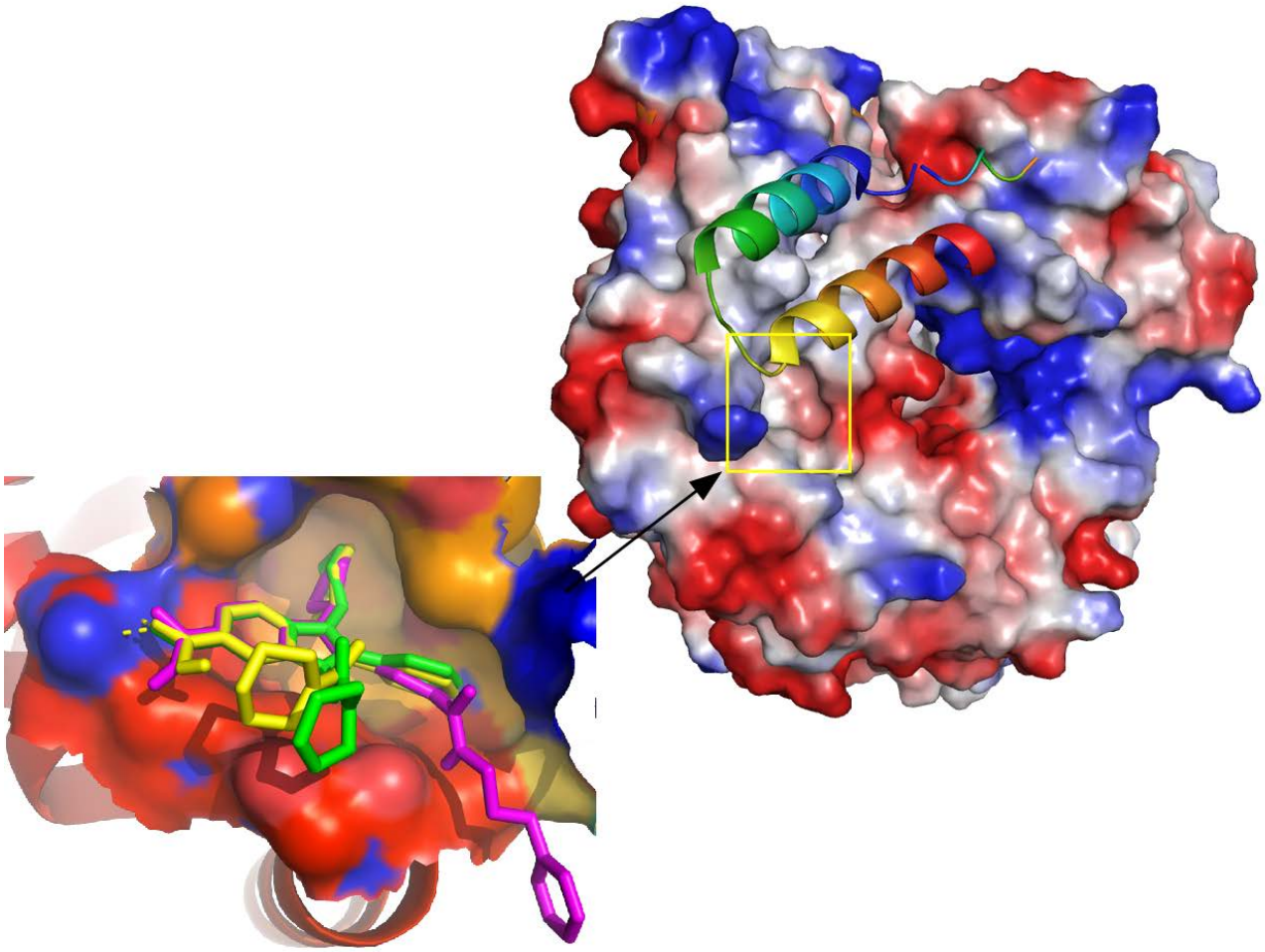
UNIVERSITAS Miguel Hernández

ANNUAL REPORT 2017



INSTITUTE OF MOLECULAR AND CELL BIOLOGY

UNIVERSITY "MIGUEL HERNÁNDEZ"

UNIVERSITAS Miguel Hernández

DIRECTOR'S FOREWORD

The Institute of Molecular and Cell Biology (IBMC) is one of the University Research Institutes at the University *Miguel Hernandez de Elche*. The IBMC is located in the University Campus in Elche, occupying a 4,000 sq. m. of laboratory in the Torregaitán Building. The Institute was created in 2002 from a transformation of the Center of Molecular and Cell Biology, thanks to the initiative and enthusiasm of its inspirator and first Director Prof. José Manuel González-Ros, who had the vision of creating a multidisciplinary research Institute in the University as a wise strategy to carry competitive and transferable research in the fields of Biomedicine and Biotechnology. This devotion to translational research has been a pivotal hallmark of the IBMC since its creation. As a result, in the past 18 years the IBMC has excelled in its scientific production, and remarkably 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 2017 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 2013-2017, that was extended for 2018.

Research groups have been active in securing funding from both governmental and private sources, publishing papers 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 have established a Master Degree in Biotechnology and Bioingeneering with the Institute of Bioingeneering that is becoming a national reference for the competences and skills tought. Notwithstanding, 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 a lead compound in phase II clinical trials in humans for pain intervention and rare diseases. To reinforce our translational activities, three 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 IBMC project.

Although we have walked a long and productive way, there is still plenty to achieve for increasing the IBMC international exposure and scientific translational excellence. In this regard, our extended Plan of Action (2017-2018), strengthens the original vision, and establishes the central mission to consolidate a multidisciplinary program in the areas of biotechnology and health. Since its implementation, we have strictly followed this plan and achieved up to 88% of the planned objectives. We will strongly continue with our comitment to become a reference Institute of transferable knowledge.

