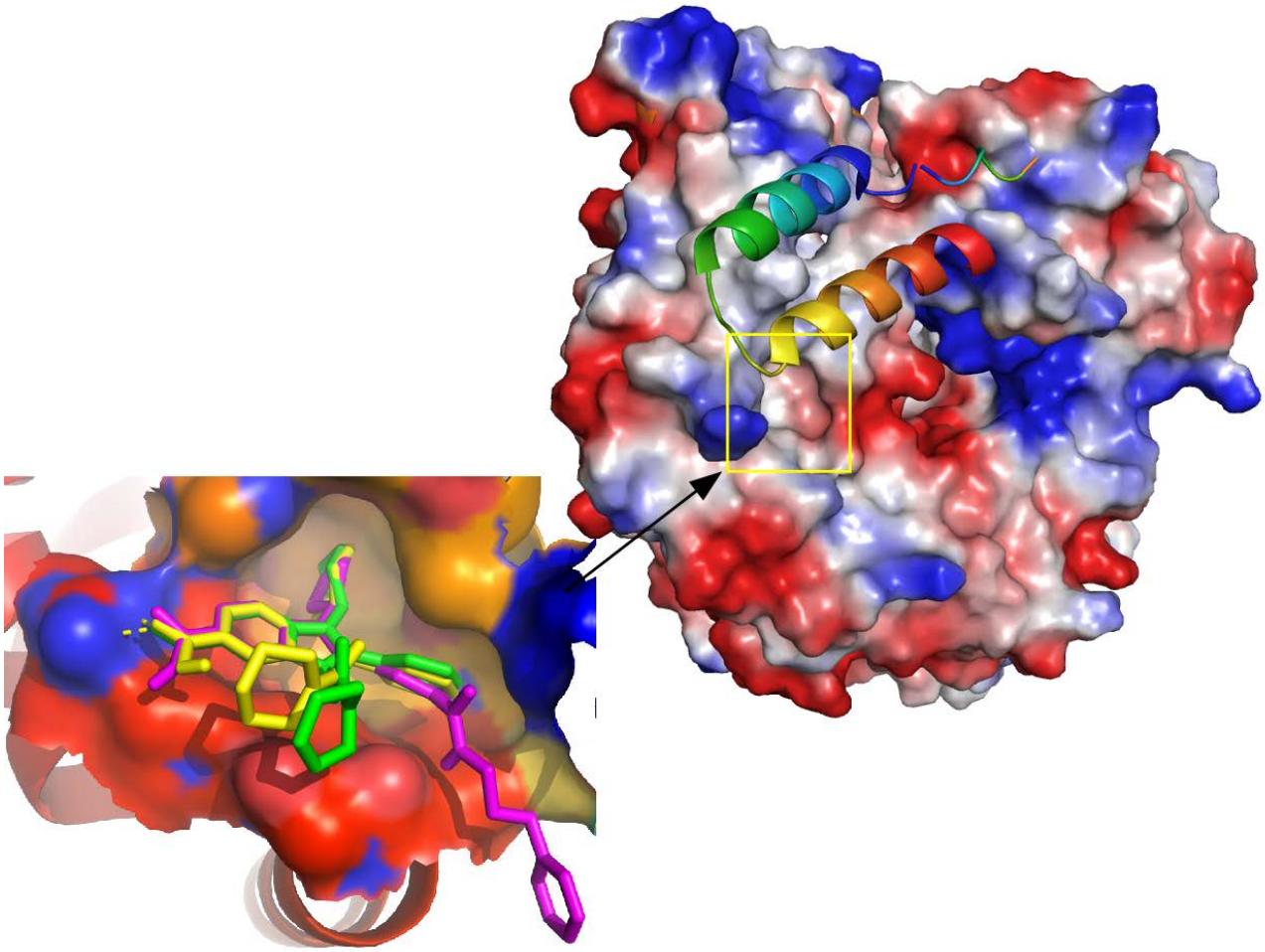
# ANNUAL REPORT 2018



INSTITUTE OF RESEARCH, DEVELOPMENT, AND INNOVATION IN HEALTHCARE BIOTECHNOLOGY IN 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. The Institute emerged in 2018 from a transformation of the Institute of Molecular and Cell Biology (IBMC), as a strategy to focus our research in Healthcare Biotechnology. IDiBE aims to become a market-oriented Research Institute that excels in translational science. In the past 19 years, the IBMC (now IDiBE) has excelled in both its scientific production, and in the exploitation of the generated results and technologies. 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 the Annual Report 2018 that describes all our achievements in research, exploitation, training and dissemination activities. All these accomplisments are in line with the objectives set in our Plan of Action 2013-2018.

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 Bioingeneering with the Institute of Bioingeneering that is becoming a national reference in the field. 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 4 lead compounds in clinical development. To reinforce our translational activities, four technological platforms have been stablished. 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.

A major milestone for 2018 has been the incorporation of new research teams to the Institute, thus reinforcing our human resources, and incorporating additional skill and competences to the existing ones. This is going to potentiate the multidisciplinarty and allow us to increase our national and international competitivity, which is essential to secure a more ambitious research program.

Although we have achieved many milestones, there is still plenty to attain for increasing the IDiBE international exposure and scientific translational excellence. In this regard, our next Plan of Action (2019-2022) approved on December 21st 2018 by the General Council, strengthens the original vision, and establishes the central mission to consolidate a multidisciplinary research program in the area of Healthcare Biotechnology.

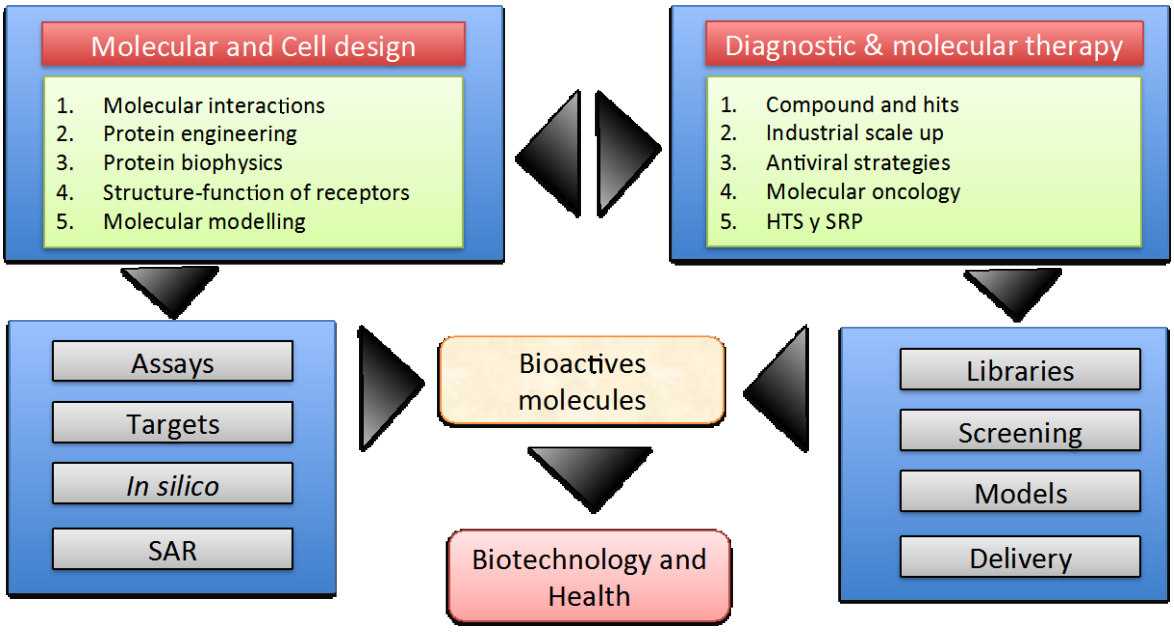
Prof. Antonio Ferrer-Montiel

IDiBE Director

# STRUCTURE AND GENERAL DESCRIPTION

## The IDiBE Scientific Program (2013-2018).

The IDiBE has established a unique research and training program, which exploits multidisciplinarity, making the most of the complementarities of the groups and using synergies as a strategy for attaining excellence and increasing competitiveness and productivity. To accomplish this aim, in the last two years, research has been organized into two complementary areas of research, namely, (i) ***molecular and cell design*** and (ii) ***molecular diagnosis and therapy***. These research lines, in turn, are organized into sub-areas, which rationally combine the groups' abilities and skills in the supplementary fields that contribute to the development of bioactive molecules, reducing scientific dispersion by grouping activities in order to carry out unique and ambitious research projects. Consequently, in the next five-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 five-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.




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

### A. Molecular and Cellular Design

Research within the line of ***Molecular and Cellular Design*** aims at advancing knowledge of relationships between structure and function in proteins, in order to be able to modify them rationally and specifically. The underlying goal is the transformation of the activity of these proteins with bio and chemo-technological purposes, or the use of the information to design targeted ligands to modulate the receptor activity acting as sensors.

The different scientific backgrounds of the researchers who develop this research line allows a reasonably and pluridisciplinary (though improved) approach to analyze problems, offering an opportunity for the development of common interests and benefiting from synergies that naturally appear in this context. This multidisciplinary approach of issues enables a broad focusing on scientific topics, ranging from a perspective of basic science to investigations with clear translational vocation.

Both the composition of the different research groups that make up this line of research as its multidisciplinarity and flexibility to raise specific scientific goals fosters a high competitiveness, both in the uptake of competitive sources and scientific production, in

the training of research personnel and in the technological transfer of research results. In this sense, strong links with research groups both national as international have been notably established, which have materialized, for example, in leadership or participation in projects coordinated with other institutions both within the different National Plans of Research and funded by the European Union and recently granted.

***Molecular and Cellular Design*** line is organized into two sub-lines, each comprising several research groups with common research interests. The first in centered around ***Molecular Recognition and Protein Biophysics and Engineering***, while the second focuses his research on ***Structure-Function Relationships in Membrane Proteins***.

