

INSTITUTO DE
INVESTIGACIÓN
SANITARIA

HOSPITAL
UNIVERSITARIO
DE LA PRINCESA



Annual Report of Scientific Activity 2023

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SPONSORS

Letter from the Scientific Director

This year 2023 has been a one of transition, after 14 years holding the scientific direction of La Princesa Health Research Institute (IIS-Princesa), in July 2023, Professor Francisco Sánchez Madrid handed over the baton to myself.

This situation represents a great honour for me, but also an enormous responsibility, since under Paco's scientific direction, this Institute has brought so much prestige and visibility to its research centres as well as to its researchers.



Isidoro González Álvaro
Scientific Director

Since July 2023, a new project seeks to adapt the Institute structure to the new challenges of our regional health service (SERMAS) and to the need for a leadership transition in most of the groups that constitute the Institute.

In terms of scientific production, the pandemic caused an increase in the number of publications due to the need of the scientific community to increase its knowledge about the biology of SARS-CoV2, the immune system's response to the virus, and how to manage COVID-19. Four years later, in 2023, things have gone back to normal and the number of annual publications in IIS Princesa has returned to the baseline of around 400 articles. Although, the overall accumulated impact factor has decreased compared to the three previous years, the relative impact per article improved to 6.7. All in all, we have returned to the pre-pandemic number of publications, but now our researchers are able to publish in better journals.

This improvement in the quality of our publications is supported by 28% of publications in D1 and 69% in Q1, clearly higher than in 2022. In addition, more than 50% of the publications were led by IIS-IP researchers, which shows

that the scientific leadership of the members of our Institute is being consolidated. Furthermore, following the strategy established in 2022, we have achieved that 63% of our articles were published in Open Access format.

After the success in the 2022 Investigo calls of SEPE and CAM, in 2023 we limited the application for new human resources grants, obtaining 9 new collaborators.

The number of contracts signed for clinical studies this year has been 118, of which 83 correspond to clinical trials and 35 to observational studies.

Regarding academic output, 21 doctoral theses have been defended, 4 of them with a European mention.

Finally, I would like to highlight that the impact that the pandemic has given to collaboration between clinical and basic researchers has continued in 2023. This close interaction contributes to developing new ideas and research hypotheses with the aim of offering the best service to citizens and quality training for future generations. My hope for the next 4 years is that the "Princess Spirit", as we call this close cohesion and interaction between the different lines of research, will continue.



Members of the Institute

Organization chart

The Health Research Institute of the University Hospital La Princesa was constituted on December 15, 2009 under an agreement signed by the Madrid Health Service - representing the University Hospitals La Princesa, Santa Cristina, and the children's Hospital Niño Jesús - the Autonomous University of Madrid, the Biomedical Research Foundation of the University Hospital La Princesa and the Agency "Pedro Laín Entralgo" of the Community of Madrid for Training, Research and Health

Studies. Almost a year later, after an audit from the Institute of Health Carlos III, it got the Accreditation as a Health Research Institute.

In 2013 the activity of the Agency of Training, Research and Health Studies of the Community of Madrid "Pedro Laín Entralgo" was finished, and its functions were assumed by the Ministry of Health of the Community of Madrid, in particular by its the General Directorate of Research, Training and Documentation.



 **Hospital Universitario de La Princesa**

 **Hospital Universitario Santa Cristina**

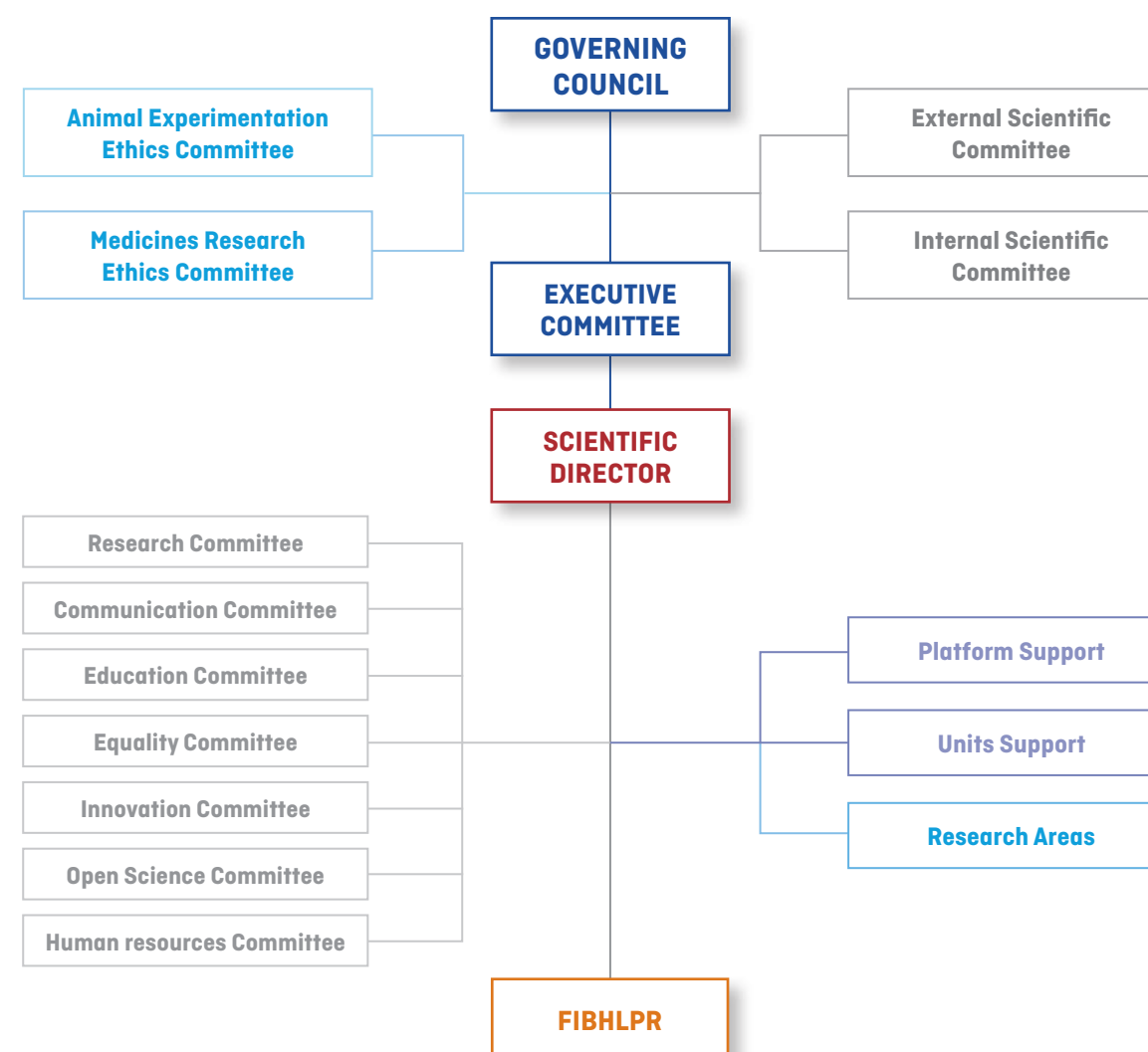
 **Hospital Universitario Niño Jesús**



Dirección General de Investigación,
Docencia y Documentación
CONSEJERÍA DE SANIDAD



Universidad Autónoma de Madrid



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Quality Coordinator, La Princesa University Hospital.

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Director of Fundación de Investigación Biomédica Hospital Universitario La Princesa

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SECRETARY

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Isidoro González Álvaro

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Purificación Muñoz Cánoves
Professor Universida Pompeu Fabra

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Associate Professor Centro Nacional de Investigaciones Cardiovasculares Carlos III

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Fundación para la Investigación Biomédica Hospital U. de La Princesa

Petronila Penela Márquez
Universidad Autónoma de Madrid

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Gastroenterology Department, Hospital Universitario La Princesa

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MEMBERS

Ángel Carlos Abanades Cuenca
Patient representative

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Gynecology and Obstetrics Department, Hospital Universitario Santa Cristina.

Carmen del Arco Galán
Emergency Department, Hospital U. La Princesa

Ángela de la Hoz Rodríguez
Emergency Department, Hospital U. La Princesa

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Family and Community Medicine, Primary Care

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Eva María Nicolás Carrillo
Patient representative

Pablo Montalvo Rebuelta
Lawyer, ASJUSA

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Biobank, Hospital Universitario La Princesa

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Ángel Núñez Pagán

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Rosario Ortiz de Urbina Barba

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PROJECTS MANAGEMENT DEPARTMENT

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Jesús Santamaría Pérez

María Joanne Dumanlag Reyes

ACCOUNTING DEPARTMENT

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CLINICAL TRIALS MANAGEMENT DEPARTMENT

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Alberto Sebastián Martínez-Caba

Marta Pérez Díaz

LEGAL

María Jesús Bono Sahuquillo

Verónica Grela Golpe

RESEARCH MANAGEMENT DEPARTMENT

Beatriz Ovejero Álvarez

Cora Llanos Manzanero

SECRETARY

Ana Aroca Martínez

WARD STAFF

José Corrochano de la Cruz



The following table shows information about the expenses and income of the Foundation, followed by the Situation Balance:

	2023	2022
Income	11.837.345	9.032.684
Expenses	11.814.603	9.016.873

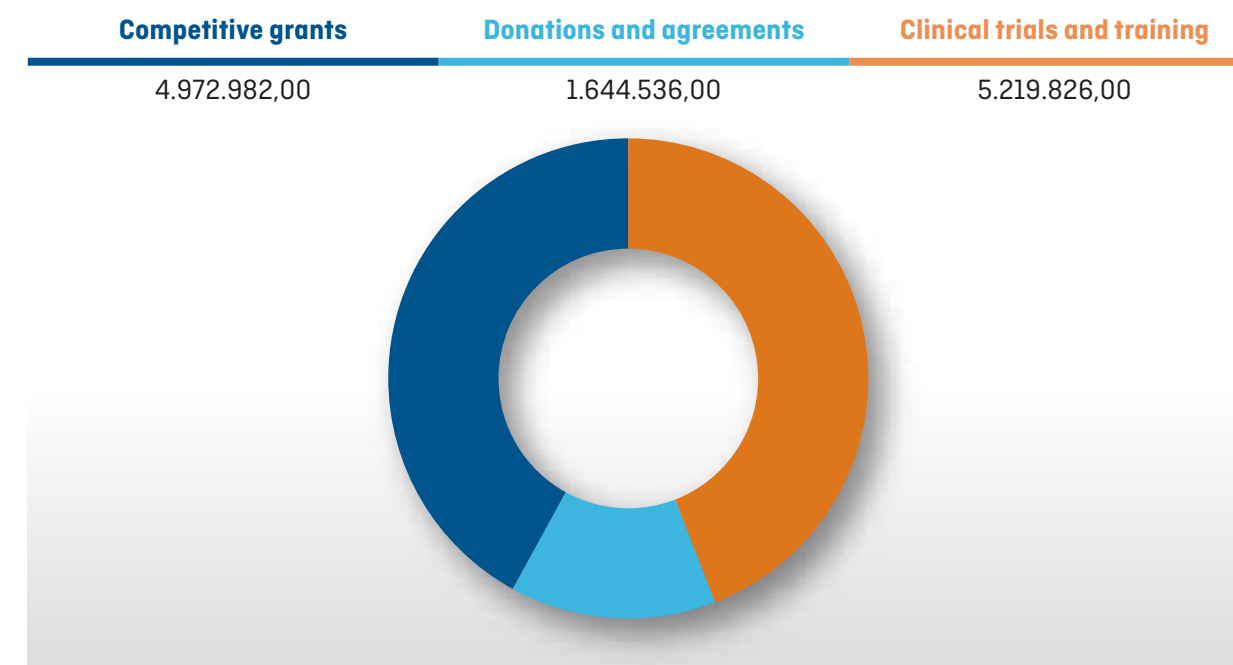
ACTIVE ASSETS

Non-current active asset	
Intangible fixed assets	60.590
Material fixed assets	868.776
Current active assets	
Debtors and Client to collect	1.713.234
Financial short term investments	0
Cash	24.913.962
Total Active Assets	27.556.563

PASSIVE ASSETS

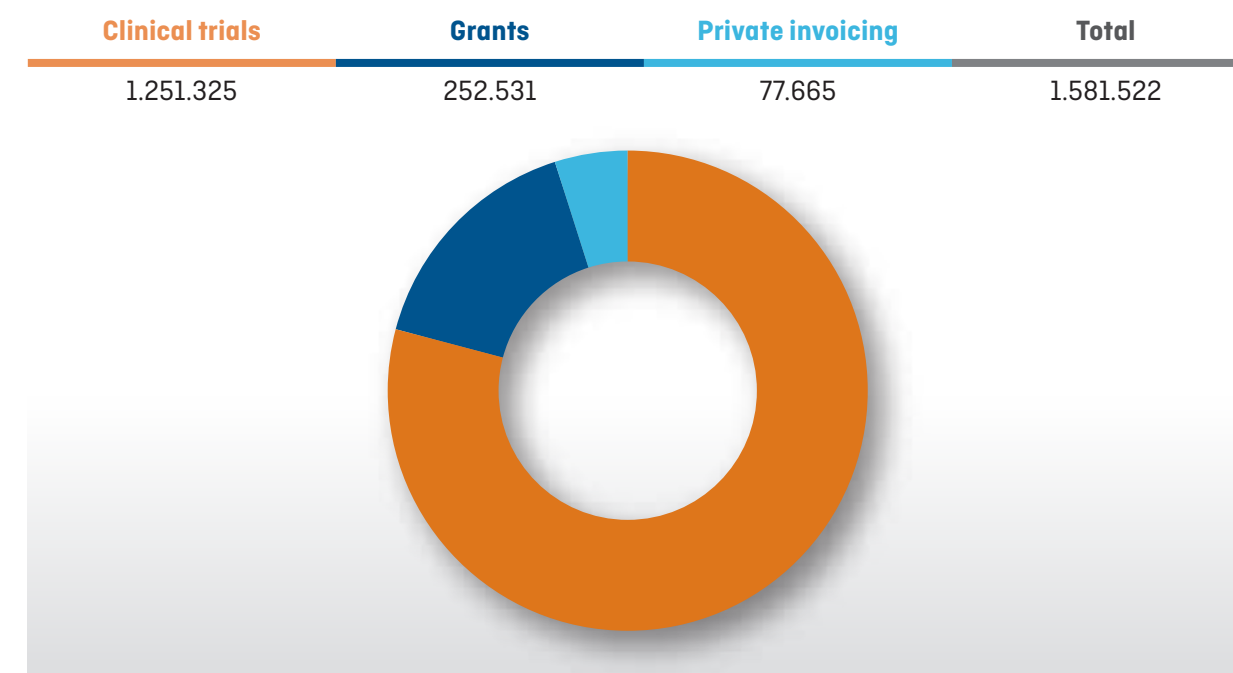
Net Worth	
Own funds	2.474.517
Non-refundable grants	796.776
Non-current passive asset	
Long term debts	0
Current active assets	
Short term provisions	9.545.591
Refundable grants	14.209.331
Creditors to pay	530.346
Total Passive Assets	27.556.563

Below is shown the information on the income obtained by the Foundation for Biomedical Research, with the income sources grouped as obtained through competitive grants, clinical trials, private invoicing, donations, or other income.



Finally, a graph is shown with the overhead income according to its origin and use.

Overhead income according to its origin:



Use of overhead income:

Personnel - Research (Platforms + Research programs)	76,7 %
Products and services - Equipment - Repairs	23,3 %

Scientific Platforms

PLATFORM SUPPORT

BIOBANK

The main mission of Biobank is focused on the development of collections of quality biological samples for the use by the scientific community. Its main tasks are: foster the setting of new collections, provide the scientific community access to biological samples and associated data, guarantee the rights of patients donating samples, and advice to investigators about the use and handling of biological samples.

SCIENTIFIC COORDINATOR

Mara Ortega Gómez

SCIENTIFIC COMMITTEE

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Scientific Management Support Unit, Hospital Universitario La Princesa

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Medical Oncology Department

Isidoro González Álvaro

Rheumatology Department

José A. Jiménez Heffernan

Pathology Department

Carlos Manuel Olivier Gómez

Urology Department

TECHNICAL STAFF

Violeta Casas Ramón

Marina Invernón Monedero

METHODOLOGICAL UNIT

It aims to provide to IP research teams support for the development and implementation of research projects in order to increase the excellence of the scientific activity of IIS-Princesa.

COORDINATOR

Francisco Javier Aspa Marco

TECHNICAL STAFF

Nuria Montes Casado

MEDICAL WRITER

Manuel Gómez Gutiérrez

SCIENTIFIC MANAGEMENT SUPPORT UNIT

The Scientific Management Support Unit of IIS-Princess has as main objective the organization, planning and coordination of all structures of support for the scientific environment and the researchers of the Institute, under the supervision of the Scientific Director of the Institute.

COORDINATOR

Francisco Javier Aspa Marco

"WHITE" ROOM

The "white" room located in the Niño Jesús Hospital, is a facility specialized to work with minimal or absent levels of contamination that meets the requirements of Good Manufacturing Practices (GMP). The "white" Room has Certification of Compliance with GMP since April 2010, both for Cell Therapy and Gene Therapy.

COORDINATOR OF THE ADVANCED THERAPIES UNIT

Manuel Ramírez Orellana

FLOW CYTOMETRY UNIT

The Flow Cytometry Unit is located in the Department of Immunology and Molecular Biology, University Hospital of La Princesa and has recently joined the Network of Laboratories of Public Research Organizations (RED-LAB) of the Community of Madrid.

The unit provides instrumentation and technical assistance to the researchers to perform both immunophenotype analysis and cell sorting based on fluorescence parameters.

COORDINATOR

Cecilia Muñoz Calleja

GENOMIC UNIT

The Genomics Unit is responsible for the development and implementation of technologies for molecular biology and genomics, equipment maintenance, and provision of technical advice on various technologies to research groups. It uses different technologies as spectrophotometry, automated extraction of nucleic acids, RNA integrity determination, conventional PCR and RT-PCR, real time PCR and RT-PCR, software for search and integration of experimental data and, recently, massive sequencing.

TECHNICAL DIRECTOR

Fernando Carrasco Ramiro

ELECTRONIC MICROSCOPE SERVICE

The Electron Microscopy Service of UAM provides technical assistance and scientific support to research groups interested in using electron microscopy techniques for ultrastructural analysis of biological samples and immunodetection of antigens. It has a transmission electron microscope and the material needed for sample preparation.

TECHNICAL DIRECTOR

María Teresa Rejas Marco

PROTEOMIC UNIT

Proteomics service's objectives are to provide the research groups with support and scientific and technical advice in the identification and characterization of proteins by mass spectrometry (MS) techniques.

COORDINATOR

Ana Isabel Marina Ramírez

HIGH DEFINITION VIDEOMICROSCOPY

The Institute Videomicroscopy Service provides the infrastructure and scientific expertise needed for studies of fluorescence, confocal and evanescent wave microscopy, with special emphasis on the observation of dynamic processes in living cell.

COORDINATOR

Noa B. Martín Cofreces

TECHNICIAN

Francisca Molina Jiménez

ANIMAL FACILITY

The Veterinary Office of the Universidad Autónoma de Madrid offers its services to our Institute. It is a service whose purpose is to maintain, produce and control animals for experimental research.

DIRECTOR

David Muñoz Valverde

DATA ANALYSIS UNIT

The Data Analysis Unit (DAU) has the objective of supporting the research groups of the Institute. The main objective of the DAU is to implement and develop numerical algorithms for the analysis and visualization of biomedical data. The UAD collaborates actively with the groups that need this expertise, and provides advice on specific issues in everything related to the analysis of data. It also carries out training activities related to data analysis tools

COORDINATOR

Guillermo J. Ortega Rabbione



UNITS

BIOLOGICAL AND TARGETED THERAPIES UNIT

Targeted biological and synthetic therapies (TBST) are the result of the great parallel advances in the knowledge of the pathogenesis of various chronic inflammatory and autoimmune diseases and biotechnology. Their discovery and development constitute one of the most relevant changes that have occurred in various medical fields over the last two decades. Their incorporation into the therapeutic armamentarium has been a crucial milestone in the history of many immune-mediated inflammatory diseases, not only in terms of the availability of drugs with new mechanisms of action, but also due to the development of strategies that improve outcomes and efficient use of all drugs. Their great effectiveness determines that there is a growing number of patients who require access to these treatments, while security requires constant and meticulous risk management. Taking this into account as well as their high cost, increasing the rigor in the selection and follow-up of patients who need them, including cost-effectiveness criteria, is considered essential. This multidisciplinary Unit, which was granted a qualification of good practice by the Spanish National Health System in 2016, coordinates the best use of these high-cost therapies based on criteria of scientific rigour, safety and efficiency. Along with sustainability, the Unit promotes research and innovation to improve knowledge and optimal use of these drugs. Thus, during the year 2022, projects to understand and measure the patient experience (PREMS) during the COVID19 pandemic, and Home delivery strategies have been carried out; an economic evaluation project for TBST has also begun in the most complex patients. Additionally, a doctoral thesis is being carried out on the real-life use of Jak kinase inhibitors, and we continue to increase the collection of biological samples of the BIOIMID project, which studies prognostic biomarkers and therapeutic response to the most recently incorporated drugs.

COORDINATOR

Alberto Morell Baladrón
Hospital Pharmacy Department

MULTIDISCIPLINAR TEAM

María Chaparro Sánchez
Gastroenterology Department

Esteban Daudén Tello
Dermatology Department

Rosario García de Vicuña
Rheumatology Department

María del Mar Llamas Velasco
Dermatology Department

Virginia Meca Lallana
Neurology Department

Rosario Ortiz de Urbina Barba
Fundación para la Investigación Biomédica Hospital Universitario La Princesa

Francisco Javier Pérez Gisbert
Gastroenterology Department

Esther Ramírez Herraiz
Hospital Pharmacy Department

Gloria María Torralbo Caballero
Hospital Medical Direction

CLINICAL TRIALS UNIT

The Clinical Trials Unit was created with the primary objective of promoting clinical research as well as providing support to researchers. Clinical trials or observational studies promoted and/or led by researchers are considered independent clinical research.

SCIENTIFIC DIRECTOR

Francisco Abad Santos

DIRECTOR

Dolores Ochoa Mazarro

DEPUTY DIRECTOR

Manuel Román Martínez

COORDINATOR

Sergio Luquero Bueno

LAB MANAGER

Samuel Martín Vilchez

CLINICAL PHARMACOLOGIST

Paola Camargo Mamani

Antía Gómez Fernández

Diana María Campodónico

PHYSICIANS

Samuel Alejandro Jiménez Guardiola

Tamara Michelle Moreno Silva

QUALITY ASSURANCE

Jaime Pérez Calvo

LAB TECHNICIAN

Alejandro de Miguel Cáceres

NURSE

Carmen Mendez-Benegassi Cid

Raquel Saiz Martínez

Tamara de La Torre Muñoz

STUDY COORDINATORS

Marina Aldama Martín

Carmen Candau Ramos

CLINICAL TRIAL ASSISTANT

Irene Román Martínez

Rebeca Manzanares López

INNOVATION UNIT

The Innovation Unit of the Hospital de La Princesa was born with the foundation of the Research Institute, and is responsible, with the existing resources, to analyze

new technological trends and their implementation at the Institute.

The Innovation Unit of the Health Research Institute Hospital Universitario de La Princesa was consolidated when it joined the Platform for Innovation in Medical and Health Technologies (ITEMAS), getting access to the funding of the 2013 call for grants from the Strategic Action in Health, from Institute of Health Carlos III.

COORDINATOR

Eduardo Pacios Blanco

Radiodiagnosis Unit, Hospital Universitario La Princesa

Sonia Sobrino Pacheco

Fundación de Investigación Biomédica Hospital Universitario La Princesa

COMMITTEES

QUALITY COMMITTEE

To achieve objective results of excellence and get a continuous improvement, the Quality Commission not only elaborates, but also continuously monitors the implementation of quality procedures established in our Institute.

COORDINATOR

María Mercedes Vinuesa Sebastián

Quality Coordinator, La Princesa University Hospital.

QUALITY COMMITTEE

Arantzazu Alfranca González

Immunology Department

Francisco Javier Aspa Marco

Scientific Management Support Unit

Ramón Colomer Bosch

Medical Oncology Department

Mara Ortega Gómez

Biobank

SECRETARY

Technical secretary, IIS Princesa, Instituto de Investigación Biomédica Hospital U. La Princesa.

EDUCATION COMMITTEE

One of the priorities set by the IIS-Princesa is the promotion and development of training programs for professionals who are part of the Centre, with a focus on training for translational research to improve the competitiveness of institutions and the qualifications of the personnel that integrates them.

In this sense, all entities that are part of the Health

Research Institute Hospital Universitario de La Princesa have an established training and teaching track, and have a wide training offer at all levels (training of undergraduate, graduate, and Continuing Specialized Health).

COORDINATOR

Fernando Ramasco Rueda

Continuous Training Coordinator

EDUCATION COMMITTEE

Francisco Javier Aspa Marco

Scientific Management Support Unit, Hospital Universitario La Princesa

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Molecular Biology Department

Alicia González Martínez

Neurology Department

Elena Martín Pérez

Head of studies Resident Doctor

José Luis Muñoz de Nova

General and Gastrointestinal Surgery

Jesús Miguel Novalbos Reina

Clinical pharmacology department

Mara Ortega Gómez

Biobank

Pablo Rodríguez Camero

Radiodiagnosis department

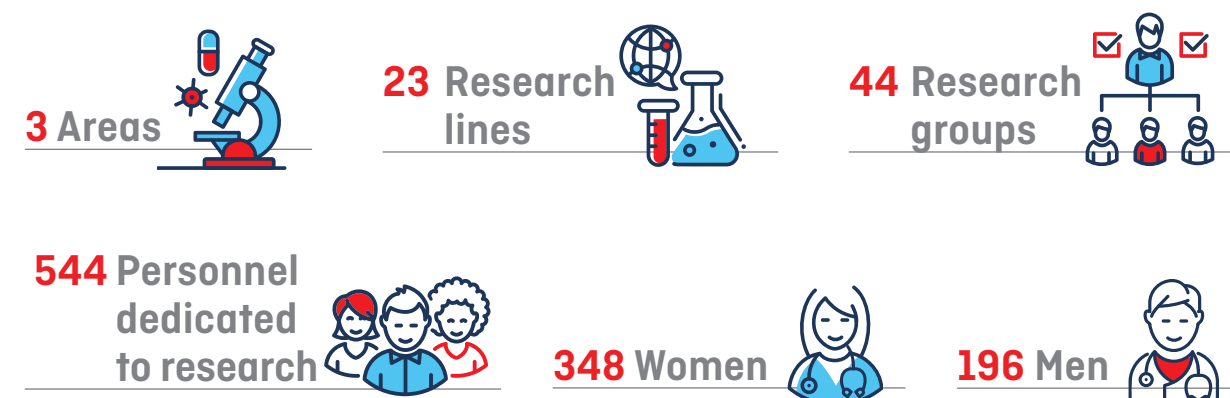
Manuel Román Martínez

Clinical pharmacology department

SECRETARY

Technical secretary, IIS Princesa, Instituto de Investigación Biomédica Hospital U. La Princesa.

Research Areas



Area 1 Cellular and molecular etiopathogenic mechanisms in inflammatory and autoimmune diseases

COORDINATOR

Francisco Sánchez Madrid

DEPUTY DIRECTOR

Julie Ann Chowen King

GENERAL OBJECTIVES

1. Unravel the molecular and cellular mechanisms that control crucial biological processes in inflammatory / autoimmune based diseases.
2. Identify molecular entities and cellular processes that can be used as targets for the action of new drugs for inflammatory / autoimmune based diseases.
3. Implement advanced experimental techniques and new animal models of disease that will allow improving basic studies to analyse pathophysiological mechanisms, and perform pre-clinical studies.
4. Promote translational research by fostering interactions between basic and clinical groups.

Five most relevant publications of the area:

Grupo 1 – Francisco Sánchez Madrid

Calzada-Fraile D, Iborra S, Ramírez-Huesca M, Jorge I, Dotta E, Hernández-García E, Martín-Cófreces N, Nistal-Villán E, Veiga E, Vázquez J, Pasqual G, Sánchez-Madrid F. **Immune synapse formation promotes lipid peroxidation and MHC-I upregulation in licensed dendritic cells for efficient priming of CD8+ T cells.** Nat Commun. 25;14(1):6772. 2023. PMID: 37880206. IF: 14,7. doi: 10.1038/s41467-023-42480-3.

Grupo 1 – Noa B. Martín-Cófreces

Rojas-Gómez A, Dosil SG, Chichón FJ, Fernández-Gallego N, Ferrarini A, Calvo E, Calzada-Fraile D, Requena S, Otón J, Serrano A, Tarifa R, Arroyo M, Sorrentino A, Pereiro E, Vázquez J, Valpuesta JM, Sánchez-Madrid F, Martín-Cófreces NB. **Chaperonin CCT controls extracellular vesicle production and cell metabolism through kinesin dynamics.** J Extracell Vesicles. 12(6):e12333. 2023. PMID: 37328936. IF: 15,5. doi: 10.1002/jev2.12333.

HUMAN RESOURCES COMMITTEE

COORDINATOR

María del Mar Martín Cuena
Human Resources Department

HUMAN RESOURCES COMMITTEE

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Sergio Luquero Bueno
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Nuria Romero Laorden
Medical Oncology Department

SECRETARY

Technical secretary, IIS Princesa, Instituto de Investigación Biomédica Hospital U. La Princesa.

COMMITTEE FOR EQUAL OPPORTUNITIES AND DIVERSITY MANAGEMENT

The Committee for Equal Opportunities acts as the main body responsible for promoting and coordinating the Institute's gender equality policies.

COORDINATOR

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Human Resources Department

Sara Cardenal Rodríguez
Clinical Trial Department

María Chaparro Sánchez
Gastroenterology Department,

Sergio Luquero Bueno
Clinical Trial Unit

Noa Beatriz Martín Cofreces
Immunology Department

María del Mar Martín Cuena
Human Resources Department

María del Rosario Ortiz de Urbina Barba
Director Fundación para la Investigación Biomédica Hospital Universitario de La Princesa

Nuria Romero Laorden
Medical Oncology Department

SECRETARY

Technical secretary, IIS Princesa, Instituto de Investigación Biomédica Hospital U. La Princesa.

OPEN SCIENCE COMMITTEE

The Open Science Committee will act as the main body responsible for promoting and coordinating Open Science policies within the framework of the IIS Princesa.

María Chaparro Sánchez
Gastroenterology Department,

Noa Beatriz Martín Cofreces
Immunology Department

Enrique Martín Gayo
Immunology Department

Rosa Ana Muñoz Codoceo
Gastroenterology Department

Pablo Rodríguez Camero
Radiodiagnosis department

Nuria Romero Laorden
Medical Oncology Department

Pablo Zubiaur Precioso
Clinical pharmacology department

SECRETARY

Technical secretary, IIS Princesa, Instituto de Investigación Biomédica Hospital U. La Princesa.



Area 2 Translational neuroscience

COORDINATOR

José Luis Ayuso Mateos

DEPUTY DIRECTOR

María Dolores Ochoa Mazarro

GENERAL OBJECTIVES

1. Design, synthesis and characterization of new compounds with potential neuroprotective effect on neurodegenerative diseases and stroke.
2. Search for biomarkers for early diagnosis, study of progression and response to treatment in these diseases.
3. Drug characterization in preclinical studies in animal models and in clinical trials in humans
4. Expand the knowledge about affective disorders in the population, studying risk factors, clinical evolution and response to treatment, in order to improve the mental health of the population.

Five most relevant publications of the area:

Grupo 32 – Francisco Abad Santos / Grupo 35 – José A. Vivancos Mora

Hernández-Jiménez M, Abad-Santos F, Cotgreave I, Gallego J, Jilma B, Flores A, Jovin TG, Vivancos J, Hernández-Pérez M, Molina CA, Montaner J, Casariego J, Dalsgaard M, Liebeskind DS, Cobo E, Castellanos M, Portela PC, Masjuán J, Moniche F, Tembl JI, Terceño Izaga M, Arenillas JF, Callejas P, Olivot JM, Calviere L, Henon H, Mazighi M, Piñeiro D, Pugliese M, González VM, Moro MA, García-Tornel A, Lizasoain I, Ribo M. **Safety and Efficacy of ApTOLL in Patients With Ischemic Stroke Undergoing Endovascular Treatment: A Phase 1/2 Randomized Clinical Trial.** JAMA Neurol. 1;80(8):779-788. 2023. PMID: 37338893. IF: 20,4. doi: 10.1001/jamaneurol.2023.1660.

Grupo 16 – Manuela García López

Crisman E, Duarte P, Dauden E, Cuadrado A, Rodríguez-Franco MI, López MG, León R. **KEAP1-NRF2 protein-protein interaction inhibitors: Design, pharmacological properties and therapeutic potential.** Med Res Rev. 43(1):237-287. 2023. PMID: 36086898. IF: 10,9. doi: 10.1002/med.21925.