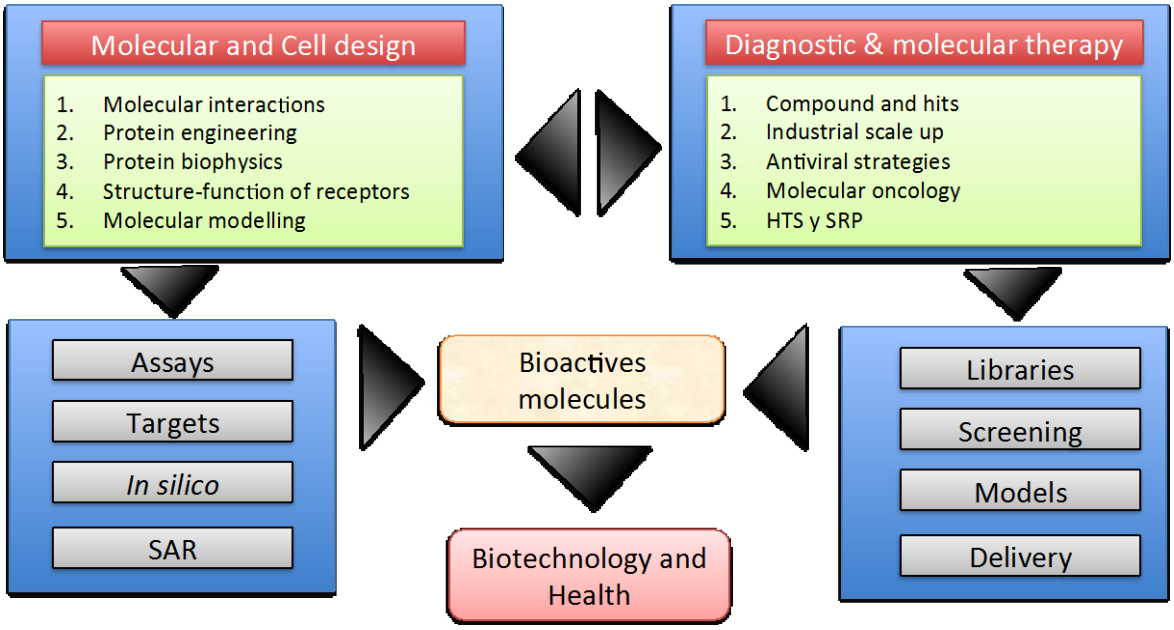
Prof. Antonio Ferrer-Montiel

IBMC Director

STRUCTURE AND GENERAL DESCRIPTION

The IBMC Scientific Program.

The IBMC 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 IBMC 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 IBMC 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.

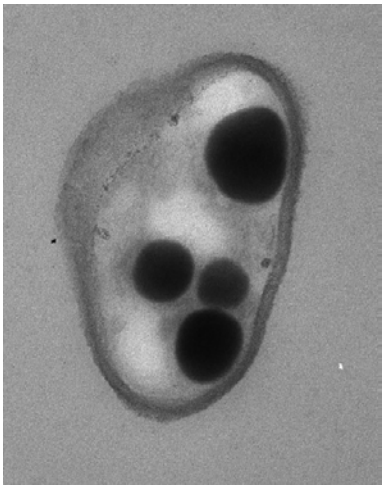
Molecular Recognition and Protein Biophysics and Engineering.

Group name: PROTEIN BIOTECHNOLOGY.

We develop basic research on the structure and folding of proteins by the acquisition of structural and thermodynamic data. Many of our results are oriented towards technological transfer, more precisely those dealing with the design of new antibiotics and the setup of novel systems of purification and immobilization of recombinant proteins. Our studies are centered basically in three lines:

1. Design, selection and evaluation of new antimicrobials against Streptococcus pneumoniae (pneumococcus) based on small molecules or in multivalent nanoparticles.

2. The C-LytA affinity tag, that serves as a model to study the folding and engineering of repeat proteins and constitutes an efficient affinity tag for the single-step chromatographic purification and immobilization of recombinant proteins from nano- to macrosurfaces, including enzymatic electrodes.



3.- Bioplastics. Natural, biodegradable plastics of bacterial origin that may constitute an alternative to the use of petroleum derivatives. We study the structure and function of several proteins involved in the synthesis, stability and degradation of these bioplastics, and the immobilization of proteins on these polymers.

Laboratory expertise includes:

- Thermodynamic analysis of protein stability.

- Spectroscopy (absorption, fluorescence, circular dichroism).

- Protein engineering.

- Nanobiotechnology.

Staff.

Jesús Miguel Sanz Morales

Manuel Sánchez Angulo (Visiting scientist)

Postdoctoral scientists.

Beatriz Maestro

Ph. D Students.

Emma Roig Molina

Technicians.

Maite Garzón Cabrerizo

Publications.

Sanz JM, Maestro B. Microbes go nano. Microb Biotechnol. 2017 Jan;10(1):17-18.

Maestro B, Sanz JM. Polyhydroxyalkanoate-associated phasins as phylogenetically heterogeneous, multipurpose proteins. Microb Biotechnol. 2017 Nov;10(6):1323-1337.

Governmental Projects and Funding.

Programa Estatal De Investigación, Desarrollo E Innovación Orientada A Los Retos De La Sociedad. Ministerio de Economía y Competitividad. "Remodelacion de la pared celular de Streptococcus pneumoniae: estudios estructurales de las proteinas StkP y LytA como objetivo para el desarrollo de nuevos antimicrobianos (BIO2016-79323-R; 2016-2019). IP: Jesús M. Sanz

Scientific and Educational Commities.

Miembro de tribunal evaluador del programa de Becas de Formación de Personal Investigador del Gobierno Vasco (2015-actualidad). Jesús M. Sanz

Vocal de la Comisión de Acreditación de Ciencias Experimentales de la Agencia de Evaluación del Sistema Universitario Vasco (2015-actualidad) Entidad de realización: Gobierno vasco. Jesús M. Sanz.

Number of Congress Communications.

National contributions: 1

Oral presentations: 1

International contributions: 4

Oral presentations: 3

Poster presentations: 1.

Editorial Boards.

Member of the Editorial Board of Microbial Biotechnology (Jesús M. Sanz).

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

Postdoctoral Scientists.

Rocío Esquembre Tomé

Ph. D Students.

Felipe Hornos Adán

Publications.

Neira JL, Bintz J, Arruebo M, Rizzuti B, Bonacci T, Vega S, Lanas A, Velázquez-Campoy A, Iovanna JL, Abián O. Identification of a drug targeting an intrinsically disordered protein involved in pancreatic adenocarcinoma. Sci. Reports, 2017, 7:39732.

Medina-Carmona E, Neira JL, Salido E, Fuchs JE, Palomino-Morales R, Timson DJ, Pey AL Site-to-site interdomain communication may mediate different loss-of-function mechanisms in a cancer-associated NQO1 polymorphism. Sci. Reports, 2017, 7:44532.

Neira JL, Cámara-Artigas, A. Trifluoroethanol-induced conformational transition of the c-terminal sterile alpha motif (SAM) of human p73. Arch. Biochem. Biophysics, 2017, 619: 1-9.

Forcada-Nadal A, Palomino-Schätzlein M, Neira JL, Pineda-Lucena A, Rubio V The PIPX protein, when not bound to its targets, has its signaling c-terminal helix in a flexed conformation. Biochemistry 2017, 56: 3211-3224

Neira JL, Florencio FJ, Muro-Pastor MI The isolated, twenty-three-residue-long, N-terminal region of the glutamine synthetase inactivating factor binds to its target. Biophysical Chemistry 2017, 228: 1-9.

Hinck, A, Neira JL An introduction to the special issue on biomolecular NMR. Arch. Biochem. Biophysics, 2017, 628: 1-2.

