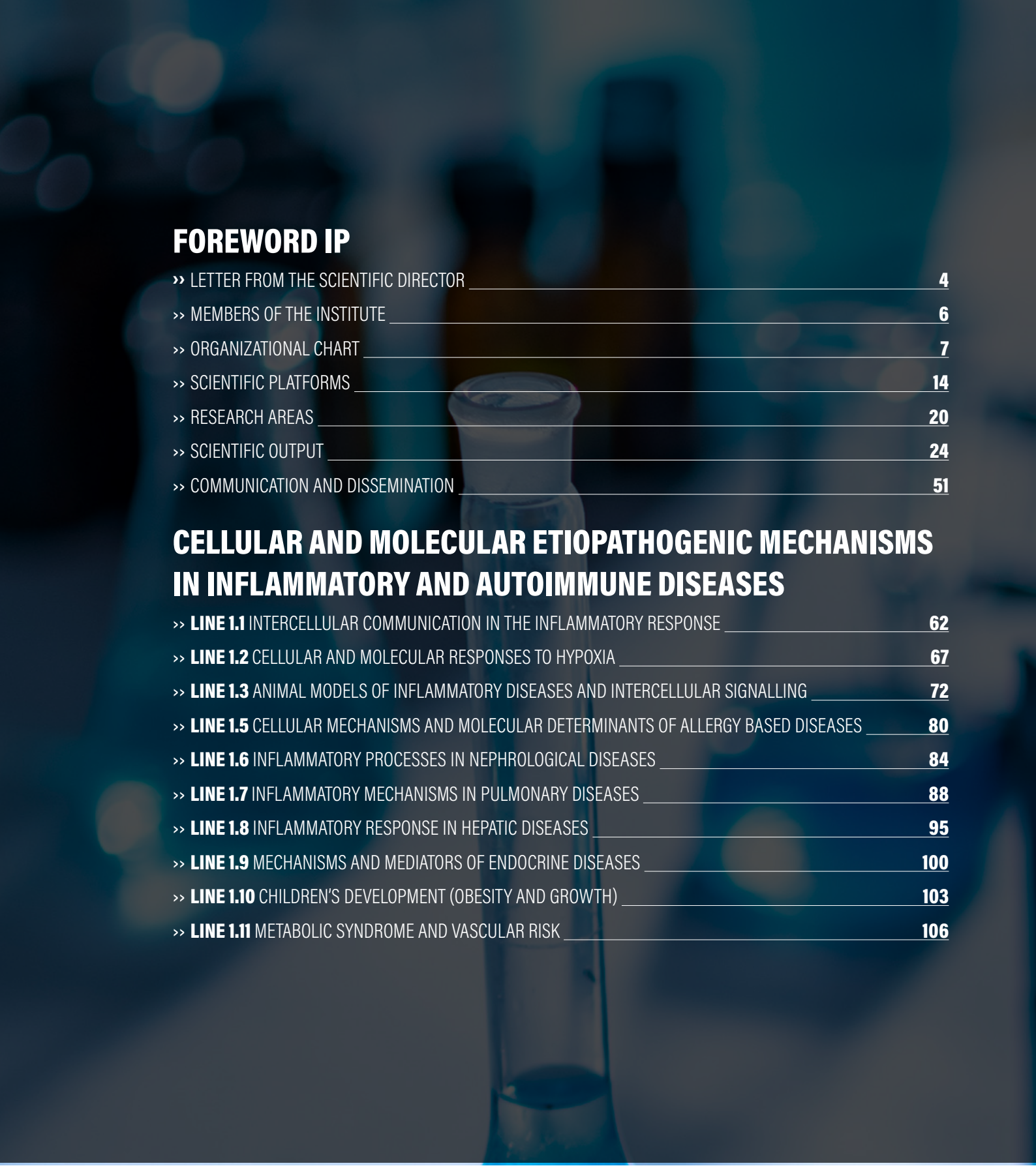
ANNUAL REPORT

OF SCIENTIFIC ACTIVITY

2022

INSTITUTO DE INVESTIGACIÓN SANITARIA
HOSPITAL UNIVERSITARIO DE LA PRINCESA
IP



FOREWORD IP

CELLULAR AND MOLECULAR ETIOPATHOGENIC MECHANISMS IN INFLAMMATORY AND AUTOIMMUNE DISEASES

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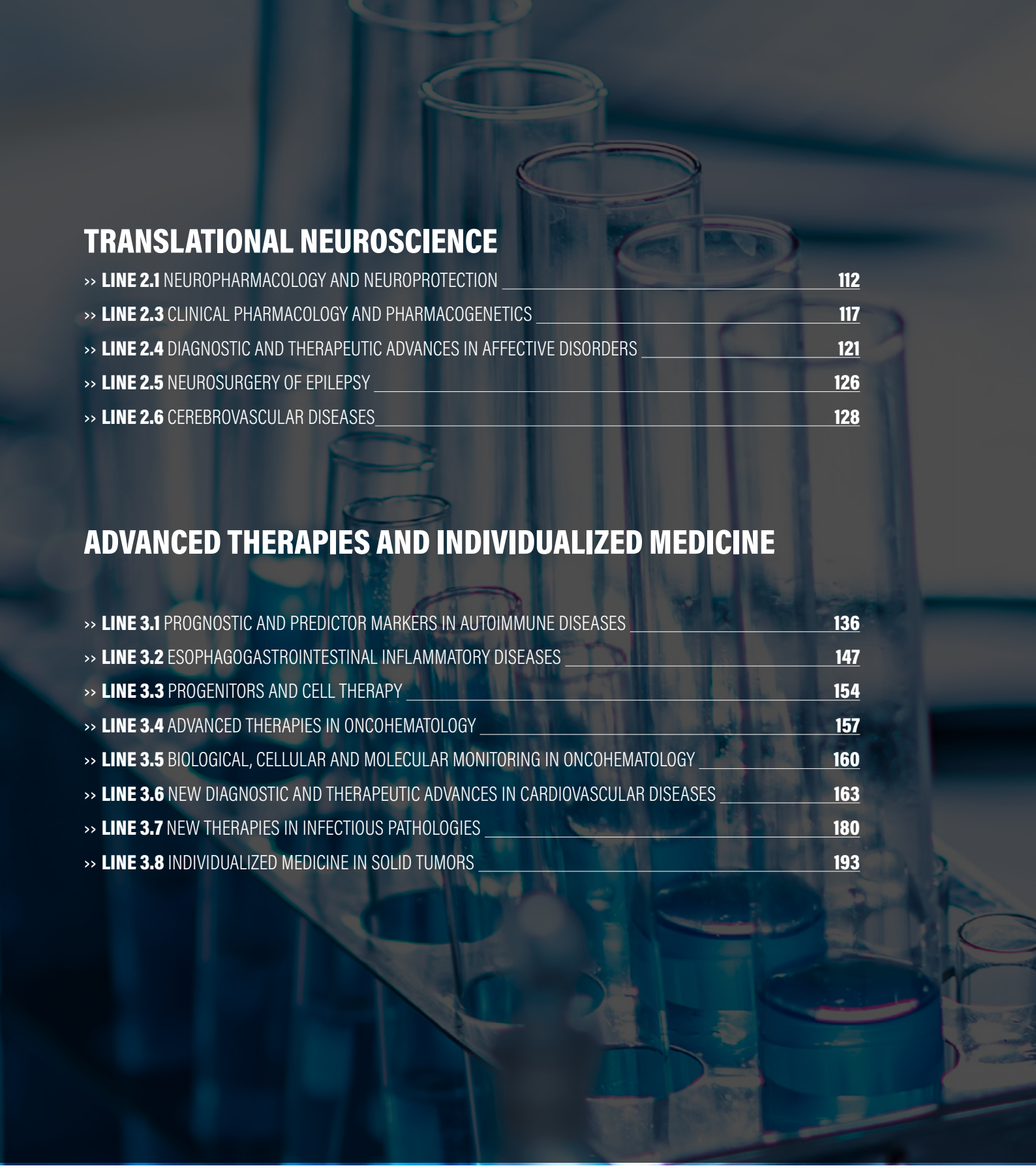


TRANSLATIONAL NEUROSCIENCE

ADVANCED THERAPIES AND INDIVIDUALIZED MEDICINE

LETTER FROM THE SCIENTIFIC DIRECTOR

FRANCISCO SÁNCHEZ MADRID
SCIENTIFIC DIRECTOR

In 2022, 13 years have passed since the first agreement for the creation of La Princesa Health Research Institute (IIS-IP) was signed. Throughout this time, I have had the immense pleasure of holding the scientific direction of this Institute, which has brought so much prestige and visibility to its research centres as well as to its researchers.

In this year 2022, regarding scientific output, I would like to highlight that, although the number of publications is 10% lower than in 2021, the overall accumulated impact factor has increased, thereby resulting in an increase of the relative impact per article up to 8.8.

As in previous years, the IIS-IP has implemented different initiatives to encourage Open Access publication. As a result, 65% of our articles were published in Open Access format. In addition, 44% of the total number of our publications were led by researchers of IIS-IP, which shows the scientific leadership of the members of our Institute.

Among the achievements to highlight during this year, is the granting to the *ISRET Platform project* of financing by the call for funding of *Singular Scientific Infrastructures 2022* (Instituto de Salud Carlos III). This funding places our Institute as a reference for cell and tissue imaging. Another achievement has been obtaining funding from the 2022 *Investigo calls* of SEPE and CAM to hire 42 new professionals.

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, 15 doctoral theses have been defended, 4 of them with a European mention.

As in previous years, I would like to make a special mention of the rest of the activities carried out by the members of the Institute, such as teaching and clinical assistance. They contribute to generating new ideas and research hypotheses, with the aim of providing the best service to citizens and quality training for the next generations.

In 2022, the Institute will continue its efforts to address, in particular, the generational renewal, as well as the requirements of open science, data management plans and the improvement of our participation in projects of the Horizon Europe programme.

In 2022, the Institute will continue its efforts to address, in particular, the generational renewal, as well as the requirements of open science, data management plans and the improvement of our participation in projects of the Horizon Europe programme.

I would like to pay special tribute to Dr. Gómez Zamora, who passed away in September of this year. Jorge Gómez Zamora was the driving force in the creation of the Biomedical Research Foundation (FIB), and of the gestation of the IIS-IP during his time as Managing Director of the Hospital. During the last years he has dedicated all his creative capacity and inexhaustible energy to his role as coordinator of the IIS-IP Innovation Unit and the Hospital Humanization Unit.

As every year, I would not like to end without thanking the work done by all the members of the Institute. Their effort and dedication have been crucial to achieve the milestone of the renewal of our accreditation, as well as the very positive data that we offer below. I also want to thank all the personnel of the Scientific Platforms and the Technical Unit for offering their support and collaborating in this success.

