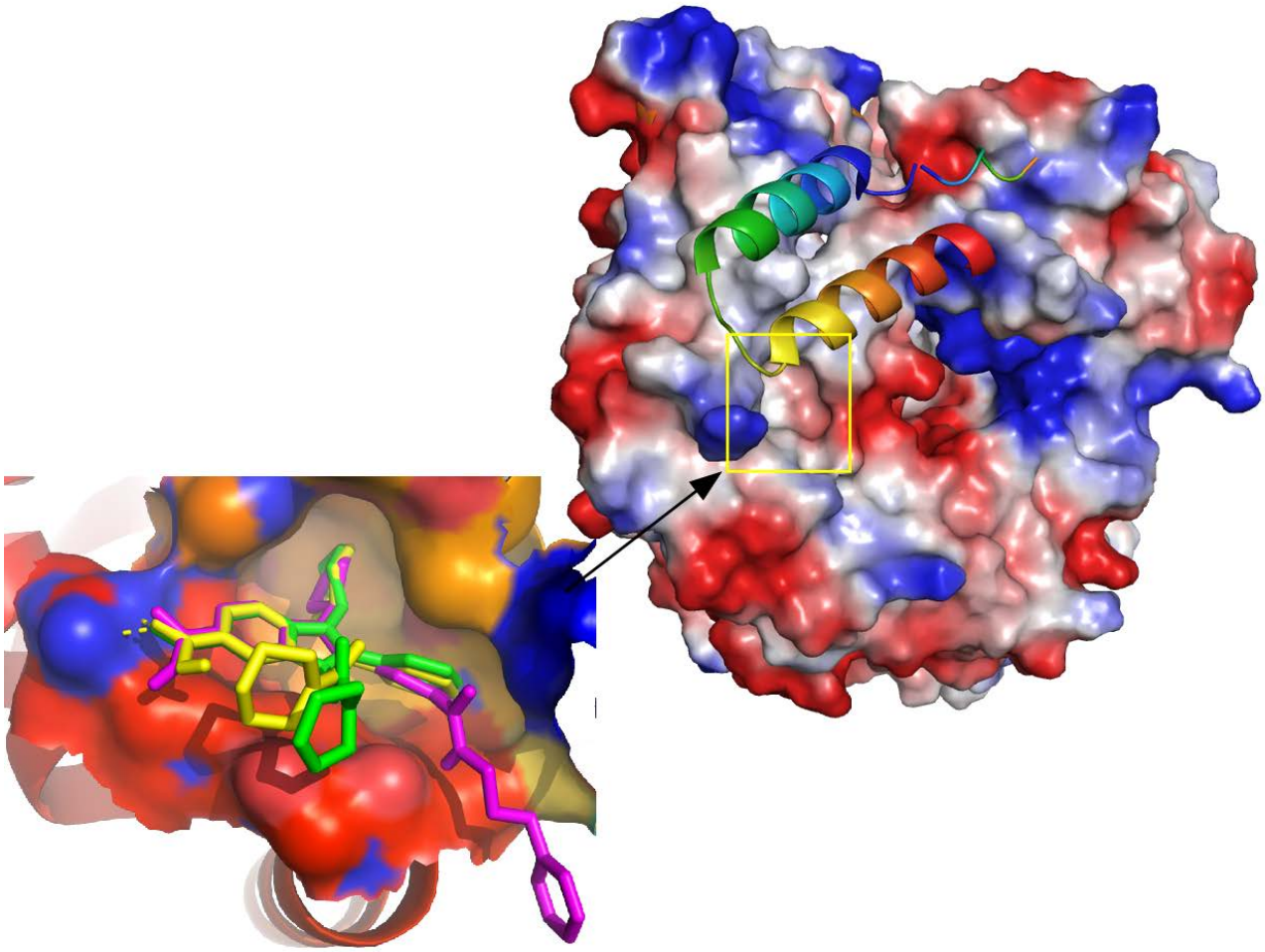
ANNUAL REPORT 2020



INSTITUTE OF RESEARCH, DEVELOPMENT, AND INNOVATION IN HEALTHCARE BIOTECHNOLOGY OF ELCHE

UNIVERSITY "MIGUEL HERNÁNDEZ"

IDiBE
UNIVERSITAS Miguel Hernández

DIRECTOR'S FOREWORD

The Institute of Research, Development, and Innovation in Healthcare Biotechnology in Elche (IDiBE) is one of the University Research Institutes at the University *Miguel Hernandez de Elche*. The IDiBE is located in the University Campus in Elche, occupying a 4,000 sq. m. of laboratory in the Torregaitán Building. IDiBE aims to become a market-oriented Research Institute that excels in translational science. In the past 23 years, the IDiBE (previously IBMC) has excelled in its scientific production, in the exploitation of the generated results and technologies and its societal disseminating programs. This translational excellence has thrust the creation of spin-off companies and Joint ventures with private enterprises and local Hospitals. This seminal vision has been kept invariable and can be fully appreciated in our Annual Reports describing all our achievements in research, exploitation, training and dissemination activities. All these accomplisments are in line with the objectives set in our Plan of Actions.

As in previous years, our groups have been active in securing funding from both governmental and private sources, publishing papers (73% in Q1) that are widely cited, training young scientists with the highest scientific standards as recognized by recent audit of our Doctorate program by the AVAP, and to disseminate our activities and achievements to society through our out-reach programs (Science with tapas; And you, what do you research on?) In addition, we consolidated the Master Degree in Biotechnology and Bioingeneering with the Institute of Bioingeneering that is becoming a national reference in the field. In addition, we initiated the Eramus+European Master on translational cosmetic and dermatological sciences with the Universities of Piemonte Orientale (Italy), Namur. (Belgium) and Humboldt (Germany). A major success of the Institute has been the commercialization of innovative products generated from the research projects in the fields of nutraceuticals, cosmeceuticals and biotechnology; and having 3 lead compounds in clinical development and one in pre-clinical. Our translational activities are reinforced with four technological platforms. This success has been possible thanks to our philosophy of potentiating communication and collaborations, and sharing all the infrastructures, as well as to the commitment of our administrative and technical personnel to the IDiBE project.

Despite the unexpected Covid-19 pandemic, the IDiBE has been able to continue working on its objectives, providing part of the deliverables. The major milestones for 2020 have been: (i) Potentiation of the technology transfer actions to the productive sectors of our society through the innovation agent; (ii) acquisition of new infrastructures funded by the GVA and the EU that have provided new technologies that will allow the Institute to embark on more competitive projects; and, (iii) award of the MCSA-ETN "PIANO" of the Horizon 2020 EU program. Furthermore, we set the basis to have a BL-2 laboratory in the Institute which will allow developing additional projects. This is in line with our current Plan of Action (2019-2022) that establishes the central mission to consolidate a multidisciplinary research program in the area of Healthcare Biotechnology elegible for a seal of excellence.

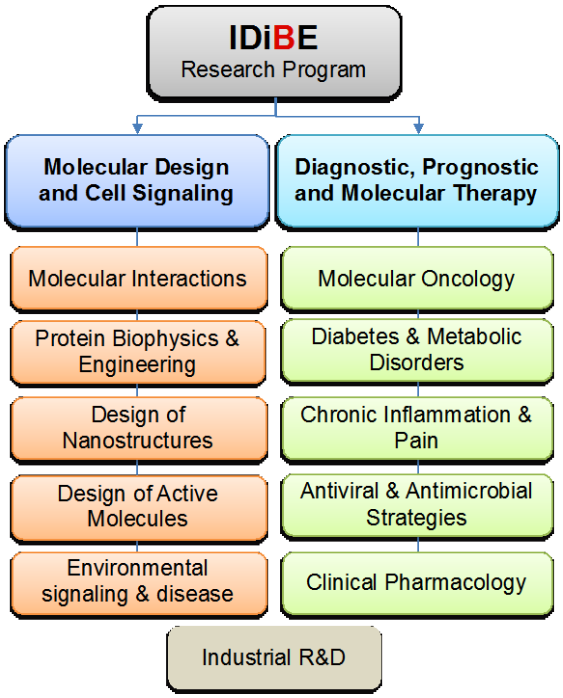
Prof. Antonio Ferrer-Montiel

IDiBE director

STRUCTURE AND GENERAL DESCRIPTION

The IDiBE Action Plan for 2019-2022

The IDiBE R&D program is organized in two major research lines that cover all the activities carried out by our teams. These lines are: (i) **Molecular Design and Cell Signaling** and, (ii) **Molecular Diagnostic, Prognostic and Therapy**. Each line is structured in specific sublines that accurately define the actions of the different groups, and also highlight the channels of communication between both research lines, which is essential for exploiting the synergies that emerge from the multidisciplinarity. **An industrial R&D** line for natural extracts complements the research lines. This organization also favors internal collaborations, sharing the infrastructures, and a more rational and productive use of all resources, including the technological platforms. Consequently, in the next four-year period, the IDiBE aspires to become a center of reference in the discovery of pharmacological and biotechnological tools, with a clear translational and transfer potential. The intense and sustain work in this line is the central objective for the next four-year period, and to so agreements with PROs will be pursued which will permit reinforcing deficient areas or those that require an impetus for their consolidation, and thereby generating a unique and unprecedented project on a national and international level.



R&D organization

In scientific terms, the targets of these research areas of the IDiBE are developed as follows:

A. Molecular Design and Cell Signaling

The main objective of this research line is to advance our knowledge in the structure-function relations of small molecules and macromolecules with the aim of transforming their activity for biotechnological purposes, and to design better ligands that modulate their function, as well as nanotechnology-based systems that help their deliver to the site of action. An additional objective of this research line is to understand the cell signaling mechanisms used by environmental signals such as endocrine disruptors and other pollutants that may be the underlying cause of diseases with an increase prevalence. These studies aim to identify the molecular composition of the signaling mechanisms and to validate targets for drug intervention. Environmentally-mediated disease or aggravation of

human disease is an emerging societal challenge directly linked to progress in western countries and heavy contamination in poor countries.

This research line involves 8 research groups. The different scientific backgrounds of the researchers involved allows for a multidisciplinary approach of the societal and technological challenges investigated. The main research fields under this core line are:

1. Molecular interactions, protein biophysics and engineering. 2. Design and validation of nanostructures. 3. Design of active molecules. 4. Environmental signaling and disease.

B. Molecular Diagnostic, Pronostic and Therapy

The research line for Molecular Diagnosis, Prognostic and Therapy pursues the identification and validation of molecular markers in human and animal pathologies of high prevalence, as well as the development of diagnostic and prognostic methods and therapeutic or preventive strategies. This research line is made up of a multi-disciplinary research team, which covers from molecular aspects to semi-industrial biological actives. This multidisciplinarity is sustained by the contribution of 8 consolidated groups, which provide a balanced composition that favors a high competitiveness in scientific contributions, raising resources, training research staff and generating exploitable and transferable technologies.

The milestones achieved in this line of research have had and have a high scientific impact as is evident from the scientific publications in internationally recognized journals, as well as the generation of unique technologies which are protected by worldwide patents and have been licensed out to interested companies. One strong point of this research line to be highlighted is the high level of national and international collaborations with public and private research organizations, which contribute to increasing the impact of the activities and their internationalization. Furthermore, the interrelation of the sub-lines which make up this line of research has reinforced the identification of synergies and common interests between groups, promoting collaborations which speed up the achievement of results and technologies.

The activities in this line clearly have a high potential for clinical translation, which has materialized in a close collaboration with the University Hospitals of Elche and Alicante, and of industrial exploitation that has led to continuous and consolidated collaborations with biotech and pharmaceutical companies. Indeed, these research lines are complemented by an additional complementary subline dealing with the industrial developments (including products and processes for healthcare biotechnology).

1. Molecular Oncology. 2. Diabetes and Metabolic disorders. 3. Chronic inflammation and pain. 4. Antiviral and antimicrobial strategies. 5. Clinical pharmacology.

MOLECULAR DESIGN AND CELL SIGNALING

MOLECULAR DESIGN AND CELL SIGNALING

Molecular Recognition and Protein Biophysics and Engineering

Group name: BIOTHERMODYNAMICS OF MOLECULAR RECOGNITION PROCESSES

Our group is involved two main research lines. On the one hand, Dr. Neira leads the research dealing with the biophysical characterization the biomolecules and interactions involved in in the phosphorylation transfer in micro-organisms, the assembly of the capsid of HIV and intrinsically disordered proteins implicated in pancreatic cancer. On the other, Dr. Gómez research activities focus on the design and characterization of nano and microparticles coated with polyelectrolytes to be used in the transport and controlled delivery of different biomolecules, the storage of labile biomolecules used as drugs and the capture and recovery of different pollutants in continental waters.