Santofimia-Castaño P, Rizzuti B, Pey AL, Soubeyran P, Vidal M, Urrutia R, Iovanna JL, Neira JL Intrinsically disordered chromatin protein NUPR1 binds to the c-terminal region of polycomb RING1B. Proc Natl. Acad Sci. USA, 2017.

Medina-Carmona E, Fuchs JE, Gavira JA, Mesa-Torres N, Neira JL, Salido E, Palomino-Morales R, Burgos M, Timson DJ & Pey AL Enhanced vulnerability of human proteins towards disease-associated inactivation through divergent evolution. Human Mol Genet 2017, 26: 3531-3544.

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.

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).

Scientific and Educational Commities.

- CONYCET, Argentina. José L. Neira.

- Israeli Science Foundation. José L. Neira.

- Czech Science Foundation. José L. Neira.

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

Ph. D Students.

Rebeca Vázquez Guilló

Amalia Mira Picó

Technicians.

Elisa Pérez García

Publications.

Z. Kahveci, M. J. Martínez-Tomé, R. Mallavia and C. Reyes Mateo. Fluorescent Biosensor for Phosphate Determination Based on Immobilized Polyfluorene-Liposomal Nanoparticles Coupled with Alkaline Phosphatase. Applied Materials & Interfaces, 9, 136 – 144. 2017.

Mira, A., Mateo, C.R., Mallavia, R., Falco, A. Poly(methyl vinyl ether-alt-maleic acid) and ethyl monoester as building polymers for drug-loadable electrospun nanofibers. Scientific Reports vol 7(1), 172015. 2017.

Science dissemination: outreach activities.

Jornadas de divulgación científica "Ciencia con tapas".

- ¿Se puede vencer el dolor crónico?, 05-04-2017

- Jugando a ser médicos: el autodiagnóstico cibernético y la cibercondria, 12-06-2017.

- Alimentos del siglo XXI: verdades y mentiras, 19-05-2017.

Mª José Martínez Tomé. Comité organizador.

PhD Theses.

Diseño de sistemas poliméricos nanoestructurados transportadores para aplicaciones biomédicas. Programa: Programa de Doctorado en Biología Molecular y Celular 1393/2007. Amalia Mira Carrió. Supervisor: Ricardo Mallavia y Alberto Falcó. 15/09/2017.

Governmental Projects and Funding.

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

Ministerio de Economía, industria y Competitividad. "Diseño de nanomateriales fluorescentes para el desarrollo de nuevas formulaciones terapéuticas y descubrimiento de nuevos fármacos". (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 muestras, identificación de sustancia clave e informe técnico. Prestaciones de servicio. (1090/17-242/18), Particular: Samuel Sanchez Gonzalez. Universidad Miguel Hernández. (2 meses Nov/2017; Feb 2018), IP: R. Mallavia Marín.

Number of Congress Communications.

National contributions: 2.

Poster presentations: 2.

International contributions: 5.

Poster presentations: 5.

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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

Marcela Giudici

Technicians.

Eva Martínez

Publications.

Montoya E., Renart M.L., Giudici A.M., Poveda J.A., Fernandez. A.M., Morales A. and González-Ros J.M. Differential binding of monovalent cations to KcsA: deciphering the mechanisms of potassium channel selectivity. BBA Biomembranes 1859, 779-788 (2017).

Poveda J.A.; Giudici A.M.; Renart M.L.; Morales A and Gonzalez-Ros J.M. Towards understanding the molecular mechanisms of ion channel modulation by lipids: mechanistic models and current paradigms. BBA Biomembranes 1859, 1507-1516 (2017).

Renart M.L., Montoya E., Giudici A.M., Poveda J.A., Fernandez. A.M., Morales A. and González-Ros J.M. Selective exclusion and selective binding contribute to ion selectivity in KcsA, a model potassium channel. J. Biol. Chem. 292, 15552-15560 (2017).

Governmental Projects and Funding.

Bases Moleculares de la Modulación de

Awards.

Premio "Universidad Miguel Hernández" al Rendimiento Investigador (J. M. González Ros, Primer clasificado, Edición 2016).

Number of Congress Communications.

National contributions: 1

Poster presentations: 1

Molecular modeling platform.

Group name: STRUCTURAL BIOCOMPUTING.

The platform for molecular modeling and virtual screening arises as a unit that brings the capabilities of groups in bioinformatics methods based on biomolecular structures. Its mission is to integrate efforts to the use (databases) or the construction of macromolecular structures (homology modeling) to be used for rational protein modification (computer design), to determine protein interaction maps (protein-protein interactions), or to identify novel active compounds (molecular docking and virtual screening) from libraries of compounds (chemical libraries). Additionally, simulation (Molecular Dynamics) recreates the macromolecules in their native environment, including lipids, water and ions.

The high resolution (3D) structural data are used to extract useful information about protein-protein interactions to elucidate protein interaction networks, and to understand the formation of the macromolecular complex. The modeling of macromolecular structures, in which the target is treated as a single molecule or a ligand-receptor complex, allows the determination of structure-function relationships of the soluble and membrane proteins, mechanical molecular simulations of complex systems, the binding ligand, or even enzyme mechanism.

For this purpose, there is dedicated room endowed with an air-conditioned machine and a proper electrical installation to house two high performance servers and two "cluster" of computers with 182 processors, as well as the programs needed to address the management, editing and modification of macromolecules.

The combination of the experimental techniques of high throughput screening (HTS) with computational techniques and virtual screening bioinformatics open ways for high performance research, because the computational in silico calculations determine quickly and economically those families of compounds capable of exerting a biological effect with the chosen targets, whereas with experimental screening techniques the parameters of interaction between ligands and receptors are quantified. Once certain lead compounds, and again using computational techniques, the ligands can be redesigned to increase the specificity of action, the affinity, or both.

Staff.

Gregorio Fernández-Ballester (IBMC-UMH).

José Antonio Encinar (IBMC-UMH).

Vicente Galiano Ibarra (Departamento de Física y Arquitectura de Computadores, UMH).

Ph.D Students.

Magdalena Nikolaeva Koleva

Publications.

Jiménez-Sánchez, C., Olivares-Vicente, M., Rodríguez-Pérez, C., Herranz-López, M., Lozano-Sánchez, J., Segura-Carretero, A., Fernández Gutiérrez, A., Encinar, J.A., Micol, V. AMPK modulatory activity of olive–tree leaves phenolic compounds: Bioassay-guided isolation on adipocyte model and *in silico* approach. 2017. PLoS ONE 12(3): e0173074.

Ruiz-Torres, V., Encinar, J.A., Herranz López, M., Perez-Sánchez, A., Galiano, V., Barrajón-Catalán, E., Micol, V. An updated review on marine anticancer compounds: the use of virtual screening for the discovery of small-molecule cancer drugs. 2017. Molecules 22(7), 1037.

