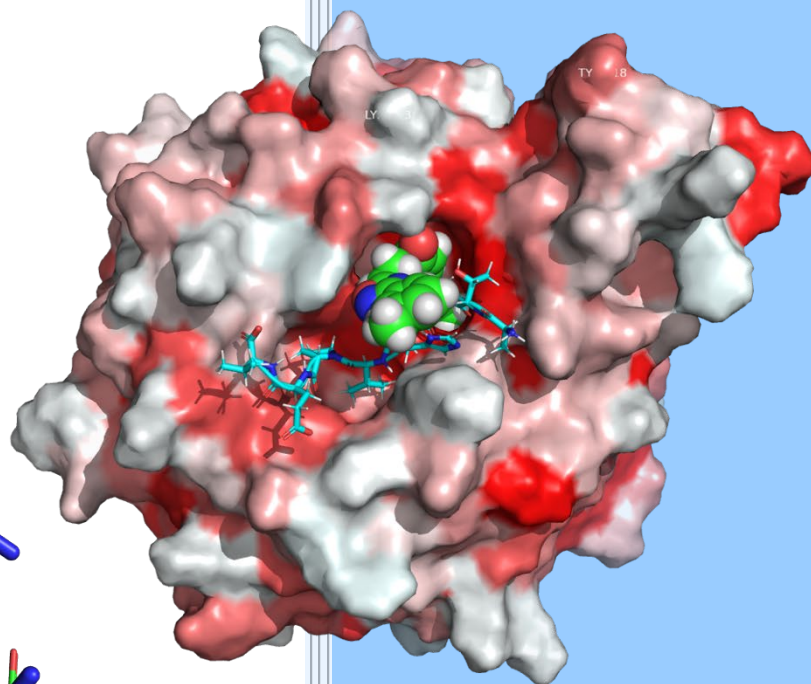
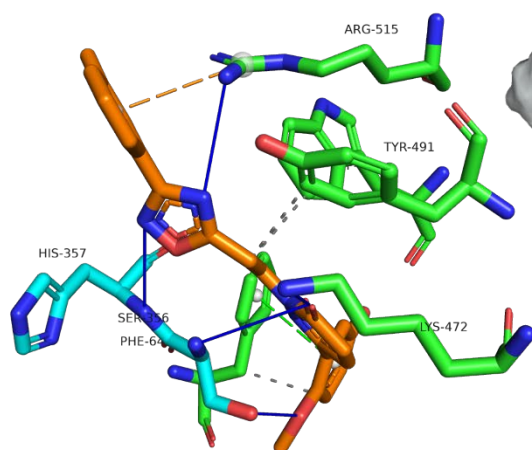


ANNUAL REPORT 2023



INSTITUTE OF RESEARCH,
DEVELOPMENT, AND
INNOVATION IN HEALTHCARE
BIOTECHNOLOGY
OF ELCHE
UNIVERSITY "MIGUEL HERNÁNDEZ"


IDiBE
UNIVERSITAS
Miguel Hernández

DIRECTOR'S FOREWORD

The Institute of Research, Development, and Innovation in Healthcare Biotechnology in Elche (IDiBE) is one of the University Research Institutes at the University Miguel Hernandez de Elche. The IDiBE is located in the University Campus in Elche, occupying a 4,000 sq. m. of laboratory in the Torregaitán Building. IDiBE aims to become a Research Institute that excels in transformative science and its translational to society. In the past 26 years, the IDiBE (previously IBMC) has excelled in its scientific production, in the exploitation of the generated results and technologies and its societal disseminating programs. This translational excellence has thrust the creation of spin-off companies and Joint ventures with private enterprises and local Hospitals. This seminal vision has been kept invariable and can be fully appreciated in our Annual Reports reporting our achievements in research, exploitation, training and dissemination activities, in line with the objectives set in our Plan of Actions.



As in previous years, our groups have been active in securing funding from both governmental and private sources (up to 2.5 M€), publishing papers in high impact journals that are widely cited, training young scientists (pre and postdoctoral) with the highest scientific standards as recognized by recent audits of our training programs, and to disseminate our activities and milestones to society through our out-reach programs (Science with tapas; And you, what do you research on?, International Day of Women and Girls in Science) In addition, we have consolidated the Master Degree in Biotechnology and Bioengineering with the Institute of Bioengineering that is becoming a national reference in the field. In addition, we continued with the Erasmus mundus European Master on translational cosmetic and dermatological sciences with the Universities of Piemonte Orientale (Italy), Namur (Belgium) and Humboldt (Germany). A major success of the Institute has been the commercialization of innovative products generated from the research projects in the fields of nutraceuticals, cosmeceuticals and biotechnology; and having 3 lead compounds in clinical development and one in pre-clinical. Our translational activities are reinforced with four technological platforms. This success has been possible thanks to our philosophy of potentiating communication and collaborations, and sharing all the infrastructures, as well as to the commitment of our administrative and technical personnel to the IDiBE project.

The major milestones for 2023 have been: (i) incrementing our technology transfer actions to the productive sectors of our society through the innovation office; (ii) strengthening the unit for business development (UCIE) funded by the AVI-GVA to further potentiate translation and exploitation of results; (iii) maintaining an 80% of publications in Q1 journals and 32% in D1; (iv) acquisition of innovative infrastructures funded by the GVA and the EU that have provided new technologies such as a mass cytometry (Hyperion) unit for single cell proteomics, that will allow the Institute to embark on more competitive projects; (iii) presenting our new Plan of action (2023-2026) centered in the development and exploitation of human-based microphysiological systems to excellence María de Maeztu program; and (vi) we received the review and input of our external advisory board for increasing the visibility and international recognition. Furthermore, we concluded the accommodation of a BL-2 laboratory in the Institute which will allow developing additional projects.

Prof. Antonio Ferrer-Montiel, Director

STRUCTURE AND GENERAL DESCRIPTION

The IDiBE Action Plan for 2023-2026

IDiBE aspires in this period to become an international leader in preclinical healthcare biotechnology by achieving an ambitious Research Technology Development (RTD) program that will foster translation and exploitation, internationalization, and social impact. It will also attract talented students to be trained, and promising early career scientists that will bring new skills, ideas, and excellence to IDiBE. Our progress towards excellence in translational science has been possible due to a rigorous commitment to our 3 previous strategic plans that set the basis of an interdisciplinary, and innovative RTD in molecular and preclinical biotechnology directed to transform the generated knowledge into health assets that increase societal wellbeing. The strategic plan (2023-2026) sets the objectives and actions necessary to reinforce the strengths, correct the weaknesses, and exploit current opportunities to become an international leader in preclinical biotechnology.

The IDiBE R&D program is organized into two inter-related departments to promote integration and collaboration among IDiBE members: (i) **Molecular biotechnology** to provide a tailored molecular toolbox of pharmacological tools, biosensors, and delivery systems for preclinical research; (ii) **Preclinical biotechnology** to strengthen research on diabetes mellitus and obesity, endocrine disruptors, hard-to-treat cancers (i.e. glioblastoma, hepatocarcinoma), liver and gastrointestinal (GI) diseases (chronic inflammation and intestinal microbiome), peripheral neuropathies (chronic pain), and anti-infective strategies for human and animal health (Figure 1). This organization also favors internal collaborations, sharing the infrastructures, and a more rational and productive use of all resources, including the technological platforms.

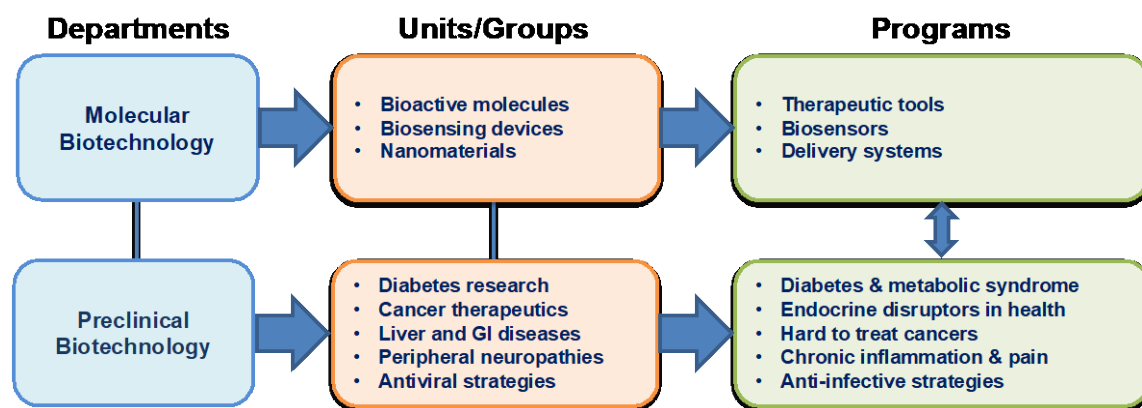


Figure 1. IDiBE RTD organization

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

A. Molecular Biotechnology

Its main objective is to advance our knowledge in the structure-function relations of small molecules and macromolecules to transform their activity for biotechnological purposes and to design better ligands that modulate their function, as well as nanotechnology-based systems that help their deliver to the site of action.

Three groups carry out their research in this molecular biotechnology department: the bioactive molecules group led by Prof. Vicente Micol; the biosensing and biorecognition group led by Prof. Reyes Mateo; and the nanobiomaterials group led by Prof. Ricardo Mallavia. The different scientific backgrounds of the researchers involved allow for a multidisciplinary approach to the societal and technological challenges investigated.

B. Preclinical Biotechnology

Its goal is to strengthen research on health societal challenges that require interdisciplinary teams to deliver innovative solutions. These challenges include human and animal health as well as the identification of environmental pollutants thus focusing on the concept of OneHealth. This research line is made up of a multi-disciplinary research team, which covers from molecular aspects to semi-industrial biological actives. This multidisciplinaryity is sustained by the contribution of consolidated groups, which provide a balanced composition that favors high competitiveness in scientific contributions, raising resources, training research staff, and generating exploitable and transferable technologies. Five groups are involved in this department, the diabetes research unit led by Prof. Ángel Nadal; the cancer therapeutic unit led by Prof. Miguel Saceda; the liver and GI disease group led by Prof. Rubén Francés; the group of Peripheral Neuropathies led by Prof. Antonio Ferrer; and the group of antiviral strategies led by Prof. M^a del Mar Ortega-Villaizán.

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

The activities in this line clearly have a high potential for clinical translation, which has materialized in the creation of clinical joint units with the University Hospitals of Elche (Joint Research Unit IDiBE-UMH/ HGUE-FISABIO) and Alicante (Joint Research Unit IDiBE-UMH/ HGUA-ISABIAL), and of industrial exploitation that has led to continuous and consolidated collaborations with biotech and pharmaceutical companies. Indeed, these research lines are complemented by an additional complementary subline dealing with industrial developments (including products and processes for healthcare biotechnology).

C. Core Technologies

The Action Plan has organized the core technology in three major platforms (Figure 2) that assemble complementarily all the generated and acquired technologies and infrastructures for a shared and synergistic use.

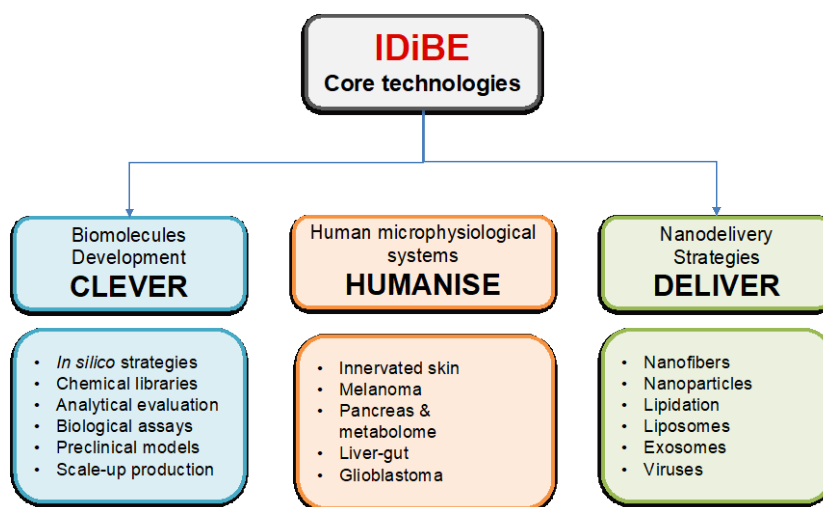


Figure 2. Technological Platforms

MOLECULAR BIOTECHNOLOGY

MOLECULAR BIOTECHNOLOGY

Development of therapeutic tools from both natural and synthetic sources

Unit/Group name: DESIGN AND DEVELOPMENT OF BIOACTIVE MOLECULES

The Design and Development of Bioactive Molecules Group is an interdisciplinary team focused on the design, extraction, purification and evaluation of bioactive molecules from natural sources, always based on scientific evidence and pursuing excellence in all our work and projects. Our group also has a strong track record of technology transfer to the business world, participating in joint developments and translational research projects.

Staff

Vicente Micol Molina (ORCID: 0000-0001-8089-0696)

Jose Antonio Encinar Hidalgo (ORCID: 0000-0002-7219-3863)

Enrique Barraji3n Catal3n (ORCID: 000-0001-8113-0795)

María Herranz López (ORCID: 0000-0002-1819-7978)

Postdoctoral Researchers

Francisco Javier 3lvarez Mart3nez (ORCID: 0000-0002-5275-1282)

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María Dolores Olivares Vicente (ORCID: 0000-0002-2792-9181)

María Losada Echeberria (ORCID: 0000-0002-9083-3692)

Ph. D Students

Irene Pomares Bri (ORCID: 0009-0005-2137-9018)

Noelia S3nchez Marzo (ORCID: 0000-0001-7486-3886)

Jessica Mart3nez Godfrey (ORCID: 0000-000-9828-3883)

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Marta Fern3ndez-Oliver (ORCID: 0000-0002-9937-3135)

Celia Mei Moreno Gonz3lez (ORCID: 0009-0006-3672-7094)

Paula De Juan Maci3 (ORCID: 0009-0005-1902-5464)

Technicians

María Teresa Garz3n Cabrerizo

Isabel Serrano Toribio

Publications

Menendez JA, Cuy3s E, Encinar JA, Vander Steen T, Verdura S, Llop-Hern3ndez 3, L3pez J, Serrano-Herv3s E, Osuna S, Martin-Castillo B, Lupu R. The Fatty Acid Synthase (FASN) signalome: A molecular guide for precision oncology. *Molecular Oncology* 29 December 2023. doi: 10.1002/1878-0261.13582

3lvarez-Mart3nez FJ, Borr3s-Rocher F, Micol V, Barraji3n-Catal3n E. Artificial Intelligence Applied to Improve Scientific Reviews: The Antibacterial Activity of Cistus Plants as Proof of Concept. *Antibiotics* 2023; 12 (2), 327, pp. 1 -32.

Raus de Baviera D, Ru3z-Candales A, Barraji3n-Catal3n E. Cistus albidus L.—Review of a Traditional Mediterranean Medicinal Plant with Pharmacological Potential. *Plants* 2023; 12, 2988, pp. 1 - 43. doi.org/10.3390/plants12162988

Bulbianskova D, D3az-Puertas R, 3lvarez-Mart3nez FJ, Herranz-L3pez M, Barraji3n-Catal3n E, Micol V. Hallmarks and Biomarkers of Skin Senescence: An Updated Review of Skin Senotherapeutics. *Antioxidants* 2023; 12 (2), 444, pp. 1 - 26. DOI: 10.3390/antiox12020444

D3az-Puertas R, 3lvarez-Mart3nez FJ, Falc3 A, Barraji3n-Catal3n E, Mallavia R. Phytochemical-Based Nanomaterials against Antibiotic-Resistant Bacteria: An Updated Review. *Polymers* 2023; 15, 1392., pp. 1 - 22. doi.org/10.3390/polym15061392

Sarmiento-Ma3us R, Fontcuberta-Cervera S, Gonz3lez-Bay3n R, Hannah MA, 3lvarez-Mart3nez FJ, Barraji3n-Catal3n E, Micol V, Quesada V, Ponce MR, Micol JL. Analysis of the Arabidopsis venosa4-0 mutant supports the role of VENOSA4 in

dNTP metabolism. *Plant Science* 2023; Volume 335, 111819. doi.org/10.1016/j.plantsci.2023.111819

Boix-Castejón M, Roche E, Olivares-Vicente M, Álvarez-Martínez FJ, Herranz-López M, Micol V. Plant compounds for obesity treatment through neuroendocrine regulation of hunger: A systematic review. *Phytomedicine* 2023; 113, 154735. <https://doi.org/10.1016/j.phymed.2023.154735>

Carrera-Quintanar L, Funes L, Herranz-López M, Vicente-Salar N, Bonet-García R, Blasco-Peris C, Micol V, Pons A, Roche E. Modulation of Oxidative Stress and Antioxidant Response by Different Polyphenol Supplements in Five-a-Side Football Players. *Nutrients* 2023; 15, 177. <https://doi.org/10.3390/nu15010177>

Patents

Patent applied for in 2023 (33% of the co-invention) "Uses of protein tyrosine phosphatase receptor kappa inhibitors (PTPRK Inhibitors)". UMH- Université Libre de Bruxelles.

PhD Theses

Título: Ingredientes basados en polifenoles vegetales con aplicaciones en patologías asociadas a la obesidad. Student: Marina Boix Castejon. Supervisors: Dr. E. Roche Collado and Dra. M. Herranz López. Qualification: Sobresaliente Cum Laude. 14/12/2023.

Invited Talks and Courses

"Looking for new ingredients in nature screening and cosmetic applications". Summer Course. Cosmetic: from bench to business, The Faculty of Pharmacy Universitas Gadjah Mada (Indonesia, online session, 07/07/23). Speaker: EBC.

Science Dissemination: Outreach Activities

"Soluciones circulares para la paja de arroz, desde la inteligencia artificial a la economía circular". Sesión CV+i sobre sector agroalimentario, Valencia (26/10/23). Entidad organizadora: Asociación RUVID: Red de Universidades Valencianas para el fomento de la I+D+i. Speaker: EBC.

"Nuevos desarrollos biotecnológicos para las extracciones vegetales: desde la inteligencia artificial a la economía circular". Jornadas de Divulgación IDiBE 2023. (20/7/23). Speaker: EBC.

"Del mar al laboratorio, historia de nuestra lucha contra el cáncer". Eureka Birras (Elche, 12/01/23). Speaker: EBC.

"Herramientas para la gestión integrada de la investigación y la innovación en la gobernanza universitaria". Semana de la Investigación. III Encuentro anual de investigación. Universidad Agraria de la Molina, Lima (Perú) (23/10/23). Speaker: VMM.

I Encuentro Investigación Cáncer IDiBE. Evaluación de compuestos marinos en cáncer de colon asociado a obesidad (26/05/2023). Speaker: MHL.

Proyecto OBRAINSITY: "Nuevos enfoques terapéuticos frente a enfermedades metabólicas" (9 y 13 de marzo-2023). Radio-UMH y SER-Radio. Speaker: MHL.

Investigadores de la UMH estudian la valorización del quitosano para la producción de plásticos sostenibles y nuevas formulaciones para la industria cosmética. Servicio de Comunicación UMH. (28-11-2023). MHL.

Number of Congress Communications

International contributions: 14

Poster presentations: 5

Oral presentations: 9

National contributions: 6

Poster presentations: 3

Oral presentations: 3

Governmental Projects and Funding

CPP2022-009795. "Valorización del quitosano para la producción de plásticos sostenibles para la industria cosmética y para ecologizar las propiedades de los cosméticos". Proyectos de Colaboración Público-Privada, 2023. MINISTERIO DE CIENCIA E INNOVACIÓN (2023-2025). IP at UMH: MHL. Funding: 184.863 €.

NeurotechEU Research and Innovation (NeurotechRI). European Commission. Project related to "The European University of Brain and Technology-NeurotechEU". European Commission, ERASMUS+ (2021-24). IP: J. Gallar. Funding: 249,894.15 € (UMH); 1.999.732,90 € (total).

INNEST/2022/103. "Development of advanced recycling techniques for rice straw to be used by footwear industry". AGENCIA VALENCIANA DE INNOVACIÓN. IP: EBC. Funding: 154,125.22 €.

PROMETEO/2021/059. "New therapeutic approaches in metabolic diseases: modulation of food intake and energy balance through nutraceuticals and neurotechnology". GENERALITAT VALENCIANA (2021-24). IPs: VMM y MHL. Funding: 548,816.10 €.

TED2021-129932B-C32. "Valorization of rice straw byproduct through the development of new biotechnological uses for cosmetic industries". MINISTERIO DE CIENCIA E INNOVACIÓN. IPs: EBC y VMM. Funding: 230,000.00 €.

PID2021-125188OB-C32. "A multi-omic approach to evaluate the healthy effects of encapsulated olive leaf extracts on obesity (ObeOMic)". MINISTERIO DE CIENCIA E INNOVACIÓN (2022-2024). IPs: EBC and VMM. Funding: 198,000 €.

Estudio farmacogenómico para el tratamiento de las enfermedades inflamatorias intestinales. FUNDACIÓN ILISABIO (2023). IP: VMM. Funding: 5,000 €.

LiCiaBetes: Metabolitos antioxidantes de la Lippia citriodora y su contribución frente al aumento de la interacción leucocito-endotelio en pacientes con diabetes tipo 2. FUNDACIÓN ILISABIO (2023). IP: MHL. Funding: 5.000 €.

"Regulación del estrés metabólico asociado al envejecimiento mediante polifenoles vegetales". INTERNATIONAL CENTER FOR AGING RESEARCH (ICAR) (2023). IPs: VMM and MHL. Funding: 34,155€.

Future generation Training in natUral products Research. REF: CIAPE/2022/19. GENERALITAT VALENCIANA (2023-4). IP: EBC. Funding: 10.000 €.

Private funding: Technical Services and Assistance

"Caracterización y pruebas de actividad de ingredientes de origen natural con potencial aplicación cosmética". Technological support contract for the company Innovation Labo Technologies, SL. Funding: 45.000€ (2023-2026).

6 technical services to 6 different external companies (total amount: 2.536€).

Projects Submitted

Innovative technologies to monitor and reduce Non-Exhaust Emissions, particles and microplastics of Vehicles and pavements to improve air quality and human health (LIFE NEEVE). Call: LIFE-2023-SAP-ENV. Status: This project has recently been granted. Total funding: 2.760.638,52€ (121.787,40€ at UMH). IP at UMH: EBC.

FUTURE: Future generation Training in natUral products REsearch. Call: HORIZON-MSCA-2023-DN-01. Status: waiting for resolution. IP and general coordinator: EBC.

R&D and Educational Committees

Enrique Barraón Catalán belongs to the "Comité ético y de integridad en la investigación, CEII" of the Miguel Hernández University.

María Herranz López and Enrique Barraón Catalán belong to the "Trabajos Fin de Grado Interdisciplinares" Program of the Miguel Hernandez University.

R&D Management

E. Barraón-Catalán is reviewer of PROCENCIA-Concytec, Perú (2021-act.)

E. Barraón-Catalán is reviewer of Agencia Española de Investigación (AEI), Spain (2021-act.)

M. Herranz-López is reviewer of Agencia Española de Investigación (AEI), Spain (2021-act.)

Vicente Micol is reviewer of Agencia Española de Investigación (AEI), Spain (2007-act.)

Editorial Boards

E. Barrajón-Catalán is Board Member of *Molecules* (2021-2023).

M. Herranz-López is Topical Advisor Panel Member of *International Journal of Molecular Science* (2022-2023).

Vicente Micol is member of the Editorial Board of *Antioxidants* (MDPI).

Development of biosensors for diagnostic and/or therapeutic prognosis

Unit/Group name: BIOSENSING AND BIORECOGNITION

Research group: BIO-MULTIFUNCTIONAL ASSEMBLIES GROUP

The group explores the molecular interactions among different components (biomolecules, polymers, nanomaterials/particles, etc.) within different environments (physiological media, deep eutectic solvents, etc.) in order to assemble them into devices and exploit their full potential in applications such as biosensing, controlled drug delivery or biomolecule storage.

Research Lines of the Group:

- Development of fluorescent platforms for biosensing applications.
- Development of hybrid nanomaterials for biomedicine and environmental applications.
- Characterization of biological systems in confined and non-conventional environments.
- Development of submicrometric particles with ultra-high loading capacity for long-term storage of labile biomacromolecules.
- Design of nanoparticles composites for the oral administration of insulin.

Staff

Carmen Reyes Mateo Martínez (ORCID: 0000-0002-2085-1676)

Javier Gómez Pérez (ORCID: 0000-0001-9612-5075)

M^a José Martínez Tomé (ORCID: 0000-0002-7042-2642)

Rocío Esquembre Tomé (ORCID: 0000-0002-9054-9106)

Felipe Hornos Adán (ORCID: 0000-0002-9360-4086)

Postdoctoral Researchers

Marta Rubio Camacho (ORCID: 0000-0001-5421-3050)

External collaborators integrated in the group

Francisco Montilla (ORCID: 0000-0003-4769-9130)

Ph. D Students

Yolanda Inmaculada Alacid Martínez (ORCID: 0000-0003-2762-449X)

Rául Martínez Baquero

Technicians

Elisa Pérez García

Publications

Rubio-Camacho M, Martínez-Tomé MJ, Cuestas-Ayllón C, De la Fuente JM, Esquembre R, Mateo CR. Tailoring the plasmonic properties of gold-liposome nanohybrids as a potential powerful tool for light-mediated therapies. *Colloid and Interface Science Communications* 2023; 52, 100690. doi.org/10.1016/j.colcom.2022.100690

Alacid Y, Martínez-Tomé MJ, Esquembre R, Herrero MA, Mateo CR. Portable Alkaline Phosphatase-Hydrogel Platform: From Enzyme Characterization to Phosphate Sensing. *Int J Mol Sci.* 2023; 24, 2672. doi.org/10.3390/ijms24032672

Alacid Y, Esquembre R, Montilla F, Martínez-Tomé MJ, Mateo CR. Fluorescent Nanocomposite Hydrogels Based on Conjugated Polymer Nanoparticles as Platforms for Alkaline Phosphatase Detection. *Biosensors* 2023; 13, 408. doi.org/10.3390/bios13030408

Madrid A, Martínez G, Hornos F, Bonet-Aleta J, Calvo E, Lozano A, Hueso JL. Laser-induced tuning of carbon nanosensitizers to maximize nitrogen doping and reactive oxygen species production in the visible range. *Catalysis Today* 2023; 422, 114214. doi.org/10.1016/j.cattod.2023.114214

Valls-Chiva A, Gomez J, Garcia-Peiro JI, Hornos F, Hueso JL. Enzyme-Iron Oxide Nanoassemblies: A Review of Immobilization and Biocatalytic Applications. *Catalysts* 2023; 13 (6), 980. doi.org/10.3390/catal13060980

Esquembre R, Martínez-Tomé MJ, Hornos Adán, F. Creación e implementación de una práctica de química virtual con formato de espcae room. *Educación y sociedad claves interdisciplinarias*. Ed. Octaedro 2023; 503-514. ISBN 978-84-10054-35-6

Hornos Adán F, Esquembre R. Quinnovalab: aumento de la autonomía del alumnado en el laboratorio de química mediante recursos digitales. *Desafíos de la docencia universitaria actual*. Ed. Educación Editora 2023. ISBN 978-84-15524-49-6

PhD Theses

Título: Plataformas sensoras soportadas en hidrogeles para aplicación biomédica y medioambiental. Student: Yolanda Inmaculada Alacid Martínez. Supervisors: Dra. M.J. Martínez Tomé and Dra. C.R. Mateo. Qualification: Sobresaliente Cum Laude. 15/12/2023.

Science dissemination: outreach activities

INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE DAY AT IDiBE ("CIENCIA CON TAPAS")

- "Investigadoras en biotecnología sanitaria, Centro de Congresos "Ciutat d'Elx" de Elche", 14/02/23

M^a José Martínez Tomé. Organizing committee

C. Reyes Mateo. Speaker

SCIENCE OUTREACH DAY "CIENCIA CON TAPAS":

- "Vacunas y otras estrategias de control de la malaria en África subsahariana", librería Pynchon&Co, (Alicante), 30-05-2023

M^a José Martínez Tomé. Organizing committee

SCIENCE OUTREACH DAY "CIENCIA CON TAPAS" in the framework of "Science Goes To School (Science GTS), of the European Women's Researchers' Night":

- "Del mar al plato: consumo responsable de productos del mar", librería Pynchon&Co, (Alicante), 26/09/2023

M^a José Martínez Tomé. Organizing committee

Number of Congress Communications

National contributions: 9

Oral presentations: 4

Poster presentations: 5

International contributions: 5

Oral presentations: 1

Poster presentations: 4

Awards

Teaching Talent Award 04/12/2023: Rocío Esquembre Tomé.

Teaching Talent Award 04/12/2023: M^a José Martínez Tomé.

Governmental Projects and Funding

Enzimas en hidrogeles nanocompuestos como plataformas de biodetección y biocatálisis: aplicación al descubrimiento y degradación de fármacos. 1/09/2023 – 31/08/2026. PROYECTOS DE GENERACIÓN DE CONOCIMIENTO 2022 (PID2022-138507OB-I00). AGENCIA ESTATAL DE INVESTIGACIÓN MINISTERIO DE CIENCIA E INNOVACIÓN. IPs: C. Reyes Mateo/M^a José Martínez. Funding: 125.000 €.

Proteínas en hidrogeles como plataformas con capacidad de reconocimiento molecular: aplicación para el desarrollo de biosensores fluorescentes. 2023 – 2025. Subvenciones a grupos de investigación consolidados (AICO) (CIAICO/2022/131). CONSELLERIA

DE INNOVACIÓN, UNIVERSIDADES, CIENCIA Y SOCIEDAD DIGITAL. IPs: C. Reyes Mateo/F. Javier Gómez. Funding: 90.000 €.

Biosensors for marine environmental monitoring: control of the ecotoxicological status of coral reefs (BioSensReef). 1/12/2022 - PROYECTOS DE TRANSICIÓN ECOLÓGICA Y TRANSICIÓN DIGITAL 2021 (TED2021-129894B-I00) UA-UMH AGENCIA ESTATAL DE INVESTIGACIÓN MINISTERIO DE CIENCIA E INNOVACIÓN. IPs: Montilla Jiménez (UA)/C. Reyes Mateo Martínez (UMH). Funding: 195.500 €.

Biosensores de transducción combinada basados en matrices híbridas multienzimáticas (BioFLEC). 25/09/2022 - EXPRESIONES DE INTERÉS DE PROYECTOS DEL PROGRAMA DE I+D+i DE MATERIALES CON FUNCIONALIDADES AVANZADAS PARA LA NUEVA TRANSFORMACIÓN TECNOLÓGICA. (MFA/2022/058). UA-UMH CONSELLERIA DE INNOVACIÓN, UNIVERSIDADES, CIENCIA Y SOCIEDAD DIGITAL. GENERALITAT VALENCIANA. IPs: Montilla Jiménez (UA)/C. Reyes Mateo Martínez (UMH). Funding: 163.534 €.

Síntesis de nuevos eutectogel-SinEuTeG 01/01/2023- 31/12/2023 AYUDAS PARA PROYECTOS DE INVESTIGACIÓN 2023 DEL VICERRECTORADO DE INVESTIGACIÓN. UMH. (VIPROY23/05). IP: Rocío Esquembre. Funding: 2.225 €.

Nanocompuestos como plataformas de biodetección y administración de fármacos para patologías asociadas al envejecimiento. 1/01/2023 – 31/12/2023. PROGRAMA DE AYUDAS PARA LA INVESTIGACIÓN DEL ENVEJECIMIENTO DE LA FUNDACIÓN ICAR, CONVOCATORIA 2023 (AgingPharm). IPs: M^a José Martínez/Rocío Esquembre. Funding: 22.882 €.

Procesos sostenibles energéticamente en la industria química: captura y uso de CO₂ asistidos por calentamiento microondas. 1/09/2023 – 31/08/2026. PROYECTOS DE GENERACIÓN DE CONOCIMIENTO 2022 (PID2022-138336OB-C21). AGENCIA ESTATAL DE INVESTIGACIÓN MINISTERIO DE CIENCIA E INNOVACIÓN. IPs: Reyes Mallada/José Luis Hueso. Proyecto externo (Universidad de Zaragoza). Funding: 195.000 €.

R&D Management

Reviewer of nanomaterials (CRM)

Reviewer of Chemosensors (CRM)

Research group: STRUCTURE-FUNCTION RELATIONSHIP OF ION CHANNELS

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

Staff

José Manuel González-Ros (ORCID: 0000-0002-4804-6855)

José Antonio Poveda Larrosa (ORCID: 0000-0003-0722-3752)

Ana Marcela Giudici Besseghini (ORCID: 0000-0002-3753-4861)

Ph. D Students

Carlos Coll Díez

Technicians

Eva Martínez Martínez

Publications

Renart ML, Giudici AM, Coll-Díez C, González-Ros JM, Poveda JA. Anionic Phospholipids Shift the Conformational Equilibrium of the Selectivity Filter in the KcsA Channel to the Conductive Conformation: Predicted Consequences on Inactivation. *Biomedicine* 2023; MDPI. 11. ISSN 2227-9059. <https://doi.org/10.3390/biomedicine11051376>

Number of Congress Communications

International contributions: 2

Oral presentations:

Poster presentation: 2

Governmental Projects and Funding

Nuevos antibióticos peptídicos que actúan sobre lípidos de membrana de bacterias patógenas. Agencia Estatal de Investigación AEI, Proyecto de Colaboración Público-Privada (CPP2022-009522). (NAPALM-BP). 01/12/2023-30/11/2026. Grant: 106.898,00 €. Participation: Investigator. Institution: UMH.

Nuevas estrategias contra el cáncer: inhibición de las interacciones moleculares de las proteínas de imininas de arginina (InterPAtH), CIAICO/2021/135, GVA. 01/01/2022-31/21/2024. IP: Camino de Juan Romero y José Luis Neira Faleiro.

PROGRAMA INVESTIGO GVA (INVEST/2022/108). 01/11/2022 a 31/10/2024. Proyectos competitivos de subvención pública cuyo objeto es, exclusivamente, la contratación de personal. IP: José Antonio Poveda Larrosa.

R&D Management

Reviewer for Membranes (JAPL)

Reviewer for "Archives of Biochemistry and Biophysics" (JAPL, AMG, MLR)

Reviewer for "International Journal of Molecular Sciences" (JMGR)

Evaluator for FWF Austrian Science Fund (JMGR)

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

Evaluator for MINECO (JMGR)

Reviewer for "Oncotarget" (JMGR)

Editorial Boards

Associated Editor of International Journal of Molecular Sciences (JMGR, 2019-...).

Associated Editor of International Journal of Molecular Sciences (JAPL, 2019-...).

Design of nanomaterials for efficient delivery systems on nanostructures (nanomaterials) and DNA-based vaccines

Unit/Group name: DESIGN AND VALIDATION OF NANOBIMATERIALS

Our group works in the design, synthesis and characterization of polymeric materials with potential biological applications. We are now focusing on the preparation of nanostructures, mainly nanofibers, based on polymeric biomaterials. At all times we are looking for the training of graduate students in pharmacy and biotechnology.

Staff

Ricardo Mallavia Marin (ORCID: 0000-0001-8058-1009)

Rocío Díaz Puertas (ORCID: 0000-0002-3288-5697)

Postdoctoral Researchers

Amalia Mira Carrió (ORCID: 0000-0002-1909-5498)

External collaborators integrated in the group

Juan Alberto Falcó Graciá (ORCID: 0000-0001-7726-6577)

Ph. D Students

Rocío Díaz Puertas (ORCID: 0000-0002-3288-5697)

Juan Suardíaz Muro (ORCID: 0000-0003-0648-2541)

Pedro Valentin Badia Hernandez

Technicians

Elisa Pérez García

Publications

Díaz-Puertas R, Álvarez-Martínez FJ, Falcó A, Barrajon-Catalán E, Mallavia R.

Phytochemical-Based Nanomaterials against Antibiotic-Resistant Bacteria: An Updated Review. *Polymers* 2023; 15, 1392. DOI:10.3390/polym15061392

Araujo-Abad S, Manresa-Manresa A, Rodríguez-Cañas E, Fuentes-Baile M, García-Morales P, Mallavia R, Saceda M, de Juan Romero C. Glioblastoma derived small extracellular vesicles: Nanoparticles for glioma treatment. *Int. J. Mol. Sci.* 2023; 24(6), 5910. DOI:10.3390/ijms24065910

Araujo-Abad S, Manresa-Manresa A, Rodríguez-Cañas E, Fuentes-Baile M, García-Morales P, Mallavia R, Saceda M, de Juan Romero C. New pancreatic ductal adenocarcinoma treatment based on small extracellular vesicles derived from RWP-1. *Biomedicine & Pharmacotherapy* 2023; 162, 114657. Doi:10.1016/j.biopha.2023.114657

Díaz-Puertas R, Rodríguez-Cañas E, Bello-Pérez M, Fernández-Oliver M, Mallavia R, Falcó A. Viricidal Activity of Thermoplastic Polyurethane Materials with Silver Nanoparticles. *Nanomaterials* 2023; 13 (9), 1467. DOI:10.3390/nano13091467

Díaz-Puertas R, Adamek M, Mallavia R, Falcó A. Fish Skin Mucus Extracts: An Underexplored Source of Antimicrobial Agents. *Marine Drugs* 2023; 21(6), 350. DOI: 10.3390/md21060350

Medina-Gali RM, Martínez-Pinna J, Marroqui L, Ciordia S, Soriano S, Mallavia R, Grimaldi M, Balaguer P, Nadal A. Proton transfer from ligands activates extranuclear-initiated estrogen receptor signaling 2023; Preprint Dic2023. DOI:10.1101/2023.12.23.573228

Organization of Meetings

XI Congreso de Jóvenes Investigadores en Polímeros (JIP 2023) "Científicas & Polímeros". RMM: President of the Congress Organization and member of the Scientific Committee RD-P; AMC, JAFG, PVBH: members of the Organizing Committee. Hotel Port Alicante & Beach Alicante. 02-05/10/2023.

Number of Congress Communications

National contributions: 3

Oral presentations: 1

Poster presentations: 2

International contributions: 3

Oral presentations: 2

Poster presentations: 1

Awards

Award of the IDiBE PhD Programme "AMPARO ESTEPA" 2023: Rocío Díaz-Puertas.

Governmental Projects and Funding

Terapias metabólicas para el tratamiento de enfermedades infecciosas en peces de cultivo REF: MetDisFish. FONDO EUROPEO MARÍTIMO, DE PESCA Y DE ACUICULTURA (FEMPA). MINISTERIO DE AGRICULTURA, PESCA Y ALIMENTACIÓN. 30/12/2021 – 15/10/2023. Proyecto Coordinado CSIC-UMH. IP UMH: Ricardo Mallavia Marín. IP coordinator: Beatriz Novoa García.

Biopolímeros para la administración de tratamientos contra el glioblastoma Biopolymers for delivery of glioblastoma treatments. MINISTERIO DE CIENCIA E INNOVACIÓN, PDI-2011-12353OB-C21. 01/09/2022-31/12/2025. IP: Ricardo Mallavia Marín.

Identificación de nuevas dianas terapéuticas para el pronóstico y mejora del tratamiento de glioblastoma. Identification of new therapeutic targets for the prognosis and improvement of glioblastoma treatment. FIS, PI-22-00824. 01/01/2023-31/12/2025. IP Meuri del Camino de Juan Romero (IP1) y Miguel Saceda (IP2).

Estudio comparativo de la expresión génica diferencial asociada a enfermedades neurodegenerativas como base para el desarrollo de nuevas terapias para el glioblastoma. CONSELLERIA DE EDUCACIÓN GENERALITAT VALENCIANA, CIAICO/2022/081 Ene2023-Dic 2025. IPs: Miguel Saceda Sánchez y M^a Salud García Ayllón.

"Valorización del quitosano para la producción de plásticos sostenibles para la industria cosmética y para ecologizar las propiedades de los cosméticos". Proyectos de Colaboración Público-

Privada, 2023. CPP2022-009795.
MINISTERIO DE CIENCIA E INNOVACIÓN
(2023-2025). IP at UMH: María Herranz.

R&D Management

Reviewers for different journals (number of revised manuscripts in 2023): RMM (12)

Editorial Boards

Special issue editor:

Ricardo Mallavia Marin (RMM) (2):
Nanomaterials (MDPI) and Polymers
(MDPI).

PRECLINICAL BIOTECHNOLOGY

PRECLINICAL BIOTECHNOLOGY

Anti-infective strategies

Unit/Group name: **ANTIVIRAL STRATEGIES**

Research group: **ANTIVIRAL STRATEGIES IN AQUACULTURE**

The major goal of the group is de design, development and testing of novel vaccines for viral diseases of aquacultured fish species, with emphasis on the zebrafish and rainbow trout models.

In year 2023 the initial phases of the new PID2021 project 2022-2025 (1) have been developed, where the major effort has been done in setting up the equipment, systems and procedures to manipulate the green algae *Chlamydomonas reinhardtii* as a new biotechnological platform for the production of recombinant viral antigens for fish. Production and characterization of the viral pathogens of salmonid fish such as IHNV and SAV viruses not previously used in our lab.

The "Proof of Concept" project PdC 2022 (2) has delivered a formulated-feed oral vaccine against VHSV for rainbow trout that will be tested in 2024.

Finally, in 2023 the group joined a newly created epidemiology network (3) for surveillance and detection of marine viruses in Spain.

Staff

Luis Perez García-Estañ (ORCID: 0000-0003-4078-8763)

María del Mar Ortega-Villaizán (ORCID: 0000-0003-2065-0601)

Ph. D Students

María E. Salvador Mira (ORCID: 0000-0002-8877-2018)

Ainhoa Gómez Quintanilla

Yeray Cerpa Damas

Publications

Gómez-Quintanilla A, Talavera D, Perez L. A Cell Membrane Fusion Assay for the Fish Pathogen Spring Viremia of Carp Virus (SVCV). *Methods Mol Biol.* 2023; 2610:49-

56. ISBN: 978-1-0716-2894-2; doi: 10.1007/978-1-0716-2895-9_4

Science dissemination: outreach activities

"Vacunas y otras estrategias de control de la malaria en África subsahariana", Diego Torrús and Luis Perez, May 30th 2023. Alicante. "Ciencia con Tapas" divulgation talks. IDiBE-UMH.

"Contraste de Fases"- a monthly radio program on science news. Pilar García, Miguel Saceda, Luis Perez and Manuel Sánchez. UMH Radio.

IDIBE-UMH Open doors/Guided tours for high school and college students: x 4.

Number of Congress Communications

National contributions: 2

Poster presentations: 2

International contributions: 2

Oral presentations: 1

Poster presentations: 1

Governmental Projects and Funding

Novel *Chlamydomonas*-encapsulated recombinant protein oral vaccines for IHNV and SAV. Antiviral efficacy compared to injectable nanopellet (NPs) vaccination. PROYECTOS DE GENERACIÓN DE CONOCIMIENTO 2021 - PID2021-126710OB-C22. MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES. P.I.s: Luis Perez, María del Mar Ortega-Villaizán.

Pre-market testing of NanoPellet (NP)-formulated feed vaccines for viral diseases in aquaculture. PROYECTOS PRUEBA DE CONCEPTO - PDC2022-133194-C22. MINISTERIO DE CIENCIA INNOVACIÓN Y UNIVERSIDADES. P.I.s:

María del Mar Ortega-Villaizán and Luis Perez.

Red de Epidemiología en el medio acuático natural: Vigilancia de virus de riesgo en acuicultura. MINISTERIO DE CIENCIA E INNOVACIÓN. Redes de Investigación 2022. RED2022-134796-T. Investigador Principal: Carlos Pereira Dopazo (Univ. Santiago de Compostela)

Research group: RED BLOOD CELLS IN ANTIVIRAL IMMUNOLOGY

Fish are the phylogenetically oldest vertebrate group with an immune system with clear similarities to the immune system of mammals. However, it is an actual matter of fact that the current knowledge of the fish immune system seems to lack the key piece to complete the puzzle. In an attempt to solve this question, our group have demonstrated that rainbow trout RBCs can respond to viral infections by themselves with an innate immune response, by means of producing antiviral molecules and exerting a paracrine antiviral communication with other cells, and with a potential adaptive immune response, by means of antigen processing and presentation and complement system regulation. Apart from this, we also focus our investigation on the search of prophylactics or therapeutics to treat the major aquaculture viral infections.

Staff

María del Mar Ortega-Villaizán Romo (ORCID: 0000-0003-2065-0601)

Postdoctoral Researchers

Verónica Chico Gras (ORCID: 0000-0001-6983-2786)

Ph. D Students

Maria Elizabeth Salvador Mira (ORCID: 0000-0002-8877-2018)

Celia García Quintanilla (ORCID: 0009-0005-2461-5637)

Adrián López Murcia (ORCID: 0009-0002-0673-1069)

Publications

Visedo A, Hernandez FT, Pardo J, Gosalbez J, Ortega-Villaizán M, Medina-Gali RM, Gonzalez D, Perez-Fernandez A.

R&D Management

Reviewer of Agencia Estatal de Investigación (AEI, Spain). Proyectos de Generación de Conocimiento 2022. Project Category: General Unoriented Research (Investigación No Orientada), Type B. Agri-Food Sciences Panel.

A combination of Polypodium leucotomos extract with vitamin A, vitamin C and selenium as an immune adjuvant against recurrent infections. Food and Agricultural Immunology 2023; 34.

doi.org/10.1080/09540105.2023.2249261

Liu F, Dixon B, Ortega-Villaizán M, Tafalla C, Xu H, Secombes CJ, Wang T. Novel insights into the cytokine network of rainbow trout *Oncorhynchus mykiss* using cell lines and primary leukocyte populations. Fish and Shellfish Immunology 2023; 137. <https://doi.org/10.1016/j.fsi.2023.108755>

Ortega-Villaizán M, Mercado L, Chico V. Editorial: Antiviral immune response in fish and shellfish. Front Immunol. 2023; doi.org/10.3389/fimmu.2023.1155538

Puente-Marin S, Cazorla D, Chico V, Coll J, Ortega-Villaizán M. Innate immune response of rainbow trout erythrocytes to spinyecterins expressing a downsized viral fragment of viral haemorrhagic septicaemia virus. Aquaculture 2023; 568. doi.org/10.1016/j.aquaculture.2023.739303

Organization of Meetings

Workshop Organization "Acuicultura segura: cultivando el futuro acuícola. Investigación y prevención". Parque Científico de la Universidad Miguel Hernández de Elche. 22/11/2023.

Number of Congress Communications

International contributions: 1

Poster presentations: 1

Awards

Special award of the 12th UMH Start-up Creation Marathon: proyecto Acuicultura Segura. Parque Científico de la UMH. 2023.

Governmental Projects and Funding

Evaluación del RNA y proteoma de eritrocitos humanos en el contexto de la Gripe A (ERIVIRUS). 2022i001. CONSELLERIA DE EDUCACION, INVESTIGACIÓN, CULTURA Y DEPORTE (GENERALITAT VALENCIANA). IPs: María del Mar Ortega-Villaizan Romo (UMH), Marta Gómez Ferrer (Hospital La Fe, Valencia)

Training fish nucleated erythrocytes for innovative antiviral solutions in aquaculture. TRAININGERY. CNS2022-135920. AGENCIA ESTATAL DE INVESTIGACIÓN. CNS-2022. IP: Maria del Mar Ortega-Villaizan Romo.

Scaling up NanoPellet (NP) based vaccine production to meet industrial requirements and european regulatory standards. 2022-2024. PDC2022-133194-C22. MINISTRY OF SCIENCE, INNOVATION AND UNIVERSITIES. IPs: Maria del Mar Ortega-Villaizan Romo; Luis Perez Garcia-Estañ

Antiviral Proteins Applied as Therapeutics in Aquaculture (AntiVirFish). 2022-2023. 101069282. ERC PROOF OF CONCEPT. EUROPEAN RESEARCH COUNCIL. IP: María del Mar Ortega-Villaizan Romo.

REDFLAG - Salmonid red blood cells - sensors of stress and infection. NORWEGIAN RESEARCH COUNCIL. NRC# 302551. IP: Maria K. Dahle. Partner: María del Mar Ortega-Villaizán.

Research group: ANTIVIRAL STRATEGIES AGAINST ENVELOPED VIRUSES USING HIGH-PERFORMANCE BIOCOMPUTING

- Study of the structure and interaction with biomembranes of proteins and peptides derived from enveloped viruses (DENV, SARS, ZIKA) that comprise both structural and non-structural viral proteins, with the aim of identifying their molecular mechanism and biological function.

Extractos naturales para aplicación como antivirales en acuicultura (NaturAcuiVir). GVA-THINKINAZUL/ 2021/020. GENERALITAT VALENCIANA. Estrategia Conjunta de Investigación e Innovación en Ciencias Marinas - Plan Complementario de I+D+i -Plan de Recuperación, Transformación y Resiliencia. IP: María del Mar Ortega-Villaizán.

Projects Submitted

Training fish nucleated erythrocytes to turn into immunocyte-like cells for novel antiviral solutions in aquaculture. FishEryStem. ERC-2023-ADG. IP: María del Mar Ortega-Villaizán.

Functional Feeds and Biomarkers for Welfare and Fish Protection against Broad Pathogen Spectrum in Aquaculture: A Heuristic Approach to Holistic Assessments of Fish Health and Welfare. HORIZON-CL6-2022-FARM2FORK-01-06. Coordinator: María del Mar Ortega-Villaizán.

R&D Management

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

Editorial Boards

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

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

Editorial Board member of Vaccines (2020- ongoing).

Editor in Intechopen (2020-ongoing).

Screening of peptide libraries to identify membranotropic determinants, characterize the interactions in structural terms and perform a detailed study of the interaction, modulation and structure of these peptide segments with membranes and cells.

- Development of molecular dynamics bioinformatics tools to study the interaction of proteins from viruses with biomembranes with the aim of finding new antiviral molecules and therapeutic targets to develop new leading compounds useful for improving combination therapies.

Staff

José Villalaín Boullón (ORCID: 0000-0002-5148-141X)

Publications

Villalaín J. Phospholipid binding of the dengue virus envelope E protein segment containing the conserved His residue. *Biochim Biophys Acta Biomembr.* 2023 Oct;1865(7):184198. doi: 10.1016/j.bbmem.2023.184198

Villalaín J. Labyrinthopeptin A2 disrupts raft domains. *Chem Phys Lipids* 2023 Jul;253:105303. doi: 10.1016/j.chemphyslip.2023.105303

Villalaín J. SARS-CoV-2 Protein S Fusion Peptide Is Capable of Wrapping Negatively-Charged Phospholipids.

Membranes (Basel) 2023 Mar 16;13(3):344. doi: 10.3390/membranes13030344

Villalaín J. Bergamottin: location, aggregation and interaction with the plasma membrane. *J Biomol Struct Dyn.* 2023;41(21):12026-12037. doi: 10.1080/07391102.2022.2164521

Governmental Projects and Funding

Molecular dynamics study of aging, oxidation and pH of the lipid structure of the mitochondrial membrane. Fundación ICAR, call 2023, Project MITMEN. IP: José Villalaín

Towards Sustainable Oral Antiviral Vaccines: nanostructured proteins versus microalgae-encapsulated antigens (TSUNAMI). 2022-2025. PID2021-126710OB-C22. Ministry of Science, Innovation and Universities. Ps: Luis Perez Garcia-Estañ; Maria del Mar Ortega-Villaizan Romo.

Research group: PROTEIN ARCHITECTURE GROUP

Use of bioinformatics and experimental methods in:

- Identification of small molecules and peptides with pharmacological potential.
- Identification and biochemical, biophysical and structural characterization of macromolecules as therapeutic targets.
- Molecular characterization of protein-ligand interactions with pharmacological potential.

Staff

Ana María Fernández Escamilla (ORCID: 0000-0002-6615-4913)

External collaborators integrated in the group

Ph.D. Luis Serrano Pubull. Director CRG Centro de Regulación Genómica (CRG) Barcelona, Spain.

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

Prof. Ana Martínez Gil and Carmen Gil. Ph.D. Elnaz Aledavood. Translational Medicinal and Biological Chemistry Group CIB Margarita Salas, Spanish National Research Council (CSIC) Madrid, Spain.

Ph.D. Maria D. Ferrer García. Senior researcher Foundation for the Promotion of Health and Biomedical Research (FISABIO) Alicante, Spain.

Ph.D. Maria D. Ferrer García. Senior researcher Foundation for the Promotion of Health and Biomedical Research (FISABIO) Valencia, Spain.

Patents

Title: Combination therapy against SARS-CoV-2 and other coronaviruses. PAT: P202330781. Contributors: Ana Grande;

Enrique Viguera; Ana María Fernández-Escamilla; Gregorio Fernández Ballester; Sergio Ortega del Campo; Clara M Blanes Mira; M Isabel Viciano Ramos; Encarnación Clavijo Frutos; Jesús Leandro Santos González.

Science Dissemination: Outreach Activities

Identificación de nuevos inhibidores del virus del Zika mediante la combinación de estrategias computacionales y experimentales. FUNDACION INSTITUTO TEOFILO HERNANDO. XLIII GENN. Reunión del Grupo Español de Neurotransmisión y Neuroprotección 13/12/2023.

Molecular design of non-immunogenic inhibitors of SARS-CoV-2 nsp14 and nsp16 proteins for combination antiviral therapy Universidad Miguel Hernández de Elche. XV JORNADAS SAN ALBERTO MAGNO 15/11/2023.

Molecular design of non-immunogenic inhibitors of SARS-CoV-2 nsp14 and nsp16 proteins for combination antiviral therapy. XVII International Congress of the Spanish Biophysical Society 27/06/2023.

Number of Congress Communications

National contributions: 3

Oral presentations: 1

Poster presentations: 2

International contributions: 1

Research group: VIRAL IMMUNOLOGY & THERAPEUTICS

Development of new DNA vaccines to prevent pediatric diseases of high prevalence.

Staff

Pablo Garcia Valtanen (ORCID: 0000-0003-4382-6446)

Ph. D Students

Inmaculada Gómez González (ORCID: 0000-0003-1537-3830)

Publications

Perkins GB, Tunbridge MJ, Chai CS, Hope CM, Yeow AEL, Salehi T, Singer J, Shi B,

Poster presentations: 1

Governmental Projects and Funding

Halting aging and neurodegeneration through the development of SGK1 inhibitors. 2023-01 to 2023-12 | SGK4END. Grants for Research on Aging, ICAR 2023. ICAR Foundation Grants Program for Research on Aging, International Centre for Ageing Research (ICAR). IP: Ana María Fernández Escamilla, ColP: Ana Martínez Gil.

R&D Management

Agencia Nacional de Evaluación y Prospectiva (ANEP).

Scientific Society Councils

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

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

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

Editorial Boards

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

Masavuli MG, Mekonnen ZA, Garcia-Valtanen P, et al. mTOR inhibition improves the formation of functional T cell memory following COVID-19 vaccination of kidney transplant recipients. Preprint. doi: <https://doi.org/10.1101/2023.03.27.23287773>

Governmental Projects and Funding

Development of new vaccines to attack the biggest viral threats to newborns and infants. 23/06/2015 – Plan Gen T (CIDEAGENT) - GVA 2022

(CIDEXG/2022/40). Conselleria de Innovación, Universidades, Ciencia y Sociedad Digital. IP: Pablo García Valtanen

R&D Management

Reviewer for Vaccine, Kidney International, Scientific Reports, Applied Microbiology and Biotechnology, Helminthologia, Pharmaceutical Research, Fish and Shellfish Immunology, Bioscience Reports. P. García Valtanen.

Diabetes and obesity / Endocrine disruptors in health

Unit/Group name: DIABETES RESEARCH UNIT (UNIBAD)

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 a gene by environment interaction. Our research unit works to understand how different environmental factors such as high fat diet and endocrine disrupting chemicals work to increase diabetes susceptibility.

We work on four different research lines:

1- The role that endocrine disrupting chemicals (EDCs) in the etiology of Diabetes. We study how exposure to EDCs at different times during life, from

pregnancy to adulthood, affects insulin sensitivity as well as the function of the endocrine pancreas. We address this problem by investigating in mice how these chemicals change the expression of genes related to β -cell function, death and division, during fetal development as well as during adulthood. We combine in vivo research with ex vivo and in vitro approaches to molecularly understand how EDCs alter β -cell function, division and death.

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

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

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

3. The role of interferon- α (IFN α) in pancreatic α - and β -cells in early stages of type 1 diabetes. Type 1 diabetes (T1D) is a chronic autoimmune disease characterized by pancreatic islet

inflammation and specific destruction of insulin-producing beta-cells by the immune system. In early stages of T1D IFN α plays a critical role in the initiation of the disease but the molecular mechanisms underlying IFN α effects directly on pancreatic cells are largely unknown. The results of this project will provide a better understanding of the effects of IFN α exposure on alpha- and beta-cell function and will develop new therapeutic strategies selecting small molecules that inhibit TYK2-mediated IFN α signaling pathway in alpha- and beta-cells.

4. Maternal metabolic adaptations during pregnancy: implications for the development of gestational diabetes mellitus. Gestational diabetes mellitus (GDM) is the most common metabolic disorder of pregnancy. In addition to the transient maternal hyperglycaemia during pregnancy, GDM predisposes the mother and the offspring for increased risk of developing T2D and obesity. Using animal and in vitro models we aim to understand the molecular basis of this disease and to identify altered signaling pathways leading to the development of GDM. We also aim to explore potential therapeutic tools which may present beneficial effects in the prevention and control of GDM.

Staff

Ángel Nadal (ORCID: 0000-0003-4178-2152)

Cristina Ripoll Orts (ORCID: 0000-0003-0935-8722)

Esther Fuentes Marhuenda (ORCID: 0000-0002-9113-739X)

Iván Quesada Moll (ORCID: 0000-0002-9808-514X)

Paloma Alonso Magdalena (ORCID: 0000-0003-1065-5388)

Laura Marroquí Esclapez (ORCID: 0000-0003-2931-9317)

Postdoctoral Researchers

Hilda Ferrero Hidalgo (ORCID: 0000-0001-7960-7523)

Reinaldo Sousa dos Santos (ORCID: 0000-0002-3219-4730)

Regla María Medina Gali (ORCID: 0000-0001-9401-8292)

Talía Boronat Belda (ORCID: 0000-0002-6548-5251)

Cristina Quereda Galvañ (ORCID:0000-0003-2970-6712)

External collaborators (Universidad de Alicante)

Juan Martínez-Pinna

Sergi Soriano Úbeda

Ph. D Students

Ignacio Babiloni Chust (ORCID: 0000-0003-1714-7650)

Atenea Alexandra Pérez Serna (ORCID: 0000-0002-7594-6365)

Roberto Sempere Navarro (ORCID: 0009-0005-4317-4945)

Daniel Guzmán Llorens (ORCID: 0000-0003-1734-9383)

Technicians

María Luisa Navarro García

María Salomé Ramón Penalva

Beatriz Bonmatí Botella

Publications

Martínez-Pinna J, Sempere-Navarro R, Medina-Gali RM, Fuentes E, Quesada I, Sargis RM, Trasande L, Nadal A. Endocrine disruptors in plastics alter β -cell physiology and increase the risk of diabetes mellitus. *Am J Physiol Endocrinol Metab.* 2023 Jun 1;324(6):E488-E505. doi: 10.1152/ajpendo.00068.2023

Martins JRN, Lopes S, Hurtado HN, da Silva FN, Villard DR, Taboga SR, Souza KLA, Quesada I, Soriano S, Rafacho A. Acute and chronic effects of the organophosphate malathion on the pancreatic α and β cell viability, cell structure, and voltage-gated K⁺ currents. *Environ Toxicol Pharmacol.* 2023 Mar; 98:104046. doi:10.1016/j.etap.2022.104046

Bruxel MA, da Silva FN, da Silva RA, Zimath PL, Rojas A, Moreira ELG, Quesada I, Rafacho A. Preconception exposure to malathion and glucose homeostasis in rats: Effects on dams during pregnancy and post-term periods, and on their

progeny. *Environ Pollut.* 2023 Jan 1;316(Pt 2):120633. doi: 10.1016/j.envpol.2022.120633

Crouzet T, Grignard E, Brion F, Blanc EB, Podechard N, Langouet S, Alonso-Magdalena P, Hubert P, Kim MJ, Audouze K. ReadEDTest: A tool to assess the readiness of in vitro test methods under development for identifying endocrine disruptors. *Environ Int.* 2023 Apr;174:107910. doi: 10.1016/j.envint.2023.107910

Dos Santos RS, Guzman-Llorens D, Perez-Serna AA, Nadal A, Marroqui L. Deucravacitinib, a tyrosine kinase 2 pseudokinase inhibitor, protects human EndoC- β H1 β -cells against proinflammatory insults. *Front Immunol.* 2023 Oct 3;14:1263926. doi: 10.3389/fimmu.2023.1263926

Al-Abdulla R, Ferrero H, Boronat-Belda T, Soriano S, Quesada I, Alonso-Magdalena P. Exploring the Effects of Metabolism-Disrupting Chemicals on Pancreatic α -Cell Viability, Gene Expression and Function: A Screening Testing Approach. *Int J Mol Sci.* 2023 Jan 5;24(2):1044. doi: 10.3390/ijms24021044

Perez-Serna AA, Dos Santos RS, Ripoll C, Nadal A, Eizirik DL, Marroqui L. BCL-XL Overexpression Protects Pancreatic β -Cells against Cytokine- and Palmitate-Induced Apoptosis. *Int J Mol Sci.* 2023 Mar 16;24(6):5657. doi: 10.3390/ijms24065657

Muncke J, Andersson AM, Backhaus T, Belcher SM, Boucher JM, Carney Almroth B, Collins TJ, Geueke B, Groh KJ, Heindel JJ, von Hippel FA, Legler J, Maffini MV, Martin OV, Peterson Myers J, Nadal A, Nerin C, Soto AM, Trasande L, Vandenberg LN, Wagner M, Zimmermann L, Thomas Zoeller R, Scheringer M. A vision for safer food contact materials: Public health concerns as drivers for improved testing. *Environ Int.* 2023 Oct;180:108161. doi: 10.1016/j.envint.2023.108161

Dos Santos RS, Babiloni-Chust I, Marroqui L, Nadal A. Screening of Metabolism-Disrupting Chemicals on Pancreatic α -Cells Using In Vitro Methods. *Int J Mol Sci.* 2023 Jan; 24(1): 231 doi: 10.3390/ijms24010231

Heindel JJ, Alvarez JA, Atlas E, Cave MC, Chatzi VL, Collier D, Corkey B, Fischer D, Goran MI, Howard S, Kahan S, Kayhoe M, Koliwad S, Kotz CM, La Merrill M, Lobstein T, Lumeng C, Ludwig DS, Lustig RH, Myers P, Nadal A, Trasande L, Redman LM, Rodeheffer MS, Sargis RM, Stephens JM, Ziegler TR, Blumberg. *Obesogens and Obesity: State-of-the-Science and Future Directions Summary from a Healthy Environment and Endocrine Disruptors Strategies Workshop.* *Am J Clin Nutr.* 2023 Jul;118(1):329-337. doi: 10.1016/j.ajcnut.2023.05.024

PhD Theses

Title: Papel de los receptores de estrógenos ER α , ER β y el receptor de estrógenos acoplado a proteínas G (GPER) en la viabilidad de la célula beta. Student: Ignacio Babiloni Chust. Supervisors: Dr. Ángel Nadal and Dra. Laura Marroquí. Qualification: Sobresaliente Cum Laude. 24/03/2023.

Organization of meetings

Reunión Anual CIBERDEM, Mataró (Barcelona), Noviembre 2023. Member of the Organizing Committee: Angel Nadal.

CIBERDEM Young Investigators, Mataró (Barcelona), Noviembre 2023. Member of the Organizing Committee: Laura Marroquí.

International Workshop on Diabetes and Related Metabolic Disorders Prometeo-Prometeo-Generalitat Valenciana, Elche, Octubre 2023. Member of the Organizing Committee: Ángel Nadal, Paloma Alonso-Magdalena and Everardo Magalhães Carneiro.

V Workshop ¿What is going on in diabetes research? Elche, Noviembre 2023. Member of the Organizing Committee: Laura Marroquí, Reinaldo S. dos Santos.

Gordon Research Conference on Environmental Endocrine Disruptors. June 2024. Member of the Organizing Committee: Angel Nadal (<https://www.grc.org/environmental-endocrine-disruptors-conference/2024/>).

Invited Talks and Courses

Endocrine-Disrupting Chemicals and metabolic diseases. 39ème Congrès de la Société Française d'Endocrinologie, Marseille, Francia 2023. Plenary Lecture. Ángel Nadal.

Disruptors endocrins i diabetis. XVLLÈ CONGRES DE L'ASSOCIACIO CATALANA DE DIABETIS, Terrassa (Barcelona) 2023. Opening Lecture. Angel Nadal.

Altered beta cell physiology and risk of diabetes from endocrine disrupting chemicals. The Finnish Endocrine Society's Endodays, Helsinki (Finlandia), 2023. Ángel Nadal.

How do endocrine disruptors upset our metabolic system? European Society of Endocrinology (Online), 2023. Ángel Nadal.

Plastics and Plasticity of Pancreatic Beta-Cells. 14TH CIBERDEM ANNUAL MEETING, Mataró (Barcelona) 2023. Ángel Nadal.

Identifying the effects of endocrine disruptors in human health. 64 CONGRESO SOCIEDAD ESPAÑOLA DE ENDOCRINOLOGIA Y NUTRICION. Barcelona, 2023. Ángel Nadal.

Efecto de los disruptores endocrinos sobre la función alfa y beta pancreática. VIII CURSO DE ACTUALIZACION EN ENDOCRINOLOGIA Y NUTRICION. Madrid, 2023. Ángel Nadal.

Alteración de la masa funcional de la célula beta pancreática por disruptores endocrinos. CICLO DE SEMINARIOS INIBICA. Fundación para la Gestión de la Investigación Biomédica Cádiz. Online. 2023. Ángel Nadal.

Diabetes, obesity and diabetes epidemic: overview of endocrine disruptors as contributing factor. Obesity and Comorbidities Research Center Annual Symposium. UNICAMP, Brazil, 2023. Paloma Alonso-Magdalena.

¿Qué hay de nuevo en la fisiología de las células de los islotes? WEBINAR "Novedades En Diabetes De La Reunión

Anual De La EASD 2023". SED October 2023. Laura Marroquí.

Screening of metabolism-disrupting chemicals on pancreatic β -cells. 25th European Congress of Endocrinology. May 2023. Istanbul, Turkey. Reinaldo S. dos Santos.

Science Dissemination: Outreach Activities

Últimos avances en terapias para la diabetes tipo 1. Jornadas ADEC. Elche, October 2023. Laura Marroquí.

¿Se puede prevenir la diabetes tipo 1?. Twitch tv SHEREZADE MR #JUSTSCIENCING. June 2023. Laura Marroquí.

Promesas y realidad de las terapias para la diabetes tipo 1. Lo que la ciencia puede aportar. II CICLO DE INVESTIGACION Y CIENCIA EN DIABETES. Murcia April 2023. Laura Marroquí.

Los disruptores endocrinos y su papel en el desarrollo de la diabetes. II Ciclo de Investigación y Ciencia en Diabetes. Murcia April 2023. Reinaldo S. dos Santos.

Career development in diabetes research: an EASD Early Career Academy panel discussion, EASD 59th Annual Meeting, Hamburgo, Alemania. Paloma Alonso-Magdalena

Participación en el proyecto Midnight, programa Researchers Back To School; Colegio Santa María, Instituto Maciá Abela. Paloma Alonso-Magdalena

Number of Congress Communications

National contributions: 7

Oral presentations: 2

Poster presentations: 5

International contributions: 4

Oral presentations: 2

Poster presentations: 2

Governmental Projects and Funding

Regulación de la viabilidad y la función de las células β y α pancreáticas por los receptores de estrógenos ER β y GPER:

papel en la terapia de la diabetes mellitus. 2020-2023-PROGRAMA DE EXCELENCIA PROMETEO, Generalitat Valenciana. IP: Ángel Nadal.

Beating Goliath: Generation Of Novel, Integrated and Internationally Harmonised Approaches for Testing Metabolism Disrupting Compounds. 01/01/2019-31/06/2024- EUROPEAN COMMISSION. REF.: GA 825489. IP: Ángel Nadal.

Relación entre ERalpha, ERbeta y GPER en las células beta del páncreas y su papel en la regulación de los canales de potasio y la apoptosis inducida por estrógenos ambientales. 01/09/2021-31/08/2024-MINISTERIO DE CIENCIA E INNOVACIÓN. AGENCIA ESTATAL DE INVESTIGACIÓN. IPs : Ángel Nadal y Juan Martínez-Pinna.

An integrative strategy of testing systems for identification of EDs related to metabolic disorders (OBERON). 01/01/2019 – 31/06/2024- EUROPEAN COMMISSION, Horizon 2020 -Research and Innovation Framework Programme. IP: Paloma Alonso-Magdalena.

Papel de la señalización mediada por TGFbeta en las adaptaciones metabólicas maternas durante el embarazo: implicaciones para el desarrollo de la diabetes mellitus gestacional. 01/09/2021- 31/08/2024-Proyectos I+D+i 2020 -MODALIDADES "RETOS INVESTIGACIÓN" Y "GENERACIÓN DE CONOCIMIENTO" PID2020 -AEI/MCI. AGENCIA ESTATAL DE INVESTIGACION (PID2020-113112RB-I00). IP: Paloma Alonso-Magdalena.

La vía de señalización mediada por TGFβ y su relación con la etiología de la diabetes mellitus gestacional: explorando nuevos biomarcadores de diagnóstico. 01/01/2023-31/12/2023-Acciones preparatorias para la exploración y formulación de futuros proyectos de investigación/innovación 2022. Subprograma ILISABIO. IPs: Paloma Alonso-Magdalena y Rubén Betoret Gustems.

Descifrando las respuestas inducidas por interferón-alfa de las células alfa y beta pancreáticas: una oportunidad para buscar nuevas dianas terapéuticas para

la diabetes tipo 1. 01/09/2021-31/08/2024- AGENCIA ESTATAL DE INVESTIGACIÓN (PID2020-117569RA-I00). IP: Laura Marroquí.

Unravelling interferon-alpha-induced responses of pancreatic alpha-and β-cells: an opportunity to seek for new therapeutic approaches for type 1 diabetes (UnravelingIFNa). 01/01/2023 – 31/12/2024- GENERALITAT VALENCIANA. CIAPE/2022/2. IP: Laura Marroquí.

Interfiriendo al Interferón alfa en Diabetes tipo 1 (InterfiriendoIFNa). 01/09/2023 – 31/08/2025- AGENCIA ESTATAL DE INVESTIGACIÓN (CNS2022-135505). IP: Laura Marroquí.

Abordando el papel del páncreas endocrino en el envejecimiento: nuevas estrategias y perspectivas. 01/01/2023-31/12/2023- PROGRAMA DE AYUDAS PARA LA INVESTIGACIÓN DEL ENVEJECIMIENTO DE LA FUNDACIÓN ICAR, Convocatoria 2023. Fundación Centro Internacional para la Investigación del Envejecimiento (ICAR). IPs: Sergi Soriano e Iván Quesada.

Ayuda UMH para proyectos de difusión de la ciencia, la tecnología y la innovación 1/01/2023 -31/12/2023. IP: Laura Marroquí.

Proyecto de internacionalización en casa UMH (PRODIC-UMH). Co-tutela de un proyecto final de Máster en un ambiente internacional entre IDiBE-UMH/ULB-CDR desde la UMH. El Trabajo Final de Master tendrá como título: Desarrollo de nuevos inhibidores de TYK2 para la prevención de la Diabetes tipo 1. IP: Laura Marroquí.

Projects Submitted

Cellular resilience in type 1 diabetes: unveiling adaptive stress mechanisms triggered by IFNa exposure (IFNa-T1D-ADAPT). Proyectos de Generación de Conocimiento-2023. IP: Laura Marroquí.

Understanding the role of endocrine disruptors in the transition from pregnancy to postpartum: an opportunity to prevent maternal diabetes. PROGRAMA PROMETEO PARA GRUPOS DE INVESTIGACIÓN DE EXCELENCIA (PROMETEO)-Generalitat Valenciana. IPs:

Paloma Alonso-Magdalena y Ángel Nadal.

Physiological effects of selective extranuclear estrogen receptor signaling in pancreatic β -cells and hypothalamic neurons. Proyectos de Generación de Conocimiento-2023. IPs: Ángel Nadal y Juan Martínez-Pinna.

Challenges for maternal diabetes prevention after gestational diabetes: deciphering the molecular and functional endocrine pancreas remodelling during pregnancy and postpartum. Proyectos de Generación de Conocimiento-2023. IPs: Paloma Alonso-Magdalena e Iván Quesada.

R&D Management

Grant Reviewer of: Instituto de Salud Carlos III (España), ANR / L'Agence Nationale de la Recherche (France). Laura Marroquí Esclapez.

Grant Reviewer of: Swiss National Foundation (Switzerland), German Research Foundation (Germany), Instituto de Salud Carlos III (España), Agencia Estatal de Investigación (España). Paloma Alonso-Magdalena.

Grant reviewer: Fonds de la Recherche Scientifique- FNRS (Belgium), Agencia Estatal de Investigación (España). Ivan Quesada.

Grant Reviewer: Agencia Estatal de Investigación (España). Ángel Nadal.

Reviewer of Journals: BMC Molecular and Cell Biology, Frontiers in Endocrinology, Frontiers in Physiology, Biomedicines. Laura Marroquí.

Reviewer of Journals: Metabolism-Clinical and Experimental, Science of the Total Environment, International Journal of Molecular Sciences, Endocrinology. Paloma Alonso-Magdalena.

Reviewer of Abstracts. 23th European Congress of Endocrinology. Istanbul. Mayo 2023. Paloma Alonso-Magdalena.

Reviewer of Journals: Am. J. Physiol. Endoc. Metab, Chemosphere, Ecotox. Environ. Safety, Metabolism. Ivan Quesada.

Membership of: Sociedad Española de Diabetes (SED), European Association for

the Study of Diabetes (EASD), Islet Society. Laura Marroquí.

Membership of: Sociedad Española de Diabetes (SED), European Association for the Study of Diabetes (EASD), Societat Catalana de Biologia. Iván Quesada.

Membership of: Sociedad Española de Diabetes (SED), European Association for the Study of Diabetes (EASD), Sociedad Española para el estudio de la Obesidad (SEEDO), Sociedad Española de Ciencias Fisiológicas (SECF). Paloma Alonso-Magdalena.

Membership of: Sociedad Española de Diabetes (SED), Sociedad Española para el estudio de la Obesidad (SEEDO), Sociedad Española de Ciencias Fisiológicas (SECF), Endocrine Society, European Society for Endocrinology, Sociedad Española de Endocrinología y Nutrición (SEEN), Sociedad Española para el Estudio de la Obesidad (SEEDO), Sociedad Española de Bioquímica y Biología Molecular (SEBBM). Ángel Nadal.

Scientific Society Councils

Member of the Endocrine Disrupting Chemicals Advisory Group of the Endocrine Society. Angel Nadal.

Member of the Endocrine Disrupting Chemicals Working Group European Society of Endocrinology. Angel Nadal.

Member of the Scientific Advisory Board Food Packaging Forum Foundation, Zurich, Switzerland. Angel Nadal.

External Advisory Board member. Instituto de Biomedicina y Genética Molecular, Universidad de Valladolid-CSIC. Ángel Nadal.

Editorial Boards

Editorial Board Member: Frontiers in Endocrinology, Frontiers in Physiology, Biomedicines. Laura Marroquí Esclapez.

Editorial Board Member: Scientific Reports, Endocrine Connections, International Journal of Molecular Sciences, Frontiers in Physiology. Paloma Alonso-Magdalena.

Editorial Board Member: Frontiers in Physiology, Frontiers in Endocrinology, Frontiers in Neuroscience. Angel Nadal.

Development of new tools in the area of cancer, especially in tumours as glioblastoma or pancreatic and breast cancer

Unit/Group name: HARD TO TREAT CANCERS UNIT

Research group: HARD TO TREAT CANCERS UNIT

Dr. Miguel Saceda and Dr Camino de Juan are leading this group, both are staff researchers at the Foundation for the Promotion of Health and Biomedical Research of the Valencian Community (FISABIO). Our group has developed a line of research focused on the search for alternative treatments in tumors that have acquired resistance to antineoplastic treatments. Within this line, we have started the generation of primary cultures of particularly aggressive and resistant tumors, such as glioblastoma and pancreatic carcinoma. Such cultures have been constituted in a model of predictive test of response applicable *ex vivo* to patients. In addition, we are isolating exosomes and obtaining organoids from patients' samples and developing new animal models as study models closest to the patient. Likewise. Actual research lines:

- Search and development of biomarkers of sensitivity and/or resistance to chemo and radiation therapy in glial and pancreatic tumors.
- Development of nanotechnological-based enzyme treatments for chemo and radio resistant tumors.
- Development of alternative therapies for chemo and radio resistant tumors based on signal transduction pathways and cellular epigenetic control.
- Evaluation of exosomes as drug transporters for patient treatment and as potential liquid biopsies.
- Development of preclinical *in vitro* and *in vivo* models.