Thank you very much and let's keep doing a professional and dedicated job. ▪

MEMBERS

OF THE INSTITUTE

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. ▪

SaludMadrid

Hospital Universitario de La Princesa

Hospital Universitario Santa Cristina

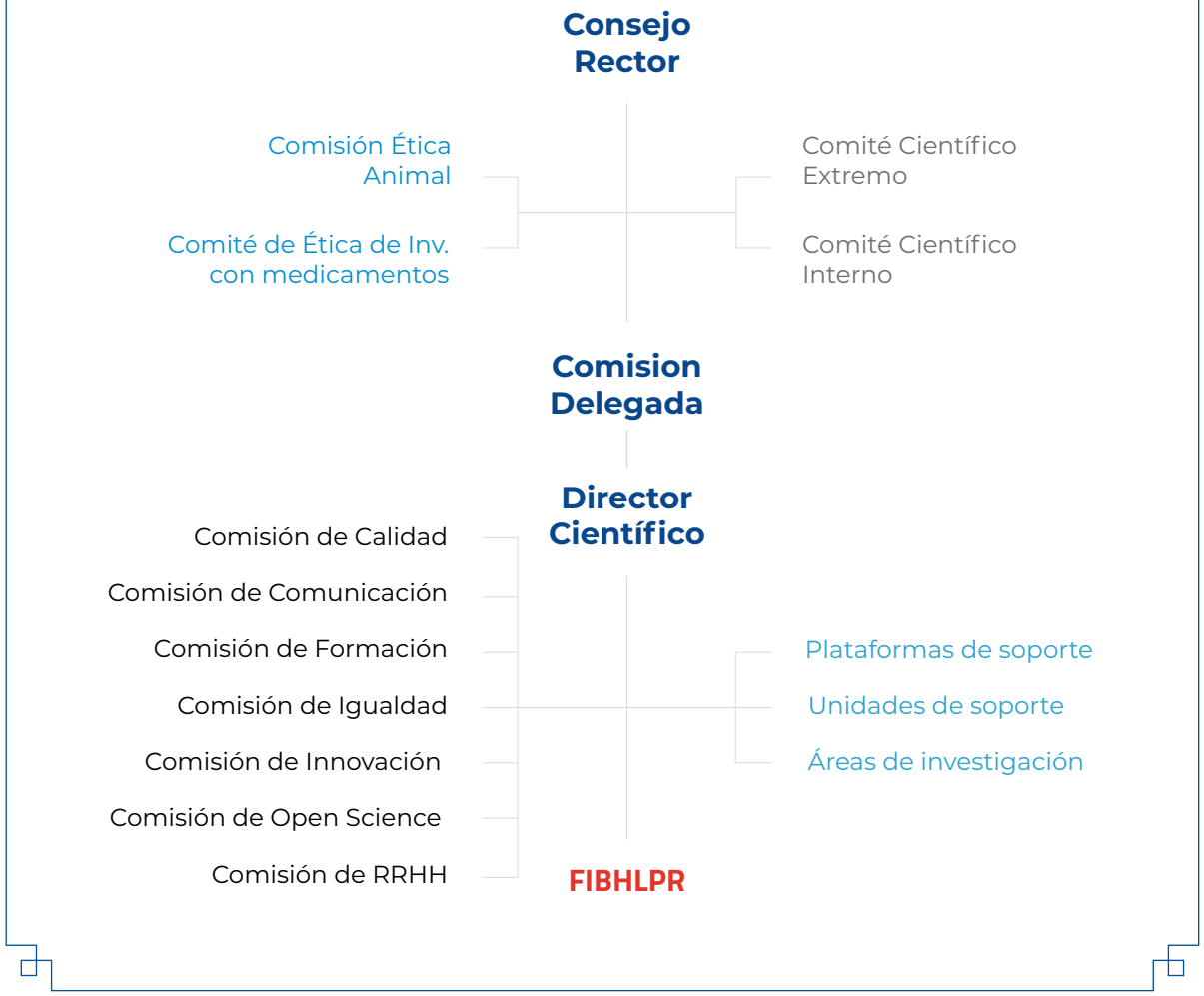
Hospital Universitario Niño Jesús

UAM Universidad Autónoma de Madrid

FIB FUNDACIÓN DE INVESTIGACIÓN BIOMÉDICA hospital universitario la princesa

Comunidad de Madrid

Dirección General de Investigación, Docencia y Documentación
CONSEJERÍA DE SANIDAD


Consejo Rector
Comisión Ética Animal
Comité de Ética de Inv. con medicamentos
Comité Científico Extremo
Comité Científico Interno
Comision Delegada
Director Científico
Comisión de Calidad
Comisión de Comunicación
Comisión de Formación
Comisión de Igualdad
Comisión de Innovación
Comisión de Open Science
Comisión de RRHH
Plataformas de soporte
Unidades de soporte
Áreas de investigación
FIBHLPR

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General Director, Hospital Universitario Santa Cristina

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Centro de Biología Molecular Severo Ochoa, Madrid

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Director of Government Affairs, Roche Farma España

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Asociación Española de Portadores de Válvulas Cardiacas y Anticoagulados

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Scientific Director of Instituto de Investigación Sanitaria Hospital Universitario La Princesa

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Director of Fundación de Investigación Biomédica Hospital Universitario La Princesa

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General Director, Hospital Universitario La Princesa

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Centro de Biología Molecular Severo Ochoa, Madrid

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Universidad Autónoma de Madrid

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Director of Continuity of Care, Hospital Universitario Santa Cristina

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Scientific Director of Instituto de Investigación Sanitaria Hospital Universitario La Princesa

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Quality Coordinator, Hospital Universitario La Princesa

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Director of Fundación de Investigación Biomédica Hospital Universitario La Princesa

SCIENTIFIC DIRECTOR

Francisco Sánchez Madrid

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Professor Universidad de Valencia

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Professor Universidad Pompeu Fabra. Scientific Director IMIM, Barcelona.

Purificación Muñoz Cánoves
Professor Universidad Pomapeu Fabra

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Francisco Sánchez Madrid
Scientific Director of Instituto de Investigación Sanitaria Hospital Universitario La Princesa

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Scientific Management Support Unit, Hospital Universitario La Princesa

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Professor, Universidad Autónoma de Madrid

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Rheumatology Department, Hospital Universitario La Princesa

Mónica Marazuela Azpiroz
Endocrinology Department, Hospital Universitario La Princesa

Cecilia Muñoz Calleja
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Internal Medicine Department, Hospital Universitario La Princesa

SECRETARY

Mª Ángeles Vallejo Rodríguez
Immunology Department, Hospital Universitario La Princesa

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Clinical Pharmacology Department, Hospital Universitario La Princesa

VICE-CHAIRMAN

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Anesthesiology Department, Hospital Universitario La Princesa

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Patient representative

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Gynecology and Obstetrics Department, Hospital Universitario Santa Cristina.

Carmen del Arco Galán
Emergency Department, Hospital Universitario La Princesa

Sara Cardenal Rodríguez
Clinical Trials Department, FIB, Hospital Universitario La Princesa

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Internal Medicine Department, Hospital Universitario La Princesa

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Family and Community Medicine, Primary Care

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Gastroenterology Department, Hospital Universitario La Princesa

Pablo Montalvo Rebuelta
Lawyer, ASJUSA

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General and Gastrointestinal Surgery, Hospital Universitario de La Princesa

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Clinical Pharmacology Department, Hospital Universitario La Princesa

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Carolina Pozuelo González
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Internal Medicine Department, Hospital Universitario La Princesa

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Mara Ortega Gómez
Biobank, Hospital Universitario La Princesa

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Ángel Núñez Pagán

FOUNDATION FOR BIOMEDICAL RESEARCH (FIBHLPR)

DIRECTOR

Rosario Ortiz de Urbina Barba

HUMAN RESOURCES DEPARTMENT

María Mar Martín Cuena

Silvia Duque Sánz

PROJECTS MANAGEMENT DEPARTMENT

María del Carmen Barrio Fuentes

Jesús Santamaría Pérez

ACCOUNTING DEPARTMENT

Jorge Gómez Juan

CLINICAL TRIALS MANAGEMENT DEPARTMENT

Sara Cardenal Rodríguez

Alberto Sebastian Martínez-Caba

Marta Pérez Díaz

LEGAL

María Jesús Bono Sahuquillo

RESEARCH MANAGEMENT DEPARTMENT

Jesús Capa Algara

Silvia González Herráez

Isabel Barrio Villa

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:

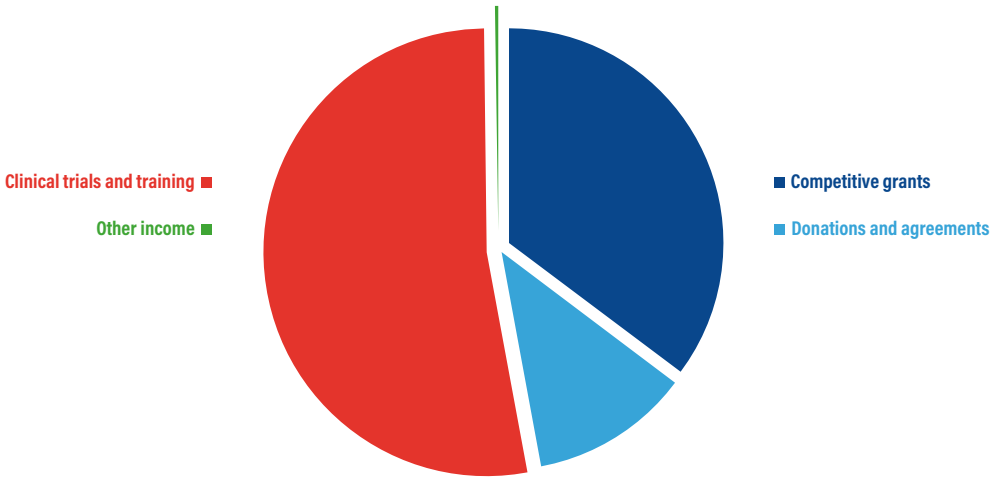
	2022	2021
Income	9.032.684	10.431.539
Expenses	9.016.873	10.416.006

ACTIVE ASSETS	
Non-current active assest	
Intangible fixed assets	69.808
Material fixed assets	565.943
Current active assets	
Debtors and Client to collect	1.666.063
Financial short term investments	0
Cash	23.142.026
Total Active Assets	**25.443.840**

PASSIVE ASSETS	
Net Worth	
Own funds	2.451.775
Non-refundable grants	751.681
Non-current Passive Assets	
Long term debts	0
Current Passive Assets	
Short term provisions	7.786.647
Refundable grants	14.014.912
Creditors to pay	323.927
Short term accruals	114.898
Total Passive Assets	**25.443.840**

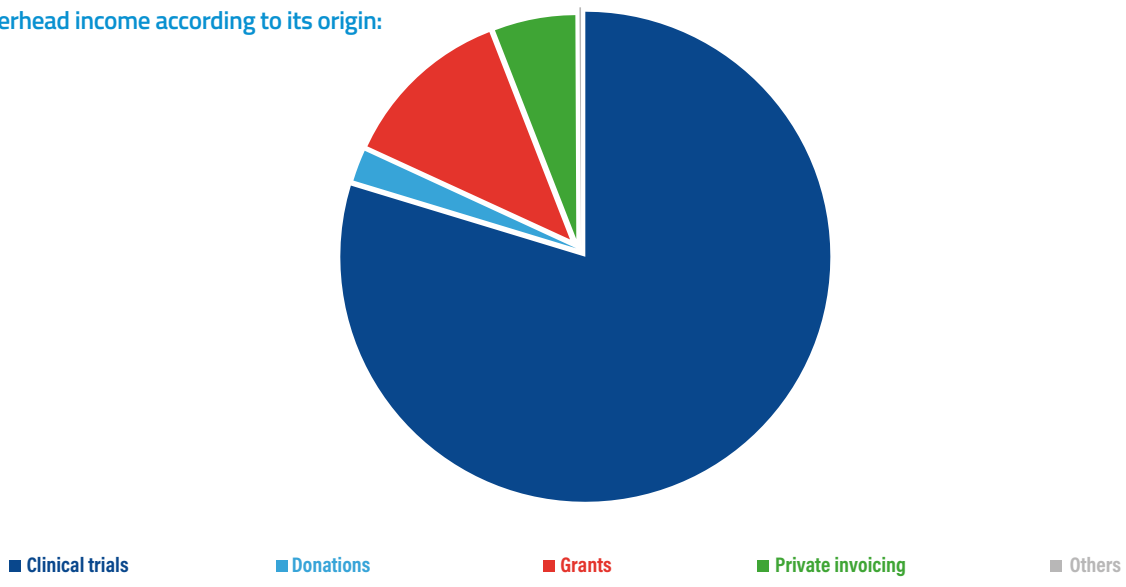
Below is shown the information on the income obtained by the Foundation for Biomedical Research, with the income sources grouped as obtained through competitive grants, clinical trials, private invoicing, donations, or other income.

Competitive grants	Donations and agreements	Clinical trials and training	Other income
3.182.467	1.069.753	4.762.991	17.473



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)	42%
Products and services – Equipment – Repairs	40%
Reserves	18%

SCIENTIFIC PLATFORMS

3. 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

Javier Aspa Marco
Scientific Management Support Unit, Hospital Universitario La Princesa

Ramón Colomer Bosch
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

Laura Gómez Cabañas

Ángel Lancho Sánchez

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

Ancor Sanz García
Núria 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.

Coordinador de la Unidad de Terapias Avanzadas

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 (REDLAB) 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 microsopy, 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

BIOINFORMATICIAN

Jorge García Martínez

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 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

Rosario García de Vicuña Pinedo
Rheumatology Department

MULTIDISCIPLINAR TEAM

María Chaparro Sánchez
Gastroenterology Department

Esteban Daudén Tello
Dermatology Department

Isidoro González Álvaro
Rheumatology Department

María del Mar Llamas Velasco
Dermatology Department

Virginia Meca Lallana
Neurology Department

Alberto Morell Baladrón
Hospital Pharmacy 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

STAFF

Gina Paola Mejía
Abril Paola Camargo
Mamani Ana Casajus Rey
Antía Gómez Fernández
Diana María Campodónico

Samuel Alejandro Jiménez Guardiola
Tamara Michelle Moreno
Silva Carmen Méndez-Benegassi Cid
Tamara de la Torre Muñoz
Carmen Candau Ramos
Marta de los Ríos Rodríguez
Marina Aldama Martin
Samuel Martin Vílchez
Alejandro de Miguel Cáceres
Raquel Saiz Martínez
Jaime Pérez Calvo
Yao Yuan Chang

Secretary-CTA

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

Francisco Sánchez Madrid
Scientific Director of Instituto de Investigación Sanitaria Hospital Universitario La Princesa

Jorge Gómez Zamora
Internal Medicine Department, Hospital Universitario La Princesa

Cristina García-Serna Cortes
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

Mª Angels Figuerola Tejerina
Preventive Medicine Deparment

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

Jesús Capa Algara
Research Managment

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

Elena Fernández Ruiz
Molecular Biology Department

Alicia González Martínez
Neurology Department

Elena Martín Pérez
Head of studies Resident Doctor

Ramón Moreno Balsalobre
Thoracic Surgery Service

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Mara Ortega Gómez
Biobank

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Radiodiagnosis department

Francisco Rodríguez Salvanés
Diagnosis Training Unit

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Clinical pharmacology department

Jesús Sanz Sanz
Internal Medicine Department

SECRETARY

Jesús Capa Algara
Research Managment

HUMAN RESOURCES COMMITTEE

COORDINATOR

María del Mar Martín Cuena
Human Resources Department

HUMAN RESOURCES COMMITTEE

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Clinical Trial Department

María Chaparro Sánchez
Gastroenterology Department

Sergio Luquero Bueno
Clinical Trial Unit

Noa Beatriz Martín Cofreces
Inmunology 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

Jesús Capa Algara
Research Managment

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Gastroenterology Department

Elena Español Pueyo
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Human Resources Department

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Director Fundación para la Investigación Biomédica Hospital Universitario de La Princesa

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Nursing Department

Nuria Romero Laorden
Medical Oncology Department

SECRETARY

Jesús Capa Algara
Research Managment

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.

Sara Cardenal Rodríguez
Clinical Trial Department

María Chaparro Sánchez
Gastroenterology Department

Sergio Luquero Bueno
Clinical Trial Unit

Noa Beatriz Martín Cofreces
Inmunology 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

Jesús Capa Algara
Research Managment

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.

Sara Cardenal Rodríguez
Clinical Trial Department

María Chaparro Sánchez
Gastroenterology Department

Sergio Luquero Bueno
Clinical Trial Unit

Noa Beatriz Martín
Cofreces Inmunology Department

Enrique Martín Gayo
Inmunology 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

Jesús Capa Algara
Research Managment

RESEARCH AREAS

Areas:	Research lines:	Research groups:	Personnel dedicated to research:	Men:	Women:
3	23	48	505	200	305

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 22 - **Joan Bautista Soriano Ortiz**

Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. **A clinical case definition of post-COVID-19 condition by a Delphi consensus**. Lancet Infect Dis. 2022. 22(4): e102-e107. doi: 10.1016/S1473-3099(21)00703-9. IF: 71,42.

Grupo 10- **Susana Cadenas Álvarez**

Cadenas S. **Mitochondria rescue cells from ischemic injury**. Science. 2022. 5; 377(6606):579-580. doi: 10.1126/science.add4629. IF: 63,71.

Grupo 1- **Enrique Martín Gayo**

Calvet-Mirabent M, Sánchez-Cerrillo I, Martín-Cófreces N, Mar-tínez-Fleta P, de la Fuente H, Tsukalov I, Delgado-Arévalo C, Calzada MJ, de Los Santos I, Sanz J, García-Fraile L, Sánchez- Madrid F, Alfranca A, Muñoz-Fernández MÁ, Buzón MJ, Martín-Gayo E. **Antiretroviral therapy duration and immunometabolic state determine efficacy of ex vivo dendritic cell-based treatment restoring functional HIV-specific CD8+ T cells in people living with HIV**. EBioMedicine. 2022. 81:104090. doi: 10.1016/j.ebiom.2022.104090. IF: 11,20.

Grupo 1 – **Francisco Sánchez Madrid**

Jiménez-Fernández M, Rodríguez-Sinovas C, Cañes L, Ballester-Servera C, Vara A, Requena S, de la Fuente H, Martínez-González J, Sánchez-Madrid F. **CD69-ox-LDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in human CD4 + T lymphocytes**. Cell Mol Life Sci. 2022. 5; 79 (8): 468. doi: 10.1007/s00018-022-04481-1. IF: 9,20.

Grupo 8 – **María Josefa Calzada García**

Sevilla-Montero J, Munar-Rubert O, Pino-Fadón J, Aguilar-Latorre C, Villegas-Esguevillas M, Climent B, Agrò M, Choya-Foces C, Martínez-Ruiz A, Balsa E, Muñoz-Calleja C, Gómez-Punter RM, Vázquez-Espinosa E, Cogolludo A, Calzada MJ. **Cigarette smoke induces pulmonary arterial dysfunction through an imbalance in the redox status of the soluble**

guanylyl cyclase. Free Radic Biol Med. 2022. 193 :9-22. doi: 10.1016/j.freeradbiomed.2022.09.026. IF: 7,40.

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**

Group 10 – **Susana Cadenas Álvarez**

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 Íñiguez 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 Azpíroz**

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**

Group 42 – **Águeda González Rodríguez**

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 neurodegenative 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 each area:

Grupo 33 – **José Luis Ayuso Mateos.**

Delgado-Parada E, Alonso-Sánchez M, Ayuso-Mateos JL, Robles-Camacho M, Izquierdo A. **Liaison psychiatry before and after the COVID-19 pandemic**. Psychiatry Res. 2022. 314: 114651. doi: 10.1016/j.psychres.2022.114651. IF: 11,225.

Grupo 41 – **Francisco Javier Egea Maiquez**

Palomino-Antolin A, Narros-Fernández P, Farré-Alins V, Sevilla-Montero J, Decouty-Pérez C, Lopez-Rodriguez AB, Fernández N, Monge L, Casas AI, Calzada MJ, Egea J. **Time-dependent dual effect of NLRP3 inflammasome in brain ischaemia**. Br J Pharmacol. 2022. 179 (7):1395-1410. doi: 10.1111/bph.15732. IF: 9,47.

Grupo 41 – **Francisco Javier Egea Maiquez**

Narros-Fernández P, Chioua M, Petcu SA, Diez-Iriepa D, Cerrada-Gálvez L, Decouty-Pérez C, Palomino-Antolín A, Ramos E, Farré-Alins V, López-Rodríguez AB, Romero A, Marco-Contelles J, Egea J. **Synthesis and Pharmacological Evaluation of New *N*-Sulfonylureas as NLRP3 Inflammasome Inhibitors: Identification of a Hit Compound to Treat Gout**. J Med Chem. 2022. 65(8):6250-6260. doi: 10.1021/acs.jmedchem.2c00149. IF: 8,04.

Grupo 32 – **Francisco Abad Santos**

Zubiaur P, Figueiredo-Tor L, Villapalos-García G, Soria-Chacartegui P, Navares-Gómez M, Novalbos J, Matas M, Calleja S, Mejía-Abril G, Román M, Ochoa D, Abad-Santos F. **Association between CYP2C19 and CYP2B6 phenotypes and the pharmacokinetics and safety of diazepam**. Biomed Pharmacother. 2022. 155:113747. doi: 10.1016/j.biopha.2022.113747. IF: 7,42.

Grupo 16 – **Manuela García López**

Luengo E, Trigo-Alonso P, Fernández-Mendívil C, Nuñez Á, Campo MD, Porrero C, García-Magro N, Negredo P, Senar S, Sánchez-Ramos C, Bernal JA, Rábano A, Hoozemans J, Casas AI, Schmidt HHHW, López MG. **Implication of type 4 NADPH oxidase (NOX4) in tauopathy**. Redox Biol. 2022. 49: 102210. doi: 10.1016/j.redox.2021.102210. IF: 10,79.

Line 1 Neuropharmacology and neuroprotection.

Group 16 – **Manuela García López**

Group 28 – **Cristóbal de los Ríos Salgado**

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**

AREA 3: ADVANCED THERAPIES AND INDIVIDUALIZED MEDICINE

COORDINATOR: Isidoro González Álvaro

DEPUTY DIRECTOR: María Chaparro Sánchez

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 each area:

Grupo 53 – **Almudena Zapatero Laborda**

Zapatero A, Guerrero A, Maldonado X, Álvarez A, San-Segundo CG, Rodríguez MÁC, Solé JM, Olivé AP, Casas F, Boladeras A, de Vidales CM, de la Torre MLV, Vara S, Sanz JL, Calvo FA. **High- dose radiotherapy and risk-adapted androgen deprivation in localised prostate cancer (DART 01/05): 10-year results of a phase 3 randomised, controlled trial**. Lancet Oncol. 2022. 23(5):671-681. doi: 10.1016/S1470-2045(22)00190-5. IF: 54,43.

Grupo 38 – **María Chaparro Sánchez**

Chaparro M, Kunovský L, Aguas M, Livne M, Rivière P, Bar-Gil Shitrit A, Myrelid P, Arroyo M, Barreiro-de Acosta M, Bautista M, Biancone L, Biron IA, Boysen T, Carpio D, Castro B, Dragoni G, Ellul P, Holubar SD, de Jorge MÁ, Leo E, Manceñido N, Moens A, Molnár T, Ramírez de la Piscina P, Ricanek P, Sebkova L, Sempere L, Teich N, Gisbert JP, Julsgaard M. **Surgery due to Inflammatory Bowel Disease During Pregnancy: Mothers and Offspring Outcomes From an ECCO Confer Multicentre Case Series [Scar Study]**. J Crohns Colitis. 2022. 16(9):1428-1435. doi: 10.1093/ecco-jcc/jjac050. IF: 10,02.

Grupo 48 – **Beatriz López Melgar**

López-Melgar B, Mass V, Nogales P, Sánchez-González J, Entrekin R, Collet-Billon A, Rossello X, Fernández-Friera L, Fernández-Ortiz A, Sanz J, Bentzon JF, Bueno H, Ibáñez B, Fuster V. **New 3-Dimensional Volumetric Ultrasound Method for**

Accurate Quantification of Atherosclerotic Plaque Volume. JACC Cardiovasc Imaging. 2022. 15(6):1124-1135. doi: 10.1016/j.jcmg.2022.01.005. IF: 16,05.

Grupo 52 – **Laura María Cardeñoso Domingo**

Cardeñoso Domingo L, Roy Vallejo E, Zurita Cruz ND, Chicot Llano M, Ávalos Pérez-Urria E, Barrios A, Hernando Santos J, Ortiz J, Rodríguez García SC, Martín Ramírez A, Ciudad Sañudo M, Marcos C, García Castillo E, Fontán García-Rodrigo L, González B, Méndez R, Iturrate I, Sanz García A, Villa A, Sánchez Azofra A, Quicios B, Arribas D, Álvarez Rodríguez J, Patiño P, Trigueros M, Uriarte M, Triguero Martínez A, Arévalo C, Galván Román JM, García-Vicuña R, Ancochea J, Soriano JB, Canabal A, Muñoz Calleja C, De la Cámara R, Suarez Fernández C, González Álvaro I, Rodríguez-Serrano DA; PREDINMUN-COVID Group. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol. 2022. 94(11):5260-5270. doi: 10.1002/jmv.27989. IF: 20,69.

Grupo 36 – **Cristina Valero Martín**

Valero C, Baldivieso JP, Gonzalez-Alvaro I, Tomero E, Castañeda S, García-Vicuña R. **Effectiveness and safety of combined biological therapy in patients with refractory multidomain spondyloarthritis**. Ann Rheum Dis. 2022. 81(6):899-901. doi: 10.1136/annrheumdis-2021- 221812. IF: 27,97.

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 54 – **Laura Cerezo Padellano**

Group 59 – **Carlos Manuel Olivier Gómez**

Group Asociado 3 – **José Cordero Ampuero**

SCIENTIFIC OUTPUT

GLOBAL ANALYSIS

Publications:

	Total	Impact Factor	Main Impact Factor	% D1	%Q1	% IF>10	% International collaborations	% Open Access	% Leadership
Publications	**549**	**4854,52**	**8,84**	**18**	**52**	**15**	**38**	**64**	**44**
Articles	495	4440,73	8,97	19	52	15	37,5	65	41
Editorial	30	250,72	8,35	17	53	20	37	40	87
Review	24	163,07	6,79	12,5	38	8	50	67	54

New Projects:

New Research projects in 2022: 31.

New Human Resources grants in 2021: 9.

Clinical Trials:

Ongoing Clinical Trials during the year 2022: 549.

Clinical Trial agreements signed in 2022: 118.

Clinical Practice Guidelines:

Clinical practice guidelines: 6

Patents:

Number of patents applications: 2.

Theses:

Number of theses defended: 15.

Number of theses with European mention: 4.

Communication: ELENA ESPAÑOL

Number of sessions / communication conferences held: 42 Number of news published in printed press: 12

News in other audiovisual media (TV / Radio): 22

Number of news in specialised and non-specialised digital media: 117

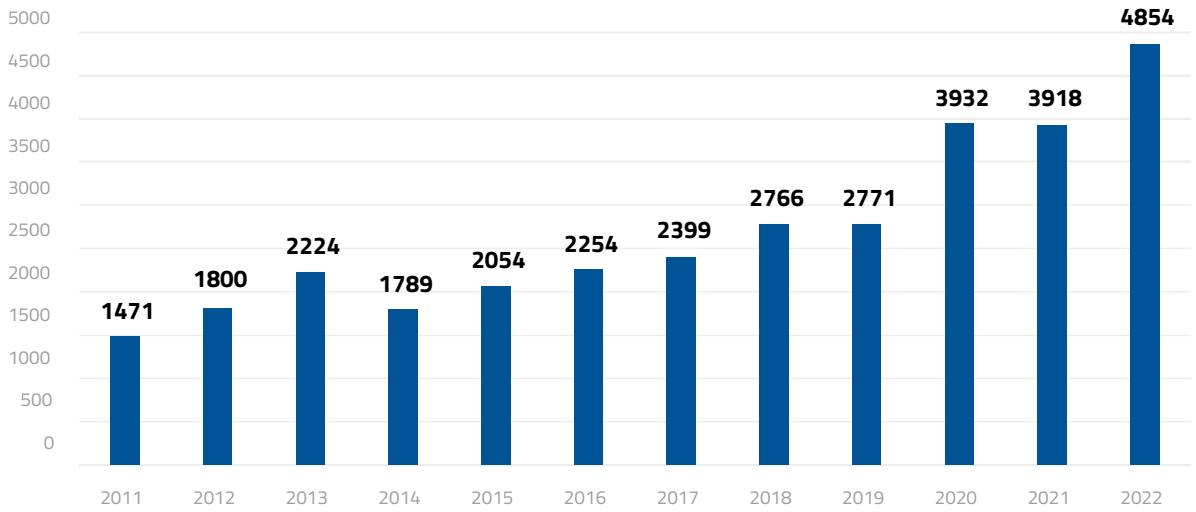
Number of Research Bulletin "Factor de Impacto" with the last scientific news with wide dissemination among patients, researchers and media: 3

	01/01/2022	31/12/2022
First Stage Researcher (R1):	53	58
Recognised Researcher (R2)	157	151
Established Researcher (R3)	35	32
Leading Researcher (R4)	69	65

PUBLICATIONS

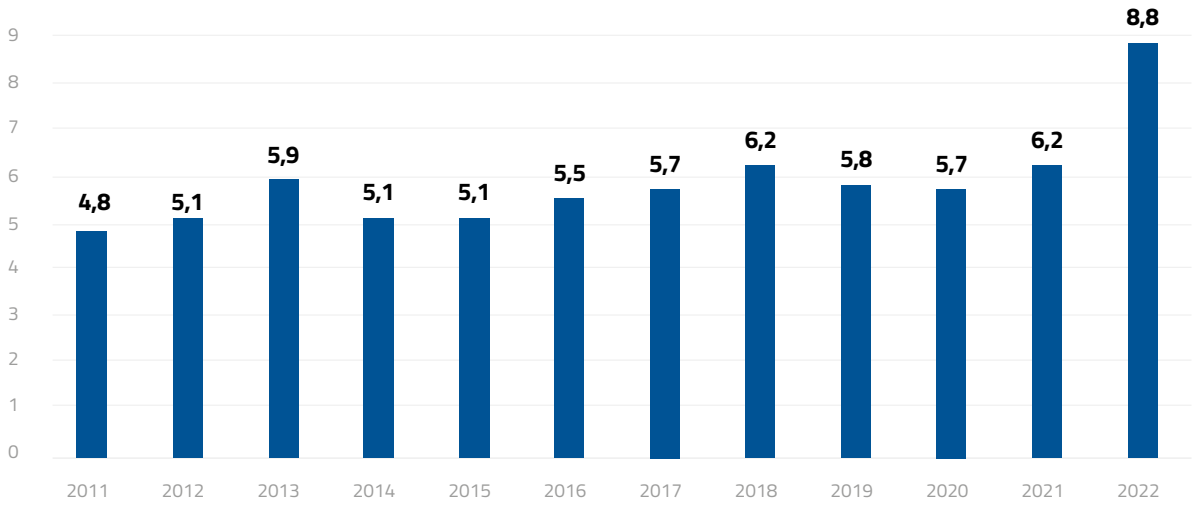
The number of publications increased in 2020, due to the number of articles published on COVID-19. These dates were followed in 2021 by a 10% decrease in the number of publications by Institute members. In 2022 this trend continues, with a decrease in publications compared to the previous year. However, the cumulative impact factor has shown a considerable increase compared to previous years, reaching 4854.52. This figure shows the high quality of the journals in which our work has been published.

The following graph shows the historical evolution from 2011 to 2022.



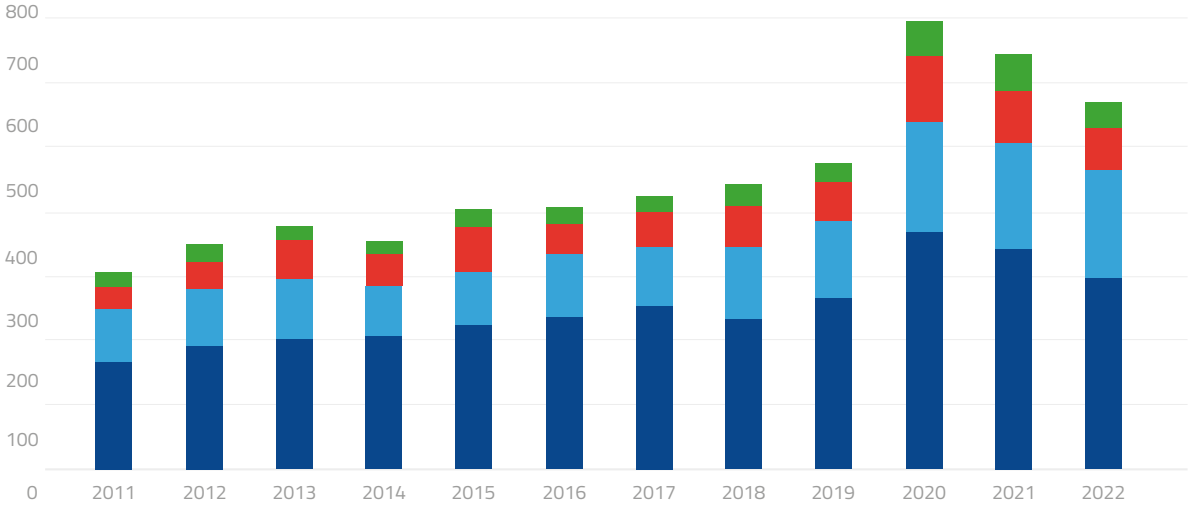
The decrease in the number of articles combined with the stability in the cumulative impact factor have caused a significant increase in the average impact factor. This parameter was the highest in the history of our Institute, exceeding 8 points.

The following table shows the evolution of the mean impact factor from 2010 to 2021.



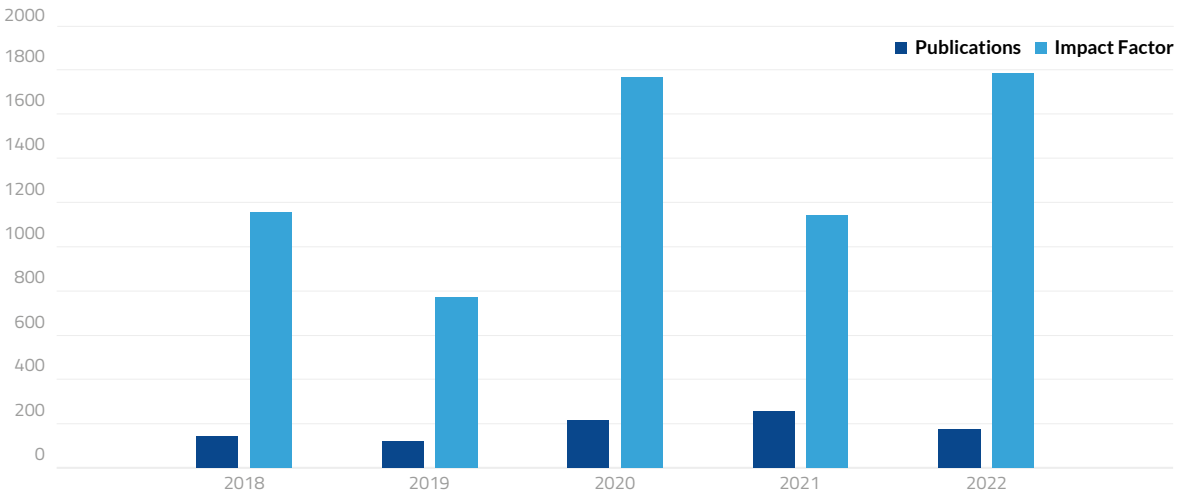
Regarding the distribution by quartiles, 52% of the all publications were published in first quartile journals and 82% of them were published in first and second quartile journals.

The following table shows a graph with the distribution of publications by quartile from 2010 to 2022.

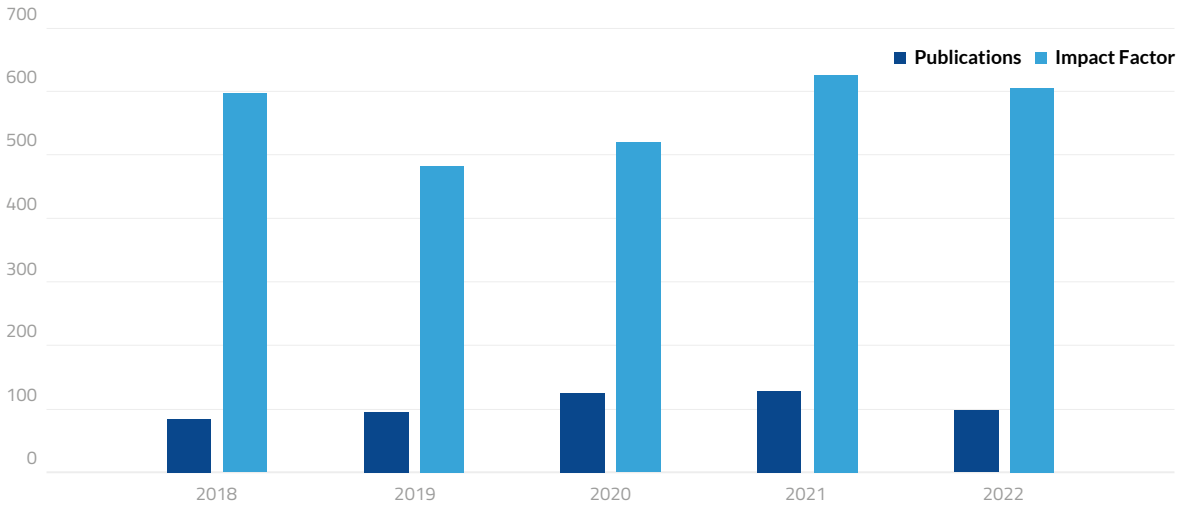


The scientific output of areas 1 to 3 has remained stable in 2021 compared to 2020, whereas in 2022 the number of publications has decreased, accompanied by a proportional increase in the average impact factor.

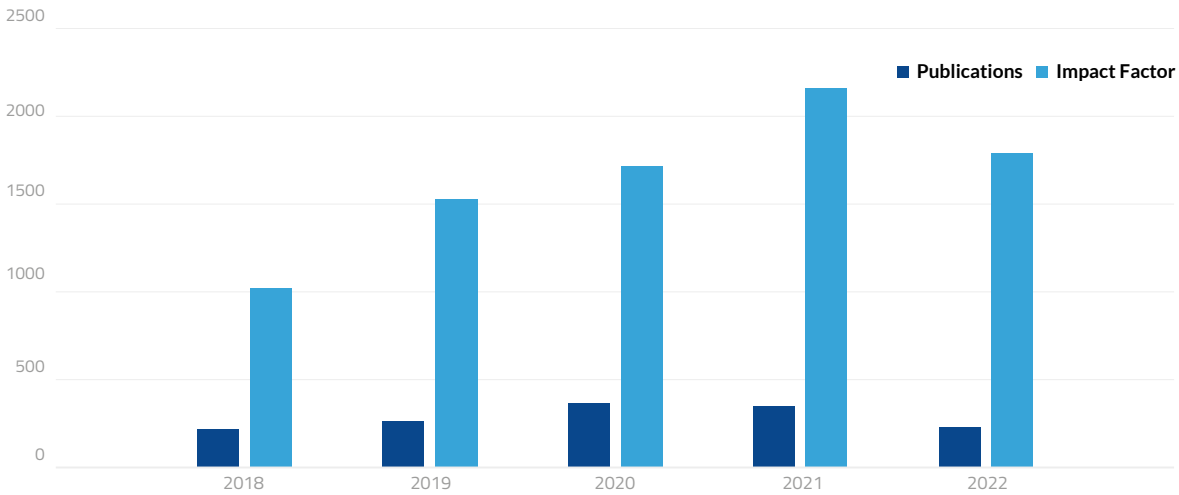
Area 1: Cellular and molecular etiopathogenic mechanisms in inflammatory and autoimmune diseases



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	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
NEW ENGLAND JOURNAL OF MEDICINE	2	176,08	352,16
JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	1	157,34	157,34
NATURE MEDICINE	1	87,24	87,24
Lancet Psychiatry	1	77,06	77,06
LANCET INFECTIOUS DISEASES	1	71,42	71,42
SCIENCE	1	63,71	63,71
LANCET ONCOLOGY	2	54,43	108,87
ANNALS OF ONCOLOGY	1	51,77	51,77
Nature Reviews Cardiology	1	49,42	49,42
LANCET GASTROENTEROLOGY & HEPATOLOGY	1	45,04	45,04
INTENSIVE CARE MEDICINE	2	41,79	83,57
NATURE GENETICS	1	41,31	41,31
Circulation	2	39,92	79,84
JOURNAL OF INFECTION	1	38,64	38,64
EUROPEAN HEART JOURNAL	2	35,86	71,71
EUROPEAN RESPIRATORY JOURNAL	5	33,8	168,98
JAMA oncology	1	33,01	33,01
Gut	1	31,79	31,79
AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	1	30,53	30,53
JOURNAL OF HEPATOLOGY	2	30,08	60,17
ANNALS OF THE RHEUMATIC DISEASES	1	27,97	27,97
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY	1	27,2	27,2
Blood	1	25,48	25,48
EUROPEAN UROLOGY	5	24,27	121,34
Journal of Hematology & Oncology	1	23,17	23,17
CLINICAL INFECTIOUS DISEASES	2	21	42

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
JOURNAL OF MEDICAL VIROLOGY	1	20,69	20,69
JOURNAL OF CLINICAL INVESTIGATION	1	19,46	19,46
Nature Communications	3	17,69	53,08
Advanced Science	1	17,52	17,52
JACC-CARDIOVASCULAR IMAGING	1	16,05	16,05
JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY	2	15,49	30,97
INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS	1	15,44	15,44
BIOMATERIALS	1	15,3	15,3
ALLERGY	2	14,71	29,42
JOURNAL OF CLINICAL VIROLOGY	1	14,48	14,48
EMBO Molecular Medicine	1	14,26	14,26
METABOLISM-CLINICAL AND EXPERIMENTAL	1	13,93	13,93
CLINICAL CANCER RESEARCH	1	13,8	13,8
Clinical Gastroenterology and Hepatology	2	13,58	27,15
ENVIRONMENT INTERNATIONAL	1	13,35	13,35
Leukemia	1	12,88	12,88
PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF; AMERICA	1	12,78	12,78
Journal for ImmunoTherapy of Cancer	1	12,47	12,47
CELL DEATH AND DIFFERENTIATION	1	12,07	12,07
JAMA DERMATOLOGY	1	11,82	11,82
NEUROLOGY	1	11,8	11,8
PSYCHIATRY RESEARCH	1	11,23	11,23
EBioMedicine	3	11,21	33,62
BMC MEDICINE	1	11,15	11,15
BRITISH JOURNAL OF DERMATOLOGY	1	11,11	11,11
JACC-CARDIOVASCULAR INTERVENTIONS	2	11,08	22,15
HAEMATOLOGICA	2	11,05	22,09
Redox biology	1	10,79	10,79
PSYCHOLOGICAL MEDICINE	1	10,59	10,59
Diabetologia	1	10,46	10,46

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
THROMBOSIS RESEARCH	1	10,41	10,41
Annals of Intensive Care	1	10,32	10,32
MOLECULAR THERAPY-NUCLEIC ACIDS	1	10,18	10,18
JOURNAL OF CROHNS & COLITIS	6	10,02	60,12
Hypertension	1	9,9	9,9
BLOOD CANCER JOURNAL	1	9,81	9,81
INTERNATIONAL JOURNAL OF EPIDEMIOLOGY	1	9,69	9,69
ALIMENTARY PHARMACOLOGY & THERAPEUTICS	3	9,52	28,57
Jci Insight	1	9,48	9,48
BRITISH JOURNAL OF PHARMACOLOGY	5	9,47	47,37
JOURNAL OF NANOBIOTECHNOLOGY	1	9,43	9,43
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY	2	9,23	18,46
CELLULAR AND MOLECULAR LIFE SCIENCES	1	9,21	9,21
GENETICS IN MEDICINE	1	8,86	8,86
Frontiers in immunology	11	8,79	96,65
ONCOGENE	1	8,76	8,76
ELIFE	1	8,71	8,71
Biomarker Research	1	8,63	8,63
BRITISH JOURNAL OF HAEMATOLOGY	1	8,62	8,62
Circulation-Cardiovascular Imaging	1	8,59	8,59
ENVIRONMENTAL RESEARCH	1	8,43	8,43
JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY	4	8,19	32,74
DEPRESSION AND ANXIETY	1	8,13	8,13
FREE RADICAL BIOLOGY AND MEDICINE	1	8,1	8,1
JOURNAL OF MEDICINAL CHEMISTRY	2	8,04	16,08
European Journal of Internal Medicine	1	7,75	7,75
EUROINTERVENTION	6	7,73	46,37
JOURNAL OF THE AMERICAN SOCIETY OF ECHOCARDIOGRAPHY	2	7,72	15,44
Antioxidants	7	7,68	53,73

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
Cells	1	7,67	7,67
CLINICAL NUTRITION	1	7,64	7,64
Journal of Intensive Care	1	7,52	7,52
Circulation-Cardiovascular Interventions	3	7,51	22,54
BIOMEDICINE & PHARMACOTHERAPY	4	7,42	29,68
HEART	1	7,37	7,37
INFLAMMATORY BOWEL DISEASES	1	7,29	7,29
NEPHROLOGY DIALYSIS TRANSPLANTATION	2	7,19	14,37
RESPIRATORY RESEARCH	2	7,16	14,32
RHEUMATOLOGY	5	7,05	35,23
COMPUTER METHODS AND PROGRAMS IN BIOMEDICINE	1	7,03	7,03
IEEE JOURNAL OF BIOMEDICAL AND HEALTH INFORMATICS	1	7,02	7,02
REVISTA ESPANOLA DE CARDIOLOGIA	8	6,98	55,8
RADIOTHERAPY AND ONCOLOGY	3	6,9	20,7
UNITED EUROPEAN GASTROENTEROLOGY JOURNAL	2	6,87	13,73
NUTRIENTS	5	6,71	33,53
EUROPEAN JOURNAL OF IMMUNOLOGY	1	6,69	6,69
JOURNAL OF NEUROLOGY	1	6,68	6,68
FRONTIERS IN PLANT SCIENCE	1	6,63	6,63
CANADIAN JOURNAL OF CARDIOLOGY	2	6,61	13,23
Cancers	8	6,58	52,6
Pharmaceutics	4	6,53	26,1
Frontiers in Public Health	2	6,46	12,92
NANOMEDICINE-NANOTECHNOLOGY BIOLOGY AND MEDICINE	1	6,46	6,46
ARCHIVOS DE BRONCONEUMOLOGIA	17	6,33	107,61
EUROPEAN JOURNAL OF NEUROLOGY	1	6,29	6,29
Kidney International Reports	1	6,23	6,23
AMERICAN JOURNAL OF CLINICAL DERMATOLOGY	1	6,23	6,23
JOURNAL OF PHYSIOLOGY-LONDON	1	6,23	6,23
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	9	6,21	55,87

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM	1	6,13	6,13
CHINESE MEDICAL JOURNAL	2	6,13	12,27
Journal of the American Heart Association	1	6,11	6,11
CEPHALALGIA	1	6,08	6,08
Biomolecules	1	6,06	6,06
FRONTIERS IN MICROBIOLOGY	2	6,06	12,13
Frontiers in endocrinology	3	6,06	18,17
EUROPEAN JOURNAL OF CELL BIOLOGY	1	6,02	6,02
JOURNAL OF LEUKOCYTE BIOLOGY	1	6,01	6,01
Frontiers in Pharmacology	5	5,99	29,94
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY	1	5,94	5,94
Epidemiology and health	1	5,92	5,92
ENDOCRINE-RELATED CANCER	1	5,9	5,9
Gastroenterologia y Hepatologia	3	5,87	17,61
CLINICAL KIDNEY JOURNAL	5	5,86	29,3
Frontiers in Cardiovascular Medicine	3	5,85	17,54
Rmd Open	1	5,81	5,81
Life Science Alliance	3	5,78	17,34
JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY	3	5,76	17,27
Frontiers in oncology	1	5,74	5,74
Journal of Fungi	1	5,72	5,72
FRONTIERS IN AGING NEUROSCIENCE	1	5,7	5,7
EXPERT OPINION ON BIOLOGICAL THERAPY	3	5,59	16,77
FOODS	1	5,56	5,56
Journal of Cystic Fibrosis	1	5,53	5,53
JOURNAL OF PARKINSONS DISEASE	2	5,52	11,04
NEUROLOGIA	3	5,49	16,46
SEMINARS IN ARTHRITIS AND RHEUMATISM	3	5,43	16,29
EUROPEAN NEUROPSYCHOPHARMACOLOGY	1	5,42	5,42
JOURNAL OF NEUROSURGERY	1	5,41	5,41

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
CLINICAL AND EXPERIMENTAL ALLERGY	1	5,4	5,4
WORLD JOURNAL OF GASTROENTEROLOGY	1	5,37	5,37
ANNALS OF MEDICINE	1	5,35	5,35
EMERGENCIAS	3	5,35	16,04
BEHAV RES THER	1	5,32	5,32
BIOORGANIC CHEMISTRY	1	5,31	5,31
JOURNAL OF NUTRITION HEALTH & AGING	1	5,29	5,29
JOINT BONE SPINE	1	5,26	5,26
JOURNAL OF PSYCHIATRIC RESEARCH	3	5,25	15,75
ANTIBIOTICS-BASEL	3	5,22	15,67
Pharmaceuticals	1	5,22	5,22
PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY	1	5,2	5,2
BONE MARROW TRANSPLANTATION	2	5,17	10,35
ONCOTARGET	1	5,17	5,17
EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES	1	5,1	5,1
INTERNATIONAL JOURNAL OF PUBLIC HEALTH	1	5,1	5,1
Frontiers in Medicine	6	5,06	30,35
Health Information Science and Systems	1	5,02	5,02
Scientific Reports	11	5	54,96
AMERICAN JOURNAL OF NEURORADIOLOGY	1	4,97	4,97
Journal of clinical medicine	18	4,96	89,35
Vaccines	2	4,96	9,92
MOLECULES	1	4,93	4,93
ARCHIVES OF DISEASE IN CHILDHOOD	1	4,92	4,92
JOURNAL OF MEDICAL SYSTEMS	1	4,92	4,92
CLINICAL AND EXPERIMENTAL RHEUMATOLOGY	5	4,86	24,31
SLEEP MEDICINE	1	4,84	4,84
MULTIPLE SCLEROSIS AND RELATED DISORDERS	1	4,81	4,81
OBESITY FACTS	1	4,81	4,81

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
THERAPEUTIC ADVANCES IN GASTROENTEROLOGY	1	4,8	4,8
JOURNAL OF HYPERTENSION	1	4,78	4,78
Biomedicines	7	4,76	33,3
Frontiers in Physiology	1	4,76	4,76
PSYCHONEUROENDOCRINOLOGY	1	4,69	4,69
Digital Health	1	4,69	4,69
EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY	1	4,53	4,53
Movement Disorders Clinical Practice	1	4,51	4,51
Neurology and Therapy	3	4,45	13,34
CTS-CLINICAL AND TRANSLATIONAL SCIENCE	1	4,44	4,44
REVIEWS IN CARDIOVASCULAR MEDICINE	1	4,43	4,43
Open forum infectious diseases	1	4,42	4,42
Journal of Cardiovascular Development and Disease	1	4,42	4,42
PARKINSONISM & RELATED DISORDERS	1	4,4	4,4
SURGERY	1	4,35	4,35
ANNALS OF SURGICAL ONCOLOGY	2	4,34	8,68
JOURNAL OF CLINICAL SLEEP MEDICINE	1	4,32	4,32
Orphanet Journal of Rare Diseases	2	4,3	8,61
Expert Review of Respiratory Medicine	1	4,3	4,3
ERJ open research	3	4,24	12,72
JOURNAL OF ALZHEIMERS DISEASE	1	4,16	4,16
GENES	1	4,14	4,14
Frontiers in neurology	2	4,09	8,17
SSM - Population Health	1	4,09	4,09
Rheumatology and Therapy	1	4,08	4,08
ADVANCES IN THERAPY	3	4,07	12,21
NUTRITIONAL NEUROSCIENCE	1	4,06	4,06
CURRENT OPINION IN HIV AND AIDS	1	4,06	4,06
INTERNATIONAL JOURNAL OF CARDIOLOGY	3	4,04	12,12
EJSO	4	4,04	16,15

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
ANNALS OF HEMATOLOGY	1	4,03	4,03
Diagnostics	3	3,99	11,98
CARDIOVASCULAR PATHOLOGY	1	3,98	3,98
Endocrine	2	3,93	7,85
COLORECTAL DISEASE	1	3,92	3,92
JCR-JOURNAL OF CLINICAL RHEUMATOLOGY	2	3,9	7,8
BJS Open	1	3,88	3,88
DERMATOLOGIC THERAPY	6	3,86	23,15
INTERNATIONAL JOURNAL OF GERIATRIC PSYCHIATRY	1	3,85	3,85
PloS one	5	3,75	18,76
BRITISH JOURNAL OF RADIOLOGY	1	3,63	3,63
Therapeutic Advances in Musculoskeletal Disease	2	3,63	7,25
INTERNATIONAL JOURNAL OF FOOD SCIENCE AND TECHNOLOGY	1	3,61	3,61
RHEUMATOLOGY INTERNATIONAL	1	3,58	3,58
FRONT NEUROANAT	1	3,54	3,54
AGING & MENTAL HEALTH	1	3,51	3,51
Journal of Personalized Medicine	4	3,51	14,03
Cardiology Journal	1	3,49	3,49
DISEASE MARKERS	1	3,46	3,46
SEIZURE-EUROPEAN JOURNAL OF EPILEPSY	1	3,41	3,41
Processes	1	3,35	3,35
CLINICAL & TRANSLATIONAL ONCOLOGY	5	3,34	16,7
EPILEPSY & BEHAVIOR	2	3,34	6,67
Brain sciences	1	3,33	3,33
CANCER CHEMOTHERAPY AND PHARMACOLOGY	1	3,29	3,29
JOURNAL OF DERMATOLOGICAL TREATMENT	1	3,23	3,23
Jmir Medical Informatics	1	3,23	3,23
Endocrine connections	1	3,22	3,22
JOURNAL OF CARDIOVASCULAR TRANSLATIONAL RESEARCH	1	3,22	3,22
DRUGS IN R&D	1	3,2	3,2

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
MEDICINA CLINICA	4	3,2	12,8
Journal of Geriatric Cardiology	2	3,19	6,38
JOURNAL OF CLINICAL GASTROENTEROLOGY	1	3,17	3,17
Healthcare	1	3,16	3,16
Respiratory Medicine and Research	1	3,15	3,15
Systematic Reviews	1	3,14	3,14
AMERICAN JOURNAL OF CARDIOLOGY	7	3,13	21,93
Frontiers In Bioscience-Landmark	2	3,12	6,23
KOREAN CIRCULATION JOURNAL	1	3,1	3,1
HIV MEDICINE	1	3,09	3,09
NEFROLOGIA	5	3,08	15,42
REVISTA CLINICA ESPANOLA	2	3,06	6,13
Journal Of Asthma And Allergy	2	3,03	6,05
BMJ OPEN	1	3,01	3,01
EPILEPSY RESEARCH	1	2,99	2,99
INTERNATIONAL JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY	1	2,99	2,99
MEDICINA-LITHUANIA	1	2,95	2,95
JOURNAL OF CARDIOVASCULAR ELECTROPHYSIOLOGY	1	2,94	2,94
CURRENT DRUG TARGETS	1	2,94	2,94
LANGENBECKS ARCHIVES OF SURGERY	1	2,9	2,9
JOURNAL OF CARDIOTHORACIC AND VASCULAR ANESTHESIA	1	2,89	2,89
INTERNATIONAL JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE	3	2,89	8,68
CANCER EPIDEMIOL	1	2,89	2,89
CURRENT OPINION IN PULMONARY MEDICINE	2	2,87	5,74
Journal of Pain Research	1	2,83	2,83
EUROPEAN JOURNAL OF DERMATOLOGY	1	2,81	2,81
Archives of Public Health	1	2,74	2,74
Updates in Surgery	1	2,69	2,69
Electronics	1	2,69	2,69

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
JOURNAL OF STROKE & CEREBROVASCULAR DISEASES	2	2,68	5,35
Arquivos Brasileiros de Cardiologia	1	2,67	2,67
Pharmacogenomics	2	2,64	5,28
Progress in Brain Research	2	2,62	5,25
J VIROL METHODS	1	2,62	2,62
INTERNAL MEDICINE JOURNAL	1	2,61	2,61
EUROPEAN JOURNAL OF GASTROENTEROLOGY & HEPATOLOGY	1	2,59	2,59
CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS	2	2,59	5,17
REVISTA ESPANOLA DE QUIMIOTERAPIA	3	2,52	7,55
GACETA SANITARIA	1	2,48	2,48
REVISTA ESPANOLA DE ENFERMEDADES DIGESTIVAS	4	2,39	9,56
INTERNATIONAL JOURNAL OF HEMATOLOGY	1	2,32	2,32
INTERNATIONAL JOURNAL OF CARDIOVASCULAR IMAGING	1	2,32	2,32
PATIENT PREFERENCE AND ADHERENCE	1	2,31	2,31
Transplant Infectious Disease	1	2,23	2,23
BMC Cardiovascular Disorders	1	2,17	2,17
JOURNAL OF CLINICAL PHARMACY AND THERAPEUTICS	1	2,15	2,15
JOURNAL OF CLINICAL MONITORING AND COMPUTING	1	1,98	1,98
INTERNATIONAL UROGYNECOLOGY JOURNAL	1	1,93	1,93
Endocrinologia Diabetes Y Nutricion	3	1,83	5,5
Medicine	1	1,82	1,82
HEART AND VESSELS	1	1,81	1,81
CORONARY ARTERY DISEASE	6	1,72	10,3
SCIENCE PROGRESS	1	1,51	1,51
JOURNAL OF CUTANEOUS PATHOLOGY	2	1,46	2,92
DIAGNOSTIC CYTOPATHOLOGY	1	1,39	1,39
CLINICAL NEUROPHARMACOLOGY	1	1,38	1,38
Revista Espanola de Salud Publica	1	1,33	1,33
EUROPEAN JOURNAL OF PSYCHIATRY	1	1,29	1,29
CYTOPATHOLOGY	2	1,29	2,57

JOURNAL	TOTAL OF PUBLICATIONS	QUARTIL	IMPACT FACTOR
REVISTA DE NEUROLOGIA	3	1,24	3,71
HEC Forum	1	1,2	1,2
Nutricion Hospitalaria	1	1,17	1,17
		2925,92	**5063,25**

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: Derivados de n-sulfonilureas y su uso terapéutico.

Number: WES22070457

Date of applicant: 14/07/2022

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (90%), CSIC (10%).

Inventors: Francisco Javier Egea Maiquez, Paloma Narros Fernandez, Laura Cerrada Galvez, Alejandra Palomino Antolin, Victor Farre Alins, Celine Decouty Perez, Ana Belén Lopez Rodriguez, Jose Luis Marco Costelle.

Title: Método predictivo de la respuesta al tratamiento farmacológico en epilepsia

Number: P202230316

Date of applicant: 07/04/2022

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (100%).

Inventors: Desiree Josefa Nava Cedeño, Maria Concepción Alonso Cerezo, Jesús Pastor Gomez. Ancor Sanz Garcia, Lorena Carolina Vega Zelaya, Paloma Pulido Rivas, Maria de Toledo Heras, Francisco Abad Santos, Rafael García Sola.

COMPETITIVE PROJECTS

Grants

Funding Institution	Call	Calls Granted
Instituto de Salud Carlos III	Proyectos de Investigación (total)	27
	Investigación Clínica Independiente	1
	Proyecto de Desarrollo Tecnológico en Salud	1
	Infraestructura de Investigación	1
Fundación CRIS contra el cáncer	Programa CRIS de talento clínico	1
FIPSE (Fundación para la Innvación Prospectiva en Salud en España)	Proyectos de Investigación	1
Agencía Estatal de Investigación	Prueba de Concepto	1
	Proyectos Colaboración Público-Privada	2
	Proyectos de Líneas Estratégicas	1
EU4Health	Proyectos de Investigación	1
Horizonte Europa	Proyectos de Investigación	1

Research staff fully or partially funded through competitive calls in 2022.

Funding Institution	Call	Calls Granted
Agencia Estatal de Investigacion	Contratos predoctorales para la formación de doctores	1
	Retos Investigación	1
	Proyectos de Líneas Estratégicas	3
Comunidad de Madrid	Programa Investigo	18
	Ayudas para la realización de programas de actividades entre grupos de investigación de la CAM en Biomedicina	2
ISCIII	Movilidad Personal Investigador (M-AES)	1
	Ayudas Sara Borrell	2
	Miguel Servet	2
	Rio Hortega	4
	Bolsa Ampliación de Estudios	2
	Investigación Clínica Independiente	1
	Proyectos de Investigación (PI)	8
	Redes de Investigación	3
	CIBER	1
	Infraestructura de Medicina de Precisión Asociada a la Ciencia y Tecnología (IMPaCT)	1
	Proyecto de Desarrollo Tecnológico en Salud	1
	Infraestructuras y equipamiento científico	1
Ministerio de Educación	Formació de Profesorado Universitario	1
EU4Health	Proyectos de Investigación	1
Horizonte Europa	Proyectos de Investigación	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 2022, a total of 15 theses have been defended by member of the IIS. Four of them was a European thesis.

THESES

Doctoral Candidate	Title	Director/s	Defense date
Bago Plaza, Ángel	Efectos de los nitro-ácidos grasos sobre la activación de los linfocitos T	Íñiguez Peña, Miguel ángel / Serrador Peiró Juan Manuel	01/27/2022
Vega de la Osada, Francisco Félix	Alergia a contrastes yodados: desarrollo de un protocolo rápido de provocaciones parenterales para identificar una alternativa segura sin uso de premedicación	Blanco Guerra, Carlos / Freira Rewyes, Alfonsa	19/05/2022
Sampedro Núñez, Miguel Antonio	Marcadores predictivos de agresividad y supervivencia en tumores neuroendocrinos gastro-enteropancreáticos	Marazuela Aspiroz, Mónica	07/09/2022
Viejo de Navas, Lucia	Implicación del intercambiador Na/Ca mitocondrial (NCLX) en las enfermedades Neurodegenerativas: estudio fisiológico y farmacológico	De los Ríos Salgado, Cristóbal	17/06/2022
Reolid Pérez, Alejandra	Búsqueda de biomarcadores epigenéticos y farmacogenómicos asociados con la respuesta a fármacos biológicos en la psoriasis moderada-gravet	Ovejero Benito, María Carmen / Daudén Tello, Esteban	03/03/2022
Mateu Albero, Tamara	Caracterización del efecto de ibrutinib en la expresión y funcionalidad del receptor CCR7 en leucemia linfocítica crónica y en la actividad antitumoral de CAP-100, el primer anticuerpo terapéutico contra CCR7	Muñoz Calleja, Cecilia / Cuesta Mateos, Carlos	15/07/2022
Serra López-Mantencio, José María	Estudio de la farmacocinética y la farmacodinámica de natalizumab: hacia la individualización del tratamiento en pacientes con esclerosis múltiple	Muñoz Calleja, Cecilia	03/11/2022
García Guimaraes, Marcos Manuel	Disección coronaria espontánea en España: datos de un registro prospectivo a nivel nacional	Alfonso Manterola, Fernando	29/04/2022
Nogales Romo, María Teresa	Diferencias en los hallazgos de resonancia magnética cardica en hombres y mujeres con miocardiopatía hipertrófica	Alfonso Manterola, Fernando / Cecconi, Alberto	23/05/2022
Rivero Crespo, Fernando	Obtención de imagen molecular intracoronaria mediante el uso de nanocompuestos funcionalizados combinados con tomografía de coherencia óptica	Aguilar Torres, Río / Alfonoso Manterola, Fernando	25/05/2022
Rubín de Célix Vargas, Cristina	Cribado de cáncer colorrectal mediante cromoendoscopia en los pacientes con enfermedad inflamatoria intestinal	Pérez Gisbert, Francisco Javier / Chaparro Sánchez, María	30/05/2022