Micol, V. and Encinar, J.A. Nutraceuticals molecular targets (II). A novel way of approaching health by using nutraceuticals: Combined -omics and virtual screening. 2017. Agro FOOD Industry Hi Tech - vol. 28(2) - March/April 2017.

Herranz-López, M., Olivares-Vicente, M., Encinar, J.A., Barrajón-Catalán, E., Segura-Carretero, A., Joven, J. and Micol, V. Multi-targeted molecular effects of Hibiscus sabdariffa polyphenols: an opportunity for a global approach to obesity. 2017. Nutrients, 9(8), 907.

Bello-Perez, M., Falco, A., Medina-Gali, R., Pereiro, P., Encinar, J.A., Novoa, B., Perez, L., Coll, J. Neutralization of viral infectivity by zebrafish C-reactive protein isoforms. 2017. Molecular Immunology 91: 145-155.

Micol, V., Encinar, J.A. and Herranz-López, M. Nutraceuticals molecular targets (III) – targeting protein receptors with polyphenols as new anti-obesity therapies. 2017. Agro FOOD Industry Hi Tech - vol. 28(5) - September/October 2017.

R de la Torre-Martínez, MA Bonache, PJ Llabrés-Campaner, B Balsera, A Fernandez-Carvajal, G Fernandez-Ballester, A Ferrer-Montiel, MJ Pérez de Vega, R Gonzalez-Muniz. Synthesis, high-throughput screening and pharmacological characterization of β–lactam derivatives as TRPM8 antagonists. Scientific reports. (2017) 7:10766.

Governmental Projects and Funding.

Searching for applications of fish innate memory ("trained immunity"): immunomodulators, therapeutic agents and vaccines. Convocatoria 2014 - Proyectos I+D+I - Programa Estatal de Investigación, Desarrollo e Innovación orientada a los retos de la sociedad. Ref.: AGL2014-51773-C3-1-R. N° invest. 3. Investigador coordinador: Dr. Luiz Pérez. Subvención concedida: 140.000 euros. Fechas: 2015-2017. Entidad

financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

Nutraceúticos de 2ª generación de plantas comestibles basados en extractos polifenólicos moduladores del metabolismo energético: aplicaciones en la prevención de la obesidad. Convocatoria 2016 - Proyectos I+D+I - Programa Estatal de Investigación, Desarrollo e Innovación orientada a los retos de la sociedad. Ref.: AGL2015-67995-C3-1-R. Nº invest. 3. Investigador coordinador: Dr. Vicente Micol. Subvención concedida: 127.050 euros. Fechas: 2016-2018. Entidad financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

El carácter multifactorial de los polifenoles: una oportunidad para el desarrollo de herramientas terapéuticas frente a la obesidad y las enfermedades infecciosas. Ref.: PROMETEO/2016/006. Nº invest. 6. Investigador coordinador: Dr. Vicente Micol. Subvención concedida: 219.478 euros. Fechas: 2016-2019. Entidad financiadora: Ministerio de Ciencia e Innovación. Investigador: J.A. Encinar.

Mecanismos de modulación funcional de los canales termoreceptores en la patogénia del dolor crónico: Diseño de nuevas intervenciones terapéuticas (TRPAIN) (PROMETEOII/2014/011). IP: Antonio Ferrer Montiel. 2014-2017. UMH. Investigador: G.J. Fernández-Ballester.

Sensibilización algésica de nociceptores en dolor crónico: mecanismos e intervención farmacológia. IP: Antonio Ferrer Montiel. 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. Investigador: G.J. Fernández-Ballester.

Private funding: Contracts.

Adenda al contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Antalgenics SL (ANTALGENICS4.16D; 28/10/2016). Finalización: 30/04/2017. IP: G. Fernandez-Ballester. Instituto de Biología Molecular y Celular. UMH.

PhD Theses.

Cambios a nivel epigenético y proteómico en pez cebra en respuesta a la infección con virus de la viremia primaveral de la carpa (SVCV). Regla María Medina Gali. Universidad Miguel Hernández de Elche. 03/07/2017. Dirección: Perez Garcia Estañ, Luis (Director), Ortega-Villaizán Romo, María del Mar (Codirector), Encinar Hidalgo, José Antonio (Codirector).

Scientific and Educational Commities.

Agencia Nacional de Evaluación de la Calidad y Acreditación (ANECA). J.A. Encinar.

Number of Congress Communications.

International contributions, poster presentations: 10.

National contributions, poster presentations: 6.

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.

Personal.

Vicente Micol Molina, IP

Domingo Saura López

Nuria Martí Bruña

Enrique Barrajón Catalán

Manuel Valero Roche

María Herranz López

Postdoctoral Fellows.

Salud Vegara Gómez

Almudena Pérez López

Ph. D Students.

Verónica Ruiz Torres

Mariló Olivares Vicente

Luz Agulló Chazarra

Sara Gea Botella

Technicians.

Mª Teresa Garzón Cabrerizo

Publications.

Cádiz-Gurrea, ML, Alañón-Pardo, E., Arráez-Román, D., Fernández-Arroyo, S., Micol, V. Roche, E., Segura-Carretero, A. Bioactive compounds from Lippia citriodora: Application in diseases prevention. In Occurrences, Structure, Biosynthesis, and Health Benefits Based on Their Evidences of Medicinal Phytochemicals in Vegetables and Fruits (Vol. 7). Motohashi, N. (series editor). Nova Science Publishers, NY, USA. 2017

Martínez, A., Vegara, S., Herranz-López, M., Martí, N.; Valero, M., Micol, V., Saura, D. Kinetic changes of polyphenols, anthocyanins and antioxidant capacity in forced aged hibiscus ale beer. Journal of the Institute of Brewing 2017. doi.org/10.1002/jib.387.

Ruiz-Torres V.; Encinar J.A.; Herranz-López M.; Pérez-Sánchez A.; Galiano V.; Barrajón-Catalán E.; Micol V. An Updated Review on Marine Anticancer Compounds: The Use of Virtual Screening for the Discovery of Small-Molecule Cancer Drugs. Molecules. 22(7):1037. 2017.

Herranz-López M, Borrás-Linares I, Olivares-Vicente M, Gálvez J, Segura-Carretero A, Micol V. Correlation between the cellular metabolism of quercetin and its glucuronide metabolite and oxidative stress in hypertrophied 3T3-L1 adipocytes. Phytomedicine 25:25-28. 2017.

Pérez-Sánchez; I. Borrás-Linares; E. Barrajón-Catalán; D. Arráez-Román; I. González-Álvarez; E. Ibáñez; A. Segura-Carretero; M. Bermejo; V. Micol. Evaluation of the intestinal permeability of rosemary (Rosmarinus officinalis L.) extract polyphenols and terpenoids in Caco-2 cell monolayers. Plos One. 12(2): e0172063. 2017.