## B. Diagnosis and Molecular Therapy.

The ***Diagnosis and Molecular Therapy*** line seeks the identification and validation of molecular markers in human and animal pathologies of high prevalence, as well as the development of diagnostic methods and therapeutic or preventive strategies. This line consists of a multidisciplinary team of researchers covering from molecular aspects to the semi-industrial production of biological actives.

Milestones achieved in this line of research have had and have a high scientific impact, as shown by scientific publications in magazines of recognized international prestige, as well as the generation of unique technologies that are protected by patents extended worldwide and have been licensed to interested companies. Also, it should be noted as a strong point of this line the high level of national and international collaborations with public bodies and private research, contributing to increase the impact of activities and its internationalization. In addition, the interrelationship of the sub-lines that make up this line of research has fostered identifying synergies and common interests between groups that have driven collaborations that accelerate the achievement of results and technologies.

Clearly, the activities of this line have a high potential for clinical translation materialized in close collaboration with the General Hospital and the University of Elche, as well as biotechnology transfer and exploitation resulting in continuous and consolidated collaborations with biotech, food, cosmetics and pharmaceutical companies.

# MOLECULAR AND CELLULAR DESIGN LINE.

## MOLECULAR AND CELLULAR DESIGN.

### 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 note exclusively, of the biomolecules currently under study in the group are: (i) those involved in the phosphorylation tranfer in micro-organisms; and (ii) those implicated in the aseembly 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.


Neira JL, Hornos F, Cozza C, Cámara-Artigas A, Abián O, Velázquez-Campoy A. The histidine phosphocarrier protein, HPr, binds to the highly thermostable regulator of sigma D protein, Rsd, and its isolated helical fragments. Arch. Biochem. Biophysics. 2018, 639:26-37.

Santofimia-Castaño P, Rizzuti B, Abián O, Velázquez-Campoy A, Iovanna JL, Neira JL. Amphipathic helical peptides hamper protein-protein interactions of the intrinsically disordered chromatin nuclear protein 1 (NUPR1). Biochim Biophys Acta Gen Subj. 2018, 1862: 1283-1295.

Neira JL, López MB, Sevilla P, Rizzuti B, Cámara-Artigas A, Vidal M, Iovanna JL. The chromatin nuclear protein NUPR1L is intrinsically disordered and binds to the same proteins as its paralogue. Biochem J., 2018, 475:2271-2291.

Contreras LM, Sevilla P, Cámara-Artigas A, Hernández-Cifre JG, Rizzuti B, Florencio FJ, Muro-Pastor MI, García de la Torre J, Neira JL. The cyanobacterial ribosomal-associated protein LrtA from Synechocystis sp. PCC 6803 is an oligomeric protein in solution with chameleonic sequence properties. Int J Mol Sci. 2018, 19. pii: E1857. doi: 10.3390/ijms19071857.

Santofimia-Castaño P, Lan W, Bintz J, Gayet O, Carrier A, Lomberk G, Neira JL, González A, Urrutia R, Soubeyran P, Iovanna JL. Inactivation of NUPR1 promotes cell death by coupling ER-stress responses with necrosis. Sci. Reports. 2018, 8:16999. doi: 10.1038/s41598-018-35020-3.

Neira JL, Giudici AM, Hornos F, Arbe A, Rizzuti B. The C Terminus of the ribosomal-associated protein LrtA is an intrinsically disordered oligomer. Int J Mol Sci. 2018, 19. E3902. doi: 10.3390/ijms19123902.


### Patents.

Inventores: Neira JL. Título: NUPR1 inhibition for treating cancer. Titular: European Patent Application. Registros: EP18305672.0. Fecha concesión: 31/05/2018.

### Governmental Projects and Funding.

Interacciones macromoleculares y "farmacobilidad" de proteínas intrinsicamente desordenadas implicadas en el desarrollo de cancer de páncreas. PROYECTOS DE I+D+i "RETOS DE LA SOCIEDAD" - MINECO 2015. Ministerio de Economía y Competitividad. IPs: Javier Gómez y José L Neira.

### Scientific and Educational Commities.

CONYCET, Argentina (2008-...). José L. Neira.

Israeli Science Foundation (2016-...). José L. Neira.

Czech Science Foundation (2010-...). José L. Neira.

ERC (2018-....). José L. Neira.

Italian PRIM program (2018-...). José L. Neira.

Belgian Ministry of Science (2018-...). José L. Neira.

Process Biochemistry. R. Esquembre.

Journal of Luminescence. R. Esquembre.

## Editorial Boards.

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

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 TO BIOLOGICAL SYSTEMS.

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.

## Staff.

Carmen Reyes Mateo Martínez

Ricardo Mallavia Marin

Mª José Martínez Tomé

## Postdoctoral Researchers.

Juan Alberto Falcó Graciá

## Ph. D Students.

Marta Rubio Camacho

Yolanda Inmaculada Alacid Martínez

## Technicians.

Elisa Pérez García

## Publications.

Vázquez-Guilló R, Falco A, Martínez-Tomé MJ, Mateo CR, Herrero MA, Vázquez E, Mallavia R. Advantageous Microwave-Assisted Suzuki Polycondensation for the Synthesis of Aniline-Fluorene Alternate Copolymers as Molecular Model with Solvent Sensing Properties. Polymers. 2018, 10, 215; doi:10.3390/polym10020215.

Vázquez-Guilló R, Martínez-Tomé MJ, Kahveci, Z, Torres I, Falco A, Mallavia R, Mateo CR. Synthesis and Characterization of a Novel Green Cationic Polyfluorene and Its Potential Use as a Fluorescent Membrane Probe. Polymers. 2018, 10, 938; doi:10.3390/polym10090938.

## Patents.

Inventores: Antonio Figueras Huerta, Maria Gasset Vega, Beatriz Novoa García, Magalí Rey Campos, Ricardo Mallavia Marin, Regla Maria Medina Gali, Alicia Martínez López. Título: Péptido de miticina y su uso en regeneración celular. Titular: Consejo Superior de Investigaciones Científicas y Universidad Miguel Hernández. Registros: P201831154. Fecha concesión: 28/11/2018.

## Invited Talks and Courses.

IRICA, Facultad de Ciencias y Tecnologías Químicas, Ciudad Real, Universidad Castilla la Mancha. 2018. R. Mallavia.

## Science dissemination: outreach activities.

Jornadas de divulgación científica "Ciencia con tapas".

- Contaminantes en aguas y alimentos: ¿debemos alarmarnos?, 25-01-2018.

- Ambiente, genes y diabetes, 11-04-2018.

- ¿Qué aporta la genética en la práctica clínica?, 12-06-2018.

- Anorexia y bulimia: El papel de los medios de comunicación, 16-10-2018.

- Adicciones: Una perspectiva neurobiológica, psicológica y social, 12-12-2018.

- Resistencia a los antibióticos ¿Le ganaremos la partida a las superbacterias?, 04-05-2018. MÓDULO "CIENCIA, SALUD Y TECNOLOGÍA" DESARROLLADO EN LA III FERIA DE LA CIENCIA Y LA TECNOLOGÍA DE ELCHE (FeCiElx).

Mª José Martínez Tomé. Comité organizador.

## Number of Congress Communications.

National contributions: 6.

Poster presentations: 6.

International contributions: 1.

Poster presentations: 1.

## Governmental Projects and Funding.

Desarrollo de nanoestructuras basadas en polielectrolitos para su aplicación como herramientas de diagnóstico, transporte de fármacos y diseño de biosensores. Ministerio de Economía y Competitividad (MAT-2014-53282) (Enero 2015- Dic-2017; Prórroga concedida hasta Jul-2018). IP: Ricardo Mallavia Marín y Co-IP: Carmen Reyes Mateo Martinez.

Diseño de nanomateriales fluorescentes para el desarrollo de nuevas formulaciones terapéuticas y descubrimiento de nuevos fármacos. Ministerio de Economía, industria y Competitividad (MAT-2017-86805-R) (Enero 2018- Dic-2020). IP: Carmen Reyes Mateo Martinez y Co-IP: Ricardo Mallavia Marín.

## Private funding. Technical Services and Assistance.

Preparación y Análisis de 5 muestras, identificación de sustancia clave e informe técnico. Prestaciones de servicio. (242/18), Particular: Samuel Sanchez Gonzalez. Universidad Miguel Hernández. (1 mes Feb 2018), IP: R. Mallavia Marín.

## Scientific and Educational Commities.

Polymers. C. R. Mateo.

Journal of Molecular Liquids. C. R. Mateo.

Journal of Physical Chemistry. C. R. Mateo.

Nano-Micro Letters. C. R. Mateo.

## Editorial Boards.

Board member Nanomaterials, special issue in MDPI (Oct. 2018-...). R. Mallavia (Editor invitado).

## Group name: PROTEIN ARCHITECTURE.

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

biomedicine, bioengineering and in the most recent areas of nanoscience.

Proteins are dynamic nanomolecular machines ubiquitous in all living systems that adopt distinct three-dimensional (3D) structures to perform multitude of biological functions. Advance in modern molecular biology and biotechnology have improved our understanding of basic functional and architectural principles of proteins, making them attractive candidates as concept generators for technological development in biomedicine, bioengineering and in the most recent areas of nanoscience. Appling "rational design", protein engineering is the most powerful approach to obtain proteins with new or desirable functions and properties. In biomolecular engineering is of particular interest, the protein biochemical and biophysical characterization by thermodynamic, kinetic, spectroscopic and structural methods allowing us to better understanding the rules that govern the processes of interest, and the degree of involvement of proteins in these processes.

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

Our studies are focused on three main lines of research:

- Protein structure regularization and effect on function.

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

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

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

### Staff.

Ana María Fernández Escamilla

### Number of Congress Communications.

National contributions: 2.

Oral presentations: 1.

Poster presentations: 1.

### Scientific and Educational Commities.

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.