Staff

Javier Gómez Pérez

José Luis Neira Faleiro

Rocío Esquembre Tomé

Postdoctoral Researchers

Felipe Hornos Adán

Technicians

Elisa Pérez García

Publications

Hornos, F, Esquembre, R, Gómez, J. Competitive inhibition of protein adsorption to silica surfaces by their coating with high density charge polyelectrolytes. Colloids and Surfaces B: Biointerfaces. 2020, 191, art. no. 110993. DOI: 10.1016/j.colsurfb.2020.110993.

Díaz-García, C, Hornos, F, Giudici, AM, Cámara-Artigas, A, Luque-Ortega, JR, Arbe, A, Rizzuti, B, Alfonso, C, Forwood, JK, Iovanna, JL, Gómez, J, Prieto, M, Coutinho, A, Neira, JL. Human importin α3 and its N-terminal truncated form, without the importin-β-binding domain, are oligomeric species with a low conformational stability in solution. Biochimica et Biophysica Acta - General Subjects. 2020, 1864 (7), art. no. 129609. DOI: 10.1016/j.bbagen.2020.129609.

Giudici, AM, Hernández-Cifre, JG, Cámara-Artigas, A, Hornos, F, Martínez-Rodríguez, S, Carlos Alvarez-Pérez, J, Díaz-Cano, I, Esther Fárez-Vidal, M, Neira, JL. The isolated armadillo-repeat domain of Plakophilin 1 is a monomer in solution with a low conformational stability. Journal of Structural Biology. 2020, 211 (3), art. no. 107569. DOI: 10.1016/j.jsb.2020.107569.

PhD Theses

Diseño y optimización de nanopartículas con aplicaciones biotecnológicas: captura de contaminantes, transporte y almacenamiento de biomoléculas. Felipe Hornos Adán. Advisor: Javier Gómez. 05/11/2020.

Governmental Projects and Funding

Diseño de nuevos antibióticos basados en un sistema de fosforilación exclusivo de Bacterias 01/01/2019-21/07/2019 - PROYECTOS I+D+i «RETOS INVESTIGACIÓN» DEL PROGRAMA ESTATAL DE I+D+i ORIENTADA A LOS RETOS DE LA SOCIEDAD- MICIU 2019. MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES (RTI2018-097991-B-I00). UMH. IPs: Jose Luis Neira Faleiro, F. Javier Gómez Pérez.

R&D Management

Reviewer of CONICET (JLN) (2008-...).

Reviewer of Israeli Science Foundation (JLN) (2016-...).

Reviewer for Czech Science Foundation (JLN) (2010-...).

Reviewer of ERC (JLN) (2018-...).

Editorial Boards

Board member Archives of Biochemistry and Biophysics (2010-2013). José L. Neira.

Executive Editor Archives of Biochemistry and Biophysics (2013-...). José L. Neira.

Group name: FLUORESCENT NANOMATERIALS APPLIED BIOTECHNOLOGY - FISH BIOMEDICAL NANOAPPLICATIONS

Our group is interested in the development of new fluorescent materials with applications in biological systems. On one hand, we design and develop fluorescent biosensors with high sensitivity, based on the entrapment of organic molecules and biomolecules in inorganic matrices, and characterize these hybrid materials at a molecular level in order to improve their applications. On the other hand, we work on the design, synthesis and characterization of novel fluorescent conjugated polyfluorenes, to be used as nanoparticles and nanofibers in applications such as bioimaging, drug delivery, clinical diagnosis and sensing devices for biomolecules. Other group activities include the characterization of macromolecular interactions, especially in non-conventional systems, such as ionic liquids as well as the synthesis of conjugated polymers to be applied in photonics and optoelectronics devices.

Study of animal mucosa bioactive compounds. Nanostructures for biomedical and veterinary skin applications. Evolutionary studies on short pentraxins (CRP and SAP).

Staff

Carmen Reyes Mateo Martínez

Ricardo Mallavia Marin

Mª José Martínez Tomé

Juan Alberto Falcó Graciá

Postdoctoral Researchers

Amalia Mira Carrió

Ph. D Students

Marta Rubio Camacho

Yolanda Inmaculada Alacid Martínez

Rocío Díaz Puertas

Technicians

Elisa Pérez García

Publications

Rubio-Camacho M, Encinar JA, Martínez-Tomé MJ, Esquembre R, Mateo CR. The Interaction of Temozolomide with Blood Components Suggests the Potential Use of Human Serum Albumin as a Biomimetic Carrier for the Drug. Biomolecules. 2020, 10(7): 1015. doi:10.3390/biom10071015.

Falcó A, Mallavia R. Electrospun Nanomaterials: Applications in Food, Environmental Remediation, and Bioengineering. 2020, Nanomaterials, 10(9), 1714. https://doi.org/10.3390/nano10091714.

Mira A, Sainz-Urruela C, Codina H, Jenkins SI, Rodriguez-Diaz JC, Mallavia R, Falcó A. Physico-Chemically Distinct Nanomaterials Synthesized from Derivates of a Poly(Anhydride) Diversify the Spectrum of Loadable Antibiotics. Nanomaterials. 2020, 10(3), 486. https://doi.org/10.3390/nano10030486.

Torres-Moya I, Vázquez-Guilló R, Fernández-Palacios S, Carrillo JR, Díaz-Ortiz JR, Navarrete JTL, Ortiz RP, Delgado MC, Mallavia R, Prieto P. Fluorene-Based Donor-Acceptor Copolymers Containing Functionalized Benzotriazole Units: Tunable Emission and their Electrical Properties. 2020, Polymers 2(2), 256. https://doi.org/10.3390/polym12020256.

Belló-Pérez M, Sola I, Novoa B, Klionsky DJ, Falcó A. Canonical and Noncanonical Autophagy as Potential Targets for COVID-19. Cells. 2020, Jul 5;9(7):1619. doi: 10.3390/cells9071619.

Belló-Pérez M, Pereiro P, Coll J, Novoa B, Perez L, Falcó A. Zebrafish C-reactive protein isoforms inhibit SVCV replication by blocking autophagy through interactions with cell membrane cholesterol. Sci Rep. 2020, Jan 17;10(1):566. doi: 10.1038/s41598-020-57501-0.

Science dissemination: outreach activities

Jornadas de divulgación científica "Ciencia con tapas".

- El coronavirus de China y otros virus que vienen de fuera: ¿hay que temerles?, 18/02/2020.

- "¿Cómo se defiende nuestro cuerpo del SARS? La respuesta inmunológica frente a virus, 05/11/2020.

Mª José Martínez Tomé. Comité organizador.

Number of Congress Communications

National contributions: 4

Oral presentations: 2

Poster presentations: 2

International contributions: 4

Oral presentations: 2

Poster presentations: 2

Governmental Projects and Funding

Desarrollo y evaluación traslacional de nanofibras de extractos mucilaginosos de pez con potencial terapéutico para aplicaciones en acuicultura y ganadería (MUCIPEUTICS). 01/10/2019 – PROYECTOS DE I+D+I "RETOS DE LA SOCIEDAD" 2018 (RTI2018-101969-J-I00). FEDER / Ministerio de Ciencia, Innovación y Universidades – Agencia Estatal de Investigación. UMH. IP: Juan Alberto Falcó Graciá.

Diseño de nanomateriales fluorescentes para el desarrollo de nuevas formulaciones terapéuticas y descubrimiento de nuevos fármacos. PROYECTOS DE I+D+I "RETOS DE LA SOCIEDAD" - MAT-2017-86805-R (Enero 2018- Sept2021). Ministerio de Economía, industria y Competitividad. IP: Carmen Reyes Mateo Martinez y Co-IP: Ricardo Mallavia Marín.

Plataforma en nanotecnología traslacional (Patent). Proyectos de Equipamiento científico-técnico. GVA-IDIFEDER_2018/2020, una forma de hacer Europa. CONSELLERIA DE EDUCACION, INVESTIGACION, CULTURA Y DEPORTE GENERALITAT VALENCIANA. IP: Antonio Ferrer Montiel.

Microscopía correlativa óptico-electrónica para dotar la plataforma en nanotecnología traslacional (PATENT). Agencia Estatal de Investigación. EQC2019-005842-P. 2020. IP: Antonio Ferrer.

Editorial Boards

Special Issue editors:

"Electrospun Nanomaterials: Applications in Food, Environmental Remediation, and Bioengineering", Nanomaterials (MDPI), 2019-2020. Ricardo Mallavia and Alberto Falcó.

Reviewer for the following journals in 2020 (number of revised manuscripts):

Reviewers for different journals in 2020 (number of revised manuscripts):

Mª José Martínez: Molecules (1)

C.Reyes Mateo (6)

Ricardo Mallavia (9)

Alberto Falcó (9)

Reviewer Board member of Nanomaterials (MDPI) (2020-...) (Alberto Falcó).

Reviewer Board member of Marine Drugs (MDPI) (2020-...) (Alberto Falcó).

Group name: PROTEIN ARCHITECTURE

This newly created group is led by Ph.D. Ana María Fernández Escamilla who has joined IDiBE recently. The group´s expertise lies in the field of protein engineering by combining theoretical (computational) and experimental approaches, for biochemical, biophysics and structural characterization of macromolecules aimed at engineering of polypeptides and peptides with new or desirable functions and properties for technological applications in biomedicine, bioengineering and in the most recent areas of nanoscience.

Proteins are dynamic nanomolecular machines ubiquitous in all living systems that adopt distinct three-dimensional (3D) structures to perform multitude of biological functions. Advance in modern

molecular biology and biotechnology have improved our understanding of basic functional and architectural principles of proteins, making them attractive candidates as concept generators for technological development in biomedicine, bioengineering and in the most recent areas of nanoscience. Appling “rational design”, protein engineering is the most powerful approach to obtain proteins with new or desirable functions and properties. In biomolecular engineering is of particular interest, the protein biochemical and biophysical characterization by thermodynamic, kinetic, spectroscopic and structural methods allowing us to better understanding the rules that govern the processes of interest, and the degree of involvement of proteins in these processes.

The efforts of the group are leading to get insights into the relationship between protein structure and function (or dysfunction), as well as to the creation of novel biomolecules with desirable properties to study. We approach this from a variety of angles and employ state-of-the-art in silico (protein rational design, protein modeling and molecular docking for identification of novel active compounds) and in vitro molecular methods for biophysical, biochemical and structural characterization of diverse recombinant proteins by using spectroscopic techniques (Circular Dichroism, Fluorescence, Dynamic Light Scattering) and thermodynamic techniques (DSC and ITC Calorimetry).

Our studies are focused on three main lines of research:

- Protein structure regularization and effect on function.

- Protein stability, folding and oligomerization with the final aim of understanding the molecular basis of the aggregation contribution to allergenic properties of food allergens.

- Zika and dengue viruses. New direct-acting antivirals through computational and experimental tools.

Our Molecular Recognition and Protein Biophysics and Engineering division possess a protein-protein interaction facility equipped, among others, with a recently acquired TA DSC (Differential scanning nanocalorimeter), VP ITC (Isothermal Titration Calorimeter), two Circular Dichroism Spectrophotometers (J-810 and J815) and also a recently acquired Malvern nano-ZS DLS (Dynamic Light Scattering).

Staff

Ana María Fernández Escamilla

External collaborators integrated in the group

Prof. Ana Grande and Prof. Enrique Viguera. Instituto de Hortofruticultura Subtropical y Mediterránea. Departamento de Biología Celular, Genética y Fisiología. Universidad de Málaga.

Prof. Salvador Ventura Zamora. Director of IBB Barcelona. Protein Folding and Conformational Diseases Group. Universidad Autónoma de Barcelona.

Ph.D. Tomás Mayoral Ortega. Director Técnico del Laboratorio de Genética Molecular. Laboratorio Central de Veterinaria de Madrid. Ministerio de Agricultura, Pesca y Alimentación.

Number of Congress Communications

National contributions: 2

Oral presentations: 2

Governmental Projects and Funding

Zika y Dengue: Identificación de nuevos inhibidores enzimáticos combinando estrategias computacionales y experimentales. AICO/2020/026, 01/01/2020-31/12/2021. IP: Ana María Fernández Escamilla.

Terapia antiviral de combinación de mutagénesis letal e inhibidores de las actividades correctoras ExoN y MTasa del coronavirus SARS-CoV-2 para impedir su evasión de la defensa inmunitaria innata antiviral. CV20-10932, 11/11/2020-11/11/2021. IP: Ana Grande Pérez.

Plataforma en nanotecnología traslacional (Patent). Proyectos de Equipamiento científico-técnico. GVA-IDIFEDER_2018/2020, una forma de hacer Europa. CONSELLERIA DE EDUCACION, INVESTIGACION, CULTURA Y DEPORTE GENERALITAT VALENCIANA. IP: Antonio Ferrer Montiel.