MB Ibitihel; MH Hussan-Qasem; E Barrajón-Catalán; V Micol; JV García-Pérez; MA Ayadi. Kinetic improvement of olive leaves' bioactive compounds extraction by using power ultrasound in a wide temperature range. Ultrasonic sonochemistry. 34:466-473. 2017.

M. Herranz-López; M. Olivares-Vicente; J.A. Encinar; E. Barrajón-Catalán; A. Segura-Carretero; J. Joven; V. Micol. Multi-Targeted Molecular Effects of Hibiscus sabdariffa Polyphenols: An Opportunity for a Global Approach to Obesity. Nutrients. 9(8):907. 2017.

Fernández-Ochoa; I. Borrás-Linares; A. Pérez-Sánchez; E. Barrajón-Catalán; I. González-Álvarez; D. Arráez-Román; V. Micol; A. Segura-Carretero. Phenolic compounds in rosemary as potential source of bioactive compounds against colorectal cancer: In situ absorption and metabolism study. Journal of Functional Foods. 33:202-210. 2017.

Di Bari C; Forni C; Di Carlo A.; Barrajón-Catalán E.; Micol V.; Teolli F.; Nota P; Matteocci F.; Frattarelli A.; Caboni E.; Lucioli S. Pigments for natural dye-sensitized solar cells from in vitro grown shoot cultures. Journal of Photonics for Energy. 7(2): 025503. 2017.

O. Tahiri; D. Atmani-Klani; S. Sánchez-Fidalgo; M. Aparicio-Soto; C. Alarcó-de-la-Lastra; E. Barrajón-Catalán; V. Micol; D. Atmani. The flavonol-enriched Cistus albidus chloroform extract possesses in vivo anti-inflammatory and anti-nociceptive activity. Journal of Ethnopharmacology. 209, 210-218. 2017.

Carrera-Quintanar L, Funes L, Sánchez-Martos M, Martinez-Peinado P, Sempere JM, Pons A, Micol V, Roche E. Effect of a 2000-m running test on antioxidant and cytokine response in plasma and circulating cells. J. Physiol. Biochem 73(4):523-530. 2017

Valdés A, García-Cañas V, Pérez-Sánchez A, Barrajón-Catalán E, Ruiz-Torres V, Artemenko KA, Micol V, Bergquist J, Cifuentes A. Shotgun proteomic analysis to study the decrease of xenograft tumor growth after rosemary extract treatment. J Chromatogr A. 1499:90-100. 2017.

Castro-Puyana M, Pérez-Sánchez A, Valdés A, Ibrahim OHM, Suarez-Álvarez S, Ferragut JA, Micol V, Cifuentes A, Ibáñez E, García-Cañas V. Pressurized liquid extraction of Neochloris oleoabundans for the recovery of bioactive carotenoids with anti-proliferative activity against human colon cancer cells. Food Res Int. 99(Pt 3):1048-1055. 2017.

Khemakhem I, Ahmad-Qasem MH, Catalán EB, Micol V, García-Pérez JV, Ayadi MA, Bouaziz M. Kinetic improvement of olive leaves' bioactive compounds extraction by using power ultrasound in a wide temperature range. Ultrason Sonochem. 34:466-473. 2017.

Jiménez-Sánchez C, Olivares-Vicente M, Rodríguez-Pérez C, Herranz-López M, Lozano-Sánchez J, Segura-Carretero A, Fernández-Gutiérrez A, Encinar JA, Micol V. AMPK modulatory activity of olive-tree leaves phenolic compounds: Bioassay-guided isolation on adipocyte model and in silico approach. PLoS One 12(3):e0173074. 2017.

Micol, V. Nutraceuticals molecular targets (I). The divorce between legislation, market and science. Agro FOOD Industry Hi-Tech 28(2): 52-53. 2017.

Micol, V; Encinar, J.A. Nutraceuticals molecular targets (II). A novel way of approaching health by using nutraceuticals: Combined -omics and virtual screening. Agro FOOD Industry Hi-Tech 28(4): 12-13. 2017.

Micol, V; Encinar, J.A; Herranz, M. Nutraceuticals molecular targets (III). Targeting protein receptors with polyphenols as new anti-obesity therapies. Agro FOOD Industry Hi-Tech 28(5): 44-45. 2017.

Losada-Echeberría M, Herranz-López M, Micol V, Barrajón-Catalán E. Polyphenols as Promising Drugs against Main Breast Cancer Signatures. Antioxidants (Basel) 6(4). pii: E88 (2017).

Patents.

Inventores: Vegara-Gómez, S., Martínez, R., Barrajón-Catalán, E., Micol, V., Saura, D., Berenguer-Martínez, M.D.R., Martí, N., Valero, M. Título: Extracción de compuestos biológicamente activos a partir de residuos de la industria de la vinificación. Titular: UMH. Fecha concesión: 21/09/2017.

Inventores: Enrique Roche, María Herranz, Vicente Micol, Nuria Caturla, Jonathan Jones. Título: Composición para el control del peso a través de la modulación de los niveles de péptidos involucrados en saciedad y/o apetito. Titular: Monteloeder. Registros: 20170294/2026 (Fecha solicitud:

25/09/2017). Fecha concesión: pendiente. Referencia patente: P201731147.

PhD Theses.

In vitro and *in vivo* anticancer activity of a *Rosmarinus officinalis* L. extract in colon cancer cell models. Almudena Pérez Sánchez. Supervisors: Enrique Barrajón-Catalán and Vicente Micol Molina. 28/04/2017.

Science dissemination: outreach activities.

Feria de la Ciencia de Torrevieja. Uso de plantas medicinales para combatir la obesidad: mecanismo de acción y dianas moleculares. Vicente Micol. 07/11/2017.

Feria de divulgación científica "Un paseo por la Ciencia". "Valoración nutricional de la dieta", "Medidas del índice de masa corporal y porcentaje de grasa", y "Recomendaciones diarias de alimentos (con base científica)". Enrique Barrajón Catalán y María Herranz López. 11/11/2017.

Number of Congress Communications.

National contributions, oral presentations: 1 and poster presentations: 1.

International contributions, oral presentations: 1 and poster presentations: 19.

Awards.

Premio de investigación doctoral "Profesora Amparo Estepa" UMH. Theses: In vitro and in vivo anticancer activity of a Rosmarinus officinalis L. extract in colon cancer cell models. Almudena Pérez Sánchez. Supervisors: Enrique Barrajón-Catalán and Vicente Micol Molina. 28/04/2017.

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: Dirección General de Investigación. MICINN (AGL2015-67995-C3-1-R). Cantidad concedida: 127.050 €. Duración: 01/01/2016-31/12/2018. Investigador responsable: 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: 51.050 € (2016), 62.655 € (2017), 43.738 € (2018), 62.034 € (2019). Total: 219477 €. Duración: 01/01/2016 – 31/12/2019. Investigador responsable: 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: 15.000 €. Duración: 01/11/2017-31/08/2019. Investigador responsable: Vicente Micol.