## Structure-Function Relationships in Membrane Proteins.

### Group name: STRUCTURE-FUNCTION RELATIONSHIP OF ION CHANNELS.

Structure/Function relationships in membrane proteins: Neuroreceptors and ion channels. Lipid-Protein and Protein-Protein interactions in biological membranes. Modulation of ion channels. Potential applications to drug discovery.

## Staff.

José Manuel González-Ros

José Antonio Poveda Larrosa

## Postdoctoral Researchers.

Mª Lourdes Renart Pérez

Ana Marcela Giudici Besseghini

## Ph. D Students.

Clara Díaz García

## Technicians.

Eva Martínez

## Publications.

Cobo R, Nikolaeva M, Alberola-Die A, Fernández-Ballester G, González-Ros JM, Ivorra I, Morales A. Mechanisms Underlying the Strong Inhibition of Muscle-Type Nicotinic Receptors by Tetracaine. Front Mol Neurosci. 2018. doi: 10.3389/fnmol.2018.00193. eCollection 2018.

## Number of Congress Communications.

National contributions: 2.

Oral presentations: 1.

Poster presentations: 1.

International contributions: 3.

Oral presentations: 2

Poster presentations: 1.

## Governmental Projects and Funding.

Bases Moleculares de la modulación de canales iónicos. PROYECTOS DE I+D+I "Subprograma Estatal de Generación de conocimiento" - MINECO 2015. Ministerio de Economía y Competitividad. Ref.: BFU2015-66612-P. Duración: 2016-2018. Subvención concedida: 124.509,00 €. IPs: José Manuel González Ros y José Antonio Poveda Larrosa.

Plataforma en nanotecnología traslacional (Patent). CONSELLERIA DE EDUCACION, INVESTIGACION, CULTURA Y DEPORTE, GENERALITAT VALENCIANA. Ref.: IDIFEDER/2018/020. Duración: 01/01/2018 - 31/10/2020. Subvención concedida: 770.000 €.

## Scientific and Educational Commities.

Archives of Biochemistry and Biophysics. J. A. Poveda.

International Journal of Molecular Sciences. J. A. Poveda.

Protein Expression and Purification. J. A. Poveda.

Biopolymers. J. A. Poveda.

AIMS Biophysics. J. A. Poveda.

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

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

MINECO. J. M. González-Ros.

Oncotarget. J. M. González-Ros.

# MOLECULAR DIAGNOSIS AND THERAPY LINE.

## MOLECULAR DIAGNOSIS AND THERAPY.

### Bioactive Molecules.

### Group name: NATURAL BIOACTIVE COMPOUNDS.

The relationship between the biological activity of natural dietary compounds and its effects on chronic human diseases is under intense debate. The research target of our group is to characterize the wide biological activity of natural bioactive compounds using cellular and animal models and to understand the mechanism underlying their health effects. The characterization and identification of natural compounds in complex matrixes, especially polyphenols, is also our target. Our group is focused on:

The capacity of polyphenols to ameliorate metabolic disturbances associated to obesity (oxidative stress and insulin resistance) in cellular models and hyperlipidemic mice.

Bioguided screening of antimicrobial herbal extracts and compounds for applications in cosmetics, hygiene or medical devices. Searching for natural compounds for dermocosmetic applications.

The antiproliferative and apoptotic effects of polyphenols in cancer cellular models using global OMICs. Nano-encapsulation of potential anticarcinogenic compounds.

Characterization of food and herbal materials by chromatography coupled to mass spectrometry. Semi-industrial scale production of herbal extracts deriving from plants or vegetal by-products.

Optimization of juice extraction processes and integral exploitation of by-products.

### Staff.

Vicente Micol Molina, IP

Jose Antonio Encinar Hidalgo

Enrique Barrajón Catalán

María Herranz López

### Postdoctoral Researchers.

Almudena Pérez Sánchez

### Ph. D Students.

Verónica Ruiz Torres

María Losada Echeberría

Maria Dolores Olivares Vicente

Luz María Agulló Chazarra

Javier Álvarez Martínez

Noelia Sánchez Marzo

### Technicians.

Mª Teresa Garzón Cabrerizo

### Publications.

Bello-Pérez, M.; Falcó, A.; Galiano, V.; Coll, J.; Perez, L.; Encinar, J. A. Discovery of nonnucleoside inhibitors of polymerase from infectious pancreatic necrosis virus (IPNV). Drug Design, Development and Therapy 2018, 12, 2337-2359 DOI: 10.2147/DDDT.S171087.

Boix-Castejón, M.; Herranz-López, M.; Gago, A. P.; Olivares-Vicente, M.; Caturla, N.; Roche, E.; Micol, V. Correction: Hibiscus and lemon verbena polyphenols modulate appetite related biomarkers in overweight subjects: a randomized controlled trial (Food Funct., (2018) 9 (3173–3184) DOI: 10.1039/c8fo00367j). Food and Function 2018, 9 (7), 4037 DOI: 10.1039/c8fo90028k.

Boix-Castejón, M.; Herranz-López, M.; Pérez Gago, A.; Olivares-Vicente, M.; Caturla, N.; Roche, E.; Micol, V. Hibiscus and lemon verbena polyphenols modulate appetite-related biomarkers in overweight subjects: A randomized controlled trial. Food and Function 2018, 9 (6), 3173-3184 DOI: 10.1039/c8fo00367j.

Cádiz-Gurrea, M. D. L. L.; Olivares-Vicente, M.; Herranz-López, M.; Román-Arráez, D.; Fernández-Arroyo, S.; Micol, V.; Segura-Carretero, A. Bioassay-guided purification of Lippia citriodora polyphenols with AMPK modulatory activity. Journal of Functional Foods 2018, 46, 514-520 DOI: 10.1016/j.jff.2018.05.026.

Corominas-Faja, B.; Cuyàs, E.; Lozano-Sánchez, J.; Cufí, S.; Verdura, S.; Fernández-Arroyo, S.; Borrás-Linares, I.;

Martin-Castillo, B.; Martin, A. G.; Lupu, R.; Nonell-Canals, A.; Sanchez- Martinez, M.; Micol, V.; Joven, J.; Segura-Carretero, A.; Menendez, J. A. Extra-virgin olive oil contains a metabolo-epigenetic inhibitor of cancer stem cells. Carcinogenesis 2018, 39 (4), 601-613 DOI: 10.1093/carcin/bgy023.

Lama, R.; Pereiro, P.; Costa, M. M.; Encinar, J. A.; Medina-Gali, R. M.; Pérez, L.; Lamas, J.; Leiro, J.; Figueras, A.; Novoa, B. Turbot (Scophthalmus maximus) Nk-lysin induces protection against the pathogenic parasite Philasterides dicentrarchi via membrane disruption. Fish and Shellfish Immunology 2018, 82, 190-199 DOI: 0.1016/j.fsi.2018.08.004.

Lucioli, S.; Di Bari, C.; Forni, C.; Di Carlo, A.; Barrajón-Catalán, E.; Micol, V.; Nota, P.; Teoli, F.; Matteocci, F.; Frattarelli, A.; Caboni, E. Anthocyanic pigments from elicited in vitro grown shoot cultures of Vaccinium corymbosum L., cv. Brigitta Blue, as photosensitizer in natural dyesensitized solar cells (NDSSC). Journal of Photochemistry and Photobiology B: Biology 2018, 188, 69-76 DOI: 10.1016/j.jphotobiol.2018.09.002.

Medina-Gali, R.; Belló-Pérez, M.; Martínez-López, A.; Falcó, A.; Ortega-Villaizan, M. M.; Encinar, J. A.; Novoa, B.; Coll, J.; Perez, L. Chromatin immunoprecipitation and high throughput sequencing of SVCV-infected zebrafish reveals novel epigenetic histone methylation patterns involved in antiviral immune response. Fish and Shellfish Immunology 2018, 82, 514-521 DOI: 10.1016/j.fsi.2018.08.056.

Micol, V.; Barrajón-Catalán, E.; Herranz, M. Nutraceuticals for skin care: How much science is behind to be reliable? Agro Food Industry Hi-Tech 2018, 29 (1), 25.

Micol, V.; Herranz, M.; Vicente-Salar, N.; Roche, E. Polyphenols for skeletal muscle recovery in sports. Agro Food Industry Hi-Tech 2018, 29 (1), 37.

Ruiz-Torres, V; Losada-Echeberría, M.; Herranz-López, M.; Barrajón-Catalán, E.; Galiano, V.; Micol, V.; Encinar, JA. New mammalian target of rapamycin (mTOR) modulators derived from natural product databases and marine extracts by using molecular docking techniques. Mar. Drugs 2018, 16(10), 385; https://doi.org/10.3390/md16100385.

Pérez-Sánchez, A.; Barrajón-Catalán, E.; Herranz-López, M.; Micol, V. Nutraceuticals for Skin Care: A Comprehensive Review of Human Clinical Studies. Nutrients 2018, 10(4), 403; https://doi.org/10.3390/nu10040403.

Olivares-Vicente, M.; Barrajon-Catalan, E.; Herranz-Lopez, M.; Segura-Carretero, A.; Joven, J.; Encinar, JA.; Micol, V. Plant-Derived Polyphenols in Human Health: Biological Activity, Metabolites and Putative Molecular Targets. Current Drug Metabolism 2018, 19(4) 351-369. https://doi.org/10.2174/1389200219666180220095236.

Álvarez-Martínez, F.J., Barrajón-Catalán, E., Encinar. J.A., Rodríguez-Díaz, J.C. and Micol, V. Antimicrobial Capacity of Plant Polyphenols against Gram-positive Bacteria: a Comprehensive Review. Curr Med Chem 2018. doi:10.2174/0929867325666181008115650

Verdura S, Cuyàs E, Llorach-Parés L, Pérez-Sánchez A, Micol V, Nonell-Canals A, Joven J, Valiente M, Sánchez-Martínez M, and Menéndez, J.A. Silibinin is a direct inhibitor of STAT3. Food Chem Toxicol. 2018, 116(Pt B):161-172.

## Creation of Spin-Off Firms.

Micol, V.; Herranz-López, M.; Barrajón-Catalán, E. Illice Effitech S.L. (September 2018).

## Organization of Meetings.

Barrajón-Catalán, E. Member of the scientific committee of 21st International Drying Symposium, Valencia (2018).

## Invited talks and courses.

Influence of drying temperature and harvesting season on phenolic content, antioxidant activity and antiproliferative capacity in cancer cell models of olive (Olea europaea) leaf extracts. Barrajón-Catalán, E. 21st International Drying Symposium, Valencia (2018).

## Number of Congress Communications.

National congress: 1.

International congress: 12.

## Governmental Projects and Funding.

Título del proyecto: Nutraceuticos de 2ª generacion de plantas comestibles basados en extractos polifenolicos moduladores del metabolismo energetico: aplicaciones en la prevencion de la obesidad. Entidad financiadora: Ministerio de Economía y Competitividad. MICINN (AGL2015-67995-C3-1-R). Cantidad concedida: 105.000 €. Duración: 01/01/2016-31/12/2018. IP: Vicente Micol.

Título del proyecto: El carácter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terapéuticas frente a la obesidad y las enfermedades infecciosas. Entidad financiadora: Conselleria de Educación, Formación y Empleo (GV). PROMETEO/2016/006. Cantidad concedida total: 219.478 €. Duración: 01/01/2016 – 31/12/2019. IP: Vicente Micol.

Título del proyecto: Subvenciones para la contratación de personal de apoyo vinculado a un proyecto de trasferencia tecnológica (APOTIP/2017/003). Entidad financiadora: Proyectos competitivos de subvención pública para contratación de personal. Consellería de Educación. GV. Cantidad concedida: 18.000 €. Duración: 01/11/2017-31/08/2019. IP: Vicente Micol.

## Private funding: Contracts.

Título del proyecto: Contrato para la realización del proyecto CDTI: "Investigación y desarrollo experimental de nuevos alimentos más saludables y envases avanzados." Entidad financiadora: MONTELOEDER, SL. Importe anualidad: 30.000 €. Duración: 01/09/2015-01/09/2019. Investigador responsable: Vicente Micol. Participan como investigadores: Barrajón-Catalán, E., María Herranz-López, Marti, N., Roche, E. Saura, D.

Título del proyecto: "Identificación de metabolitos intracelulares en la hoja y el fruto de pimiento alterados tras tratamiento con bioestimulante 1". Entidad financiadora: Grupo AGROTECNOLOGÍA. Cantidad concedida: 15.175 €. Duración: 28/09/2017-28/03/2018. IP: Enrique Barrajón. Participan como investigadores: Micol, V, María Herranz-López.

## Private funding: Technical Services and Assistance.

Scientific Advisor MONTELOEDER, SL (2002-2018). V. Micol.

Scientific Advisor MITRA SOL TECHNOLOGIES (2013-2018). V. Micol.

Scientific Advisor INVITROTECNIA (2016-2018). V. Micol, E. Barrajón, M. Herranz.

14 provisions of services with different companies in 2018.

## R&D and Educational Committees.

Enrique Barrajón Catalán. Vocal científico en Órgano Evaluador de Proyectos (órgano habilitado) de la Universidad Miguel Hernández de Elche.

Vicente Micol. Evaluador de la Agencia Nacional de Evaluación y Prospectiva (ANEP).

## R&D Management.

R&D Management of the Company Ilice Effitech, SL. V. Micol, E. Barrajón, M. Herranz.

## Editorial Boards.

AgroFOOD Industry Hi Tech – Teknoscience (2010-2018). V. Micol.

## 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

## Ph. D Students.

Sara Gea Botella

## External collaborators integrated in the group.

Concepción Martínez Madrid (UMH)

## Publications.

Giménez T, Mula D, Gea-Botella S, Martínez-Madrid MC, Marti N, Valero M, Saura D. Lipase catalyzed deacidification of tocopherol-rich distillates obtained from natural Vitamin E sources. Process Biochemistry. 2018, I.S.S.N.: 1359-5113.

## Patents.

Inventores: Martí, N., Barrajón-Catalán, E., Berenguer-Martínez, M.D.R., Martínez, R.,

Micol, V., Saura, D., Valero, M., Vegara-Gómez, S. Título: Contrato de Licencia de Know-how para la obtención de compuestos con actividad biológica a partir de subproductos de la industria enológica. Titular: MITRA SOL TECHNOLOGIES SL. Fecha concesión: 27/03/2013.

Inventores: Saura, D., Barrajón-Catalán, E., Martí, N., Martínez, R., Micol, V, Valero, M., Vegara Gomez, S. Título: Contrato de licencia de patente 201300578 "Combinación sinérgica de flavonoides y vitamina C". Titular: MITRA SOL TECHNOLOGIES SL. Fecha concesión: 13/05/2016. Referencia patente: 201300578.

Inventores: Saura, D., Barrajón-Catalán, E., Rodríguez Díaz, J.L., 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 concesión: 13/05/2016. Referencia patente: 201301181.

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

Inventores: Saura, D., Martí, N., Micol, V, Valero, M. Título: Contrato de licencia patente 201500423. Titular: MITRA SOL TECHNOLOGIES SL. Fecha concesión: 27/03/2013. 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 concesión: 13/05/2016. Referencia patente: 201200830.

## Chronic inflammation & pain.

## 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.

## 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 Barrajón y María Herranz. Participan como investigadores: Nuria Martí, Enrique Roche y Domingo Saura.

Título del proyecto: (793/18) Caracterización y estudio de la aptitud de un extracto de pimiento para su uso en cosmética. Cantidad concedida: 1.950 €. Fecha concesión: 14/07/2018. IP: Nuria Martí.

## Private funding: Technical Services and Assistance.

Domingo Saura, Nuria Martí y Manuel Valero. Technical Assistance to Cool Vega Company S.L.

## Group name: DRUG DESING ON THERMOTRPs AND PAIN SIGNALLING.

Our group is interested in understanding the cellular and molecular basis underlying pain transduction in the peripheral nervous system, and to use this knowledge to design and validate novel therapeutic strategies for pain control. Our research is hypothesis-based and combines cellular and molecular approaches, using from animal models to purified proteins. Identification of the signalplexes involved in sensory and pain transduction allows us to identify new druggable targets that enter our drug discovery program for hit identification.

To refine lead development, we are also interested in unveiling the protein structure of the selected targets, mostly thermoreceptor channels (thermoTRPs). This information is essential for accelerating the identification and development of lead compounds. Complementarily, we also characterize the biophysics of channel activity to further understand how ion channels work in terms of their underlying protein structure and the antagonists modulate their activity.

### Staff.

Antonio Ferrer-Montiel.

Gregorio Fernández-Ballester

Asia Fernández Carvajal

### Postdoctoral Researchers.

Maite Artero Morales

Sara González Rodríguez

### Ph. D Students.

Magdalena Nikolaeva Koleva

Simona Giorgi

David Alarcón Alarcón

Alicia Medina Peris

Gloria Briceño Vega

Eva Villalba Riquelme

Mariana Dionissi

### Collaborators integrated in the group.

Laura Butrón García

### Technicians.

Irene Mudarra Fraguas

Antonio Manuel Zafra Pinto

### Publications.

Felipe A, Ferrer-Montiel A. The Spanish Ion Channel Initiative (SICI) Consortium: Ten Years (2008–2018) of a Network of Excellence on Ion Channel Research. Int J Mol Sci. 2018 Nov 8;19(11). pii: E3514. doi: 10.3390/ijms19113514.

Pérez de Vega MJ, Ferrer-Montiel A, González-Muñiz R. Recent progress in non-opioid analgesic peptides. Arch Biochem Biophys. 2018 Dec 15;660:36-52. doi: 10.1016/j.abb.2018.10.011. Epub 2018 Oct 17. Review.

Artero-Morales M, González-Rodríguez S, Ferrer-Montiel A.TRP Channels as Potential Targets for Sex-Related Differences in Migraine Pain. Front Mol Biosci. 2018 Aug 14;5:73. doi: 10.3389/fmolb.2018.00073. eCollection 2018. Review.

Bertamino A, Iraci N, Ostacolo C, Ambrosino P, Musella S, Di Sarno V, Ciaglia T, Pepe G, Sala M, Soldovieri MV, Mosca I, Gonzalez-Rodriguez S, Fernandez-Carvajal A, Ferrer-Montiel A, Novellino E, Taglialatela M, Campiglia P, Gomez-Monterrey I. Identification of a Potent Tryptophan-Based TRPM8 Antagonist With in Vivo Analgesic Activity. J Med Chem. 2018 Jul 26;61(14):6140-6152. doi: 10.1021/acs.jmedchem.8b00545. Epub 2018.

Serafini M, Griglio A, Aprile S, Seiti F, Travelli C, Pattarino F, Grosa G, Sorba G, Genazzani AA, Gonzalez-Rodriguez S, Butron L, Devesa I, Fernandez-Carvajal A, Pirali T, Ferrer-Montiel A. Targeting Transient Receptor Potential Vanilloid 1 (TRPV1) Channel Softly: The Discovery of Passerini Adducts as a Topical Treatment for Inflammatory Skin Disorders. J Med Chem. 2018 May 24;61(10):4436-4455. doi: 10.1021/acs.jmedchem.8b00109. Epub 2018 May 15.

Balsera B, Mulet J, Sala S, Sala F, de la Torre-Martínez R, González-Rodríguez S, Plata A, Naesens L, Fernández-Carvajal

A, Ferrer-Montiel A, Criado M, Pérez de Vega MJ, González-Muñiz R. Amino acid and peptide prodrugs of diphenylpropanones positive allosteric modulators of α7 nicotinic receptors with analgesic activity. Eur J Med Chem. 2018 Jan 1;143:157-165. doi: 10.1016/j.ejmech.2017.10.083. Epub 2017 Nov 2.

R. Cobo; M. Nikolaeva; A. Alberola-Die; G. Fernandez-Ballester; J.M. González-Ros; I. Ivorra; A. Morales. Mechanisms underlying the strong inhibition of muscle-type nicotinic receptors by tetracaine. Frontiers in Molecular Neuroscience. 11:193 (2018) pp: 1-21. Doi: 10.3389/fnmol.2018.00193.

## Creation of Spin-Off Firms.

Antonio Ferrer. Administrador de PROSPERA BIOTECH y FASTBASE SOLUTIONS.

## Patents.

Inventores: Antonio Ferrer Montiel, A. Fernández-Carvajal, Isabel Devesa, Tracey Pirali, Armando Genazzani. Título: TRPV1 modulator compounds. Titular: AntalGenics SL. Registros: WO2018206742.

Inventores: Antonio Ferrer Montiel, van den Nest, Wim, DOMENECH, Nuria Alminana, Consuelo Garcia. Título: Compounds useful for the treatment and/or care of the skin, hair, nails and/or mucous membranes. Titular: LUBRIZOL ADVANCED MATERIALS, INC. Registros: WO2018071640.

Inventores: Antonio Ferrer Montiel. Título: Compounds useful for the treatment and/or care of the skin, hair, nails and/or mucous membranes. Ampliación: US2018369115.

Inventores: Antonio Ferrer Montiel. Título: Cosmetic and/or pharmaceutical composition containing a bacterial extracellular product from pseudoalteromonas antarctica, and use thereof. Ampliación: US10265348.

Inventores: Antonio Ferrer Montiel. Título: Ferment extract of a bacterial strain for the increase of adiponectin levels. Ampliación: US10159641.

## PhD Theses.

Título: Herramientas para el estudio del dolor. Maite Artero Morales. Supervisor: Antonio Ferrer-Montiel. 23 noviembre 2018.

## Invited Talks and Courses.

¿Podemos vencer el dolor? Que puede o no puede hacer la ciencia. Antonio Ferrer Montiel. La Madraz, Centro de Cultura Contemporánea. Universidad de Granada. Granada, 20 de febrero de 2018.

Curso de Verano: La responsabilidad social en la investigación, un compromiso y una oportunidad profesional. Antonio Ferrer Montiel. UMH. Campus de Elche. 10 al 13 julio, 2018.

Kærtor Workshop: Advancing Transformative Drug Discovery. Sessión: Disruptive Technologies to Accelerate Translation. Antonio Ferrer Montiel. Centro de Estudios Avanzados (CEA). Santiago de Compostela. November 20th-21st, 2018.

Mesa redonda sobre la inclusión de nuevas competencias en el curriculum académico. Asia Fernández-Carvajal. Curso Cultura científica y divulgación de la ciencia, Elche 10-13 julio 2018.

## Science Dissemination: Outreach Activities.

Ciencia con Tapas. Monthly outreach activity of IDiBE.

X Jornadas de San Alberto. Facultad de Ciencias Experimentales. UMH. 15 noviembre 2018.

Jornadas de Puertas Abiertas del IBMC. 13 julio 2018.

Canales iónicos: de la investigación básica a la aplicación. Jornada Y TÚ, ¿QUÉ INVESTIGAS? IBMC. 27 y 28 septiembre, 2018.

## Number of Congress Communications.

National contributions: 2.

Poster presentations: 2.

International contributions: 8.

Oral presentations: 4.

Poster presentations: 4.

## Governmental Projects and Funding.

Sensibilización algésica de nociceptores en dolor crónico: mecanismos e intervención farmacológia. 23/06/2015 - PROYECTOS DE I+D+I "RETOS DE LA SOCIEDAD" - MINECO 2015 (SAF2015-66275-C2-1-R). UMH-CSIC MINISTERIO DE ECONOMIA Y COMPETITIVIDAD. IP: Antonio Ferrer Montiel (coordinador, SP_01).

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). IP: Antonio Ferrer Montiel.

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

La Iniciativa Española en Canales Iónicos. MINECO (BFU2015-70067-REDC). Universidad Miguel Hernández, CSIC. 2016-2017. IP: Antonio Ferrer Montiel.

## 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. 2018. 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.

## R&D and Educational Committees.

Antonio Ferrer Montiel. Comité científico del 6th International Iberian Biophysics Congress and X Iberoamerican Congress of Biophysics. Castellón 20-22 de junio.

Asia Fernández Carvajal. Evaluación convocatoria de proyectos sinérgicos de la Comunidad de Madrid. BBRR Sinérgicos.

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

## R&D Management.

Red Nacional de Canales Iónicos. Coordinador: Antonio Ferrer Montiel. (2011-2018).

## Scientific Society Councils.

Sociedad Española de Biofísica. (2014-2018). A. Ferrer. President.

## Editorial Boards.

Journal of Pharmacological Sciences (2018). A. Ferrer.

The Open Journal of Pain (2018). A. Ferrer.

Frontiers in Pharmacology (2018). A. Ferrer.

Frontiers in Neurosciences (2018). A. Ferrer.

Scientific Reports (2014-2018). A. Fernandez-Carvajal.

Frontiers in Physiology (2015-2018). A. Fernandez-Carvajal.

## Antiviral Strategies.

**Group name: ANTIVIRAL STRATEGIES.**

The group of Virology at the IBMC was established fourteen years ago. The group members have proven expertise over 20 years in the field of viral diseases of fish in aquaculture. The group's interest is focused on the study of viruses, fish immune response related to virus infections and antiviral strategies for disease prevention and treatment:

- Study of the early steps of rhabdovirus infections.
- Design of new antivirals using combinatorial chemistry or molecules related to the innate immune response such as AMPs (antimicrobial peptides).
- Development of environmentally friendly DNA vaccines. Characterization of the immune response induced by DNA vaccines using genomic and proteomic approaches (microarrays) to determine the molecular bases of protection conferred by these vaccines.

## Staff.

Luis Pérez García-Estañ

## Postdoctoral Researchers.

Regla María Medina Gali

## Ph. D Students.

Melissa Belló Pérez

## Technicians.

Ángeles Gómez Martínez

## Publications.

Bello-Perez M, Falco A, Galiano V, Coll J, Perez L, Encinar JA. Discovery of nonnucleoside inhibitors of polymerase from infectious pancreatic necrosis virus (IPNV). Drug Des. Devel. Ther. 2018, 12:2337-2359.

Medina-Gali, R, Ortega-Villaizan M, Mercado L, Novoa B, Coll J, Perez L. Beta-glucan enhances the response to SVCV infection in zebrafish. Dev. Comp. Immunol. 2018, 84:307-314.

Medina-Gali R, Bello-Perez M, Martinez-Lopez A, Falco A, Ortega-Villaizan M, Encinar JA, Novoa B, Coll J, Perez L. Chromatin immunoprecipitation and high throughput sequencing of SVCV-infected zebrafish reveals novel epigenetic histone methylation patterns involved in antiviral immune response. Fish Shellfish Immunol. 2018, 82:514-521.

## Science dissemination: outreach activities.

WORKSHOP "LA RESPONSABILIDAD SOCIAL EN LA INVESTIGACIÓN: UN COMPROMISO Y UNA OPORTUNIDAD PROFESIONAL". L. Pérez. Vicerrectorado de Cultura y Extensión Unversitaria, UMH. Participación. Ponente Mesa Redonda sobre Cultura y Divulgación Científicas. Elche 10 julio 2018.

NOCHE DE LOS INVESTIGADORES. INVESTIGACION APLICADA A ACUICULTURA. L. Pérez. Fundación MUDIC, Ayuntamiento de Orihuela. Participación. Ponente Mesa Redonda sobre Cultura y Divulgación Científicas. Orihuela 28 septiembre 2018.

## Group name: VIRAL MEMBRANE PROTEINS.

Among the pathogens which cause the higher rates of mortality and morbidity on humans and animals we can name the viruses. However, in the vast majority of cases, there are no vaccines or effective therapeutic treatments. Flaviviridae constitute a large family of viruses to which medically highly relevant human pathogens belong. Viruses such as the hepatitis C virus, the Yellow Fever Virus, West Nile virus, Tick-Borne Encephalitis Viruses, Zika and Dengue belong to this family. Dengue (DENV), as well as Zika (ZIKV), cause the most prevalent arthropod-borne viral disease among humans affecting millions of people per year. These diseases have evolved from a sporadic occurrence to a global public health problem. The number of reported cases is increasing geometrically due to environmental and geographical changes and many countries, including ours, have a direct risk to them. Significantly, all processes inherent to the

viral replication cycle are directly or indirectly related to membrane systems or membranes derived from them. Anything that might interfere with any one of these processes would be potentially useful in ensuring that the virus cannot get in or out of the cell. Our group aims to study the structure and interaction with different types of model biomembrane systems of several peptide domains derived from the structural and non-structural proteins of DENV and ZIKV viruses. Our goal will be to distinguish and correlate the effects on both the peptides and the membrane components, with the specific aims of obtaining, on the one hand, the knowledge of the molecular mechanism of the biological function of the original proteins and on the other, effective antiviral and bioactive molecules against them. Relaying on the knowledge we have about the structural and non-structural proteins of DENV, our experimental approach and objectives will consist of using in silico molecular dynamics to find the specific interacting three dimensional structure of selected peptides of DENV and ZIKV with biomembrane model systems, in vitro obtain exhaustive information about its structure and specific lipid interaction, in silico screening and peptide docking methodologies to obtain antiviral peptides and bioactive molecules against those obtained structure, and test them to check their effectivity using different model biomembrane compositions. These data will permit us the development of new leading compounds useful for improved combined therapies in order to achieve the ultimate goal, eradicate the DENV and ZIKV viral infections.

### Staff.

José Villalaín Boullón

### Ph. D Students.

Laureano Emilio Carpio Mulas

### Publications.

Villalaín J. “Epigallocatechin-3-gallate Location and Interaction with Late Endosomal and Plasma Membrane Model Membranes by Molecular Dynamics”, J BIOMOL STRUCT DYN. 2018 Aug 6:1-46. doi: 10.1080/07391102.2018.1508372.