Microscopía correlativa óptico-electrónica para dotar la plataforma en nanotecnología traslacional (PATENT). Agencia Estatal de Investigación. EQC2019-005842-P. 2020. IP: Antonio Ferrer.

R&D and Educational Committees

Agencia Nacional de Evaluación y Prospectiva (ANEP). A. M. Fernández Escamilla.

Scientific Society Councils

Name of the society: Red temática de Estructura y Función de Proteínas. http://redproteinas.iqfr.csic.es/

Name of the society: Sociedad Española de Biofísica (SBE). http://www.sbe.es/

Name of the society: Sociedad Española de Bioquímica y Biología Molecular (SEBBM). http://www.sebbm.es/

Editorial Boards

Review Editor in Frontiers in Physiology - Membrane Physiology and Membrane Biophysics (2018-.....). A. M. Fernández Escamilla.

Structure-Function Relationships in Membrane Proteins

Group name: STRUCTURE-FUNCTION RELATIONSHIP OF ION CHANNELS

Our group studies the structure-function relationships in membrane proteins, especially neuroreceptors and ion channels. The final aim is to understand how these proteins work at the molecular level and how they are modulated by lipids, ligands or other proteins in order to find new potential targets for drug discovery.

Staff

José Manuel González-Ros

José Antonio Poveda Larrosa

Postdoctoral Researchers

Mª Lourdes Renart Pérez

Ana Marcela Giudici Besseghini

Ph. D Students

Clara Díaz García

Technicians

Eva Martínez

Publications

Renart ML, Giudici AM, Díaz-García C, Molina ML, Morales A, González-Ros JM, Poveda JA. Modulation of Function, Structure and Clustering of K+ Channels by Lipids: Lessons Learnt from KcsA. Int J Mol Sci. 2020, Apr 7;21(7):2554. doi: 10.3390/ijms21072554.

Giudici AM, Hernández-Cifre JG, Cámara-Artigas A, Hornos F, Martínez-Rodríguez S, Carlos Alvarez-Pérez J, Díaz-Cano I, Esther Fárez-Vidal M, Neira JL. The isolated armadillo-repeat domain of Plakophilin 1 is a monomer in solution with a low conformational stability. J Struct Biol. 2020, Sep 1;211(3):107569. doi: 10.1016/j.jsb.2020.107569. Epub 2020 Jul 7.

Díaz-García C, Hornos F, Giudici AM, Cámara-Artigas A, Luque-Ortega JR, Arbe A, Rizzuti B, Alfonso C, Forwood JK, Iovanna JL, Gómez J, Prieto M, Coutinho A, Neira JL. Human importin α3 and its N-terminal truncated form, without the importin-β-binding domain, are oligomeric species with a low conformational stability in solution. Biochim Biophys Acta Gen Subj. 2020 Jul;1864(7):129609. doi: 10.1016/j.bbagen.2020.129609. Epub 2020 Mar 29.

Number of Congress Communications

International contributions: 1

Oral presentations: 1

Governmental Projects and Funding

Estudio de los estados conformacionales del filtro de selectividad de los canales iónicos: hacia la comprensión de la permeación, selectividad e inactivación. Ref. PGC2018-093505-B-I00. 01/01/2019-31/12/2021. PROYECTOS DE I+D – GENERACIÓN DE CONOCIMIENTO, MINISTERIO DE CIENCIA, INNOVACIÓN. IPs: José Manuel González-Ros y José Antonio Poveda Larrosa.

Plataforma en nanotecnología traslacional (Patent). Proyectos de Equipamiento científico-técnico. 01/01/2018-31/10/2020. CONSELLERIA DE EDUCACION, INVESTIGACION, CULTURA Y DEPORTE GENERALITAT VALENCIANA. IP: Antonio Ferrer Montiel.

Microscopia correlativa óptico-electrónica para dotar la Plataforma en Nanotecnología Traslacional (PATENT) de microscopia de superresolución. Ayudas a infraestructuras y equipamiento científico-técnico cofinanciadas con fondos FEDER – 2019; 2019- 2020. IP: Antonio Ferrer-Montiel.

R&D Management

Reviewer for Biomedicines (JAPL)

Reviewer for Molecules (JAPL)

Reviewer for Pharmaceuticals (JAPL)

Reviewer for “Archives of Biochemistry and Biophysics” (JAPL, AMG)

Reviewer for “International Journal of Molecular Sciences” (JAPL, JMGR)

Reviewer for “Protein Expression and Purification” (JAPL)

Reviewer for “Biopolymers” (JAPL)

Revierwer for “AIMS Biophysics” (JAPL)

Evaluator for FWF Austrian Science Fund (JMGR)

Evaluator for “Agència de Gestió d'Ajuts Universitaris i de Recerca” (JMGR)

Evaluator for MINECO (JMGR)

Reviewer for “Oncotarget” (JMGR)

Editorial Boards

Associated Editor of International Journal of Molecular Sciences (J. M. González-Ros, 2019-...).

Associated Editor of International Journal of Molecular Sciences (J. A. Poveda, 2019-...).

MOLECULAR DIAGNOSTIC, PROGNOSTIC AND THERAPY

MOLECULAR DIAGNOSTIC, PROGNOSTIC AND THERAPY

Bioactive Molecules

Group name: DESIGN AND DEVELOPMENT OF BIOACTIVE MOLECULES

The research target of our group is to characterize the wide biological activity of natural bioactive compounds using analytical techniques and cellular and animal models, and to understand the mechanism underlying their health effects. Our group is mainly focused on the relationship between the biological activity of bioactive molecules and its effects on chronic human diseases related to metabolic stress.

Staff

Vicente Micol Molina

Jose Antonio Encinar Hidalgo

Enrique Barrajón Catalán

María Herranz López

Postdoctoral Researchers

Verónica Ruiz Torres

Maria Dolores Olivares Vicente

María Losada Echeberría

Ph. D Students

Javier Álvarez Martínez

Noelia Sánchez Marzo

Marina Boix Castejón

Technicians

Mª Teresa Garzón Cabrerizo

Publications

Capó C, Martorell M, Ferrer MD, Sureda A, Pons V, JC Domingo JC, Drobnic F, Martinez-Rodriguez A, Leyva-Vela B, Sarabia JM, Herranz-López M, Roche E, Tur JA, Pons A. Calorie Restriction Improves Physical Performance and Modulates the Antioxidant and Inflammatory Responses to Acute Exercise. Nutrients. 2020, 12, 930.

Herranz-Lopez M, Barrajón-Catalán E. Antioxidants and skin protection. Antioxidants. 2020, 9, 704.

Herranz-López M, Olivares-Vicente M, Rodríguez-Gallego E, Encinar JA, Pérez-Sánchez A, Ruiz-Torres V, Joven J, Roche E, Micol V. Quercetin metabolites from Hibiscus sabdariffa contribute to alleviate glucolipotoxicity-induced metabolic stress in vitro. Food and Chemical Toxicology. 2020, 144:111606.

Carrera-Quintanar L, Funes L, Herranz-López M, Martínez-Peinado P, Pascual-García S, Sempere JM, Boix-Castejón M, Córdova A, Pons A, Micol V, Roche E. Antioxidant supplementation modulates neutrophil inflammatory response to exercise-induced stress. Antioxidants. 2020, 9, 1242.

Díaz-Echave, P, Vezza, T, Rodríguez-Nogales A, Ruiz-Malagon AJ, Hidalgo-García L, Garrido-Mesa J, Molina-Tijeras JA, Romer M, Robles_Vera I, Pimentel-Moral S, Borrás-Linares I, Arráez-Román D, Segura-Carretero A, Micol V, García F, Duarte J, Rodríguez-Cabezas ME, Gálvez J. The prebiotic properties of Hibiscus sabdariffa extract contribute to the beneficial effects in diet-induced obesity in mice. Food Res. Int. 2020, 127:108722.

Barrajón-Catalán E, Álvarez-Martínez FJ, Borrás F, Pérez D, Herrero N, Ruiz JJ, Micol V. Metabolomic analysis of the effects of a commercial complex biostimulant on pepper crops. Food Chemistry. 2020, 310:125818.

Sánchez-Marzo N, Pérez-Sánchez A, Barrajón-Catalán E, Castillo J, Herranz-López M, Micol V. Rosemary Diterpenes and Flavanone Aglycones Provide Improved Genoprotection against UV-Induced DNA Damage in a Human Skin Cell Model. Antioxidants. 2020, 9(3):255.

Agulló-Chazarra L, Borrás-Linares I, Lozano-Sánchez J, Segura-Carretero A, Micol V, Herranz-López M, Barrajón-Catalán E. Sweet Cherry Byproducts Processed by Green Extraction Techniques as a Source of Bioactive Compounds with Antiaging Properties. Antioxidants. 2020, 9(5):418.

Diez-Echave P, Vezza T, Rodríguez-Nogales A, Hidalgo-Garcia L, Garrido-Mesa J, Ruiz-Malagon A, Molina-Tijeras JA, Romero M, Robles-Vera I, Leyva-Jiménez

FJ, Lozano-Sanchez J, Arráez-Román D, Segura-Carretero A, Micol V, García F, Morón R, Duarte J, Rodríguez-Cabezas ME, Gálvez J. The Beneficial Effects of Lippia Citriodora Extract on Diet-Induced Obesity in Mice Are Associated with Modulation in the Gut Microbiota Composition. Mol Nutr Food Res. 2020, 64(13):e2000005.

Álvarez-Martínez FJ, Barrajón-Catalán E, Micol V. Tackling Antibiotic Resistance with Compounds of Natural Origin: A Comprehensive Review. Biomedicines. 2020, 8 (10):E405.

Álvarez-Martínez FJ, Barrajón-Catalán E, Encinar JA, Rodríguez-Díaz JC, Micol V. Antimicrobial Capacity of Plant Polyphenols against Gram-positive Bacteria: A Comprehensive Review. Curr Med Chem. 2020, 27(15):2576-2606.

Jebabli H, Nsir H, Abu-Reidah I, Álvarez-Martínez FJ, Losada-Echeberria M, Barrajón-Catalán E, Mhamdi R. Industrial-Scale Study of the Chemical Composition of Olive Oil Process-Derived Matrices. Processes. 2020, 8 - 701, pp.1 – 14.

Verdura S, Cuyàs E, Cortada E, Brunet J, Lopez-Bonet E, Martin-Castillo B, Bosch-Barrera J, Encinar JA, Menendez JA. Resveratrol targets PD-L1 glycosylation and dimerization to enhance antitumor T-cell immunity. Aging. 2020, 12(1): 8-34.

Galiano V, Encinar JA, Villalaín J. Location, orientation and aggregation of Bardoxolone-ME, CDDO-ME, in a complex phospholipid bilayer membrane. The Journal of Membrane Biology. 2020, 1-14.

Cuyàs A, Gumuzio J, Verdura S, Brunet J, Bosch-Barrera J, Martin-Castillo B, Alarcon T, Encinar JA, Martin AG, Menendez JA. The LSD1 inhibitor iadademstat (ORY-1001) targets SOX2-driven breast cancer stem cells: a potential epigenetic therapy in luminal-B and HER2-positive breast cancer subtypes. Aging. 2020, 12(6): 4794-4814.

Encinar JA, Menendez JA. Potential Drugs Targeting Early Innate Immune Evasion of SARS-Coronavirus 2 via 2'-O-Methylation of Viral RNA. Viruses. 2020, 12(5), 525.

Bosch-Barrera J, Martin-Castillo B, Buxó M, Brunet J, Encinar JA, Menendez JA. Silibinin and SARS-CoV-2: Dual targeting of host cytokine storm and virus replication machinery for clinical management of COVID-19 patients. J. Clin. Med. 2020, 9(6), 1770.

Rubio-Camacho M, Encinar JA, Martínez-Tomé MJ, Esquembre R, Mateo CR. The interaction of temozolomide with blood components suggests the potential use of human serum albumin as a biomimetic carrier for the drug. Biomolecules. 2020, 10(7), 1015.

Fuentes-Baile M, Ventero-Martín MP, Encinar JA, García-Morales P, Poveda-Deltell M, Pérez-Valenciano E, Barberá VM, Gallego-Plazas J, Rodríguez-Lescure A, Martín-Nieto J, Saceda M. Differential effects of IGF-1R small molecule tyrosine kinase inhibitors BMS-754807 and OSI-906 on human cancer cell lines. Cancers. 2020, 12(12), 3717.

Creation of Spin-Off Firms

Innovation Labo Technologies, SL (Advanced microbiome technologies). Spin-off company of the UMH Scientific Park. OTRI code 2021/IPR/00001. July 2020.