Título del proyecto: Subprograma CIBER. Instituto de Salud Carlos III (ISCIII). Spanish Ministry of Health. Fisiopatología de la Obesidad y la Nutrición, CIBERobn, Spain (CIBER: CB12/03/30038). Entidad financiadora: Instituto de Salud Carlos III (ISCIII). Duración: 01/01/2015-31/12/2017. Investigador responsable: J. A. Tur (participan Vicente Micol y Enrique Roche por la UMH).

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. Cantidad concedida: 120.000 €. Duración: 01/09/2015-01/09/2019. Investigador responsable: Vicente Micol. Participan como investigadores: Enrique Barrajón y María Herranz.

Título del proyecto: Cátedra de empresa: "Bioestimulantes Naturales". Entidad financiadora: Grupo AGROTECNOLOGÍA (IBERFOL, SL). Cantidad concedida: 30.000 €. Duración: 12/05/2017-12/05/2018. Investigador responsable: Vicente Micol (Director de la Cátedra).

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 (IBERFOL, SL). Cantidad concedida: 15.175 €. Duración: 28/09/2017-28/03/2018. Investigador responsable: Enrique Barrajón. Participa como investigador: Vicente Micol.

Título del proyecto: Contrato para la realización del proyecto "Desarrollo de estrategias antimicrobianas y de esterilización". Entidad financiadora: MITRA SOL TECHNOLOGIES SL. Cantidad concedida: 3.750 €. Duración: 28/11/2016-27/11/2017. Investigador responsable: Domingo Saura. Participan como investigadores: Vicente Micol, Enrique Barrajón y María Herranz.

Título del proyecto: Contrato para la realización del trabajo "Caracterización de preparaciones a base de extractos de uso agrícola como biofertilizantes y biocidas". Entidad financiadora: AGROZYMES, SL. Cantidad concedida: 12.000 € Duración: 22/11/2016-21/11/2017. Investigador responsable: Domingo Saura. Participan: Vicente Micol.

Private funding: Technical Services and Assistance.

Vicente Micol. Technical Assistance to Monteloeder SL.

Vicente Micol, Enrique Barrajón, María Herranz. Technical Assistance to Invitrotecnia SL.

Editorial Boards.

AgroFOOD Industry Hi Tech – Teknoscience (2010-2012). V. Micol.

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

Ph. D Students.

Maite Artero Morales

Gloria Briceño

Verónica Rivero Hernández

Eva Villalba

Simiona Giorgi

Technicians.

Irene Mudarra Fraguas

Antonio Manuel Zafra Pinto

Publications.

R de la Torre-Martínez, MA Bonache, PJ Llabrés-Campaner, B Balsera, A Fernandez-Carvajal, G Fernandez-Ballester, A Ferrer-Montiel, MJ Pérez de Vega, R Gonzalez-Muniz. Synthesis, high-throughput screening and pharmacological characterization of β–lactam derivatives as TRPM8 antagonists. Scientific reports. (2017) 7:10766.

E Montoya, ML Renart, AM Giudici, JA Poveda, Asia M Fernandez, A Morales and JM Gonzalez-Ros. Differential binding of monovalent cations to KcsA: Deciphering the mechanisms of potassium channel selectivity. Biochim Biophys Acta. (2017) 1859(5):779-788.

ML Renart, E Montoya, AM Giudici, JA Poveda, Asia M Fernandez, A Morales and JM Gonzalez-Ros. Selective exclusion and selective binding contribute to ion selectivity in KcsA, a model potassium channel. J. Biol. Chem. (2017) 292(37):15552-15560.

S Quarta, M Camprubí-Robles, R Schweigreiter, D Matusica, RV Haberberger, RL Proia, CE Bandtlow, A Ferrer-Montiel, M Kress. Sphingosine-1-Phosphate and the S1P3 Receptor Initiate Neuronal Retraction

via RhoA/ROCK Associated with CRMP2 Phosphorylation. Front Mol Neurosci. (2017) 10:317.

MG Ciardo, A Ferrer-Montiel. Lipids as central modulators of sensory TRP channels. Biochim Biophys Acta. (2017) 1859 (9 Pt B):1615-1628.

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: EP17382266.

Inventores: Antonio Ferrer Montiel, A. Fernández-Carvajal, R. de la Torre, M.A. Juana Gallar, Carlos Belmonte, Gian Cesare Tron, Valentina Mercali, Armando Genazzani. Título: Compuestos agonistas del receptor trpm8 y sus aplicaciones. Titular: UMH. Registros: PCT/ES2017/070026

PhD Theses.

Título: Identificación de moduladores de canales de sodio activados por voltaje. Verónica Rivero Hernández. Supervisor: Antonio Ferrer-Montiel. 1 septiembre 2017.

Organization of Meetings.

16th International Congress of SBE. Comité Científico. 6-8 de junio 2017. Sevilla, España.

VI Reunión Red Nacional de Canales Iónicos. Comité Científico. 6-8 de septiembre 2017. Santiago Compostela, España.

6th Worshop in Biophysics and Molecular Biology of Ion Channels and Transporters. Comité Científico. 10-13 de septiembre 2017. Seté, Francia.

Invited Talks and Courses.

37th Congreso de la SEF/BPS. Conferencia clausura: A novel pharmacological paradigm for chronic pain. Foro del Emprendedor. Barcelona (Spain). Junio, 2017

Science Dissemination: Outreach Activities.

Ciencia con Tapas. Monthly outreach activity of IBMC.

IX Jornadas de San Alberto. Facultad de Ciencias Experimentales. UMH. 15 noviembre 2017.

Jornadas de Puertas Abiertas del IBMC. 7 julio 2017.

I FORO DE INNOVACION PROVINCIA DE ALICANTE /INNOVATE-T. Desarrollo de nuevos compuestos activos para tratamientos de alergias de contacto. Octubre 2017.

Number of Congress Communications.

National contributions, poster presentations: 4.

International contributions, poster presentations: 5.

Awards.

Placa de Honor de la Asociación Española de Científicos. Antonio Ferrer Montiel. 23 noviembre 2017.

Governmental Projects and Funding.

Mecanismos de modulación funcional de los canales termoreceptores en la patogénia del dolor crónico: Diseño de nuevas intervenciones terapéuticas (TRPAIN) (PROMETEOII/2014/011). 2014-2017. UMH. IP: Antonio Ferrer Montiel.

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)

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

Private funding: Contracts.

Adenda al contrato para la realización del trabajo "Modelización molecular de interacciones proteína-proteína en el receptor muscarínico de acetilcolina". Antalgenics SL (ANTALGENICS4.16D; 28/10/2016). Finalización: 30/04/2017. IP: G. Fernandez-Ballester. Instituto De Biología Molecular Y Celular. UMH.

Adenda al contrato para la realización de un proyecto de investigación y desarrollo titulado "Identificación y desarrollo de

productos cosméticos". Funded by LIPOTEC S.A. (DIVERDRUGS1.17D). IP: Antonio Ferrer Montiel. Instituto de Biología Molecular y Celular. UMH.

Identificación y Desarrollo moduladores TRPV1. AntalGenics, SL. 2017. IP: Antonio Ferrer Montiel. Instituto de Biología Molecular y Celular. UMH.

Identificación y Desarrollo De Productos Cosméticos. Diverdrugs, SL. 2017. IP: Antonio Ferrer Montiel. Instituto de Biología Molecular y Celular. UMH.

Technical Services and Assistance.

Antonio Ferrer Montiel. Technical Assistance to AntalGenics SL

Scientific Society Councils.

Red Nacional de Canales Iónicos. Coordinador: Antonio Ferrer Montiel. (2011-2017).

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

Editorial Boards.

Journal of Pharmacological Sciences (2017). A. Ferrer.

The Open Journal of Pain (2017). A. Ferrer.

Frontiers in Pharmacology (2017) A. Ferrer.

Frontiers in Neurosciences (2017) A. Ferrer.

Scientific Reports (2014-2017). A. Fernandez-Carvajal.

Frontiers in Physiology (2015-2017) 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

Ph. D Students.

Melissa Belló Pérez

PhD Theses.

Cambios a nivel epigenético y proteómico en pez cebra en respuesta a la infección con virus de la viremia primaveral de la carpa (SVCV). Regla María Medina Gali. Universidad Miguel Hernández de Elche. 03/07/2017. Dirección: Perez Garcia Estañ, Luis (Director), Ortega-Villaizán Romo, María del Mar (Codirector), Encinar Hidalgo, José Antonio (Codirector).

Technicians.

Ángeles Gómez

Publications.

Ricardo Parreño, Lucía Almagro, Melissa Belló-Perez, Regla M. Medina-Gali, Amparo Estepa & Luis Perez. Restricted replication of viral hemorrhagic septicaemia virus (VHSV) in a birnavirus-carrier cell culture. Arch. Virol (2017)162: 1037-1041.

Melissa Belló-Perez, Alberto Falcó, Regla Medina, José A. Encinar, Beratriz Novoa, Luis Perez, Amparo Estepa, Julio Coll. Structure and functionalities of the human c-reactive protein compared to the zebrafish multigene family of c-reactive-like proteins. Dev. Comp. Immunol. (2017) 69: 33-40.

Melissa Belló-Perez, Alberto Falcó, Regla Medina-Gali, Patricia Pereiro, José A. Encinar, Beratriz Novoa, Luis Perez, Julio Coll. Neutralization of viral infectivity by zebrafish c-reactive protein isoforms. Mol. Immunol. (2017) 91: 145-155.

Governmental Projects and Funding.

Project: Buscando aplicaciones para la memoria innata ("trained immunity") en peces: inmunomoduladores, agentes terapeùticos y vacunas. Proyectos de I+D+I "Retos de la sociedad" - MINECO 2014\AGL2014-51773-C3-1-R.

Number of Congress Communications.

International contributions, poster presentations: 1 and oral presentations: 1.

Science dissemination: outreach activities.

Contraste de Fases. UMH-Radio broadcast on science.

Group name: ENVELOPED VIRUSES. BIOMEMBRANES, PROTEINS AND DESIGN ON NOVEL ANTIVIRALS.

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

Vicente Galiano Ibarra

Postdoctoral Fellows.

Enmanuel Fajardo Sánchez

Publications.

Fajardo-Sánchez E, Galiano V, Villalaín J. Spontaneous membrane insertion of a

dengue virus NS2A peptide. Arch Biochem Biophys. 2017 Aug 1; 627:56-66.

Fajardo-Sánchez E, Galiano V, Villalaín J. Location of the bioactive pentacyclic triterpene ursolic acid in the membrane. A molecular dynamics study. J Biomol Struct Dyn. 2017 Sep; 35(12):2688-2700.

Fajardo-Sánchez E, Galiano V, Villalaín J. Molecular dynamics study of the membrane interaction of a membranotropic dengue virus C protein-derived peptide. J Biomol Struct Dyn. 2017 May;35(6):1283-1294.

Governmental Projects and Funding.

Caracterizacion de la interacción proteína-membrana en el virus del dengue. una herramienta para el desarrollo de antivirales (BFU2013-43198-P).

Number of Congress Communications.

National contributions: 2 Poster.

Group name: FISH ERYTHROCYTES 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 Fellows.

Verónica Chico Gras

Ph. D students.

Iván Nombela Díaz

Sara Puente Marín

Publications.

I Nombela; S Puente-Marin; V Chico; AJ Villena; B Carracedo; S Ciordia; MC Mena; L Mercado; L Perez; J Coll; A Estepa; M Ortega-Villaizan (2017). Identification of diverse defense mechanisms in rainbow trout red blood cells in response to halted replication of VHS virus. F1000Research. 6 - 1958.

I Nombela; A Carrion; S Puente-Marin; V Chico; L Mercado; L Perez; J Coll; M Ortega-Villaizan (2017). Infectious pancreatic necrosis virus triggers antiviral immune response in rainbow trout red blood cells, despite not being infective. F1000Research. 6 - 1968.

MH Jung; J Lee; M ORTEGA-VILLAIZAN; L Perez; SJ Jung (2017). Protective immunity against Megalocytivirus infection in rock bream (*Oplegnathus fasciatus*) following CpG ODN administration. Vaccine. 35 - 30, pp. 3691 - 3699.

García-Valtanen P; Martinez-Lopez A; Lopez-Muñoz A; Bello M; Medina-Gali RM; Ortega-Villaizan M; Varela M; Figueras A; Mulero V; Novoa B; Coll JM (2017). Zebrafish lacking adaptive immunity acquire an anti-viral alert state characterized by upregulated gene expression of apoptosis, multi-gene families and interferon-related genes. Frontiers in Immunology. 8:668.

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.

PhD Theses.

Cambios a nivel epigenético y proteómico en pez cebra en respuesta a la infección con virus de la viremia primaveral de la carpa (SVCV). Regla María Medina Gali. Universidad Miguel Hernández de Elche. 03/07/2017. Dirección: Perez Garcia Estañ, Luis (Director), Ortega-Villaizán Romo, María del Mar (Codirector), Encinar Hidalgo, José Antonio (Codirector).

Number of Congress Communications.

International contributions: 2 Oral presentations and 1 poster presentation.

Editorial Boards.

Frontiers in Immunology (Topic Editor) (2017-2018).