Grupo 33 – José Luis Ayuso Mateos

Javier-David Lopez-Morinigo, Hilario Blasco-Fontecilla, Philippe Courtet, José-Luis Ayuso-Mateos. **In-**

vestigating the relationship between cross-national suicide rates and COVID-19 first and second waves spread across the world: An exploratory study. Span J Psychiatry Ment Health. 16(2):95-101. 2023. PMID: 35251385. IF: 5,2. doi: 10.1016/j.rpsm.2022.02.002.

Grupo 35 – Alicia González Martínez

González-Martínez A, Bose G, Lokhande H, Saxena S, Healy BC, Polgar-Turcsanyi M, Weiner HL, Chitnis T. **Early miR-320b and miR-25-3p miRNA levels correlate with multiple sclerosis severity at 10 years: a cohort study.** J Neuroinflammation. 1;20(1):136. 2023. PMID: 37264432. IF: 9,3. doi: 10.1186/s12974-023-02816-8.

Grupo 41 – Francisco J. Egea Maiquez

Damiano Rocchi, Juan F González, Olmo Martín-Cámara, María Grazia Perrone, Morena Miciaccia, Antonio Scilimati, Celine Decouty-Pérez, Esther Parada, Javier Egea, J Carlos Menéndez. **m-Terphenylamines, Acting as Selective COX-1 Inhibitors, Block Microglia Inflammatory Response and Exert Neuroprotective Activity.** Molecules. 13;28(14):5374. 2023. IF: 4,2. doi: 10.3390/molecules28145374.

Line 1 Neuropharmacology and neuroprotection

Group 16 Manuela García López

Group 41 Javier Egea Maiquez

Line 3 Clinical pharmacology and pharmacogenetics

Group 32 Francisco Abad Santos

Line 4 Diagnostic and therapeutic advances in affective disorders

Group 33 José Luis Ayuso Mateos

Line 5 Neurosurgery of epilepsy

Group 34 Jesús Pastor Gómez

Line 6 Cerebrovascular diseases

Group 35 José Aurelio Vivancos Mora

Grupo 24 – Pedro Majano Rodríguez

Molina-Jiménez F, Ugalde-Triviño L, Arias-González L, Relaño-Rupérez C, Casabona S, Pérez-Fernández MT, Martín-Domínguez V, Fernández-Pacheco J, Laserna-Mendieta EJ, Muñoz-Hernández P, Arias-Arias Á, Cano A, Muñoz J, Lucendo AJ, Santander C, Majano P. **Proteomic analysis of the esophageal epithelium reveals key features of eosinophilic esophagitis pathophysiology.** Allergy. 78(10):2732-2744. 2023. PMID: 37287363. IF: 12,6. doi: 10.1111/all.15779.

Grupo 1 – Enrique Martín Gayo /

Grupo 36 – Santos Castañeda Sanz

Sánchez-Cerrillo I, Calzada-Fraile D, Triguero-Martínez A, Calvet-Mirabent M, Popova O, Delgado-Arévalo C, Valdivia-Mazeyra M, Ramírez-Huesca M, de Luis EV, Benguría A, Aceña-Gonzalo T, Moreno-Vellisca R, de Llano MA, de la Fuente H, Tsukalov I, Delgado-Wicke P, Fernández-Ruiz E, Roy-Vallejo E, Tejedor-Lázaro R, Ramiro A, Iborra S, Sánchez-Madrid F, Dopazo A, Álvaro IG, Castañeda S, Martín-Gayo E. **MICA/b-dependent activation of natural killer cells by CD64+ inflammatory type 2 dendritic cells contributes to autoimmunity.** EMBO J. 1;42(23):e113714. 2023. PMID: 37916875. IF: 9,4. doi: 10.15252/embj.2023113714.

Grupo 18 – Miguel Ángel Iñiguez Peña

Bago Á, Cayuela ML, Gil A, Calvo E, Vázquez J, Queiro A, Schopfer FJ, Radi R, Serrador JM, Iñiguez MA. **Nitro-oleic acid regulates T cell activation through post-translational modification of calcineurin.** Proc Natl Acad Sci U S A. 24;120(4):e2208924120. 2023. PMID: 36652486. IF: 9,4. doi: 10.1073/pnas.2208924120

Line 1 Intercellular communication in the inflammatory response

Group 1 Francisco Sánchez Madrid

Group 3 María Yáñez Mó

Group 56 Ana Carmen Urzainqui Mayayo

Line 2 Cellular and molecular responses to hypoxia

Group 9 Julián Aragonés López

Group 7 Antonio Martínez Ruiz

Group 8 María Josefa Calzada García

Line 3 Animal models of inflammatory diseases and intercellular signalling

Group 11 Federico Mayor Menéndez

Group 12 Manuel Fresno Escudero

Group 13 Petronila Penela Márquez

Group 17 Cristina Murga Montesinos

Group 18 Miguel Ángel Iñiguez Peña

Line 5 Cellular mechanisms and molecular determinants of allergybased diseases

Group 20 Carlos Blanco Guerra

Group 15 María Dolores Ibáñez Sandín

Line 6 Inflammatory processes in nephrological diseases.

Group 21 Guillermina Barril Cuadrado

Line 7 Inflammatory mechanisms in pulmonary diseases

Group 22 Julio Ancochea Bermúdez

Line 8 Inflammatory response in hepatic diseases

Group 24 Pedro Lorenzo Majano Rodríguez

Group 23 Luisa Consuelo García Buey

Line 9 Mechanisms and mediators of endocrine diseases

Group 25 Mónica Marazuela Azpiroz

Line 10 Children's development (obesity and growth)

Group 26 Jesús Argente Oliver

Line 11 Metabolic syndrome and vascular risk

Group 5 Carmelo García Monzón



Area 3 Advanced therapies and individualized medicine

COORDINATOR

María Chaparro Sánchez

DEPUTY DIRECTOR

Isidoro González Álvaro

GENERAL OBJECTIVES

1. Identification of biomarkers that allow predicting the prognosis and / or response to treatment in inflammatory, infectious or tumor diseases.
2. Optimization of biological therapies by identifying biomarkers predictive of therapy response.
3. Identification of new drugs and / or therapeutic targets.
4. Search for new treatments and improvement in the efficacy and safety of treatments and in the management of their effects on the quality of life of patients.

Five most relevant publications of the area:

Grupo 38 – Javier Pérez Gisbert

Burgos-Santamaría D, Nyssen OP, Gasbarrini A, Vaira D, Pérez-Aisa Á, Rodrigo L, Pellicano R, Keco-Huerga A, Pabón-Carrasco M, Castro-Fernández M, Boltin D, Barrio J, Phull P, Kupcinskis J, Jonaitis L, Ortiz-Polo I, Tepes B, Lucendo AJ, Huguet JM, Areia M, Jurecic NB, Denkovski M, Bujanda L, Ramos-San Román J, Cuadrado-Lavín A, Gómez-Camarero J, Jiménez Moreno MA, Lanas A, Martínez-Dominguez SJ, Alfaro E, Marcos-Pinto R, Milivojevic V, Rokkas T, Leja M, Smith S, Tonkić A, Buzás GM, Doulberis M, Venerito M, Lerang F, Bordin DS, Lamy V, Capelle LG, Marlicz W, Dobru D, Gridnyev O, Puig I, Mégraud F, O'Morain C, Gisbert JP; Hp-EuReg Investigators. **Empirical rescue treatment of *Helicobacter pylori* infection in third and subsequent lines: 8-year experience in 2144 patients from the European Registry on *H. pylori* management (Hp-EuReg).** Gut. 72 (6): 1054-1072. 2023. PMID: 36591610. IF: 23. doi: 10.1136/gutjnl-2022-328232.

Grupo 40 – Ramón Colomer Bosch

Colomer R, Miranda J, Romero-Laorden N, Hornedo J, González-Cortijo L, Mouron S, Bueno MJ, Mondéjar R, Quintela-Fandino M. **Usefulness and real-world outcomes of next generation sequencing testing in patients with cancer: an observational study on the impact of selection based on clinical judgement.** ECLI-

nicalMedicine. 1;60:102029. 2023. PMID: 37304496. IF: 9,6. doi: 10.1016/j.eclinm.2023.102029.

Grupo 44 – Rafael de la Cámara Llanza

Greco R, Snowden JA, Knelange NS, Tridello G, Cacciatore C, Xhaard A, Ciceri F, Collin M, Ferra C, De Becker A, Badoglio M, Averbuch D, Alexander T, Ljungman P, De la Camara R; European Society for Blood and Marrow Transplantation (EBMT) COVID19 Task Force, Autoimmune Diseases Working Party (ADWP) and Infectious Diseases Working Party (IDWP). **Outcome of SARS-CoV2 infection in hematopoietic stem cell transplant recipients for autoimmune diseases.** J Autoimmun. 136:103024. 2023. PMID: 37001437. IF: 7,9. doi: 10.1016/j.jaut.2023.103024.

Grupo 58 – Fernando Alfonso Manterola

Alfonso F, Fernández-Pérez C, Del Prado N, García-Guimaraes M, Bernal JL, Bastante T, Del Val D, Rosillo N, Elola J. **Primary Percutaneous Coronary Intervention in Patients With Spontaneous Coronary Artery Dissection vs Coronary Artery Disease.** JACC Cardiovasc Interv. 14;16(15):1860-1869. 2023. PMID: 37587593. IF: 11,7. doi: 10.1016/j.jcin.2023.05.044. PMID: 37587593.

Grupo 38 – María Chaparro Sánchez

Chaparro M, Acosta D, Rodríguez C, Mesonero F, Vicuña M, Barreiro-de Acosta M, Fernández-Clotet A, Hernández Martínez Á, Arroyo M, Vera I, Ruiz-Cerulla A, Sicilia B, Cabello Tapia MJ, Muñoz Villafranca C, Castro-Pocheiro J, Martínez Cadilla J, Sierra-Ausín M, Vázquez Morón JM, Vicente Lidón R, Bermejo F, Royo V, Calafat M, González-Muñoz C, Leo Carnerero E, Manceñido Marcos N, Torrealba L, Alonso-Galán H, Benítez JM, Ber Nieto Y, Diz-Lois Palomares MT, García MJ, Muñoz JF, Armesto González EM, Calvet X, Hernández-Camba A, Madrigal Domínguez RE, Menchén L, Pérez Calle JL, Piqueras M, Dueñas Sadornil C, Botella B, Martínez-Pérez TJ, Ramos L, Rodríguez-Grau MC, San Miguel E, Fernández Forcelledo JL, Fradejas Salazar PM, García-Sepulcre M, Gutiérrez A, Llaó J, Sesé Abizanda E, Boscá-Watts M, Iyo E, Keco-Huerga A, Martínez Bonil C, Peña González E, Pérez-Galindo P, Varela P, Gisbert JP; To-ReWard Study Group. **Real-World Evidence of Tofacitinib in Ulcerative Colitis: Short-Term and Long-Term Effectiveness and Safety.** Am J Gastroenterol. 1;118(7):1237-1247. 2023. PMID: 36716287. IF: 8. doi: 10.14309/ajg.0000000000002145.

Line 1 Prognostic and predictor markers in autoimmune diseases

Group 36 *Isidoro González Álvaro*

Group 37 *Esteban Daudén Tello*

Line 2 Esophagogastrointestinal inflammatory diseases

Group 38 *Javier Pérez Gisbert*

Line 3 Progenitors and cell therapy

Group 39 *Luis Madero López*

Line 4 Advanced therapies in oncohematology

Group 44 *Juan Luis Steegmann Olmedillas*

Line 5 Biological, cellular and molecular monitoring in oncohematology

Group 45 *Elena Fernández Ruiz*

Group 46 *Cecilia Muñoz Calleja*

Line 6 New diagnostic and therapeutic advances in cardiovascular diseases

Group 58 *Fernando Alfonso Manterola*

Group 48 *Luis Jesús Jiménez Borreguero*

Group 57 *Carmen Suárez Fernández*

Group 49 *Blanca Novella Arribas*

Line 7 New therapies in infectious pathologies

Group 50 *Ignacio de los Santos Gil*

Group 51 *Javier Aspa Marco*

Group 52 *Teresa Alarcón Cavero*

Line 8 Individualized medicine in solid tumors

Group 40 *Ramón Colomer Bosch*

Group 53 *Almudena Zapatero Laborda*

Group Asociado 3 *José Cordero Ampuero*



Scientific Output

GLOBAL ANALYSIS

Publications:

	Total	Impact Factor	Mean Impact Factor	% D1	%Q1	% IF>10	% International collaborations	% Open Access	% Leadership
Publications	387	2584,6	6,67	28,16	69	12,14	32,82	63,82	54,79
Articles	319	2037,6	6,39	26,96	69,60	10,34	31,97	65,20	52,35
Editorial	27	289,3	10,71	55,56	70,37	29,63	29,62	40,74	81,48
Review	41	257,7	6,28	19,51	63,41	14,63	41,46	68,29	56,09

New Projects:

New Research projects in 2023: 18

New Human Resources grants in 2023: 9

Clinical Trials:

Ongoing Clinical Trials during the year 2023: 509

Clinical Trial agreements signed in 2023: 118

Patents:

Number of patents applications: 2

Theses:

Number of theses defended: 21

Number of theses with European mention: 4



Communication: ELENA ESPAÑOL

Number of news published in printed press: 6

News in other audiovisual media (TV / Radio): 33

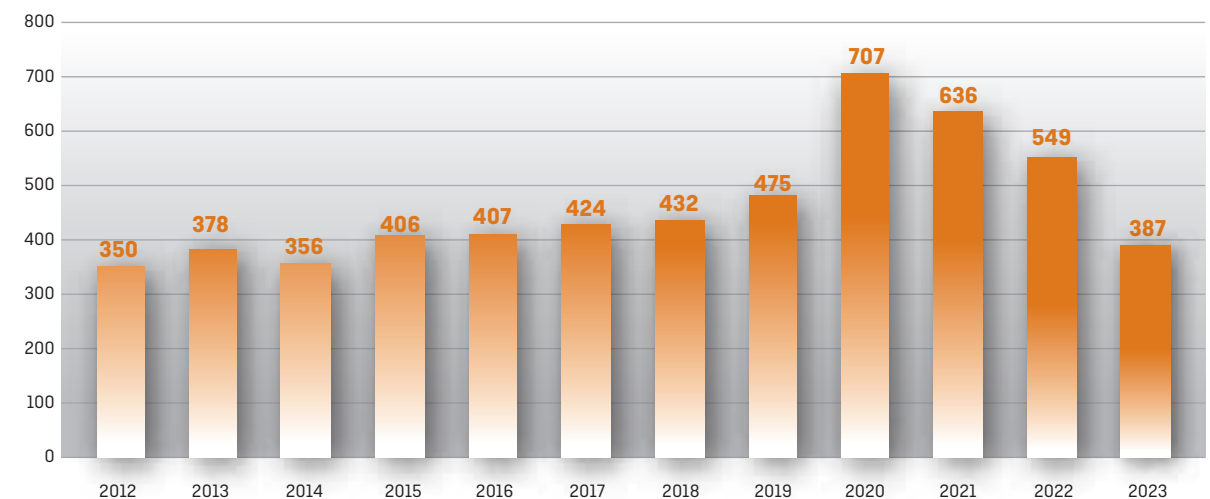
Number of news in specialised and non-specialised digital media: 133

Number of Research Bulletin "Factor de Impacto" with the last scientific news with wide dissemination among patients, researchers and media: 4

PUBLICATIONS

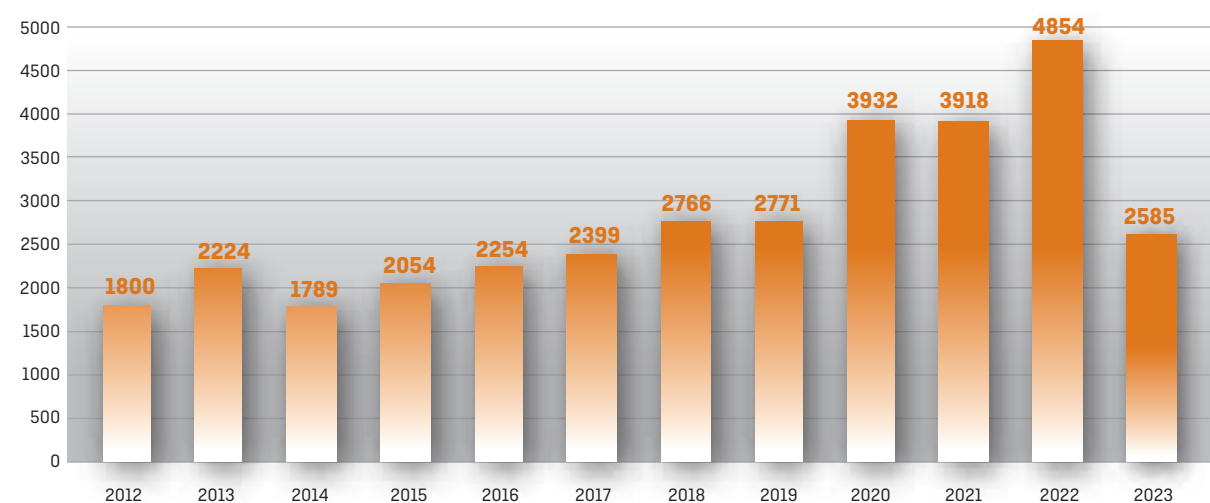
Following the trend started in 2021, the number of publications in 2023 experienced a decrease compared to 2022. Obviously, the pandemic caused an outstanding influence in the number of articles published by the scientific community all over the world. Our Institute was deeply involved in the scientific effort to improve the knowledge and, therefore, the management of COVID-19. This effort led to a striking increase in publications during 2020. As shown in the graph below, then the number of publications gradually decreased reaching the prepandemic levels in 2023. .

Number of publications per year. Historical evolution from 2012 to 2023



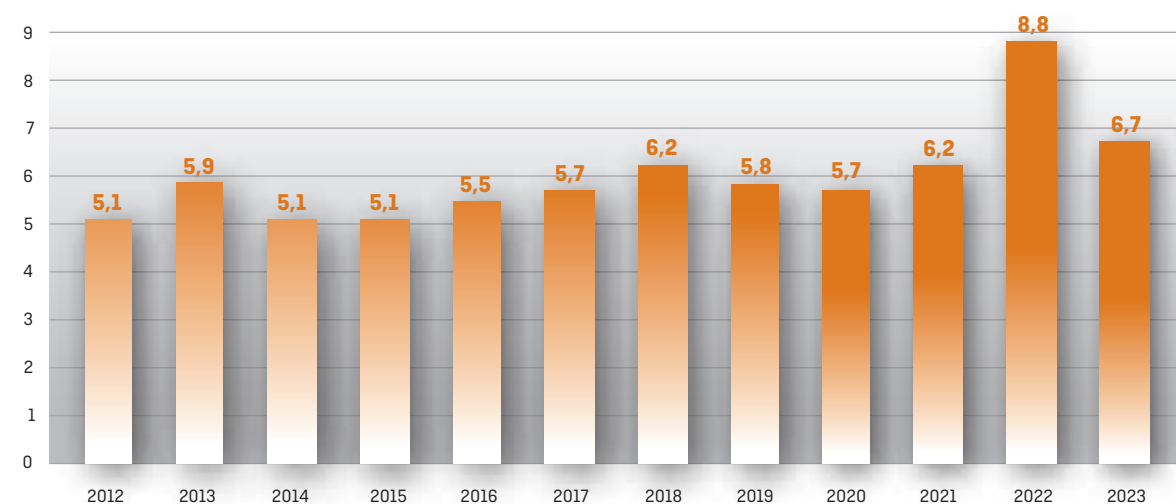
Due to the decrease in the number of publications, the cumulative impact factor (IF) has also decreased compared to the pandemic years (2020-2022). Compared to 2022, the cumulative IF in 2023 seems to have decreased dramatically. However, the reason is that most journals had a transient increase in the IF due to the excessive number of COVID-19-related publications in 2020 and 2021 worldwide. In 2023, the IF assigned by the Journal Citation Reports has returned to normal values. The historical evolution of the cumulative IF at the IIS Princesa is shown in the graph below.

Cumulative impact factor per year. Historical evolution from 2012 to 2023



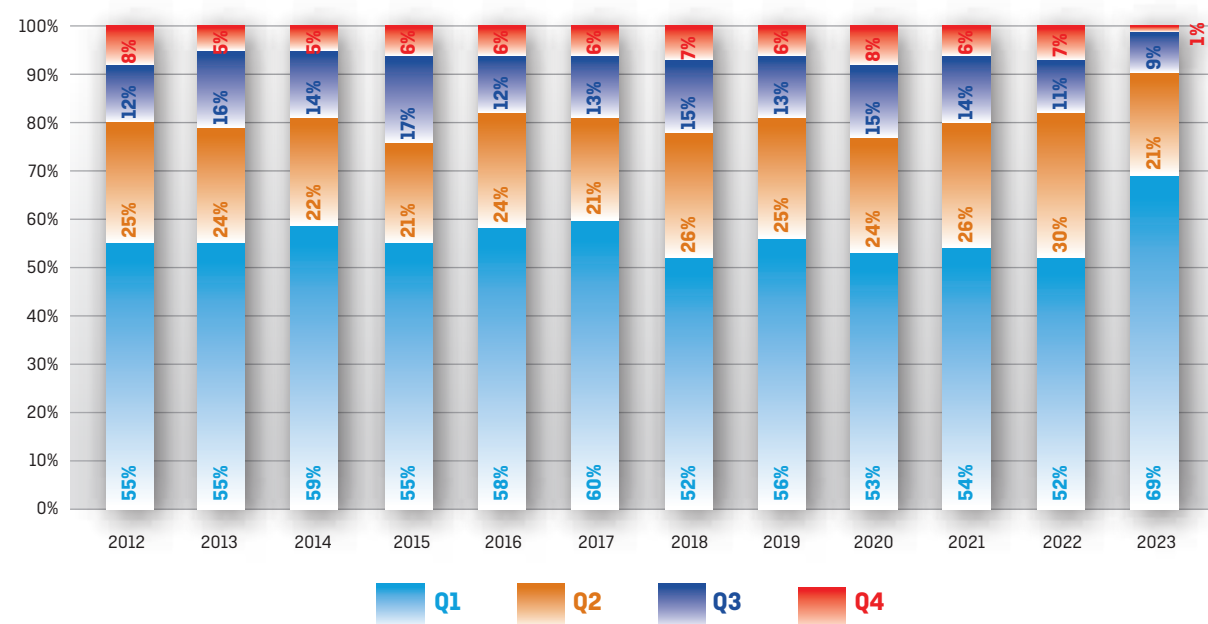
Despite the decrease in the number of publications and the cumulative impact factor, the average impact factor of publications has remained proportionally stable and high. If, for the reasons mentioned in the previous paragraph, we exclude the year 2022, as shown in the graph below, 2023 maintains the trend of increasing average IF per article, suggesting that the quality of our researchers' publications is continuously increasing.

Mean impact factor per article and year. Historical evolution from 2012 to 2023



The proportional distribution of publications by quartiles confirms the improvement in the quality of the scientific production of our researchers. Almost 70% of all articles were published in journals ranked at Q1, and, remarkably, 28% of them were published in journals classified in the first decil.

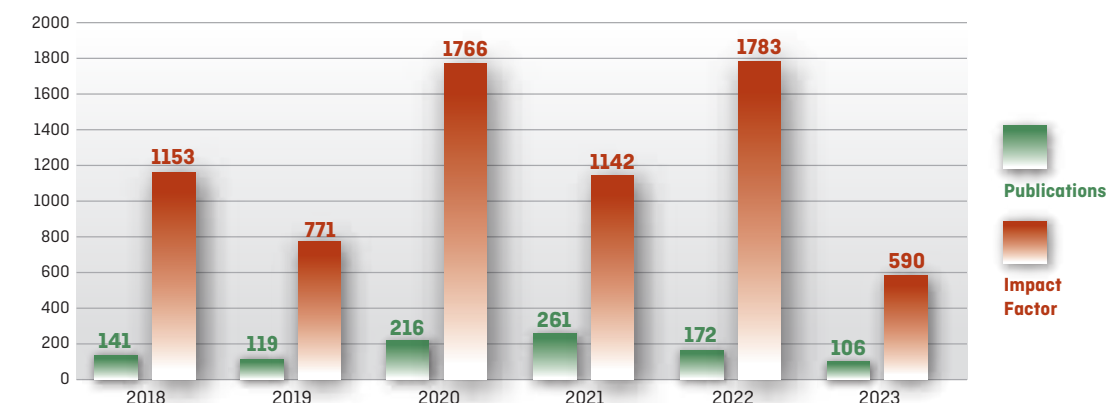
Mean impact factor per article and year. Historical evolution from 2012 to 2023



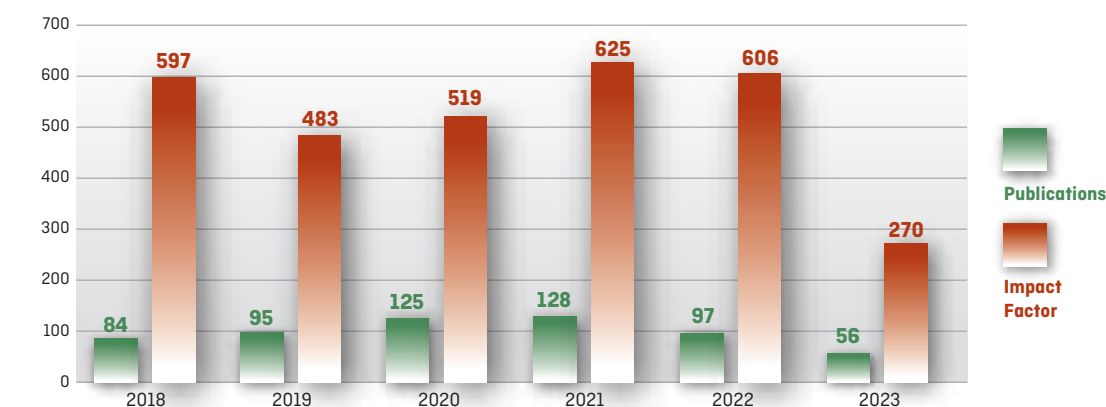
The analysis of scientific production by areas reveals that areas 1 and 2 have been those in which the number of publications has clearly decreased. Area 3 maintained the number of publications and the cumulative impact factor compared to 2022. The average impact factor per area was slightly higher than in year 2021 in areas 1 and 3, but lower than in 2022 by the reasons mentioned above.

Below is the historical evolution of the number of publications and the cumulative impact factor for each of the areas of the Institute:

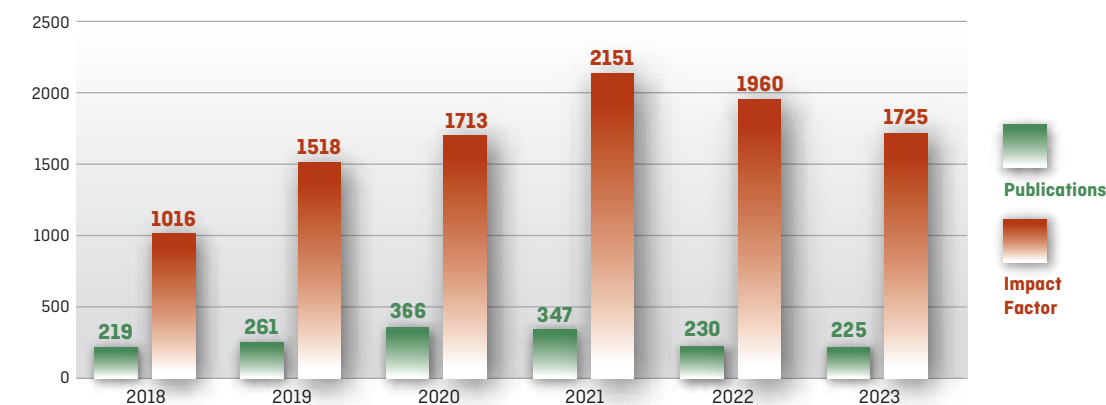
Area 1 Cellular and molecular etiopathogenic mechanisms in inflammatory and autoimmune diseases



Area 2 Translational neuroscience



Area 3 Advanced therapies and individualized medicine



SCIENTIFIC PRODUCTION

A detailed list of the journals in which IIS articles have been published is shown below. The journals are sorted from highest to lowest by the number of publications and includes the journal quartile and its impact factor.

JOURNAL	NUMBER OF PUBLICATIONS	IMPACT FACTOR	CUMULATIVE IF
NEW ENGLAND JOURNAL OF MEDICINE	1	158,5	158,5
LANCET RESPIRATORY MEDICINE	1	76,2	76,2
LANCET ONCOLOGY	1	51,1	51,1
JOURNAL OF CLINICAL ONCOLOGY	2	45,3	90,6
EUROPEAN HEART JOURNAL	6	39,3	235,8
INTENSIVE CARE MEDICINE	1	38,9	38,9
LANCET GASTROENTEROLOGY & HEPATOLOGY	1	35,7	35,7
NATURE GENETICS	1	30,8	30,8
JAMA NEUROLOGY	1	29	29
JAMA ONCOLOGY	2	28,4	56,8
ANNALS OF THE RHEUMATIC DISEASES	1	27,4	27,4
LANCET HAEMATOLOGY	2	24,7	49,4
GUT	1	24,5	24,5
EUROPEAN RESPIRATORY JOURNAL	5	24,3	121,5
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY	2	24	48
EUROPEAN UROLOGY	1	23,4	23,4
NATURE COMMUNICATIONS	1	16,6	16,6
JOURNAL OF EXTRACELLULAR VESICLES	1	16	16
INTERNATIONAL JOURNAL OF SURGERY	1	15,3	15,3
ECLINICALMEDICINE	2	15,1	30,2
CELL REPORTS MEDICINE	1	14,3	14,3
CLINICAL MICROBIOLOGY AND INFECTION	3	14,2	42,6
AUTOIMMUNITY REVIEWS	1	13,6	13,6
HEPATOLOGY	1	13,5	13,5
MEDICINAL RESEARCH REVIEWS	1	13,3	13,3
JOURNAL OF AUTOIMMUNITY	1	12,8	12,8
JOURNAL OF MEDICAL VIROLOGY	1	12,7	12,7
ALLERGY	1	12,4	12,4
DRUGS	1	11,5	11,5
EMBO JOURNAL	1	11,4	11,4
LEUKEMIA	1	11,4	11,4
JACC-CARDIOVASCULAR INTERVENTIONS	2	11,3	22,6
BIOMARKER RESEARCH	1	11,1	11,1
PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	1	11,1	11,1
JOURNAL FOR IMMUNOTHERAPY OF CANCER	1	10,9	10,9
AMERICAN JOURNAL OF GASTROENTEROLOGY	2	9,8	19,6
SCIENCE OF THE TOTAL ENVIRONMENT	1	9,8	9,8
JOURNAL OF CLINICAL MICROBIOLOGY	2	9,4	18,8

JOURNAL	NUMBER OF PUBLICATIONS	IMPACT FACTOR	CUMULATIVE IF
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY	4	9,2	36,8
SPANISH JOURNAL OF PSYCHIATRY AND MENTAL HEALTH	1	5,2	5,2
JOURNAL OF CLINICAL IMMUNOLOGY	1	9,1	9,1
CLINICAL IMMUNOLOGY	1	8,6	8,6
EUROPEAN JOURNAL OF CANCER	3	8,4	25,2
EUROPEAN UROLOGY ONCOLOGY	1	8,2	8,2
JOURNAL OF CROHNS & COLITIS	9	8	72
ARCHIVOS DE BRONCONEUMOLOGIA	3	8	24
CELLULAR AND MOLECULAR LIFE SCIENCES	1	8	8
EUROPEAN JOURNAL OF INTERNAL MEDICINE	1	8	8
WORLD JOURNAL OF EMERGENCY SURGERY	1	8	8
VACCINES	1	7,8	7,8
EMBO REPORTS	1	7,7	7,7
ALIMENTARY PHARMACOLOGY & THERAPEUTICS	3	7,6	22,8
BIOMEDICINE & PHARMACOTHERAPY	3	7,5	22,5
FREE RADICAL BIOLOGY AND MEDICINE	1	7,4	7,4
JOURNAL OF HEADACHE AND PAIN	1	7,4	7,4
FRONTIERS IN IMMUNOLOGY	7	7,3	51,1
JOURNAL OF PATHOLOGY	1	7,3	7,3
JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY	5	7,2	36
ANTIOXIDANTS	3	7	21
OSTEOARTHRITIS AND CARTILAGE	1	7	7
BIODRUGS	1	6,8	6,8
TRANSLATIONAL PSYCHIATRY	1	6,8	6,8
CLINICAL PHARMACOLOGY & THERAPEUTICS	1	6,7	6,7
JOURNAL OF INFECTION AND PUBLIC HEALTH	1	6,7	6,7
JOURNAL OF AFFECTIVE DISORDERS	2	6,6	13,2
HEMASPHERE	1	6,6	6,6
AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY	1	6,4	6,4
CLINICAL NUTRITION	1	6,3	6,3
JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM	1	6,3	6,3
EUROINTERVENTION	4	6,2	24,8
EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING	3	6,2	18,6
NEPHROLOGY DIALYSIS TRANSPLANTATION	2	6,1	12,2
CHINESE MEDICAL JOURNAL	1	6,1	6,1
REVISTA ESPANOLA DE CARDIOLOGIA	3	5,9	17,7
NUTRIENTS	1	5,9	5,9
ISCIENCE	1	5,8	5,8
FRONTIERS IN CELLULAR AND INFECTION MICROBIOLOGY	1	5,7	5,7
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	9	5,6	50,4
CIRCULATION-CARDIOVASCULAR INTERVENTIONS	1	5,6	5,6
FRONTIERS IN PHARMACOLOGY	1	5,6	5,6

JOURNAL	NUMBER OF PUBLICATIONS	IMPACT FACTOR	CUMULATIVE IF
PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY	1	5,6	5,6
EMERGENCIAS	5	5,5	27,5
RHEUMATOLOGY	3	5,5	16,5
CONTACT DERMATITIS	1	5,5	5,5
EUROPEAN JOURNAL OF CLINICAL INVESTIGATION	1	5,5	5,5
FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY	1	5,5	5,5
PHARMACEUTICS	3	5,4	16,2
JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION	2	5,4	10,8
BJPSYCH OPEN	1	5,4	5,4
JOURNAL OF THE AMERICAN HEART ASSOCIATION	1	5,4	5,4
CURRENT NEUROPHARMACOLOGY	1	5,3	5,3
CANCERS	6	5,2	31,2
JOURNAL OF PARKINSONS DISEASE	3	5,2	15,6
DERMATITIS	1	5,2	5,2
FRONTIERS IN ENDOCRINOLOGY	1	5,2	5,2
JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY	1	5,2	5,2
MOLECULAR NEUROBIOLOGY	1	5,1	5,1
SEMINARS IN ARTHRITIS AND RHEUMATISM	4	5	20
FRONTIERS IN NUTRITION	3	5	15
NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY	1	5	5
INFLAMMATORY BOWEL DISEASES	2	4,9	9,8
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY	1	4,9	4,9
CEPHALALGIA	1	4,9	4,9
BONE MARROW TRANSPLANTATION	7	4,8	33,6
AMERICAN HEART JOURNAL	1	4,8	4,8
ANTIBIOTICS-BASEL	1	4,8	4,8
IRBM	1	4,8	4,8
SLEEP MEDICINE	1	4,8	4,8
BIOMEDICINES	5	4,7	23,5
VIRUSES-BASEL	2	4,7	9,4
FRONTIERS IN PSYCHIATRY	1	4,7	4,7
JOURNAL OF EPIDEMIOLOGY	1	4,7	4,7
CLINICAL KIDNEY JOURNAL	4	4,6	18,4
ERJ OPEN RESEARCH	1	4,6	4,6
EXPERT OPINION ON BIOLOGICAL THERAPY	1	4,6	4,6
MOLECULES	1	4,6	4,6
SCIENTIFIC REPORTS	1	4,6	4,6
DIGESTIVE AND LIVER DISEASE	2	4,5	9
BMC PUBLIC HEALTH	1	4,5	4,5
HUMAN RESOURCES FOR HEALTH	1	4,5	4,5
BMC PSYCHIATRY	1	4,4	4,4
EXPERT REVIEW OF CLINICAL IMMUNOLOGY	1	4,4	4,4
EXPERT REVIEW OF CLINICAL PHARMACOLOGY	1	4,4	4,4

JOURNAL	NUMBER OF PUBLICATIONS	IMPACT FACTOR	CUMULATIVE IF
PANMINERVA MEDICA	1	4,3	4,3
RESPIRATORY MEDICINE	1	4,3	4,3
JOINT BONE SPINE	1	4,2	4,2
BMJ OPEN RESPIRATORY RESEARCH	3	4,1	12,3
BONE	1	4,1	4,1
EUROPEAN HEART JOURNAL-ACUTE CARDIOVASCULAR CARE	1	4,1	4,1
NEUROENDOCRINOLOGY	1	4,1	4,1
CANCER MEDICINE	1	4	4
INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY	1	4	4
JOURNAL OF PAIN	1	4	4
JOURNAL OF CLINICAL MEDICINE	8	3,9	31,2
MEDICINA CLINICA	2	3,9	7,8
CTS-CLINICAL AND TRANSLATIONAL SCIENCE	1	3,9	3,9
EXPERT REVIEW OF RESPIRATORY MEDICINE	1	3,9	3,9
FRONTIERS IN MEDICINE	1	3,9	3,9
NEUROLOGIA	1	3,9	3,9
ADVANCES IN THERAPY	2	3,8	7,6
CLINICAL AND EXPERIMENTAL RHEUMATOLOGY	7	3,7	25,9
ENDOCRINE	2	3,7	7,4
KIDNEY DISEASES	1	3,7	3,7
MICROBIOLOGY SPECTRUM	1	3,7	3,7
PLOS ONE	1	3,7	3,7
FRONTIERS IN CARDIOVASCULAR MEDICINE	3	3,6	10,8
ACTA DERMATO-VENEREOLOGICA	1	3,6	3,6
AMERICAN JOURNAL OF EMERGENCY MEDICINE	1	3,6	3,6
EUROPEAN JOURNAL OF PEDIATRICS	1	3,6	3,6
JOURNAL OF PERSONALIZED MEDICINE	4	3,508	14,032
INTERNATIONAL JOURNAL OF CARDIOLOGY	3	3,5	10,5
CLINICAL & TRANSLATIONAL ONCOLOGY	2	3,4	6,8
DERMATOLOGY AND THERAPY	2	3,4	6,8
FRONTIERS IN NEUROLOGY	2	3,4	6,8
BRAIN SCIENCES	1	3,3	3,3
CURRENT OPINION IN PULMONARY MEDICINE	1	3,3	3,3
HEMATOLOGICAL ONCOLOGY	1	3,3	3,3
JOURNAL OF RENAL NUTRITION	1	3,2	3,2
PARKINSONS DISEASE	1	3,2	3,2
BRAIN AND BEHAVIOR	1	3,1	3,1
CLINICAL AND TRANSLATIONAL RADIATION ONCOLOGY	1	3,1	3,1
EUROPEAN JOURNAL OF HAEMATOLOGY	1	3,1	3,1
JOURNAL OF CLINICAL NEUROLOGY	1	3,1	3,1
THROMBOSIS JOURNAL	1	3,1	3,1
NEFROLOGIA	4	3,084	12,336
MEDICINA INTENSIVA	1	3	3

JOURNAL	NUMBER OF PUBLICATIONS	IMPACT FACTOR	CUMULATIVE IF
REVISTA CLINICA ESPANOLA	2	2,9	5,8
BMJ OPEN	1	2,9	2,9
ENDOCRINE CONNECTIONS	1	2,9	2,9
AMERICAN JOURNAL OF CARDIOLOGY	1	2,8	2,8
ALLERGY ASTHMA AND CLINICAL IMMUNOLOGY	1	2,7	2,7
DISASTER MEDICINE AND PUBLIC HEALTH PREPAREDNESS	1	2,7	2,7
REVIEWS IN CARDIOVASCULAR MEDICINE	1	2,7	2,7
CURRENT ONCOLOGY	1	2,6	2,6
PAIN PRACTICE	1	2,6	2,6
UPDATES IN SURGERY	1	2,6	2,6
WORLD JOURNAL OF SURGERY	1	2,6	2,6
NEUROSCIENCE LETTERS	1	2,5	2,5
RESP CARE	1	2,5	2,5
CARDIOVASCULAR DIAGNOSIS AND THERAPY	2	2,4	4,8
DERMATOLOGIC SURGERY	1	2,4	2,4
JOURNAL OF APPLIED RESEARCH IN INTELLECTUAL DISABILITIES	1	2,4	2,4
JOURNAL OF NEUROIMAGING	1	2,4	2,4
PREHOSPITAL EMERGENCY CARE	1	2,4	2,4
CURRENT MEDICAL RESEARCH AND OPINION	1	2,3	2,3
BMC CARDIOVASCULAR DISORDERS	1	2,1	2,1
INTERNATIONAL JOURNAL OF CARDIOVASCULAR IMAGING	1	2,1	2,1
REVISTA ESPANOLA DE ENFERMEDADES DIGESTIVAS	4	2	8
AUSTRALASIAN JOURNAL OF DERMATOLOGY	1	2	2
GASTROENTEROLOGIA Y HEPATOLOGIA	2	1,9	3,8
REVISTA ESPANOLA DE QUIMIOTERAPIA	2	1,9	3,8
BMC SPORTS SCIENCE MEDICINE AND REHABILITATION	1	1,9	1,9
CARDIOLOGY	1	1,9	1,9
CIRUGIA ESPANOLA	1	1,9	1,9
ENDOCRINOLOGIA DIABETES Y NUTRICION	1	1,9	1,9
JOURNAL OF NEUROSURGICAL SCIENCES	1	1,9	1,9
CORONARY ARTERY DISEASE	2	1,8	3,6
JOURNAL OF INTEGRATIVE NEUROSCIENCE	2	1,8	3,6
FRONTIERS IN SURGERY	1	1,8	1,8
INTERNATIONAL UROGYNECOLOGY JOURNAL	1	1,8	1,8
JOURNAL OF CUTANEOUS PATHOLOGY	2	1,7	3,4
NEUROREPORT	1	1,7	1,7
JOURNAL OF CARDIAC SURGERY	1	1,6	1,6
MEDICINE	1	1,6	1,6
HEART AND VESSELS	1	1,5	1,5
CYTOPATHOLOGY	4	1,3	5,2
REVISTA DE NEUROLOGIA	3	1,2	3,6
AMERICAN JOURNAL OF DERMATOPATHOLOGY	1	1,1	1,1

PATENTS

Innovation improves the quality of life of the citizens, through the improvement of the healthcare and it is used for the launching of new products and services. In this sense, IIS Princesa is actively committed to Innovation and the transfer of innovative advances to industry. As a sign of this commitment, researchers at our center, in collaboration with other institutions, have developed the patents shown below..

NATIONAL PATENT APPLICATIONS

Title: Dispositivo de implante para tratamiento de patologías mediante campos eléctricos.

Number: P202331078.

Date of application: 22/12/2023.

Owners: Universidad Politécnica de Madrid (60.0%), Fundación de Investigación Hospital Universitario de La Princesa (40%).

Inventors: Miguel Jiménez Carrizosa, Ricardo Gil Simoes, María Regina Ramos Hortal.

Title: Dispositivo de inmovilización personalizada para radioterapia.

Number: P202330774.

Date of application: 14/09/2023.

Owners: Fundación de Investigación Hospital Universitario de La Princesa (55%), Asociación “HullProject” (45%).

Inventors: Miguel Ángel Muñoz Torrijos, Carlos Izquierdo Rodríguez, David Hernández González, Pablo Castro Tejero.

COMPETITIVE PROJECTS

Grants

FUNDING INSTITUTION	CALL	CALLS GRANTED
Instituto de Salud Carlos III	Proyectos de I+D+I en Salud (PI)	3
	Proyectos de investigación de medicina personalizada de precisión (IMPACT)	2
Agencia Estatal de Investigación	Proyectos Líneas Estratégicas (PLEC)	1
EU4Health	Proyectos de Investigación	2
Fundación Caixa Impulse	Proyecto de Investigación	1
Fundación Eugenio Rodríguez Pacual	Programa de investigación	1
Fundación Alfonso X el Sabio	Proyecto de investigación	1
Fundación Lovexair	Beca “Respirar es Vida”. Proyecto de investigación	1

Research staff fully or partially funded through competitive calls in 2023

FUNDING INSTITUTION	CALL	CALLS GRANTED
Agencia Estatal de Investigacion	Contratos predoctorales para la formación de doctores	1
	Contratos predoctorales de formación en investigación en salud (PFIS)	3
Instituto de Salud Carlos III	Ayudas Sara Borrell	2
	Juan Rodés	2
	Río Hortega	1
	Contratos para la intensificación de la actividad investigadora en el SNS	1

DEFENDED DOCTORAL THESES

The thesis represents a systematic and exhaustive research work on a subject, which is considered a crucial step in the training of new generations of researchers. During 2023, a total of 21 theses have been defended by member of the IIS. Four of them was a European thesis.

THESES

Doctoral Candidate	Title	Director/s	Defense date
Muñoz Aceituno, Ester	Búsqueda de biomarcadores farmacogenéticos para el uso de fármacos biológicos en la psoriasis moderada a grave	Daudén Tello, Estevan / Ovejero Benito, María Carmen	04/10/2023
Bazire Batiz, Raphaëlle	Seguimiento de la inmunoterapia sublingual con alérgenos mediante herramientas ómicas	Blanco Guerra, Carlos / Villaseñor Solis, Alma	17/07/2023
Ortiz del Castillo, Belén	The role of GRK2 in orienting cell division and cell cycle decision-making to proliferation	Penela Márquez, Petronila	09/03/2023
González Martínez, Alicia	Clinical neuroimaging and serum biomarkers to predict disease course and treatment response in neurological diseases	Sánchez Madrid, Francisco / Vivancos Mora, José Aurelio	15/02/2023
De Toledo Heras, María	Variabilidad farmacocinética de los nuevos fármacos anticrisis levetiracetam y eslicarbazepina en una unidad de cirugía de la epilepsia	Sobrado, Mónica / Ovejero, Carmen / Lagares, Alfonso	12/04/2023
Aguirre, Clara	Topografía de la isquemia en TC multimodal como posible factor predictor de evolución en pacientes con ictus isquémico agudo de circulación anterior tratados mediante trombectomía mecánica	Vivancos Mora, José Aurelio / Ximénez-Carrillo Rico, Álvaro	18/10/2023
Marinero Martínez-Lázaro	Prevalencia y Gravedad de la Enfermedad Hepática Crónica en los Pacientes con Fibrosis Quística en edad adulta en un Hospital terciario	García Buey, Luisa / Girón Moreno, Rosa María	26/05/2023
Muñoz Callejas, Antonio	Estudio de la interacción del eje PSGL-1/ selectina P en la regulación de la muerte celular de los neutrófilos y monocitos en los pacientes con lupus eritematoso sistémico	Urzainqui Mayayo, Ana / Castañeda Sanz, Santos	09/10/2023
Guberna Blanco, Laura	Frecuencia y efectividad de la intensificación del tratamiento anti-TNF en la enfermedad inflamatoria intestinal: revisión sistemática y metaanálisis	Pérez Gisbert, Francisco Javier / Nyssen Pérez, Olga	13/03/2023
García Donday, María	Seguridad de los tratamientos para la enfermedad inflamatoria intestinal durante el embarazo (Registro DUMBO)	Pérez Gisbert, Francisco Javier / Chaparro Sánchez, María	18/12/2023
García Prieto, Teresa	Las isoformas de Akt y TLR5 en la función de la barrera intestinal y la enfermedad inflamatoria intestinal	Fresno Esvudero, Manuel	10/06/2023
Triguero Martínez, Ana	El papel de la Galectina 1 en la patogenia de las Enfermedades Inflamatorias Mediadas por Mecanismos Inmunes y su posible función como biomarcador	González Álvaro, Isidoro / Lamana Dominguez, Amalia	10/03/2023
García Castillo, Elena	Cambios en la tendencia en la prevalencia en la Enfermedad Pulmonar Obstructiva Crónica en España en 1997, 2007 y 2017.	Ancochea Bermúdez, Julio / Soriano, Joan B	27/06/2023

Doctoral Candidate	Title	Director/s	Defense date
Alonso Pérez, Tamara	Características diferenciales de la Enfermedad Pulmonar Obstructiva Crónica en la mujer.	Ancochea Bermúdez, Julio / Soriano, Joan B	18/09/2023
Martínez Vergara, Adrián	Impacto de la pandemia por el virus SARS-CoV-2 sobre el número y gravedad de agudizaciones en pacientes con bronquiectasias no debidas a fibrosis quística.	Girón Moreno, Rosa / Martínez Gracia, Miguel Ángel	23/06/2023
García Prieto, Teresa	Las isoformas de Akt y TLR5 en la función de la barrera intestinal y la enfermedad inflamatoria intestinal.	Fresno Escudero, Manuel	10/06/2023
Torres Gérica, Patricia	Role of galectin-1 in adipose tissue development and adipocyte metabolism.	Fresno Escudero, Manuel	22/09/2023

EUROPEAN THESES

Doctoral Candidate	Title	Director/s	Defense date
Albitre Sanz, Ángela	Redes señalizadoras de GRK2 en el desarrollo de la glándula mamaria y el cáncer de mama	Penela Márquez, Petronila / Mayor Menéndez, Federico	12/15/2023
Del Sastre López, Eric	ND523, a novel NRF2 inducer through KEAP1 inhibition, for the treatment of Alzheimer's and age-related diseases	García López, Manuela	15/12/2023
Mayo Mariscal de Gante, Paloma	Diseño, síntesis y evaluación farmacológica de nuevos fármacos multidiana inhibidores de GSK3β e inductores de Nrf2 para el tratamiento de la enfermedad del Alzheimer	García López, Manuela / León Martínez, Rafael	05/05/2023
Torres Gérica, Patricia	Role of galectin-1 in adipose tissue development and adipocyte metabolism	Fresno Escudero, Manuel	22/09/2023

CLINICAL TRIALS

Clinical Trials represent an indication of being at the forefront of R+D in the health sector. They provide a benefit to society based on the most innovative treatments and the most advanced techniques, with special aim of improving the health and well-being of citizens. During 2023, 118 new agreements have been signed for clinical trials led by IIS members.

Gullón Ojesto, Alejandra. **“Evaluación de la seguridad de Edoxabán en pacientes ancianos con criterios de fragilidad.”** Antonio Domingo Pose Reino. EDO-FRAG-001.

Romero Laorden, Nuria. **“Estudio observacional del tratamiento con inhibidores de PARP en pacientes con cáncer de ovario avanzado y/o metastásico dentro de práctica clínica habitual.”** Rodrigo Sánchez-Bayona.

Loscertales Pueyo, Javier. **“Un ensayo abierto de fase Ia/b de escalada de dosis seguido de expansión de la dosis sobre la seguridad y tolerabilidad de CAP-100, un anticuerpo humanizado contra el receptor 7 de la quimiocina C-C, administrado como monoterapia en sujetos con leucemia linfocítica crónica r/r.”** Catapult. CAP-100-1.

de la Cámara de Llanza, Javier. **“Análisis retrospectivo del uso en la práctica real de cefiderocol para el tratamiento de infecciones por gramnegativos como parte del programa de acceso precoz (estudio PERSEUS).”** Shionogi S.L.U. 2020-266-4.

Llamas Velasco, Mar. **“Estudio obsrevacional retrospectivo para evaluar los datos en entorno real sobre el uso de mogamulizumab en España y Portugal para el tratmiento de Micosis Fungoide(MF) y Síndrome de Sézary (SS) (MIBERIC).”** Kyowa Kirin Pharmaceuticals. MIBERIC.

Pérez Gisbert, Javier. **“Ensayo de fase IIa, aleatorizado, doble ciego y comparado con placebo para evaluar la**

seguridad, la eficacia, la farmacocinética y la farmacodinámica de BI 706321 administrado por vía oral durante 12 semanas en pacientes con enfermedad de Crohn (EC) que reciben tratamiento de inducción con ustekinumab.” Boehringer Ingelheim International GmbH . 1425-0003 .

Ochoa Mazarro, Dolores. “Estudio de cohortes no aleatorizado, abierto e internacional para describir la seguridad de las participantes que recibieron o la vacuna para inmunización materna RSVPreF3 (cualquier dosis) o el placebo (grupo control) en los estudios RSV MAT anteriores (RSV MAT-001, RSV MAT-004, RSV MAT-010, RSV MAT-011, RSV MAT-009, RSV MAT-012 y RSV MAT-039), durante cualquier embarazo posterior a la vacunación con la vacuna RSVPreF3 o el placebo.” GlaxoSmithKline Biologicals S.A.. 219510 [RSV-MAT015].

Loscertales Pueyo, Javier. “Estudio MACRO. Estudio retrospectivo observacional del tratamiento de la Macroglobulinemia de Waldenström con Ibrutinib en la práctica clínica habitual en España.” Janssen. 54179060WAL4004.

Ochoa Mazarro, Dolores. “ENSAYO CLÍNICO ALEATORIZADO DE BIOEQUIVALENCIA DE SACUBITRIL/VALSARTAN 97 MG/103 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN AYUNAS CON DISEÑO CRUZADO REPLICADO.” Laboratorios Normon. N-SACVAL-22-275.

de Argila Fernández-Durán, Diego . “Estudio de fase III, multicéntrico y abierto: monitorización ambulatoria de la presión arterial en pacientes adultos con urticaria crónica espontánea inadecuadamente controlada con antihistamínicos H1 y tratados con remibrutinib hasta 12 semanas.” NOVARTIS FARMACÉUTICA S.A . CLOU064A2305.

Alegre Amor, Adrián. “ESTUDIO EN FASE III, ABIERTO, DE 2 GRUPOS, MULTICÉNTRICO Y ALEATORIZADO PARA EVALUAR LA EFICACIA Y LA SEGURIDAD DE ELRANATAMAB (PF-06863135) + DARATUMUMAB + LENALIDOMIDA EN COMPARACIÓN CON DARATUMUMAB + LENALIDOMIDA + DEXAMETASONA EN PARTICIPANTES CON MIELOMA MÚLTIPLE DE DIAGNÓSTICO RECIENTE NO APTOS PARA TRASPLANTE.” Pfizer Inc. C1071006.

Keough Delgado, Elena. “Preservación del volumen pulmonar durante la extubación. Ensayo clínico multicéntrico prospectivo, controlado y aleatorizado.” Dr. Carlos Subirà. NCT055260053.

Trillo Senin, Santiago. “Continuación del tratamiento anticoagulante en la fase aguda del infarto cerebral cardioembólico.” FIB HOSPITAL LA PAZ. RRBAP-2020-01.

Trillo Senin, Santiago. “Ensayo fase III multicéntrico, internacional, aleatorizado, controlado con placebo, doble ciego, de grupos paralelos y determinado por

eventos, del inhibidor oral del FXIa -Asundexian (BAY 2433334), para la prevención de ictus isquémicos en pacientes de ambos sexos mayores de edad, tras un ictus isquémico no cardioembólico agudo o AIT de alto riesgo.” Bayer. BAY 2433334/20604.

Alegre Amor, Adrián. “Primer estudio Fase 1 en seres humanos de aumento escalonado de la dosis de ampliación del BMF-219, un inhibidor oral covalente de la menina, en pacientes adultos con leucemia aguda (LA), linfoma difuso de células B grandes (LBDCG), mieloma múltiple (MM) y leucemia linfocítica crónica (LLC)/linfoma linfocítico pequeño (LLP).” Biomea Fusion Inc.. COVALENT-101.

Rivero Crespo, Fernando. “Tratamiento de placas vulnerables funcionalmente no significativas en pacientes con infarto de miocardio con elevación del ST y enfermedad multivascular. (Estudio VULNERABLE).” Fundación Epic. EPIC28.

Ramírez Herraiz, Esther. “ADHERENCE: Estudio observacional para evaluar la adherencia a TREMFYA® (guselkumab) en la práctica clínica en pacientes con psoriasis moderada a grave.” Janssen. CNT01959PS04024.

Ciudad Sañudo, Marianela. “Estudio de fase 3, multicéntrico, prospectivo, aleatorizado, con enmascaramiento doble, en el que se comparan dos tratamientos para la candidemia y/o la candidiasis invasiva: una equinocandina por vía intravenosa, seguida de ibrexafungerp por vía oral, frente al tratamiento con una equinocandina por vía intravenosa, seguida de fluconazol por vía oral (MARIO).” SCYNEXIS. SCY-078-302.

García de Vicuña, Rosario. “Estudio observacional multicéntrico sobre la eficacia (en la afectación axial) y seguridad del tratamiento con ustekinumab, guselkumab y risankizumab en pacientes con artritis psoriásica axial y/o mixta en práctica clínica habitual en España: APXIS 12-23.” RAQUEL ALMODÓVAR. APXIS12-23.

Rubín de Célix Vargas, Cristina. “Infección por Clostridioides difficile en pacientes con Enfermedad Inflamatoria Intestinal bajo tratamiento con Vedolizumab y en tratamiento con anti-TNF: riesgo comparado y evolución de la enfermedad.” CONSORCI MAR PARC DE SALUT.

Alfonso Manterola, Fernando. “Estrategia intervencionista para las lesiones no culpables con criterios de vulnerabilidad mayores identificados mediante tomografía de coherencia óptica en pacientes con síndrome coronario agudo.” Fondazione Centro Lotta contro Infarto. INTERCLIMA.

Pérez Abanades, María. “Análisis de utilización de células madre mesenquimales para el tratamiento de complicaciones post-alotrasplante de progenitores hematopéyicos en hospitales españoles.” Sociedad Española de Farmacia Hospitalaria. FEF-MS-2022-01.

Lopez Manzanares, Lydia. “Estudio de fase IIb, multi-

céntrico, aleatorizado, doble ciego y controlado con placebo para determinar la eficacia y la seguridad de BIIB122 en participantes con enfermedad de Parkinson.” Biogen. 283PD201.

Llamas Velasco, Mar. “Estudio de fase 3 aleatorizado, controlado con placebo y doble ciego de 24 semanas de duración para evaluar la eficacia, seguridad y tolerabilidad de rocatinlimab (AMG 451) en monoterapia en sujetos adultos con dermatitis atópica (DA) de moderada a grave (ROCKET-Ignite).” Amgen Inc.. 20210142.

Ochoa Mazarro, Dolores. “ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE APIXABAN 5 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN AYUNAS.” Laboratorios Normon. N-API-23-276.

Ramos García, Tania. “Estudio observacional prospectivo para evaluar la seguridad de “Modigoid®” y “Modigoid Plus®” en pacientes mono o polialérgicos con rinitis/rinoconjuntivitis alérgica, con o sin asma asociada.” ROXALL Medicina España S.A. ROX-ALTCUPA1-2022.

García Fraile, Lucio. “Estudio Fase I/II, observador ciego, aleatorizado, controlado con placebo y multinacional para evaluar la seguridad y eficacia de la vacuna en investigación de GSK frente a Neisseria gonorrhoeae GMMa (NgG) cuando se administra en adultos sanos de 18 a 50 años de edad.” GlaxoSmithKline Biologicals SA. 216156.

Arranz Canales, Elena. “Memoria para el estudio de esplenomegalia y pacientes esplenectomizados no filiados en población adulta.” Fundación Española de Hematología y Hemoterapia”. PREDIGA2.

Vieira Campos, Alba. “Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo, de prevención de las recaídas, para evaluar la seguridad y la eficacia de KarXT para el tratamiento de la psicosis asociada a la demencia de Alzheimer.” Karuna Therapeutics Inc. KAR-031.

Suárez Fernández, Carmen. “Ensayo fase III multicéntrico, internacional, aleatorizado, controlado con un comparador activo, doble ciego, con doble simulación y 2 grupos paralelos, para comparar la eficacia y la seguridad del inhibidor oral de FXIa asundexian (BAY 2433334) con apixaban para la prevención del ictus o embolia sistémica en participantes masculinos y femeninos de 18 años o más con fibrilación auricular y riesgo de ictus.” Bayer. BAY 2433334/19767.

López Manzanares, Lydia. “Estudio adaptativo en fase II con doble enmascaramiento, aleatorizado, controlado con placebo y multicéntrico para evaluar la seguridad, tolerabilidad, inmunogenicidad y los efectos farmacodinámicos de ACI-7104.056 en pacientes en

fases incipientes de la enfermedad de Parkinson.” AC Immune S.A . ACI-7104-PD-2103.

Aguado Bueno, Beatriz. “Análisis retrospectivo del uso en la práctica real de cefiderocol para el tratamiento de infecciones por gramnegativos como parte del programa de acceso precoz (estudio PERSEUS).” Shionogi S.L.U. 2020-266-4.

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Communication and Dissemination

The concept of communicating science in journals or scientific congresses is deeply rooted in the field of scientific research, but scientists are becoming increasingly more aware of the need to disseminate science among citizens, which partly finance research with their taxes.

Communication of biomedical research allows the population to know and understand biomedical advances with application or possible application in human health, making the citizen more knowledgeable about the diseases that affect society.

The IIS Princesa uses two main tools to carry out this task: the web (www.iis-princesa.org) and the newsletter “Impact Factor”. The Institute website www.iis-princesa.org, renewed in 2016 to adapt to the new trends of users, presents the most important news about its members, as well as information about courses, congresses, job offers or detailed information of research groups. In addition, the website offers other services, such as the research calls alert service, which provides up to date information to subscribers about public and private, national or international calls.

The Impact Factor newsletter, published by the IIS Princesa since 2011, both in paper and electronic formats, shows the most outstanding scientific advances, the most relevant news and the successes of our researchers.

These activities are reinforced with the active participation of the IIS Princesa in the Science Week of the Community of Madrid which offers entertaining, interesting and important talks about the latest scientific research, in a format accessible to the public.

COURSES

TITLE	DATE		SPEAKER
Curso SVCA/ACLS de la AHA	7/02/2023	9/02/2023	Dr. Mariano Aguilar Mulet
Curso SVCA/ACLS de la AHA	7/03/2023	9/03/2023	Dr. Mariano Aguilar Mulet
Curso Soporte Vital Avanzado ERC SEDAR	10/03/2023	11/03/2023	Dr. Mariano Aguilar Mulet
Centro de Competencias en Ecografía Clínica para Atención Primaria	23/03/2024	24/03/2024	Dr. Andrés von Wernitz Teleki
Análisis estadístico en investigación biomédica con Stata 14.0. Nivel básico.	27/03/2023	27/04/2023	Dr. Isidoro González Álvaro
Curso de ecografía	16/05/2023	17/05/2023	Dr. Mariano Aguilar Mulet
Centro de Competencias en Ecografía Clínica para Medicina de Familia	23/05/2023	23/05/2023	Dr. Andrés von Wernitz Teleki
Curso R1 protección radiológica básica para residentes	30/05/2023	30/05/2023	Dña. Paula García Castañón
Curso de Análisis Estadístico en Investigación Biomédica con "R" Nivel Básico	23/05/2023	06/06/2023	Dña. Nuria Montes Casado
	30/05/2023	13/06/2023	
		20/06/2023	
		27/06/2023	
		28/06/2023	
Curso de Cefaleas para residentes	29/09/2023	30/09/2023	Dra. A. González Martínez

TITLE	DATE		SPEAKER
CURSO DE PROVEEDOR DE SOPORTE CARDIOVASCULAR AVANZADO (SVCA/ACLS) DE LA AHA	3/10/2023	5/10/2023	Dr. Mariano Aguilar Mulet
Competencias en Ecografía Clínica para Atención Primaria: Edición VIII	09/10/2023	n.d.	Juan Mariano Aguilar Mulet Fernando Alfageme Jiménez José Ignacio Alonso González Sonia González Del Val Iñigo Guerra Molina Ana María Martínez Molina Jorge Sorando Ortín Javier Val De Santos Andres Von Wernitz Teleki
Simulación en el manejo de la vía aérea 7ª Ed (2023)	10/10/2023	27/11/2023	Noemí Díaz Velasco Jesús Manuel Nieves Alonso Diana Parrado Fernando Ramasco Rueda Elena Rojo Rodríguez Sheila Santidrián
Código Sepsis Princesa (EDICIÓN 09)	17/10/2023	02/12/2023	Marta Chicot Llano Natalia Pascual Gómez Alberto Pizarro Portillo
Centro de Competencias en Ecografía Clínica para Atención Primaria	19/10/2023	20/10/2023	Dr. Andrés von Wernitz Teleki
Curso Soporte Vital Avanzado	21/10/2023	21/10/2023	Dr. Fernando Ramasco Rueda
Curso de Análisis Estadístico en Investigación Biomédica con "R" Nivel Avanzado	19/10/2023 26/10/2023 31/10/2023	23/11/2023	Dña. Nuria Montes Casado
XX CURSO DE FORMACIÓN MIR DE HEMATOLOGÍA	22/11/2023	22/11/2023	Dr. Adrián Alegre Amor
Curso Ecografía	23/11/2023	23/11/2023	Dr. Andrés von Wernitz Teleki



WORKSHOPS

DATE	TITLE	SPEAKER
17 ene	Taller para pacientes Embarazo y lactancia en esclerosis múltiple	Dra. Clara Aguirre Hernández
21 mar	Reciente diagnóstico de esclerosis múltiple	Dra. Virginia Meca Lallana
23 may	Taller para pacientes con reciente diagnóstico de esclerosis múltiple	Dra. Virginia Meca Lallana
20 jun	Taller para pacientes Deterioro cognitivo en Esclerosis Múltiple	Ana Gesteira
27 jun	Taller para pacientes Dolor en Esclerosis Múltiple	Dra. Clara Aguirre Hernández
11 jul	Taller para pacientes Síntomas invisibles de la Esclerosis Múltiple	Dña. Beatriz del Río Muñoz

SESSIONS

DATE	TITLE	SPEAKER
3 feb	Jornada Nefrología - "Por qué no en tu casa"	Dra. Guillermina Barril
8 mar	El ejercicio físico y sus beneficios en la Esclerosis Múltiple	Dra. M. José Arriaza
11 mar	Jornada del Dolor	Dra. Concepción Pérez
21 mar	World Down Syndrome Day	Dr. Diego Real de Asúa
20 y 21 abril	I Jornadas de Actualización de Medicina Interna	Dr. José Mº Galván Román
26 may	V MADRID DEB SYMPOSIUM	Dr. Fernando Alfonso Manterola
29 may	Conoce la migraña: Una visión actual	Dra. Ana Gago
8 jun	Jornada Proyecto ICOP	Dr. Diego Real de Asúa
28 sep	VI Reunión Madrileña de Coloproctología	Dr. J. García Septiem
5 oct	VI Jornada de Puertas Abiertas del Servicio de Reumatología para médicos de Atención primaria	Dra. Rosario García de Vicuña
6 oct	VISIONARIOS: Innovación y futuro en enfermedades respiratorias	Dr. Ancochea
26 oct	II Jornada Científica de la Dirección de Enfermería	Dir. Enfermería
2 nov	Neurorrestauración: estimulación cerebral profunda para los trastornos psiquiátricos refractarios	Dr. Cristina V. Torres Díaz
7 nov	VIII JORNADA NETS, Día mundial de los tumores	Dr. Elena Martín Pérez
21 nov	Jornada de Humanización	Dir. Enfermería
25 y 26 noviembre	XVIII Simposio NERC	Dra. Guillermina Barril
27 nov	V Jornada de Neurogastroenterología	Dr. Cecilio Santander
30 nov	II Jornada de Cooperación Internacional y Colaboración Humanitaria AEC, SEDAR, SECOT	Dra. Esperanza Mata
18 dic	Jornada para pacientes Esclerosis	Dra. Virginia Meca Lallana
17 ene	Taller para pacientes Embarazo y lactancia en esclerosis múltiple	Dra. Clara Aguirre Hernández
17 ene	Taller para pacientes Embarazo y lactancia en esclerosis múltiple	Dra. Clara Aguirre Hernández

SEMINARS

DATE	TITLE	SPEAKER
26 ene	CCR6 and CCR9 expression define a population of SARS-CoV-2-specific TReg with pathogenic potential	Laura Esparcia Pinedo
2 feb	Involvement of Tyrosine Kinase 2 (TYK2) in splenic B cell function	Dra. Elena Fernández Ruiz
9 feb	Novel insights in the BTK and MyD88 crosstalk in B cell dynamics and lymphomas	Dra. Yolanda Carrasco
16 feb	Biomarcadores asociados a asma grave y poliposis nasosinusal	María Isabel Delgado Dolset
23 feb	El papel de la Galectina-1 en la patogenia de las Enfermedades Inflamatorias Mediadas por Mecanismos Inmunes y su posible función como biomarcador	Ana Triguero
9 mar	RAPTOR como diana de un microRNA novel	Dra. Hortensia de la Fuente
16 mar	New insights into the role of LAT1 amino acid transporter as a regulator of immune cells and inflammation	Dra. Danay Cebrián
23 mar	Los sistemas del insulín-like growth factor (IGF) central y periférico en la respuesta metabólica a los cambios dietéticos	Dr. Santiago Guerra
30 mar	Differential expression of ligands for checkpoint receptor in myeloid cells from people living with HIV: regulation during chronic inflammation and lymphoid tissue distribution	Marta Calvet
20 abr	Predicción de la respuesta a tratamientos anti-CGRP en migraña utilizando estrategias de machine-learning: nueva herramienta en cefaleas	Dra. Alicia González Martínez
27 abr	Implicación de las proteínas morfogenéticas óseas en la fisiopatología hepática	Patricia Marañón Barnusell
4 may	Papel del transportador de aminoácidos SLC7A5 en escenarios biológicos no tumorales	Dr. Julián Aragonés
18 may	Efectos moleculares del humo del tabaco sobre la arteria pulmonar, su relación con la Enfermedad Pulmonar Obstructiva Crónica y sus posibles dianas terapéuticas	Onofre Munar
25 may	GWC to unravel new molecular candidates involved in Extracellular Vesicles uptake	Víctor Toribio Serrano
1 jun	Regulación de la función de la quinasa Lck por las fosfatasa de regeneración hepática	Carlos Carrasco Padilla
8 jun	Serum profiles of PSGL-1, ADAM8 and selectins as diagnostic markers for Systemic lupus erythematosus and Systemic sclerosis: an observational study	Dra. Esther Santoantonio
15 jun	End-Binding 1 regulates the metabolic fate of CD4+ T lymphoblast and Jurkat T cells and the organization of the mitochondrial network	Álvaro Gómez Morón
7 sep	Identification of Novel Innate, Immunometabolic and Inflammatory Modulators Improving Dendritic Cell-based Preventive Vaccine and Immunotherapy to Boost Cytotoxic CD8+ T Cells Against HIV-1	Marta Calvet Maribent
12 sep	CCT como modulador de la producción de vesículas extracelulares y del metabolismo de linfocitos T a través de las dinámicas de kinesina	Amelia Rojas Gómez
21 sep	MicroRNAs as immunotherapeutic agents: from basics to clinics	Dra. Lola Fernández Messina
28 sep	Primary cilia in pituitary neuroendocrine tumours: A potential biomarker of tumour behaviour	Dra. Rebeca Martínez Hernández

DATE	TITLE	SPEAKER
5 oct	Estudio de la interacción del eje PSGL-1/Selectina P en la regulación de la muerte celular de los neutrófilos y monocitos en los pacientes con lupus eritematoso sistémico	Antonio Muñoz Callejas
26 oct	Desarrollo de una nueva inmunoterapia para cáncer colorrectal metastásico	Dra. Marta Jaén Castaño
2 nov	Unraveling the molecular landscape in autoimmune thyroid diseases at spatial transcriptomics resolution	Pablo Sacristán y Nuria Sánchez de la Blanca
23 nov	Caracterización de la respuesta inmunitaria adaptativa generada tras la vacunación frente al virus SARS-CoV-2 en sujetos sanos y poblaciones de riesgo	Laura Esparcia Pinedo
30 nov	Microbial metabolism of food allergens in IgE responses	Elisa Sánchez Martínez
14 dic	Próxima generación de inmunoterapias contra el cáncer basadas en linfocitos instruidos con bacterias	Dr. Esteban Veiga

CONTINUING EDUCATION LA PRINCESA

TITLE	DATE	SPEAKER
Competencias en Ecografía Clínica para Atención Primaria: Edición VII	13/02/2023 24/02/2023	
Código Sepsis Princesa (EDICIÓN 08)	17/04/2023 29/05/2023	Dr. Fernando Ramasco Rueda
Curso de Soporte Vital Básico para personal sanitario 1ª Edición 2023	26/04/2023 12/05/2023	
CURSO SOBRE RETOS EN ANTIBIOTERAPIA EN EL PACIENTE CRÍTICO - 3ª Edición. Mayo 2023	27/04/2023 30/05/2023	David Arribas Méndez Sonia Expósito Carazo Elena Fernández Martínez Carlos Figueroa Yusta Esther García Villabona Rafael González de Castro Julia Hernando Santos Emilio Maseda Garrido Rosa Méndez Hernández Mar Orts Rodríguez Diana Parrado Sheila Santidrián María Semiglia Alejandro Suárez de La Rica Gonzalo Tamayo Medel Carmen Vallejo Lantero Nelly Zurita Cruz
Centro de Competencias en Ecografía Clínica para Medicina de Familia: Curso de Formación Inicial Edición I	12/05/2023 24/06/2023	Andres Von Wernitz Teleki
Curso de Soporte Vital Avanzado para personal sanitario 2023	22/05/2023 30/06/2023	
Curso de Bienvenida a los nuevos Residentes 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda Ignacio Redondo Pascual
Curso de Historia Clínica Electrónica - 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda

TITLE	DATE	SPEAKER
Soporte Vital Inmediato para Residentes 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda Raquel Caminero García Marta Caño Hortonedá Lydia Chao Ricoy Teresa Coco Carrascal Elvira Contreras Murillo María Cruzate Aparicio Ana del Rey Ubago Noemí Díaz Velasco Verónica Espiga Prieto Luis Aníbal Gómez Arredondo Beatriz González Chesa Sonia González Del Val Javier Martín Ruiz Ana María Martínez Molina Mónica Negro Rúa Diana Parrado Luis Picazo García María Isabel Puca Briones Bárbara Retana Fernández Elena Rojo Rodríguez
Curso de Traumatología para nuevos residentes - 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda Rafael Carbonell
Cirugía para nuevos Residentes - 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda Iñigo García Sanz
ELECTROCARDIOGRAFÍA - 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda Amparo Benedicto Buendía
Curso de interpretación básica de radiología simple - 2023	22/05/2023 n.d.	Juan Mariano Aguilar Mulet Fernando Ramasco Rueda
Metodología en investigación Hospital Universitario de la Princesa	22/05/2023 28/06/2023	María Apellániz Ruiz Administrador del Campus Apoyo Docente Victor Fanjul Alicia González Martínez Mariana Hernández González Fernando Ramasco Rueda Miguel Antonio Sampredro Nuria Sánchez de la Blanca Carrero Ancor Sanz García
Mejora de la atención a las personas mayores en el Servicio de Urgencias. Hospital Amable	26/06/2023 30/06/2023	
Curso Avanzado en eLearning: Creación de Minivideos Docentes - 5ª Edición	01/09/2023 30/09/2023	Elena Fernández Martínez Fernando Ramasco Rueda
eLearning en Sanidad - 6ª Edición	01/09/2023 10/11/2023	Elena Fernández Martínez Fernando Ramasco Rueda
Lectura crítica de artículos para residentes - Edición I	11/09/2023 24/09/2023	María Apellániz Ruiz Alicia González Martínez Jesus Novalbos Reina Fernando Ramasco Rueda Miguel Antonio Sampredro Nuria Sánchez de la Blanca Carrero

TITLE	DATE		SPEAKER
Actualización en cuidados de enfermería del paciente crítico: UCI, REA y UCC	25/09/2023	15/11/2023	Laura Cañal Sainz Elena Espíritu Jiménez Raquel Fernández Leal María Mercedes García Franco Sonia Guinaldo Martín David Jiménez Jiménez María José López Yolanda López González Celia Martín Almazán Rosa Méndez Hernández Mar Puente Cepeda Begoña Quicios Dorado Fernando Ramasco Rueda María Jesús Rodríguez Alonso María Dolores Rodríguez Huerta María José Rubio Pérez Laura Torrent Cristina Yepes Temiño Beatriz Yuste Lozano
Soporte Mecánico Cardiopulmonar	02/10/2023	31/10/2023	Bea Abad Santamaría Río Jorge Aguilar Torres Begoña Bernal Gallego Nieves de Antonio Pablo Díez Villanueva Carlos Figueroa Yusta Judith Iglesias Franco María José López Manuel Emilio Monguio Santin Nuria Oliva Illescas Mar Orts Rodríguez Guillermo Reyes Copa Fernando Rivero Emilia Rosas Carvajal Jorge Salamanca Vilorio Marta Sánchez Galindo Juan Antonio Sánchez Giralt Fernando Suárez Sipmann Tania Tineo Drove Olinda Gladys Tupac Yupanqui López Pablo Villamayor Tirado
Introducción a la metodología de la enseñanza en ciencias de la salud - 1ª edición	02/10/2023	16/10/2023	Beatriz Gal Iglesias Damián García Olmo Joaquín García-Estañ López Héctor Guadalajara Labajo Montiel Jiménez Fuertes Jesús Millán Nuñez-Cortes Antonio Planas Alfredo Prieto Martín Fernando Ramasco Rueda Ricardo Rigual Roger Ruiz Moral
Tutoría profesional en Sanidad - Edición I	23/10/2023	23/11/2023	María Isabel González Anglada Jorge Mendoza Jiménez-Ridruejo Fernando Ramasco Rueda

TITLE	DATE		SPEAKER
Cómo presentar un proyecto de investigación a un CEIm	23/10/2023	31/10/2023	Francisco Abad José Luis Muñoz de Nova Mara Ortega Fernando Ramasco Rueda
Ecografía Clínica en Pacientes Con Patología Aguda: Formación Inicial	25/10/2023	25/10/2023	Juan Mariano Aguilar Mulet Sonia González Del Val Iñigo Guerra Molina Ana María Martínez Molina Fernando Ramasco Rueda Jorge Sorando Ortín Javier Val De Santos Andres Von Wernitz Teleki
Neurorestauración: estimulación cerebral profunda para los trastornos psiquiátricos refractarios	02/11/2023	02/11/2023	Mónica Lara Almunia Marta Navas García Rodrigo Rodríguez Rodríguez Luis Mariano Rojas Medina Alejandra Roldán Purificación Salgado Serrano Cristina Torres Díaz Gloria Villalba
Código Sepsis Princesa para Residentes (Edición 1)	06/11/2023	03/12/2023	Marta Chicot Llano Iñigo García Sanz Rosa Méndez Hernández Sara Navarro Ausere Natalia Pascual Gómez Alberto Pizarro Portillo Fernando Ramasco Rueda María José Rubio Pérez Carmen Sáez Bejar María del Pilar Sanz Martín María Semiglia Andres Von Wernitz Teleki Nelly Zurita Cruz
Introducción a la metodología de la enseñanza en ciencias de la salud - 2ª edición	30/11/2023	13/11/2023	Beatriz Gal Iglesias Damián García Olmo Joaquín García-Estañ López Héctor Guadalajara Labajo Montiel Jiménez Fuertes Jesús Millán Nuñez-Cortes Antonio Planas Alfredo Prieto Martín Fernando Ramasco Rueda Ricardo Rigual Roger Ruiz Moral

GENERAL SESSIONS

DATE	TITLE	SPEAKER
20 ene	Sesión General – 20 de enero de 2023 – Servicio de Medicina Preventiva	Servicio de Medicina Preventiva
27 ene	Sesión General – 27 de enero de 2023 – Servicio de Cardiología	Servicio de Cardiología
3 feb	Sesión General – 3 de febrero de 2023 – Comité de Ética	Comité de Ética
	SaludMadrid – Código Ictus	
	SaludMadrid – Código Infarto	
10 feb	Sesión General – 10 de febrero de 2023 – Servicio de Traumatología	Servicio de Traumatología
24 feb	Sesión General – 24 de febrero de 2023 – Servicio de Medicina Nuclear	Servicio de Medicina Nuclear
3 mar	Sesión General – 3 de marzo de 2023 – Servicio de Prevención de Riesgos Laborales	Servicio de Prevención de Riesgos Laborales
10 mar	Sesión General – 10 de marzo de 2023 – Servicio de Neumología	Servicio de Neumología
17 mar	Sesión General – 17 de marzo de 2023 – Servicio de Farmacología Clínica	Servicio de Farmacología Clínica
24 mar	Sesión General – 24 de marzo de 2023 – Servicio de Oftalmología	Servicio de Oftalmología
31 mar	Sesión General – 31 de marzo de 2023 – Servicio de Oncología médica	Servicio de Oncología médica
14 abr	Sesión General – 14 de abril de 2023 – Servicio de Alergología	Servicio de Alergología
21 abr	Sesión General – 21 de abril de 2023 – Servicio de Farmacia	Servicio de Farmacia
5 may	Sesión General – 05 de mayo de 2023 – Servicio de Nefrología	Servicio de Nefrología
12 may	Sesión General – 12 de mayo de 2023 – Servicio de Oncología Radioterápica	Servicio de Oncología Radioterápica
19 may	Sesión General – 19 de mayo de 2023 – Servicio de Neurofisiología	Servicio de Neurofisiología
25 may	Sesión General – 25 de mayo de 2023 – Servicio de Reumatología	Servicio de Reumatología
2 jun	Sesión General – 2 de junio de 2023 – Servicio de Admisión, Archivo y Documentación Clínica	Servicio de Admisión, Archivo y Documentación Clínica
9 jun	Sesión General – 9 de junio de 2023 – Servicio de Medicina Intensiva	Servicio de Medicina Intensiva
16 jun	Sesión General – 16 de junio de 2023 – Servicio de Neurología	Servicio de Neurología
23 jun	Sesión General – 23 de junio de 2023 – Cirugía General y del Aparato Digestivo	Cirugía General y del Aparato Digestivo
30 jun	Sesión General – 30 de junio de 2023 – Cirugía Dermatológica	Cirugía Dermatológica
20 oct	Sesión General – 20 de octubre de 2023 – Medicina interna	Medicina interna
27 oct	Sesión General – 27 de octubre de 2023 – Servicio de Aparato Digestivo	Servicio de Aparato Digestivo
3 nov	Sesión General – 3 de noviembre de 2023 – Servicio de Inmunología	Servicio de Inmunología
17 nov	Sesión General – 17 de noviembre de 2023 – Servicio de Endocrinología	Servicio de Endocrinología
1 dic	Sesión General – 1 de diciembre de 2023 – Servicio de Angiología y Cirugía Vascular	Servicio de Angiología y Cirugía Vascular
15 dic	Sesión General – 15 de diciembre de 2023 – Servicio de Hematología	Servicio de Hematología



Area 1 Cellular and molecular etiopathogenic mechanisms in inflammatory and autoimmune diseases

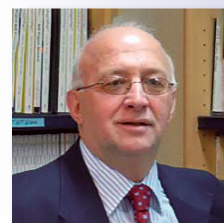
- Line 1.1** Intercellular communication in the inflammatory response
- Line 1.2** Cellular and molecular responses to hypoxia
- Line 1.3** Animal models of inflammatory diseases and intercellular signalling
- Line 1.5** Cellular mechanisms and molecular determinants of allergybased diseases
- Line 1.6** Inflammatory processes in nephrological diseases
- Line 1.7** Inflammatory mechanisms in pulmonary diseases
- Line 1.8** Inflammatory response in hepatic diseases
- Line 1.9** Mechanisms and mediators of endocrine diseases
- Line 1.10** Children’s development (obesity and growth)
- Line 1.11** Metabolic syndrome and vascular risk



Line 1.1

Intercellular communication in the inflammatory response

GROUP 1



Francisco Sánchez Madrid
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RESEARCH INTEREST

Activation of the adaptive immune response requires the formation of intimate contacts between antigen-bearing cells (e.g. dendritic cells, DC) and T lymphocytes. These contacts ('immune synapses') act as hubs that transmit activating signals from the DC to the T cell, driving its differentiation and proliferation. However, information also travels in reverse, from the T cell to the DC. Reverse transmission depends of receptor-dependent adhesive contacts, soluble factors, and vesicles, e.g. exosomes. Exosomes are small extracellular vesicles biosynthesized from multi-vesicular bodies (MVB) and released towards the DC through MVB fusion with the plasma membrane. This group aims to determine the extent, nature and function of the information transferred from T cells towards DCs in exosomes through synaptic contacts. We will characterize the role of specific bits of information originated within the T cell and carried by exosomes, e.g. membrane transporters for specific metabolites, captured by the DC during the

establishment and maintenance of synaptic contacts. The regulation of anti-viral and anti-bacterial genes determining the ability of DCs to respond to these challenges will define their Alert State. We are assessing the role of epigenetic changes at a DNA level in function of post-synaptic DCs, alone and in combination with metabolic changes and post-translational modifications to specific proteins, for example, Ubiquitin-like modifiers such as ISGylation. Cell viability, survival, and migration of post-synaptic DCs will be determined in vivo. We will also characterize the role of ISGylation on the Alert state during T-DC synapsis and inflammation. Finally, the role of the L-type amino-acid transporter 1 molecule (LAT1) and L-tryptophan metabolism and important T cell immunoregulatory molecules will be analyzed in the context of the immune response associated to atherosclerosis and skin-inflammatory diseases in animal models to identify the molecular basis of these autoimmune diseases. These studies will open new avenues for vaccination strategies and novel therapies to treat autoimmune-related diseases.



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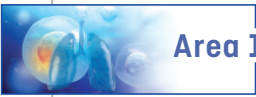
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Line 1.1

Intercellular communication in the inflammatory response

GROUP 3



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RESEARCH INTEREST

Our group is focused on the role of tetraspanin-enriched membrane nanodomains in extracellular vesicles (EVs). We pursue both biotechnological applications for EV detection, isolation or characterization as well as fun-damental knowledge on tetraspanin involvement in the

molecular mechanisms of EV biogenesis, cargo selection and uptake. Our latest data suggest that tetraspanins fi-nely regulate the dynamics of endosomal compartments and their interrelation with autophagy and mitophagy pa-thways. Thus, tetraspanins emerge as potent regulators of the metabolic fitness of the cell, with novel therapeutic implications in the fight against cancer.



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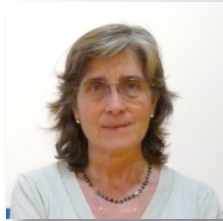
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Line 1.1
Intercellular communication in the inflammatory response

GROUP 56



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RESEARCH INTEREST

P-Selectin Glycoprotein Ligand-1 (PSGL-1) is a leukocyte receptor that interacts with P-, E-, and L-Selectins and is responsible for the initial steps of leukocyte extravasation to inflammation sites. Our laboratory has demonstrated that PSGL-1 acts as an immunoregulatory receptor that participates in the generation of regulatory T cells (Treg) and contributes to the maintenance of peripheral tolerance in mice. Additionally, our group discovered that ADAM8 associates with and cleaves PSGL-1 (Dominguez-Luis et al., Eur J Immunol 2011). Importantly, we found that PSGL-1 knock-out (KO) mice develop a progressive autoimmune disease similar to systemic sclerosis (SSc) (Pérez-Frías et al., Arthritis and Rheumatol 2014)

Moreover, we observed that the absence of P-Selectin, the main PSGL-1 ligand, causes an autoimmune syndrome similar to human systemic lupus erythematosus (SLE), characterized by the generation of anti-dsDNA autoantibodies, immune complex deposits in skin and kidney, and hypersensitivity to UV light, which are characteristics of SLE (González-Tajuelo et al., Sci Reports 2017). Interestingly, we have recently reported that aged PSGL-1 KO females develop pulmonary arterial hypertension (PAH), the most severe form of connective tissue-related autoimmune diseases. This condition is associated with increased levels of Angiotensin II and endothelial dysfunction, along with low production of NO (González-Tajuelo et al., Arthritis and Rheumatol. 2019).

Remarkably, clinical studies with patients indicate that PSGL-1 and P-Selectin expression are altered in both diseases. SSc patients exhibit reduced PSGL-1 expression in B cells and increased expression in monocytes, dendritic cells, and T cells. Additionally, our data show a correlation between high PSGL-1 expression and the presence of interstitial lung disease (ILD) in SSc patients, with over 75% of circulating pDCs expressing ADAM8 associated with SSc presence (Silván J et al., J Invest Dermatol, 2018). Lupus patients present reduced expression of P-Selectin in skin vessels and reduced expression of PSGL-1 in neutrophils and monocytes, which is associated with disease activity.

Our recent data indicate that specific ratios of ADAM8 and L-selectin serum levels indicate the presence of SLE, and specific ratios of ADAM8 serum levels and percentage of neutrophils expressing ADAM8 can distinguish SLE from SSc (San Antonio E et al., Frontiers Immunol, 2024, in press). Given all these findings, our main goal is to study the molecular and cellular alterations that underlie the pathology of SSc and SLE

Main Research Lines:

Studies with patient samples:

- Characterization of idiopathic ILD, SSc-ILD and SLE-ILD and expression of PSGL-1 and its ligands in lung and blood cells, serum, and BAL supernatant

- Analysis of the expression of PSGL-1 and its ligands in circulating cells and serum of PAH patients (idiopathic or associated with SSc)
- Study of the signaling pathways elicited by PSGL-1/P-Selectin interaction in monocytes and neutrophils of healthy donors, SSc patients, and SLE patients, and its relevance to cell proteostasis

Studies with PSGL-1 and P-selectin KO mice:

- Characterization of ILD developed by PSGL-1 and P-Selectin KO mice and study of PSGL-1 signaling pathways and cell proteostasis in different lung immune cell subsets.



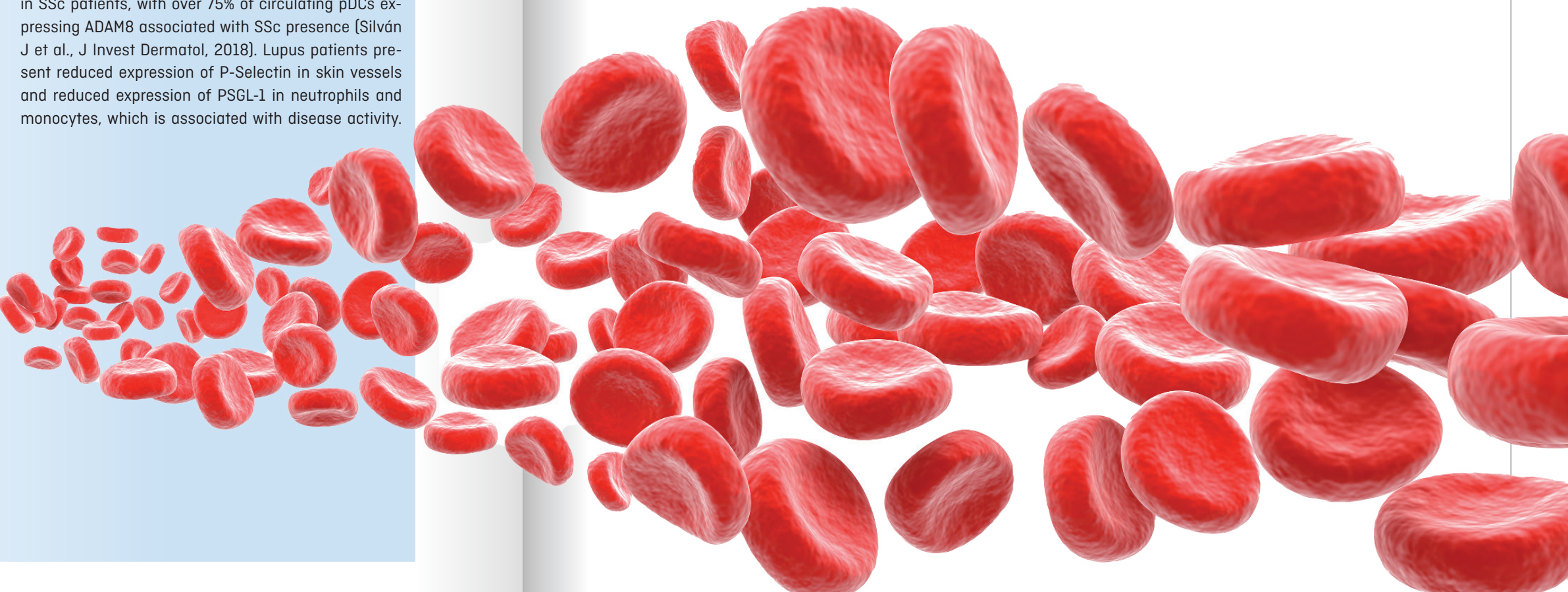
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Line 1.2

Cellular and molecular responses to hypoxia

GROUP 9



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Claudia Mesa Ciller
Andrés Amalio Urrutia Elorduy
Esther Fuertes Yebra
Florinda del Coral Meléndez Rodríguez



RESEARCH INTEREST

An insufficient oxygen supply (hypoxia) is a hallmark of numerous life-threatening pathologies with unmet medical needs such as solid tumor growth, chronic obstructive pulmonary disease (COPD), ischemic diseases and tumor growth. Cells are equipped with oxygen-sensing systems to mount a programmed response when oxygen becomes limited. Hypoxia-inducible factors (HIF1, HIF2 and HIF3) are central regulators of this cellular response to oxygen fluctuations.

Our research interest is focused on the role of the HIF oxygen sensing pathways in cancer, pulmonary disease and metabolic disease. In particular, we are mainly interested in cellular metabolic reprogramming, which is one the central biological functions executed by the HIF factors. 1) HIF factors and renal cell carcinoma: the HIF factors are induced in hypoxic areas in the inner core of the solid tumors but in clear cell renal cell carcinoma (ccRCC) - which loss Vhl (the main repressor of HIFs in normoxia) - show constitutive HIF expression irrespectively of the oxygen levels of the tumor. In these tumors HIF1 shows its cell autonomous anti-proliferative capability, whereas HIF2 acts as an oncoprotein. We

are interested in the metabolic rewiring executed by HIF1a and HIF2a responsible of this contrasting properties of both HIF isoforms, a topic in which we have published the following studies (Elorza et al. 2012 Molecular Cell; Meléndez Rodríguez et al. 2019 Cell Reports; Urrutia et al. 2024 Cell Reports) 2) HIF factors and airway dysfunction in pulmonary disease: Pulmonary diseases such as chronic obstructive pulmonary disease (COPD) and sleep-apnea hypoapnea syndrome (SAHS) are the most common respiratory diseases causing illness and death, and are being projected to be the third leading cause of death worldwide by 2020. They are characterized by an insufficient level of oxygen in the blood (hypoxemia), continuous in the COPD and intermittent in the SAHS, and they are associated to pulmonary oxidative damage, an exaggerated inflammatory response in the lung and systemically. Surprisingly, despite the fact that lung tissue - bronchial epithelium - Along this line, we have reinitiated a research line focused on the role of HIF in bronchial epithelial cells biology, a topic in which we have published the following study (Torres-Capelli et al. Scietific Reports 2016). 3) In line with our interest in the role of HIF oxygen sensing pathways in cellular adaptation to hypoxia through the

mitochondrial reprogramming and metabolic disease, we already unveiled the role of HIF1 in obesity (Soro et al. Cell Reports 2016). Along this line, NDUFA4L2 is a target gene of hypoxia-inducible factors (HIF) that has the ability to decrease overall mitochondrial oxygen

consumption through the inhibition of mitochondrial complex I and some members of the group are actively working on the role NDUFA4L2 in vivo, a topic in which Dr. Urrutia alrerady published the following study (Mesa-Ciller et al. Scietific Reports 2016).



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Line 1.2
Cellular and molecular responses to hypoxia

GROUP 7



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Head of laboratory



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Susana Delgado Martín
Carmen Choya Foces.



RESEARCH INTEREST

Our research line studies redox signalling and oxidative stress in hypoxia and ischemic events (especially stroke), and in inflammation, with a main focus on the actions of the mitochondrial sodium/calcium exchanger NCLX.

While searching the source of redox signals in the response to acute hypoxia we have discovered the key role of mitochondrial Na⁺ import by NCLX in controlling the activity and superoxide production of the mitochondrial electron transport chain.

We now study the role of NCLX in oxidative damage in ischemia-reperfusion injury (IRI), applying specific NCLX inhibitors (developed in the IIS-IP) and genetic deletion in cell culture and animal models of stroke. A

specific project studies the role of NCLX in ferroptosis, a novel type of cell death related with oxidative stress in IRI. We envision to advance the knowledge of the molecular mechanisms as well as to try innovative approaches to diminish stroke damage.

As NCLX is also a lithium transporter, we are studying the mitochondrial effects of lithium that may depend on NCLX activity, and their consequences in mitochondrial and cellular functions.

We also study the role of NCLX and the importance of redox signalling mediated by specific cysteine residues in the regulation of the NLRP3 inflammasome.

In an international collaboration, we also study the role of protein sulphydration, an oxidative modification of cysteines with sulphydric acid (H₂S), in neurogenesis in Down syndrome.



MAJOR GRANTS

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Line 1.2
Cellular and molecular responses to hypoxia

GROUP 8



María Josefa Calzada García
Head of laboratory



GROUP MEMBERS

María Josefa Calzada García
Jorge Rodríguez Pérez
Noelia López García

Leila Pérez Sánchez
Héctor Milian Goicoechea



RESEARCH INTEREST

Hypoxia plays critical roles in the pathobiology of many diseases, these including cancer and chronic lung disease, with a high prevalence and morbidity. Understanding how cells sense and respond to changes in oxygen availability and the physiologic or pathologic consequences in the context of chronic diseases will have a positive impact in the diagnosis and treatment of these pathologies.

Currently, our main line of research is focused on studying the involvement of hypoxia and tobacco smoke in chronic and inflammatory lung diseases and some of the comorbidities, in particular pulmonary hypertension.

These pathologies are rapidly progressive pulmonary

vascular diseases with a multifactorial etiopathogenesis that result in loss of pulmonary function and emphysema, right-sided heart failure and ultimately death. However, the underlying cellular and molecular mechanisms are largely unknown. Our previous results demonstrate that cigarette smoke has direct effects on pulmonary vascular tone homeostasis and contribute to pulmonary arterial dysfunction. This is in part due to altered activity of the voltage-dependent K⁺ channel, an exacerbated production of reactive oxygen species and a diminished antioxidant response which promotes a switch in the sGCs redox state.

Our current studies aim to delve deeper into the molecular pathways involved in the vascular impairment induced by cigarette smoke exposure and their contribution to calcium signaling and cellular contractile machinery in pulmonary arteries and bronchi.



MAJOR GRANTS

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Line 1.3

Animal models of inflammatory diseases and intercellular signalling

GROUP 11



Federico Mayor Menéndez
Head of laboratory



GROUP MEMBERS

Federico Mayor Menéndez
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Natalia Reglero Real
Cristina Delgado Arévalo

Irene García Higuera
Inmaculada Navarro Lérda
Alejandro Asensio López
Catalina Ribas Núñez



RESEARCH INTEREST

An integrated knowledge of the complex functioning of cellular signalling networks and of their alterations or maladaptive rewiring in pathological conditions is key for understanding the molecular basis of disease and for the design of targeted therapeutic strategies. Regulatory nodes or hubs within these signalling networks are particularly relevant since these proteins display a complex interactome and thus integrate multiple upstream inputs and trigger pleiotropic downstream outputs. The main aim of our group is to better understand the role of the G protein-coupled receptor kinase 2 (GRK2) hub in the onset or progression of prevalent diseases and the molecular mechanisms involved. GRK2 is a versatile protein that modulates signalling mediated by many members of the large G protein-coupled receptor (GPCR) superfamily and also via phosphorylation or scaffolding interactions with a growing array of non-GPCR cellular partners. From a pathophysiological perspective, GRK2 is emerging as an oncomodulator, functionally interacting with signalling networks related to the hallmarks of

cancer in a tumour and cell type-dependent way. On the other hand, GRK2 levels and activity are convergently upregulated in the heart and in tissues that are key for metabolic control during cardiovascular pathologies and in obesity and insulin resistance-related contexts, which are frequent clinical co-morbidities, pointing to this protein as a potentially relevant "synergic" therapeutic target. The group pursues the following lines of investigation: 1) Integrative role of GRK2 in the crosstalk of signalling cascades acting within the breast tumour microenvironment 2) GRK2 in epidermal homeostasis and in keratinocyte-immune cells crosstalk and potential pathological implications in skin inflammatory diseases and in squamous cell carcinomas. 3) GRK2 in obesity and insulin resistance-related contexts: participation of GRK2 in determining the pro-inflammatory profile of macrophages and impact of myeloid GRK2 in inter-organ crosstalk in cardiometabolic disease. 4) Explore the functional implications of the Galphag interactome on autophagy and nutrient sensing and on oxidative stress processes and its impact on endothelial cell function and cardiovascular disease.



MAJOR GRANTS

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Marolda, V.; Asensio López, A.; Murga Montesinos, C.; Mayor Menéndez, F. Redes de señalización de GRK2 y mecanismos moleculares de procesos patológicos. PID2020-117218RB-I00. Agencia Estatal de Investigación.

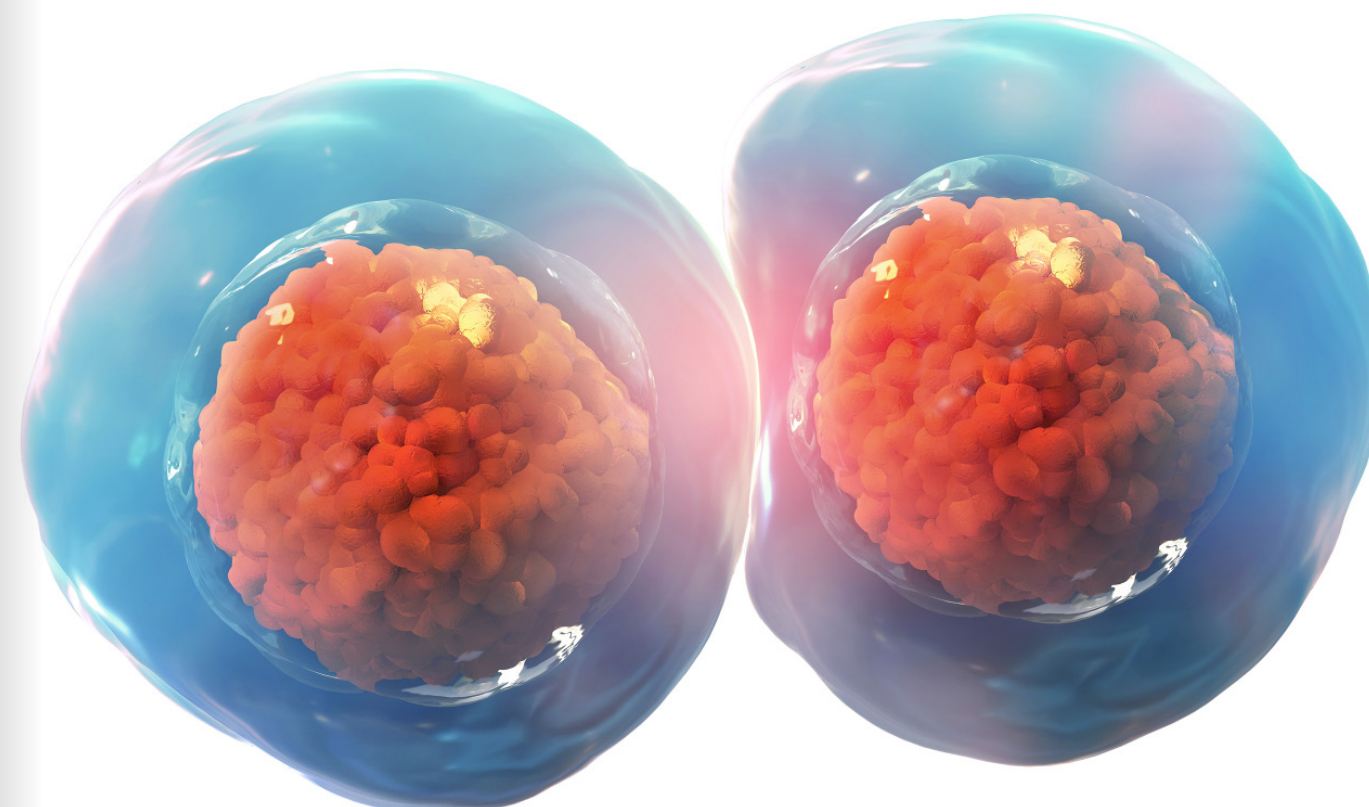
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Portilla Y, Mulens-Arias V, Daviu N, Paradelo A, Pérez-Yagüe S, Barber DF. **Interaction of Iron Oxide Nanoparticles with Macrophages Is Influenced Distinctly by "Self" and "Non-Self" Biological Identities**. ACS Appl Mater Interfaces. 2023 Aug 2;15(30):35906-35926. IF: 8,3. doi: 10.1021/acsami.3c05555.





Line 1.3

Animal models of inflammatory diseases and intercellular signalling

GROUP 12



Manuel Fresno Escudero
Head of laboratory



GROUP MEMBERS

Manuel Fresno Escudero
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Alfonso Herreros Cabello
Javier Merino Valverde
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Teresa García Prieto

Patricia Torres Gérica
Francisco Callejas Hernández
Javier Galán Martínez
María del Carmen Maza Moreno
Natalia Cuesta Rubio
Nuria Gironès Pujol



RESEARCH INTEREST

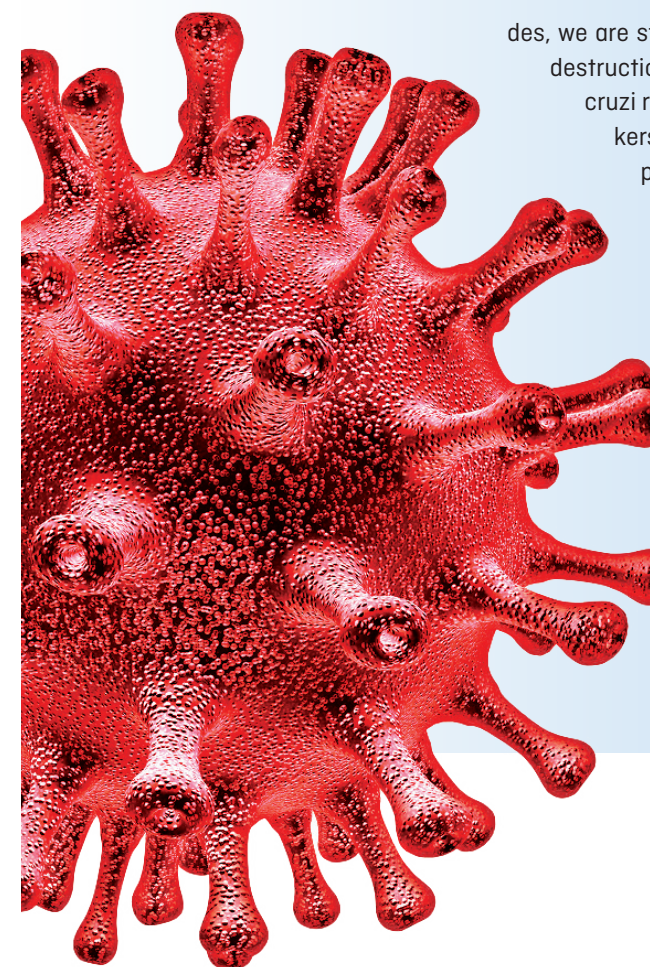
We are analyzing the involvement of Pathogen recognition receptors (TLRs or galectin) in the immune system and inflammatory pathologies such as obesity, cancer, and sepsis. We have found that galectin-1 (Gal-1) deficiency abolished diet-induced obesity and insulin resistance in mice. Gal-1 is needed to differentiate preadipocytes by regulation of the key proadipogenic transcription factor PPAR- γ and in the differentiation of brown adipocytes. We studied the immune evasion through TLR4 by atypical LPS from α 2-proteobacteria. On the other hand, TCFL5 is a member of the bHLH transcription factor family with multiple isoforms in humans and mice. Complete deletion of the isoforms drastically reduces the tumor properties of colon cancer cells. Interestingly, the two major isoforms (TCFL5 and CHA) showed reciprocal regulation and different functions in the cell, with CHA exercising a protumoral effect. TCFL5 / CHA expression is essential for NF κ B2 activity regulating the expression of anti-apoptotic genes such as BCL2 and controlling the expression of the pluripotency markers SOX2, NANOG, and KLF4.

We have also defined a set of genes regulated by TCFL5/CHA in leukemia cell lines and established their role in the prognosis and development of B- and T-acu-

te lymphoblastic leukemia and normal hematopoiesis. The expression of TCFL5 and CHA was associated with greater severity in lymphoma and myeloma samples from patients. Last but not least, using Tcfl5 deficient mice, we found that TCFL5 is involved in the formation of germinal centers and in the stage of differentiation of pro-B to pre-B cells, two processes that are not only characterized by a high proliferation rate but are also MYC dependent. The lack of TCFL5 caused a radical decrease in the levels of the most important molecules in BCR signaling, such as SYK and BLNK, resulting in an inability to respond to stimuli, an increase in cell death, and an abnormal cell cycle.

Using Tcfl5 deficient mice, we found that TCFL5 is expressed in early mouse embryonic development during the preimplantation period and plays a role in the differentiation of embryonic cells to germline precursors by controlling the expression of genes important in this differentiation.

In the infection by the protozoan parasite *T. cruzi* we are working on the impact of *T. cruzi* genetic variability on the clinical outcome and immunopathology of Chagas' disease and drug susceptibility. All are intended for improved understanding and prevention of Chagas' disease. We have identified different immune responses, which depend on the infecting strain. Besi-



des, we are studying how the parasite enters, infects, and escapes destruction by myeloid cells, defining Slamf1 (CD150) as a new *T. cruzi* receptor. Circulating miRNAs are also excellent biomarkers of Chagas' disease progression, and transcriptomics, proteomics, and metabolomics studies are in progress in macrophages and metabolomics in serum from Chagasic patients, in collaboration with different hospitals, to identify new therapeutic targets and prognosis markers, respectively.

Finally, we tested different approaches to fight infections in collaboration with other research groups. For *T. cruzi* infection we studied the contribution of Sec22b to cross-presentation. For SARS-CoV-2 infection, we tested the anti-viral effect of senolytics, and bacterial dextran sulfate in the k18-hACE2 mice experimental model. Moreover, we studied antibodies in the serum of COVID-19 patients after repeated vaccination, and in children. We plan to continue with these collaborative projects.



PUBLICATIONS

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Line 1.3
Animal models of inflammatory diseases and intercellular signalling

GROUP 13



Petronila Penela Márquez
Head of laboratory



GROUP MEMBERS

Petronila Penela Márquez
M^a Teresa González Muñoz

Ángela Albitre Sanz
Belén Ortiz del Castillo



RESEARCH INTEREST

Breast cancer is a heterogeneous disease at both the molecular and histopathological levels, leading to varied clinical outcomes that complicate the identification and development of targeted therapies. Different molecular alterations underlie the onset and progression of this disease by progressively weakening the cellular processes that maintain genome stability and homeostasis. In breast cancer, key proteins that impact genomic instability and tumor cell heterogeneity include ATM kinase, BRCA1 ligase, and the tumor suppressor transcription factor p53. Notably, in approximately 80% of ductal breast carcinomas, p53 is restrained by the activation or amplification of the ligase Mdm2. However, therapies targeting these molecules have not yet proven satisfactory. Additionally, adaptive mechanisms involving the dynamic rewiring of cell signaling networks through posttranslational modifications of proteins, such as ubiquitination, acetylation, and phosphorylation, can contribute to cellular instability and malignancy. This signaling rewiring also contributes to the emergence of resistance across all breast cancer subtypes, accompanied by increased genomic instability and

metabolic reprogramming of tumors. This complexity underscores the need for a deeper understanding of signal transduction plasticity in breast cancer development and progression. Our group has identified G protein-coupled receptor kinase 2 (GRK2) as a critical signalling node that is upregulated in breast cancer (BC), promoting growth and survival. Our laboratory is investigating the interplay of this kinase with ligases such as Mdm2, examining its role in cell-autonomous malignant transformation and the communication of tumor cells with the tumour micro-environment. Our results indicate that GRK2 and these ligases modulate each other differently in normal epithelial cells compared to tumour cells, responding distinctively to signals that activate adrenergic receptors and other G-protein coupled receptors (GPCR) or growth factor tyrosine kinase receptors (RTK).

We aim to understand the impact of modified proteins resulting from the regulatory feedback between GRK2 and Mdm2 in various cellular processes such as cell cycle control and cell division, differentiation, energy metabolism, and senescence, which are crucial for maintaining normal cell behaviour. Additionally, we are exploring the connection of these molecules with hormonal (adrenergic, estrogenic) and metabolic stress by analysing their impact on proteins related to genomic stability as BRCA1. Furthermore, we are studying their unforeseen influence on stromal remodeling processes, such as tumor angiogenesis, which collectively contribute to tumor dissemination.



MAJOR GRANTS

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PUBLICATIONS

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Line 1.3
Animal models of inflammatory diseases and intercellular signalling

GROUP 17



Cristina Murga Montesinos
Head of laboratory



GROUP MEMBERS

Cristina Murga Montesinos

María del Carmen Vida Rueda



RESEARCH INTEREST

Cellular responses to nutrients and to changes in metabolism are increasingly being regarded as key modulators of immunity and inflammatory processes. In particular, it is well established that nutritional stress can mount a sterile inflammatory response called metaflammation that affects different tissues and is both low grade and chronic. Obesity and metabolic dysregulation, and, in particular, metaflammation underlies an increased risk to different pathologies.

An important point of control of intracellular signaling routes in response to metabolic, stress and inflammatory signals is the node of the G protein-coupled receptor kinase 2 (GRK2), that emerges as a pivotal control point in the onset and/or progression of prevalent cardiovascular, metabolic and inflammatory diseases.

Consequently, our research efforts are focused on the following lines:

1. Analysis of the phenotypical differences in the response of mice with decreased or increased levels of GRK2 towards several types of metabolic challenges under physiological and pathological conditions. We are unveiling whether the response of relevant tissues to these challenges varies with GRK2 dosage. Also whether the levels of GRK2

itself may allow for a better adaptation of each tissue to different nutrient stress situations or even serve as biomarkers of disease. Our latest research describes the influence of GRK2 on the influence of perivascular adipose tissue on vascular dysfunction in mice fed a high fat diet, on the control of pancreatic insulin secretion and on glucagon-induced hepatic glucose production.

2. We are also studying how changes in the levels of GRK2 protein in neutrophils, macrophages and other cells of the immune system may contribute to the control of insulin sensitivity and metabolic homeostasis in animal models of disease. We have published how myeloid GRK2 affects whole body responses to nutrient stress such as glycaemic control and hepatic inflammation. We are currently investigating how the levels and activity of GRK2 can shape the different populations of immune system cells that infiltrate adipose tissue after feeding mice with high fat high fructose diets. We are posing particular emphasis on the study of myeloid cell phenotypic landscape using OMIC techniques. We are also assessing the influence of GRK2 on diet-induced egression of myeloid cells and precursors from the bone marrow towards the circulation and the molecular mechanisms implicated.



MAJOR GRANTS

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Line 1.3
Animal models of inflammatory diseases and intercellular signalling

GROUP 18



Miguel Ángel Iñiguez Peña
Head of laboratory



GROUP MEMBERS

Miguel Ángel Iñiguez Peña

Ángel Bago Plaza

Ana Renshaw Calderón



RESEARCH INTEREST

Fatty acid modification results in the production of bioactive lipids as oxo or nitro fatty acids, agents that can modulate the activation, differentiation and function of different cell types, as those involved in the inflammatory process and the immune response. Their actions take place through their ability to covalently modify transcriptional regulatory proteins and enzymes and to activate various nuclear and membrane receptors, finally modifying protein function and altering patterns of gene expression.

Enzymatic oxygenation of fatty acids generates signalling mediators, as those of the eicosanoids lipid family, which includes prostaglandins and leukotrienes. Current knowledge shows their key role as signalling molecules in an array of pathophysiological processes, being regarded as critical mediators in a variety of inflammatory diseases such as arthritis, atherosclerosis and cancer. Our current research is focused on a particular class of electrophilic compounds named cyclopentenones (CyPGs), which play an important role in

the inflammatory process, acting as anti-inflammatory pro-resolving agents.

Electrophilic fatty acid species also include nitro-containing fatty acids as nitroalkene derivatives of linoleic and oleic acid (LN02 and OA-N02). These compounds are a novel class of endogenous, electrophilic mediators that can also exert adaptive anti-inflammatory signalling reactions.

Our research is aimed to the study of the molecular mechanisms involved in the actions displayed by these electrophilic fatty acids as modulators of inflammation and the immune response. To this end, we analyze their influence on diverse parameters of macrophage and T lymphocyte function, focusing on their effects on transcriptional activation and gene expression and their consequences on cell activation and differentiation.

Research on the molecular and cellular basis of the actions of electrophilic fatty acids in inflammation and the immune response is required to clearly understand the potential benefits and risks of pharmaceutical intervention with these lipids in the onset and progress of inflammatory diseases.



MAJOR GRANTS

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Line 1.5

Cellular mechanisms and molecular determinants of allergy based diseases

GROUP 20



Carlos Alberto Blanco Guerra
Head of laboratory



GROUP MEMBERS

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María Teresa Belver González
María Victoria Múgica García

Álvaro Daschner
María Consolación de Frutos Moreno
Tania María Ramos García
Ana María Valls Sánchez
Francisco Félix Vega de la Osada
Celia López Sanz



RESEARCH INTEREST

Allergic diseases are increasing worldwide, related to a complex interaction between genetic and environmental factors, and reaching prevalence rates higher than 30%. Among them, respiratory allergy, including bronchial asthma and rhinoconjunctivitis, is a research priority target for most health organizations. Nowadays, allergen specific immunotherapy is the only way to modify the natural course of allergic respiratory diseases. Meanwhile, food & drug allergies are also rising problems, due to both the potential severity of reactions and to their great impact on patient quality of life. In this context, our group has the following main research lines, in collaboration with the allergy research network ARADyAL (ISCIII RD16/0006):

- Searching for biomarkers of allergy severity: multicentric BIOGRAL study led by Dr. Barber from San Pablo CEU University and funded by ISCIII, including

patients with respiratory- food- and drug-allergies, is now ongoing.

- Immunotherapy for respiratory allergy: a 2-yr placebo controlled clinical trial has been finished, checking immunological changes induced by grass-pollen immunotherapy on respiratory allergy, a doctoral thesis is in the writing phase.
- A study on severe bronchial asthma treated with biological drugs, cooperating with San Pablo CEU university, is ongoing.
- Cross-reactivity between Cupressus arizonica and Cryptomeria japonica has been checked in collaboration with ALK-Abello.
- A study on adverse reactions to iodinated- and gadolinium-contrasts led by Dr. Vega is ongoing, in which tolerance to alternative contrasts is assessed by means of a protocol of fast challenge tests at full dose. First results have been already published and

a doctoral thesis will soon be presented.

- We have participated in a research project (Retos Investigación: Proyectos I+D+i 2017, MINECO) with Dra. Cuadrado from INIA (National Food Research Institute), focused on nut allergy. Both DNA- and immunological- biosensors will be developed.
- Possible cross-reactivity between peanut and the new food called miracle berry has been checked in collaboration with the biotechnology Dept. of Madrid Polytechnic University.
- Flaxseed allergy has been characterized in collaboration with Madrid Complutense University.
- Dra. Múgica and Dra. Ramos are collaborating with the Spanish Allergy Society in the Allergodata study, recording patients treated with biological drugs.
- Dr. Daschner continues with its productive research lines on Anisakis allergy, which made it possible, in

a collaborative study with the ISCIII, to perform an epidemiological analysis of Hospitalizations due to Anisakiasis and establish a new estimate of nationwide allergy cases. He continues to work in the field of Evolutionary Medicine with a multidisciplinary approach and in collaboration with the National Museum of Natural Sciences.

- The incorporation of Dr. Rodrigo Jiménez-Saiz two years ago has enhanced the group's capabilities. His interest is to understand immunological principles of Th2 immunity in the context of allergic disease, particularly as it pertains to acute allergic reactions (anaphylaxis) and its modulation by the microbiota, the mast cell-neuron axis during allergen immunotherapy and the impact of allergic disease on the development of atherosclerosis. (<https://www.jimenezsaizlab.com/>).



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Jiménez Saiz, Rodrigo. "Estudio integrativo de la inflamación aguda y crónica en enfermedad alérgica y su asociación con dislipemia y aterosclerosis". FIS.22/00236. Instituto de Salud Carlos III.

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PUBLICATIONS

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Line 1.5
Cellular mechanisms and molecular determinants of allergy based diseases

GROUP 15



María Dolores Ibáñez Sandín
Head of laboratory



GROUP MEMBERS

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Carmelo Escudero Díez

Pablo Rodríguez del Río
Silvia Sánchez García



RESEARCH INTEREST

Study of biomarkers for allergic prediction in new-borns (BIOPAL): In the present study we will identify biomarkers, by -omic tools, related to the development of atopic dermatitis; allergic asthma (or its equivalent in newborns, recurrent wheezing); and food allergy (both IgE-mediated or non-IgE-mediated). We will describe the qualitative and quantitative differences of gut microbiota in allergic versus control individuals by genomic techniques. We intent to validate the metabolites observed with the panel of severity biomarkers that we already have obtained in previous projects and correlate this data with gut microbiota profiles, identified by -omic tools.

Evaluation of the efficacy and safety of the combined treatment of anti-IgE antibodies and low-dose oral immunotherapy in children with persistent and severe allergy to cow's milk protein in order to optimize treatment related outcomes. Several evaluations will be carried out including changes in reactivity thresholds, immunological parameters, dietary and quality of life changes evolution, as well as a novel assessment of patients' experience in the "Day Hospital".

Safety and Efficacy Study of **Viaskin Peanut in Peanut-allergic** Children 4-7 Years of Age: VITESSE study: this is an international sponsored study exploring the

safety and efficacy of epicutaneous peanut immunotherapy in schoolers.

Harmonization of clinical outcomes of efficacy in Food AIT trials. Food immunotherapy is currently the only aetiological treatment of food allergy, and despite the extensive research carried out in the last decade, there are still some gaps to fill in such as understanding the clinical outcomes that should be used in the field. This project aims at reviewing currently used clinical outcomes of efficacy in Food immunotherapy trials and proposing the most suitable to be used in the future research.

Peanut allergy oral immunotherapy studies. We have conducted several trials to investigate the short- and long-term efficacy and safety of oral immunotherapy with peanut (recently marketed as Palforzia). These trials have ended in 2023

In a clinical trial, CQGE031G12301, and its open lable follow-up study, CQGE031G12303B, we are investigating the clinical efficacy and safety of **ligelizumab**, and optimized monoclonal antibody against IgE, as monotherapy in peanut allergy.

Efficacy and Safety Study of **Tezepelumab, a monoclonal antibody against the TSLP**, in 5 to < 12 Year Old Children With Severe Uncontrolled Asthma. We are currently recruiting patients for this multicenter international Phase III clinical trial.



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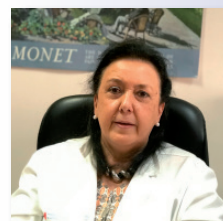
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Line 1.6

Inflammatory processes in nephrological diseases

GROUP 21



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RESEARCH INTEREST

Peritoneal Dialysis (PD): Our main line of work is focused on the study of the mechanisms involved in the damage induced by PD on the peritoneal membrane. Also, we studied the influence of several drugs (Paricalcitol, Tamoxifen, Roxiglitazone) in preventing and repairing damage to the peritoneal membrane. In the next years we will try to clarify which are the mechanisms responsible for the hyalinizing vascular disease, the role of alternatively activated macrophages in the progression of peritoneal damage and we will analyze the morphological and immunohistochemical findings in peritoneal biopsies from patients treated with conventional or bio-compatible liquids. An ongoing project aims to design a microchip for early noninvasive diagnosis of mesothelial to mesenchymal transition in peritoneal membrane using the peritoneal effluent. Preliminary data have shown that peritoneal dialysis, in animals subjected to a cerebral ischemic damage, is able to decrease the cerebral damage induced by high glutamate levels. In collaboration with the Neurology Service we are conducting a clinical trial in patients to determine whether peritoneal dialysis can protect from ischemic brain damage in the acute phase of ischemic stroke.

Nutrition in Renal disease: We have studied the importan-

ce of exercise in proper nutrition and survival of patients with advanced chronic kidney disease and the effect of physical training. We have studied the introduction of new scores for nutritional assessment of renal patients and we intend to study the balance of myocytokines and its relation to muscle strength and functionality.

Alterations of Bone and Mineral Metabolism in Chronic Kidney Disease (CKD): FGF23 is a molecule involved in the metabolism of phosphorus but can be important as a marker of cardiovascular pathology and survival in renal disease. We have designed a clinical trial, which is already funded, to analyze the behavior of FGF23 and PTH fragments in patients with chronic kidney disease on peritoneal dialysis program treated with cinacalcet.

Down's Syndrome. We are developing a study to evaluate renal function in a large group of these patients followed regularly in a monographic consultation. The incidence of cardiovascular complications and bone mineral metabolism will also be studied.

Hepatorenal polycystosis of the adult. New drugs have been introduced in the last few years that have demonstrated, in preliminary trials, that they improve the prognosis of patients with polycystosis. We are trying to determine the mechanisms that significantly affect the progression of these patients towards renal failure, and implement measures to prevent this progression.



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Line 1.7

Inflammatory mechanisms in pulmonary diseases

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RESEARCH INTEREST

Inflammation and reparative process in lung diseases. Chronic obstructive pulmonary disease (COPD). Apnea-Hypopnea Syndrome. Asthma. Idiopathic pulmonary fibrosis (IPF). Non-cystic fibrosis Bronchiectasis and Bronchiectasis related to cystic fibrosis. Immunopathogeny. Molecular diagnosis. Cellular diagnosis. New therapeutic approaches. New care models. COVID-19 and Post-COVID-19.

Pulmonary diseases are an important social and healthcare issue, related to their high prevalence and associated morbimortality. In recent years, our group has worked on different topics related to lung diseases, as it is reflected in our publications from studies carried out in collaboration with other research groups.

General objectives:

1. Promote research on lung diseases.

2. Promote quality of care in the therapeutic approach to patients with chronic lung diseases.
3. Promote transfer of lung disease research.
4. Create new research lines in coordination with other research groups.

Research interests: The Pulmonology Department of La Princesa Hospital is part of the R+D Biomedicine Programme. HUP ConSEPOC-CM: Inflammation and hypoxia: mechanisms of COPD and SAHS development and progression. Several active clinical trials will be developed during next years on different respiratory diseases (COPD, asthma, idiopathic pulmonary fibrosis, bronchiectasis and cystic fibrosis).

Additionally, persistent COVID is currently a new disease with a major impact on public health in Spanish society. In Spain, it is estimated that between 400,000 and 800,000 people suffer or will suffer from persistent COVID, as 10-16% of patients still have symptoms

one year after overcoming acute COVID. For this reason, our team has also been interested in studying the long-term sequelae of persistent COVID.

Several projects received grants from the Spanish Society of Respiratory Pathology (SEPAR) and other funding entities.

Plan of actions for 2020-2022

- Further develop, maintain and strengthen the research group on chronic respiratory conditions at the Health Research Institute Princesa (IP).
- Complete the M-BREATH study (COPD Monitoring

and Biomarkers) funded by the European Union Horizon 2020 programme.

- unCoVer Project: Unravelling Data for Rapid Evidence-Based Response to COVID-19. Funded by Horizon 2020.
- TackSHS Project: Tackling secondhand tobacco smoke and e-cigarette emissions: exposure assessment, novel interventions, impact on lung diseases and economic burden in diverse European populations. Topic: Global Alliance for Chronic Diseases. Prevention and treatment of lung diseases. Reference: HCO-06-2015.



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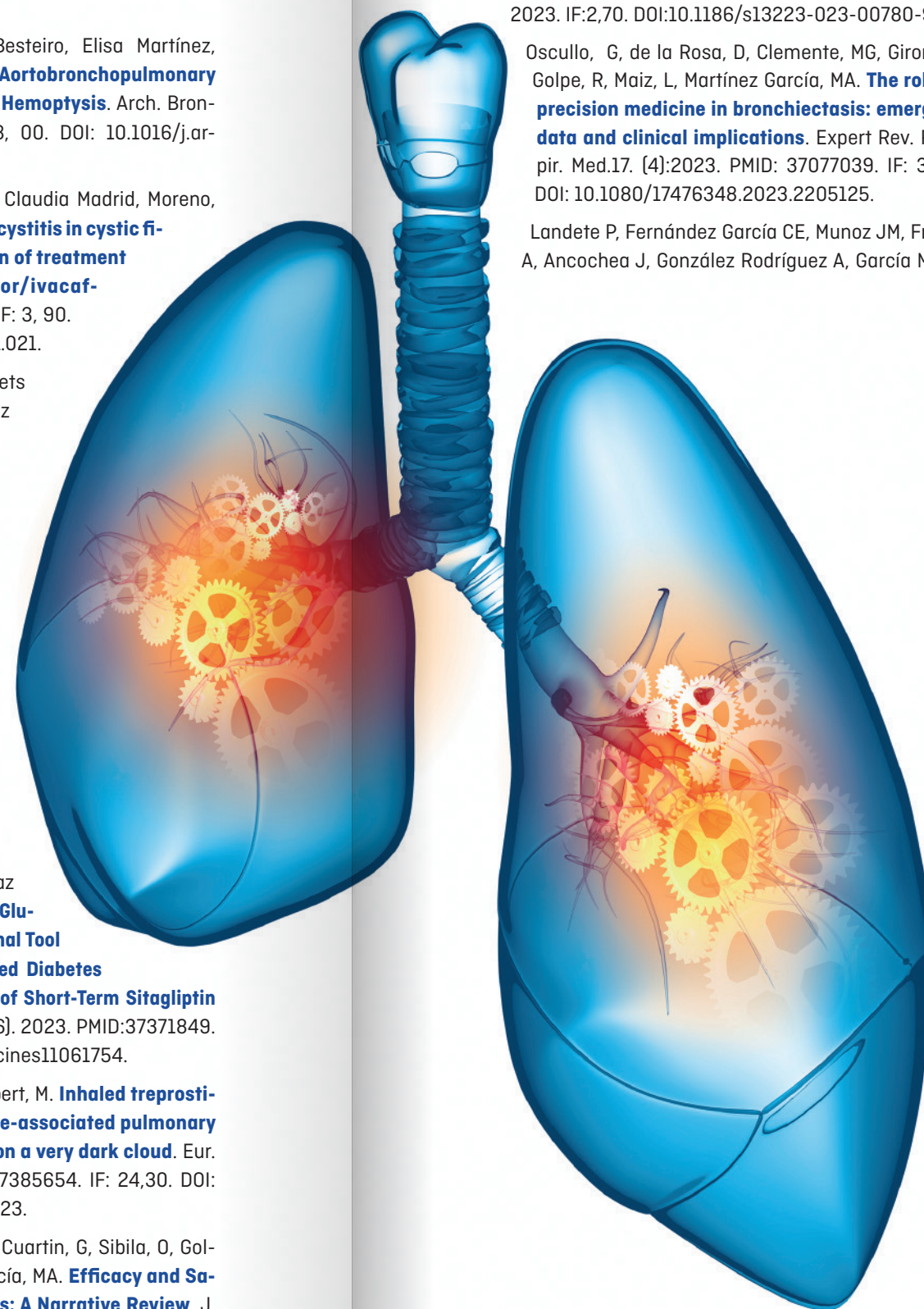
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Line 1.8

Inflammatory response in hepatic diseases

GROUP 24



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RESEARCH INTEREST

Eosinophilic Esophagitis (EoE) is a chronic inflammatory disease of the esophagus with an immune-allergic basis. EoE is clinically characterized by symptoms of esophageal dysfunction, and histologically by an eosinophil-predominant inflammatory infiltrate. In the absence of treatment, the natural history of EoE consists in a progressive fibrous remodeling of the organ into the formation of strictures that reduce the esophageal caliber and aggravate the symptoms. Currently, endoscopic biopsies are the only reliable method to diagnose the disease and monitor the response to therapy.

In this project, we aim to analyze changes in the expression of genes and proteins in esophageal biopsies of adult patients with EoE, induced after being treated as recommended in European clinical practice guidelines, and compared with healthy subjects. Changes in the expression of mRNA (mRNAseq), proteins (proteomic) and in the secreted proteins (multiplexed Elisa) will be measured, and lymphocyte populations in both esophageal tissue and peripheral blood of EoE patients will be characterized (flow cytometry). Data obtained by these

massive analysis techniques, together with markers of the progression of esophageal fibrosis and alteration in esophageal distensibility (as determined by EndoFLIP) will allow us selecting a series of candidate markers related to the presence of the disease, its inflammatory activity and fibrotic changes, as well as predicting response to treatment. As a final aim, we will try to define a set of biomarkers to be further studied in a larger cohort (validation).

SECONDARY:

Gastroesophageal reflux disease (GERD) is the most prevalent gastrointestinal disorder in industrialized countries. Key mechanisms of disease include abnormaloesophagogastric junction structure and function, and impaired oesophageal clearance. Recent studies have challenged the traditional notion that reflux esophagitis develops only when esophageal surface epithelial cells are exposed to chemical injury from refluxed acid. In this line, we wanted to characterize lymphocyte populations in both esophageal tissue and peripheral blood of GERD patients by multiplexed flow cytometry. Data obtained by these techniques will be related to the presence of the disease and its inflammatory activity.

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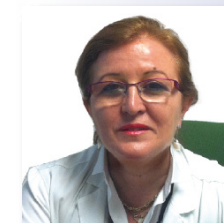
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Line 1.8

Inflammatory response in hepatic diseases

GROUP 23



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RESEARCH INTEREST

During the last years our research group has been particularly focused on identifying non-invasive prognostic biomarkers of chronic liver disease (CLD) progression to cirrhosis and hepatocellular carcinoma (HCC).

HCC is the second leading cause of cancer death worldwide and has a high mortality rate because it is only diagnosed in advanced stages, at which available treatments are no longer effective. Therefore, new tools that improve the diagnosis and treatment of HCC patients are needed.

The altered expression of angiogenic and fibrogenic-related factors during the course of CLD to HCC may provide a valuable tool for the non-invasive assessment of liver fibrosis, key for clinical decision-making. Among other clinical and demographic variables, we found that peripheral levels of angiopoietins significantly correlated with hepatic fibrosis in patients with chronic hepatitis C (CHC). Such finding allowed us to develop a novel index for non-invasive evaluation of liver fibrosis, AngioScore, which was further validated in an independent series of patients. In addition, our group reported a significant increment of TIE2-expressing monocytes (TEMs) in the peripheral blood of patients with CHC. Monocytes, essential precursors of antigen-presenting cells, notably contribute to the pathogenesis of chronic inflammatory diseases and cancer. We proposed that chronic expansion of TEMs, which are characterized by their marked proangiogenic properties and notable immunosuppressive nature, might prevent proper im-

mune response and promote mechanisms that cause liver damage. The expression of the angiopoietin receptor Tie2 in the surface of this subtype of monocytes might serve as useful "tag" for the non-invasive monitoring of CLD progression in a simple blood test. Moreover, we believe that a more in depth understanding of TEM regulation can lead to important therapeutic advances. Interestingly, in the meantime, other authors described that TEMs might work as a useful cellular diagnostic and prognostic biomarker for HCC. Furthermore, we have also characterized the significance of certain genetic variants of HDACs and other angiogenic factors, receptors and mediators, in relation to fibrosis progression.

Therapeutic options and diagnostic procedures in hepatology have quickly advanced during the last decade, in particular, the management of viral hepatitis. Hepatitis C has become a curable disease with a sustained 99% response using direct-acting antiviral therapeutic regimens. With the increasing number of individuals with diabetes and obesity, non-alcoholic fatty liver disease (NAFLD) is becoming increasingly prevalent, affecting more than one-quarter of adults in the world. In addition to liver cancer, we have other research lines:

- Actions for micro-elimination of HCV infection.
- Interaction between DAA for Chronic Hepatitis C infection and hepatocellular carcinoma.
- Non invasive evaluation of non alcoholic fatty liver disease.
- Chronic cholestatic liver disease: Primary Sclerosing Cholangitis and Primary Biliary Cholangitis.



PUBLICATIONS

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Line 1.9

Mechanisms and mediators of endocrine diseases

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RESEARCH INTEREST

Our current and future work involves different research fields in endocrine diseases. In the last years we have discovered that patients with AITD present altered populations of regulatory T cells (Treg), augmented Th17 cells, a reduced number of Tr1 regulatory cells and abnormalities in NK cell subset levels [Endocrine 2016 51(3):478-89; J Clin Endocrinol Metab. 2017 Feb 1; 102(2):672-680; J Clin Endocrinol Metab. 2018 103: 3359 -3367; J Clin Endocrinol Metab., 2020, Vol. 105, No. 11, 1 -11], and the description of alterations in Tr1 lymphocytes in patients with type 2 diabetes mellitus [J Endocrinol Invest. 2024 Jan 6. doi: 10.1007/s40618-023-02250-w].

The group's leaders also participated as principal investigators in a collaborative project with the departments of Immunology, Rheumatology and Dermatology of Hospital la Princesa in the study of immunoregulatory molecules and miRNAs in different immune-mediated inflammatory diseases (IMID). We have investigated new predictive biomarkers (immuno-regulatory molecules) of IMID severity and responsiveness to biological

therapies in different IMIDs including rheumatoid arthritis, psoriasis, inflammatory bowel disease and AITD [BIOIMID Project-PIE13/00041, Journal of Autoimmunity 111 (2020) 102472]. In these projects, we have developed novel analytical approaches using exosomes and microvesicles as targets containing these relevant biomarkers. We have demonstrated that microvesicles may have a relevant role in AITD as modulators of the immune response, mainly through the inhibition of Treg cell differentiation and the induction of Th17 cells [J Clin Endocrinol Metab. 2015 Dec;100(12):E1531-9]. Furthermore, we have identified a 5-miRNA signature that could be an independent risk factor for developing AITD and for predisposition to a worse prognosis in Graves' Disease (GD) patients [J Clin Endocrinol Metab. 2018 Mar 1;103(3):1139-1150]. By integrating miRNA and mRNA data we have observed, for the first time, the important role of genes involved in cilia regulation in the etiopathogenesis of AITD [EBioMedicine. 2019 Dec;50:329-342]. Furthermore, we have discovered the importance of the role of HDAC9 in the altered function of the immune regulatory mechanisms observed in these patients [J Clin Endocrinol Metab. 2021 Oct 21;106(11):3213-3227]. The group also has a strong



collaborative record with specialists of thyroid disorders including Drs. Mercedes Robledo (Centro Nacional de Investigaciones Oncológicas [CNIO]), Pilar Santisteban and Susana Alemany (Instituto de Investigaciones Biomédicas Alberto Sols [IIBM]) in pathophysiology in projects from Programas de Actividades de I+D de grupos de la Comunidad de Madrid [S2010/BMD-2328 TIRONET-CM and TIRONET2 B2017/BMD3724] [J Clin Endocrinol Metab. 2018 Mar 1;103(3):1139-1150 and EBioMedicine. 2019 Dec;50:329-34; J Clin Endocrinol Metab. 2021 Oct 21;106(11):3213-3227]. In regard of the coronavirus pandemic we have documented cases of concurrent presentation of SARS-CoV-2 infection and GD [J Endocrinol Invest. 2021 Feb;44(2):387-388; Rev Endocr Metab Disord. 2020 Dec;21(4):495-507 and Rev Endocr Metab Disord. 2021 Jul 31;1-14.]. In this line we have recently obtained another grant from Comunidad de Madrid [iTIRONET P2022/BMD7379] together with M. Robledo and Fátima Al-Shahrour (from CNIC) and Hospital Ramon y Cajal (P. Valderrabano). This consortium provides the translational implementation of the basic research in AITD, resulting in approval of research projects, publications, exchange researcher programs and predoctoral & postdoctoral scholarships.

The group's second line of research is aimed to the study of thyroid eye disease (TED), also known as Graves' ophthalmopathy. TED is an autoimmune disease that often occurs as a secondary manifestation of Graves' disease, affecting to the thyroid gland. It is characterized by ocular symptoms such as exophthalmos, eyelid retraction, conjunctival edema and various visual function defects, which in severe cases can impair the visual function. Recently, Dr. Martínez Hernández was awarded with the SEEN Fellowship for Clinical Research in General Endocrinology and Metabolism. It is a multicenter project coordinated by the Hospital de La Princesa involving professionals from 8 different hospitals across 4 geographical nodes. Our aim is to gather a comprehensive collection of patient samples in order to search for biomarkers and predictors of the clinical involvement.

The third line of study is the search of novel biomarkers of diagnosis and aggressiveness that could have a role in the proliferation and metastatic capacity of neuroendocrine tumours. In line with this research, we have found that PD-1 expression is detected in a small but significant proportion of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) and that the presence of this receptor is significantly associated to increased malignancy [Scientific Reports (2018) 8:17812]. Furthermore, we have confirmed that mechanisms that increase nutrient uptake, such as the ami-

noacid transporters LAT-1 and GLUT-1, are increased in GEP-NETs, which might be related to their proliferation and metastatic capacity [Cancers 2020, 12, 2968]. We have also evaluated whether the body composition could be used to as a predictor for poor prognosis in these patients. We found that loss in normal-density muscle and increase in low-density muscle during follow-up are independently associated with an increase in mortality [Cancers 2022, 14.5189.10.3390/cancers14215189], also concluding that nutritional management during the follow-up should be mandatory for these patients.

The group is also part of the CIBERER (clinical group GCV14/ER/12) working on pituitary tumours. Our group also leads the Spanish Molecular Registry of Pituitary Adenomas (REMAH) with 1,400 registered patients. This strategy allows for comparative and relational analysis between the molecular profile of the different types of adenoma and the clinical phenotype of patients, which may provide a better understanding of the condition and potentially help in treatment selection. Regarding this research line, we also closely participated in a recently obtained fellowship of personalized medicine from the ISCIII-PMP program (ACROMICS project PMP22/00021, funded by ISCIII). This project is coordinated by Dr. Manel Puig from Germans Trias i Pujol Research Institute and has national collaborators with extensive experience in acromegaly including our group in Madrid, Dra. Susan Webb from Barcelona (Institut de Recerca de l'Hospital Sant Pau), Dr. Ignacio Bernabeu and Dra Clara Alvarez from Santiago de Compostela (Health Research Institute of Santiago de Compostela), Dr. Antonio Picó from Alicante (Health and Biomedical Research Institute of Alicante), Dr. Elias Delgado from Asturias (Health Research Institute of the Principality of Asturias), Dr. G. Serra from Balearic Islands (Son Espases University Hospital) and Dr. Cristina Lamas from Albacete (Albacete University Hospital Complex). In this project, we collaborate with the Bioinformatic department (Dra.Fátima Sánchez Cabo) of the National Center for Cardiovascular Research (CNIC, Madrid). In turn, this same project will include its data in the national platform IMPaCT-Data, in the area of predictive medicine. This translational research consortium aims to develop new tools to provide personalized diagnosis and treatment to people suffering from pituitary tumours. This knowledge will allow us to better understand this condition and adopt more appropriate decisions on the treatment and follow-up of patients with pituitary tumours.

Moreover, our group has recently discovered a novel diagnostic marker for aggressive tumour behavior

prediction in pituitary tumours. A European patent has been requested for this biomarker as a method for diagnosis and prognosis [EP22382079]: "In vitro method for the diagnosis and/or prognosis of pituitary neuroendocrine tumours". Inventors: Rebeca Martínez Hernández and Mónica Marazuela (main inventors), Ana Serrano, Miguel Sampedro, Ancor Sanz. Registration date: 31/01/2022. Rights holder entity: Universidad Autónoma de Madrid / Instituto Investigación La Princesa.

The fourth line focuses in the assessment of big data analysis on the settlement of diabetic and nutritional



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diseases. In this context, several bioinformatics projects in our laboratory analyses big data sets of the electronic health registries including the assessment of radiologic images. Recently, we have published some articles [BMC Med. 2024, PMID: 38273326; Endocr Pract. 2024 Apr;30(4):372-379.PMID: 38307457; Acta Diabetol. 2024 Mar;61(3):343-350. PMID: 37930420; Endocrinol Diabetes Nutr (Engl Ed). 2023 Oct;70(8):548-555.PMID: 37858412] and a grant for new the development of new technologies on diabetes have been awarded to our center by the Spanish Society of diabetes on 2024.

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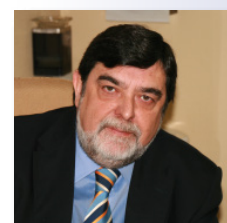




Line 1.10

Children's development (obesity and growth)

GROUP 26



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RESEARCH INTEREST

How the genetic make-up of an individual interacts with the early maternal/neonatal and postnatal environments to culminate in obesity and its secondary complications, is being studied with both clinical and basic approaches. Genetic studies are performed to identify mutations in genes involved in monogenic obesity, to identify new candidate genes and to analyze polygenic and epigenetic causes of obesity. Diverse new candidate genes have been identified and are being further investigated, as well as the interaction genotype/phenotype and ethnic influences. Metabolomic studies are underway to better understand the processes involved in the development of insulin resistance and type 2 diabetes in obese children. Metabolites that may be involved in this process have been identified and will be further studied. In addition, it appears that this process may differ between males and females even prepubertally and this will be further explored. We have recently identified a new monogenic cause of

pathological human growth that courses with skeletal abnormalities. The underlying cause is due to affectation of the insulin-like growth factor (IGF) system and this new syndrome will be thoroughly analyzed and new concepts of the physiological functioning of the IGF system pursued.

Animal models are employed to analyze how poor maternal and/or neonatal nutrition, stress or changes in specific hormones during neonatal life affect adult metabolism, with special attention focused on the differential responses of males and females. Studies analyzing the effect of increased central leptin levels on insulin signaling in the CNS and adipose tissue demonstrate a relationship between insulin resistance, hypothalamic inflammation and energy homeostasis. Hypothalamic glial cells are a main focus of investigation for their newly recognized role in metabolic control. We have shown them to respond to weight gain and metabolic hormones such as leptin. Current interest includes analysis of glial responses to specific nutrients and how this could influence the metabolic out-



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ty being different between males and females. Future studies are planned to determine the role of astrocytes in mediating the protective and/or detrimental responses to high fat diet intake on neurodegeneration.

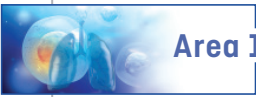
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Line 1.11

Metabolic syndrome and vascular risk

GROUP 5



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RESEARCH INTEREST

Nonalcoholic fatty liver disease (NAFLD) is an increasingly common chronic liver disease around the world with a diverse histopathological spectrum ranging from simple steatosis without significant inflammation to steatohepatitis (NASH) with varying stages of fibrosis and, ultimately, cirrhosis and hepatocellular carcinoma. It is well known that NAFLD occurs more frequently in obese and diabetics, being currently considered as the hepatic manifestation of the metabolic syndrome. Although the molecular mechanisms involved in the pathogenesis of NAFLD and progression to NASH remain incompletely defined, most investigations indicate that insulin resistance plays a pivotal role in NAFLD setup. Since NASH is becoming one of the most frequent causes of cirrhosis and liver transplantation in the developed countries, it is crucial to identify populations at risk for NASH in order to prioritize the diagnostic and therapeutic interventions on those patients with an increased risk for liver disease progression.

Our group seeks three main research lines for the next five years. 1) To unravel the molecular mechanisms involved in the pathogenesis of NASH searching for potential therapeutic targets. We are exploring the role of autophagy in the development of NASH. We recently reported that autophagic flux is impaired in hepatocytes from NASH patients and murine models of NASH and we are, therefore, proposing to investigate in the next future whether therapies aimed to restore the autophagic flux might prevent or attenuate the progression of NAFLD. We are also addressing the role of intermittent hypoxia in the pathogenesis of NAFLD by analyzing the expression levels of hypoxia-inducible factors 1 and 2 in liver biopsies and serum of NASH patients and murine models of NASH as well as the impact of hypoxia on the mitochondrial function in human hepatocytes under experimental conditions of lipid overload. 2) Identification of biomarkers able to be used for noninvasive diagnosis of NASH. We have shown that genetic variants of SLC2A1 are associated with NAFLD and that circulating levels of soluble CD36 is an independent factor associated with advanced steatosis in NAFLD but not in



patients with chronic hepatitis C virus (HCV) infection. More recently, we have reported that the combination of ultrasound and HOMA score is useful for noninvasive diagnosis of patients with NASH. We are now pursuing diagnostic tools based on ELISA multiplex using proteins of pathogenic relevance in chronic liver diseases. 3) Impact of the new direct-acting antivirals on carbohydrate and lipid metabolism in patients with chronic hepatitis C treated with these highly effective antiviral drugs: Implications for the cardiovascular morbidity and mortality.

It is well known that chronic HCV infection is associated with insulin resistance and type 2 diabetes mellitus together with alterations in hepatic lipid metabolism. The discovery of new direct-acting antiviral agents has become a huge advance in the treatment of HCV infection. Among them, sofosbuvir and other new antivirals

in combination with ribavirin has improved considerably the sustained virological response of HCV infection. However, little is known about their effects on carbohydrate and lipid metabolic profiles in patients treated with these new direct-acting agents and their potential mechanistic actions. On that basis, we propose to determine the effects of sofosbuvir and other direct-acting antivirals on HCV-induced metabolic complications such as insulin resistance, hyperglycemia and dyslipidemia. Moreover, the impact of therapy with sofosbuvir and other related agents on metabolic disturbances induced by the impairment of autophagic flux in HCV infection will be analyzed. In summary, we believe that our lines of investigation could shed light, in the next future, on key aspects for the pathogenesis and therapy of NAFLD and other chronic liver diseases as well as for the noninvasive diagnosis of NASH.

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Area 2 Translational neuroscience

- Line 2.1** Neuropharmacology and neuroprotection
- Line 2.3** Clinical pharmacology and pharmacogenetics
- Line 2.4** Diagnostic and therapeutic advances in affective disorders
- Line 2.5** Neurosurgery of epilepsy
- Line 2.6** Cerebrovascular diseases

Line 2.1

Neuropharmacology and neuroprotection

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RESEARCH INTEREST

Neurodegenerative disorders like Alzheimer’s disease, Parkinson’s disease, amyotrophic lateral sclerosis and stroke represent an appalling cost, both in financial and human terms. Treatments for neurodegenerative diseases are destined to become the most significant health challenge for this generation. To date, no therapeutic strategy has proven effective and millions have been invested in therapeutic trials that have failed. There is therefore an urgent and pressing need to identify novel therapeutic strategies that might protect or rescue vulnerable neurons in these dreadful diseases. In this context, our main research lines are:

1. Identification of therapeutic targets to develop new drugs for neurodegeneration. We are particularly interested in understanding how oxidative stress, neuroinflammation and changes in the autophagic flux participate in neurodegeneration, in order to develop pharmacological interventions to regulate these pathological conditions.

2. Development of in vitro a in vivo preclinical models that better mimic the human neurodegenerative disease. Availability of preclinical models that better represent the human disease will greatly improve translation of preclinical results to human disease.
3. Search of novel therapeutic strategies for neurodegeneration based on medicinal chemistry, combination therapy and drug repurposing. Since oxidative stress, neuroinflammation and impairment of autophagy have been implicated in neurodegeneration, impacting on several of these processes with multitarget compounds or combination of drugs with complementary mechanisms of action is sought, to have better therapeutic profile than just impacting on a single target. For example, Nrf2 inducers combined with scavenger effect, the inhibition of several enzymes related to neurological disorders and agonist of the nicotinic acetylcholine receptors are currently being developed in our group.



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Line 2.1

Neuropharmacology and neuroprotection

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RESEARCH INTEREST

Acute brain injuries, such as stroke and traumatic brain injury, account for 10% of deaths and are the leading cause of disability worldwide (GBD 2013 Mortality and Causes of Death Collaborators, 2015). The pathophysiology of acute brain injuries is complex and multifactorial and, currently, it is difficult to treat pharmacologically and represent an unmet need at clinical level. In recent years, inflammatory processes (pronounced in this type of pathologies) have become the main agents that contribute to aggravate acute brain injuries and, therefore, have become very promising therapeutic targets.

Our group focuses on studying the role of inflammation and immunity in the pathogenesis of these diseases. Specifically, we study the mechanisms that control the activation of the innate immune system and its application to the search for new therapeutic targets and new prognostic / diagnostic biomarkers in stroke, traumatic brain injury and neurodegenerative diseases.

1. Study of the mechanisms that control the activation of the innate immune system.

Inflammasomes are multi-protein molecular platforms involved in the activation of caspase-1. After activation of caspase-1, interleukins pro-IL-1 β and pro-IL-18 are processed and released to initiate the inflammatory process. NLRP3 is the only NOD receptor (NLR, NOD-like receptors) that responds to both danger-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs). NLRP3 is activated in response to a wide variety of infectious stimuli or cellular stress caused by different signs of sterile danger, such as high concentrations of extracellular ATP, oxidative

stress, and β -amyloid aggregates. Our main work focuses on studying the transduction of the signals that activate inflammation and, specifically, the participation of mitochondria in this process.

2. Search for new therapeutic targets to treat acute brain injuries.

The mechanisms studied in line 1 are validated in "in vitro" and "in vivo" models of cerebral ischemia (transient middle cerebral artery occlusion, tMCAO model) and traumatic brain injury (closed head injury model).

3. Search for new diagnostic/prognostic biomarkers of inflammatory origin.

We study the potential role of new biomarkers in samples of traumatic brain injury patients and we try to validate them using the models described in line 2.



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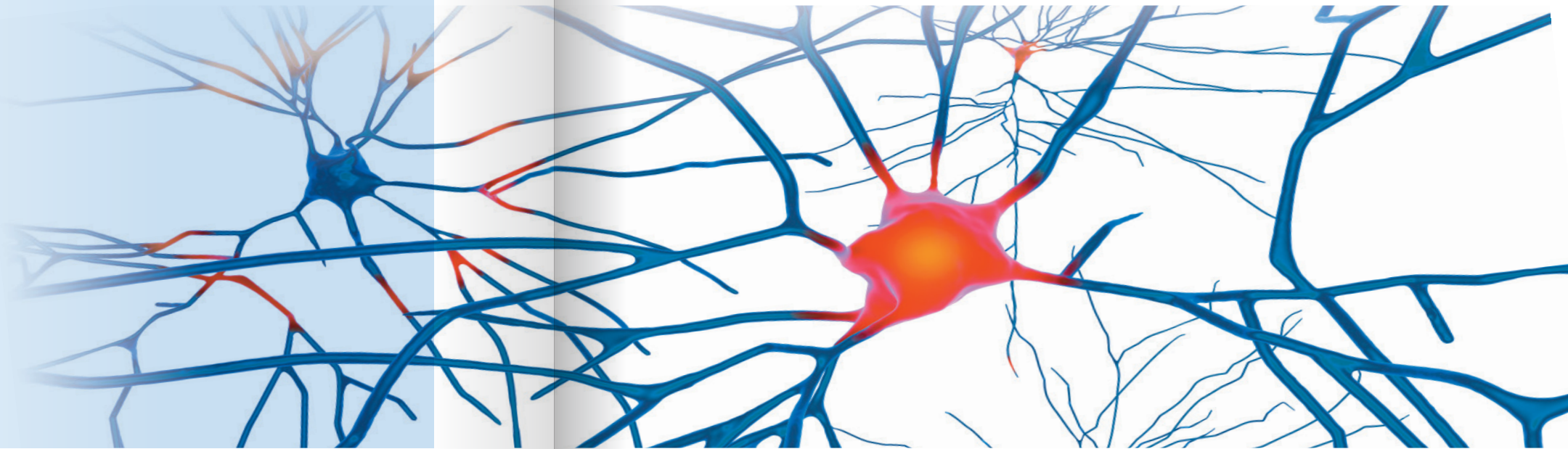
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Line 2.3

Clinical pharmacology and pharmacogenetics

GROUP 32



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RESEARCH INTEREST

The aim of the research conducted by this group is to increase pharmacogenetic, pharmacokinetic and pharmacodynamic knowledge of drugs in order to predict patients' response in terms of effectiveness and safety. Our group has extensive experience in conducting phase I, II and III clinical trials. We have a clinical trials unit (UECHUP), with capacity for 18 subjects on the 7th floor of the Hospital Universitario de la Princesa. The clinical trials conducted include phase I clinical trials (e.g. bioequivalence or first in human trials), and clinical trials in patients to evaluate the effectiveness of new drugs, in collaboration with various specialists at the hospital and with primary care. Our group conducts more than 18 clinical trials each year, and this number

is expected to increase due to demand from the pharmaceutical industry. Last years, several clinical trials on the vaccines were conducted in our unit.

The group's research focuses mainly on the pharmacogenetics of several drugs prescribed for the treatment of various diseases, so that eventually this knowledge could help physicians to prescribe the best treatment for each patient in a personalised way. This research is focused on several therapeutic areas such as: pain, cardiovascular diseases, neuropsychiatry, gastroenterology, endocrinology and dermatology. In 2023, 613 patients benefited from pharmacogenetic testing.

We have also implemented pharmacogenetic testing through OpenArray using a customised chip that can simultaneously analyse 180 SNPs located in 63 different genes.

This technology has enabled us to significantly increase our portfolio of available pharmacogenetic tests to support physicians in prescribing medicines. Another important line of research focuses on therapeutic drug monitoring, mainly for antipsychotics and tyrosine

kinase inhibitors. Ten funded projects were active in 2023. In addition to projects funded in previous years, Francisco Abad Santos was awarded with 1 new grants in 2023.



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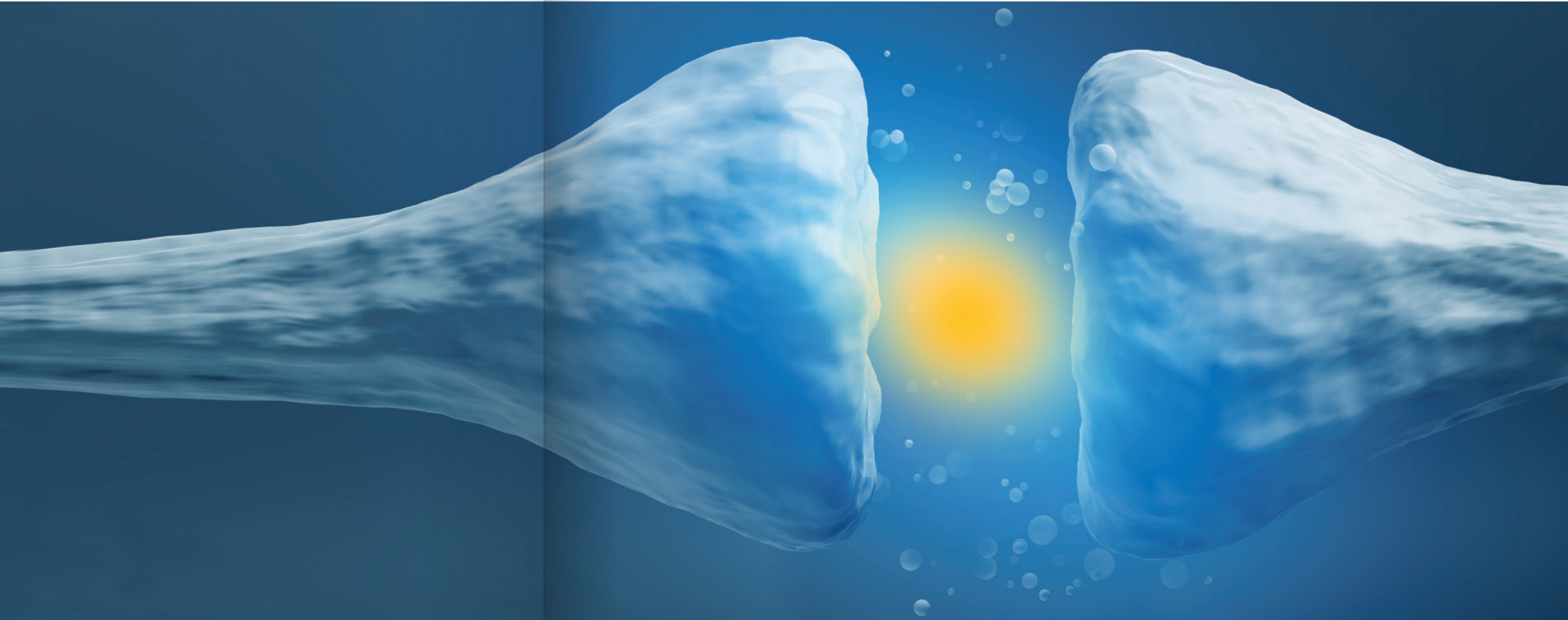
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Line 2.4

Diagnostic and therapeutic advances in affective disorders

GROUP 33



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 Iosune Torio Palmero
 María Cabello Salmerón



RESEARCH INTEREST

Our team has been devoted to researching the nosology of mental disorders, the epidemiology of mental disorders in general population, the study of the efficacy and efficiency of clinical interventions in affective disorders and the assessment of the health status, quality of life and well-being by means of analysing large population's data.

On the one hand, in 2017 we have maintained some projects and research lines: we have sustained our collaboration with the WHO and have contributed to the

revision of the International Classification of Diseases 11th edition (ICD-11). Furthermore, we have intended to contribute to the promotion of mental health not only at a European level but also in Low and middle income countries (LAMICs) and focused in improvement of health systems. We have participated in an international project (EMERALD project) funded by the EU aimed to enhance mental health in LAMICs by means of improvement of all the systems related to health care.

Following H2020 strategic plan, we have consolidated our research line on active aging and wellbeing. We have been working in the project ATHLOS - Ageing

Trajectories of Health: Longitudinal Opportunities and Synergies, and PATHWAYS - Participation To Healthy Workplaces And inclusive Strategies in the Work Sector. In addition, we have been conducting a multi-approach study for the identification of the available interventions for targeting psychosocial difficulties in major depression (meta-analyses and expert consultation) (MARATONE project).

Additionally, we have maintained our interest in the study of the environmental and genetic risk factors for the development of psychotic episodes (AGES-CM project).

On the other hand, we have been working on several new research projects:

- 1) "Trajectories on mental health, physical health and functioning: Third wave survey of a Spanish cohort of the adult population", which is aimed to carry out a third time point assessment to know trajectories of health in ageing people as well as recruiting new people to make generational comparisons.
- 2) "CIBERSAM cohorts about FEP cases and controls", which is aimed to create a common cohort from different existing cohorts with first episode patients and controls, and follow-up the common cohort at 5, 10 and 15 years.
- 3) "Emotional fluctuation in daily life. Ecological

analysis of depressive symptomatology in the general population" which is aimed to analyse the mood fluctuations throughout the day in a general population sample using mobile Apps.

- 4) "European Welfare Models and Mental Wellbeing in Final Years of Life", which is addressed to gather information on the components of wellbeing and welfare in people older than 80 years.
- 5) "Peripheral oxidative stress and inflammatory markers in Major Depressive Disorder", focuses on finding biological markers in Major Depressive Disorder.
- 6) "Metabolic Dysfunctions associated with Pharmacological Treatment of Schizophrenia (TREATMENT)" in which we evaluate how short-term antipsychotic drug responses impact long-term metabolic control to identify and validate biomarkers with clinically predictive value for targeting drug induced metabolic dysfunctions.
- 7) "Psychiatric Ratings using Intermediate Stratified Markers (PRISM)", whose overall objective is to develop a quantitative biological approach to the understanding and classification of the endophenotypes that contribute to neuropsychiatric diseases, to accelerate the discovery and development of better treatments for patients with Alzheimer and Schizophrenia.



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Line 2.5 Neurosurgery of epilepsy

GROUP 34



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RESEARCH INTEREST

Epilepsy, movement disorders and some psychiatric pathologies are among the main targets for functional neurosurgery. They share several properties that make them interesting for our research line.

Drug-resistant epilepsy affects 20-30% of patients suffering epilepsy worldwide. One of the most efficacious treatments is surgery, including resective techniques and neuromodulation in different forms. Presurgical evaluation usually requires the use of very deep studies (e.g. morphological and functional MRI) or invasive techniques (intracranial electrodes), which are also used during treatment (electrocorticographic recordings or extracellular recordings for Deep Brain Stimulation -DBS). In the same way, several pathologies affecting basal ganglia need different ancillary tests to characterize the illness (genetic, nuclear medicine, morphological MRI) and to carry out the treatment (DBS).

Altogether, this set of human illness offers a unique opportunity to study the underlying pathophysiological processes. Understanding these processes is the first step to its rational treatment.

Our research line is integrated by clinical researchers which are part of national reference units for the treatment of refractory epilepsy and surgical treatment of movement disorders. Therefore, our scientific interests include all aspects around functional neurosurgery and, especially, epilepsy and basal ganglia pathologies.

The topics we are working on include the following:

- a) Identification of basal ganglia subnuclei by extracellular recording.
- b) Physiopathology of somatosensory thalamus, by means of somatosensory evoked potentials, electrically elicited.
- c) Connectivity in epilepsy. To do that, we are studying diffusion tensor imaging and fractional anisotropy, as well as electrophysiological recordings acquired by means of scalp or intracranial recordings.
- d) Genetics and epi-genetics in epilepsy.
- e) Quantified EEG (qEEG) to use as biomarker for different pathologies. Among those fields specially targeted by this technique are patients in Intensive Care Units and neurological and psychiatric illness.
- f) Cortico-cortical connectivity, especially for language function.



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Line 2.6

Cerebrovascular diseases

GROUP 35



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Álvaro Ximenez-Carrillo Rico
Teresa Carreras Rodríguez
Mónica Sobrado Sanz
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Florentino Nombela Merchán
Gemma Reig Roselló
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RESEARCH INTEREST

Stroke and Cerebrovascular Diseases

- Predictive models in stroke for the search of diagnostic and prognostic markers:
- Application of machine learning techniques and search for plasma and clinical scale biomarkers.
- Acute phase treatments: Interventional neuroradiology and emerging therapies. Strategies to improve the selection of patient candidates.
- Neuroprotection: Biomolecular markers of ischemia and new therapeutic targets and strategies.
- Primary and secondary stroke prevention: Detection of atrial fibrillation using a new ECG monitoring device based on biomedical textiles (wearables). Identification of risk profiles.
- Population-based health services delivery / stroke code system Telemedicine

Headaches

- Study of the response variables to botulinum toxin and anti- CGRP therapies
- Glutamate and headaches
- Non-invasive outpatient monitoring of biometric and biophysical variables as a method for prediction of migraine crises.

Neuromuscular diseases:

- Immunopathogenesis of myasthenia gravis
- Multiple Sclerosis
- Outcome markers and new therapies
- Immunopathogenesis of multiple sclerosis and monoclonal antibody therapies.
- Therapeutic compliance of first line disease-modifying therapies in patients with multiple sclerosis.



Cognitive impairment and dementia

- Detection of early Alzheimer's disease and search for new therapeutic targets
- Language disorders of neurodegenerative origin
- Management of behavior alteration in the context of patients with dementia

Movement Disorders

- Parkinson disease in young patients
- Parkinson disease. Follow-up and control helped by new technologies

Epilepsy

- Adult-onset temporal lobe epilepsy
- Drug-refractory epilepsy
- Genetic alterations in refractory epilepsy
- Non-convulsive epileptic status
- Neuroimaging in the emergency epileptic patient

Translational Biomarker Research in Neurological Disorders

- Identification, multimodal analysis and validation of clinical, neuroimaging and serum biomarkers to predict disease course and treatment response in neurological disorders



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Area 3 Advanced therapies and individualized medicine

- Line 3.1** Prognostic and predictor markers in autoimmune diseases
- Line 3.2** Esophagogastrintestinal inflammatory diseases
- Line 3.3** Progenitors and cell therapy
- Line 3.4** Advanced therapies in oncohematology
- Line 3.5** Biological, cellular and molecular monitoring in oncohematology
- Line 3.6** New diagnostic and therapeutic advances in cardiovascular diseases
- Line 3.7** New therapies in infectious pathologies
- Line 3.8** Individualized medicine in solid tumors



Line 3.1

Prognostic and predictor markers in autoimmune diseases

GROUP 36



Isidoro González Álvaro
Head of laboratory



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RESEARCH INTEREST

The main goal for our group is personalized medicine in the field of autoimmune/inflammatory rheumatic disorders (mainly rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus, giant cell arteritis and scleroderma). Our efforts are focused on providing new knowledge about two unmet needs for rheumatologists: severity biomarkers and predictors of response to disease modifying anti-rheumatic drugs, either synthetic or biological. For the last five years, to achieve these objectives, we have consolidated our collaborations both at a local level in our Institute, as well as, at national and international levels.

Regarding the first, in 2013 we were involved in the development of BiolMID project that was granted by the PIE program (Integrated Projects for Excellence at Health Research Institutes) from the Instituto de Salud

Carlos III (ISCIII). This is a project that intends to deepen in personalized medicine in the field of biological therapies for immune mediated inflammatory diseases. Although the project ended in 2018, our group remains including patients in the IIS-IP Biobank, in order to expand the sample collection to JAK-inhibitors.

On the other hand, we maintain an intense collaborative effort with groups of the Network of Inflammatory Diseases (REI; RD21/0002), which belongs to the RICORS program of the ISCIII. Our research has mainly focused on the detection of prognostic and cardiovascular risk factors in rheumatoid arthritis, as well as the study of security aspects in biological therapies. On the other hand we have open our collaboration to the understanding of mechanism of action of methotrexate (Dra Amaya Puig Kröguer), as well as to the development of efficient biomarkers to predict response to these biological therapies (Dra. Rosario Lopez Pedrera and Dra

Cristina Ruiz Romero). In addition, many other rheumatologic diseases such as scleroderma, systemic lupus erythematosus, systemic vasculitis, osteoporosis, and osteoarthritis, are objectives of our research work. As a result of the intense activity of the group, some of its members have been called to participate in the elaboration of several documents establishing consensus guidelines for the rational use of biological therapies or imaging techniques in which the establishment of proper cost/benefit ratio is of great importance in the current economic situation.

During 2023, the COVID-19 outbreak still has marked

our research activity Deeping into the genetic factors involved in COVID severity and presence of SARS-Cov-2 viremia We have also studied the effect of MTX withdrawal in the effectiveness of COVID-19 vaccination.

For the next years, our efforts will continue to focus on discovering new biomarkers that may allow to more efficiently treat patients with immune mediated inflammatory disorders. Specially, with our involvement in the project SPIDeRR funded by the Horizon Europe program, coordinated by Prof. Rachel Knevel from Leyden University Medical Center, The Netherlands.



MAJOR GRANTS

Ahijón Lana, María. PROYECTO BECA SORCOM-MSD CONVOCATORIA AÑO 2022 PARA EL PROYECTO: "DESARROLLO Y VALIDACION DE UNA ESTRATEGIA PARA MEJORAR LA ADHERENCIA TERAPEUTICA EN ARTRITIS REUMATOIDE". PROY.BECA SORCOM-MSD.

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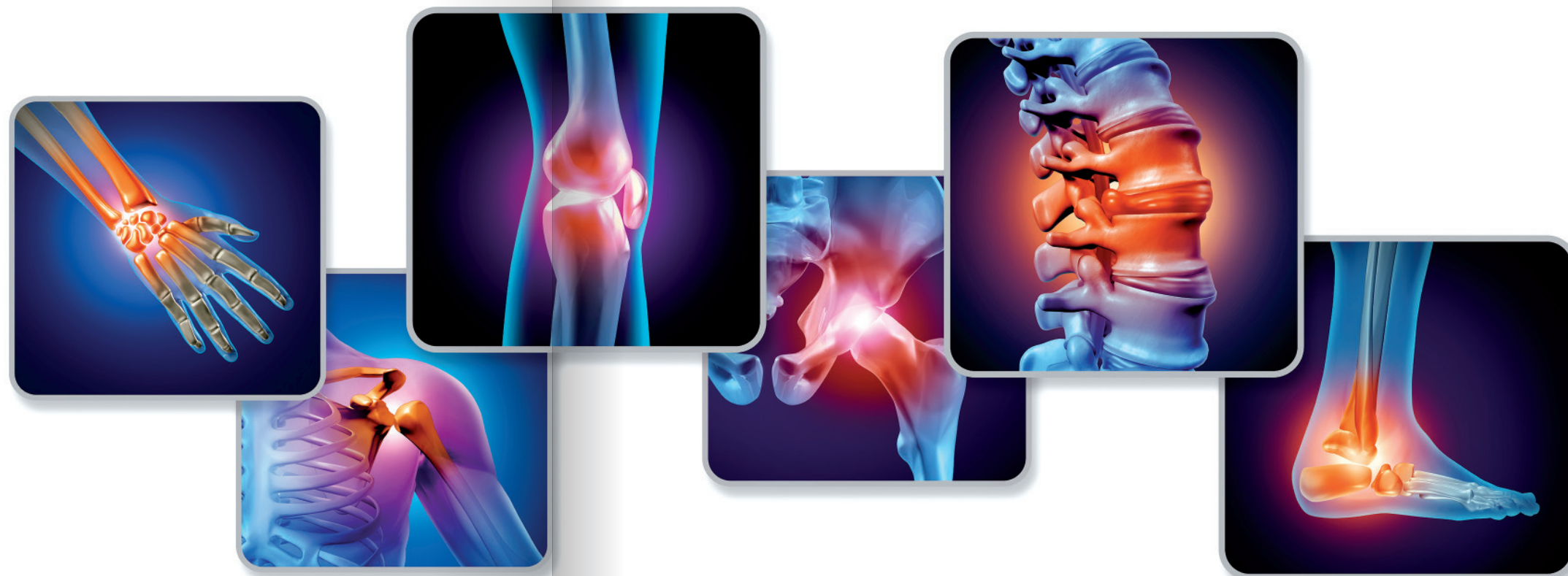
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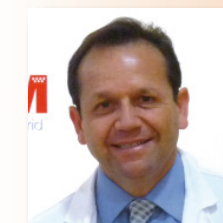
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Line 3.1

Prognostic and predictor markers in autoimmune diseases

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RESEARCH INTEREST

The investigation activity of the Group at present and for the following years is focused on:

- 1 Immune-mediated inflammatory diseases (IMID), particularly including psoriasis, atopic dermatitis and hidradenitis. The main lines of investigation are:
 - a) Immunoregulatory molecules as biomarkers predicting response to biological therapies and disease severity in IMIDs. These are a group of diseases that display inflammation as a major pathogenic mechanism. Their long-term impact has been alleviated by the implementation of biological therapy. Despite the growing knowledge on the etiopathogenesis of these diseases and the marked improvement in their management represented by biologic therapy, markers of the severity of the disease or to predict whether patients will be refractory to treatment are lacking. We are searching for new predictive biomarkers of IMID severity and responsiveness to biologics; b) Gene Expression Profile in patients with IMIDs c) Epigenetic biomarkers as predictors of therapeutic response to biologic drugs in psoriasis; d) Immunoregulatory molecules and their therapeutic potential. We investigate

the possible role of GADD45, ICOSL, TSP-1, and galectins in the immunopathogenesis of psoriasis, and the possibility of finding new therapeutic targets for the treatment of this disease; e) Survival analysis of conventional systemic therapies and biologics in psoriasis; f) Identification of Copy-Number Variants associated with the risk of developing psoriasis and psoriatic arthritis, using a genome-wide analysis approach; g) Study of optimization strategies (dose reduction, increase of the administration interval) in the treatment of moderate-to-severe psoriasis with systemic agents; h) Regulation of CXCL12 and RAPTOR by novel miRNAs and their role during the inflammatory process in Psoriasis; i) Integrative study of systemic inflammation in chronic inflammatory skin diseases and its association with cardiovascular disease.

- 2) Eczematous dermatitis. Study on the prevalence of allergens as responsible for allergic contact dermatitis in the Spanish population
- 3) Connective Tissue Diseases. Determination of the association of myositis-specific autoantibodies and myositis-associated autoantibodies with clinically amyopathic dermatomyositis.
- 4) Photobiology. Studies on epidemiology, clinical phenotypes, and photobiology of solar urticaria.



MAJOR GRANTS

Daudén Tello, Esteban; de la Fuente Flores, Hortensia. Estudio integrativo de la inflamación sistémica en Dermatitis Atópica e Hidradenitis Suppurativa y su asociación con la enfermedad cardiovascular. FIS.21/01583. Instituto de Salud Carlos III.

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Line 3.2 Esophagogastrointestinal inflammatory diseases

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Ana Isabel Garre Vázquez
María José Beceiro Pedreño
María Chaparro Sánchez
Almudena Durán Vegue



RESEARCH INTEREST

The Gastrointestinal Inflammatory Diseases Group focuses mainly on the understanding and management of Inflammatory Bowel Disease and *Helicobacter pylori* infection. The Group's Clinical and epidemiological research area is specialized in coordinating large-scale collaborative networks of Gastroenterologists from over 100 hospitals in Spain, over 300 hospitals in Europe, and many others around the world.

The Translational research area leads multiple projects in collaboration with several Services at Hospital Universitario de La Princesa (Immunology, Pathology, Microbiology, Clinical Pharmacology, Pharmacy, Rheumatology, Dermatology, Neurology, Anaesthesia, Haematology, etc.), Coagulopathies and Haemostasis Disorders Research Group at the Hospital Universitario La Paz, Organic Chemistry Department at the

Complutense University, CIC BioGUNE (Proteomics Platform, Precision Medicine and Metabolism Lab and Genome Analysis Platform), Metagenomics Platform at CIBER-IBIMA, the Galician Genomics Foundation, Bioinformatic Unit at National Center for Cardiovascular Research (CNIC) (part of the IMPaCT-Data Science Infrastructure), the National Center for Oncology Research (CNIO), the Asturian Institute of Dairy Products (IPLA-CSIC), the Institute of Food Science Research (CIAL-CSIC) and the Institute of Molecular Biology and Genetics (IBGM, University of Valladolid-CSIC). Internationally, the group leads projects with the National Institutes of Health of U.S.A. (U.S. N.I.H.) and the Karolinska Institute (Sweden), and has collaborative projects and interactions with the Imperial College London & St Mark's Institute (UK), the University of Manchester (UK) and the University of Lund (Sweden).

Finally, the Group is strongly oriented to the transferen-



ce to society and the scientific community, founding several programs for the advancement of biomedical research and evidence-based clinical practice. The Group has promoted multiple collaboration agreements between: 1) National scientific societies: Asociación Española Gastroenterología (AEG), Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa (GETECCU), Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHNP), Sociedad Española de Medicina de Familia y Comunitaria (SEMFyC), Sociedad Española de Médicos de Atención Primaria (SEMERGEN), Sociedad Española de Médicos Generales y de Familia (SEMG); 2) International scientific societies: European Helicobacter and Microbiota Study Group (EHMSG), European Crohn's and Colitis Organisation (ECCO), European Society for Primary Care Gastroenterology (ESPCG); 3) Institutions: Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Universidad Autónoma de Madrid (UAM), Vanderbilt University; 4) Patient advocacy groups; and 5) The private sector.

The Group's research lines are organized as follows:

1. Inflammatory Bowel Disease (IBD)

1.1 Understanding the mechanisms underlying IBD, based on systems biology and supported by omics technologies.

- Identification of new therapeutic targets in IBD.
- Identification of proteins (serum, extracellular serum vesicles and urine) with potential as biomarkers in IBD.
- Determination of immunoregulatory molecules as predictors of IBD severity and prognosis.
- Characterization of biomarkers by proteomics at diagnosis [PI16/01296, FI17/00143, PI19/01034].
- Analysis of the metabolome in serum and urine [PI16/01296, FI17/00143, PI19/01034].
- Metagenomic analysis of fecal microbiota [PI19/01034, CD19/00247].
- Analysis of the effect of immunomodulatory peptides secreted by the gut microbiota on mucosal dendritic cells in IBD patients.
- Transcriptomics from intestinal biopsies as markers.

1.2. Epidemiology in IBD.

- Evaluation of the incidence of IBD in Spain [PI16/01296, FI17/00143].
- International collaborative efforts to describe the epidemiology of IBD and the costs derived from its management.

1.3. Real world evidence studies to produce knowledge about the effectiveness, safety and use of therapeutic agents in IBD.

- International and national leadership on real world evidence studies.
- International collaborations in real world evidence studies.

1.4. Strategies for patient selection and optimization of treatment in patients with IBD.

- Switching to biosimilar drugs.
- Identification of biomarkers of response to treatment with biological drugs and tofacitinib in IBD using a multi-omic and cytometry approach [PI18/00622 and intramural CIBEREHD project].
- Comparative study of the immunomodulatory effect of the combination of biological drugs in inflammatory bowel disease [COMBINE] [PI22/01069, CD23/00075, FI23/00071].

1.5. Strategies for advanced therapies cycling in IBD.

- Discontinuation of anti-TNF drugs in IBD patients [PI15/00560].
- Identification of predictive biomarkers of relapse after discontinuation of anti-TNF therapy in IBD patients.
- Coordination of international initiatives on treatment cycling.

1.6. Safety of IBD treatments

- Safety during pregnancy and lactation (coordination of the national registry DUMBO [ICI19/0083]).
- Risk of thromboembolic events in patients treated with JAK inhibitors [PI21/01086].

2. Helicobacter pylori infection

- Implementation Science and evaluation of clinical practice: evidence based recommendations on real routine practice.
- International coordination of the European Registry on *H. pylori* management, a prospective study of clinical practice including 300 hospitals of 40 European countries.
- International coordination of the World Registry on *H. pylori* management, including hundreds of hospitals from the 5 continents.
- Primary Care: Surveys on practitioners, evaluation of clinical registries and development of dissemination programs.
- Prevalence, transmission, resistance, and socio-sanitary factors of infection.



MAJOR GRANTS

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Chaparro Sánchez, María. "Estudio comparativo del efecto inmunomodulador de la combinación de fármacos biológicos en la enfermedad inflamatoria intestinal [COMBINE]".FIS.22/01069. Instituto de Salud Carlos III.



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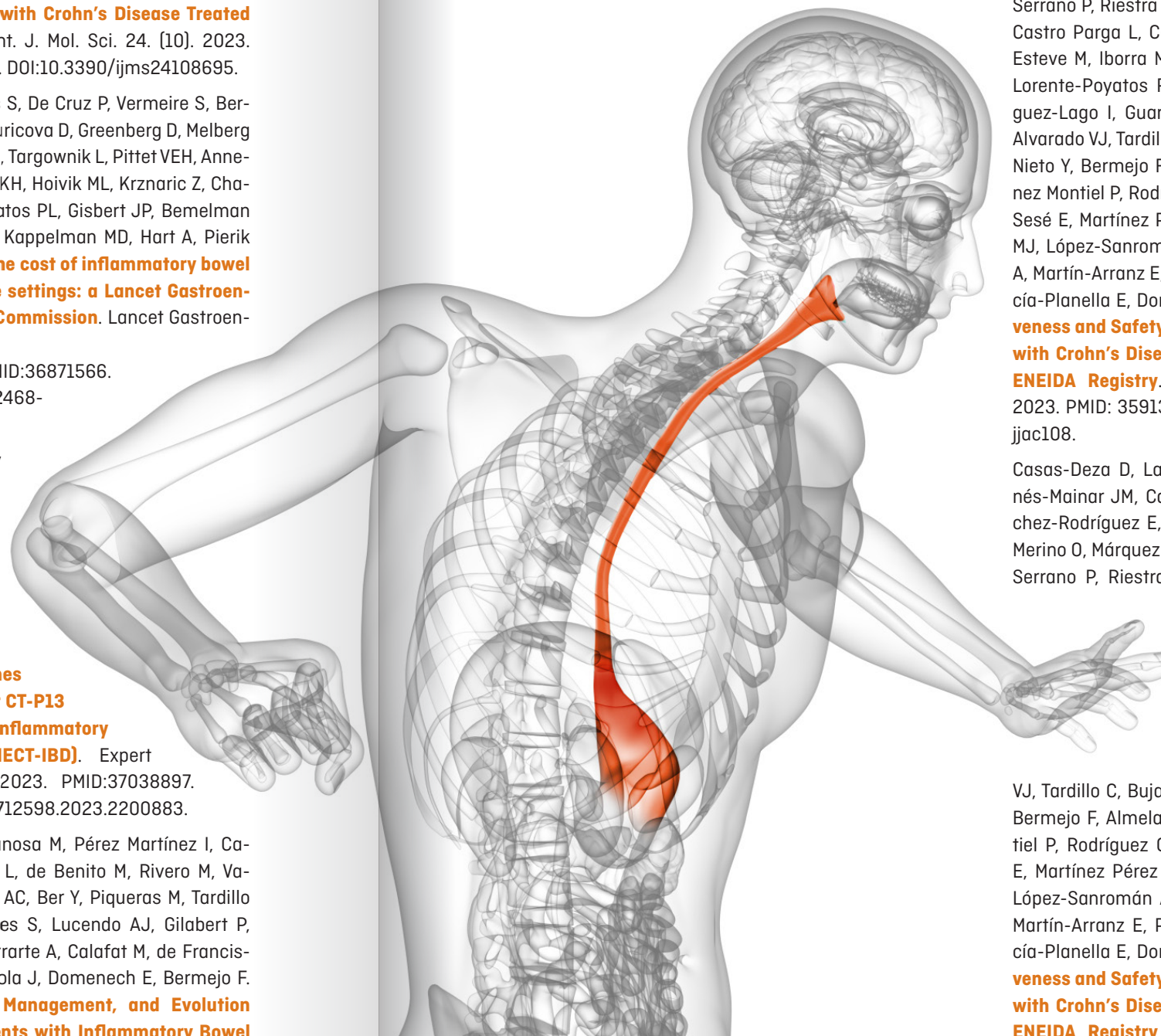
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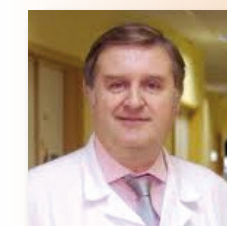
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Line 3.3 Progenitors and cell therapy

GROUP 39



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RESEARCH INTEREST

Although more than half of children and adolescents diagnosed with cancer survive, neoplasias remain the main cause of death from disease in these patients. Those with metastasis at any time during their evolution, who present genetic markers of poor prognosis, or recurrent/refractory tumors, have a very negative prognosis. Our research group is convinced that translational research is the best strategy to provide solutions to these patients.

The team is a multidisciplinary group, with proven experience in the diagnosis and treatment of childhood cancer, the development of research projects in advanced therapies applied to refractory pediatric cancer, and implementation of clinical trials in pediatric oncology. In summary, it has know-how and previous expertise that ensure the impact of newly developed Advanced Therapies and individualized medicine to any child or adolescent with cancer in Spain.

The group is focused on the following lines of research:

- Advanced Therapies: We have designed, preclinically tested [10.18632/oncotarget.27401]

and clinically translated a new antitumor treatment strategy: Celyvir, mesenchymal stem cells (MSCs) carrying an oncolytic adenovirus. The first clinical experience was a Compassionate Use Program authorized by the Spanish Medicines Agency [10.1038/cgt.2010.4 and 10.1016/j.canlet.2015.11.036]. We have also finished the first academic clinical trial (NCT01844661; reported at 10.1016/j.ymthe.2020.01.019). This program is testing currently a new version of the ATMP in 3 independent trials: EudraCT 2019-001154-26; EudraCT 2020-004838-37, and NCT05047276. We are exploring other ATMP developments, mostly autologous MSCs, for pediatric diseases in Neurology [10.24966/SRDT-2060/100030 and 2021-003607-17] and orthopedics and traumatology [10.1007/s12094-017-1752-9].

Childhood leukemias: The laboratory is one of the 2 reference laboratories of the Spanish Acute Leukemia Group, which centralizes and coordinates laboratories involved in the diagnosis and follow-up of children with the disease. We studied the process of resistance, especially in the central nervous system and found that the application of flow cytometry to CSF samples de-



tested a subgroup of patients at high risk of relapse [10.1002/ajh.23407]. In addition, the profile of chemokine receptors expressed by leukemic blasts and their signaling ability may have a role in relapses [10.1016/j.bcmd.2015.07.001]. More recently we have further characterized anatomically and functionally leukemic

infiltration of the CNS [10.1002/path.5510; 10.1182/blood.2021013506; 10.3324/haematol.2021.279383] and assessed mechanisms of childhood leukemogenesis in collaboration with Dr. Isidro Sánchez [10.1038/s41598-020-76206-y; 10.1158/0008-5472.CAN-21-3386; 10.1016/j.trecan.2022.06.012].



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Line 3.4 Advanced therapies in oncohematology

GROUP 44



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María Reyes Arranz Sáez
María Jimena Cannata Ortiz
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Valle Gómez García de Soria
Jimena Jiménez Braña
Javier Loscertales Pueyo



RESEARCH INTEREST

The Group of Advanced Therapies in Oncohematology of the Research Institute of the Hospital de la Princesa has the mission of promoting clinical, epidemiological and translational research in hematologic malignancies.

The scope of the group is broad, reflecting the variegated nature of each member's interests, and spans from genetic studies to the commitment in the development of new drugs.

The Group has a differential interest in:

- Epidemiological studies on chronic myeloid leukemia.
- Study of the efficacy and safety of new drugs in hematologic malignancies.
- Immunological and genetic studies in hematologic malignancies.

- Analysis of conditioning regimes in bone marrow transplants (BMT)
- Analysis of infectious complications of BMT.

During the past 5 years, Dr. Steegmann has focused his clinical research activity in two fields. The first, as Spanish IP of the European Leukemia Net EUTOS projects, in epidemiological studies and good clinical practice recommendations. Secondly, as president of the Spanish CML group (GELMC), to foster clinical research in this group. In the next 5 years, the targets are, on one hand, to follow this path. We have constructed a mobile app for IOS, Windows, and Android for exchanging information between GELMC members.

On the other hand, locally, our aim is to establish common projects which could cover all the hematologic malignancies cared by our group. In this regard the plan is to set studies of quality of life, comorbidities, and pharmacology.



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Line 3.5

Biological, cellular and molecular monitoring in oncohematology

GROUP 45



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RESEARCH INTEREST

Chromosomal translocations and gene mutations are frequently associated with the etiology of hematologic neoplasms. The JAK family of non-receptor tyrosine kinases (which comprises four members: JAK1, JAK2, JAK3 and TYK2) are involved in cytokine signaling on immune and hematopoietic cells and are crucial to normal hematopoiesis through the recruitment of downstream effectors of cell proliferation and survival. Recently, it has been reported that 10% of high risk pediatric acute lymphoblastic leukemia (ALL) cases bear activated JAK2 mutations, and could be potential candidates for JAK2 inhibitor therapeutic intervention. Acute lymphoblastic leukemia (ALL) is the most common neoplasm in childhood and although most cases respond to treatment, 20% relapse, shortening survival. Therefore, we analyzed high risk ALL samples with next generation sequencing (NGS) to determine the percentage of JAK-family receptor mutations in the Spanish population. ALL samples were obtained from hospitals throughout the country. We found that mutations in TP53 and JAK2 are independent prognostic biomarkers

in B-cell ALL. Furthermore, for TYK2, we provide evidence of naturally occurring catalytic loss-of-function TYK2 variants and reduced expression of TYK2 in B-ALL patients. On the other hand, it has been reported that Tyk2 deficiency in mouse increases the susceptibility to develop Abelson-induced B lymphoid leukemia/lymphoma linked to a diminished cytotoxic capacity of CD8+T, NK and NKT cells as a consequence of IFN-gamma decreased production. Taken together, these data suggest that TYK2 deficiency in humans is clinically silent, but could predispose to tumor formation, and patients with leukemia might be a target population in which TYK2 deficiency is enriched. Given the importance of maintaining an accurate immunological response for appropriate tumor surveillance, and that those immune responses are based on a functional JAK-dependent signal transduction, knowing the role in this response of the complex formed by cytokine receptors, JAK proteins and their target genes is highly relevant. In this sense, it is necessary to know the role of TYK2 in the immune system, both in infection and neoplasia.



MAJOR GRANTS

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Line 3.5
Biological, cellular and molecular monitoring in oncohematology

GROUP 46



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Noelia López García



RESEARCH INTEREST

The main scientific interest of the group revolves around immunotherapy and is focused on the following lines of research:

1. Characterization of the determinants of outcome in allogeneic hematopoietic stem cell transplantation (HSCT), with special interest in the role of the immune system.

Graft-versus-host disease (GvHD) and cytomegalovirus (CMV) infection are two major complications of allogeneic hematopoietic stem cell transplantation (HSCT). In order to anticipate their development and select the best donor, we set out the following objectives:

- 1.1. To study how immune reconstitution after allogeneic HSCT conditions late CMV reactivation, GvHD development and relapse.
- 1.2. To analyze the relevance of minor histocompatibility antigens (mHAGs) discrepancies between donor and recipient in the development of GvHD after HLA-identical related and unrelated donor HSCT.
- 1.3. To determine the predictive value of mHAGs as biomarkers that anticipate the therapeutic benefit of GvL (graft vs. leukemia effect) in the same patients.

2 Assessment of the efficacy of CCR7 immunotherapy. CCR7 is a chemokine receptor with a key role in lymphocyte recirculation to secondary lymphoid organs. The group has a long track record in designing and characterizing therapeutic anti-CCR7 antibodies to treat B and T cell leukemia. This line of research has been the basis to develop a humanized antibody that is currently being tested in a phase I clinical trial by the private company Catapult Therapeutics in the context of B cell leukemia (CAP-100 for Subjects With Relapsed/Refractory Chronic Lymphocytic Leukemia, NCT04704323).

Other pathologies in which we are testing the therapeutic effect of modulating migration in response to CCR7 include the following:

- Graft-versus-host disease (GvHD) after allogeneic hematopoietic stem cell transplantation (HSCT). The group aims to confirm the prophylactic and therapeutic potential of CCR7 blockade in GvHD in a murine model of allogeneic transplantation.
- Multiple sclerosis. The aim is to provide novel, specific, target-directed therapeutic monoclonal antibodies in a field with high medical need of novel drugs. It is carried out in the frame of a project lead by the company IMMED and another participant centre.

3. The characterization of the immunomodulatory effects of the tyrosine kinase inhibitor dasatinib.

Dasatinib is used to treat chromosome Philadelphia-positive leukemias. Because of its broad spectrum it has immunomodulatory effects, including a lymphocytosis occurring in most patients that has been associated to a better outcome. Thus, the therapeutic potential of dasatinib is an exciting field of research. The group has characterized this lymphocytosis and explored the effects of this drug on the endothelium. In collaboration with Dr. Jens Stein (University of Fribourg, Switzerland), we are currently exploring whether dasatinib has direct effects in the migratory abilities of lymphocytes within the lymph node parenchyma.

4. The characterization of the interaction between innate and adaptive humoral immune responses and how it relates to the severity of different respiratory infectious diseases.

The onset of the pandemic in 2020 caused the group to focus on understanding the role of humoral immunity in the severity of COVID-19. We are exploring the relationship between components of the complement system and other inflammatory markers with the kinetics of B cells and plasmablasts response. Our goal is to find prognostic biomarkers that help to predict a worse clinical course of respiratory infectious diseases.



MAJOR GRANTS

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PUBLICATIONS

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Line 3.6

New diagnostic and therapeutic advances in cardiovascular diseases

GROUP 58



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RESEARCH INTEREST

Intracoronary imaging is an area of intense clinical research for our group. As previously described, these techniques provide unique insights on the pathophysiology of stent failure but also of vulnerable coronary plaques (thin-cap fibroatheroma, plaque erosion, calcified coronary nodules). New technological advancements on optical coherence tomography (OCT) and high-resolution intravascular ultrasound (IVUS) are currently being evaluated by our group. Moreover, we are developing different “translational” research initiatives with the group of Nanomaterials for Bio-imaging from the Material Physics Department of the Universidad Autónoma de Madrid, to develop bio-functionalized particles (gold-NanoShells) to target specific molecules on the arterial wall surface (molecular imaging).

Our group is collaborating and developing several translational research initiatives with the Department of Immunology of our center and the CNIC (Centro Nacional

de Investigaciones Cardiovasculares). We are looking for molecules promoting the expression of anti-inflammatory transcription factors involved in the development of clinical and subclinical atherosclerosis. We are also searching for novel circulating microRNAs involved in the development of acute coronary syndromes and myocarditis.

Members of the group working in the Intensive Care Department are analyzing the pathophysiology and therapeutic alternatives in patients with acute respiratory distress. Likewise, research on optimal ventilation strategies in COVID-19 patients is currently ongoing.

Different research projects are also being promoted in the area of cardiac surgery including protocols on advanced hemodynamic support.

Another area of major research interest for our group is Spontaneous Coronary Artery Dissection (SCAD). SCAD represents a rare yet increasingly recognized cause of acute coronary syndrome. For the last 7 years our group

has been leading (PI) the multicenter prospective Spanish Registry on SCAD under the auspices of the Spanish Society of Cardiology (SEC) and the association of Interventional Cardiology of SEC. All cases are reviewed in a centralized core-laboratory and events at clinical follow-up are adjudicated by an independent Clinical Events Committee. Currently 500 patients are included in this study, which represents one of the largest registries of this condition worldwide.

In the same lines, in 2021 we were awarded by the

ECAM (Ensayo Clínico Aleatorizado Multicéntrico) grant from the Spanish Society of Cardiology (SEC), the largest award ever granted by the SEC, to randomized clinical trial. The BA-SCAD (Betablockers and Antiplatelet agents in patients with Spontaneous Coronary Artery Dissection) is a pragmatic, open-label, investigators’ promoted, randomized clinical trial, assessing the value of betablockers and antiplatelet drugs in this elusive clinical entity. A total of 60 Spanish University sites are participating in this large randomized clinical trial.