Number of Congress Communications

International contributions: 1

Poster presentations: 1

Governmental Projects and Funding

Una innovadora aproximación metabonómica inductiva para la identificación de metabolitos derivados de polifenoles de la dieta y sus dianas moleculares (RTI2018-096724-B-C21). Ministerio de Ciencia, Innovación y Universidades. Cantidad concedida: 145.000 €. Duración: 01/01/2019 – 31/12/2021. IP: Vicente Micol y Co-IP: Enrique Barrajón Catalán.

Patrones cerebrales particulares en obesos con hiperfagia vs obesos sedentarios (BRAIN-SCAN). ISABIAL 2020-0282. Funding: 4.000 €. IP: Enrique Roche. Vicente Micol (participant).

Private funding: Contracts

Contrato para la realización del trabajo "Caracterización e identificación de la microflora endofítica predominante en

especies vegetales mediterráneas". Actividades de Apoyo Tecnológico (2020/CON/00162). Funding: 7.749 €. IP: Vicente Micol.

Contrato para el "Estudio de la viabilidad de la producción de un edulcorante natural mediante procesos biotecnológicos". NUTRAFUR, SA. Funding: 28.667 €. Duración: 12/12/2019-12/12/2020. IP: Vicente Micol Molina.

Contrato para la "Caracterización de la composición de nuevos ingredientes funcionales y determinación de bioactividad para los sectores nutracéutico y cosmético". Entidad financiadora: "Illice Effitech S.L. Cantidad concedida: 5.700 €. Duración: 21/01/2019-21/01/2020. IP: Enrique Barrajón Catalán.

Donación por parte de la empresa Caja Rural Central para el proyecto "Nuevos compuestos antitumorales para tratar el cáncer de colón", proyecto reconocido como de interés social por la Oficina de Mecenazgo de la Generalitat Valenciana. Funding: 32.000 €. Duración: 12/12/2019-11/12/2020. IP: Enrique Barrajón Catalán.

Donación por parte de la "Asociación de Novelda para ayuda a personas con cáncer" para el proyecto "Nuevos compuestos antitumorales para tratar el cáncer de colón", proyecto reconocido como de interés social por la Oficina de Mecenazgo de la Generalitat Valenciana. Funding: 5.000 €. Fecha donación 23/07/2020. IP: Enrique Barrajón Catalán.

Private funding: Technical Services and Assistance

9 provisions of services with different companies: Enrique Barrajón Catalán. 10.110 €.

R&D Management

Reviewer of Agencia Estatal de Investigación (MICINN, Spain) (2010-present). Vicente Micol and Enrique Barrajón Catalán.

Editorial Boards

Scientific Advisory Board of AgroFOOD Industry Hi Tech - Teknoscienze (2010-...). Vicente Micol.

Guest Editor of Special Issue "Antioxidants and Skin Protection II" in Antioxidants (MPDI). María Herranz, Enrique Barrajón, Vicente Micol.

Guest Editor of Special Issue "Development of Functional Foods from Marine Sources" in Frontiers Nutrition. Enrique Barrajón.

Guest Editor of Special Issue "Connection of Marine Natural Products and Cell Apoptosis-II" in Marine Drugs (MPDI). María Herranz, Enrique Barrajón, Vicente Micol.

Enrique Barrajón Catalán is included as Academic editor (section board member) of the journal Molecules.

Group name: INDUSTRIAL DEVELOPMENTS FOR HEALTH INGREDIENTS

In order to cover the basic activities in the field of biotechnology, it is possible to define a biotechnology product as a good or service, the development of which requires the use of one or more biotechnology techniques. On the other hand, into the specific area of "industrial biotechnology" it is convenient to highlight that scientific and technological complexity are also inherent to biotechnology and consequently, it should be understood that interfaces and overlaps among other techniques.

The main lines in that area are:

a. Optimization of industrial processes for:

- functional beverages production and
- waste management for nutraceutical ingredients with a bio economy perspective.

b. Semi-industrial scale production of nutraceuticals from plants, herbs or by-products.

c. Identification & Purification of bioactive molecules from waste management, and small-scale production herein for agricultural biological pest control

d. Identification, isolation, culture development and pilot plant scale production of microorganism for agriculture and feedstock

e. Development of new nutritional products from fermentation processes.

f. Identification & Purification of bioactive molecules in functional drinks, fermented drinks, beer and wine by Liquid and Gas Chromatography coupled to Mass Spectrometry and Olfactometry.

g. Formulation, development and pilot plant scale production of cosmetic and food functional products.

The IDiBE Pilot Extraction Biotech Platform´s is created for research, development and technology transfer to companies focused in Food, Pharmacy and Biotech business. The PEB plant is able to offer knowledge of high technological value and to give support to the industries in the life, health and agro food science areas. The know-how is directly transformed into a pipeline of products, processes, services and technological strategies that provide to the industries competitive and highly specialized products.

The PEB plant has complementary services for the companies, customer and the general market, such as; formulation of new food, beverage and nutraceutical ingredient development, technological analysis of bioactive compounds, technical consultancy and specialised training for employers.

The mission of PEB is generating technological strategies and solutions with high industrial value according with Bioeconomy Strategy of EU 2018. The objective is modernisation and strengthening of the industrial biotech base through the creation of new value chains and more cost-effective industrial processes.

The main activities of PEB platform in collaboration with consolidated companies in this business model are:

h. Quality control or development of new biotech products and process

i. Design, optimisation and industrial scale up of biotechnology process

j. Extraction, Purification and characterization of bioactive compounds produced through green technologies

Staff

Nuria Martí Bruña

Domingo Saura López

Manuel Valero Roche

External collaborators integrated in the group

Concepción Martínez Madrid. Área: EDAFOLOGÍA Y QUÍMICA AGRÍCOLA (UMH).

Prof. Dr. Francisco Martin Bermudo. UNIVERSIDAD PABLO OLAVIDE (Sevilla).

Prof. Dra. Madalina Neascu. Gut Health Theme, Rowett Institute, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen.

Prof. Dra. Farah Hosseinian. Department of Chemistry, CARLETON UNIVERSITY.

Ph. D Students

Sara Gea Botella

Julio Salazar Bermeo

Bryan Moreno Chamba

Publications

Gea-Botella S, Agulló L, Marti N, Martínez-Madrid MC, Lizama V, Martín F, Berná G, Saura D, Valero M. Carotenoids from persimmon juice processing. Food Research International. 10 Nov 2020, 141:109882. https://doi.org/10.1016/j.foodres.2020.109882.

Patents

Inventores: Saura D, Barrajón-Catalán E, Martí N, Martínez R, Micol V, Valero M, Vegara Gomez S. Título: Contrato de licencia de patente 201300578 "Combinación sinérgica de flavonoides y vitamina C". Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio:

13/05/2016. Fecha fin: 12/05/2033. Referencia patente: 201300578.

Inventores: Saura D, Barrajón-Catalán E, Rodríguez Díaz JC, Tomás Menor L, Martí N, Micol V. Título: Contrato de licencia de patente 201301181 "Preparado hecho a base de una combinación sinérgica de polifenoles con actividad antibiótica". Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio: 13/05/2016. Fecha fin: 12/05/2033. Referencia patente: 201301181.

Inventores: Saura D, Barrajón-Catalán E, Martí N, Martínez R, Micol V, Valero M, Vegara Gomez, S. Título: Contrato de licencia de patente 201301183 "Método de producción de pectina modificada de cítricos". Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio: 13/05/2016. Fecha fin: 12/05/2033. Referencia patente: 201301183.

Inventores: Saura D, Martí N, Micol V, Valero M. Título: Contrato de licencia patente 201500423. Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio: 27/03/2013. Fecha fin: 05/06/2035. Referencia patente: 201500423.

Inventores: Saura D, Berenguer Martínez MDR, Martí N, Micol V, Valero M, Vegara Gomez S. Título: Contrato de licencia 201200830 "Equipo de expansión instantánea a vacío y ultrasonidos". Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio: 13/05/2016. Fecha fin: 12/05/2032. Referencia patente: 201200830.

Governmental Projects and Funding

Simbiosis Industrial en el aprovechamiento integral del caqui (Dyospiros kaki); ejemplo de bioeconomía. Proyectos competitivos de subvención pública. MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD Subvención concedida: 64.553,50 €. Duración: 01/01/2018 – 31/12/2020. IPs: Domingo Saura y Manuel Valero.

Plataforma en nanotecnología traslacional (Patent). Proyectos de Equipamiento científico-técnico. 01/01/2018-31/10/2020. CONSELLERIA DE EDUCACION, INVESTIGACION, CULTURA Y DEPORTE GENERALITAT VALENCIANA. IP: Antonio Ferrer Montiel.

Editorial Boards

Board member Horticulturae.

Board member Journal of the Science of Food and Agriculture.

Board member Scientific Reports.

Board member Journal of Food Engineering.

Board member Food Microbiology.

Board member Food and Bioprocess Technology.

Chronic inflammation & pain

Group name: DRUG DESING ON THERMOTRPs AND PAIN SIGNALLING

This subline is centered in discovering and developing new lead compounds for the treatment of chronic inflammatory pain and chronic pruritus, two nociceptive modalities of the dysfunctional peripheral nervous system. Modulators of the thermoTRP channel TRPV1 have been identified and are currently in clinical development for the treatment of chronic postsurgical pain. This success will be extended to other chronic pain syndromes, as well as to chronic pruritus. The main focus will be towards thermoTRP channels, which are central in the generation of peripheral nociceptive signaling, and pain transduction.

Complementarily, type C phospholipases will be used to develop new analgesic and anti-inflammatory candidates for drug development. These enzymes have been traditionally considered undruggable, but we have developed a strategy that has produced hit compounds with a promising potential for clinical development.

DESIGN OF ACTIVE MOLECULES. Identifying molecular components with potential applications in healthcare. The identification and design of bioactive molecules for different applications (anti-inflammatory, analgesic and anti-pruritus)

is first based on a computational strategy using molecular modeling, docking and dynamics. In addition, in silico screening is also applied to virtual libraries composed of thousands to millions of molecules from natural and synthetic sources.

Staff

Antonio Ferrer Montiel

Gregorio Fernández Ballester

Asia Fernández Carvajal

Postdoctoral Researchers

David Cabañero

External collaborators integrated in the group

Rosario Gonzalez-Muñiz. Instituto de Química Médica (IQM-CSIC).

Ph. D Students

Magdalena Nikolaeva Koleva

Jorge de Andrés López

David Alarcón Alarcón

Simona Giorgi

Laura Butrón García

Eva María Villalba Riquelme

Alicia Medina Peris

Technicians

José Manuel Serrano García

Gema Osuna Tenorio

Irene Mudarra Fraguas

Publications

Blair Journigan V, Feng Z, Rahman S, Wang Y, Ruhul Amin ARM, Heffner CE, Bachtel N, Wang S, Gonzalez-Rodriguez S, Fernández-Carvajal A, Fernández-Ballester G, Hilton JK, Sestile S, Vazquez-Molina DA, Harper JK, Van Horn WD, Ferrer-Montiel A, Xie X-Q, Rahman T. Structure-based design of novel biphenyl amide antagonists of human Transient Receptor Potential Cation Channel Subfamily M Member 8 channels (TRPM8) with potential implications in the treatment of sensory neuropathies. ACS Chemical Neuroscience. 2020, 11:268-290. DOI:10.1021/acschemneuro.9b00404. https://pubmed.ncbi.nlm.nih.gov/31850745/

Bertamino A, Ostacolo, C, Medina, A, Di Sarno V, Lauro G, Ciaglia T, Vestuto V, Giacomo P, Basilicata MG, Musella S, Smaldone G, Cristiano C, Gonzalez-Rodriguez S, Fernández-Carvajal A, Bifulco G, Campiglia P, Gomez-Monterrey I, Russo R. Exploration of TRPM8 Binding Sites by Carboline-based Antagonists and Their In Vitro Characterization and in Vivo Analgesic Activities. J Med Chem. 2020, Sep 10;63(17):9672-9694. doi: 10.1021/acs.jmedchem.0c00816. https://pubmed.ncbi.nlm.nih.gov/32787109/

Bonache MA, Martín-Escura C, de la Torre Martínez R, Medina A, González-Rodríguez S, Francesch A, Cuevas C, Roa AM, Fernández-Ballester G, Ferrer-Montiel, A, Fernández-Carvajal A, González-Muñiz R. Highly functionalized β-lactams and 2-ketopiperazines as TRPM8 antagonists with antitumor and antiallodynic activity. 2020, Sci Rep. 2020 Aug 25;10(1):14154. doi: 10.1038/s41598-020-70691-x. https://pubmed.ncbi.nlm.nih.gov/32843690/

Fernández-Ballester G, Fernández-Carvajal A, Ferrer-Montiel A. Targeting ion channels: in silico preclinical approaches and opportunities. Expert Opinion in Therapeutic Targets. 2020, 1-19. doi: 10.1080/14728222.2020.1820987. https://pubmed.ncbi.nlm.nih.gov/32972264/

Fernández-Carvajal A, Gonzalez-Muñiz R, Fernández-Ballester G, Ferrer-Montiel A. Investigational drugs in early phase clinical trials targeting thermotrp channels. Expert Opinion in Investigational Drugs. 2020, 1-14. doi: 10.1080/13543784.2020.1825680. https://pubmed.ncbi.nlm.nih.gov/32941080/

Dionisi M, Ruffinatti FA, Riva B, Lim D, Canta A, Meregalli C, Fumagalli G, Monza L, Ferrer-Montiel A, Fernández-Carvajal A, Cavaletti G, Genazzani AA and Distasi C. Early stimulation of TREK channel transcription and activity induced by Oxaliplatin-dependent cytosolic acidification. Int J Mol Sci. 2020;

21(19):E7164. doi: 10.3390/ijms21197164. https://pubmed.ncbi.nlm.nih.gov/32998392/

Cabañero D, Ramírez-López A, Drews E, Schmöle A, Otte DM, Wawrzczak-Bargiela A, Huerga Encabo H, Kummer S, Ferrer-Montiel A, Przewlocki R, Zimmer A, Maldonado R. Protective role of neuronal and lymphoid cannabinoid CB2 receptors in neuropathic pain. Elife. 2020, Jul 20;9:e55582. doi: 10.7554/eLife.55582. https://pubmed.ncbi.nlm.nih.gov/32687056/

González-Gil I, Zian D, Vázquez-Villa H, Hernández-Torres G, Martínez RF, Khiar-Fernández N, Rivera R, Kihara Y, Devesa I, Mathivanan S, Del Valle CR, Zambrana-Infantes E, Puigdomenech M, Cincilla G, Sanchez-Martinez M, Rodríguez de Fonseca F, Ferrer-Montiel AV, Chun J, López-Vales R, López-Rodríguez ML, Ortega-Gutiérrez S. A Novel Agonist of the Type 1 Lysophosphatidic Acid Receptor (LPA1), UCM-05194, Shows Efficacy in Neuropathic Pain Amelioration. J Med Chem. 2020 Mar 12;63(5):2372-2390. doi: 10.1021/acs.jmedchem.9b01287.

https://pubmed.ncbi.nlm.nih.gov/31790581/

Cobo R, Nikolaeva-Koleva M, Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Mechanisms of blockade of the muscle-type nicotinic receptor by benzocaine, a permanently uncharged local anesthetic. Neuroscience. 2020, Jul 15;439:62-79. doi: 10.1016/j.neuroscience.2019.05.043. https://pubmed.ncbi.nlm.nih.gov/31158437/

Creation of Spin-Off Firms

ANTALGENICS (2015-actualidad).

PROSPERA BIOTECH (2014-actualidad).

FASTBASE SOLUTIONS (2015-actualidad).

Organization of Meetings

Participation in Scientific Committees:

7TH INTERNATIONAL IBERIAN BIOPHYSICS CONGRESS, June 2020. Coimbra. Postponed because of Covid. Antonio Ferrer.

Invited Talks and Courses

Programa Conoce Fundación UMH. Antonio Ferrer.

Science Dissemination: Outreach Activities

Ciencia con Tapas. Monthly outreach activity of IDiBE.

XII Jornadas de San Alberto. Facultad de Ciencias Experimentales. UMH. 11 noviembre 2020.

López-González MJ, García N, Rivero V, Sempere A, Tracey P, Genanzzani A, Fernández-Carvajal A, Ferrer-Montiel A, Devesa I. Improving a Natural Compound: Design of Innovative Neurocosmeceuticals for Sensitive Skin. 2020, vol 1: 37-44 International Federation of Societies of Cosmetic Chemists IFSCC Magazine.

Fernández-Carvajal A, Devesa I, Fernández-Ballester G, Ferrer-Montiel A.. Moduladores del termorreceptor TRPV1 desactivables metabólicamente en la farmacología. Actualidad en Farmacología y terapéutica. 2020, Vol 18 (3) 162-172. http://www.ifth.es/wp-content/uploads/2021/02/AFT18N3-WEB-2.pdf

Blanes-Mira C, Fernández-Ballester G. Búsqueda computacional de compuestos activos para el tratamiento de alteraciones cutáneas. Revista SEBBM. 2020, 206, 8-14. ISSN: 1696-473X. https://www.sebbm.es/revista/pdf.php?id=721

Articulo en Novaciencia https://novaciencia.es/un-compuesto-desarrollado-por-investigadores-de-la-umh-reduce-el-picor-de-la-psoriasis-sin-producir-efectos-secundarios/

Entrevista en el Diario medico: https://www.diariomedico.com/farmacia/hospitalaria/un-derivado-de-los-pimientos-picantes-reduce-el-picor-de-la-psoriasis-sin-efectos-secundarios.html

Entrevista en UMH-TV: https://www.youtube.com/watch?v=AXN3qFex2Kk

Entrevista en radio UMH: https://radio.umh.es/files/2021/01/250121-Podcast-INFORMATIVOS-UMH.mp3

Number of Congress Communications

National contributions: 8

Poster presentations: 8

International contributions: 3

Poster presentations: 3

Awards

Premio Alberto Sols 2020 Antonio Ferrer.

Premio al talento docente 2020 Asia Fernández.

Governmental Projects and Funding

Plataforma en nanotecnología traslacional (Patent). GENERALITAT VALENCIANA (IDIFEDER/2018/020). 2018-2020. IP: Antonio Ferrer Montiel.

Validación y desarrollo pre-clínico de nuevos tratamientos para el dolor artrítico. Proyecto Retos Colaboración del Programa Estatal de Investigación, Desarrollo e Innovación Orientada a los Retos de la Sociedad (RTC-2017-6507-1). 2018-2021 IP: Antonio Ferrer Montiel.

Valorización y traslación de los resultados del IDiBE (VALORIzE). Agencia Valenciana de Innovación. Generalitat Valenciana. INNTAL11/19/021. 2019-2020 IP: Antonio Ferrer Montiel.

Microscopia correlativa óptico-electrónica para dotar la Plataforma en Nanotecnología Traslacional (PATENT) de microscopia de superresolución. Agencia Estatal de Investigación. EQC2019-005842-P. 2019-2020. IP: Antonio Ferrer Montiel.

Un modelo pre-clínico in vitro de nociceptores humanos para investigar el dimorfismo sexual en migraña crónica y rastrear candidatos a fármacos (HEADACHE). Agencia Estatal de Investigación. RTI2018-097189-B-C21. 2019-2021. IPs: Antonio Ferrer Montiel y Asia Fernández Carvajal.

Modelos preclínicos in vitro de organoides inervados con nociceptores humanos para rastrear y validar candidatos a fármacos (OPERETTA). CONSELLERIA DE INNOVACION, UNIVERSIDADES, CIENCIA Y SOCIEDAD DIGITAL (IDIFEDER/2020/022). IP: Antonio Ferrer.

Nanoparticle-based imaging and therapy of chronic pain in the dorsal root glanglia (PIANO). Horizon 2020-MSCA training Network (Ref. nº 859938). 2021-2024. IP: Antonio Ferrer.

Private funding: Contracts

AntalGenics. Scientific supervisión on development of PLC inhibitors. Antonio Ferrer.

Fundación KERTOR. SAP Cancer Innova Program. Antonio Ferrer.

Contrato de licencia de patente "Compuestos antagonistas del receptor TRPM8 y sus aplicaciones". Antalgenics, SL. Antonio Ferrer y Asia Fernández.

Private funding: Technical Services and Assistance

Antonio Ferrer Montiel. Technical Assistance to AntalGenics SL.

(956/20) Evaluación Contenido y Ejecución como Experto Técnico del ejercicio fiscal 2019 del proyecto 852.228 "Productos sanitarios inyectables ácido hialurónico" EQA CERTIFICADOS I+D+I SLU. Asia Fernández Antonio Ferrer Montiel.

(951/20) Evaluación Contenido y Ejecución como Experto Técnico del ejercicio fiscal 2019 del proyecto 863.980 "Nuevas síntesis química de fármaco oncológico de alta efectividad para enfermedades hematológicas EQA CERTIFICADOS I+D+I SLU. Asia Fernández.

R&D and Educational Committees.

Máster: The European Master in Translational Cosmetic and Dermatological Sciences (EMOTION). An Erasmus Mundus Master. Coordinadora: Asia Fernández.

R&D Management

Coordinador de la subárea de Herramientas diagnósticas, pronósticas y terapéuticas del área de Biomedicina en la Agencia Estatal de Investigación. Antonio Ferrer Montiel.

Scientific Society Councils

Sociedad Española de Biofísica. Ex – presidente: Antonio Ferrer Montiel.

Representante Español IUPAB - Antonio Ferrer.

Sociedad Española de Bioquímica y Biología Molecular. Antonio Ferrer.

Red Española de Canales Iónicos. Coordinador: Antonio Ferrer Montiel.

Editorial Boards

Revista de la SEBBM (2020). Antonio Ferrer (Editor jefe).

Journal of Pharmacological Sciences (2020). A. Ferrer Montiel.

The Open Journal of Pain (2020). A. Ferrer Montiel.

Frontiers in Pharmacology (2020). A. Ferrer Montiel.

Frontiers in Neurosciences (2020). A. Ferrer Montiel.

Journal of Neurosciences (2020). A. Ferrer Montiel.

International Journal Molecular Science (2020). Antonio Ferrer.

Scientific Reports (2014-2020). A. Fernandez-Carvajal

Frontiers in Physiology (2015-2020). A. Fernandez-Carvajal.

UMH editorial board A. Fernandez-Carvajal.

Antiviral Strategies

Group name: ANTIVIRAL AND ANTIMICROBIAL STRATEGIES

We are carrying out research on Viral Diseases of Fish with impact on Aquaculture. Our interest is focused on the fish immune response and related topics such as viral interference, immunostimulants and antiviral drugs. The study model is zebrafish infections with spring viremia of carp virus (SVCV). Our group tries to answer questions about what genes are the major responders after viral challenge, and which ones lead to protection against disease.

During the COVID-19 pandemic, our expertise in Molecular Virology techniques was required to determine the presence of SARS-VoV-2 genetic material in samples from wastewater treatment facilities in our local area.

Staff

Luis Pérez García-Estañ

María del Mar Ortega-Villaizán

Ph. D Students

María E. Salvador Mira

Technicians

Efrén Lucas Mañogil

Publications

Bello-Perez M, Pereiro P, Coll J, Novoa B, Perez L, Falco A. Zebrafish C-reactive protein isoforms inhibit SVCV replication by blocking autophagy through interactions with cell membrane cholesterol. Sci Rep. 2020, Jan 17;10(1):566. doi: 10.1038/s41598-020-57501-0.

Science dissemination: outreach activities

TITULO: EL CORONAVIRUS DE CHINA Y OTROS VIRUS QUE VIENEN DE FUERA: ¿HAY QUE TEMERLES?

Ciclo de Conferencias Divulgativas Ciencia con Tapas (IDiBE – UMH). Alicante, 20 febrero 2020. Luis Perez y Mar Masiá.

https://idibe.es/es/ciencia-con-tapas-coronavirus-china-virus/

TITULO: ¿CÓMO SE DEFIENDE NUESTRO CUERPO DEL SARS? RESPUESTA INMUNOLÓGICA AL CORONAVIRUS.

Ciclo de Conferencias Divulgativas Ciencia con Tapas (IDiBE – UMH). Alicante, 5 noviembre 2020. Luis Perez y Rubén Francés.

https://idibe.es/es/ciencia-con-tapas-sars-respuesta-inmunologica-virus/

Governmental Projects and Funding

Enhancing antiviral responses in fish: From rational design of prophylactics to in vivo responses. PROYECTOS DE I+D+I "RETOS DE LA SOCIEDAD" – Ministerio de Ciencia Innovación y Universidades. RTI2018 –096957 –B-C22. IP: Luis Perez; Co-IP: María del Mar Ortega-Villaizán.

SARS-CoV-2 in wastewater - Convenio para la ejecución en el ejercicio 2020 de proyectos de investigación aplicada a recursos hídricos en la Comunitat Valenciana. Conselleria de Agricultura, desarrollo rural, emergencia climática y transición ecológica. Generalitat Valenciana. Investigadores: Luis Perez, María del Mar Ortega-Villaizán. Investigador Principal: José Navarro Pedreño.

R&D Management

Expert Evaluator for Agencia Estatal de Investigación, Spain (from oct 4th 2019). Luis Pérez García-Estañ.

Editorial Boards

Pathogens (ISSN 2076-0817). Special Issue "Viral Diseases of Fish", 2020. Luis Perez, Guest Editor. Pathogens | Special Issue: Viral Diseases of Fish (mdpi.com).

Group name: VIRAL MEMBRANE PROTEINS

Study of the structure and interaction of virus-derived peptide libraries comprising the viral structural and non-structural proteins with model biomembranes, aiming to identify their molecular mechanism and biological function. Screening of peptide libraries to identify membranotropic determinants, characterize the interactions in structural terms, study the structure of the membranotropic segments, and make a detailed study of the interaction, modulation and structure of these peptide segments with membranes and living cells. Developing molecular dynamics bioinformatic tools to study the interaction of viral proteins with biomembranes to find new antivirals and therapeutic targets to develop new leading compounds useful for improved combined therapies.

Staff

José Villalaín Boullón

Publications

Galiano V, Villalaín J. Aggregation of 25-hydroxycholesterol in a complex biomembrane. Differences with cholesterol. Biochim Biophys Acta Biomembr. 2020, Nov 1;1862(11):183413. doi: 10.1016/j.bbamem.2020.183413.

Galiano V, Encinar JA, Villalaín J. Location, Orientation and Aggregation of Bardoxolone-ME, CDDO-ME, in a Complex Phospholipid Bilayer Membrane. J Membr Biol. 2020, Apr;253(2):115-128. doi: 10.1007/s00232-020-00106-5.

Carpio LE, Villalaín J. Identification of the phospholipid binding regions of the envelope E protein of flaviviruses by molecular dynamics. J Biomol Struct Dyn. 2020, Oct;38(17):5136-5147. doi: 10.1080/07391102.2019.1697368.

Scientific and Educational Commities

Reviewer of CONICET, Argentina (2011 - ...). J. Villalaín.

Reviewer of ISF (2013 - ...). J. Villalaín.

Group name: RED BLOOD CELLS IN ANTIVIRAL IMMUNOLOGY

Fish are the phylogenetically oldest vertebrate group with an immune system with clear similarities to the immune system of mammals. However, it is an actual matter of fact that the current knowledge of the fish immune system seems to lack the key piece to complete the puzzle.

In an attempt to solve this question, our group have demonstrated that rainbow trout RBCs can respond to viral infections by themselves with an innate immune response, by means of producing antiviral molecules and exerting a paracrine antiviral communication with other cells, and with a potential adaptive immune response, by means of antigen processing and presentation and complement system regulation. Apart from this, we also focus our investigation on the search of prophylactics or therapeutics to treat the major aquaculture viral infections.

Staff

María del Mar Ortega-Villaizán Romo

Postdoctoral Researchers

Verónica Chico Gras

Ph. D Students

Maria Elizabhet Salvador Mira

Technicians

Efren Lucas Mañogil

Patents

IFIT5 para su uso como agente antiviral (P202031141).

Science dissemination: outreach activities

Difusión y divulgación de resultados de investigación en revistas o diarios de divulgación: Agrodiario, Canal UNED, Diario Información, ES Radio, EU Research, IPAAcuicultura, Mis Peces, 20 minutos, UMH Sapiens, UMH Tv.

Governmental Projects and Funding

ERC Starting Grant 2014. Proyecto: BloodCellsCrosstalk. "The Crosstalk Between Red and White Blood Cells: The case of fish". 2015-2020. GA639249. European Commission. IP: María del Mar Ortega-Villaizán.

Proyectos RTI- AEI/MCIU 2018. ENHANCING ANTIVIRAL RESPONSES IN FISH: From rational design of prophylactics to in vivo responses. Proyectos RTI-AEI/MCIU 2018. Ministry of Science, Innovation and Universities. RTI2018-096957-B-C22. 2019-2021. IPs: Luis Perez, María del Mar Ortega-Villaizán.

Investigation of the cellular changes induced by viral haemorrhagic septicaemia virus in rainbow trout nucleated erythrocytes using soft X-ray cryo-tomography. ALBA Synchrotron Project. Beam line BL09 – MISTRAL. 2019.

SARS-CoV-2 in wastewater - Convenio para la ejecución en el ejercicio 2020 de proyectos de investigación aplicada a recursos hídricos en la Comunitat Valenciana. Conselleria de Agricultura, desarrollo rural, emergencia climática y transición ecológica. Generalitat Valenciana. IP: José Navarro Pedreño. Investigadores: Luis Perez, María del Mar Ortega-Villaizán.

REDFLAG - Salmonid red blood cells - sensors of stress and infection. Norwegian Research Council. NRC# 302551. IP: Maria K. Dahle. Investigadores: María del Mar Ortega-Villaizán.

Los eritrocitos nucleados de peces: ¿células somáticas o madre? Abriendo camino hacia nuevas soluciones antivirales en acuicultura. 2020-2021. EUR2020-112098. Acciones de Dinamización Europa Excelencia 2020. Programa Estatal de Generación de Conocimiento y Fortalecimiento Científico y Tecnológico del Sistema de I+D+i. IP: María del Mar Ortega-Villaizán.

Private funding: Technical Services and Assistance

Ensayo para testar la actividad virucida de revestimientos de grafeno en la que se testaran dos concentraciones de grafeno y un material control. Universidad de Alicante. 01/2020.

R&D Management

Expert Evaluator for Agencia Estatal de Investigación, Spain (2019-ongoing. María del Mar Ortega-Villaizán.)

Editorial Boards

Editorial Board member of PLOS One (2019- ongoing).

Editorial Board member of Frontiers in Immunology (2018- ongoing).

Editorial Board member of Vaccines (2020- ongoing).

Editor in Intechopen (2020-ongoing).

Molecular and Cellular Oncology

Group name: MOLECULAR ONCOLOGY

The main objective of our research group is the identification of new therapeutical approaches for the treatment of different types of cancers highly resistant to conventional chemotherapy.

Glioblastomas are very resistant to either chemotherapy and radiotherapy Since it is known that PDGFR and IGF-1R pathways are important in glioblastoma, we have evaluated the effect of PDGFR and IGF-1R inhibitors on cell cycle and cell death in glioblastoma cell lines as well in primary cultures derived from patients affected with this type of tumour. Inhibition of these signal transduction pathways could become a putative alternative therapeutical strategy for glioblastoma treatment.

We have also study the role of SOCS1 and SOCS3 genes in the radiotherapy response in glioblastoma, since both genes have been associated with tumor progression in different types of cancer.

Nanotechnology appears as a promising tool for cancer treatment, allowing a better delivery of the drug and increasing specificity. In our laboratory we have been used enzimatic therapy with the D-amino acid oxidase (DAAO from Rhodotorula gracilis for the treatment of cancer. One of the main advantages of this approach is that the enzyme substrate is a D-aminoacid, not present endogenously, allowing a simple regulation of the enzymatic activity. DAAO has been immobilized on magnetic nanoparticles. The efect of this experimental approach has been tested on cells from colon carcinoma, pancreatic adenocarcinoma and glioblastoma.

Staff

Miguel Saceda Sánchez

Camino de Juan Romero

Postdoctoral Researchers

Mª del Pilar García Morales

External collaborators integrated in the group

Dr. Victor Manuel Barbera Juan

Ph. D Students

María Fuentes Baile

Elizabeth Perez Valenciano

Salomé Araujo

Publications

Fuentes-Baile M, Ventero MP, Encinar JA, García-Morales P, Poveda-Deltell M, Pérez-Valenciano E, Barberá VM, Gallego-Plazas J, Rodríguez-Lescure Á, Martín-Nieto J, Saceda M. Differential Effects of IGF-1R Small Molecule Tyrosine Kinase Inhibitors BMS-754807 and OSI-906 on Human Cancer Cell Lines. Cancers (Basel). 2020 Dec 11;12(12):3717. doi: 10.3390/cancers12123717. PMID: 33322337; PMCID: PMC7763458.

Fuentes-Baile M, García-Morales P, Pérez-Valenciano E, Ventero MP, Sanz JM, de Juan Romero C, Barberá VM, Alenda C, Saceda M. Cell Death Mechanisms Induced by CLytA-DAAO Chimeric Enzyme in Human Tumor Cell Lines. Int J Mol Sci. 2020 Nov 12;21(22):8522. doi: 10.3390/ijms21228522. PMID: 33198289; PMCID: PMC7697521.

Fuentes-Baile M, Bello-Gil D, Pérez-Valenciano E, Sanz JM, García-Morales P, Maestro B, Ventero MP, Alenda C, Barberá VM, Saceda M. CLytA-DAAO, Free and Immobilized in Magnetic Nanoparticles, induces Cell Death in Human Cancer Cells. Biomolecules. 2020 Feb 3;10(2):222. doi:

10.3390/biom10020222. PMID: 32028649; PMCID: PMC7072168.

Governmental Projects and Funding

Desarrollo de nuevas terapias y biomarcadores de utilidad para el diagnóstico y el tratamiento del glioblastoma multiforme. Nº of researchers: 4. Funding entity or bodies: FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA EN LA COMUNITAT VALENCIANA. Start-End date: 04/01/2021 - 31/12/2022. Total amount: 22.600 €. IP: Miguel Saceda Sánchez.

Evaluación del papel dual de la proteína inducida por interferon IFITM1 en la adquisición de quimiorresistencia en cáncer y en la invasividad viral. IFITMI y Sars-cov-2. Nº of researchers: 5. Funding entity or bodies: FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA EN LA COMUNITAT VALENCIANA. Start-End date: 20/01/2021 - 20/01/2022. Total amount: 5.000 €. IP: Miguel Saceda Sánchez.

Identificación y validación de los genes que participan en la resistencia a la terapia enzimática con la D-aminoácido oxidasa en modelos celulares de diferentes tipos de tumores. Nº of researchers: 2. Funding entity or bodies: FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA EN LA COMUNITAT VALENCIANA. Start-End date: 01/10/2019 - 01/10/2020. Total amount: 5.000 €. IP: Miguel Saceda Sánchez.

Editorial Boards

Board member Archives of Biochemistry and Biophysics (2010-2013).

Executive Editor Archives of Biochemistry and Biophysics (2013-...).

Diabetes & metabolic disorders

Group name: DIABETES RESEARCH UNIT

Diabetes mellitus is characterized by hyperglycaemia caused by an insulin deficiency. Its prevalence is rising, reaching 425 million people worldwide (www.idf.org). In Spain a 13.8% of adult population is diabetic and 3 of 10 people have problems with glucose metabolism (Soriguer et al, Diabetologia 2012). There are two main types of diabetes mellitus. Type 1 diabetes is caused by an autoimmune attack against β-cells, which is the cell type responsible for producing and releasing insulin, the only hormone in our organism able to decrease glucose. When the β-cell is destroyed, no more insulin is produced and, therefore, the patient depends on insulin injection. Between a 10 and 15% of diabetic persons are diagnosed as Type 1. About 80-85% of diabetics are diagnosed as Type 2, which occurs when peripheral tissues experience a decrease in insulin sensitivity or insulin resistance together with an incapacity of the β-cell to produce and secrete enough insulin to counteract such resistance. Then, hyperglycemia progresses because insulin secretion and β-cell mass are below a critical threshold.

The etiology of both diabetes types is different, but both forms are the result of genetic background and environmental factors interaction. Our research unit works to understand how different environmental factors such as high fat diet, aging and endocrine disrupting chemicals work to increase diabetes susceptibility.

We work on four different research lines:

1- The role that endocrine disrupting chemicals (EDCs) in the etiology of Diabetes. We study how exposure to EDCs at different times during life, from pregnancy to adulthood, affects insulin sensitivity as well as the function of the endocrine pancreas. We address this problem by investigating in mice how these chemicals change the expression of genes related to β-cell function, death and division, during fetal development as well as during adulthood. We combine in vivo research with ex vivo and in vitro approaches to molecularly understand how EDCs alter β-cell function, division and death.

This should give light to the hormone receptors involved as well as the molecular pathways used and end-points affected by EDCs exposure, which will help to establish harmonizing testing protocols to identify EDCs with diabetogenic effects.

The results of this research line in the last two decades have been seminal to establish the link between EDC exposure and diabetes mellitus.

2. The physiological role of estrogen receptors ERα, ERβ and GPER1 in the islet of Langerhans. Using molecular biology and electrophysiology, we study how estrogens influence the plasticity of the endocrine pancreas during the adaptation to pregnancy and obesity. This will help us to better understand sex differences in glucose regulation and the development of new chemicals that should help to stablish gender-based therapeutic for diabetes.

3. The effect of aging on pancreatic islet function and glucose homeostasis. The prevalence of diabetes and other alterations in glucose homeostasis increases with age. It is believed that this situation is mainly due to a loss of peripheral insulin sensitivity. This condition gives rise to functional and morphological adaptations to couple the plasma levels of insulin and glucagon to the new requirements imposed by insulin resistance. If these adaptations do not occur properly, glucose homeostasis is altered and this situation can progress to diabetes. In this line of research, we want to know what functional and morphological adaptations take place in the islet cells during aging and what molecular mechanisms underlie these adaptations. Likewise, we want to know the impact of these alterations on glucose homeostasis. We also aim to find possible therapeutic targets to favor these pancreatic adaptations or to prevent and treat possible harmful alterations during aging.