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 Isabel Martínez-Lacaci Fortuny

Mª Pilar García Morales

Ph. D Students.

María Fuentes Baile

María Paz Ventero Martin

Invited talks and courses.

Búsqueda de nuevas estratégias terapéuticas para el tratamiento del cáncer. Casino de Torrevieja, 26 de Mayo de 2017.

Nuevas estratégias terapéuticas para el tratamiento de tumores quimio y radiorresistentes. Facultad de Química de la Universidad de Murcia (UMU). 31 de Octubre de 2017.

Number of Congress Communications.

International contributions: 1 poster presentations.

Governmental Projects and Funding.

Título del proyecto: Desarrollo de inhibidores de PTK6 como posibles nuevos agentes terapéuticos en cáncer. Evaluación de su potencialidad en modelos celulares de tumores de mama, páncreas y colon. Entidad financiadora: FIS PI01202025. Duración, desde: 2013 hasta: 2016. 65,000 €, IP: Dr. Miguel Saceda.

Título del proyecto: Terapias antitumorales basadas en nanotecnología. Ayudas para la captación de proyectos europeos u otros programas de ámbito internacional (2016). APE/2016/028. Generalitat Valenciana. IP: Dr. Miguel Saceda.

Private funding: Contracts.

Título del proyecto: Nanotecnología, terapia enzimática y cribado de nuevas moléculas para la optimización del tratamiento radioterápico en tumores quimio y radio resistentes. Entidad Financiadora: Fundación ERESA SL. 2016 - 2017. 12,000 €, IP: Dr. Miguel Saceda.

PhD THESES (2017).

Título: Diseño de sistemas poliméricos nanoestructurados transportadores para aplicaciones biomédicas.

Autor: Amalia Mira Carrió.

Fecha de Lectura: 15/09/2017

Dirección: Ricardo Mallavia Marín, Juan Alberto Falcó Graciá.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1524300

Título: Estudio de los complejos transcripcionales que dirigen la formación del pistilo en angiospermas mediante la identificación de sus dianas moleculares y de su conservación funcional durante la evolución de las dicotiledóneas.

Autor: África Gomariz Fernández

Fecha de Lectura: 14/09/2017

Dirección: Cristina Ferrándiz Maestre

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1516845

Título: Cribado farmacológico para el síndrome de Dravet.

Autor: Verónica Rivero Hernández

Fecha de Lectura: 01/09/2017

Dirección: Antonio Vicente Ferrer Montiel (Director), Antonio Felipe Campo

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1483551

Título: Cambios a nivel epigenético y proteómico en pez cebra en respuesta a la infección con virus de la viremia primaveral de la carpa (svcv).

Autor: Regla María Medina Gali

Fecha de Lectura: 03/07/2017

Dirección: Luis Perez Garcia Estañ, María Del Mar Ortega-Villaizán Romo, José Antonio Encinar Hidalgo

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1456419

Título: Actividad Antitumoral de un Extracto de Romero (*Rosmarinus officianalis* L.) en modelos *in vitro* e *in vivo* de cáncer de colon.

Autor: Almudena Pérez Sánchez

Fecha de Lectura: 28/04/2017

Dirección: Vicente Micol Molina, Enrique Barrajón Catalán, José Antonio Ferragut.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1415100

Título: Farmacocinética Poblacional de Litio en pacientes psiquiátricos.

Autor: Maria Isabel Pérez Castelló

Fecha de Lectura: 11/04/2017

Dirección: Maria del Val Bermejo Sanz, José Luís Marco Garbayo, María Isabel González Álvarez.

https://www.educacion.gob.es/teseo/mostrarRef.do?ref=1402239

SEMINARS (2017).

Título: **Descifrando alteraciones bioquímicas en proteínas claves en el desarrollo del Alzheimer**.

Ponente / Institución: Javier Saez Valero. Dpto de Bioquímica y Biología Molelular – UMH.

Viernes, 1 diciembre 2017.

Título: **La importancia de tener vecinos para innovar. El clúster biotecnológico de Alicante**.

Ponente / Institución: José Antonio Belso Martínez. Universidad Miguel Hernández.

Viernes, 10 noviembre 2017.

Título: **Receptores y efectores de inmunidad**.

Ponente / Institución: Luis Mercado Vianco. Instituto de Biología de la Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso, Chile.

Viernes, 3 de noviembre 2017.

Título: **Proteómica y metabolómica: con qué herramientas contamos para abordar una visión más profunda de los procesos biológicos**.

Ponente / Institución: Francesc Márquez Garrido. Empresa Bruker.

Viernes, 26 de mayo 2017.

Título: **Elaboración, crianza y degustación del vinagre de Jerez.**

Ponente / Institución: Ana Troncoso y Maria del Carmen García. Universidad de Sevilla.

Miércoles 17 de mayo de 2017

Título: **La importancia de tener vecinos para innovar. El clúster biotecnológico de Alicante**.

Ponente / Institución: José Antonio Belso Martínez. Universidad Miguel Hernández.

Viernes, 28 de abril 2017.

Título: **Plataforma F1000. Una nueva forma de escribir, descubrir y compartir la ciencia**.

Ponente / Institución: Maaike Pols. Faculty of 1000.

Lunes, 10 de abril 2017.

Título: **Emergencia del iridovirus del besugo roca en Corea**.

Ponente / Institución: Myung-Hwa Jung. Universidad Nacional de Chonnam, Corea del Sur.

Viernes, 7 de abril 2017.

Título: **Deconstruyendo la enfermedad neurodegenerativa en Escherichia coli con un prionoide sintético**.

Ponente / Institución: Rafael Giraldo Suarez. Centro de Investigaciones Biológicas (CSIC, Madrid).

Viernes, 31 de marzo 2017.

Título: **Herramientas nano-biotecnológicas para investigación e innovación**.

Ponente / Institución: Daniel Pando. CEO de la empresa Nanovex Technologies S.L.
Martes, 21 de marzo 2017.

Título: **Nano y microsensores para aplicaciones biomédicas**.
Ponente / Institución: Nerea Alayo. Instituto de Investigación en Energía de Cataluña (IREC).
Viernes, 17 de marzo 2017.

Título: **Aplicaciones bioquímicas, farmacológicas y clínicas de la metabolómica**.
Ponente / Institución: Antonio Pineda Lucena. Hospital Universitario y Politécnico de la Fe (Valencia).
Viernes, 10 de marzo 2017.

Título: **Biomolecular Engineering: from Biological Processes to Biotechnological Applications**.
Ponente / Institución: Ana María Fernández Escamilla. Estación Experimental del Zaidín
Viernes, 3 de marzo 2017.

Título: **CIDAF. Del laboratorio a la empresa**.
Ponente / Institución: David Arraez Román. Universidad de Granada
Viernes, 27 de enero 2017.

ANNUAL REPORT 2017

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