Staff

Miguel Saceda Sánchez (ORCID: 0000-0002-1564-3602)

Camino de Juan Romero (ORCID: 0000-0001-7890-8447)

Dr. Pilar Garcia Morales (ORCID: 0000-0002-8424-4613)

Postdoctoral Researchers

Maria Fuentes Baile (ORCID: 0000-0003-3653-2407)

External collaborators integrated in the group

Dr. Víctor Manuel Barberá Juan (ORCID: 0000-0002-4012-6973)

Dr. José Martín Nieto

Dr. Teresa Quintanar Verdúguez

Carlos Martorell Llobregat

Ph. D Students

Elizabeth Perez Valenciano (ORCID: 0000-0001-9271-0592)

José Marcos Berna Belmonte (ORCID: 0000-0003-1571-9416)

Elena Lloret López (ORCID: 0009-0001-4814-9395)

Technicians

Lourdes Soto Conde (ORCID: 0009-0008-1534-8436)

Antonio Manresa Manresa

Publications

Araujo-Abad S, Manresa-Manresa A, Rodríguez-Cañas E, Fuentes-Baile M, García-Morales P, Mallavia R, Saceda M, de Juan Romero C. Glioblastoma-Derived Small Extracellular Vesicles: Nanoparticles for Glioma Treatment. *Int J Mol Sci.* 2023 Mar 21;24(6):5910. doi: 10.3390/ijms24065910

Araujo-Abad S, Manresa-Manresa A, Rodríguez-Cañas E, Fuentes-Baile M, García-Morales P, Mallavia R, Saceda M,

de Juan Romero C. New therapy for pancreatic cancer based on extracellular vesicles. *Biomed Pharmacother* 2023 Jun;162:114657. doi: 10.1016/j.biopha.2023.114657. Epub 2023 Apr 5. PMID: 37023623

Araujo-Abad S, Rizzuti B, Villamarin-Ortiz A, Pantoja-Uceda D, Moreno-Gonzalez CM, Abian O, Velazquez-Campoy A, Neira JL, de Juan Romero C. New insights into cancer: MDM2 binds to the citrullinating enzyme PADI4. *Protein Sci.* 2023 Jul;17(7):923-33. doi: 10.1038/nn.3729

Araujo-Abad S, Fuentes-Baile M, Rizzuti B, Bazán JF, Villamarin-Ortiz A, Saceda M, Fernández E, Vidal M, Abian O, Velazquez-Campoy A, de Juan Romero C, Neira JL. The intrinsically disordered, epigenetic factor RYBP binds to the citrullinating enzyme PADI4 in cancer cells. *Int J Biol Macromol.* 2023 Jul 2;246:125632. doi: 10.1016/j.ijbiomac.2023.125632

Araujo-Abad S, Neira JL, Rizzuti B, García-Morales P, de Juan Romero C, Santofimia-Castaño P, Iovanna J. Intrinsically Disordered Chromatin Protein NUPR1 Binds to the Enzyme PADI4. *J Mol Biol.* 2023 Apr 15;435(8):168033. doi: 10.1016/j.jmb.2023.168033. PMID: 36858171

Messé A, Hollensteiner KJ, Delettre C, Dell-Brown LA, Pieper F, Nentwig LJ, Galindo-Leon EE, Larrat B, Mériaux S, Mangin JF, Reillo I, de Juan Romero C, Borrell V, Engler G, Toro R, Engel AK, Hilgetag CC. Structural basis of envelope and phase intrinsic coupling modes in the cerebral cortex. *Neuroimage* 2023 Aug 1;276:120212. doi: 10.1016/j.neuroimage.2023.120212. Jun 1. PMID: 37269959

patents

Patent in drafting stage: Report 101704/P9604.

PhD Theses

Title: Small extracellular vesicles as a potential clinical tool for hard to treat cancer therapy. Student: Lourdes Salomé Araujo Abad. Supervisors: Dra. Pilar García Morales and Dra. Camino de Juan

Romero. Qualification: Mencion Europea, Sobresaliente Cum Laude. 24/03/2023.

Science Dissemination: Outreach Activities

"Contraste de Fases"- a monthly radio program on science news. Pilar García, Miguel Saceda, Luis Perez and Manuel Sánchez. UMH Radio.

"Investigadoras en biotecnología sanitaria, Centro de Congresos "Ciutat d'Elx" de Elche" (Elche). INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE DAY AT IDiBE ("CIENCIA CON TAPAS") 14/02/23. Speaker: Camino de Juan.

Number of Congress Communications

International contributions: 5

Oral presentations: 2

Poster presentations: 3

Awards

Salome Araujo Abad – Santander-UMH Award for young researchers for the article: Araujo-Abad S, Saceda M, de Juan Romero C*. Biomedical application of exosomes in cancer treatment. *Adv Drug Deliv Rev.* 2022. IF: 17.873 Q1D1

Governmental Projects and Funding

2020-2025. Miguel Servet 2019. Study of the mechanism underlying the tumorigenic capacity of the GBM multiforme. (CP19/00095) ISCIII. 242.500 €.

2022-2025. Health Research Projects. Identification of new therapeutic targets for the prognosis and improvement of glioblastoma treatment. (PI22/00824). ISCIII. 147.620 €.

2022-2024. AICO. New strategies against cancer: inhibition of molecular interactions of arginine protein deiminases (CIAICO 2021/135). GVA. 90.000 €.

2023-2024. APE. New generation biomimetic nanoparticles for the treatment of glioblastoma (CIAPE/2022/14). GVA 9.000 €.

2023-2025. APOTI. Development of new drugs for therapeutic targets found by transcriptomic analysis (CIAPOT/2022/3). GVA. 36.000€. Contract with the BIOARRAY company.

2023-2025. APOTI. Graphene-based anti-tumour nanoformulations. (CIAPOT/2022/7). GVA. 36000€. Contract with the Applynano Solutions S.L. company.

2022-2023. EPRIEX. PI: Camino de Juan. Internship in the public administration of Antonio Manresa Manresa (Conselleria de economía sostenible, sectores productivos, comercio y trabajo). 12 months. 32.108,92 €.

2022-2023. EPRIEX. PI: Camino de Juan. Internship in public administration by Sergio Martí Torregrosa (Conselleria de economía sostenible, sectores productivos, comercio y trabajo). 12 months. 12 months. 32.108,92 €.

2022-2023. Copper sulphide nanoformulations as therapeutic agents for tumours with poor prognosis. ILISABIO 2022 Call (UMH/FISABIO). NANOTERASUCO Project (Acronym). 5000€. IP: Miguel Saceda.

2022-2023. Response to interferon and acquisition of chemoresistance in pancreatic and colon carcinomas. Call (FISABIO/La FE). 5000€. IP: Pilar García Morales.

Private funding: Contracts

CONTRATO DE OPCIÓN DE LICENCIA Y TRANSFERENCIA DE RESULTADOS ENTRE LA FUNDACIÓN PARA EL FOMENTO DE LA INVESTIGACIÓN SANITARIA Y BIOMÉDICA DE LA COMUNITAT VALENCIANA (FISABIO) Y APPLYNANO SOLUTIONS S.L. (para la evaluación de nanoformulaciones de grafeno como transportadores de antineoplásicos y/o vectores de terapias enzimáticas antitumorales). IP: Miguel Saceda Sánchez.

Projects Submitted

AECC Lab 2024 Development of a new personalized medicine for glioblastoma treatment. IP. Dr. Camino de Juan 300.000€

HORIZON-EIC-2024-PATHFINDEROPEN-01. NEXTGENANO: Next generation personalized medicine for glioblastoma treatment. IP. Dr. Camino de Juan. Project coordinator. 3.000.000€.

CAIXA-Impulse. Organo-silanes targeting proteins to treat glioblastoma and pancreatic cancers. Group Member: Camino de Juan. 50.000€.

R&D and Educational Committees

2024- ongoing. Protect evaluator. ISCIII. Spain. Camino de Juan

2021-ongoing. Review panel member (Science/ Health). Evaluator/Area coordinator. ACSUG (Axencia para a Calidade do Sistema Universitario de Galicia). "Grants to support the predoctoral stage", "Grants to support the postdoctoral stage", "Grants for the industrial doctorate program", "Grants for the program of consolidation and structuring of competitive research units". Camino de Juan

2019- Project evaluator for the Department of Health of the Government of Navarra. Miguel Saceda

2022- Project evaluator for the Agency for the quality of the university system of Castilla y Leon (ASUCYL). Miguel Saceda

2019-Ong Project Evaluator for the National Agency for Evaluation and Prospective Studies (ANEP). Miguel Saceda

2019-ong Project evaluator for the Progress and Health Foundation of Andalusia. Miguel Saceda

2023- Project evaluator for the Research and Innovation Agency of Castilla la Mancha. Miguel Saceda

2021-Ong Project evaluator for the Biobank of the public health system of Andalusia. Miguel Saceda

2022 Project evaluator for the Spanish Cancer Association. Miguel Saceda

R&D Management

2021- ongoing. Reviewer for Cancers, Nanomaterials, Pharmaceutics, International Journal of Molecular Sciences, Viruses, Applied Sciences, Cells,

Journal of Clinical Medicine. MDPI. Camino de Juan

2020– ongoing. Reviewer for Archives of Biochemistry and Biophysics; Biomedicine & Pharmacotherapy. Elsevier. Camino de Juan

2023– ongoing. Reviewer for Scientific Reports. Nature portfolio. Camino de Juan

2023– ongoing. Reviewer for Extracellular Vesicles and Circulating Nucleic Acids. OAE Publishing Inc. Camino de Juan

2023– ongoing. Reviewer for Nanomedicine. Future medicine Ltd. Camino de Juan

2023 – ongoing. Member of the Mentoring program. FISABIO. Spain. 2023 – ongoing. Member of the Mentoring program. FISABIO. Spain. Camino de Juan

2020 – ongoing. Member of the Program for external Practice “Obsevatorio ocupacional” Miguel Hernandez University. Spain. Camino de Juan

2023 – ongoing. Scientific Advisory Board. +queuntrail. Spain. Camino de Juan

2022 – ongoing. Internal Scientific Advisory Board. FISABIO. Spain. Camino de Juan

2022 Review panel member (secretary) “Master en Biotecnología y Bioingeniería”. Miguel Hernandez University. Spain. Camino de Juan

2020 – ongoing Scientific Advisory Board for “SELLO EUROPEO de EXCELENCIA RRHH (HRS4R)”. FISABIO. Spain. Camino de Juan

2020 – ongoing Member of the Program for external Practice “Obsevatorio ocupacional” Miguel Hernandez University. Spain. Camino de Juan

2023 – ongoing Scientific Advisory Board. +queuntrail. Spain. Camino de Juan

2022 – ongoing Internal Scientific Advisory Board. FISABIO. Spain. Camino de Juan

2022 Review panel member (secretary) “Master en Biotecnología y Bioingeniería”. Miguel Hernandez University. Spain. Camino de Juan

2020 – ongoing Scientific Advisory Board for “SELLO EUROPEO de EXCELENCIA RRHH (HRS4R)”. FISABIO. Spain. Camino de Juan

2019- Reviewer for Plos One. Miguel Saceda

2020- Reviewer for Cancers. Miguel Saceda

2022- Reviewer for IJMS. Miguel Saceda

2020- Reviewer for Cancers. Miguel Saceda

2022- Reviewer for IJMS. Miguel Saceda

Research group: Structure of proteins

Solving structure of proteins and their interactions by using NMR

Staff

José Luis Neira Faleiro (ORCID: 0000-0002-4933-0428)

Publications

Rizzuti B, Abian O, Velazquez-Campoy A, Neira JL. Conformational Stability of the N-Terminal Region of MDM2. *Molecules* 2023 Nov 14;28(22):7578. doi: 10.3390/molecules28227578

Araujo-Abad S, Rizzuti B, Villamarin-Ortiz A, Pantoja-Uceda D, Moreno-Gonzalez CM, Abian O, Velazquez-Campoy A, Neira JL,

de Juan Romero C. New insights into cancer: MDM2 binds to the citrullinating enzyme PADI4. *Protein Sci.* 2023 Aug;32(8):e4723. doi: 10.1002/pro.4723

Araujo-Abad S, Fuentes-Baile M, Rizzuti B, Bazán JF, Villamarin-Ortiz A, Saceda M, Fernández E, Vidal M, Abian O, Velazquez-Campoy A, de Juan Romero C, Neira JL. The intrinsically disordered, epigenetic factor RYBP binds to the citrullinating enzyme PADI4 in cancer cells. *Int J Biol Macromol.* 2023 Aug 15;246:125632. doi: 10.1016/j.ijbiomac.2023.125632

Sobrado P, Neira JL. Paul F. Fitzpatrick: A life of editorial duties and elucidating the

mechanism of enzyme action. Arch Biochem Biophys. 2023 Jul 1;742:109635. doi: 10.1016/j.abb.2023.109635

Araujo-Abad S, Neira JL, Rizzuti B, García-Morales P, de Juan Romero C, Santofimia-Castaño P, Iovanna J. Intrinsically Disordered Chromatin Protein NUPR1 Binds to the Enzyme PADI4. J Mol Biol. 2023 Apr 15;435(8):168033. doi: 10.1016/j.jmb.2023.168033

Neira JL, Palomino-Schätzlein M. Folding of the nascent polypeptide chain of a histidine phosphocarrier protein in vitro. Arch Biochem Biophys. 2023 Mar 1;736:109538. doi: 10.1016/j.abb.2023.109538

Neira JL, Rizzuti B, Araujo-Abad S, Abian O, Fárez-Vidal ME, Velazquez-Campoy A, de Juan Romero C. The armadillo-repeat domain of Plakophilin 1 binds to human enzyme PADI4. Biochim Biophys Acta Proteins Proteom. 2023 Feb 1;1871(2):140868. doi: 10.1016/j.bbapap.2022.140868

Research group: RESEARCH GROUP ON GENETICS, EPIGENETICS AND TRANSCRIPTION IN NEUROPATHOLOGIES

Our group is interested on the identification of novel diagnostics tools in gliomas (including the aggressive glioblastomas) by analyzing biomaterial from patients (tissue, primary cultures) using transcriptomics, epigenomics, multivariable correlations and artificial intelligence. From the point of view of therapeutics, we are interested on elucidating the mechanisms of action of epigenetic-modulating drugs.

Another line of research is focused Huntington's disease: search of novel biomarkers and assessment of novel preclinical biomodels.

Staff

Luis Miguel Valor Becerra (ORCID: 0000-0002-1229-0565)

PhD Theses

Title: Descripción de nuevos correlatos transcripcionales y de nuevas fuentes de biomarcadores en la enfermedad de Huntington. Student: Andrea Gallardo Orihuela. Supervisors: Dr. L.M. Valor

Governmental Projects and Funding

Nuevas estrategias contra el cáncer: Inhibición de las interacciones moleculares de las proteínas deiminasas de arginina- PROYECTOS AICO CAICO2021/135- GENERALITAT VALENCIANA. UMH-FISABIO. IPs: Camino de Juan Romero and José Luis Neira.

R&D Management

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

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

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

Editorial Boards

Associate editor in Chief of International Journal of Biological Macromolecules (August 2023-December 2023).

Becerra and Dra. Ana I. Arroba. Qualification: Sobresaliente Cum Laude. 14/04/2023. Universidad de Cádiz.

Invited Talks and Courses

"Caracterización de biomarcadores en neuropatologías". INNOVA Summit ISABIAL. Alicante, España. 27/01/2023.

"Genética, epigenética y transcripción en neuropatologías". Research sessions ISABIAL. Alicante, España. 11/05/2023.

Science Dissemination: Outreach Activities

"¿Firma asociada a terapia epigenética en glioblastomas?". Día Mundial de las Enfermedades Raras, 02/03/2023.

"Neuroinflamación en la retina de animales modelo de la enfermedad de Huntington". Día Mundial de las Enfermedades Raras, 02/03/2023.

"Tras nuevas fuentes de biomarcadores en la enfermedad de Huntington". Jornada de Ciencia Participativa ISABIAL-

Asociación Valenciana de Enfermedad de Huntington. 20/05/2023.

Number of Congress Communications

International contributions: 4

Poster presentations: 4

Governmental Projects and Funding

Neuroinflamación en la enfermedad de Huntington: modelización en ratones y correlatos periféricos en pacientes. 01/09/2023 - 31/10/2025. CONSOLIDACIÓN INVESTIGADORA 2022 (CNS2022-136169). ISABIAL. MINISTERIO DE CIENCIA E INNOVACIÓN. IP: Luis Miguel Valor.

Plataforma Integral e Inteligente para la Medicina de Precisión aplicada a Tumores Cerebrales. 01/10/2022 - 30/09/2024. PROYECTOS ESTRATÉGICOS EN COOPERACIÓN. ISABIAL. AGÈNCIA VALENCIANA DE LA INNOVACIÓ (AVI) (INNEST/2022/168). IP: Luis Miguel Valor.

Plataforma de análisis avanzado de textos científicotécnicos para la extracción de tendencias y conocimiento mediante técnicas de PLN. 01/10/2022 - 30/09/2024. PROYECTOS ESTRATÉGICOS EN COOPERACIÓN. ISABIAL. AGÈNCIA VALENCIANA DE LA INNOVACIÓ (AVI) (INNEST/2022/54). IP: Sandra Gomis Pont.

Biomarcadores específicos de tipo celular en sangre periférica de pacientes con enfermedad de Huntington. 07/07/2022 - 06/07/2024. CONVOCATORIA EXTRAORDINARIA DE AYUDAS 2021. ISABIAL. FUNDACIÓN NAVARRO-LUCIANO TRIPODI. IP: Luis Miguel Valor.

Biomarcadores específicos de tipo celular en fluidos periféricos de enfermedades de trinucleótidos. 01/01/2020 - 31/12/2023. PROYECTOS DE I+D+I EN SALUD (PI19/00125). ISABIAL. INSTITUTO DE SALUD CARLOS III – FEDER. IP: Luis Miguel Valor.

Clasificación multiómica de pacientes y nuevos modelos de escrutinio farmacológico en la enfermedad de Huntington. 01/01/2024 – 31/12/2026. PROYECTOS DE I+D+I EN SALUD (PI23/01568). ISABIAL. INSTITUTO DE SALUD CARLOS III – FEDER. IP: Luis Miguel Valor.

Projects Submitted

Ayudas a la investigación - VIII Convocatoria de ayudas a la investigación. Fundación FEDER.

Joint Call (JTC 2023) TRANSCAN-3: "Translational research on cancer epigenetics".

Subvenciones a Grupos Consolidados CIAICO/2023. Generalitat Valenciana.

R&D Management

Reviewer of ANEP / EVALUA (2010-).

Chronic inflammation and pain

Unit/Group name: PERIPHERAL NEUROPATHIES

CHRONIC INFLAMMATION, PAIN AND PRURITUS. Understanding sensory neural signaling. This subline is centered in understanding the mechanisms underlying the pro-algesic sensitization of sensory neurons as well as their desensitization upon resolution of injury or diseases. Our hypothesis considers that chronification results from a lack or defective resolution of neural sensitization. We are focused in three pathologies: (i) chronic migraine as a paradigm of chronic inflammatory pain that additionally shows a strong sex

dimorphism; (ii) chemotherapy induced peripheral neuropathy as a model of neuropathic pain syndrome; and, (iii) psoriatic pruritus as a model of chronic itch. The common aspect of these three conditions is the involvement of the peripheral sensory system that is sensitized by increasing its electrogenic activity. We focus on the role of ion channels involved in the generation of action potentials and in their propagation, i.e. thermoTRP channels, Na, Kv and HCN channels. Furthermore, we investigate how the activity of these channels is affected by

pro-algesic agents. The aim of these studies is to validate therapeutic targets that are subsequently used in our drug discovery program to identify and develop drug candidates that restore channel activity and the neural sensitivity.

DESIGN OF BIOACTIVE MOLECULES. Discovery of drug candidates for nociceptive precision therapy.

The identification and design of bioactive molecules for different applications (anti-inflammatory, analgesic and anti-pruritus) is first based on a computational strategy using molecular modeling, docking and dynamics on the validated therapeutic targets. In addition, *in silico* screening is also applied to virtual libraries composed of thousands to millions of molecules from natural and synthetic sources. Hit compounds are validated in HTS assays, and lead compounds pharmacologically characterized *in vitro* and *in vivo*. Selected drug candidates are licensed out to biotech companies for pre-clinical and clinical development.

Staff

Antonio Ferrer Montiel (ORCID: 0000-0002-2973-6607)

Gregorio Fernández Ballester (ORCID: 0000-0002-5412-8611)

Asia Fernández Carvajal (ORCID: 0000-0003-2741-1427)

Postdoctoral Researchers

David Cabañero (ORCID: 0000-0002-1133-0908)

Olivia Gross (ORCID: 0000-0002-1299-3076)

Verónica Rivero (ORCID: 0009-0000-7167-7201)

Magdalena Nikolaeva (ORCID: 0000-0002-2617-3108)

External collaborators integrated in the group

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

Ph. D Students

Jorge de Andrés López (ORCID: 0000-0001-7797-4688)

David Alarcón Alarcón (ORCID: 0000-0002-6280-2805)

Simona Giorgi (ORCID: 0000-0001-9431-6759)

Laura Butrón García (ORCID: 0000-0001-5931-4934)

Eva María Villalba Riquelme (ORCID: 0000-0002-0301-0672)

Angela Lamberti

María López López

Technicians

José Manuel Serrano García

Publications

Fernández-Ballester G, Fernández-Carvajal A, Ferrer-Montiel A. Progress in the structural basis of thermoTRP channel polymodal gating. *International Journal of Molecular Sciences* 2023; 24(1), 743. Doi: <https://doi.org/10.3390/ijms24010743>

Martín-Escura C, Bonache MA, Medina JA, Medina-Peris A, De Andrés-López J, González-Rodríguez S, Kerselaers S, Fernández-Ballester G, Voets T, Ferrer-Montiel A, Fernández-Carvajal A, González-Muñiz R. β -Lactam TRPM8 Antagonists Derived from Phe-Phenylalaninol Conjugates: Structure-Activity Relationships and Antiallodynic Activity. *International Journal of Molecular Sciences* 2023; 24(19), 14894. Doi: <https://doi.org/10.3390/ijms241914894>

Blanes-Mira C, Fernández-Aguado P, de Andrés-López J, Fernández-Carvajal A, Ferrer-Montiel A, Fernández-Ballester G. Comprehensive survey of consensus docking for high-throughput virtual screening. *Molecules* 2023; 28, 175. doi: <https://doi.org/10.3390/molecules28010175>

Butron L, Nikolaeva-Koleva M, Sempere A, Rivero V, Fernandez-Ballester G, Espinosa A, Vergassola M, Mastrocola E, Zucchi A, Ragni L, Fernández-Carvajal A, Mangano G, Ferrer-Montiel A, Devesa I. Design and validation of neuronal exocytosis blocking peptides as potential novel antiperspirants. *Experimental Dermatology* 2023; 32(7):999-1006. doi: <https://doi.org/10.1111/exd.14804>

Angeli A, Micheli L, Carta, F, Ferraroni M, Piralì T, Fernández-Carvajal A, Ferrer-Montiel A, Di Cesare Mannlli L, Ghelardini C, Supuran CT. First in Class Dual Hybrid Carbonic Anhydrase Inhibitors and Transient Receptor Potential Vanilloid 1 Agonists Revert Oxaliplatin-Induced Neuropathy. *Journal of Medicinal Chemistry* 2023; 2023 Jan 26;66(2):1616-1633. doi: 10.1021/acs.jmedchem.2c01911

Giorgi S, Lamberti A, Butrón L, Gross-Amat O, Alarcón-Alarcón D, Rodríguez-Cañas E, Fernández-Carvajal A, Ferrer-Montiel A. Compartmented primary cultures of dorsal root ganglion neurons to model peripheral pathophysiological conditions. *Molecular pain* 2023; Aug 14:17448069231197102. doi: 10.1177/17448069231197102

Felipe A, Ferrer-Montiel A. Membrane Channels in Health and Diseases. *International Journal of Molecular Sciences* 2023; Apr 4;24(7):6719. doi: 10.3390/ijms24076719

Nikolaeva-Koleva M, Espinosa A, Vergassola M, Polenzani L, Mangano G, Ragni L, Zucchi S, Ferrer-Montiel A, Devesa I. Benzydamine plays a role in limiting inflammatory pain induced by neuronal sensitization. *Mol Pain*. 2023; Jan-Dec; 19: 17448069231204191. doi: 10.1177/17448069231204191

SPIN-OFF/START UP Companies

ANTALGENICS (2015-actualidad). Board of Directors. Antonio Ferrer (President).

PROSPERA BIOTECH (2014-actualidad). Board of Directors. Asia Fernández (member) and Antonio Ferrer (President). Scientific Advisory Board. Asia Fernández (Chair).

HAWK BIOSYSTEMS (2015-actualidad). Board of Directors. Antonio Ferrer. (President).

Patents

Compositions for treating hyperhidrosis. EP22382149.7. Antonio Ferrer.

5-fluorouracilo como agente antiviral contra virus de la familia Coronaviridae. P202330781. Gregorio Fernández.

Phospholipase C inhibitor peptides and uses thereof. EP23383327. Antonio Ferrer.

PhD Theses

Title: Involvement of transient receptor potential channels in the sexual dimorphism of a mouse model of chronic migraine. Student: David Alarcón Alarcón. Advisor: Dr. Antonio Vicente Ferrer Montiel and Dr. David Cabañero Ferri. Qualification: Sobresaliente Cum Laude 16/02/2023.

Title: Investigating chemotherapy-induced peripheral neuropathies and its sexual dimorphism using an in vitro preclinical pain model. Student: Eva María Villalba Riquelme. Advisor: Dr. Antonio Vicente Ferrer Montiel. Qualification: Sobresaliente Cum Laude 31/05/2023.

Organizing of Scientific Committees

RECI Webinars. Antonio Ferrer.

45° Congreso de la Sociedad de Bioquímica y Biología Molecular. Antonio Ferrer.

Invited Talks and Courses

XL National Meeting of the Spanish Society of Pharmacology. New pharmacological approaches to treat alterations in the sensory nervous system. Toledo, September 6 to 8 - 2023. Invited speaker: A. Fernández Carvajal.

2nd Workshop of the Neurobiology of Pain and Inflammation Program 28-29th September 2023, Alicante, Spain. Invited speaker: A. Fernández Carvajal.

XIX Congreso de la Sociedad Española del Dolor. Fabricando neuronas sensitivas humanas para estudiar el dolor. Madrid, mayo 2023. Antonio Ferrer.

45° Congreso de la Sociedad de Bioquímica y Biología Molecular. Apoyo a la ciencia traslacional y transferencia tecnológica en la SEBBM. Antonio Ferrer.

Science with and for Society in European Universities Alliances. WS3- Reforming Research Assessment. November 2023. Brussels. Antonio Ferrer.

Science Dissemination: Outreach Activities

XV Jornadas de San Alberto. Facultad de Ciencias Experimentales. UMH. November 2023. Antonio Ferrer.

60 Years of SEBBM. June 2023, Valencia and October 2023, Elche and Sax. Antonio Ferrer.

Innopropel. Parque Científico Universidad de Valencia. December 2023. Antonio Ferrer.

Jornada Biotech. Parque Científico Universidad de Valencia. December 2023. Antonio Ferrer.

Number of Congress Communications

National contributions: 6

Oral presentations: 2

Poster presentations: 4

International contributions: 48

Oral presentations: 43

Poster presentations: 5

Awards

Teaching Talent Award 04/12/2023: Gregorio Fernández.

Governmental Projects and Funding

Sex dimorphism in migraine: thermoTRPs as hormonal and drug targets (GIOCONDA). PID2021-126423OB-C21. 2022-2025 IP: Antonio Ferrer & Asia Fernández.

Prototipo de organoide funcional de piel humana inervada para investigación en dolor (OPERA) PROYECTOS PRUEBA DE CONCEPTO - MINECO 2022 PDC2022-133405-I00. 2022-2025 IP: Antonio Ferrer & Asia Fernández.

Neuropatía por quimioterapia: fisiopatología, dimorfismo sexual e intervención terapéutica. ChemoTheRapy-Induced neuropathy: pathophysiology, sex dimorphism and therapeutic intervention (TRILOGY). Generalitat Valenciana, Conselleria d'Innovació, Universitats, Ciència i Societat Digital. Programa Prometeo para grupos de investigación de excelencia –

PROMETEO 2021. PROMETEO/2021/031. 2021-2024. IP: Antonio Ferrer-Montiel y Ana Gomis García.

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

Obtención de compuestos con actividad antifúngica frente a *Candida Auris* mediante cribado computacional de alta eficacia. Ayudas para la realización de acciones preparatorias UMH/IIS La Fe 2022. UMH. Ref.: 2022i005. 2023-2024. IP: Gregorio Fernández.

Valorización de residuos de fruta a materias primas de base microalgal para obtener nuevos productos de alto valor añadido y reducir emisiones de CO₂ (Frutalga) INNEST/2023/321 IP: Antonio Ferrer & Asia Fernández.

Análisis neurosensorial de canalopatías infantiles complejas. Fundación Soledad. IP Antonio Ferrer & Asia Fernández.

PROGRAMA INVESTIGO GVA (INVEST/2023/462_1) INVEST/2023/462_1 IP: Asia Fernández.

PROGRAMA INVESTIGO GVA (INVEST/2023/462_2) INVEST/2023/462_2 IP: Asia Fernández

Private funding: R&D Contracts

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

Contrato para la realización de los trabajos de evaluación de la actividad de neurocosméticos en neuronas sensoriales que forman parte del Proyecto "DESARROLLO DE NEUROCOSMÉTICOS PARA EL CUIDADO DE LA PIEL SENSIBLE Y SUS ANEXOS". Prospera Biotech. Antonio Ferrer.

Private funding: Technical Services and Assistance

Supervisión científica desarrollo inhibidores PLC. AntalGenics SL. Antonio Ferrer

Projects Submitted

Human Vascularized Neuroimmune Microphysiological Systems To Model Tumour Microenvironment (pALADIN) HORIZON-MSCA-2023-DN-01-01. Proposal ID 101168658. Antonio Ferrer (submitted).

Human Innervated, Vascularized, and Immunized Tumours-On-Chip as Surrogates for Animal Testing (MITIGATE) HORIZON-HLTH-2024-TOOL-05-06-two-stage. Proposal ID 101155749-1 Antonio Ferrer (submitted).

Protein and insect chitin based on a beehive with electronically maintained homeostasis: a sustainable source of CO₂ - neutral functional foods (apiChitin). HORIZON-CL6-2024-FARM2FORK-01-7. Proposal ID 101182161. David Cabañero.

Preparation of proposal High impact chronic pain as a disorder of executive function: molecular to psychosocial mechanisms and translation. (Wellcome Trust discovery Awards). CIAPE-GVA (GVRTE/2023/4633822). Antonio Ferrer (Submitted).

R&D and Educational Committees

Erasmus Mundus EU master: The European Master in Translational Cosmetic and Dermatological Sciences (EMOTION). Coordinator: Asia Fernández.

IDiBE doctorate Program. Molecular and cell biology. Coordinator: Asia Fernández/Gregorio Fernández.

Scientific Society Councils

Spanish representative IUBMB - Antonio Ferrer.

SEBBM. President-elect-Antonio Ferrer.

RECI. Coordinator-Antonio Ferrer.

FEBS. Financial Committee. Antonio Ferrer.

Editorial Boards

Revista de la SEBBM (2023). Antonio Ferrer (Editor in chief).

Journal of Pharmacological Sciences (2023). A. Ferrer Montiel.

Frontiers in Pharmacology (2023). A. Ferrer Montiel.

Frontiers in Neurosciences (2023). A. Ferrer Montiel.

Journal of Neurosciences (2022). A. Ferrer Montiel.

International Journal Molecular Science (2023). Antonio Ferrer.

Scientific Reports (2014-2023). A. Fernandez-Carvajal

Frontiers in Physiology (2015-2023). A. Fernandez-Carvajal.

Frontiers in Pharmacology (2021-2023) A. Fernandez-Carvajal.

IJMS (2020-2023). A. Fernandez-Carvajal.

UMH editorial board (2019-2023). A. Fernandez-Carvajal.

Immunological aspects associated with liver and gastrointestinal diseases

Unit/Group name: LIVER AND GI DISEASES

Research group: HEPATIC AND INTESTINAL IMMUNOBIOLOGY GROUP

Our group is focused on the comprehension of the local and systemic inflammatory response underlying chronic liver disease progression, including gut-derived antigenic load arriving through the gut-liver axis, and neurocognitive complications facilitated by the liver-brain axis during decompensated stages of disease. Additionally, we are also interested in translational research on IBD,

focusing on the identification, control, and recovery of mechanisms of immune activity in the context of intestinal inflammation, with special attention to its relationship with the microbiome and the use of biologic therapeutic strategies to improve their efficacy in IBD patients.

Staff

Rubén Francés Guarinos (ORCID: 0000-0001-5105-1201)

Esther Caparrós Cayuela (ORCID: 0000-0002-9681-0408)

Isabel Gómez-Hurtado Cubillana (ORCID: 0000-0003-4305-9427)

Oriol Juanola Juárez (ORCID: 0000-0001-7432-8808)

Postdoctoral Researchers

Marina Serrano Maciá

Ph. D Students

Sebastián Martínez López (ORCID: 0000-0003-1720-845X)

Enrique Ángel Gomis (ORCID: 0000-0003-0736-7625)

Technicians

Paula Boix (ORCID: 0000-0003-2857-9790)

Publications

García-Martínez I, Alen R, Pereira L, Povo-Retana A, Astudillo AM, Hitos AB, Gomez-Hurtado I, Lopez-Collazo E, Boscá L, Francés R, Lizasoain I, Moro MÁ, Balsinde J, Izquierdo M, Valverde ÁM. Saturated fatty acid-enriched small extracellular vesicles mediate a crosstalk inducing liver inflammation and hepatocyte insulin resistance. *JHEP Rep.* 2023 Apr 7;5(8):100756. doi: 10.1016/j.jhepr.2023.100756. PMID: 37360906; PMCID: PMC10285285.

Almenara S, Lozano-Ruiz B, Herrera I, Gimenez P, Miralles C, Bellot P, Rodríguez M, Palazon JM, Tarín F, Sarmiento H, Francés R, Gonzalez-Navajas JM, Pascual S, Zapater P. Immune changes over time and survival in patients with cirrhosis treated with non-selective beta-blockers: A prospective longitudinal study. *Biomed Pharmacother.* 2023 Jul;163:114885. doi: 10.1016/j.biopha.2023.114885. Epub 2023 May 16. PMID: 37201262.

Muñoz L, Caparrós E, Albillos A, Francés R. The shaping of gut immunity in cirrhosis. *Front Immunol.* 2023 Apr 14;14:1139554. doi: 10.3389/fimmu.2023.1139554. PMID: 37122743; PMCID: PMC10141304.

Simbrunner B, Caparrós E, Neuwirth T, Schwabl P, Königshofer P, Bauer D,

Marculescu R, Trauner M, Scheiner B, Stary G, Mandorfer M, Reiberger T, Francés R. Bacterial translocation occurs early in cirrhosis and triggers a selective inflammatory response. *Hepatology Int.* 2023 Aug;17(4):1045-1056. doi: 10.1007/s12072-023-10496-y. Epub 2023 Mar 7. PMID: 36881247; PMCID: PMC10386924.

Invited Talks and Courses

Dysbiosis and immunity in the development of infections in cirrhosis. 5th AEEH Meeting of Translational Hepatology. 2023. Sevilla, Spain. Invited conference.

Hepatic Immune Dysfunction. Congreso Sociedad Española Biología Celular (SEBC). Córdoba, Spain. 2023. Invited conference.

Implicación de la microbiota en EI. Congreso Argentino de Enfermedad Inflamatoria Intestinal GADECCU. Córdoba, Argentina. 2023. Invited conference. Etiopatogenia de la enfermedad de Crohn. Congreso Argentino de Enfermedad Inflamatoria Intestinal GADECCU. Córdoba, Argentina. 2023. Invited conference.

Number of Congress Communications

National contributions: 7

Oral presentations: 1

Poster presentations: 6

International contributions: 7

Poster presentations: 7

Governmental Projects and Funding

Therapeutic targets and biomarkers from precision medicine in MAFLD (PreMed-MAFLD). MINISTERIO DE CIENCIA E INNOVACIÓN (PI21/0082). Rubén Francés. (IIS ISABIAL, Hospital General Universitario de Alicante). 01/01/2022-31/12/2023. 157.000 €.

Role of LSECTin in aging and the liver-brain axis in cirrhosis. De 01/01/2021 hasta 31/12/2024. GENERALITAT VALENCIANA - CONSELLERÍA DE INNOVACIÓN, UNIVERSIDAD Y CIENCIA (PROMETEO 2021/033). IP: Rubén Francés.

R&D and Educational Committees

Scientific Committee, Asociación Española para el Estudio del Hígado, AEEH

Scientific Committee, 2^o International Workshop on Gut-Liver Fibrosis.

R&D Management

Research group: LIVER CANCER IMMUNOLOGY AND IMMUNOTHERAPY

Our research group is dedicated to define and understand the mechanisms through which the immune system can either fight against cancer or facilitate its development, with a specific emphasis on liver cancer.

Staff

José Manuel González-Navajas (ORCID: 0000-0002-1591-939X)

Ph. D Students

Beatriz Lozano Ruiz (ORCID: 0000-0001-6714-7179)

Amalia Tzoumpa (ORCID: 0000-0003-3733-4090)

Huang Yin (ORCID: 0000-0001-6495-715X)

Joanna Picó Carrasco (ORCID: 0000-0003-0909-8094)

Publications

Wang D, Li W, Albasha N, Griffin L, Chang H, Amaya L, Ganguly S, Zeng L, González-Navajas JM, Levin M, AkhavanAghdam Z, Snyder H, Schwartz D, Tao A, Boosherhi LM, Hoffman HM, Rose M, Estrada MV, Varki N, Herdman S, Corr M, Webster NJG, Raz E, Bertin S. Long-term exposure to house dust mites accelerates lung cancer development in mice. *J Exp Clin Cancer Res.* 2023 Jan 21;42(1):26. doi: 10.1186/s13046-022-02587-9

Number of Congress Communications

National contributions: 1

Oral presentations: 1

International contributions: 1

Poster presentations: 1

Awards

Reviewer of *Liver International*, *J Hepatology*, *J Hep Reports*, *EBiomedicine*
Coordinador grupo CIBERehd.

Editorial Boards

Editorial Board: *Front Immunol* (2018-).

Best Communication Award – A-WISH Meeting 2023

Governmental Projects and Funding

CNS2023-145676. Effect of salt intake on the efficacy of immune checkpoint inhibition therapy. 01/04/2024 – 31/03/2026. CONSOLIDACIÓN INVESTIGADORA 2023 – AGENCIA ESTATAL DE INVESTIGACIÓN (AEI) - PLAN ESTATAL DE INVESTIGACIÓN CIENTÍFICA Y TÉCNICA Y DE INNOVACIÓN 2021 – 2023. MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES. IP: José Manuel González Navajas. 198.432€

R01CA276642-01A1. Chronic exposure to house dust mites: a new risk factor for lung cancer in never smokers. 06/2023 – 05/2028. RO1 GRANT PROGRAM. NATIONAL CANCER INSTITUTE (NCI) – NATIONAL INSTITUTES OF HEALTH (NIH) OF THE UNITED STATES OF AMERICA. IP: Eyal Raz. \$3.100.000

PI22/01907. A multi-cytokine blocking strategy to reduce HCC development and improve immune checkpoint inhibition therapy. 01/01/2023 – 31/12/2025. INSTITUTO DE SALUD CARLOS III – MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES. IP: José Manuel González Navajas. 245.000€

Projects Submitted

PROMETEO. The MASLD-Inflammasome axis in inflammatory disease and tumor development. SUBVENCIONES PROGRAMA PROMETEO PARA GRUPOS DE INVESTIGACIÓN DE EXCELENCIA. CIPROM. IP: José Manuel González Navajas y Rodrigo Jover Martínez.

R&D Management

Reviewer – Agencia Estatal de Investigación (AEI) (2018 – present) (JMGN).

Reviewer – Instituto de Salud Carlos III – Acción Estratégica en Salud (AES) (2013 – present) (JMGN).

Reviewer – Asociación Española Contra el Cáncer (AECC). (2021, 2023) (JMGN).

Reviewer for the Journals (in 2023): Nature Communications, Theranostics, Cancer Immunology Research (JMGN).

Member of the Research Committee of ISABIAL – Hospital General Universitario Dr. Balmis – ISABIAL (2014 – present). (JMGN).

Member of the Ethics & Research Integrity Committee of IDiBE. (2023 – present) (JMGN).

Deputy Coordinator of the Digestive Research Area of ISABIAL (2021 – present) (JMGN).

Member of the Organizing Committee – VII Researchers’ Meeting of ISABIAL (JMGN).

External Member, Ph.D. evaluation committee for Ria Pinioti – KU Leuven, Leuven, Belgium (JMGN).

Editorial Boards

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

Group name: LIVER AND GASTROINTESTINAL DISEASES

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

1. Immunoregulatory effects of beta-blockers drugs in patients with cirrhosis in risk of development of hepatocellular carcinoma.
2. Role of inflammasome in the development of hepatocellular carcinoma.
3. Mechanism of action of antibiotics used to reduce bacterial translocation in patients with cirrhosis.
4. Pharmacokinetic-pharmacodynamic relationship of biological drugs used in inflammatory bowel diseases

Staff

Pedro Zapater Hernández (ORCID: 0000-0001-7927-858X)

Ph. D Students

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Cayetano Miralles Maciá (ORCID: 0000-0003-2037-6358)

Publications

Sempere L, Bernabeu P, Cameo J, Gutiérrez A, García MG, García MF, Aguas M, Belén O, Zapater P, Jover R, van der Hofstadt C, Ruiz-Cantero MT. Gender Biases and Diagnostic Delay in Inflammatory Bowel Disease: Multicenter Observational Study. *Inflammatory Bowel Diseases* 2023 Dec 5;29(12):1886-1894. doi: 10.1093/ibd/izad001

Almenara S, Lozano-Ruiz B, Herrera I, Gimenez P, Miralles C, Bellot P, Rodriguez M, Palazon JM, Tarín F, Sarmiento H, Francés R, Gonzalez-Navajas JM, Pascual S, Zapater P. Immune changes over time and survival in patients with cirrhosis treated with non-selective beta-blockers: A prospective longitudinal study. *Biomedicine & Pharmacotherapy* 2023 Jul;163:114885. doi: 10.1016/j.biopha.2023.114885

Lluís N, Carbonell S, Villodre C, Zapater P, Cantó M, Mena L, Ramia JM, Lluís F; LUCENTUM Project Researchers*. Propensity score matching analysis of laparoscopic surgery vs. open approach

in 4 297 adult patients with acute appendicitis, acute cholecystitis or gastrointestinal tract perforation: a prospective multicentre study of nationwide outcomes. *International Journal of Surgery* 2023 Jun 1;109(6):1603-1611. doi: 10.1097/JS9.000000000000384

Mangas-Sanjuan C, de-Castro L, Cubiella J, Díez-Redondo P, Suárez A, Pellisé M, Fernández N, Zarracquiños S, Núñez-Rodríguez H, Álvarez-García V, Ortiz O, Sala-Miquel N, Zapater P, Jover R; CADILLAC study investigators. Role of Artificial Intelligence in Colonoscopy Detection of Advanced Neoplasias : A Randomized Trial. *Annals of Internal Medicine* 2023 Sep;176(9):1145-1152. doi: 10.7326/M22-2619

Seguí-Ripoll JM, Candela-Gomis A, Compañy-Catalá L, Francés-Guarinos R, Payá-Romá A, Compañ-Rosique A, Such-Ronda J, Zapater-Hernández P. Lipid peroxidation and liver damage in double and simple common bile duct ligation models in male Sprague-Dawley rats. *Life Sciences* 2023 Dec 1;334:122238. doi: 10.1016/j.lfs.2023.122238

Unit/Group name: Infectious Diseases and HIV/AIDS Research Group – Hospital General Universitario de Elche

The Infectious Diseases and HIV/AIDS Research Group of the Hospital General Universitario de Elche (HGUE), led by Dr. Félix Gutiérrez and Dr. Mar Masiá, is a consolidated research group attached to the Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (FISABIO). The group is made up of 6 postdoctoral researchers, 5 predoctoral researchers, 2 research technicians/assistants, 2 statisticians, 1 project manager and 1 research nurse.

It is a multidisciplinary group (infectious disease specialists, microbiologists, biochemists, and statisticians) with a broad experience of more than two decades in infectious disease research that has made contributions to knowledge mainly in the fields of HIV/AIDS, respiratory infections, influenza pandemic and COVID-19.

Governmental Projects and Funding

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

R&D Management

Revisor de la Agencia Estatal de Investigación (AEI).

Revisor de la Fundación Progreso y Salud, Consejería de Salud Andalucía

Miembro de la Comisión de Investigación Departamental – Hospital General Universitario de Alicante – ISABIAL

Miembro de los Comités de Ética de la Investigación de los Hospitales de San Juan y Orihuela

Miembro del Comités de Ética de la Investigación con Medicamentos del Hospital de Elche.

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Technicians

Christian Ledesma Mejías (ORCID: 0009-0000-8022-364X)

Catalina Robledano García

Araceli Adsuar García

Rafael Pascual Martínez

Publications

Fernández-González M, Agulló V, García JA, Padilla S, García-Abellán J, de la Rica A, Mascarell P, Masiá M, Gutiérrez F. T-Cell Immunity Against Severe Acute Respiratory Syndrome Coronavirus 2 Measured by an Interferon- γ Release Assay Is Strongly Associated With Patient Outcomes in Vaccinated Persons Hospitalized With Delta or Omicron Variants. *J Infect Dis.* 2023 Nov 2;228(9):1240-1252. <https://doi.org/10.1093/infdis/jiad260>

Masiá M, Gutiérrez-Ortiz de la Tabla A, Gutiérrez F. Cancer screening in people living with HIV. *Cancer Med.* 2023 Nov;12(21):20590-20603. <https://doi.org/10.1002/cam4.6585>

Masiá M, de la Rica A, Fernández-González M, García JA, Padilla S, García-Abellán J, Botella Á, Mascarell P, Gutiérrez F. Integrating SARS-CoV-2-specific interferon- γ release assay testing in the evaluation of patients hospitalized with COVID-19. *Microbiol Spectr.* 2023 Dec 12;11(6):e0241923. <https://doi.org/10.1128/spectrum.02419-23>

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disoproxil fumarate/emtricitabine and hydroxychloroquine for pre-exposure prophylaxis of COVID-19: a double-blind placebo-controlled randomized trial in healthcare workers. *Clin Microbiol Infect.* 2023 Jan;29(1):85-93. <https://doi.org/10.1016/j.cmi.2022.07.006>

Vizcarra P, Moreno A, Vivancos MJ, García AM, González RP, Gutiérrez F, Mata DC, Galindo P, Calzado S, Casado JL. Improving Recognition of Fracture Risk in People with Human Immunodeficiency Virus: Performance and Model Contribution of Two Common Risk Assessment Tools. *AIDS Patient Care STDS.* 2023 Jan;37(1):11-21. <https://doi.org/10.1089/apc.2022.0183>

Masiá M, Fernández-González M, Agulló V, Mascarell P, Padilla S, García-Abellán J, Gutiérrez F. Human Immunodeficiency Virus Type 1 RNA Levels in Rectal and Seminal Compartments After Switching to Long-Acting Cabotegravir Plus Rilpivirine: A Longitudinal Study. *Clin Infect Dis.* 2023 Feb 8;76(3):e748-e751. <https://doi.org/10.1093/cid/ciac676>

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Kolossvary M, deFilippi C, McCallum S, Fitch KV, Diggs MR, Fulda ES, Ribaud HJ, Fichtenbaum CJ, Aberg JA, Malvestutto CD, Currier JS, Casado JL, Gutierrez F, Sereti I, Douglas PS, Zanni MV, Grinspoon SK. Identification of pre-infection markers and differential plasma protein expression following SARS-CoV-2 infection in people living with HIV. *EBioMedicine.* 2023 Apr;90:104538. <https://doi.org/10.1016/j.ebiom.2023.104538>

Alonso-Navarro R, Ramírez M, Masiá M, Paredes R, Montejano R, Povar-Echeverría M, Carratalà J, Salavert M, Bernal E, Dueñas C, Flores J, Fanjul F, Gutiérrez I, Rico V, Mateu L, Cadiñanos J, Berenguer J, Soriano A. Time from symptoms onset to remdesivir is associated with the risk of ICU admission: a multicentric analyses. *BMC Infect Dis.* 2023 May 4;23(1):286. <https://doi.org/10.1186/s12879-023-08222-Y>

Santos JR, Casadellà M, Noguera-Julian M, Micán-Rivera R, Domingo P, Antela A, Portilla J, Sanz J, Montero-Alonso M, Navarro J, Masiá M, Valcarce-Pardeiro N, Ocampo A, Pérez-Martínez L, García-Vallecillos C, Vivancos MJ, Imaz A, Iribarren JA, Hernández-Quero J, Villar-García J, Barrufet P, Paredes R; INSTINCT study group. Effectiveness and safety of integrase strand transfer inhibitors in Spain: a prospective real-world study. *Front Cell Infect Microbiol.* 2023 Jun 26;13:1187999. <https://doi.org/10.3389/fcimb.2023.1187999>

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Hidalgo-Tenorio C, Pitto-Robles I, Arnés García D, de Novales FJM, Morata L, Mendez R, de Pablo OB, López de Medrano VA, Lleti MS, Vizcarra P, Lora-Tamayo J, Arnáiz García A, Núñez LM, Masiá M, Seco MPR, Sadyrbaeva-Dolgova S. Cefto Real-Life Study: Real-World Data on the Use of Ceftobiprole in a Multicenter Spanish Cohort. *Antibiotics (Basel).* 2023 Jul 21;12(7):1218. <https://doi.org/10.3390/antibiotics12071218>

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Hoffmann U, Lu MT, Ribaud HJ, Douglas PS; REPRIEVE Investigators (Mar Masiá among others). Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. *N Engl J Med.* 2023 Aug 24;389(8):687-699. <https://doi.org/10.1056/NEJMoa2304146>

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González-Cordón A, Assoumou L, Moyle G, Waters L, Johnson M, Domingo P, Fox J, Stellbrink HJ, Guaraldi G, Masiá M, Gompels M, De Wit S, Florence E, Esser S, Raffi F, Behrens G, Pozniak A, Gatell JM, Martínez E; NEAT 022 Study Group. Long-term effects on subclinical cardiovascular disease of switching from boosted protease inhibitors to dolutegravir. *J Antimicrob Chemother.* 2023 Sep 5;78(9):2361-2365. <https://doi.org/10.1093/jac/dkad247>

Sempere A, Assoumou L, González-Cordón A, Waters L, Rusconi S, Domingo P, Gompels M, de Wit S, Raffi F, Stephan C, Masiá M, Rockstroh J, Katlama C, Behrens GMN, Moyle G, Johnson M, Fox J, Stellbrink HJ, Guaraldi G, Florence E, Esser S, Gatell J, Pozniak A, Martínez E; NEAT 022 Study Group. Incidence of Hypertension and Blood Pressure Changes in Persons With Human Immunodeficiency Virus at High Risk for Cardiovascular Disease Switching From Boosted Protease Inhibitors to Dolutegravir: A Post-hoc Analysis of the 96-week Randomised NEAT-022 Trial. *Clin Infect Dis.* 2023 Oct 5;77(7):991-1009. <https://doi.org/10.1093/cid/ciad297>

Santos JR, Domingo P, Portilla J, Gutiérrez F, Imaz A, Vilchez H, Curran A, Valcarce-Pardeiro N, Payeras A, Bernal E, Montero-Alonso M, Yzusqui M, Clotet B, Videla S, Moltó J, Paredes R. A Randomized Trial of Dolutegravir Plus Darunavir/Cobicistat as a Switch Strategy in HIV-1-Infected Patients With Resistance to at Least 2 Antiretroviral Classes. *Open Forum Infect Dis.* 2023 Oct 31;10(11):ofad542. <https://doi.org/10.1093/ofid/ofad542>

Podzamczar D, Imaz A, Lopez-Lirola A, Knobel H, Masiá M, Fanciulli C, Hernández C, Lagarde M, Gutierrez A, Curran A, Morano L, Montero-Alonso M, Troya J, Rigo R, Casadellà M, Navarro-Alcaraz A, Ardila F, Parera M, Bernal E, Echeverría P, Estrada V, Hidalgo-Tenorio C, Macias J, Prieto P, Portilla J, Valencia E, Vivancos MJ, Rivero A. Switching to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) plus darunavir/cobicistat in heavily antiretroviral-experienced, virologically suppressed HIV-infected adults receiving complex regimens. *J Antimicrob Chemother.* 2023 Nov 6;78(11):2696-2701. <https://doi.org/10.1093/jac/dkad285>

Suárez-García I, Gutiérrez F, Pérez-Molina JA, Moreno S, Aldamiz T, Valencia Ortega E, Curran A, Gutiérrez González S, Asensi V, Amador Prous C, Jarrin I, Rava M; CoRIS. Mortality due to non-AIDS-defining cancers among people living with HIV in Spain over 18 years of follow-up. *J Cancer Res Clin Oncol.* 2023 Dec;149(20):18161-18171. <https://doi.org/10.1007/s00432-023-05500-9>

Viñuela L, de Salazar A, Fuentes A, Serrano-Conde E, Falces-Romero I, Pinto A, Portilla I, Masiá M, Peraire J, Gómez-Sirvent JL, Sanchiz M, Iborra A, Baza B, Aguilera A, Olalla J, Espinosa N, Iribarren JA, Martínez-Velasco M, Imaz A, Montero M, Rivero M, Suarez-García I, Maciá MD, Galán JC, Perez-Elias MJ, García-Fraile LJ, Moreno C, Garcia F. Transmitted drug resistance to antiretroviral drugs in Spain during the period 2019-2021. *J Med Virol.* 2023 Dec;95(12):e29287. <https://doi.org/10.1002/jmv.29287>

PhD Theses

Título: Evaluación de los efectos del tratamiento precoz con inhibidores de Interleucina-6 en pacientes con covid-19 y predictores de respuesta favorable. Student: Lucía Guillén Zafra. Supervisors: Dra. Mar Masiá and Dr. Félix Gutiérrez. June 2023.

Título: Determinantes de seroconversión, aclaramiento viral y cinética de la inmunidad humoral en pacientes con infección por SARS-COV-2. Student: Guillermo Telenti Rodríguez. Supervisors:

Dr. Félix Gutiérrez and dra. Mar Masiá. July 2023.

Number of Congress Communications

National contributions: 5

Oral presentations: 2

Poster presentations: 3

Awards

Alberto Sols Award for the Best Research Work in Clinical Medicine 2023: Dr. Félix Gutiérrez Rodero.

Governmental Projects and Funding

Factores inmunológicos, bacteriológicos y virológicos potencialmente implicados en la recurrencia de displasia anal de alto grado en personas con VIH. Instituto de Salud Carlos III (PI22/01949). 01/01/23 - 31/12/25. IP: Mar Masiá. Funding: 87.120,0 €.

CIBER en Enfermedades Infecciosas. Instituto de Salud Carlos. Instituto de Salud Carlos III (CB21/13/00011). Desde 01/01/2022. IP: Félix Gutiérrez (Mar Masiá y otros miembros del grupo en el equipo investigador). Funding: 60.000,0 €.

Impacto de un Programa Ampliado de Cribado en la detección de NEOplasias malignas no-sida en pacientes con infección por el VIH (IMPAC-NEO). Instituto de Salud Carlos III (PI18/01861). 01-01-2019 - 30-06-2023. IP: Mar Masiá. Funding: 220.220,0 €.

Subvenciones para grupos de investigación consolidados. AGENCIA FINANCIADORA: FUNDACIÓN PARA EL FOMENTO DE LA INVESTIGACIÓN SANITARIA Y BIOMÉDICA EN LA COMUNITAT VALENCIANA (FISABIO). 2021-2023. IP: Mar Masiá. Funding: 90.000,00 €.

Desarrollo de un asistente virtual inteligente destinado a la población con VIH. AGENCIA FINANCIADORA: FUNDACIÓN PARA EL FOMENTO DE LA INVESTIGACIÓN SANITARIA Y BIOMÉDICA EN LA COMUNITAT VALENCIANA (FISABIO). 01/01/2021-30/6/23. IP: Félix Gutiérrez (Mar Masiá y otros miembros del grupo en el equipo investigador). Funding: 13.500,0 €.

Private funding

A Clinical Trial of GSK3640254 + Dolutegravir (DTG) in Human Immunodeficiency Virus-1 Infected Treatment-naïve Adults (DYNAMIC). Agencia financiadora: GLAXOSMITHKLINE (GSK) (2021-000016-28). 09/09/2021 – 26/06/2023. IP: Félix Gutiérrez Rodero (IP de centro) (Mar Masía y otros miembros del grupo en el equipo investigador).

Phase 3 Randomized, Active-Controlled, Double-Blind Clinical Study to Evaluate the Antiretroviral Activity, Safety, and Tolerability of Doravirine/Islatravir Once-Daily in HIV-1 Infected Treatment-Naïve Participants. Merck Sharp & Dohme Corp (2019-000590-23). 26/04/2021 – Ongoing. IP: Félix Gutiérrez (IP de centro) (Mar Masía y otros miembros del grupo en el equipo investigador).

A Phase 3 Randomized, Active-Controlled, Open-Label Clinical Study to Evaluate a Switch to Doravirine/Islatravir (DOR/ISL) Once-Daily in Participants With HIV-1 Virologically Suppressed on Antiretroviral Therapy. Merck Sharp & Dohme Corp (MK-8591A-017. EudraCT 2019-000586-20). 04/2020 – Ongoing. IP: Félix Gutiérrez (IP de centro) (Mar Masía y otros miembros del grupo en el equipo investigador)

A Phase IIIb, Randomized, Multicenter, Parallel-group, Non-inferiority, Open-label Study Evaluating the Efficacy, Safety, and Tolerability of Long-acting Cabotegravir Plus Long-acting Rilpivirine Administered Every 8 Weeks or Every 4 Weeks in HIV-1-infected Adults who are Virologically Suppressed (ATLAS-2). ViiV Healthcare UK Limited (207966; EudraCT: 2017-002946-62). 18/09/2017-28/9/23. IP: Mar Masía Canuto (IP de Centro).

A Phase III, Randomized, Multicenter, Parallel-group, Open-Label Study Evaluating the Efficacy, Safety, and Tolerability of Long-Acting Intramuscular Cabotegravir and Rilpivirine for

Maintenance of Virologic Suppression Following Switch from an Integrase Inhibitor Single Tablet Regimen in HIV-1 Infected Antiretroviral Therapy Naïve Adult Participants (FLAIR). ViiV Healthcare, S.L. (201584; EudraCT 2016-001646-25). 20/10/2016-24/01/2024. IP: Mar Masía Canuto (IP de Centro)

A Phase III, randomized, multicenter, parallel-group, noninferiority, open-label study evaluating the efficacy, safety, and tolerability of switching to long-acting cabotegravir plus longacting rilpivirine from current ININRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed (ATLAS). ViiV Healthcare, S.L. (201585; EudraCT 2016-001647-39). 20/10/2016-28/9/23. IP: Mar Masía Canuto (IP de Centro)

A phase III, randomised, multicenter, open-label study to evaluate the safety and efficacy of a switch to MK-1439A in HIV-1-infected participants virologically suppressed on an anti-retroviral regimen of a ritonavirboosted protease inhibitor in combination with two nucleoside reverse transcriptase inhibitors. Merck Sharp & Dohme Corp. (1439A-024; EudraCT 2014-005550-18). 12/08/2015-ongoing. IP: Félix Gutiérrez Rodero (IP de centro) (Mar Masía y otros miembros del grupo en el equipo investigador)

Projects Submitted

Contrato Sara Borrell CD23/00136 en la convocatoria Acción Estratégica en Salud 2023.

Contrato Predoctoral de Formación en Investigación en Salud FI23/00120 en la convocatoria Acción Estratégica en Salud 2023.

Contrato para la Intensificación de la Actividad Investigadora en el Sistema Nacional de Salud INT23/0067 en la convocatoria Acción Estratégica en Salud 2023.

Unit/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:

1. Optimization of industrial processes for functional beverages production and waste management for nutraceutical ingredients with a bio-economy perspective.
2. Semi-industrial scale production of nutraceuticals from plants, herbs or by-products.
3. Identification & Purification of bioactive molecules from waste management, and small-scale production herein for agricultural biological pest control.
4. Identification, isolation, culture development and pilot plant scale production of microorganisms for agriculture and feedstock.
5. Development of new nutritional products from fermentation processes.

Staff

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Domingo Saura López (ORCID: 0000-0003-4711-0744)

Manuel Valero Roche

External collaborators integrated in the group

Prof. Dr. Francisco Martín Bermudo. Universidad Pablo Olavide (Sevilla).

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

Prof. Dra. Farah Hosseinian. Department of Chemistry, Carleton University.

Ph. D Students

Julio Salazar Bermeo (ORCID: 0000-0002-8920-9817)

Bryan Moreno Chamba (ORCID: 0000-0002-4263-2239)

Sara Gea Botella

Publications

Moreno-Chamba B, Salazar-Bermeo J, Navarro-Simarro P, Narváez-Asensio M, Martínez-Madrid MC, Saura D, Valero M. Autoinducers modulation as a potential anti-virulence target of bacteria by phenolic compounds. *International Journal of Antimicrobial Agents* 2023; 62(4), 106937. doi.org/10.1016/j.ijantimicag.2023.106937

Kilasoniya A, Garaeva L, Shtam T, Spitsyna, A, Putevich E, Moreno-Chamba B, Salazar-Bermeo J, Komarova E, Malek A, Valero M, Saura D. Potential of Plant Exosome Vesicles from Grapefruit (*Citrus paradisi*) and Tomato (*Solanum lycopersicum*) Juices as Functional Ingredients and Targeted Drug Delivery Vehicles. *Antioxidants* 2023; 12(4), 943. doi: 10.3390/antiox12040943

Salazar-Bermeo J, Moreno-Chamba B, Heredia-Hortigüela R, Lizama V, Martínez-Madrid MC, Saura D, Valero M, Neacsu M, Martí N. Green Technologies for Persimmon By-Products Revalorisation as Sustainable Sources of Dietary Fibre and Antioxidants for Functional Beverages Development. *Antioxidants* 2023; 12(5), 1085. doi.org/10.3390/antiox12051085

Salazar-Bermeo J, Moreno-Chamba B, Martínez-Madrid MC, Valero M, Rodrigo-García J, Hosseinian F, Martín-Bermudo F, Aguado M, de la Torre R, Martí N, Saura D. Preventing Mislabeling: A Comparative Chromatographic Analysis for Classifying Medical and Industrial Cannabis. *Molecules* 2023; 28(8), 3552. doi: 10.3390/molecules28083552

Patents

Persimmon Dietary Fiber for use with Beneficial Micro-Organisms. ES202131183A-2021-12-21.

Inventores: Saura D, Barrajón-Catalán E, Martí N, Martínez R, Micol V, Valero M, Vegara Gomez S. Título: Contrato de licencia de patente 201300578

"Combinación sinérgica de flavonoides y vitamina C". Titular: MITRA SOL TECHNOLOGIES SL. Fecha inicio: 13/05/2016. Fecha fin: 12/05/2033. Referencia patente: 201300578.

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

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

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

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

Inventores: Saura D, Martí N, M Martínez-Madrid MC. Título: Envase para bebidas nutricionales. Propietario: UNIVERSIDAD MIGUEL HERNANDEZ DE ELCHE. Fecha solicitud: 30/04/2020. Fecha concesión: 04/03/2022. Referencia: P202030369.

Number of Congress Communications

National contributions: 4

Poster presentations: 4

International contributions: 4

Poster presentations: 4

Private funding: Technical Services and Assistance

Contrato para la realización del trabajo "Caracterización de extractos vegetales obtenidos mediante un proceso instantáneo con un consumo energético muy reducido". Programa y Referencia: HAUSMANN1.23CC. Código OTRI: 2023/CON/00110. Fecha inicio: 29/07/2023. Fecha fin: 31/12/2023. Importe Anualidad: 32000 €. Investigadores: 3.

Editorial Boards

Board member Food Microbiology (2010-2023) Manuel Valero Roche.

PhD THESES (2023)

Title: INVOLVEMENT OF TRANSIENT RECEPTOR POTENTIAL CHANNELS IN THE SEXUAL DIMORPHISM OF A MOUSE MODEL OF CHRONIC MIGRAINE

PhD student: DAVID ALARCÓN ALARCÓN

Defense date: 16/02/2023

Supervisors: Dr. Antonio Vicente Ferrer Montiel and Dr. David Cabañero Ferri

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2385522>

Title: PAPEL DE LOS RECEPTORES DE ESTRÓGENOS ER α , ER β Y EL RECEPTOR DE ESTRÓGENOS ACOPLADO A PROTEÍNAS G (GPER) EN LA VIABILIDAD DE LA CÉLULA β

PhD student: IGNACIO BABILONI CHUST

Defense date: 24/03/2023

Supervisors: Dr. Ángel Nadal Navajas and Dra. Laura Marroquí Esclapez

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2400264>

Title: DESCRIPCIÓN DE NUEVOS CORRELATOS TRANSCRIPCIONALES Y DE NUEVAS FUENTES DE BIOMARCADORES EN LA ENFERMEDAD DE HUNTINGTON

PhD student: ANDREA GALLARDO ORIHUELA

Defense date: 14/04/2023

Supervisors: Dr. L.M. Valor Becerra and Dra. Ana I. Arroba.

Title: INVESTIGATING CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHIES AND ITS SEXUAL DIMORPHISM USING AN IN VITRO PRECLINICAL PAIN MODEL

PhD student: EVA MARÍA VILLALBA RIQUELME

Defense date: 31/05/2023

Supervisors: Dr. Antonio Vicente Ferrer Montiel

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2441634>

Title: EVALUACIÓN DE LOS EFECTOS DEL TRATAMIENTO PRECOZ CON INHIBIDORES DE INTERLEUCINA-6 EN PACIENTES CON COVID-19 Y PREDICTORES DE RESPUESTA FAVORABLE

PhD student: LUCÍA GUILLÉN ZAFRA

Defense date: June 2023

Supervisors: Dra. Mar Masiá and Dr. Félix Gutiérrez

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2455227>

Title: DETERMINANTES DE SEROCONVERSIÓN, ACLARAMIENTO VIRAL Y CINÉTICA DE LA INMUNIDAD HUMORAL EN PACIENTES CON INFECCIÓN POR SARS-COV-2

PhD student: GUILLERMO TELENTI RODRIGUEZ

Defense date: July 2023

Supervisors: Dr. Félix Gutiérrez and Dra. Mar Masiá

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2458476>

Title: SMALL EXTRACELLULAR VESICLES AS A POTENTIAL CLINICAL TOOL FOR HARD TO TREAT CANCER THERAPY

PhD student: LOURDES SALOMÉ ARAUJO ABAD

Defense date: 23/10/2023

Supervisors: Dra. Pilar García Morales and Dra. Camino de Juan Romero

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2475429>

Título: INGREDIENTES BASADOS EN POLIFENOLES VEGETALES CON APLICACIONES EN PATOLOGÍAS ASOCIADAS A LA OBESIDAD

PhD student: MARINA BOIX CASTEJON

Defense date: 14/12/2023

Supervisors: Dr. E. Roche Collado and Dra. M. Herranz López

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2489217>

Title: PLATAFORMAS SENSORAS SOPORTADAS EN HIDROGELES PARA APLICACIÓN BIOMÉDICA Y MEDIOAMBIENTAL

PhD student: YOLANDA INMACULADA ALACID MARTÍNEZ

Defense date: 15/12/2023

Supervisors: Dra. María José Martínez Tomé and Dra. Carmen Reyes Mateo Martínez

URL: <https://www.educacion.gob.es/teseo/mostrarRef.do?ref=2479188>

SEMINARS (2023)

Title: **NUTRICIÓN PERSONALIZADA, (POLI)FENOLES Y RESPUESTA CARDIOMETABÓLICA: ¿QUÉ SIGUE?**

Speaker / Institution: Pedro Mena Parreño. Universidad de Parma, Italia.

Date: 12/01/2023

Title: **INGENIERÍA DE CLOROPLASTO PARA LA PRODUCCIÓN DE GLICOLÍPIDOS BIOACTIVOS EN MICROALGAS**

Speaker / Institution: Pablo Leivar. Univ. Ramon Llull.

Date: 10/02/2023

Title: **WHEN HYPNOS MEETS THANATOS - "KOI SLEEPY DISEASE" AS A PATHOPHYSIOLOGICAL AND IMMUNOLOGICAL CONSEQUENCE OF A CARP EDEMA VIRUS INFECTION OF THE COMMON CARP GILLS**

Speaker / Institution: Dr. Mikolaj Adamek. University of Veterinary Medicine Hannover.

Date: 10/03/2023

Title: **UNDERSTANDING SENSORY PROCESSING IN THE BRAIN THROUGH IN VIVO ELECTROPHYSIOLOGY**

Speaker / Institution: Roberto de la Torre. Karolinska Institutet, Sweden.

Date: 19/04/2023

Title: **BIOMEDICAL AND BIOTECHNOLOGICAL APPLICATIONS OF METABOLOMICS**

Speaker / Institution: Carlos Leon Canseco. Universidad Carlos III de Madrid.

Date: 28/04/2023

Title: **NOCIONES BÁSICAS PARA EL ANÁLISIS BIOINFORMÁTICO DE DATOS NGS**

Speaker / Institution: Carlos Llorens. Biotechvana S.L.

Date: 02/05/2023

Title: **AUTOFAGIA EN CÉLULAS DE HUMANO Y MURCIÉLAGO EN RESPUESTA A LA INFECCIÓN POR SARS-COV-2: UN ESTUDIO COMPARATIVO**

Speaker / Institution: Ivan Nombela Diaz. Institute of Virology (Charité – Universitätsmedizin Berlin).

Date: 05/05/2023

Title: **DISEÑO DE ANTÍGENOS BASADOS EN LA ESTRUCTURA PARA EL DESARROLLO DE VACUNAS FRENTE A VIRUS RESPIRATORIOS**

Speaker / Institution: Dr. Vicente Mas Lloret. Instituto de Salud Carlos III.

Date: 11/05/2023

Title: **PERSONALISED 3D PRINTED TREATMENT FOR EARLY KNEE OSTEOARTHRITIS**

Speaker / Institution: Dr. Richie Gill. Universidad de Bath.

Date: 15/06/2023

Title: **INTRODUCCIÓN A LA CITOMETRÍA DE FLUJO MULTICOLOR**

Speaker / Institution: Fernando Alonso/Irene Martinez. BD.

Date: 06/09/2023

Title: **DISEÑOS DE PANELES MULTICOLOR EN CITOMETRÍA CON MÚLTIPLES FLUORESCENCIAS**

Speaker / Institution: Alberto Crespo. BD.

Date: 07/09/2023

Title: **FLUID BIOMAKERS MEASUREMENT**

Speaker / Institution: Paula Pérez Míguez y Bernat Coll-Martínez. "Somalogic y Diagnostica Longwood."

Date: 14/09/2023

Title: **AVANCES EN LA MEDIDA DE CAPACIDAD ANTIOXIDANTE TOTAL Y SU APLICACIÓN EN AGROALIMENTACIÓN Y BIOMEDICINA**

Speaker / Institution: Henar Muñoz Cimadevilla y Sara Menéndez Cotarelo. Bioquochem, S.L.

Date: 19/09/2023

Title: **AQUACULTURE – A NEW FEED REVOLUTION ON THE RISE?**

Speaker / Institution: Margareth Overland. Norwegian University of Life Sciences-NMBU.

Date: 27/10/2023

Title: **ENTENDER LA SEÑALIZACIÓN DISFUNCIONAL EN EL CÁNCER DE HÍGADO ASOCIADO A LA OBESIDAD: ¿EN EL BUEN CAMINO O UNA CAUSA PERDIDA?**

Speaker / Institution: Esteban Gurzov, PhD. Université Libre de Bruxelles-ULB.

Date: 03/11/2023

Title: **AVANCES EN VACUNAS Y AVANCES EN INMUNOLOGÍA: DOS CARAS DE LA MISMA MONEDA**

Speaker / Institution: Pablo García Valtanen. Viral Immunology & Therapeutics Lab IDiBE, UMH.

Date: 24/11/2023

Title: **IDENTIFICACIÓN DE NUEVAS DIANAS FARMACOLÓGICAS PARA EL TRATAMIENTO DE LA FIBROSIS HEPÁTICA: CÉLULAS ESTRELLADAS HEPÁTICAS Y COMUNICACIÓN INTERCELULAR**

Speaker / Institution: Ana Blas. Universidad de Valencia.

Date: 01/12/2023

Title: **REPURPOSING DRUG DELIVERY SYSTEMS FOR DIAGNOSTICS**

Speaker / Institution: Simon Matoori. Université de Montréal.

Date: 14/12/2023

Financial and administrative management

General Manager

María Amparo García Gutiérrez

Logistic Coordinator

Eva del Río Pons

Administration team

Vicente Lucerga (Officer)

Rosa María Balonga Rodríguez

María Teresa Prieto Ávila

Francisca Molino Tomás

María Teresa Mora Cano

Innovation Office

Gabriel Estañ Cerezo

Alejandra Lucía Terol Díaz-Rodríguez

The Innovation Office is working on the transference of the obtained research results by IDiBE's researchers. Its staff is formed by two people: Gabriel Estañ Cerezo and Alejandra Lucía Terol and it is funded by the Agencia Valenciana de la Innovación (AVI) through two projects (INNTA1/2023/17 and INNVA2/2022/8). INNTA1/2023/17 has been granted in 2023.

Its work is done by detecting funding opportunities (national and international), reviewing grant proposal, looking for new partners (universities and innovative companies) and advising about how to protect and transfer research results (one patent application has been filled and another was in preparation during 2023). During 2023, The Innovation Office has also coordinated some training activities as:

-I Patent Meeting of IDiBE – OEPM (04/10/2023).

-Avances en la medida de capacidad antioxidante total y su aplicación en agroalimentación y biomedicina – Bioquochem (19/09/2023).

-Herramienta facilitadora en búsquedas y manejo masivo de información científica – Francisco Javier Álvarez Martínez (8/06/2023).

Also, the management of the LinkedIn account of IDiBE and the uploading of the IDiBE's web page (including the publication of the news) was done by the Innovation Office staff. Other works carried out by the Innovation Office were done in order to obtain a donation from Grupo Soledad of a total amount of 35.000 euros, the signature of a Joint Unit with

the University General Hospital of Elche-FISABIO or the adhesion to AEBA, Bioval and AseBio were carried out during 2023.

Thus, the organization of the visits of some relevant stakeholders to IDiBE as the Asociación Empresarial de Biotecnología de Alicante (AEBA; 06/03/2023) and the responsible of Innovation in the regional government (14/03/2023). In addition, the Innovation Office has organized the meeting with six technological institutes (27/10/2023), the first Young Researchers day (21/12/2023), the participation of IDiBE in the specialized congresses as Foro Cosmética PCUMH (18/05/2023) or BioSpain (26-28/09/2023) and has collaborated in the organization of the I IDiBE Cancer Research Meeting (26/05/2023),

Finally, the Innovation Officer Gabriel Estañ has done some public presentations about the IDiBE capabilities such in the ISABIAL InnovaSummit (27/01/2023), in the II Foro Alicante Conexión Salud (30/11/2023), in the IDiBE research meeting (20/07/2023), in the conference Acuicultura Segura (22/11/2023) and others.

Technicians in charge of major scientific instruments of IDiBE

Microscopy and Bioprinting Units of IDiBE

Enrique Rodríguez Cañas

Mass Cytometry Unit of IDiBE

Dra. Marta Rubio Camacho

Agreements

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

Bibliometrics of publications

Number of publications (WoS)	% of Q1 (D1)	Mean impact factor	Total impact factor
85	80 (32)	6.52	424

Dissemination

- Outreach seminars "Ciencia con tapas":
 - INTERNATIONAL DAY OF WOMEN AND GIRLS IN SCIENCE DAY AT IDiBE: "Investigadoras en biotecnología sanitaria, Centro de Congresos "Ciutat d'Elx" de Elche" (Elche), 14/02/23.
 - "Vacunas y otras estrategias de control de la malaria en África subsahariana", librería Pynchon&Co, (Alicante), 30-05-2023.
 - SCIENCE OUTREACH DAY "CIENCIA CON TAPAS" in the framework of "Science Goes To School (Science GTS), of the European Women's Researchers' Night": "Del mar al plato: consumo responsable de productos del mar", librería Pynchon&Co, (Alicante), 26/09/2023.
- IDiBE-UMH Open doors/Guided tours for high school and college students, 12/05/23, 26/05/23, 20/10/23, 03/11/23.
- Jornada Científica IDiBE 2023, 20/07/2023.

Entrepreneurship

- Prospera Biotech SL
- AntalGenics SL
- Hawk Biosystems SL
- Mitra solutions technologies SL
- Innovation Labo

Clinical development

- Parentide® continues in phase II clinical trials for chronic surgical pain. Sponsor: BCN Peptides.
- Bicalutamide is advancing to phase II clinical trials for treating Sanfilippo syndrome. Sponsor BCN Peptides
- AVX-012 starts phase III clinical trial in USA for dry eye syndrome. Sponsors: Aerie Pharmaceuticals Inc. Alcon acquires Aerie Pharmaceuticals.
- Oncapsisens, a novel formulation for alleviating symptoms of chemotherapy induced neuropathy starts a clinical study to evaluate a preventive effect in 10 hospitals. Sponsor: Prospera Biotech.
- Vulvisens, a novel formulation women intimate care. A pilot study reports excellent results attenuating vulvar pruritus and erythema.
- AG1529 continues in regulated pre-clinical safety studies for chronic psoriatic pruritus. Sponsor: AntalGenics.

ANNUAL REPORT 2023

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

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