4. Discovery of new targets for the treatment of type 1 and type 2 diabetes based on pancreatic alpha-cell strategies to survive proinflammatory and metabolic stresses. Using a combination of bioinformatics and molecular biology approaches, our aim is to identify genes and signalling pathways that allow pancreatic alpha-cells to survive under different stresses related to the onset and progression of T1D (e.g. proinflammatory cytokines) and T2D (e.g. palmitate). The results of this project will provide a better understanding of the mechanisms underlying the survival of endocrine pancreatic cells upon proinflammatory and metabolic stresses. This may open the door to the development of new therapeutic strategies aimed to preventing the loss of beta cell mass observed in the early stages of these diseases.

Staff

Ángel Nadal Navajas

Iván Quesada Moll

Cristina Ripoll Orts

Esther Fuentes Marhuenda

Paloma Alonso Magdalena

Laura Marroquí Esclapez

Postdoctoral Researchers

Eva Tudurí López

Anabel García Heredia

Hilda Ferrero Hidalgo

Ruba Al Abdulla

Reinaldo Sousa dos Santos

Regla María Medina Gali

External collaborators (Universidad de Alicante)

Juan Martínez-Pinna

Sergi Soriano Úbeda

Ph. D Students

Lucía Almagro Ruz

Ignacio Babiloni Chust

Atenea Alexandra Pérez Serna

Technicians

María Luisa Navarro García

María Salomé Ramón Penalva

Beatriz Bonmatí Botella

Publications

Pozuelo-Sanchez I, Villasanta-Gonzalez A, Alcala-Diaz JF, Vals-Delgado C, Leon-Acuña A, Gonzalez-Requero A, Yubero-Serrano EM, Luque RM, Caballero-Villarraso J, Quesada I, Ordovas JM, Pérez-Martinez P, Roncero-Ramos I, Lopez-Miranda J. Postprandial Lipemia Modulates Pancreatic Alpha-Cell Function in the Prediction of Type 2 Diabetes Development: The CORDIOPREV Study. J Agric Food Chem. 2020, Feb 5;68(5):1266-1275. doi: 10.1021/acs.jafc.9b06801.

Quesada-Candela C, Tudurí E, Marroquí L, Alonso-Magdalena P, Quesada I*, Nadal Á*. Morphological and functional adaptations of pancreatic alpha-cells during late pregnancy in the mouse. Metabolism. 2020, Jan;102:153963. doi: 10.1016/j.metabol.2019.153963. *, corresponding authors.

Boronat-Belda T, Ferrero H, Al-Abdulla R, Quesada I, Gustafsson JA, Nadal Á, Alonso-Magdalena P. Bisphenol-A exposure during pregnancy alters pancreatic β-cell division and mass in male mice offspring: A role for ERβ. Food Chem Toxicol. 2020, Nov;145:111681. doi: 10.1016/j.fct.2020.111681.

Alonso-Magdalena P, Nadal A. The Commonly Overlooked Factor. Commentary on: "Environmental Obesogens and their Impact on Susceptibility to Obesity". Endocrinology. 2020, Sep 1;161(9):bqaa123. doi: 10.1210/endocr/bqaa123.

Audouze K, Sarigiannis D, Alonso-Magdalena P, Brochot C, Casas M, Vrijheid M, Babin PJ, Karakitsios S, Coumoul X, Barouki R. Integrative Strategy of Testing Systems for Identification of Endocrine Disruptors Inducing Metabolic Disorders-An Introduction to the OBERON Project. Int J Mol Sci. 2020, Apr 23;21(8):2988. doi: 10.3390/ijms21082988.

Ramzy A, Tudurí E, Glavas MM, Baker RK, Mojibian M, Fox JK, O'Dwyer SM, Dai D, Hu X, Denroche HC, Edeer N, Gray SL, Verchere CB, Johnson JD, Kieffer TJ. AAV8 Ins1-Cre can produce efficient β-cell recombination but requires consideration of off-target effects. Sci Rep. 2020, Jun 29;10(1):10518. doi: 10.1038/s41598-020-67136-w.

Legler J, Zalko D, Jourdan F, Jacobs M, Fromenty B, Balaguer P, Bourguet W, Munic Kos V, Nadal A, Beausoleil C, Cristobal S, Remy S, Ermler S, Margiotta-Casaluci L, Griffin JL, Blumberg B, Chesné C, Hoffmann S, Andersson PL, Kamstra JH. The GOLIATH Project: Towards an Internationally Harmonised Approach for Testing Metabolism Disrupting Compounds. Int J Mol Sci. 2020, May 14;21(10):3480. doi: 10.3390/ijms21103480.

Muncke J, Andersson AM, Backhaus T, Boucher JM, Carney Almroth B, Castillo Castillo A, Chevrier J, Demeneix BA, Emmanuel JA, Fini JB, Gee D, Geueke B, Groh K, Heindel JJ, Houlihan J, Kassotis CD, Kwiatkowski CF, Lefferts LY, Maffini MV, Martin OV, Myers JP, Nadal A, Nerin C, Pelch KE, Fernández SR, Sargis RM, Soto AM, Trasande L, Vandenberg LN, Wagner M, Wu C, Zoeller RT, Scheringer M. Impacts of food contact chemicals on human health: a consensus statement. Environ Health. 2020 Mar 3;19(1):25. doi: 10.1186/s12940-020-0572-5.

Rey-Campos M, Moreira R, Romero A, Medina-Gali RM, Novoa B, Gasset M, Figueras A. Transcriptomic Analysis Reveals the Wound Healing Activity of Mussel Myticin C. Biomolecules. 2020, Jan 14;10(1):133. doi: 10.3390/biom10010133.

PhD Theses

Modulación de la masa de la célula alfa pancreática en un modelo murino de diabetes autoinmune experimental. Eva María Bru Tarí. Advisor: Ivan Quesada Moll. 22/01/2020.

Adaptaciones de la célula alfa pancreática durante el final de la gestación en el ratón: papel de las hormonas gestacionales. Cristina Quesada Candela. Advisor: Ivan Quesada Moll; Co-advisor: Ángel Nadal Navajas. 24/02/2020.

Organization of meetings

Congreso: XI REUNION ANUAL CIBERDEM (CIBER DE DIABETES Y ENFERMEDADES METABOLICAS ASOCIADAS). 03/11/2020 - 05/11/2020. Moderador de sesión: Iván Quesada.

Congreso: III Jornadas SEJI jovenes investigadores de excelencia 2020: what is going on in diabetes research? 16/12/2020. Organizadores: Laura Marroquí, Reinaldo S. Dos Santos.

Invited Talks and Courses

Ponencia invitada: Alteraciones de la célula alfa pancreática en condiciones diabetogénicas. Iván Quesada. XXXI Congreso Nacional de la Sociedad Española de Diabetes. Madrid (Congreso virtual). 22-24 June de 2020.

Conferencia de clausura: Disruptores endocrinos ¿A dónde vamos? Ángel Nadal. V Curso de actualización de Endocrinología y Nutrición, Sociedad Española de Endocrinología y Nutrición. Madrid, 28-29 February de 2020.

Number of Congress Communications

National contributions: 8

Oral presentations: 8

International contributions: 2

Poster presentations: 2

Governmental Projects and Funding

Efectos de la exposición simultánea a disruptores endocrinos y dieta rica en grasa sobre la célula beta pancreática e implicaciones en la diabetes mellitus de tipo 2. Plan Nacional de I+D+I. Ministerio de Ciencia e Innovación, Agencia Estatal de Investigación. BFU2017-86579-R. 2018-2020, IP: Ángel Nadal.

Beating Goliath: Generation Of NoveL, Integrated and Internationally Harmonised Approaches for Testing Metabolism Disrupting Compounds. E Proyecto del Programa Marco de la UE, European Comission. IP: Ángel Nadal Navajas.

Función de la célula alfa pancreática durante el envejecimiento: implicaciones en la homeostasis de la glucosa. MINISTERIO DE ECONOMíA (PLAN NACIONAL DE I+D+I). REF: BFU2016-77125-R. IP: Ivan Quesada.

OBERON-An integrative strategy of testing systems for identification of EDs related to metabolic disorders. Proyecto del Programa Marco de la UE, European Comission. IP. Paloma Alonso-Magdalena.

Descubrimiento de nuevas dianas terapéuticas para el tratamiento de la diabetes tipo 1 y diabetes tipo 2 basadas en estrategias de supervivencia de la célula alfa pacreática. Programa Subvenciones a la excelencia científica de juniors investigadores-SEJI, Generalitat Valenciana y Referencia: SEJI/2018/023, 2018-2020. IP: Laura Marroquí Esclapez.

Regulación de la viabilidad y de la función de las células ß y a pancreáticas por los receptores de estrógenos ERß y GPER: papel enla terapia de la diabetes mellitus. Proyecto del Programa Prometeo de la GVA. IP: Ángel Nadal Navajas.

R&D Management

Paloma Alonso-Magdalena. Reviewer for the following journals in 2020: Toxicological Sciences, International Review of Cell and Molecular Biology, JCI Insight, Journal of Nutritional Biochemistry, Environmental Pollution, Free Radical Biology and Medicine, Metabolism-Clinical and Experimental.

Ivan Quesada. Reviewer for the following journals in 2020: Endocrine Connections.

Ivan Quesada. Reviewer of Agencia Estatal de Investigación-MINECO.

Ivan Quesada. Reviewer of Sociedad Española de Diabetes (Proyectos de Investigación).

Reinaldo S. Dos Santos. Reviewer for the following journals in 2020: Endocrinology, Scientific Reports, Biomolecules, y Cells.

Hilda Ferrero. Reviewer for the following journals in 2020: Endocrine Connections, Scientific Reports.

Laura Marroquí. Reviewer for the following journals in 2020: Nutrients, Archives Of Biochemistry And Biophysics.

Angel Nadal. Revisor de las siguientes revistas: Lancet Diabetes and Endocrinology, Nature Reviews of Endocrinology, eLife, Journal of Hazardous Materials, Chemosphere,

Environmental Pollution, reproductive Toxicology, Scientific Reports, Journal of Physiology and Biochemistry.

Evaluación de proyectos: Agencia Estatal de Investigación, España. National Science Centre, Polonia.

Editorial Boards

Editor Frontiers in Physiology. Ángel Nadal.

Editor Frontiers in Endocrinology. Ángel Nadal.

Editor Frontiers in Neuroscience. Ángel Nadal.

Senior Editor Endocrine Connections. Paloma Alonso-Magdalena.

Editor Scientific Reports. Paloma Alonso-Magdalena.

Clinical pharmacology

Group name: IMMUNOPHARMACOLOGY

We develop translational research on immunopharmacology. Our research projects are mostly devoted to study the mechanism of action and the pharmacokinetic-pharmacodynamic relationship of drugs widely used in clinical practice in inflammatory diseases and cancer, especially in digestive diseases. In 2020, our studies were centered basically in:

1. Immunoregulatory effects of beta-blockers drugs in patients with cirrhosis in risk of development of hepatocellular carcinoma.

2. Role of inflammasome in the development of hepatocellular carcinoma.

3. Mechanism of action of antibiotics used to reduce bacterial translocation in patients with cirrhosis.

4. Pharmacokinetic-pharmacodynamic relationship of biological drugs used in inflammatory bowel diseases

Staff

Pedro Zapater Hernández

José Manuel González-Navajas

Ph. D Students

Susana Almenara de Riquer

Beatriz Lozano Ruiz

Ivan Herrera Marante

Beatriz Orts Jorquera

Cayetano Miralles Maciá

Publications

Lozano-Ruiz B, González-Navajas JM. The emerging relevance of AIM2 in liver disease. Int J Mol Sci. 2020, Sep 7;21(18):6535 doi: 10.3390/ijms21186535.

Caparrós E, Juanola O, Gómez-Hurtado I, Puig-Kroger A, Piñero P, Zapater P, Linares R, Tarín F, Martínez-López S, Gracia-Sancho J, González-Navajas JM, Francés R. Liver sinusoidal endothelial cells contribute to hepatic antigen-presenting cell function and th17 expansion in cirrhosis. Cells. 2020, May 15;9(5):1227. Doi: 10.3390/cells9051227.

Lee J, Zhang J, Chung YJ, Kim JH, Kook CM, González-Navajas JM, Herdman DS, Nürnberg B, Insel PA, Corr M, Mo JH, Tao A, Yasuda K, Rifkin IR, Broide DH, Sciammas R, Webster NJ, Raz E. Inhibition of IRF4 in dendritic cells by PRR-independent and -dependent signals inhibit Th2 and promote Th17 responses. Elife. 2020, Feb 4;9:e49416. Doi: 10.7554/eLife.49416.

