La Plata (UNLP) – CONICET. Argentina. [2]Programa Ambiental de extensión universitaria (PAEU). Facultad de Ciencias Exactas UNLP. Argentina. [3]CINDECA CONICET-CIC-UNLP. Argentina.

Introduction: Recently, the component of oil cannabis CBD was found to regulate mitochondrial DNA epigenetics, biogenesis, and network dynamics. While abnormal mitochondrial function has been repeatedly linked to a wide variety of cardiovascular diseases, components of cannabis oil have proved cardioprotective, attenuating inflammatory and oxidative damage. However, the effect of cannabis oil on hypertensive cardiac hypertrophy (CH) and specially on mitochondrial function, remains elusive. Objective: To evaluate the consequences of cannabis oil on hypertrophy, mitochondrial function, and mitochondrial network dynamics in SHR hearts. Methods: Three-month old male SHR were randomized into treated (TR) and control (CR). Cannabis sativa or olive oil were orally administered for 1 month, respectively. At the end of treatment, we measured CH, mitochondrial network dynamics by qPCR, mitochondrial membrane potential by spectrofluorometry and myocardial superoxide dismutase (SOD) activity by spectrometry. Data are presented as mean±SEM. Welch's t-test was used for statistical differences ($p<0.05$).

Results: CH, determined by left ventricular weight/tibia length ratio, was reduced by treatment (mg/mm, CR:33,49±0,2 N=6; TR:30,47±0,78 N=9, $p<0,05$). Mitochondria membrane potential was improved in TR (in mV, CR: -152,9±2,622 N=8, TR:-161,6±2,821 N=7, $p<0,05$). The treatment also enhanced mitochondrial biogenesis estimated by mRNA transcripts (%ratio of PG1alpha/GAPDH : CR:100,0 ± 20,33 N=6; TR:156,6 ± 13,80 N=9, $p<0,05$) and mitochondrial network dynamics (%ratio of gene/GAPDHexpression:DRP1: CR: 100,0 ± 10,78 N=5 TR: 330,7 ± 109,3 N=6 $p=0.089$, MITO1 CR:100,0±40,20 N=4; TR:224,1±18,11 N=4, $p<0,05$, PINK CR:100,0 ± 26,24 N=5,TR:183,3 ± 20,60 N=8 $p<0,05$) in SHR hearts. Moreover, we observed a significant increase in the activity of the antioxidant SOD by treatment (% of control CR:100,0 ± 19,62 N=4, TR:269,4 ± 53,31 N=4 $p<0,05$). Conclusion: We propose that a 1-month treatment with Cannabis sativa oil is effective to reduce CH and improve mitochondrial network. These effects may be related to an increased antioxidant capacity.

SPONSORS

Physiological Societies:

Argentina, Brazil, Colombia, Cuba, Chile, Ecuador, Haití, Mexico, Peru, Uruguay, Venezuela
The International Union of Physiological Sciences (IUPS)
The Physiological Society (UK)
The American Physiological Society (APS)
Sociedad Española de Ciencias Fisiológicas (SECF)

Publishers: