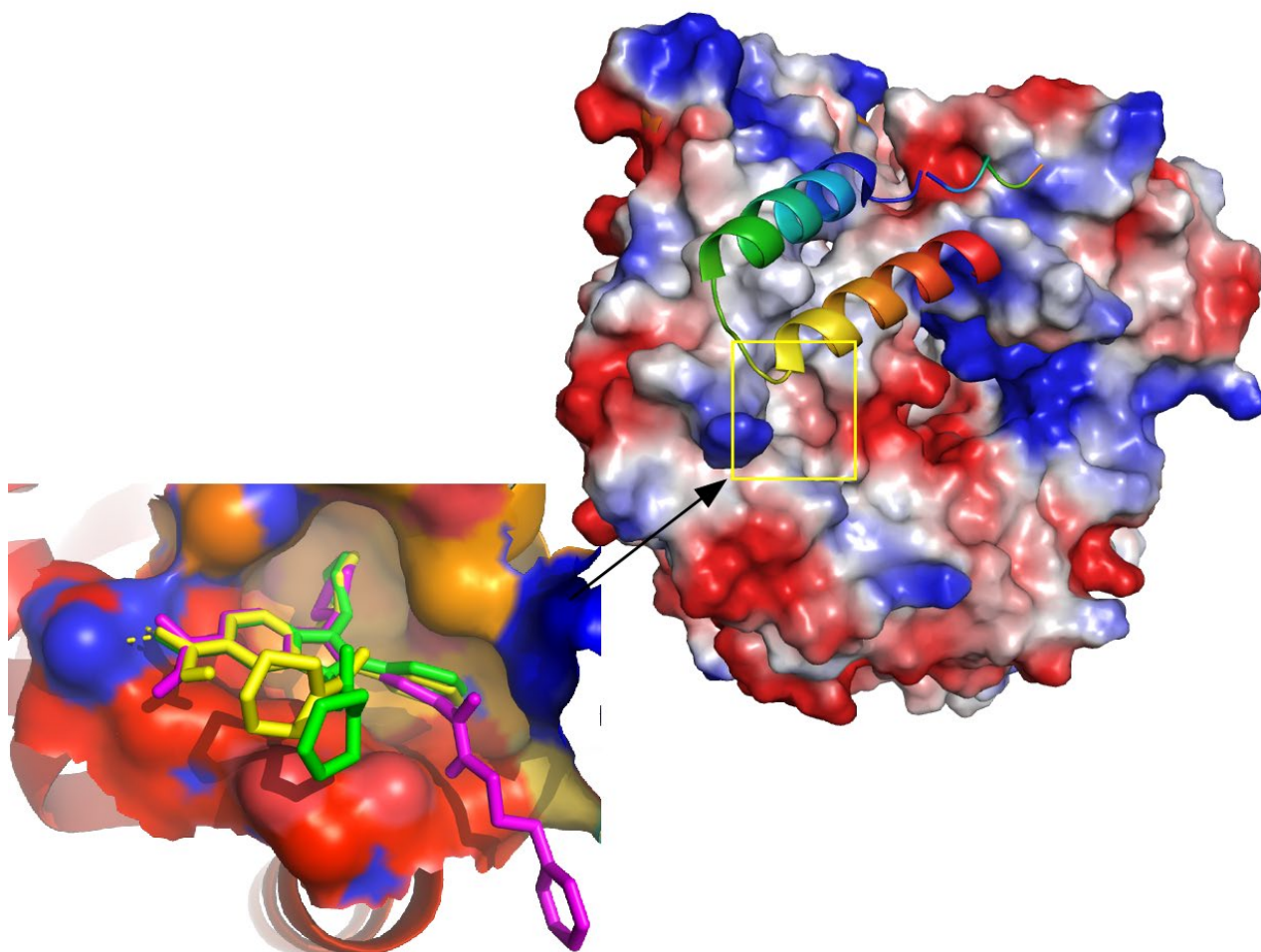


ANNUAL REPORT 2019



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 21 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 accomplishments 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 (70% 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 Bioengineering with the Institute of Bioengineering that is becoming a national reference in the field. In addition, we initiated the Erasmus+European Master on translational cosmetic and dermatological sciences with the Universities of Piemonte Orientale (Italy), Namur. (Belgium) and Humbolt (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.

Major milestones for 2019 have been: (i) the incorporation of Dr. Roberto Pascual as innovation agent funded by the AVI-GVA and the UMH, to potentiate the technology transfer actions to the productive sectors of our society; (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. In addition, we have set an agreement with the Center for Therapeutic Innovation of the University of Bath, and participated in the application for a distributed ICTS with the CRG, CNIO, Fundación Medina and CIMUS. This is going to potentiate the multidisciplinary and allow us to increase our national and international competitiveness, which is essential to secure a more ambitious research program. 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 eligible for a seal of excellence.

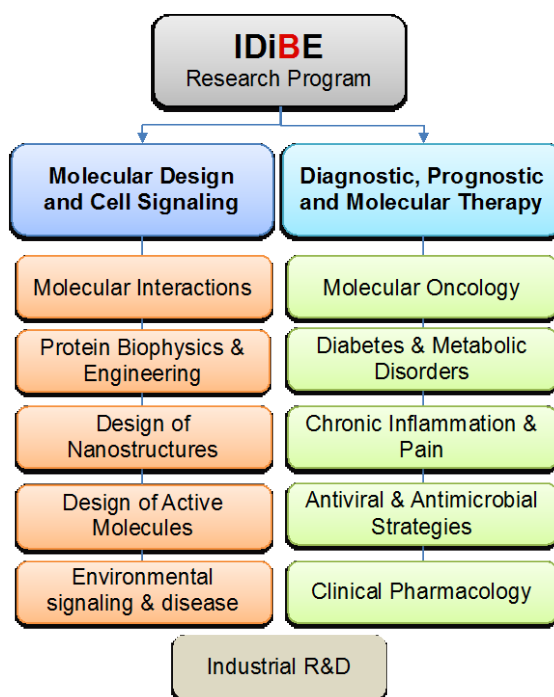
Prof. Antonio Ferrer-Montiel

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 multidisciplinary. **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, Prognostic 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 multidisciplinary nature 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: PROTEIN STRUCTURE AND THERMODYNAMICS OF MOLECULAR RECOGNITION

Our group is involved in the study, by using calorimetric and spectroscopic techniques, of macromolecular interactions. To that end, the group has the expertise in DSC, ITC, fluorescence and circular dichroism. Furthermore, the group has the knowledge to solve structures by using state-of-the-art techniques. Some, but not exclusively, of the biomolecules currently under study in the group are: (i) those involved in the phosphorylation transfer in microorganisms; and (ii) those implicated in the assembly of the capsid of HIV.

Staff

Javier Gómez Pérez

José Luis Neira Faleiro

Rocío Esquembre Tomé

Ph. D Students

Felipe Hornos Adán

Technicians

Elisa Pérez García

Publications

Yadahalli S, Neira JL, Johnson CM, Tan YS, Rowling PJE, Chattopadhyay A, Verma CS, Itzhaki LS. Kinetic and thermodynamic effects of phosphorylation on p53 binding to MDM2. *Scientific Reports*. 2019, 9 (1), art. no. 693. doi: 10.1038/s41598-018-36589-5.

Neira JL, Palomino-Schätzlein M, Ricci C, Ortore MG, Rizzuti B, Iovanna JL. Dynamics of the intrinsically disordered protein NUPR1 in isolation and in its fuzzy complexes with DNA and prothymosin a *Biochimica et Biophysica Acta - Proteins and Proteomics*. 2019, 1867 (11), art. no. 140252. doi: 10.1016/j.bbapap.2019.07.005.

García-Rodríguez FM, Neira JL, Marcia M, Molina-Sánchez MD, Toro N. A group II intron-encoded protein interacts with the cellular replicative machinery through the

β -sliding clamp. *Nucleic acids research*. 2019, 47 (14), pp. 7605-7617. doi: 10.1093/nar/gkz468.

Neira JL, Correa J, Rizzuti B, Santofimia-Castaño P, Abian O, Velázquez-Campoy A, Fernandez-Megía E, Iovanna JL. Dendrimers as Competitors of Protein-Protein Interactions of the Intrinsically Disordered Nuclear Chromatin Protein NUPR1. *Biomacromolecules*. 2019, 20 (7), pp. 2567-2576. doi: 10.1021/acs.biomac.9b00378.

Santofimia-Castaño P, Xia Y, Lan W, Zhou Z, Huang C, Peng L, Soubeyran P, Velázquez-Campoy A, Abián O, Rizzuti B, Neira JL, Iovanna J. Ligand-based design identifies a potent NUPR1 inhibitor exerting anticancer activity via necroptosis. *Journal of Clinical Investigation*. 2019, 129 (6), pp. 2500-2513. doi: 10.1172/JCI127223.

Neira JL, Díaz-García C, Prieto M, Coutinho A. The C-terminal SAM domain of p73 binds to the N terminus of MDM2. *Biochimica et Biophysica Acta - General Subjects*. 2019, 1863 (4), pp. 760-770. doi: 10.1016/j.bbagen.2019.01.019.

Pantoja-Uceda D, Neira JL, Contreras LM, Manton CA, Welch DR, Rizzuti B. The isolated C-terminal nuclear localization sequence of the breast cancer metastasis suppressor 1 is disordered. *Archives of Biochemistry and Biophysics*. 2019, 664, pp. 95-101. doi: 10.1016/j.abb.2019.01.035.

Medina-Carmona, E., Rizzuti, B., Martín-Escolano, R., Pacheco-García, J.L., Mesa-Torres, N., Neira, J.L., Guzzi, R., Pey, A.L. Phosphorylation compromises FAD binding and intracellular stability of wild-type and cancer-associated NQO1: Insights into flavo-proteome stability. *International Journal of Biological Macromolecules*. 2019, 125, pp. 1275-1288. doi: 10.1016/j.ijbiomac.2018.09.108.

Santofimia-Castaño P, Rizzuti B, Xia Y, Abian O, Peng L, Velázquez-Campoy A, Neira JL, Iovanna J. Targeting intrinsically

disordered proteins involved in cancer Cellular and Molecular Life Sciences. 2019. doi: 10.1007/s00018-019-03347-3.

Santofimia-Castaño P, Rizzuti B, Xia Y, Abian O, Peng L, Velázquez-Campoy A, Iovanna JL, Neira JL. Designing and repurposing drugs to target intrinsically disordered proteins for cancer treatment: using NUPR1 as a paradigm. *Molecular and Cellular Oncology*. 2019, 6 (5), art. no. e1612678. doi: 10.1080/23723556.2019.1612678.

Governmental Projects and Funding

Diseño de nuevos antibióticos basados en un sistema de fosforilación exclusivo de Bacterias 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-...).

Reviewer of Italian PRIM program (JLN) (2018-...).

Reviewer of Belgian Ministry of Science (JLN) (2018-...).

Reviewer for Archives of Biochemistry and Biophysics (JG).

Reviewer for Colloids and Surfaces B: Biointerfaces (JG).

Reviewer for Process Biochemistry (RE).

Reviewer for Journal of Luminescence (RE).

Editorial Boards

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

Board member of BBA Proteins and Proteomics (2018-...). José L. Neira (Editor).

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

M^a José Martínez Tomé

Juan Alberto Falcó Graciá

Postdoctoral Researchers

Amalia Mira Carrió

Ph. D Students

Marta Rubio Camacho

Yolanda Inmaculada Alacid Martínez

Helena Codina Márquez

Technicians

Elisa Pérez García

Publications

Falco A, Medina-Gali RM, Poveda JA, Bello-Perez M, Novoa B, Encinar JA. Antiviral Activity of a Turbot (*Scophthalmus maximus*) NK-Lysin Peptide by Inhibition of Low-pH Virus-Induced Membrane Fusion. *Mar Drugs*. 2019 Feb 1;17(2). pii: E87. doi: 10.3390/md17020087.

Bello-Perez M, Falco A, Novoa B, Perez L, Coll J. Hydroxycholesterol binds and enhances the anti-viral activities of zebrafish monomeric c-reactive protein isoforms. *PLoS One*. 2019 Jan 17;14(1):e0201509. doi: 10.1371/journal.pone.0201509.

Martínez-Ortega L, Mira A, Fernandez-Carvajal A, Mateo CR, Mallavia R, Falco A. Development of A New Delivery System Based on Drug-Loadable Electrospun Nanofibers for Psoriasis Treatment. *Pharmaceutics*. 2019 Jan 4;11(1). pii: E14. doi: 10.3390/pharmaceutics11010014.

Rubio-Camacho M, Alacid Y, Mallavia R, Martínez-Tomé MJ, Mateo CR. Polyfluorene-Based Multicolor Fluorescent Nanoparticles Activated by Temperature for Bioimaging and Drug Delivery. *Nanomaterials*. 2019, 9: 1485. doi:10.3390/nano9101485.

PhD Theses

Descubrimiento y caracterización de la actividad antiviral inducida por las moléculas tipo CRP de pez cebra (*Danio rerio*). Melissa Belló-Perez. Universidad Miguel Hernández. Supervisor: Juan Alberto Falcó Graciá. 23/07/2019.

Science dissemination: outreach activities

Jornadas de divulgación científica "Ciencia con tapas".

- Inmunoterapia y nuevos avances contra el cáncer, 13-02-2019.

- Una conversación con el cerebro: ¿Podemos hablar su lenguaje?, 10-04-2019.

- ¿Conoces las particularidades de los vinos de Alicante?, 13-06-2019.

- Tu 'dieta' tenía un precio. ¿Todo por perder kilos?, 11-12-2019.

- "¿El estrés físico produce cáncer?, 20-09-2019. Módulo "Ciencia, Salud y Tecnología" desarrollado en la IV Feria de la Ciencia y la Tecnología de Elche (FeCiElx).

M^a José Martínez Tomé. Comité organizador.

Number of Congress Communications

National contributions: 1

Poster presentations: 1

International contributions: 6

Oral presentations: 2

Poster presentations: 4

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- Dic-2020). Ministerio de Economía, industria y Competitividad. IP: Carmen Reyes Mateo Martínez y Co-IP: Ricardo Mallavia Marín.

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.

R&D Management

Reviewer for Spanish State Research Agency (Agencia Estatal de Investigación, AEI) (2019-...). Alberto Falcó.

Research for Spanish Agency, Agencia Nacional de Evaluación y Prospectiva (ANEP). Ricardo Mallavia.

Editorial Boards

Guest Editor of Special Issue in Nanomaterials (Basel) (2018-2020). Alberto Falcó & Ricardo Mallavia.

Reviewer for the following journals in 2019:

Developmental and Comparative Immunology, Fish and Shellfish Immunology, International -Journal of Molecular Sciences, Molecular Immunology, Nanomaterials and PLOS ONE. Alberto Falcó.

Sensors, Molecules and Micromachines. Reyes Mateo.

Polymers, Applied Sciences-Basel, Drug Delivery and Translational Research, Pharmaceutics, Nanomaterials, Materials. Ricardo Mallavia.

Molecules. M^a José Martínez.

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. Applying "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

Number of Congress Communications

National contributions: 2

Oral presentations: 1

Poster presentations: 2

Governmental Projects and Funding

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.

R&D and Educational Committees

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

Review Editor in Frontiers in Physiology - Membrane Physiology and Membrane Biophysics. 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

M^a Lourdes Renart Pérez

Ana Marcela Giudici Besseghini

Ph. D Students

Clara Díaz García

Technicians

Eva Martínez

Publications

Poveda JA, Giudici AM, Renart ML, Millet O, Morales A, González-Ros JM, Oakes V, Furini S, Domene C. Modulation of the potassium channel KcsA by anionic phospholipids: Role of arginines at the non-annular lipid binding sites. *Biochim Biophys Acta Biomembr.* 2019 Oct 1;1861(10):183029. doi: 10.1016/j.bbamem.2019.183029.

Renart ML, Giudici AM, Poveda JA, Fedorov A, Berberan-Santos MN, Prieto M, Díaz-García C, González-Ros JM, Coutinho A. Conformational plasticity in

the KcsA potassium channel pore helix revealed by homo-FRET studies. *Sci Rep.* 2019 Apr 17;9(1):6215. doi: 10.1038/s41598-019-42405-5.

Giudici AM, Renart ML, Díaz-García C, Morales A, Poveda JA, González-Ros JM. Accessibility of Cations to the Selectivity Filter of KcsA in the Inactivated State: An Equilibrium Binding Study. *Int J Mol Sci.* 2019 Feb 5;20(3). pii: E689. doi: 10.3390/ijms20030689.

Falco A, Medina-Gali RM, Poveda JA, Bello-Perez M, Novoa B, Encinar JA. Antiviral Activity of a Turbot (*Scophthalmus maximus*) NK-Lysin Peptide by Inhibition of Low-pH Virus-Induced Membrane Fusion. *Mar Drugs.* 2019 Feb 1;17(2). pii: E87. doi: 10.3390/md17020087.

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.* 2019 May 31. pii: S0306-4522(19)30373-2. doi: 10.1016/j.neuroscience.2019.05.043.

Neira JL, Díaz-García C, Prieto M, Coutinho A. The C-terminal SAM domain of p73 binds to the N terminus of MDM2. *Biochim Biophys Acta Gen Subj.* 2019 Apr;1863(4):760-770. doi: 10.1016/j.bbagen.2019.01.019.

Invited talks and courses

Interacciones lípido-proteína: Papel de los fosfolípidos aniónicos en la modulación funcional de un canal iónico, KcsA. Prof. José Manuel González Ros. Seminarios de Biología Molecular y Biotecnología, "Master en Biología Molecular y Biotecnología", Universidad de Murcia, 28 de febrero de 2019.

Number of Congress Communications

International contributions: 2

Oral presentations: 0

Poster presentations: 2

Governmental Projects and Funding

Bases Moleculares de la modulación de canales iónicos. 01/01/2016-30/06/2019. Ref. BFU2015-66612-P. PROYECTOS DE I+D – GENERACIÓN DE CONOCIMIENTO, MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES. IPs: José Manuel González-Ros y José Antonio Poveda Larrosa.

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 *Biomolecules*. J. A. Poveda.

Reviewer for "Archives of Biochemistry and Biophysics". J. A. Poveda, Ana Marcela Giudici.

Reviewer for "International Journal of Molecular Sciences". J. A. Poveda.

Reviewer for "Protein Expression and Purification". J. A. Poveda.

Reviewer for "Biopolymers". J. A. Poveda.

Reviewer for "AIMS Biophysics". J. A. Poveda.

Evaluator for FWF Austrian Science Fund. J. M. González-Ros.

Evaluator for "Agència de Gestió d'Ajuts Universitaris i de Recerca". J. M. González-Ros.

Evaluator for MINECO. J. M. González-Ros.

Reviewer for "Oncotarget". J. M. González-Ros.

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: NATURAL BIOACTIVE COMPOUNDS

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 Barraji3n Catal3n

María Herranz López

Postdoctoral Researchers

Almudena Pérez Sánchez

Ver3nica Ruiz Torres

María Dolores Olivares Vicente

Ph. D Students

Noelia Sánchez Marzo

Javier 3lvarez Mart3nez

Luz Mar3a Agull3 Chazarra

Technicians

M^a Teresa Garz3n Cabrerizo

Mar3a Losada Echeberr3a

Publications

P3rez-S3nchez A, Barraji3n-Catal3n E, Ruiz-Torres V, Agull3-Chazarra L, Herranz-L3pez M, Vald3s A, Cifuentes A, Micol V. Rosemary (*Rosmarinus officinalis*) extract causes ROS-induced necrotic cell death and inhibits tumor growth in vivo. *Sci Rep.* 2019, 9(1):808. Q1

Verdura S, Cuy3s 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.* 2019, 12(1): 8-34.

Herranz-L3pez M, Olivares-Vicente M, Boix-Casteji3n M, Caturla N, Roche E, Micol V. Differential effects of a combination of *Hibiscus sabdariffa* and *Lippia citriodora* polyphenols in overweight/obese subjects: A randomized controlled trial. *Sci Rep.* 2019, 9(1):2999. Q1

P3rez-S3nchez A, Cuy3s E, Ruiz-Torres V, Agull3-Chazarra L, Verdura S, Gonz3le 3lvarez I, Bermejo M, Joven J, Micol V, Bosch-Barrera J, Menendez JA. Intestinal Permeability Study of Clinically Relevant Formulations of Silibinin in Caco-2 Cell Monolayers. *Int J Mol Sci.* 2019, 20(7).

Montero D, Vicente-Salar N, Herranz-L3pez M, Micol V, Walther G, P3rez-Mart3n A, Vinet A, Roche E. Glutathione-dependent enzyme activities of peripheral blood mononuclear cells decrease during the winter season compared with the summer in normal-weight and severely obese adolescents. *J. Physiol. Biochem.* 2019, 75(3), 321-327.

Cuy3s E, Verdura S, Micol V, Joven J, Bosch-Barrera J, Encinar JA, Menendez JA. Revisiting silibinin as a novobiocin-like Hsp90 C-terminal inhibitor: Computational modeling and experimental validation. *Food Chem Toxicol.* 2019. Q1

S3nchez-Marzo N, Lozano-S3nchez J, C3diz-Gurrea ML, Herranz-L3pez M, Micol V, Segura-Carretero A. Relationships Between Chemical Structure and Antioxidant Activity of Isolated Phytochemicals from Lemon Verbena. *Antioxidants (Basel).* 2019, 20;8(8), 324. Q1

Ruiz-Torres V, Rodr3guez-P3rez C, Herranz-L3pez M, Mart3n-Garc3a B, G3mez-Caravaca AM, Arr3ez-Rom3n D, Segura-Carretero A, Barraji3n-Catal3n E, Micol V. Marine Invertebrate Extracts Induce Colon Cancer Cell Death via ROS-Mediated DNA Oxidative Damage and Mitochondrial Impairment. *Biomolecules.* 2019, 9(12), 771; <https://doi.org/10.3390/biom9120771>. Q1

Olivares-Vicente M, S3nchez-Marzo N, Encinar JA, C3diz-Gurrea ML, Lozano-

Sánchez J, Segura-Carretero A, Arráez-Román D, Riva C, Barrajon E, Herranz-López M, Micol V. The potential synergistic modulation of AMPK by *Lippia citriodora* compounds as a target in metabolic disorders. *Nutrients*. 2019, 11(12), 2961. DOI: 10.3390/nu11122961. Q1

Cuyàs E, Gumuzio J, Lozano-Sánchez J, Carreras D, Verdura S, Llorach-Parés L, Sanchez-Martinez M, Selga S, Pérez GJ, Scornik FS, Brugada R, Bosch-Barrera R, Segura-Carretero A, Martín AG, Encinar JA, Menendez JA. Extra Virgin Olive Oil Contains a Phenolic Inhibitor of the Histone Demethylase LSD1/KDM1A. *Nutrients*. 2019, 11(7): 1656. DOI: 10.3390/nu11071656.

Cuyàs E, Verdura S, Lozano-Sánchez J, Viciano-Gonzalo I, Llorach-Parés L, Bosch-Barrera J, Brunet J, Nonell-Canals A, Segura-Carretero A, Sánchez-Martínez M, Encinar JA, Menendez JA. The extra virgin olive oil phenolic oleacein is a dual substrate-inhibitor of catechol-O-methyltransferase. *Food Chem Toxicol*. 2019, 128: 35-45. DOI: 10.1016/j.fct.2019.03.049.

Chico V, Salvador-Mira ME, Nombela I, Puente-Marín S, Ciordia S, Mena MC, Perez L, Coll J, Guzman F, Encinar JA, Mercado L, Ortega-Villaizan MM. IFIT5 Participates in the Antiviral Mechanisms of Rainbow Trout Red Blood Cells. 2019. *Front Immunol*. 2019; 10: 613. DOI: 10.3389/fimmu.2019.00613.

Falco A, Medina-Gali RM, Poveda JA, Bello-Perez M, Novoa B, Encinar JA. Antiviral activity of a turbot (*Scophthalmus maximus*) NK-lysin peptide by inhibition of low-pH virus-induced membrane fusion. 2019. *Mar Drugs*. 17(2). DOI: 10.3390/md17020087.

Sánchez-Marzo N, Pérez-Sánchez A, Ruiz-Torres V, Martínez-Tébar A, Castillo J, Herranz-López M, Barrajon-Catalán E. Antioxidant and photoprotective activity of apigenin and its potassium salt derivative in human keratinocytes and absorption in Caco-2 cell monolayers. *Int. J. Mol. Sci*. 2019, 20(9), 2148; <https://doi.org/10.3390/ijms20092148>.

Herranz-López M, Losada-Echeberría M, Barrajon-Catalán E. The multitarget activity of natural extracts on cancer:

Synergy and xenohormesis. *Medicines*. 2019, 6(1), 6; <https://doi.org/10.3390/medicines6010006>.

Veza T, Rodriguez-Nogales A, Algieri F, Garrido-Mesa J, Romero M, Sánchez M, Toral M, Martín-García B, Gómez-Caravana AM, Arráez-Román D, Segura-Carretero A, Micol V, García F, Utrilla, MP, Duarte J, Rodriguez-Cabezas ME, Gálvez J. The metabolic and vascular protective effects of olive (*Olea europaea* L.) leaf extract in diet-induced obesity in mice are related to the amelioration of gut microbiota dysbiosis and to its immunomodulatory properties. *Pharmacol. Res*. 2019, 150, 104487. Q1

Barrajon-Catalán E, Borrás F, Pérez D, Herrero N, Ruiz JJ, Micol V. Metabolomic analysis of the effects of a commercial complex biostimulant on pepper crops. *Food Chem*. 2019, 310, 125818. Q1

Olivares-Vicente M, Sánchez-Marzo N, Encinar JA, Cádiz-Gurrea ML, Lozano-Sánchez J, Segura-Carretero A, Arráez-Román D, Riva C, Barrajon-Catalán E, Herranz-López M, Micol V. The Potential Synergistic Modulation of AMPK by *Lippia citriodora* Compounds as a Target in Metabolic Disorders. *Nutrients*. 2019, 11(12), 2961; <https://doi.org/10.3390/nu11122961>. Q1

Fernández-Calvet A, Euba B, Caballero L, Díez-Martínez R, Menéndez M, Ortiz de Solórzano C, Leiva J, Micol V, Barrajon-Catalán E, Garmendia J. Preclinical Evaluation of the Antimicrobial-Immunomodulatory Dual Action of Xenohormetic Molecules against *Haemophilus influenzae* Respiratory Infection. *Biomolecules*. 2019, 9(12), 891; <https://doi.org/10.3390/biom9120891>. Q1

PhD Theses

Estudio de la capacidad antiproliferativa en modelos celulares de cáncer de mama de un extracto de hoja de olivo enriquecido en polifenoles. María Losada Echeberria. Universidad Miguel Hernández. Supervisor: Enrique Barrajon-Catalán y Vicente Micol. 10/10/2019.

Polifenoles de plantas comestibles como reprogramadores metabólicos en condiciones de glucolipototoxicidad. María

Dolores Olivares Vicente. Universidad Miguel Hernández. Supervisor: María Herranz-López y Vicente Micol. 28/10/2019.

The stress-mediated antiproliferative effects of marine invertebrate extracts in human colon cancer cell models. Veronica Ruiz Torres. Universidad Miguel Hernández. Supervisor: Enrique Barraji3n-Catal3n y Vicente Micol. 08/11/2019.

Organization of Meetings

Barraji3n-Catal3n, E. Organizing committee of XV Congress of pharmacy Students. San Juan (Spain), 2019.

Invited talks and courses

The use of natural compounds to beat supebacteria: "The Cistus connection". Enrique Barraji3n-Catal3n. Wageningen (Netherlands), september 2019.

Number of Congress Communications

National contributions: 1

Oral presentations: 1

Poster presentations: 0

International contributions: 6

Oral presentations: 4

Poster presentations: 2

Governmental Projects and Funding

T3tulo del proyecto: Una innovadora aproximaci3n metab3n'mica inductiva para la identificaci3n de metabolitos derivados de polifenoles de la dieta y sus dianas moleculares. Entidad financiadora: Ministerio de Ciencia, Innovaci3n y Universidades. (RTI2018-096724-B-C21). Cantidad concedida: 145.000 €. Duraci3n: 01/01/2019 – 31/12/2021. IP: Vicente Micol y Co-IP: Enrique Barraji3n Catal3n.

T3tulo del proyecto: El car3cter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terap3uticas frente a la obesidad y las enfermedades infecciosas. Entidad financiadora: Conselleria de Educaci3n, Formaci3n y Empleo (GV). PROMETEO/2016/006. Cantidad

concedida total: 219.478 €. Duraci3n: 01/01/2016 – 31/12/2019. IP: Vicente Micol.

T3tulo del proyecto: Subvenciones para la contrataci3n de personal de apoyo vinculado a un proyecto de transferencia tecnol3gica (APOTIP/2017/003). Entidad financiadora: Proyectos competitivos de subvenci3n p3blica para contrataci3n de personal. Conselleria de Educaci3n. GV. Cantidad concedida: 18.000 €. Duraci3n: 01/11/2017-31/08/2019. IP: Vicente Micol.

Private funding: Contracts

T3tulo del proyecto: Contrato para el "Estudio de la viabilidad de la producci3n de un edulcorante natural mediante procesos biotecnol3gicos". Entidad financiadora: NUTRAFUR, SA. Importe: 28.667 €. Duraci3n: 12/12/2019-12/12/2020. IP: Vicente Micol Molina.

T3tulo del proyecto: Donaci3n a trav3s del plan de mecenazgo para el proyecto "Nuevos compuestos antitumorales para tratar el c3ncer de colon". Entidad financiadora: Caja Rural Central. Importe: 32.000 €. Duraci3n: 12/12/2019-12/12/2020. IP: Enrique Barraji3n Catal3n.

T3tulo del proyecto: Contrato para la "Caracterizaci3n de la composici3n de nuevos ingredientes funcionales y determinaci3n de bioactividad para los sectores nutrac3utico y cosm3tico". Entidad financiadora: "Illice Effitech S.L. Cantidad concedida: 5.700 €. Duraci3n: 21/01/2019-21/01/2020. IP: Enrique Barraji3n Catal3n.