### Scientific and Educational Commities.

CONICET, Argentina (2005-…). J. Villaín.

Israeli Science Foundation, Israel (2012-…). J. Villaín.

## 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, 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

### Ph. D students.

Iván Nombela Díaz

Sara Puente Marín

### Technicians.

Efren Lucas Mañogil

Remedios Torres Montero

### Publications.

Chico V, Nombela I, Puente-Marín S, Ortega-Villaizan M. Nucleated Red Blood Cells Contribute to the Host Immune Response Against Pathogens, Immune Response Activation and Immunomodulation, Rajeev K. Tyagi and Prakash S. Bisen, IntechOpen. 2018, DOI: 10.5772/intechopen.80545.

Puente-Marin S, Nombela I, Chico V, Ciordia S, Mena MC, Coll J, Mercado L, Ortega-Villaizan M. Rainbow Trout Erythrocytes ex vivo Transfection With a DNA Vaccine Encoding VHSV Glycoprotein G Induces an Antiviral Immune Response. Front Immunol. 2018. DOI: 10.3389/fimmu.2018.02477.

Medina-Gali R, Belló-Pérez M, Martínez-López A, Falcó A, Ortega-Villaizan M, Encinar JA, Novoa B, Coll J, Perez L. Chromatin immunoprecipitation and high throughput sequencing of SVCV-infected zebrafish reveals novel epigenetic histone methylation patterns involved in antiviral immune response. Fish Shellfish Immunol. 2018, 82:514-521. doi: 10.1016/j.fsi.2018.08.056.

Nombela I, Ortega-Villaizan M. Nucleated red blood cells: Immune cell mediators of the antiviral response. PLoS Pathog. 2018.

Chico V, Puente-Marin S, Nombela I, Ciordia S, Mena MC, Carracedo B, Villena A, Mercado L, Coll J, Ortega-Villaizan M. Shape-Shifted Red Blood Cells: A Novel Red Blood Cell Stage? Cells. 2018, 19;7(4).

Puente-Marin S, Nombela I, Ciordia S, Mena MC, Chico V, Coll J, Ortega-Villaizan M. In Silico Functional Networks Identified in Fish Nucleated Red Blood Cells by Means of Transcriptomic and Proteomic Profiling. Genes (Basel). 2018, 9;9(4).

Medina-Gali RM, Ortega-Villaizan M, Mercado L, Novoa B, Coll J, Perez L. Beta-glucan enhances the response to SVCV infection in zebrafish. Dev Comp Immunol. 2018, 84:307-314.

### Governmental Projects and Funding.

ERC Starting Grant 2014. Proyecto: BloodCellsCrosstalk. "The Crosstalk Between Red and White Blood Cells: The case of fish". GA639249. European Commission.

### Editorial Boards.

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

## Molecular and Cellular Oncology.

**Group name: MOLECULAR AND CELLULAR ONCOLOGY.**

The main objectives of our research group are, first, the study of the molecular mechanisms associated to chemo and radio resistance in cancer, and second, the search of new therapeutical strategies for the treatment of chemo

and radiorresistant tumours. We propose different experimental approaches to raise these objectives:

1. Development of celular models closer to the patient, allowing ex vivo tests of the treatments.
2. Development of the several models in order to determine the presence of tumour stem cells in primary cultures.
3. Use of novel therapies such as epigenetic and enzimatic therapies, in celular models from glioblastoma and pancreatic carcinoma.
4. Study of signal transduction pathways involved in resistance acquisition in glioblastoma and pancreatic carcinoma. This experimental approach allows the identification of genes involved in this process that can be considered as putative therapeutical targets.

During the last years, nanotechnology development has gained an important boom as a putative therapeutical approach for the treatment of several tumours. The use of immunodirected nanoparticles, will allow:

- To increase of the local doses and to decrease of the secondary effects.
- To direct the treatments to celular subpopulations of interest on the tumour, such as tumour stem cells or stroma cells.
- To combine and direct different and novel therapeutical strategies against the tumours of interest, such as epigenetic and enzimatic therapies.
- To explore the possibilities of these nanoparticles to potentiate the immunogenic effects observed with classical chemotherapeutical treatments as well as with radiotherapical treatments.

### Staff.

Miguel Saceda Sánchez

Mª Pilar García Morales

### Ph. D Students.

María Fuentes Baile (predoctoral-ISABIAL)

María Paz Ventero Martin (predoctoral-ISABIAL)

Elizabeth Perez Valenciano

### Genetic board from the General University Hospital of Elche.

Victor Manuel Barbera Juan

### Publications.

Carrasco-Garcia E, Martinez-Lacaci I, Mayor-López L, Tristante E, Carballo-Santana M, García-Morales P, Ventero Martin MP, Fuentes-Baile M, Rodriguez-Lescure Á, Saceda M. PDGFR and IGF-1R Inhibitors Induce a G2/M Arrest and Subsequent Cell Death in Human Glioblastoma Cell Lines. Cells. 2018, Sep 6;7(9). pii: E131. doi: 10.3390/cells7090131. PubMed PMID: 30200644; PubMed Central PMCID: PMC6162497.

### Number of Congress Communications.

International contributions: 4.

Poster presentations: 4.

## Diabetes & metabolic disorders.

### Group name: DIABETES RESEARCH UNIT.

Diabetes mellitus is characterized by hyperglycaemia caused by an insulin deficiency. Its prevalence is rising, reaching 425 million people worldwide (www.idf.org). In Spain a 13.8% of adult population is diabetic and 3 of 10 people have problems with glucose metabolism (Soriguer et al, Diabetologia 2012). There are two main types of diabetes mellitus. Type 1 diabetes is caused by an autoimmune attack against β-cells, which is the cell type responsible for producing and releasing insulin, the only hormone in our organism able to decrease glucose. When the β-cell is destroyed, no more insulin is produced

and, therefore, the patient depends on insulin injection. Between a 10 and 15% of diabetic persons are diagnosed as Type 1. About 80-85% of diabetics are diagnosed as Type 2, which occurs when peripheral tissues experience a decrease in insulin sensitivity or insulin resistance together with an incapacity of the β-cell to produce and secrete enough insulin to counteract such resistance. Then, hyperglycemia progresses because insulin secretion and β-cell mass are below a critical threshold.

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

We work on four different research lines:

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

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

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

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

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

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

observed in the early stages of these diseases.

## Staff.

Ángel Nadal Navajas

Iván Quesada Moll

Esther Fuentes Marhuenda

Cristina Ripoll Orts

Paloma Alonso-Magdalena

## Postdoctoral Researchers.

Laura Marroquí Esclapez

Eva Tudurí López

Hilda Ferrero Hidalgo

Reinaldo Sousa dos Santos

## Ph. D Students.

Cristina Quesada Candela

Eva Bru Tari

Lucía Almagro Ruz

Talía Boronat Belda

Ignacio Babiloni Chust

## External collaborators (Universidad de Alicante)

Juan Martínez-Pinna

Sergi Soriano Úbeda

## Technicians.

Mª Luisa Navarro García

Salomé Ramón Penalva

## Publications.


Soriano S, Castellano-Muñoz M, Rafacho A, Alonso-Magdalena P, Marroquí L, Ruiz-Pino A, Bru-Tarí E, Merino B, Irles E, Bello-Pérez M, Iborra P, Villar-Pazos S, Vettorazzi JF, Montanya E, Luque RM, Nadal A, Quesada I. Cortistatin regulates glucose-induced electrical activity and insulin secretion in mouse pancreatic beta-cells. Molecular and Cellular Endocrinology. 2018, pii: S0303-7207(18)30277-6. doi: 10.1016/j.mce.2018.09.009.

Stahlhut RW, Myers JP, Taylor JA, Nadal A, Dyer JA, Vom Saal FS. Experimental BPA Exposure and Glucose-Stimulated Insulin Response in Adult Men and Women. Journal of The Endocrine Society. 2018, 2(10):1173-1187.

Marroqui L, Tuduri E, Alonso-Magdalena P, Quesada I, Nadal A, Dos Santos RS. Mitochondria as a target of endocrine-disrupting chemicals: implications for type 2 diabetes. Journal of Endocrinology. 2018, 239: R27–R45.

Nadal A, Fuentes E, Ripoll C, Villar-Pazos S, Castellano-Muñoz M, Soriano S, Martinez-Pinna J, Quesada I, Alonso-Magdalena P. Extranuclear-initiated estrogenic actions of endocrine disrupting chemicals: Is there toxicology beyond paracelsus?. Journal of Steroid Biochemistry and Molecular Biology. 2018, 176:16-22.

Nuñez P, Fernandez T, García-Arévalo M, Alonso-Magdalena P, Nadal A, Perillan C, Arguelles J.. Effects of bisphenol A treatment during pregnancy on kidney development in mice: a stereological and histopathological study. Journal of Develpmental Origins of Health and Disease. 2018, 9(2):208-214.

Gallo F, Fossi C, Weber R, Santillo D, Sousa J, Ingram I, Nadal A, Romano D. Marine litter plastics and microplastics and their toxic chemicals components: the need for urgent preventive measures. Environmental Science Europe. 2018, 30(1):13.

Martinez-Pinna J, Soriano S, Tudurí E, Nadal A, de Castro F. A Calcium-Dependent Chloride Current Increases Repetitive Firing in Mouse Sympathetic Neurons. Frontiers in Physiology. 2018, May 14;9:508. doi: 10.3389/fphys.2018.00508.

Tudurí E, Marroqui L, Dos Santos RS, Quesada I, Fuentes E, Alonso-Magdalena P. Timing of Exposure and Bisphenol-A: Implications for Diabetes Development. Front Endocrinol (Lausanne). 2018, 9: 648.