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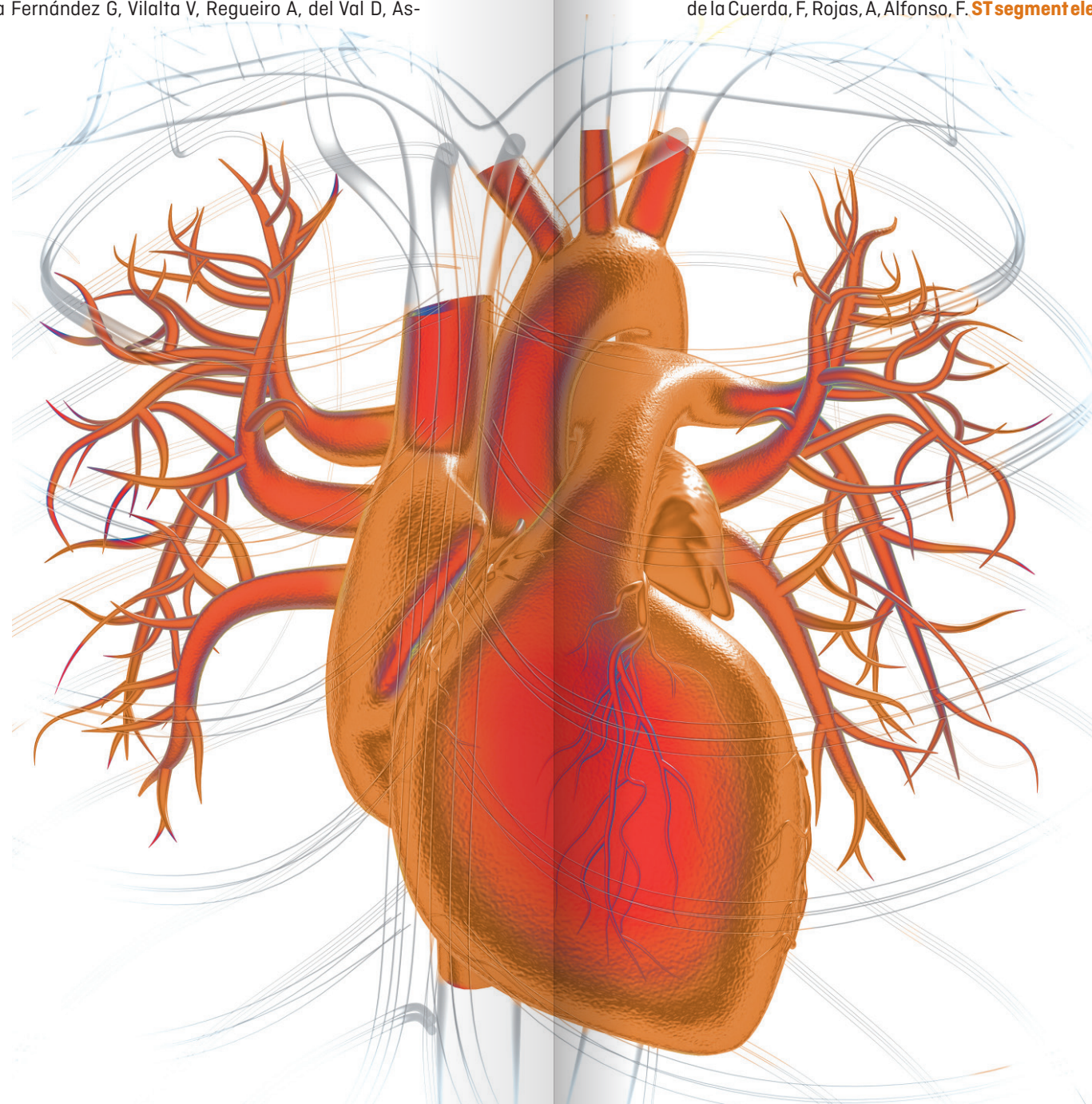
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Line 3.6

New diagnostic and therapeutic advances
in cardiovascular diseases

GROUP 48



Luis Jesús Jiménez
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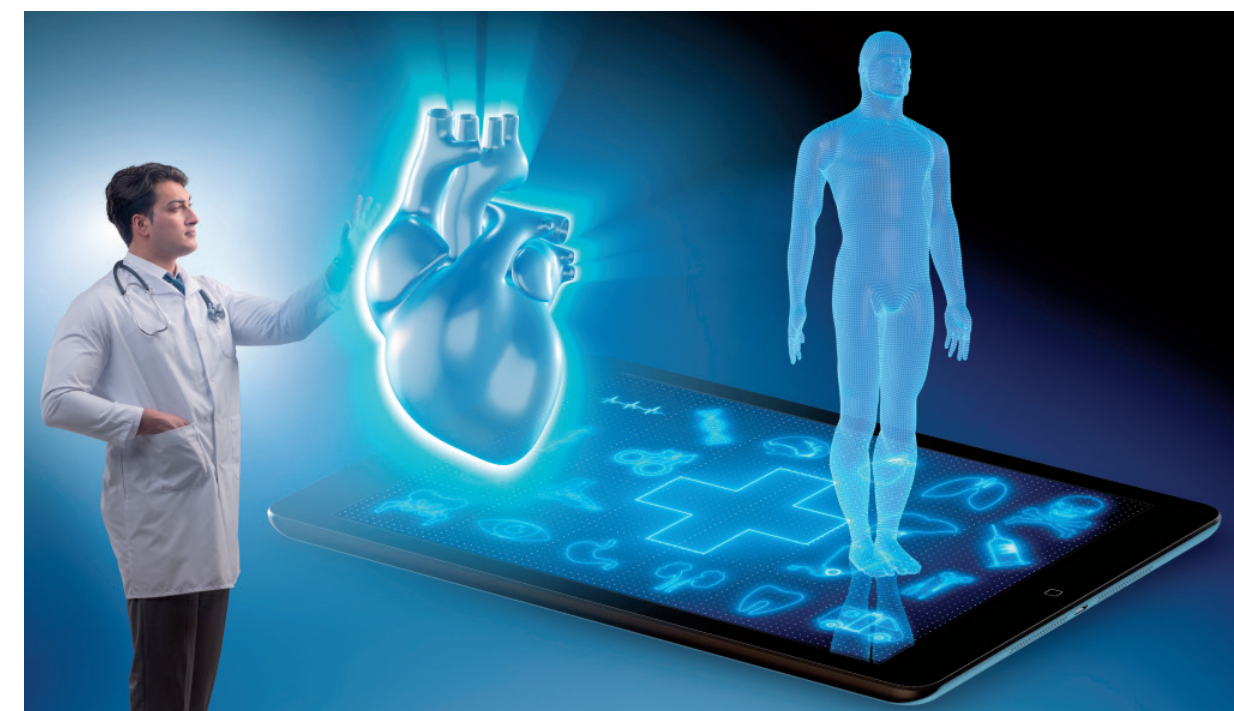
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RESEARCH INTEREST

In the last 4 years we have consolidated a new line of research based on the use of artificial intelligence (AI) methods. In this field we already have 4 original publications and a patent for the prediction of the first event of atrial fibrillation by means of AI analysis of an ECG. For its commercialization, we have the signature of bu-

siness interest from Google UK LDT and the health services company Atrys Health. In addition to AI projects with the ECG, we have obtained preliminary results from new original AI projects for cardiovascular diagnostic imaging and its databases. The consolidation of our research using AI is made possible by close and harmonious multidisciplinary collaboration with doctors, nurses, physicists and engineers.





MAJOR GRANTS

Jiménez Borreguero, Luis Jesús; Ortega Rabbione, Guillermo José. Detección de nuevos marcadores pronósticos sub-clínicos y precoces mediante inteligencia artificial de > 400.000 electrocardiogramas de la base de datos de un hospital terciario. FIS.20/00792. Instituto de Salud Carlos III.

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Line 3.6

New diagnostic and therapeutic advances in cardiovascular diseases

GROUP 57



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RESEARCH INTEREST

Cardiovascular diseases (CVD) are the main cause of mortality in developed countries. The prevalence and incidence of CVD are increasing. There are a great variety of new cardiovascular drugs that are targeted to dyslipidaemia, arterial and venous thrombosis and diabetes, and can modify the natural history of CVD.

Age is an important determinant of arterial and venous outcomes. However, usual clinical practice in a general setting reveals a disproportionately low use of cardiovascular medications and intensive treatment in elderly patients that could otherwise benefit from their use. On the other hand, there probably is an excessive

use of these medications in patients with cognitive impairment and short life expectancy. There is not enough information about cardiovascular therapies in very elderly patients with multiple comorbidities/diseases.

The purpose of this group is:

- 1) To investigate the efficacy of new cardiovascular treatments in different settings
- 2) To evaluate the risks and benefit obtained from antithrombotic treatment in elderly patients with venous thromboembolic disease and atrial fibrillation.
- 3) To describe the natural history of CVD in very elderly patients (over 90).



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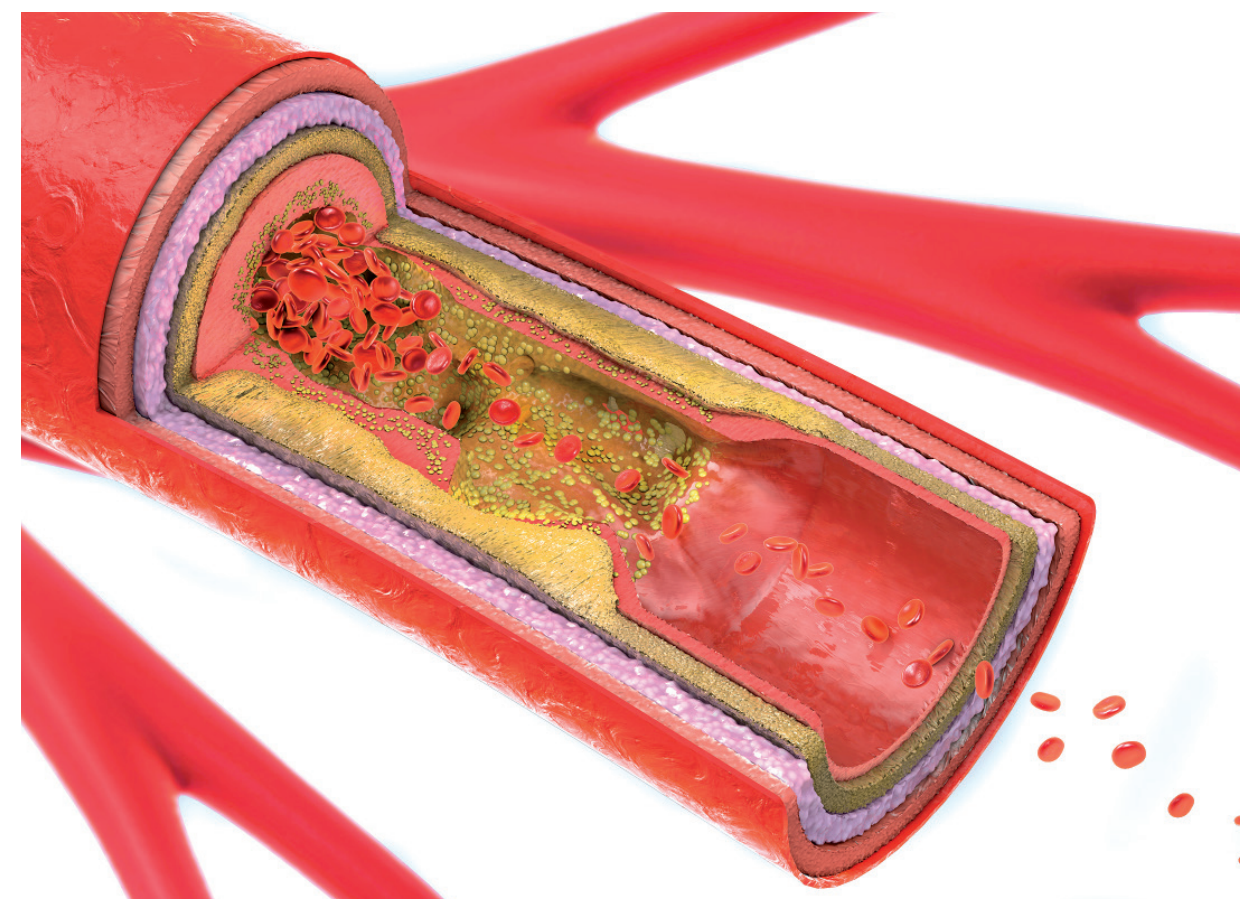
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Line 3.6

New diagnostic and therapeutic advances in cardiovascular diseases

GROUP 49



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María Lourdes Ruiz Díaz
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RESEARCH INTEREST

Our investigation addresses the genesis of scientific evidence on RCV in general and specific population, as well as evaluating the transfer of evidence both professionals and population.

My research projects directed to this are "Development, implementation and evaluation of a guide clinical practice in global cardiovascular risk" with 2 publications and publishing the results of the primary endpoint and a doctoral thesis; "Evaluation in Terms of Morbimortality and control of CVRF implementation of an adaptation of a GPC RCV" under analysis and a doctoral thesis and "A Clinical Trial Of Two Educational Strategies In Cardiovascular Health In Child Population (SAVINHEARTS)" assessment received CAIBER number extramurales2010 10 projects and has generated two publications. In analysis of the primary endpoint and two doctoral theses.

Collaborate with other groups of the institute with the project "Effect of oral nitrates on pulse pressure and arterial elasticity in patients older than 65 years with isolated systolic hypertension refractory. Ministry funding for non-commercial clinical trials. "Launch and publication. Also in projects from other institutions related to the RCV. "Project Prevention of Early Complications of Dia-

betes in Europe. European Project e-PREDICT" Hospital La Paz as a member of node ISCIII Cardiovascular Diseases Network and the Hospital 12 October through "CARDIORISK / MAPAPRES Project" and I am a member of the international group RISC (research in insulin resistance).

We promote the investigation of the other group members in these lines. Thus, we have participated in the project "Control of blood pressure in diabetic patients: a comparative study between treatment based on BP measured in the medical consultation and based on self-measurement of BP in the patient's home" and Development from primary care model risk stratification in patients with heart failure for predicting disability and hospitalization" within the network of Health in Chronic Disease.

With the research network Diabetes AP (GEDAPS) with studies PREDIMERC and CHAMBS and the IASB in the FOCUS trial led to the fixed-dose combination of drugs for secondary prevention of IHD. Over the next five years, thanks to the experience gained in these projects, we plan to start a project assessment tool doctor-patient communication addressed to the measurement and control of RCV, besides analyzing and publishing the results of studies launched over the years and continue to cooperate with other groups of the Institute.



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Line 3.7

New therapies
in infectious pathologies

GROUP 50



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Azucena Bautista Hernández
Marianela Ciudad Sañudo
Rafael de la Cámara de Llanza



RESEARCH INTEREST

Our group has been working on the study of HIV infection for more than 20 years. We have participated in several clinical trials and international research projects. Currently, we continue working in the Research Network on AIDS (CoRIS) collecting data for epidemiological studies from HIV-infected patients who come to our clinic for the first time, and periodically sending blood samples to the Biobank Network of AIDS, for virological and immunological studies. This project will keep going for years, and we will also continue collecting the data necessary for these studies. Since two years ago we belong to the CIBERINFEC consortium, which also includes members of the Immunology Laboratory and the Research Laboratory of the Carlos III Health Institute.

We are involved in clinical trials of new drugs and new therapeutic strategies for HIV, including the combination of two drugs Dolutegravir and lamivudine for nai-

ve and experienced patients, and the new maturation inhibitor in a very early phase, as well as a new clinical trial with a therapeutic vaccine for early treated HIV patients.

In addition, another field of interest, in which we have more than ten years of experience, is HIV / HCV co-infection. We are collaborating with the HEPAVIR cohort of co-infected patients, along with various centres in the Spanish territory, where we have treated more than 600 patients so far.

The study of new drugs in real life is very important because it can reveal side effects not seen before in clinical trials. In this sense, and also in a multicentre group, we are studying the impact of sustained viral response in cardiovascular risk and inflammation markers, as well as its impact in appearance of liver cancer and cancer survival. Other fields of interest are bacterial endocarditis, non-HIV immunosuppressive patients and the study of pre-exposure prophylaxis for HIV.



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Line 3.7

New therapies in infectious pathologies

GROUP 51



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RESEARCH INTEREST

Community-Acquired Pneumonia (CAP): From 1990 to 2015, the research group focused on various evolutionary aspects of CAP, primarily related to clinical management and innate immune response. As a result of this work, the group continues to collaborate with the CAP group of SEPAR, specifically in the study of genetic factors associated with polymorphisms and their correlation with severity and hospitalization risk. In their latest publication on CAP, a simple prognostic marker (the ratio of neutrophils to total leukocytes) was validated, demonstrating predictive capacity for short- and long-term mortality. These results have directly benefited the institution by improving the profile of prognostic indices for CAP, thereby determining the appropriate intensity of medical care for patients requiring hospitalization.

Non-coding RNAs (ncRNAs): Leveraging the knowledge on inflammation and pathophysiology of CAP, the research group explored the study of circulating ncRNAs as clinical biomarkers. On one hand, the response patterns of miRNAs were analyzed as predictors of mortality in CAP; on the other hand, their differences in immune response to COVID-19 infection and the pa-

thways involved were characterized. Studies on soluble biomarkers and microRNAs in the prognosis of CAP have formed the basis for two doctoral theses within the research group. In this same line, the group collaborated in the search for a molecular signature based on ncRNAs that could discriminate between bacterial and viral pneumonias, such as COVID-19.

COVID-19: The SARS-CoV-2 pandemic disrupted work and allowed the group to collaborate with the scientific community on several studies related to understanding the immune response to this infection. Notable collaborations include studies on the relationship between genetic polymorphisms, viremia, and prognosis of severe COVID-19 infection.

Cancer: In 2015, the leader of the research group concluded his management in the healthcare field and, after a period as an "Honorary Visitor" at the Royal Marsden Cancer Hospital in London, dedicated his professional and research career to lung cancer. Currently, several group members participate in the Thoracic Tumors Committee at the Hospital Universitario de la Princesa, participating in and leading various projects related to the study of ncRNAs in lung cancer and their diagnostic and therapeutic applications. Additionally, there are significant collaborations with the Oncology



group of the institution, including several studies on the response to immunotherapy in patients with non-small cell lung cancer (NSCLC):

- Circulating mononuclear subpopulations as predictors of immunotherapy response in NSCLC.

- Normal-high body weight in NSCLC patients treated with anti-PD-1 as a predictor of good prognosis.
- Relationship between immune-related adverse effects following anti-PD-1 oncological treatment and better prognosis.



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Line 3.7 New therapies in infectious pathologies

GROUP 52



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RESEARCH INTEREST

A great interest in the role of human microbiome in health and disease exists due to the accessibility of high throughput sequencing methods. Several studies indicate that the human microbiome may contribute to the regulation of multiple neuro-chemical and neuro-metabolic pathways through a complex series of highly interactive and symbiotic host-microbiome signaling systems that mechanistically interconnect the gastrointestinal tract, skin, liver, and other organs with the central nervous system. Several studies suggest that the stomach contains an unexpected diversity of microorganisms but their relationship with Helicobacter pylori, and with other human diseases is not well established.

H. pylori infects 50% of the population worldwide and colonizes the gastric mucosa causing many gastrointestinal diseases such as severe gastritis, peptic ulcer disease, gastric cancer and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. It is identified as a Group I carcinogen by the International Agency for Research on Cancer of the World Health Organization. Several treatment regimens have been used to eradicate this microorganism. Resistance to antibiotics is considered the main cause of treatment failure.

Since the beginning of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) pandemic, a large quantity of studies has been performed to develop and validate real-time PCR (RT-PCR) techniques capable of

providing an accurate diagnosis in respiratory samples. However, SARS-CoV-2 has also been detected in other types of samples such as blood. Assessment of commercial RT-PCR techniques in serum and plasma samples has been one of the aims of our group, which has provided satisfactory results. We performed a multidisciplinary study to assess detection of SARS-CoV-2 viremia as a marker to identify patients who are at risk of developing severe COVID-19 and mortality. This marker has shown better results than other biomarkers such as SEIMC score, interleukin-6, or lymphopenia.

This group includes members of the Microbiology Department with interest in diagnosis and treatment of several infectious diseases caused by pathogens such as fungi, Mycobacterium spp or CMV, as well as in infections in cystic fibrosis patients. Since March 2020, a huge interest in SARS-CoV-2 infection has emerged.

The main lines of research are: (1) Study of gastric microbiome and its relationship with H. pylori infection and other human diseases with potential therapeutic applications. (2) Detection of antimicrobial resistance in H. pylori (national and international surveys) and molecular methods for detection of clarithromycin resistance and heteroresistance. (3) Study of the in vitro activity of wine phenolic compounds against H. pylori. (4) Determination of the role of Non-Tuberculous Mycobacteria on the development of several diseases. (5) Detection of SARS-CoV-2 viremia as a marker to identify patients who are at risk of developing severe COVID-19 and mortality.



PUBLICATIONS

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Line 3.8

Individualized medicine in solid tumors

GROUP 40



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Ramón Moreno Balsalobre
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Francisco Eduardo Viamontes Ugalde
Verónica Jiménez Renard



RESEARCH INTEREST

Our line of clinical research is focused on the development of innovative cancer therapies. We have contributed to the clinical evaluation of neoadjuvant Pertuzumab, currently the standard of therapy in HER2+ breast cancer, or Neratinib in advanced HER2+ breast cancer. We have evaluated in phase I and phase II trials novel drugs such as Nintedanib or Dovitinib, and monoclonal antibodies such as Durvalumab. We have developed

medical and surgical protocols for lung, breast and pancreatic cancers.

Our line of translational research is focused on the discovery of biomarkers for assessing the effects of anticancer immunotherapy and biomarkers of cancer, including an immunophenotype profile in patients with advanced cancer and the rare double amplification of FGFR-1 and CCND1 in breast cancer. By using a systems biology approach, we are clustering breast cancer into subtypes defined by biologic features that constitute therapeutic targets.



MAJOR GRANTS

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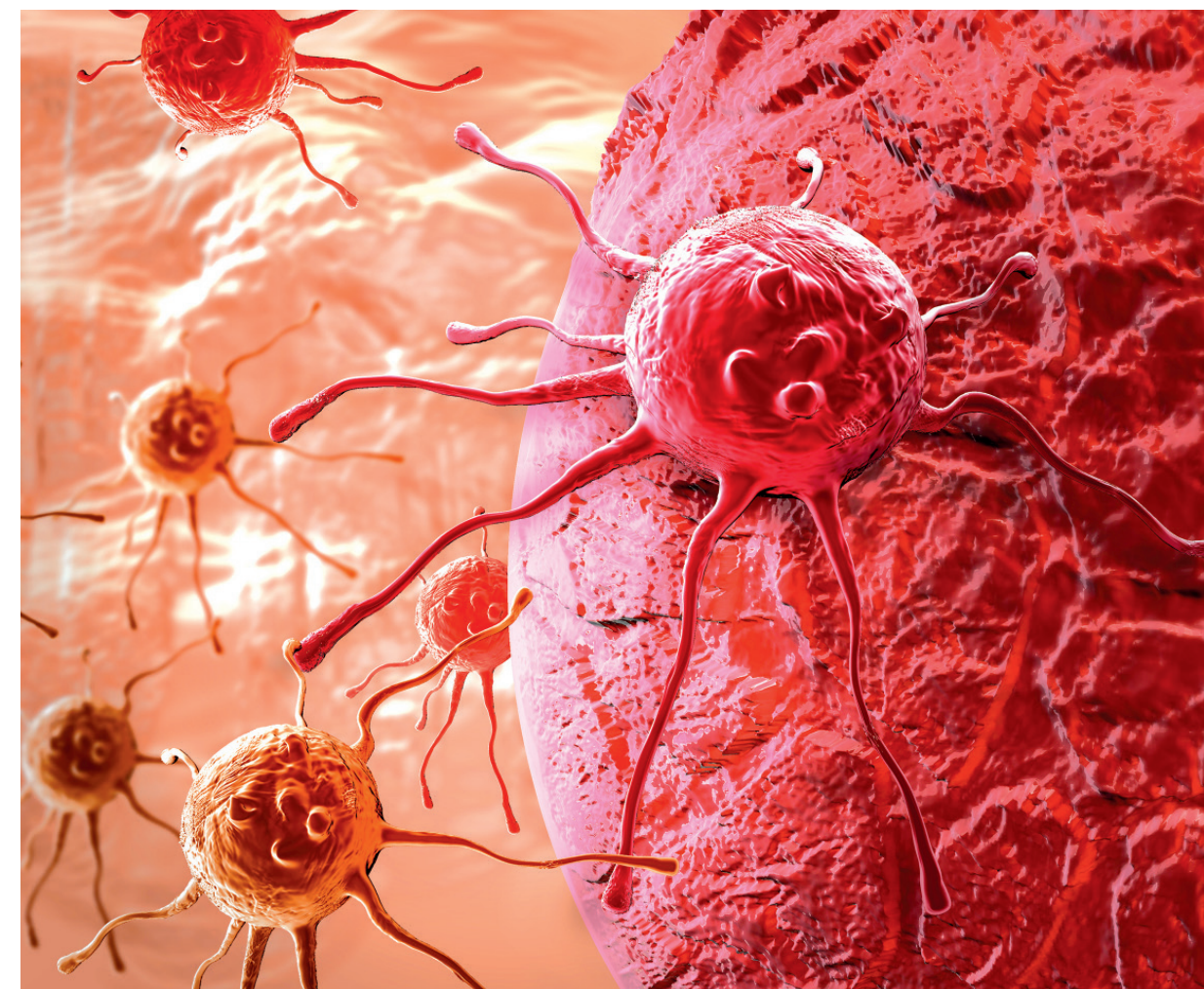
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Line 3.8

Individualized medicine in solid tumors

GROUP 53



Almudena Zapatero Laborda
Head of laboratory



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RESEARCH INTEREST

This group is focused on four research lines:

1) Identification of clinical and Biological Markers as risk and predictive factors in Prostate Cancer.

- Cooperative projects with Fundación Centro Nacional de Investigaciones Oncológicas (CNIO) to determine the prognostic value of expression of molecular markers in patients with high-risk localized prostate cancer (REF CaPr-HLP-RT-01/ PI 197) and metastatic cancer (PROCURE platform).
- We have just completed a project in collaboration with HU Santiago de Compostela and HU 12 de Octubre, Madrid, about the prognostic and predictive role of CTCs in high-risk non-metastatic prostate cancer (CaPr-RTCTC-01/PI 197). Results presented in abstract form in IJROBP 2019. Manuscript in preparation.
- IRONMAN-ES: "Estudio prospectivo observacional de parámetros clínicos y biomarcadores en cáncer de próstata avanzado en hospitales de España"; in collaboration with CNIO (co-sponsor).
- Collection of biological markers within the EORTC research project platform 1822 E2-RADlatE- OligoCare: A pragmatic observational cohort study to

evaluate radical radiotherapy for oligo-metastatic cancer patients.

2) Advances in Prostate Cancer Treatment:

- A phase III clinical trial to determine the optimum duration of androgen deprivation alongside high-dose radiotherapy in localized intermediate and high-risk PCa patients ("Phase III Trial comparing Long-Term Versus Short-Term Androgen Deprivation Combined With High-Dose Radiotherapy For Localized Prostate Cancer: GICOR Protocol DART01/05". EudraCT 2005-000417-36 ClinicalTrials.gov, number NCT02175212). 5-year data reported in Lancet Oncol 2015 and In J Radiat Oncol Biol Phys 2016. Substudy analysis of prognostic and predictive value of Testosterone nadir is ongoing.
- Collaboration with the ICECaP Working Group, a multidisciplinary team of academic cancer researchers from the Dana-Farber Cancer Institute-Harvard Medical School:
 - "Intermediate Clinical Endpoints In Cancer Of The Prostate (ICECaP) Initiative", a Meta-analysis. Published in JCO 2017.
 - "Event-Free Survival, a PSA-Based Composite Endpoint, is Not a Surrogate for Overall Survival in Localized Prostate Cancer". Sent to publication.



c. Participation in 6 Randomized Phase III clinical trials in several treatment and disease scenarios: localized-high risk prostate cancer, prostate cancer without metastasis with biochemical failure after radical treatment, in M0 castration resistant prostate cancer and in metastatic prostate cancer (MDV3100-14, MDV3100-13, JNJ-56021927, TALAPRO-2 [C3441021] EORTC 1333 and EORTC 1531).

3) High Technology and Innovation:

- Over the last 10 years we have actively worked in Intensity Modulated Radiation Treatment - Image Guided Radiotherapy (IMRT-IGRT) versus three-dimensional conformal radiotherapy (3DCRT): comparative results on patients treated in a single institution, which demonstrate the significant reduction in acute and late genitourinary and rectal toxicity in patients with prostate cancer treated with IMRT-IGRT. The results have been presented in international meetings and reported in indexed journals.
- Implementation of the new technology VMAT (Volumetric Modulated Arc Therapy) and Stereotactic Body Radiation Therapy for the treatment of localized and oligometastatic PCa
- Design and implementation of a Phase II clinical trial: Dose Intensification With a Focal Boost to Dominant Intraprostatic Lesion Using Volumetric Modulated Arc Therapy /Image Guided Radiotherapy in Patients With Localized Prostate Cancer, Protocol ID: CaP-VMAT-DIL. ClinicalTrials.gov Identifier: NCT03030625. Active recruitment.

- Participation in a Phase II clinical trial: Tratamiento de las Oligo-metástasis de Cancer de Prostata Mediante SBRT- Código SBRT-SG 05. NCT02192788 STAGE: Recruitment completed.
- Participation in a Phase II clinical trial EC/2018/0130PEACE V/STORM: A randomized phase II trial for the Salvage Treatment of OligoRecurrent nodal prostate cancer Metastases (STORM).PROMOTOR: Ghent University. GICOR

4) Multi-Institutional Data Base Register in PCa:

- National Register of Prostate Cancer Treated with Radiotherapy (RECAP)
- EORTC research project 1822 E²-RADlatE - OligoCare: A pragmatic observational cohort study to evaluate radical radiotherapy for oligo-metastatic cancer patients. Activation phase

5) BLADDER CANCER- BLADDER SPARING PROGRAM

- Our team is one of the most active and successfully experienced groups in the conservative treatment of invasive bladder cancer. We continue to study the optimal sequence of treatment concerning tumor control, bladder preservation, quality of life and efficient delivery. The results have been presented in international meetings and reported in indexed journals.
- Collaboration- inclusion in clinical trial of Radio-Immunotherapy in this context. "Eficacia del atezolizumab con radioterapia concomitante en pacientes con cáncer de vejiga músculo-invasivo."Code: SOGUG-2017-A-IEC(VEJ)-4EudraCT: 2018-004348-47



MAJOR GRANTS

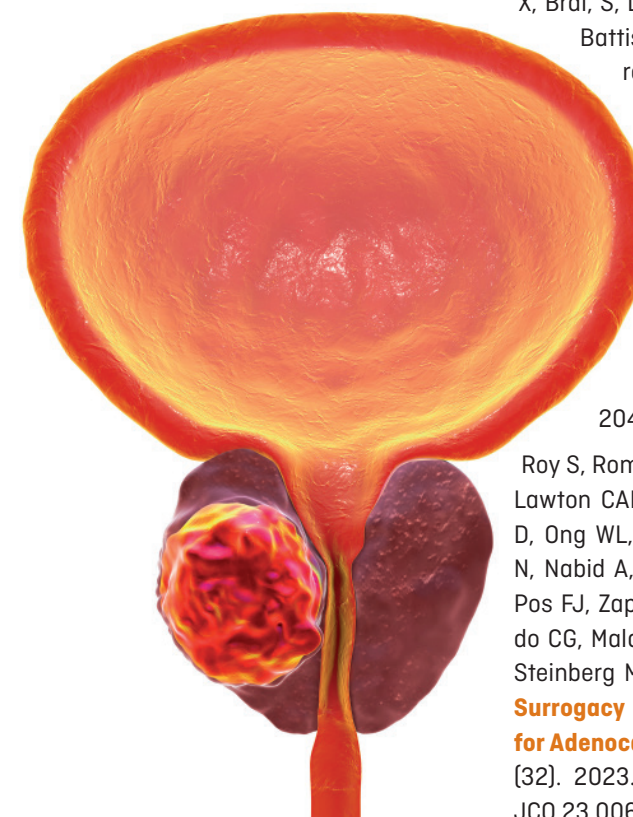
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Line 3.8
Individualized medicine in solid tumors

GROUP 59



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RESEARCH INTEREST

Our group focused on different research areas.

Erectile dysfunction: Endothelial dysfunction is one of the first symptoms of erectile dysfunction (ED) and is closely related to atherosclerosis and risk factors such as diabetes mellitus (DM), both of them characterized by inflammatory and oxidative advanced state. Vardenafil is one of the more effective 5-phosphodiesterase inhibitors in patients with ED and DM. We have determined plasma proteome of patients with DM and the effect of vardenafil administration in the expression of proteins related to inflammatory oxidative stress and cellular homeostasis.

We have observed a significant negative correlation between plasma levels of betatropomyosin and IIEF-EF score. Elevated levels of beta-tropomyosin in plasma indicate cell damage and loss of cellular regenerative capacity.

Urothelial cancer: Exosomes extracellular vesicles are potent intercellular mediators containing membrane and cytosolic proteins, mRNA and specific miRNA, which in turn can be obtained from fluids such as urine. We have analyzed urinary exosomes, miRNA and protein content in order to find diagnostic markers for bladder urothelial cancer. Some of the miRNAs that are involved in tumor cell proliferation, inhibition of tumor suppressor genes, activation of EMT and metastatic state, are significantly reduced in urinary exosomes from patients with bladder urothelial carcinoma and may be useful as non-invasive diagnostic biomarkers in bladder cancer.

With regard to surgical techniques, we have optimized the diagnosis and therapeutic endourologic approach to the upper urothelial tract cancer.



PUBLICATIONS

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