T3tulo del proyecto: Contrato para la realizaci3n del proyecto titulado "Investigaci3n y desarrollo experimental de nuevos alimentos m3s saludables y envases avanzados". Entidad financiadora: Monteloeder S.L. Cantidad concedida: 30.000 €. Duraci3n: 01/02/2018-31/08/2019. IP: Vicente Micol Molina.

Private funding: Technical Services and Assistance

Scientific Advisor MONTELOEDER, S.L. (2002-2019). V. Micol.

Scientific Advisor ILICE EFFITECH, S.L. (2018-). E. Barraji3n, M. Herranz and V. Micol.

10 provisions of services with different companies: Enrique Barrajon Catalán.

Editor of the journal Antioxidants and Molecules. Enrique Barrajon Catalán.

Editorial Boards

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 (Profs. Domingo Saura López and Nuria Martí Bruñá).
- 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. 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

Laura Agulló Anton

Patents

Inventores: Saura, D., Barraión-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., Barraión-Catalán, E., Rodríguez Díaz, J.C., 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., Barraión-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, M.D.R., 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.

El carácter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terapéuticas frente a la obesidad y las enfermedades infecciosas. Conselleria de Educación, Formación y Empleo (GV). PROMETEO/2016/006. Subvención concedida: 51.050 € (2016), 62.655 € (2017), 43.738 € (2018), 62.034 € (2019). Total: 219.477 €. Duración: 01/01/2016 – 31/12/2019. IP: Vicente Micol.

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.

Private funding: Contracts

Título del proyecto: Contrato para la realización del proyecto titulado "Investigación y desarrollo experimental de nuevos alimentos más saludables y envases avanzados". Entidad financiadora: MONTELOEDER, SL. Cantidad concedida: 30.000 €. Duración: 01/02/2016-31/08/2019. IPs: Vicente Micol, Enrique Barraión y María Herranz. Participan como investigadores: Nuria Martí, Enrique Roche y Domingo Saura.

R&D Management

Scientific Advisor in Mitra Sol Tech S.L. and Cool Vega Company S.L.

Scientific Society Councils.

Food Microbiology.

Editorial Boards

Chronic inflammation & pain

Group name: DRUG DESIGN 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

Clotilde Ferrándiz Huertas

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

González-Gil I, Zian D, Vázquez-Villa H, Hernández-Torres G, Martínez RF, Khair-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.* 2019 Dec 16. doi: 10.1021/acs.jmedchem.9b01287.

Pérez de Vega MJ, Fernandez-Mendivil C, de la Torre Martínez R, González-Rodríguez S, Mullet J, Sala F, Sala S, Criado M, Moreno-Fernández S, Miguel M, Fernández-Carvajal A, Ferrer-Montiel A, López MG, González-Muñiz R. 1-(2',5'-Dihydroxyphenyl)-3-(2-fluoro-4-hydroxyphenyl)-1-propanone (RGM079): A Positive Allosteric Modulator of $\alpha 7$

Nicotinic Receptors with Analgesic and Neuroprotective Activity. *ACS Chem Neurosci*. 2019 Aug 21;10(8):3900-3909. doi: 10.1021/acscchemneuro.9b00364. Epub 2019 Aug 2.

Solé L, Roig SR, Sastre D, Vallejo-Gracia A, Serrano-Albarrás A, Ferrer-Montiel A, Fernández-Ballester G, Tamkun MM, Felipe A. The calmodulin-binding tetraleucine motif of KCNE4 is responsible for association with Kv1.3. *FASEB J*. 2019 Jul;33(7):8263-8279. doi: 10.1096/fj.201801164RR. Epub 2019 Apr 10.

Aribas-Blázquez M, Olivos-Oré LA, Barahona MV, Sánchez de la Muela M, Solar V, Jiménez E, Gualix J, McIntosh JM, Ferrer-Montiel A, Miras-Portugal MT, Artalejo AR. Overexpression of P2X3 and P2X7 Receptors and TRPV1 Channels in Adrenomedullary Chromaffin Cells in a Rat Model of Neuropathic Pain. *Int J Mol Sci*. 2019 Jan 3;20(1). pii: E155. doi: 10.3390/ijms20010155.

Cordero-Sánchez C, Mudarra-Fraguas I, Fernández-Carvajal A. Fluorescence-Based Functional Assays for Ca²⁺-Permeable ThermoTRP Channels. *Methods Mol Biol*. 2019;1987:99-110. doi: 10.1007/978-1-4939-9446-5_7.

Martínez-Ortega L, Mira A, Fernández-Carvajal A, Mateo CR, Mallavia R, Falco A. Development of A New Delivery System Based on Drug-Loadable Electrospun Nanofibers for Psoriasis Treatment. *Pharmaceutics*. 2019 Jan 4;11(1). pii: E14. doi: 10.3390/pharmaceutics11010014.

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*. 2019 May 31. pii: S0306-4522(19)30373-2. doi: 10.1016/j.neuroscience.2019.05.043.

Nikolaeva Koleva M, Fernández-Ballester G. In Silico Approaches for TRP Channel Modulation. *Methods Mol Biol*. 2019;1987:187-206. doi: 10.1007/978-1-4939-9446-5_12.

Creation of Spin-Off Firms

ANTALGENICS (2015-actualidad).

PROSPERA BIOTECH (2014-actualidad).

FASTBASE SOLUTIONS (2015-actualidad).

Patents

Título: TRPV1 modulator compounds. Registros: KR20197032699 20180510.

Título: Compound useful for the treatment and/or care of the skin, hair, nails and/or mucous membranes. Registros: WO2019008452 (A1).

Título: Peptides and compositions for use in cosmetics and medicine. Registros: WO2019166347 (A1).

Título: Compositions for the treatment of pain and/or inflammation. Registros: CY20191100041T 20190115.

Título: Bicalutamide analogs or (s)bicalutamide as exocytosis activating compounds for use in the treatment of a lysosomal storage disorder or glycogenosis. Registros: PT3086784 (T).

Título: Therapeutic pharmaceutical composition for treatment of dry eyes. Registros: JP20190094210 20190520

Organization of Meetings

Participation in Scientific Committees:

VII Congreso Red Española de Canales Iónicos. Cáceres. 15-17 May 2019.

Joint 12th EBSA 10th ICBP-IUPAP Biophysics Congress. Madrid 20-24 July 2019.

7th Spanish-Italian-Portuguese-French International. Workshop (SIPF-SIF). Genova (Italy) 2-5 October 2019.

Invited Talks and Courses

Targeting the TRPV1 channel with soft drugs". Antonio Ferrer. 4th German Pharm-Tox Summit. Stuttgart (Germany). 25-28 February 2019.

"Drug development of topical TRPV1 soft drugs for skin disorders"CTI-Bath International Showcase. Antonio Ferrer. University of Bath. Bath (UK). 25 June 2019.

Emprender desde el conocimiento científico, trasladar la ciencia a la sociedad. Asia Fernández Carvajal. CURSO INVIERNO UMH. AVANCES EN CIENCIA Y TECNOLOGIA. March 2019.

Nuevos fármacos para el dolor: del laboratorio al paciente. Asia Fernández Carvajal. XI SEMANA DE LA CIENCIA EN TORREVIEJA. November 2019.

Science Dissemination: Outreach Activities

Ciencia con Tapas. Monthly outreach activity of IDiBE.

XI Jornadas de San Alberto. Facultad de Ciencias Experimentales. UMH. 13 noviembre 2019.

Jornadas de Puertas Abiertas del IBMC. 19 julio 2019.

Number of Congress Communications

National contributions: 2

Poster presentations: 2

International contributions: 11

Oral presentations: 4

Poster presentations: 7

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.

Microscopía correlativa óptico-electrónica para dotar la Plataforma en Nanotecnología Traslacional (PATENT) de microscopía de superresolución. Agencia Española 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 Española de Investigación. RTI2018-097189-B-C21. 2019-2021. IPs: Antonio Ferrer Montiel y Asia Fernández Carvajal.

Private funding: Contracts

Convenio de colaboración para la constitución del Grupo de Investigación Mixto "Investigación en nuevas tecnologías en el tratamiento y diagnóstico del cáncer" FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA DE LA COMUNIDAD VALENCIANA (FISABIO) (FISABIO3.15X). Finalización: 07/2019. IP: Antonio Ferrer Montiel. IDiBE. UMH.

Contrato de licencia para explotación de la patente "Nuevas dianas terapéuticas y su uso para el tratamiento del dolor". AntalGenics, SL. 2019. IP: Antonio Ferrer Montiel. Instituto De Biología Molecular Y Celular. UMH.

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

Private funding: Technical Services and Assistance

Antonio Ferrer Montiel. Technical Assistance to AntalGenics SL.

Antoni Ferrer Montiel. Assitance to Fasbase Solutions SL

Antonio Ferrer Montiel. Asistance to Prospera Biotech SL.

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

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

Antonio Ferrer Montiel. Member of the General University Council

Antonio Ferrer Montiel. Member of the General Council of the Fundación UMH

Antonio Ferrer Montiel. Advisor of the Kaertor Foundation

Antonio Ferrer Montiel. Advisor of the Bind4.0 Program of the Basque Government.

Scientific Society Councils

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

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

Editorial Boards

Journal of Pharmacological Sciences (2019). A. Ferrer Montiel.

The Open Journal of Pain (2019). A. Ferrer Montiel.

Frontiers in Pharmacology (2019). A. Ferrer Montiel.

Frontiers in Neurosciences (2019). A. Ferrer Montiel.

Journal of Neurosciences (2019-). A. Ferrer Montiel.

Scientific Reports (2014-2019). A. Fernandez-Carvajal

Frontiers in Physiology (2015-2019). 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.

Staff

Luis Pérez García-Estañ

María del Mar Ortega-Villaizán

Ph. D Students

María E. Salvador Mira

Technicians

Efrén Lucas Mañogil

Publications

Belló-Pérez M, Medina-Gali R, Coll J, Perez L. Viral interference between infectious pancreatic necrosis virus and spring viremia of carp virus in zebrafish. *Aquaculture*. 2019, 500:370-377. doi.org/10.1016/j.aquaculture.2018.10.039 CLAVE: A.

Medina-Gali R, Belló-Pérez M, Ciordia S, Mena MC, Coll J, Novoa B, Ortega-Villaizán MM, Perez L. Plasma proteomic analysis of zebrafish following spring viremia of carp virus infection. *Fish Shellfish Immunol*. 2019, 86:892-899.

Bello-Perez, M, Falco A, Novoa B, Perez L, Coll J. Hydroxycholesterol binds and enhances the anti-viral activities of zebrafish monomeric c-reactive protein isoforms. *PLoS ONE*. 2019. doi: 10.1371/journal.pone.0201509.

Chico V, Salvador-Mira ME, Nombela I, Puente-Marín S, Ciordia S, Mena MC, Perez L, Guzmán F, Encinar JA, Mercado L y Ortega-Villaizán MM. IFIT5 participates in the antiviral mechanisms of rainbow trout red blood cells. *Front. Immunol*. 2019. 10: doi.org/10.3389/fimmu.2019.00613.

Nombela I, Requena-Platek R, Morales-Lange B, Chico V, Puente-Marín S, Ciordia S, Mena MC, Coll J, Perez L, Mercado L y Ortega-Villaizán MM, Rainbow Trout Red Blood Cells Exposed to Viral Hemorrhagic Septicemia Virus Up-Regulate antigen-Processing Mechanisms and MHC I&II, CD86, and CD83 Antigen-presenting Cell Markers. *Cells*. 2019. 8, 386. doi:10.3390/cells8050386.

Puente-Marín S, Nombela I, Chico V, Ciordia S, Mena MC, Perez L, Coll J, Ortega-Villaizan MM. Potential Role of Rainbow Trout Erythrocytes as Mediators in the Immune Response Induced by a DNA Vaccine in Fish. *Vaccines*. 2019. doi:10.3390/vaccines7030060.

Nombela I, Lopez-Lorigados M, Salvador-Mira ME, Puente-Marín S, Chico V, Ciordia S, Mena MC, Mercado L, Coll J, Perez L, y Ortega-Villaizan MM. Integrated Transcriptomic and Proteomic Analysis of Red Blood Cells from Rainbow Trout Challenged with VHSV Point Towards Novel Immunomodulant Targets. *Vaccines*. 2019. doi: 10.3390/vaccines7030063.

Acute phase protein response to viral infection and vaccination. Perez L. *Arch. Biochem. Biophys.* 2019, 671:196-202. doi: 10.1016/j.abb.2019.07.013.

PhD Theses

Descubrimiento y caracterización de la actividad antiviral inducida por las moléculas tipo CRP de pez cebra (*Danio rerio*). Melissa Belló-Perez. Universidad Miguel Hernández. Supervisor: Luis Pérez García-Estañ. 23/07/2019.

Invited Talks and Courses

ENFERMEDADES VÍRICAS DE PECES: UNA AMENAZA PARA LA ACUICULTURA. Luis Pérez García-Estañ. Ciclo de Conferencias Aulas de la Experiencia. Universidad Miguel Hernández de Elche.

Elche, Altea, Benidorm, Ibi, Orihuela. March-may, 2019.

INTERFERENCIA VIRAL EN PECES: EL CASO DE BIRNAVIRUS Y RHABDOVIRUS. Luis Pérez García-Estañ. Instituto de Biología, Universidad Católica de Valparaíso. Valparaíso, Chile. Nov 14th, 2019.

Science dissemination: outreach activities

"Ciencia con Tapas" Science Talks. IDiBE – UMH. M^a José Martínez Tomé, Angeles Gómez, Luis Perez. Organizer.

Number of Congress Communications

International contributions: 3

Poster presentations: 3

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.

R&D Management

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

Group name: VIRAL PROTEINS, ANTIVIRALS AND MOLECULAR DYNAMICS

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

Villalaín J. Epigallocatechin-3-gallate location and interaction with late endosomal and plasma membrane

model membranes by molecular dynamics. *J Biomol Struct Dyn*. 2019 Aug;37(12):3122-3134. doi: 10.1080/07391102.2018.1508372. Epub 2018 Nov 17.

Scientific and Educational Committees

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 1953 Nelson described a new role of human red blood cells (RBCs) which would go beyond the simple transport of O₂ to the tissues. This new role, involved in the defence against microbes, described the antibody and complement-dependent binding of microbial immune complexes to RBCs. Regardless of the importance of this finding in the field of microbial infection, this phenomenon has been poorly evaluated. Just recently, a set of biological processes relevant to immunity have been described in the RBCs of a diverse group of organisms, which include: pathogen recognition, pathogen binding and clearance and cytokines production.

Furthermore, it has been demonstrated that nucleated erythrocytes from fish and avian species develop specific responses to different pathogen associated molecular patterns and produce soluble factors that modulate leukocyte activity.

In the light of these pieces of evidences, and in an attempt to improve the knowledge of the immune mechanism(s) responsible for fish protection against viral infections, we raised the question: could nucleated fish erythrocytes be the key mediators of the antiviral responses? To answer this question, we decided to focus our work on the evaluation of the crosstalk between red and white blood cells in the scenario of fish viral infections and prophylaxis. For that we chose a working model composed of the rainbow trout,

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

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

the viral haemorrhagic septicaemia virus (VHSV) and the glycoprotein G of VHSV (GVHSV), the antigen encoded by this DNA vaccine.

Staff

María del Mar Ortega-Villaizán Romo

Postdoctoral Researchers

Verónica Chico Gras

Technicians

Efren Lucas Mañogil

Remedios Torres Montero

Publications

Puente-Marin S, Thwaite R, Mercado L, Coll J, Roher N, ORTEGA-VILLAIZAN M. Fish red blood cells modulate immune genes in response to bacterial inclusion bodies made of TNF α and a g-VHSV fragment. *Frontiers in Immunology*. 2019. SJR: 2.021 (Q1).

Chico V, Salvador-Mira M, Nombela I, Puente-Marin S, Ciordia S, Mena M, Perez L, Coll J, Guzman F, Encinar J, Mercado L, ORTEGA-VILLAIZAN M. IFIT5 participates in the antiviral mechanisms of rainbow trout red blood cells. *Frontiers in Immunology*. 2019. SJR: 2.021 (Q1).

Puente-Marin S, Nombela I, Chico V, Ciordia S, Mena M, Perez L, Coll J, ORTEGA-VILLAIZAN M. Potential role of rainbow trout erythrocytes as mediators in the immune response induced by a DNA vaccine in fish. *Vaccines*. 2019. SJR: 2.136 (Q1).

Nombela I, Lopez-Lorigados M, Salvador-Mira M, Puente-Marin S, Chico V, Ciordia S, Mena M, Mercado L, Coll J, Perez L, ORTEGA-VILLAIZAN M. Integrated transcriptomic and proteomic analysis of

red blood cells from rainbow trout challenged with VHSV point towards novel immunomodulant targets. *Vaccines*. 2019. SJR: 2.136 (Q1).

Nombela I, Requena-Platek R, Morales-Lange B, Chico V, Puente-Marin S, Ciordia S, Mena MC, Coll J, Perez L, Mercado L, ORTEGA-VILLAIZAN M. Rainbow Trout Red Blood Cells Exposed to Viral Hemorrhagic Septicemia Virus Up-Regulate Antigen-Processing Mechanisms and MHC I&II, CD86, and CD83 Antigen-presenting Cell Markers. *Cells*. 2019. JCR: 5.656 (Q1).

Myung-Hwa J, Chico V, Ciordia S, Mena MC, Jung SJ, ORTEGA-VILLAIZAN M. The Megalocytivirus RBIV Induces Apoptosis and MHC Class I Presentation in Rock Bream (*Oplegnathus fasciatus*) Red Blood Cells. *Frontiers in Immunology*. 2019. SJR: 2.021 (Q1).

Medina-Gali R, Belló-Pérez M, Ciordia S, Mena MC, Coll J, Novoa B, Ortega-Villaizán M, Perez L. Plasma proteomic analysis of zebrafish following spring viremia of carp virus infection. *Fish Shellfish Immunol*. 2019.

PhD Theses

Los eritrocitos nucleados de peces en la inmunización frente a rhabdovirus. Sara Puente Marin. Universidad Miguel Hernández de Elche. Supervisor: María del Mar Ortega-Villaizán Romo. 26/07/2019.

Los eritrocitos nucleados de peces en la respuesta inmune frente a infecciones víricas. Ivan Nombela Diaz. Universidad Miguel Hernández de Elche. Supervisor:

María del Mar Ortega-Villaizán Romo. 24/07/2019.

Number of Congress Communications

International contributions: 6

Oral presentations: 3

Poster presentations: 3

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.

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.

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.

Editorial Boards

Frontiers in Immunology (Topic Editor) (2018-2019).

Molecular and Cellular Oncology

Group name: MOLECULAR ONCOLOGY

Dr. Miguel Saceda is staff researcher at the Foundation for the Promotion of Health and Biomedical Research of the Valencian Community (FISABIO). Dr. Saceda began studying the Molecular and Cellular Cancer Biology at the NCI (National Cancer Institute of the USA), continuing his training at the Vincent. T. Lombardi Cancer Center of Georgetown University and at the Department of Biochemistry and Molecular Biology of the same University (1986-1993 and 1996-

1997). Dr. Saceda has developed a line of research focused on the search for alternative treatments in tumors that have acquired resistance to antineoplastic treatments. Within this line, he started the generation of primary cultures of particularly aggressive and resistant tumors, such as glioblastoma multiforme and pancreatic carcinoma. Such cultures have been constituted in a model of predictive test of response applicable ex

vivo to patients Likewise. Actual research lines:

- Search and development of biomarkers of sensitivity and/or resistance to chemo and radiation therapy in glial and pancreatic tumors.
- Development of nanotechnological-based enzyme treatments for chemo and radio resistant tumors.
- Development of alternative therapies for chemo and radio resistant tumors based on signal transduction pathways and cellular epigenetic control.

Staff

Miguel Saceda Sánchez

Postdoctoral Researchers

M^a Pilar García Morales

External collaborators integrated in the group

Dr. Victor Manuel Barbera Juan.

Dr. José Martin Nieto.

Ph. D Students

María Fuentes Baile

Elizabeth Perez Valenciano

Publications

Fuentes-Baile M, Bello-Gil D, Pérez-Valenciano E, Sanz JM, García-Morales P, Maestro B, Ventero MP, Alenda C, Barberá VM, Saceda M. CLyA-DAAO, Free and Immobilized in Magnetic Nanoparticles, induces Cell Death in Human Cancer Cells. *Biomolecules*. 2020 Feb 3;10(2). pii: E222. doi: 10.3390/biom10020222. PubMed PMID: 32028649.

PhD Theses

Evaluación de los genes MGMT, SOCS1 y SOCS3 como marcadores moleculares de quimio y radorresistencia en modelos

celulares de glioblastoma humano. Maripaz Ventero Martin. Universidad Miguel Hernández de Elche. Supervisor: Miguel Saceda Sánchez. Co-Supervisor: Victor Manuel Barbera Juan. 11/07/2019.

Invited Talks and Courses

Radio UMH program "Contraste de fases" each month for the last 3 years. Miguel Saceda.

Number of Congress Communications

International contributions: 4

Poster presentations: 4

Governmental Projects and Funding

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. 2019-2020. Convocatoria grupos asociados de FISABIO (UGP-19-063), IP: Miguel Saceda Sánchez.

Desarrollo de nuevos tratamientos para tumores de mal pronóstico. 2018-2020. Plataforma precipita de la FECYT (UGP-18-298). IP: Miguel Saceda Sánchez.

R&D and Educational Committees

Member of the scientific committee of the Elche's university general hospital.

Editorial Boards

Reviewer of Stragmed, Poland. Miguel Saceda.

Reviewer of ANEP. Miguel Saceda.

Reviewer of ASUCYL. Miguel Saceda.

Reviewer of „Fundación progreso de Andalucía“. Miguel Saceda.

Guest Editor of *Biomolecules*. Miguel Saceda.

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 ER α , ER β 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 establish 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

Ph. D Students

Lucía Almagro Ruz

Ignacio Babiloni Chust

External collaborators (Universidad de Alicante)

Juan Martínez-Pinna

Sergi Soriano Úbeda

Technicians

María Luisa Navarro García

María Salomé Ramón Penalva

María Del Carmen Alonso Fuentes

Beatriz Bonmatí Botella

Atenea Alexandra Pérez Serna

Publications

Bru-Tari E, Cobo-Vuilleumier N, Alonso-Magdalena P, Dos Santos RS, Marroqui L, Nadal A, Gauthier BR, Quesada I. Pancreatic alpha-cell mass in the early-onset and advanced stage of a mouse model of experimental autoimmune diabetes. *Sci Rep.* 2019 Jul 2;9(1):9515. doi: 10.1038/s41598-019-45853-1.

Martinez-Pinna J, Marroqui L, Hmadcha A, Lopez-Beas J, Soriano S, Villar-Pazos S, Alonso-Magdalena P, Dos Santos RS, Quesada I, Martin F, Soria B, Gustafsson JÅ, Nadal A. Oestrogen receptor β mediates the actions of bisphenol-A on ion channel expression in mouse pancreatic beta cells. *Diabetologia.* 2019 Sep;62(9):1667-1680. doi: 10.1007/s00125-019-4925-y.

Soriano S, Marroqui L, Alonso Magdalena, P., Fuentes, E., Jan-Ake Gustafsson, Nadal A, Martinez-Pinna J. Bisphenol A Regulates Sodium Ramp Currents in Mouse Dorsal Root Ganglion Neurons and Increases Nociception. *Sci Rep.* 2019 Jul 16;9(1):10306. doi: 10.1038/s41598-019-46769-6.

Esteban J, Serrano-Maciá M, Sánchez-Pérez I, Alonso-Magdalena P, Pellín MC, García-Arévalo M, Nadal Á, Barril J. In utero exposure to bisphenol-A disrupts key elements of retinoid system in male mice offspring. *Food Chem Toxicol.* 2019 Apr;126:142-151. doi: 10.1016/j.fct.2019.02.023.

Zoeller RT, Doan L, Demeneix B, Gore AC, Nadal A, Tan S. Update on Activities in Endocrine Disruptor Research and Policy. *Endocrinology.* 2019 Jul 1;160(7):1681-1683. doi: 10.1210/en.2019-00166.

Gibert Y, Sargis RM, Nadal A. Editorial: Endocrine Disruptors and Metabolism. *Front Endocrinol (Lausanne).* 2019 Dec 10;10:859. doi: 10.3389/fendo.2019.00859.

Tudurí E, Glavas MM, Asadi A, Baker RK, Ellis CE, Soukhatcheva G, Philit M, Huynh FK, Johnson JD, Verchere CB, Kieffer TJ. AAV GCG-EGFP, a new tool to identify glucagon-secreting alpha-cells. *Scientific Reports.* 04/07/2019. DOI: 10.1038/s41598-019-46735-2.

Glavas MM, Hui Q, Tudurí E, Erener S, Kasteel NL, Johnson JD, Kieffer TJ. Early overnutrition reduces Pdx1 expression and induces beta-cell failure in Swiss Webster mice. *Scientific Reports*. 9- 3619.

Dos Santos RS, Marroqui L, Velayos T, Olazagoitia-Garmendia A, Jauregi-Miguel A, Castellanos-Rubio A, Eizirik DL, Castaño L, Santin I. DEXI, a candidate gene for type 1 diabetes, modulates rat and human pancreatic beta cell inflammation via regulation of the type I IFN/STAT signalling pathway. *Diabetologia*. 2019 Mar;62(3):459-472. doi: 10.1007/s00125-018-4782-0.

Al-Ali R, Bauer K, Park JW, Al Abdulla R, Fermi V, von Deimling A, Herold-Mende C, Mallm JP, Herrmann C, Wick W, Turcan Ş. Single-nucleus chromatin accessibility reveals intratumoral epigenetic heterogeneity in IDH1 mutant gliomas. *Acta Neuropathol Commun*. 2019 Dec 5;7(1):201. doi: 10.1186/s40478-019-0851-y.

Organization of meetings

II Jornadas SEJI jóvenes investigadores de excelencia 2019: what is going on in diabetes? (21/11/2019).

Young investigators symposium, Ciber del Área de Diabetes y Enfermedades Metabólicas (CIBERDEM) (6/11/2019).

Invited Talks and Courses

Endocrine Disrupting Chemicals in the Aetiology of Diabetes. Ángel Nadal. INTERNATIONAL DIABETES FEDERATION CONGRESS 2019, Busan, Corea del Sur, 1/12/2019.

Unconventional actions of environmental estrogens via estrogen receptors. Ángel Nadal. 2ND AFRICAN CONFERENCE ON HEALTH EFFECTS OF ENDOCRINE DISRUPTORS, Pretoria, Africa, 04/11/2019.

EDC disturbance of beta-cells and risk of diabetes. Ángel Nadal. 2ND AFRICAN CONFERENCE ON HEALTH EFFECTS OF ENDOCRINE DISRUPTORS, Pretoria, Africa, 05/11/2019.

Endocrine Disrupting Chemicals and Diabetes Mellitus. Ángel Nadal. 21ST EUROPEAN CONGRESS OF ENDOCRINOLOGY, Lyon, Francia, 18/05/2019.

The role of Endocrine Disrupting Chemicals in the etiology of Diabetes Mellitus. Ángel Nadal. 6TH SYMPOSIUM ON BIOMEDICAL RESEARCH "ADVANCES AND PERSPECTIVES IN MOLECULAR ENDOCRINOLOGY", Madrid, 31/05/2019.

Bisphenol-A modulates ion channel expression and function via estrogen receptor β in mouse pancreatic beta cells. Ángel Nadal. VII REUNIÓN DE LA RED ESPAÑOLA DE CANALES IÓNICOS / RECI VI, Cáceres, Spain, 15/05/2019.

Contaminantes ambientales y obesidad. Paloma Alonso-Magdalena. XV CONGRESO SOCIEDAD ESPAÑOLA DE OBESIDAD, Vigo, Spain, 13/03/2019.

La amenaza silenciosa de los disruptores endocrinos: un problema de salud pública. Paloma Alonso-Magdalena. Conferencia inaugural. XIII CONGRESO DE LA SOCIEDAD CANARIA DE ENDOCRINOLOGIA Y NUTRICION, Tenerife, Spain, 4/10/2019.

Disruptores endocrinos y resistencia a la insulina. Laura Marroquí Esclapez. V JORNADAS DE LA SENMO, Valencia, Spain 09/11/2019.

Diabetes y desórdenes metabólicos: viejos problemas, nuevas soluciones. Laura Marroquí Esclapez. JORNADA CIENTIFICA IDIBE 2019, Elche, Spain, 19/07/2019.

Discovery of new therapeutic targets for the treatment of type 1 diabetes and type 2 diabetes based on pancreatic alpha cell survival strategies. Laura Marroquí Esclapez. CICLO DE SEMINARIOS ANTÔNIO LUIZ VIANNA, Rio de Janeiro, Brazil, 06/08/2019.

Interfering with beta-cells or: how type 1 interferons are implicated in type 1 diabetes. Reinaldo Sousa dos Santos. CICLO DE SEMINARIOS ANTÔNIO LUIZ VIANNA, Rio de Janeiro, Brazil, 06/08/2019.

Interfering with β -cells or: how type 1 interferons are implicated in type 1 diabetes. Reinaldo Sousa dos Santos. Young Investigator Symposium-CIBERDEM, Barcelona, Spain, 6/11/2019.

¿Puede el Bisfenol-A modular la sensación dolorosa? Sergi Soriano Úbeda. CICLO DE SEMINARIOS IDiBE, Elche, 22/11/2019.

Number of Congress Communications

National contributions: 10

Oral presentations: 2

Poster presentations: 8

International contributions: 5

Oral presentations: 1

Poster presentations: 4

Awards

Paloma Alonso-Magdalena. Medalla de Honor Dr Balmis del Ateneo Científico, Literario y Artístico de Alicante.

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, BFU2017-86579-R, 2018-2020, IP: Ángel Nadal.