Villamayor L, Rodríguez-Seguel E, Araujo R, Carrasco M, Bru-Tarí E, Mellado-Gil JM, Gauthier BR, Martinelli P, Quesada I, Soria B, Martín F, Cano DA, Rojas A. GATA6 Controls Insulin Biosynthesis and Secretion in Adult β-Cells. Diabetes. 2018, 67: 448-460.

Alonso-Magdalena P, Tudurí E, Marroqui L, Quesada, I, Sargis R, Nadal, A. Toxic

Effects of Common Environmental Pollutants in Pancreatic b-Cells and the Onset of Diabetes Mellitus. Encyclopedia of Endocrine Diseases. 2018, I.S.B.N: 978-0-12-475570-3.

Colli ML, Hill JLE, Marroqui L, Chaffey J, Dos Santos RS, Leete P, Coomans de Brachène A, Paula FMM, Op de Beeck A, Castela A, Marselli L, Krogvold L, Dahl-Jorgensen K, Marchetti P, Morgan NG, Richardson SJ, Eizirik DL. PDL1 is expressed in the islets of people with type 1 diabetes and is up-regulated by interferons-α and-γ via IRF1 induction. EbioMedicine. 2018, 36:367-375. doi: 10.1016/j.ebiom.2018.09.040.

Juan-Mateu J, Alvelos MI, Turatsinze JV, Villate O, Lizarraga-Mollinedo E, Grieco FA, Marroquí L, Bugliani M, Marchetti P, Eizirik DL. SRp55 Regulates a Splicing Network That Controls Human Pancreatic β-Cell Function and Survival. Diabetes. 2018 Mar;67(3):423-436. doi: 10.2337/db17-0736.

Fuentes E, Quesada I. Salud Nutricional en el envejecimiento. En: Cuestiones básicas en gerontología. ISBN: 978-84-16024-68-1. 2018.

Alonso-Magdalena P. La exposición a disruptores endocrinos en el embarazo es un factor de riesgo en la aparición de diabetes. Revista: Diabetes-Sociedad Española de Diabetes I.S.S.N.: 0417-3988. 2018.

## Organization of meetings.

Symposium: Jornadas Prometeo-Generalitat Valenciana 2018 of the Diabetes Research Unit-UMH.

Jornadas SEJI Jóvenes Investigadores de Excelencia: New approaches in diabetes research (30/11/2018).

## Invited Talks and Courses.

Discussion Leader EED Toxicology and Modes of Action: Mechanisms of Inheritence and Novel Paradigms. Ángel Nadal. 11th GORDON RESEARCH CONFERENCE. ENVIRONMENTAL ENDOCRINE DISRUPTORS, Les Diablerets, Suiza 03/06/2018.

Endocrine-Disrupting Chemicals, ACTION ON ENDOCRINE-DISRUPTING CHEMICALS BRIEFING. Ángel Nadal. Parlamento Europeo, Bruselas, Bélgica 20/11/2018.

Exposure to endocrine disrupting chemicals during pregnancy and risk of obesity in the offspring. Ángel Nadal. FESBE 2018 XXXIII REUNIAO ANNUAL, Campos do Jordao, Brasil 03/09/2018.

Revisando los dogmas de la toxicología a través del efecto de los disruptores endocrinos en la célula beta pancreática. Ángel Nadal. Jornadas Prometeo-Generalitat Valenciana 2018 of the Diabetes Research Unit-UMH,13/11/2018.

La gestación como periodo de susceptibilidad a los efectos de los disruptores endocrinos. Paloma Alonso-Magdalena. Conferencia inaugural. XLV REUNION DE LA SOCIEDAD DE PEDIATRIA DEL SURESTE DE ESPAÑA, 17/03/2018.

¿Programación metabólica en el adulto?: Disrupción endocrina, cambiando paradigmas. Paloma Alonso-Magdalena. XXIX CONGRESO NACIONAL DE LA SOCIEDAD ESPAÑOLA DE DIABETES, 18/04/2018.

Disruptores endocrinos en el origen de la diabetes. Paloma Alonso-Magdalena. X SEMANA DE LA CIENCIA, 14/11/2018.

Endocrine disruptors, obesity and diabetes. Paloma Alonso-Magdalena. IX SYPOSIUM CIBER FISIOPATOLOGIA DE LA OBESIDAD Y NUTRICION, 21/11/2018.

## Awards.

Paloma Alonso Magdalena. Premio José Antonio Hedo de investigación básica junior-Sociedad Española de Diabetes.

## Governmental Projects and Funding.

Papel de los receptores de estrógenos en la regulación de la masa de células beta y alfa pancreáticas durante el embarazo. PROMETEOII/2015/016, 2015-2018, IP: Ángel Nadal.

Efectos del ambiente estrogénico materno en la masa y la función de la célula beta pancreática de la descendencia: implicaciones en la etiología de la diabetes. SAF2014-58335-P, 2015-2018, IP: Ángel Nadal.

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.

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.

Proyecto de Investigación de la Dra. Laura Marroquí Esclapez (Programa Juan de la Cierva Incorporación). Programa y Referencia: IJCI-2015-24482. Anualidad: 6000 €.

Descubrimiento de nuevas dianas terapéuticas para el tratamiento de la diabetes tipo 1 y diabetes tipo 2 basadas en estrategias de supervivencia de la célula alfa pacreática. Programa y Referencia: SEJI/2018/023, 2018-2020. IP: Laura Marroquí.

## R&D and Educational Committees.

Ángel Nadal. Member of the Direction Committee of CIBERDEM.

Ángel Nadal. Scientific Advisory Board-Food Packaging Forum Foundation, Zurich, Suiza.

## R&D Management.

Ángel Nadal. Colaborador de la División de Coordinación, Evaluación y Seguimiento Científico Técnico. Agencia Estatal de Investigación. Ministerio de Economía, Industria y Competitividad.

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

Iván Quesada Reviewer of the Sociedad Española de Diabetes (Ayudas SED a Proyectos de Investigación Básica).

Paloma Alonso-Magdalena. Reviewer of Universidad de Oviedo.

Paloma Alonso-Magdalena. Reviewer of Deakin University.

Laura Marroquí. Reviewer of Agencia Nacional de Promoción Científica y Tecnológica (Ministerio de Educación, Ciencia y Tecnología de Argentina).

## Scientific Society Councils.

Head of the Endocrine Disrupting Chemicals Advisory Group, Endocrine Society, USA.

## Editorial Boards.

Senior Editor Endocrine Connections. Ángel Nadal.

Reviewing Editor Frontiers in Endocrinology. Ángel Nadal.

Reviewing Frontiers in Neuroscience. Ángel Nadal.

Associate Editor Frontiers in Physiology. Ángel Nadal.

Editor Journal of Physiology and Biochemistry. Ángel Nadal.

Editor Plos One. Ángel Nadal.

Reviewer for the following journals in 2018: Molecular and Cellular Endocrinology, American Journal of Physiology-Endocrinology and Metabolism. Iván Quesada.

Reviewer for the following journals in 2018: International Journal of Molecular Sciences, Endocrine Connections, Environmental Research, Molecular and Cellular Endocrinology, Plos One, Frontiers in Endocrinology, Environmental Pollution, Environmental Science and Technology, Toxicology Letters, Ecotoxicology and Environmental Safety, Scientific Reports, Nutrients, Journal of Clinical Medicine, Chemosphere. Paloma Alonso-Magdalena.

Editor Scientific Reports. Paloma Alonso-Magdalena.

## Clinical pharmacology.

### Group name: IMMUNOPHARMACOLOGY.

We develop translational research on immunopharmacology. Our research projects are mostly devoted to study the mechanism of action and the

pharmacokinetic-pharmacodynamic relationship of drugs widely used in clinical practice in inflammatory diseases and cancer, especially in digestive diseases. In 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

## Postdoctoral Researchers.

José Manuel González-Navajas

## Ph. D Students.

Susana Almenara de Riquer

Beatriz Lozano Ruiz

## Publications.


Juanola O, Piñero P, Gómez-Hurtado I, Caparrós E, García-Villalba R, Marín A, Zapater P, Tarín F, González-Navajas JM, Tomás-Barberán FA, Francés R. Regulatory T Cells Restrict Permeability to Bacterial Antigen Translocation and Preserve Short-Chain Fatty Acids in Experimental Cirrhosis. Hepatol Commun. 2018, Oct 22;2(12):1610-1623. doi: 10.1002/hep4.1268.

Murcia O, Juárez M, Rodríguez-Soler M, Hernández-Lllán E, Giner-Calabuig M, Alustiza M, Egoavil C, Castillejo A, Alenda C, Barberá V, Mangas-Sanjuan C, Yuste A, Bujanda L, Clofent J, Andreu M, Castells A, Llor X, Zapater P, Jover R. Colorectal cancer molecular classification using BRAF, KRAS, microsatellite instability and CIMP status: Prognostic implications and response to chemotherapy. PLoS One. 2018, Sep 6;13(9):e0203051. doi: 10.1371/journal.pone.0203051.

Martínez-Cardona C, Lozano-Ruiz B, Bachiller V, Peiró G, Algaba-Chueca F, Gómez-Hurtado I, Such J, Zapater P, Francés R, González-Navajas JM. AIM2 deficiency reduces the development of hepatocellular carcinoma in mice. Int J Cancer. 2018, Dec 1;143(11):2997-3007. doi: 10.1002/ijc.31827.

Mangas-Sanjuan C, Zapater P, Cubiella J, Murcia Ó, Bujanda L, Hernández V, Martínez-Ares D, Pellisé M, Seoane A, Lanas Á, Nicolás-Pérez D, Herreros-de-Tejada A, Chaparro M, Cacho G, Fernández-Díez S, Marín-Gabriel JC, Quintero E, Castells A, Jover R; COLONPREV study investigators. Importance of endoscopist quality metrics for findings at surveillance colonoscopy: The detection-surveillance paradox. United European Gastroenterol J. 2018, May;6(4):622-629. doi: 10.1177/2050640617745458.