Gómez-Hurtado I, Gallego-Durán R, Zapater P, Ampuero J, Aller R, Crespo J, Arias-Loste M, Garcia-Monzón C, Bellot P, González-Rodriguez Á, Juanola O, Romero-Gómez M, Francés R. Bacterial antigen translocation and age as BMI-independent contributing factors on systemic inflammation in NAFLD patients. Liver Int. 2020, Jul;40(9):2182–93. Doi: 10.1111/liv.14571.

Almenara S, Lozano B, Gimenez P, Herrera I, Miralles C, Bellot P, Rodríguez M, Francés R, Gonzalez-Navajas JM, Pascual S, Zapater P. Functionality of beta-adrenergic receptors in patients with cirrhosis treated chronically with non-selective beta-blockers. Hepatology

International. 2020, Sep 1;14(5):858–68. Doi: 10.1007/s12072-020-10083-5.

Picó, MD, Sánchez-Heras, AB., Castillejo, A, Giner-Calabuig, M, Alustiza, M, Sánchez, A, Moreira, L, Pellise, M, Castells, A, Llort, G, Yagüe, C, Cajal, TRY, Gisbert-Beamud, A, Cubiella, J, Rivas, L, Herraiz, M, Garau, C, Salces, I, Carrillo-Palau, M, Bujanda, L, López-Fernández, A, Alvarez-Urturi, C, López, MJ, Alenda, C, Zapater, P, Lacueva, FJ, Balaguer, F, Soto, JL, Murcia, O, Jover, R. Risk of cancer in family members of patients with lynch-like syndrome. Cancers. 2020, Aug 1;12(8):1–12. Doi: 10.3390/cancers12082225.

Governmental Projects and Funding

Estudio experimental del efecto modulador del sistema adrenérgico sobre el proceso de hepatocarcinogénesis. PROYECTO DE INVESTIGACIÓN DE SALUD. 01/01/2018 – 31/12/2020. INSTITUTO DE SALUD CARLOS III – ACCIÓN ESTRATÉGICA EN SALUD 2017 (PI17/01617). IP: Pedro Zapater Hernández.

Effect of high salt intake in the development of hepatocellular carcinoma and the immunological profile of patients with compensated cirrhosis. 01/01/2020 – 31/12/2022 – PROYECTOS DE INVESTIGACIÓN EN SALUD – ACCIÓN ESTRATÉGICA EN SALUD 2019 (PI19/01554) – INSTITUTO DE SALUD CARLOS III. IP: José Manuel González Navajas.

The Salt-Th17 axis in tumor growth and response to immunotherapy. 01/01/2020 – 31/12/2023. PLAN GenT (CDEI-03/20-A) – CONSELLERIA DE SANITAT – GENERALITAT VALENCIANA. IP: José Manuel González Navajas.

R&D Management

Reviewer of Cells (JMGN) (2020).

Reviewer of Frontiers in Immunology (JMGN) (2020).

Reviewer of International Journal of Molecular Sciences (JMGN) (2020).

Reviewer of Advances in Therapy (PZH) (2020).

Reviewer of Biomarkers (PZH) (2020).

Reviewer of British Journal of Clinical Pharmacology (PZH) (2020).

Reviewer of Clinics and Research in Hepatology and Gastroenterology (PZH) (2020).

Reviewer of Frontiers Cellular (PZH) (2020).

Reviewer of Liver International (PZH) (2020).

Reviewer of World Journal of Gastroenterology (PZH) (2020).

Reviewer of World Journal of Hepatology (PZH) (2020).

Editorial Boards

Associate Editor – Frontiers in Immunology (JMGN) (2020-…).

Topic Editor – International Journal of Molecular Sciences (JMGN) (2020-…).

Group name: RECEPTORS AND MECHANISMS INVOLVED IN ANALGESIA

Our group is formed by professors of the University Miguel Hernández and physicians of the Department of Anaesthesia, Resuscitation and Pain Relief Therapy of the General University Hospital of Alicante. We develop translational and clinical research on pain therapy and anaesthesia. Present lines of research are:

1. Regarding translational research we are interested in the neurobiological basis of the variability in opiate actions in normal and pathological conditions, at molecular level.

2. The analgesic efficacy of radiofrequency for the relief of the Greater Trochanteric Pain Syndrome

3. Ambispective comparative study of post operative cognitive dysfunction after anaesthesia using inhalatory anaesthesics in bariatric surgery

Staff

Juan José Ballesta Payá

Ph. D Students

Luis Gómez Salinas

Physicians from the General University Hospital of Alicante

Yolanda Sastre Peris

PhD THESES (2020)

Título: FUNCIONES DE LAS CÉLULAS T REGULADORAS EN EL CONTROL INFLAMATORIO E INTEGRIDAD DE LA BARRERA INTESTINAL EN LA CIRROSIS

Autor: ORIOL JUANOLA JUAREZ

Fecha de Lectura: 24/01/2020

Dirección: Rubén Francés Guarinos/ Esther Caparrós Cayuela

Dirección web: https://idibe.es/wp-content/uploads/2020/01/TESIS-Oriol-Juanola-IDiBE-24enero2020.pdf

Título: INFLUENCIA DE LOS EXCIPIENTES EN LA BIODISPONIBILIDAD ORAL.

Autor: ALEJANDRO RUIZ PICAZO

Fecha de Lectura: 31/01/2020

Dirección: Mª del Val Bermejo Sanz/ Mª Isabel González Álvarez

Dirección web: https://idibe.es/es/influencia-excipientes-biodisponibilidad-oral-tesis-doctoral-alejandro-ruiz-picazo/

Título: ESTUDIO ESTRUCTURAL Y APLICACIONES BIOMÉDICAS DE LOS MÓDULOS DE UNIÓN A COLINA: ANTIMICROBIANOS FRENTE A STREPTOCOCCUS PNEUMONIAE

Autor: EMMA ROIG MOLINA

Fecha de Lectura: 28/02/2020

Dirección: Jesús Sanz Morales/Mª Beatriz Maestro García-Donas

Dirección web: https://idibe.es/estudio-estructural-colina-antimicrobianos-streptococcus-pneumoniae-tesis-emma-roig/

Título: DISEÑO Y OPTIMIZACIÓN DE NANOPARTÍCULAS CON APLICACIONES BIOTECNOLÓGICAS: CAPTURA DE CONTAMINANTES, TRANSPORTE Y ALMACENAMIENTO DE BIOMOLECULAS.

Autor: FELIPE HORNOS ADÁN

Fecha de Lectura: 05/11/2020

Dirección: Francisco Javier Gómez Pérez

Dirección web: https://idibe.es/nanoparticulas-aplicaciones-contaminantes-biomoleculas-tesis-doctoral-felipe-hornos/

SEMINARS (2020)

Título: **CÓMO ESCRIBIR UN GRAN MANUSCRITO CIENTÍFICO, Y QUE SEA ACEPTADO EN UNA BUENA REVISTA / EL PROCESO DE LA "REVISIÓN POR PARES".**

Ponente / Institución: Anthony Newman, Editorial Elsevier, Ámsterdam (Países Bajos).

Lunes, 13 de Enero de 2020.

Título: **INTERACCIÓN INMUNO-REPRODUCTORA EN PECES TELEÓSTEOS.**

Ponente / Institución: Elena Chaves Pozo, Instituto Español de Oceanografía, Murcia (España).

Viernes, 17 de Enero de 2020.

Título: **MICROBIOTA: DEL LABORATORIO A LA CLÍNICA. Efecto antiinflamatorio intestinal de cepas probióticas.**

Ponente / Institución: Julio Juan Gálvez Peralta, Departamento de Farmacología de la Universidad de Granada.

Viernes, 21 de Febrero de 2020.

Título: **NAMPT y PARP1: NUEVAS DIANAS TERAPÉUTICAS Y BIOMARCADORES DE PRONÓSTICO PARA LA PSORIASIS.**

Ponente / Institución: Víctor Mulero Méndez, Instituto Murciano de Investigación Biosanitaria. Universidad de Murcia.

Viernes, 28 de febrero de 2020.

Título: **EL PUNTO CIEGO DE LA NEUROCIENCIA: MAGIA Y A.I. PARA ESTUDIAR NUESTRA PROPIA MENTE.**

Ponente / Institución: Álex Gómez Marín, Instituto de Neurociencias de Alicante (CSIC-UMH), San Juan de Alicante.

Viernes, 6 de Marzo de 2020.

Título: **FROM BASIC NEUROSCIENCE TO NEURO-ONCOLOGY.**

Ponente / Institución: Camino De Juan Romero, Fundación FISABIO e IDIBE, Elche.

Viernes, 13 de Marzo de 2020.

Título: **MICROBIOTA EN EL ENTORNO MATERNOINFANTIL: INFLUENCIA DE LA LACTANCIA.**

Ponente / Institución: Mª Carmen Collado Amores, Instituto de Agroquímica y Tecnología de Alimentos (IATA-CSIC), Valencia.

Martes, 26 de Mayo de 2020.

Título: **MECANISMOS DE PATOGÉNESIS DE CORONAVIRUS HUMANOS.**

Ponente / Institución: Isabel Sola, Centro Nacional de Biotecnología (CNB-CSIC), Madrid.

Martes, 10 de Noviembre de 2020.

Título: **INGENIERÍA DE GENOMAS DE CORONAVIRUS HUMANOS PARA EL DESARROLLO DE VACUNAS.**

Ponente / Institución: Melissa Belló, Centro Nacional de Biotecnología (CNB-CSIC), Madrid.

Martes, 10 de Noviembre de 2020.

Título: **LAS NEURONAS ESPINALES PTF1A EVITAN EL DESARROLLO DE PICOR CRÓNICO AUTOINDUCIDO.**

Ponente / Institución: Augusto Escalante, Instituto de Neurociencias, CSIC-UMH, San Juan de Alicante.

Viernes, 4 de Diciembre de 2020.

Título: **III WORKSHOP SEJI JÓVENES INVESTIGADORES DE EXCELENCIA: WHAT IS GOING ON IN DIABETES RESEARCH?**

Ponente / Institución:

Dr. Carlos Guillén Viejo (Facultad de Farmacia de la Universidad Complutense de Madrid) - Hyperactivation of mTORC1, aging and pancreatic β cells.

Dra. Noèlia Téllez Besolí (CIBER del área de diabetes y enfermedades metabólicas asociadas – CIBERDEM; Instituto de Investigación Biomédica de Bellvitge) - Pancreatic beta cell regeneration in aging.

Dr. David Sebastián (Instituto de Investigación Biomédica de Barcelona) - Dinámica mitocondrial y su papel en enfermedades metabólicas y envejecimiento.

Dra. Irene Miguel-Escalada (Centre for Genomic Regulation, Barcelona) - Modeling human non-coding mutations reveals new insights into diabetes and pancreas development.

Miércoles, 16 de Diciembre.

Agreements

- Center for Therapeutic Innovation (CTI) University of Bath for the secondments of researchers and PhD students.
- KAERTOR foundation.

Bibliometric of publications

Number of publications (WoS)	% of Q1	Mean impact factor	Total impact factor
59	73	4.57	269.41

Dissemination

Out-reach seminars “Sciencie with tapas”:

- El coronavirus de China y otros virus que vienen de fuera: ¿hay que temerles?, 18/02/2020.
- “¿Cómo se defiende nuestro cuerpo del SARS? La respuesta inmunológica frente a virus, 05/11/2020.

Entrepreneurship

- Prospera Biotech SL starts its activity developing neurocosmetics.

Clinical development

- Parentide® continuues in phase II clinical trials for chronic surgical pain. Sponsor: BCN Peptides.
- Bicalutamide is advancing to phase II clinical trials for treating Sanfilippo syndrome. Sponsor BCN Peptides
- AVX-012 starts the phase II clinical trial in USA for dry eye syndrome and it is preparing aphase II clinical trial. Sponsors Avizorex Pharma and Aerie Pharmaceuticals Inc.
- Nocisens, a neurocosmetic for skin care, formulating a soft TRPV1 antagonist is marketed for alleviating sensitive sking. Sponsor: Prospera Biotech.
- PB-02 is a novel formulation for alleviating symptoms that suffer cancer patients that have developed paclitaxel-induced peripheral neuropathy. Sponsor: Prospera Biotech.
- AG1529 continues in regulated pre-clinical safety studies for chronic psoriasic pruritus. Sponsor: AntalGenics.

ANNUAL REPORT 2020

INSTITUTE OF RESEARCH, DEVELOPMENT, AND INNOVATION IN HEALTHCARE BIOTECHNOLOGY IN ELCHE

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