'Beating Goliath: Generation Of Novel, Integrated and Internationally Paloma Alonso-Magdalena. Reviewer of Sociedad Española de Diabetes.

Paloma Alonso-Magdalena. Reviewer of Universidad de Oviedo.

Harmonised Approaches for Testing Metabolism Disrupting Compounds' — 'GOLIATH'. Proyecto del Programa Marco de la UE, European Comission. IP. Ángel Nadal.

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.

Proyecto de Investigación de la Dra. Laura Marroquí Esclapez (Programa Juan de la Cierva Incorporación).Programa y Referencia: IJCI-2015-24482.

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 pancreática. Programa y Referencia: SEJI/2018/023, 2018-2020. IP: Laura Marroquí Esclapez.

R&D Management

Ángel Nadal. Reviewer of Agencia Estatal de Investigación (Ministerio de Ciencia, Innovación y Universidades).

Ángel Nadal. Miembro del Comité de Dirección del CIBER de Diabetes y Enfermedades Metabólicas Asociadas.

Ángel Nadal. Coordinador Grupo Asesor sobre Disruptores Endocrinos de la "Endocrine Society", Washington DC, USA.

Ángel Nadal. Miembro del Comité Científico Externo de "Food Packaging Forum", Zurich, Suiza.

Ángel Nadal. Vice-Presidente de la "Gordon Reserach Conference on Environmental Endocrine Disruptors" que se celebrará en Maine, USA, 2020.

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

Iván Quesada. Reviewer of the FONDS DE LA RECHERCHE SCIENTIFIQUE – FNRS.

Paloma Alonso-Magdalena. Reviewer of Sociedad Española de Diabetes.

Paloma Alonso-Magdalena. Reviewer of Universidad de Oviedo.

Paloma Alonso-Magdalena. Reviewer of Fundación Robles Chillida.

Paloma Alonso-Magdalena. Reviewer of Netherlands Organisation for Scientific Research (NWO).

Paloma Alonso-Magdalena. Reviewer of Roaltain Foundation.

Laura Marroquí Esclapez. Keypoint in diabetes (SED)-congress review ADA 2019- San Francisco.

Reinaldo Sousa dos Santos. Reviewer of Universidad de Oviedo.

Juan Martínez-Pinna. Reviewer of Agencia Nacional de Evaluación y Prospectiva (ANEP).

Juan Martínez-Pinna. Reviewer of Universidad Autónoma de Madrid.

Editorial Boards

Editor Frontiers in Physiology. Ángel Nadal.

Editor Frontiers in Endocrinology. Ángel Nadal.

Editor Journal of Physiology and Biochemistry. Ángel Nadal.

Reviewer for the following journals in 2019: Molecular and Cellular Endocrinology, Scientific Reports, Nutrients. Iván Quesada.

Senior Editor Endocrine Connections. Paloma Alonso-Magdalená.

Editor Scientific Reports. Paloma Alonso-Magdalená.

Reviewer for the following journals in 2019: Toxicology, Frontiers in Endocrinology, Journal of Diabetes and its Complications, Environmental Research, Food and Chemical Toxicology, Free Radical Biology and Medicine, Science and the Total Environment. Paloma Alonso-Magdalená.

Reviewer for the following journals in 2019: Scientific Reports, Frontiers In Endocrinology, Nutrients, Marine Drugs. Laura Marroquí Esclapez.

Reviewer for the following journals in 2019: Molecules, Cells. Reinaldo Sousa dos Santos.

Editor Membrane Physiology and Biophysics. Sergi Soriano Úbeda.

Editor Membrane Physiology and Biophysics. Juan Martínez-Pinna.

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 2018, 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

Publications

Juanola O, Ferrusquía-Acosta J, García-Villalba R, et al. Circulating levels of butyrate are inversely related to portal hypertension, endotoxemia, and systemic inflammation in patients with cirrhosis. *FASEB J.* 2019;33(10):11595–11605. doi:10.1096/fj.201901327R.

Mangas-Sanjuan C, Santana E, Cubiella J, et al. Variation in Colonoscopy Performance Measures According to Procedure Indication [published online ahead of print, 2019 Aug 22]. *Clin Gastroenterol Hepatol.* 2019;S1542-3565(19)30910-3. doi:10.1016/j.cgh.2019.08.035.

Zapater P, Almenara S, Gutiérrez A, et al. Actual Anti-TNF Trough Levels Relate to Serum IL-10 in Drug-Responding Patients With Crohn's Disease. *Inflamm Bowel Dis.* 2019;25(8):1357–1366. doi:10.1093/ibd/izz012.

Seguí-Ripoll JM, Zapater-Hernández P, Candela-Gomis A, Compañ-Catalá L, Francés-Guarinos R, Payá-Romá A, et al. Single versus double experimental bile duct ligation model for inducing bacterial translocation. *Am J Surg.* 2019;218(2):380–7.

Sternby H, Bolado F, Canaval-Zuleta HJ, et al. Determinants of Severity in Acute Pancreatitis: A Nation-wide Multicenter Prospective Cohort Study. *Ann Surg.* 2019;270(2):348–355. doi:10.1097/SLA.0000000000002766.

Gómez-Hurtado I, Zapater P, Portune K, et al. Improved hemodynamic and liver function in portal hypertensive cirrhotic rats after administration of *B. pseudocatenuatum* CECT 7765. *Eur J Nutr.* 2019;58(4):1647–1658. doi:10.1007/s00394-018-1709-y.

Rodríguez-Laiz GP, Zapater P, Melgar P, et al. Bacterial DNA translocation contributes to systemic inflammation and to minor changes in the clinical outcome of liver transplantation. *Sci Rep.* 2019;9(1):835. Published 2019 Jan 29. doi:10.1038/s41598-018-36904-0.

Cossarizza A, Chang HD, Radbruch A, et al. Guidelines for the use of flow cytometry and cell sorting in immunological studies (second edition). *Eur J Immunol.* 2019 Oct;49(10):1457-1973.

PhD Theses

Función del inflamasoma AIM2 en el desarrollo de carcinoma hepatocelular. Claudia Martínez Cardona. Universidad de Alicante. Supervisor: José Manuel González Navajas. 01/02/2019.

Governmental Projects and Funding

Estudio experimental del efecto modulador del sistema adrenérgico sobre el proceso de hepatocarcinogénesis. PROYECTO DE INVESTIGACIÓN DE SALUD. INSTITUTO DE SALUD CARLOS III. PI17/01617. 2018-2020. IP: Pedro Zapater Hernández.

Evaluación de una nueva diana terapéutica en carcinoma hepatocelular: mecanismos implicados y efecto en el desarrollo de infecciones bacterianas. PROYECTO DE INVESTIGACIÓN DE SALUD. INSTITUTO DE SALUD CARLOS III. PI16/01833. 02/01/2017 - 31/12/2019. IP: José Manuel González Navajas.

Dianas para la recuperación de la inmunovigilancia hepática en cirrosis. Generalitat Valenciana. Prometeo - Ayudas para Grupos de Excelencia de la C.V. Prometeo/2016/001. 01/01/2017 - 31/12/2019. IP: Rubén Francés Guarinos.

Función del inflamasoma AIM2 en el desarrollo de fibrosis y carcinoma hepático. Ministerio de Educación, Cultura y Deporte. Becas de Formación del Profesorado Universitario (FPU). 01/09/2015 - 31/08/2019. IP: José Manuel González Navajas.

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 anaesthetics 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 (2019)

Título: PREDISPOSICIÓN GENÉTICA A LA INFLAMACIÓN Y TRASLOCACIÓN BACTERIANA EN ENFERMEDAD HEPÁTICA E INTESTINAL

Autor: PAULA PIÑERO ROMERO

Fecha de Lectura: 23/04/2019

Dirección: RUBÉN FRANCÉS GUARINÓS

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1776705>

Título: EVALUACIÓN DE LOS GENES MGMT, SOCS1, SOCS3 COMO MARCADORES MOLECULARES DE QUIMIO Y RADIORRESISTENCIA EN MODELOS CELULARES DE GLIOBLASTOMA HUMANO

Autor: María Paz Ventero Martín

Fecha de Lectura: 11/07/2019

Dirección: MIGUEL SACEDA SANCHEZ/ VICTOR MANUEL BARBERA JUAN

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1794102>

Título: DESCUBRIMIENTO Y CARACTERIZACIÓN DE LA ACTIVIDAD ANTIVIRAL INDUCIDA POR LAS MOLÉCULAS TIPO CRP DE PEZ CEBRA (DANIO RERIO)

Autor: Melissa Belló Pérez

Fecha de Lectura: 23/07/2019

Dirección: LUIS PEREZ GARCIA-ESTAÑ/ JUAN ALBERTO FALCO GRACIA

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1798671>

Título: LOS ERITROCITOS NUCLEADOS DE PECES EN LA RESPUESTA INMUNE FRENTE A INFECCIONES VÍRICAS

Autor: Iván Nombela Díaz

Fecha de Lectura: 24/07/2019

Dirección: MARIA DEL MAR ORTEGA-VILLAIZAN ROMO y JULIO COLL MORALES

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1799748>

Título: ESTUDIO DE LA CAPACIDAD ANTIPROLIFERATIVA EN MODELOS CELULARES DE CÁNCER DE MAMA DE UN EXTRACTO DE HOJA DE OLIVO ENRIQUECIDO EN POLIFENOLES

Autor: María Losada Echeberría

Fecha de Lectura: 08/10/2019

Dirección: ENRIQUE BARRAJÓN CATALÁN Y VICENTE MICOL MOLINA

Título: METAGENOMES AND GENOMES OF THE MEDITERRANEAN SEA PELAGIC MICROBIOTA

Autor: José Manuel Haro Moreno

Fecha de Lectura: 22/11/2019

Dirección: FRANCISCO EDUARDO RODRIGUEZ VALERA Y MARIO LOPEZ PEREZ

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1807854>

Título: LOS ERITROCITOS NUCLEADOS DE PECES EN LA INMUNIZACIÓN FRENTE A RHABDOVIRUS

Autor: Sara Puente Marín

Fecha de Lectura: 26/07/2019

Dirección: MARIA DEL MAR ORTEGA-VILLAIZAN ROMO y JULIO COLL MORALES

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1799694>

Título: POLIFENOLES DE PLANTAS COMESTIBLES COMO REPROGRAMADORES METABÓLICOS EN CONDICIONES DE GLUCOLIPOTOXICIDAD

Autor: OLIVARES VICENTE, MARÍA DOLORES

Fecha de Lectura: 28/10/2019

Dirección: VICENTE MICOL MOLINA Y MARÍA HERRANZ LÓPEZ

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1825707>

Título: THE STRESS-MEDIATED ANTIPROLIFERATIVE EFFECTS OF MARINE INVERTEBRATE EXTRACTS IN HUMAN COLON CANCER CELL MODELS

Autor: Verónica Ruiz Torres

Fecha de Lectura: 08/11/2019

Dirección: MICOL MOLINA, VICENTE y BARRAJON CATALAN, ENRIQUE

<https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1825491>

SEMINARS (2019)

Título: **FIGHTING SICKNESS WITH IMMUNOLOGY KNOWLEDGE.**

Ponente / Institución: Dra. Cristiane Monteiro da Cruz, Profesora de Investigación del Centro Universitario Cesmac, Alagoas, (Brasil).

Viernes, 11 de enero de 2019.

Título: **GENÓMICA Y BIOINFORMÁTICA EN EL CÁNCER: LOS DESAFÍOS DE LAS ENFERMEDADES COMPLEJAS CON DATOS COMPLEJOS.**

Ponente / Institución: Dr. Javier De Las Rivas, Centro de Investigación del Cáncer (CiC-IBMCC, CSIC/USAL) Consejo Superior de Investigaciones Científicas (CSIC) y Universidad de Salamanca (USAL).

Viernes, 18 de enero de 2019.

Título: **SISTEMAS PSEUDO-ORDENADOS. SU INTERÉS COMO SOPORTES PARA MANIPULACIÓN CELULAR.**

Ponente / Institución: Dr. Alberto Gallardo Ruiz, ICTP-CSIC, Madrid (España).

Viernes, 1 de febrero de 2019.

Título: **OPIOID-BASED STRATEGIES TO TREAT CHRONIC PAIN.**

Ponente / Institución: Dra. Sara González Rodríguez, IDiBE, Elche (España).

Viernes, 1 de febrero de 2019.

Título: **EL PICOR, UN SÍNTOMA INFRAVALORADO.**

Ponente / Institución: Dr. Isabel Devesa, Chief Scientist Officer at AntalGenis, S.L.

Viernes, 8 de febrero 2019.

Título: **NANO POLÍMEROS DE COORDINACIÓN CON RECONOCIMIENTO MOLECULAR Y RESPUESTA A ESTÍMULOS. DESDE COLOIDES IMPRIMIBLES EN 3D Y NANOTRANSPORTADORES A AEROGEL.**

Ponente / Institución: Dra. Pilar Amo Ochoa, Universidad de Autónoma de Madrid.

Viernes, 22 de febrero de 2019.

Título: **ANGIOTENSINA II Y TRÁFICO LEUCOCITARIO. NUEVAS PERSPECTIVAS INMUNOLÓGICAS DE UN CONOCIDO MEDIADOR VASCULAR.**

Ponente / Institución: Prof. María Jesús Sanz Ferrando, Catedrática de Farmacología, Universidad de Valencia.

Viernes, 12 de abril de 2019.

Título: **TARGETED STRATEGIES IN POOR PROGNOSTIC MOLECULAR SUBGROUPS OF COLORECTAL CANCER.**

Ponente / Institución: Dra. Sandra Van Schaeuybroeck, Queen's University Belfast, United Kingdom.

Viernes, 17 de mayo de 2019.

Título: **MANUFACTURACIÓN AVANZADA DE POLÍMEROS FUNCIONALES: DE LA MOLÉCULA A LA APLICACIÓN A TRAVÉS DEL PROCESADO.**

Ponente / Institución: Dr. Carlos Sánchez Somolinos, Instituto de Ciencia de materiales de Aragón (ICMA), CSIC-UNIZAR, Zaragoza.

Viernes, 24 de mayo de 2019.

Título: **DISRUPTORES ENDOCRINOS: CAROS PARA LA ECONOMÍA Y LA SALUD PÚBLICA, PERO HAY OPORTUNIDAD PARA LA PREVENCIÓN.**

Ponente / Institución: Dr. Leonardo Trasande, Department of Pediatrics, New York University, USA.

Martes, 4 de junio de 2019.

Título: **TRANSLATING RESULTS TO MAKE NEW CANCER THERAPEUTICS: FROM THE FARM TO THE LAB AND BEYOND.**

Ponente / Institución: Dr. Pablo García Valtanen, Experimental Therapeutics Laboratory (Adelaide, SA).

Viernes, 14 de junio de 2019.

Título: **THE DANGEROUS LIAISON BETWEEN EARLY LIFE STRESS AND TYPE 2 DIABETES.**

Ponente / Institución: Dr. Stefano Loizzo, National Center for Global Health, ISS, Roma (Italy).

Viernes, 21 de junio de 2019.

Título: **APPLICATIONS OF PLANT TISSUE CULTURE AND MICROPROPAGATION.**

Ponente / Institución: Dr. Simona Lucoli, Consiglio per la ricerca in agricoltura e l'analisi dell'economia agraria (CREA) National Council for Agriculture.

Martes, 25 de junio de 2019.

Título: **MARCADORES MOLECULARES DE RESPUESTA INMUNE CONTRA EL PATÓGENO PISCIRICKETTSIA SALMONIS: UN ESTUDIO EN CAMPO DEL PRINCIPAL PATÓGENO DE LA SALMONICULTURA EN CHILE.**

Ponente / Institución: Luis Mercado Vianco. National Center for Global Health, ISS, Roma (Italy).

Miércoles, 25 de septiembre de 2019.

Título: **REGULACIÓN DEL TRÁFICO DE RECEPTORES: NUEVAS PERSPECTIVAS SOBRE LA MAQUINARIA SNARE POSTSINÁPTICA.**

Ponente / Institución: Sandra Jurado Sánchez. Instituto de Neurociencias CSIC-UMH, Alicante, España.

Lunes, 7 de octubre de 2019.

Título: **NEW INSIGHTS INTO INFLAMMASOME ACTIVATION, INTERLEUKIN-1 β RESEASE AND INFLAMMATORY CELL DEATH.**

Ponente / Institución: Pablo Pelegrín Vivancos. Instituto Murciano de Investigación Biosanitaria (IMIB-Arrixaca), Murcia, España.

Viernes, 25 de octubre de 2019.

Título: **EL PESTICIDA ORGANOFOSFORADO ES UN FACTOR DE RIESGO PARA LA DIABETES GESTACIONAL, ¿ES POSIBLE? LA EVIDENCIA NO CLÍNICA.**

Ponente / Institución: Álex Rafacho. Laboratório de Investigaçã de Doenças Crônicas – LIDoC, Universidade Federal de Santa Catarina, Brasil.

Viernes, 15 de noviembre de 2019.

Título: **¿PUEDE EL BISFENOL-A MODULAR LA SENSACIÓN DOLOROSA?**

Ponente / Institución: Sergi Soriano Úbeda. Departamento de Fisiología, Genética y Microbiología, Universidad de Alicante.

22 de noviembre de 2019.

Título: **LA ACTIVACIÓN DEL FACTOR DE TRANSCRIPCIÓN 3 MUESTRA UNA RELACIÓN ENTRE EL ESTRÉS CELULAR Y LA REPROGRAMACIÓN EPIGENÉTICA EN CÁNCER PANCREÁTICO.**

Ponente / Institución: Christopher Pin. Departamentos de Pediatría, Fisiología y Farmacología, y Oncología en la Universidad de Western Ontario, Canadá.

Viernes, 29 de noviembre de 2019.

Título: **II Workshop SEJI Jóvenes Investigadores de Excelencia: what is going on in diabetes research?**

Ponente / Institución: Dra. Rajaa El Bekay (Institute of Biomedical Research in Malaga, Malaga, España).

Dr. Jonàs Juan-Mateu (Centre for Genomic Regulation, Barcelona, España).

Dra. Elaine Vieira (Universidade Católica de Brasília, Brasília, Brasil).

Dr. Bruno Ramos Molina (Institute of Biomedical Research in Malaga, Malaga, España).

Jueves, 21 de noviembre 2019.

Agreements

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

-Distributed ICTS on **Pre-clinical drug design and development (InsPIRED)** with the CRG (Barcelona), CNIO (Madrid), CIMUS (University of Santiago Compostela) and Fundación Medina (Granada).

Bibliometric of publications

Number of publications (WoS)	% of Q1	Mean impact factor	Total impact factor
67	70	5.21	218.65

Dissemination

Out-reach seminars "Science with tapas":

- Inmunoterapia y nuevos avances contra el cáncer, 13-02-2019.
- Una conversación con el cerebro: ¿Podemos hablar su lenguaje?, 10-04-2019.
- ¿Conoces las particularidades de los vinos de Alicante?, 13-06-2019.
- "¿El estrés físico produce cáncer?, 20-09-2019.
- Tu 'dieta' tenía un precio. ¿Todo por perder kilos?, 11-12-2019.

Entrepreneurship

-Prospera Biotech SL becomes a fully owned start-up and moves its address to the University Campus from Barcelona to market neurocosmetics.

Clinical development

- Parentide® is in phase II clinical trials for chronic surgical pain. Sponsor: BCN Peptides.
- Bicalutamide is preparing phase II clinical trials for treating Sanfilippo syndrome. Sponsor BCN Peptides
- AVX-012 successfully finished a phase I/IIa clinical trial for dry eye syndrome and it is preparing a phase II clinical trial. Sponsors Avizorex Pharma and Aerie Pharmaceuticals Inc.
- PB-01 successfully finished the safety studies for topical application and it is preparing a proof-of-concept clinical trial for skin satisfaction of cancer patients suffering paclitaxel-induced peripheral neuropathy. Sponsor: Prospera Biotech
- AG1529 is currently in regulated pre-clinical safety studies for chronic psoriasis pruritus. Sponsor: AntalGenics

ANNUAL REPORT 2019

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

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