Gimenez P, Garcia-Martinez I, Francés R, Gonzalez-Navajas JM, Mauri M, Alfayate R, Almenara S, Miralles C, Palazon JM, Carnicer F, Pascual S, Such J, Horga JF, Zapater P. Treatment with non-selective beta-blockers affects the systemic inflammatory response to bacterial DNA in patients with cirrhosis. Liver Int. 2018, Dec;38(12):2219-2227. doi: 10.1111/liv.13890.

Zapater P. Genetic studies and alcoholic liver disease. Rev Clin Esp. 2018, May; 218(4):190-191. doi: 10.1016/j.rce.2018.03.007.

Roca R, Esteban P, Zapater P, Inda MD, Conte AL, Gómez-Escolar L, Martínez H, Horga JF, Palazon JM, Peiró AM. B2-adrenergic receptor functionality and genotype in two different models of chronic inflammatory disease: Liver cirrhosis and osteoarthritis. Mol Med Rep. 2018, Jun;17(6):7987-7995. doi: 10.3892/mmr.2018.8820.

Ranieri L, Contero C, Peral ML, Calabuig I, Zapater P, Andres M. Impact of diuretics on the urate lowering therapy in patients with gout: analysis of an inception cohort. Arthritis Res Ther. 2018, Mar

22;20(1):53. doi: 10.1186/s13075-018-1559-2.

de-Madaria E, Herrera-Marante I, González-Camacho V, Bonjoch L, Quesada-Vázquez N, Almenta-Saavedra I, Miralles-Maciá C, Acevedo-Piedra NG, Roger-Ibáñez M, Sánchez-Marin C, Osuna-Ligero R, Gracia Á, Llorens P, Zapater P, Singh VK, Moreu-Martín R, Closa D. Fluid resuscitation with lactated Ringer's solution vs normal saline in acute pancreatitis: A triple-blind, randomized, controlled trial. United European Gastroenterol J. 2018, Feb;6(1):63-72. doi: 10.1177/2050640617707864.

Gómez-Hurtado I, Gimenez P, García I, Zapater P, Francés R, González-Navajas JM, Manichanh C, Ramos JM, Bellot P, Guarner F, Such J. Norfloxacin is more effective than Rifaximin in avoiding bacterial translocation in an animal model of cirrhosis. Liver Int. 2018, Feb;38(2):295-302. doi: 10.1111/liv.13551.

## 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.

## Private funding. Contracts.

Estudio de la relación entre la activación sistémica inmunoinflamatoria-adrenérgica y los cambios en la estructura articular observados en pacientes con artrosis en diferentes estadios de evolución y con distintos tratamientos. Contrato para actividades de apoyo tecnológico entre la Universidad Miguel Hernández de Elche y Bioibérica S.A. 2018. IP: Pedro Zapater.

## Technical Services and Assistance.

Informe de experto para registro de un gel vaginal con estriol. Contrato para actividades de asesoramiento y asistencia técnica entre la Universidad Miguel Hernández de Elche y la Fundación Teófilo Hernando. 2018-2019. IP: Pedro Zapater.

Efecto de una leche infantil para lactantes suplementada con la CEPA BPL1 inactiva sobre la composición corporal: ensayo clínico multicéntrico y aleatorizado. Contrato para actividades de asesoramiento y asistencia técnica entre la Universidad Miguel Hernández de Elche y la Fundación Teófilo Hernando. 2018-2019. IP: Pedro Zapater.

Asesoramiento y asistencia técnica sobre el ensayo clínico titulado “Multicenter, Open-Label, Single Arm, Phase II Exploratory Study to Evaluate the Effect of a One-Year Consolidation Treatment with Ponatinib 15 mg on Treatment Free-Remission Rate in Patients with Philadelphia-Positive Chronic Myeloid Leukemia, who had previously Achieved a Deep Molecular Response with Imatinib. Contrato para actividades de asesoramiento y asistencia técnica entre la Universidad Miguel Hernández de Elche y la Fundación Teófilo Hernando. 2018-2019. IP: Pedro Zapater.

## Number of Congress Communications.

National contributions: 2

Oral presentations: 1.

Poster presentations: 1.

International contributions: 6.

Oral presentations: 3,

Poster presentations: 3.

## Group name: RECEPTORS AND MECHANISMS INVOLVED IN ANALGESIA.

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

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

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

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

## Staff.

Juan José Ballesta Payá

## Ph. D Students.

Luis Gómez Salinas

## Physicians from the General University Hospital of Alicante.

Yolanda Sastre Peris

## Invited Talks and Courses.

Tratamiento del dolor isquémico vascular con sevoflurano tópico. Luis Gómez Salinas. XV congreso de la Sociedad española del dolor. Palacio de Congresos de Palma de Mallorca. 26/5/2018.

Utilidad de los test viscoelásticos para la monitorización de la coagulación. Luis Gómez Salinas. II Jornada de Actualización en Anestesiología y Reanimación. Hospital Clínico Universitario Virgen de la Arrixaca y Universidad de Murcia. 09/10/2018.

## Number of Congress Communications.

National contributions: 4.

Poster presentations: 4.

# PhD THESES (2018).

Título: Herramientas para el estudio del dolor.

Autor: Maite Artero Morales.

Fecha de Lectura: 23/11/2018

Dirección: Antonio Ferrer Montiel.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1720005#

Título: Citoarquitectura y dinámica del citoesqueleto de F-actina en el proceso de secreción en el modelo neuroendocrino.

Autor: Yolanda Giménez Molina

Fecha de Lectura: 23/11/2018

Dirección: José Heliodoro Villanueva Roig

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1715796

# SEMINARS (2018).

Título: **Investigación en farmacocinética en preclínica, ensayos clínicos, y rutina clínica**.

Ponente / Institución: Dr. Ricardo Nalda. Universidad Miguel Hernández.

Viernes, 19 enero 2018.

Título: **¿Nosotros podemos hacer experimentos de biomedicina en el sincrotrón Alba?**

Ponente / Institución: Ana J. Pérez Berná. MISTRAL Beamline Experiments Division, ALBA Synchrotron Light Source, Cerdanyola del Vallès, Barcelona.

Lunes, 12 febreo 2018.

Título: **Nanoparticle-neuron interactions: molecular basis of neuronal activity modulation**.

Ponente / Institución: Carla Distasi. Department of Pharmacological Science, UPO, Italy.

Viernes, 16 de febrero 2018.

Título: **Trends and Opportunities in Food Fermentation**.

**Adulteration of Olives and olive oil.**

Ponente / Institución: Dra. Farah Hosseinian. Associate Professor, Institute of Biochemistry. Carleton University (Canadá).

Miércoles, 21 de febrero 2018.

Título: **My Journey from Medical Sciences to Business: A Marketing Primer for Biotec.**

Ponente / Institución: Dr. Michel Rod. Associate Dean, Research and International. Sprott School of Business, Carleton University (Canadá).

Miércoles, 21 de febrero 2018.

Título: **Presentación de las líneas de investigación del IBMC.**

Ponente / Institución: Profesores del Instituto de Biología Molecular y Celular.

Viernes, 23 de febrero 2018.

Título: **Molecular mechanism of angiogenesis adaptations to exercise in adipose tissue: basis of physical activity as efficient as anti-obesity therapy?**

Ponente / Institución: Dr. Catherine Riva. Laboratoire de Pharm-ecologie Cardiovasculaire. Université d'Avignon (France).

Martes, 27 de febrero 2018.

Título: **Cardiac ectopic fat depots and myocardial function: translational approach and effect of exercise training**

Ponente / Institución: Dr. Philippe Obert. Laboratoire de Pharm-ecologie Cardiovasculaire. Université d'Avignon (France).

Miércoles, 28 de febrero 2018.

Título: **"¿Son las plantas y los productos naturales recursos interesantes para la investigación farmacéutica?**

Ponente / Institución: Dr. Víctor López. Departamento de Farmacia, Facultad de Ciencias de la Salud. Universidad San Jorge (Zaragoza).

Viernes, 2 de marzo 2018.

Título: **Aproximaciones bioinformáticas en la identificación de marcadores de utilidad clínica en gliomas.**

Ponente / Institución: Dr. Víctor Manuel Barberá Juan Dr. Eduardo Larriba Tornel. Unidad de Genética Molecular, Hospital General Universitario de Elche.

Viernes, 13 de abril 2018.

Título: **¿Qué podemos hacer con NANOmateriales en un mundo MACROScópico?**

Ponente / Institución: Dra. María Antonia Herrero Chamorro.

Viernes, 18 de mayo 2018.

Título: **Respuesta inmunitaria de peces frente a Nodavirus.**

Ponente / Institución: Dr. Alberto Cuesta.

Viernes, 25 de mayo 2018.

Título: **Jerusalem artichoke: an ancient plant for future clean sugar.**

Ponente / Institución: Dra. Farah Hosseinian. Associate Professor, Institute of Biochemistry. Carleton University (Canadá).

Martes, 29 de mayo 2018.

Título: **Respuesta inmune en campo contra Piscirickettsia salmonis: Un desafió del PGSA en Chile.**

Ponente / Institución: Luis Alberto Mercado Vianco.

Miércoles, 3 de octubre 2018.

Título: **Fármacos metabolo-epigenéticos: Un nuevo paradigma en el abordaje del envejecimiento y el cáncer.**

Ponente / Institución: Prof. Javier Menéndez del Instituto de Oncología de Girona.

Miércoles, 5 de diciembre 2018.

Título: **Claves en la redacción de patentes para el sector biotecnológico y químico-farmacéutico.**

Ponente / Institución: Javier Agulló Pastor. Qualified European Patent Attorney.

Jueves, 13 de diciembre 2018.

# ANNUAL REPORT 2018

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

**UNIVERSITY "MIGUEL HERNÁNDEZ"**

Avda. de la Universidad s/n, Edificio Torregaitán
03202 Elche (Alicante). Spain.

**Phone:** (+34) 96 665 8759
**Fax:** (+34) 96 665 8478
https://idibe.es/

IDiBE
UNIVERSITAS
Miguel Hernández