EUROPEAN THESES

Doctoral Candidate	Title	Director/s	Defense date
Sevilla Montero, Javier	Cigarette smoke impact on the pulmonary artery: implications on COPD-related pulmonary hypertension	Calzada García, María Josefa	31/03/2022
Trigo Alonso, Paula	Microglia-based therapeutic strategies for Alzheimer's disease and related tauopathies	García López, Manuela	01/07/2022
Guerra Cantera, Santiago	Los sistemas de IGF central y periférico en la respuestametabólica a los cambios dietéticos	Argente Oliver, Jesús / Chowen King, Julie Ann	28/04/2022
Narros Fernández, Paloma	Nuevas estrategias farmacológicas dirigidas a la inhibición del inflamasoma NLRP3	Egea Máiquez, Francisco Javier / Martínez Ruíz, Antonio	24/05/2022

CLINICAL GUIDELINES

Clinical Guidelines are the compendium of recommendations based on the systematic review of evidence and the evaluation of benefits and risks of different alternatives, with the aim of improving patients´ healthcare. During 2022, IIS Princesa researchers have participated in the development of 6 clinical guidelines.

Ayuso, J. L. **Who guidelines on mental health.** World Health Organization. 2022. PMID: https://www.who.int/publications/i/item/9789240053052. DOI: https://www.who.int/publications/i/item/9789240053052

Gisbert JP, Alcedo J, Amador J, Bujanda L, Calvet X, Castro-Fernández M, Fernández-Salazar L, Gené E, Lanas Á, Lucendo AJ, Molina-Infante J, Nyssen OP, Pérez-Aisa A, Puig I. **V Spanish Consensus Conference on Helicobacter pylori infection treatment**. Gastroenterol Hepatol 45 (5): 392-417. 2022. PMID: 34629204. IF: 5,867. doi: 10.1016/j.gastrohep.2021.07.011.

Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, Gasbarrini A, Hunt RH, Leja M, O'Morain C, Rugge M, Suerbaum S, Tilg H, Sugano K, El-Omar EM; European Helicobacter and Microbiota Study group. **Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report**. Gut. 2022. PMID: 35944925. IF: 31,795. doi: 10.1136/gutjnl- 2022-327745.

Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, Bachmann O, Bettenworth D, Chaparro M, Czuber-Dochan W, Eder P, Ellul P, Fidalgo C, Fiorino G, Gionchetti P, Gisbert JP, Gordon H, Hedin C, Holubar S, Iacucci M, Karmiris K, Katsanos K, Kopylov U, Lakatos PL, Lytras T, Lyutakov I, Noor N, Pellino G, Piovani D, Savarino E, Selvaggi F, Verstockt B, Spinelli A, Panis Y, Doherty G. **ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment**. J Crohns Colitis 16 (1): 2-17. 2022. PMID: 34635919. IF: 10,020. doi: 10.1093/ecco-jcc/jjab178.

Spinelli A, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, Bachmann O, Bettenworth D, Chaparro M, Czuber-Dochan W, Eder P, Ellul P, Fidalgo C, Fiorino G, Gionchetti P, Gisbert JP, Gordon H, Hedin C, Holubar S, Iacucci M, Karmiris K, Katsanos K, Kopylov U, Lakatos PL, Lytras T, Lyutakov I, Noor N, Pellino G, Piovani D, Savarino E, Selvaggi F, Verstockt B, Doherty G, Raine T, Panis Y. **ECCO Guidelines on Therapeutics in Ulcerative Colitis: Surgical Treatment**. J Crohns Colitis 16 (2): 179-189. 2022. PMID: 34635910. IF. 10.020. doi: 10.1093/ecco-jcc/jjab177.

Palacio-Portilla EJ, Roquer J, Amaro S, Arenillas JF, Ayo-Martín O, Castellanos M, Freijo MM, Fuentes B, García-Pastor A, Gomis M, Gómez-Choco M, López-Cancio E, Martínez-Sánchez P, Morales

A, Rodríguez-Yáñez M, Segura T, Serena J, Vivancos-Mora J, de Leciñana MA; Comité ad hoc del Grupo de Estudio de Enfermedades Cerebrovasculares de la Sociedad Española de Neurología. **Dyslipidemias and stroke prevention: Recommendations of the Study Group of Cerebrovascular Diseases of the Spanish Society of Neurology**. Neurologia 37(1):61-72. 2022. PMID: 35074190. IF: 5,486. doi: 10.1016/j.nrleng.2020.07.021.

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 2022, 118 new agreements have been signed for clinical trials led by IIS members.

Daudén Tello, Esteban. **"Estudio no intervencionista, retrospectivo y multicéntrico en dermatología, realizado mediante big data para describir la proporción y el recorrido asistencial de pacientes con psoriasis, urticaria crónica, hidradenitis supurativa y dermatitis atópica en departamentos de dermatología en hospitales terciarios de España. (DERMACLEAR)".** Sponsored by: Novartis. Sponsored's protocol code: DERMACLAIR.

Alegre Amor, Adrián. **"ESTUDIO EN FASE III, ABIERTO, MULTICÉNTRICO, ALEATORIZADO Y DE 3 GRUPOS PARA EVALUAR LA EFICACIA Y LA SEGURIDAD DE ELRANATAMAB (PF-06863135) EN MONOTERAPIA Y ELRANATAMAB + DARATUMUMAB EN COMPARACIÓN CON DARATUMUMAB + POMALIDOMIDA + DEXAMETASONA EN PARTICIPANTES CON MIELOMA MÚLTIPLE RECIDIVANTE/REFRACTARIO QUE HAN RECIBIDO AL MENOS 2 LÍNEAS PREVIAS DE TRATAMIENTO QUE INCLUYAN LENALIDOMIDA Y UN INHIBIDOR DEL PROTEASOMA".** Sponsored by: Pfizer INC. Sponsored's protocol code: C1071005.

Loscertales Pueyo, Javier. **"Estudio multicéntrico, abierto, de fase 2 para evaluar la eficacia y seguridad del retratamiento con venetoclax-obinituzumab en pacientes con leucemia linfocítica crónica recurrente".** Sponsored by: ABBVIE DEUTSCHLAND GMBH & CO. KG. Sponsored's protocol code: M20-356.

Cannata Ortiz, Jimena. **Efectividad y seguridad para el retratamiento con brentuximab-vedotin en pacientes con linfomas CD30+ en recaída/refractariedad: estudio retrospectivo de revisión de historias clínicas en España.** Sponsored by: TAKEDA FARMACÉUTICA ESPAÑA, S.A. Sponsored's protocol code: C25023.

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García Buey, Luisa. **Estudio Fase 11, simple ciego, aleatorizado, controlado e internacional para evaluar la seguridad, reactogenicidad, eficacia y respuesta inmune tras el tratamiento secuencial con un oligonucleótido antisentido (ASO) para la hepatitis B crónica (HBC) seguido de inmunoterapia dirigida contra la hepatitis B crónica (HBC-IT) en pacientes con HBC en tratamiento con análogos de nucleós(t)idos (AN).** Sponsored by: GlaxoSmithKline. Sponsored's protocol code: 21702.

Ochoa Mazarro, Dolores. **Ensayo clínico cruzado, aleatorizado de bioequivalencia de tadalafilo 20 mg comprimidos bucodispersbables, tras su administración oral en dosis única a voluntarios sanos en presencia de alimentos.** Sponsored by: Laboratorios Alter. Sponsored's protocol code: UECHUP-TADODT/22-2.

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Paola Mejia Abril, Gina. **"INFECCIONES BACTERIANAS Y RESISTENCIA A LOS ANTIMICROBIANOS EN LA ERA DE LA PANDEMIA DE COVID-19: UN ANÁLISIS RETROSPECTIVO DE VARIOS PAÍSES**

(BI-AMR-COVID)". Sponsored by: AMR Insights B.V. Sponsored's protocol code: BI-AMR-COVID.

Ochoa Mazarro, Dolores. **Estudio Fase III, para evaluar la no inferioridad de la respuesta inmune y la seguridad de la vacuna candidata de GSK (RSVPreF3 OA) frente al virus respiratorio sincitial (VRS) en adultos de 18 a 59 años de edad, incluyendo aquellos con mayor riesgo de enfermedades del tracto respiratorio inferior causadas por VRS, en comparación con adultos de 60 años de edad o más.** Sponsored by: GlaxoSmithKline. Sponsored's protocol code: 218280 (RSV OA=ADJ-014).

Gullón Ojesto, Alejandra. **"Ensayo controlado con placebo que evalúa el impacto de inclisirán en los acontecimientos cardiovasculares adversos mayores (MACE) en participantes con enfermedad cardiovascular establecida (ECV) (VICTORION-2 PREVENT)".** Sponsored by: NOVARTIS. Sponsored's protocol code: CKJX839B12302.

Ochoa Mazarro, Dolores. **"ENSAYO CLÍNICO DE BIOEQUIVALENCIA DE TICAGRELOR 90 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS**

ÚNICA A VOLUNTARIOS SANOS EN AYUNAS.". Sponsored by: Laboratorios Normon. Sponsored's protocol code: N-TIC-22-272.

Santander Vaquero, Cecilio. **"Ensayo de fase III a doble ciego, doble simulación, aleatorizado, de grupos paralelos y sin prioridades, sobre la eficacia y la tolerabilidad de 2 mg una vez al día frente a 1 mg dos veces al día de comprimidos orodispersables de budesonida para la inducción de la remisión histológica en adultos con esofagitis eosinofílica".** Sponsored by: Dr. Falk Pharma GmbH. Sponsored's protocol code: Falk_BUL-8/EEA.

Marazuela Aspíroz, Mónica. **"Ensayo de grupos paralelos, controlado con placebo (doble ciego) y con tratamiento activo (abierto) para comparar la eficacia y seguridad de lonapegsomatropina una vez a la semana frente a placebo una vez a la semana y un producto de somatropina diaria en adultos con deficiencia de hormona del crecimiento".** Sponsored by: ASCENDIS PHARMA. Sponsored's protocol code: TCH-306.

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Reyes Copa, Guillermo. **"Estudio clínico de fase 2 controlado con placebo y de grupos paralelos para evaluar la eficacia y la seguridad de RMC-035 en pacientes con alto riesgo de lesión renal aguda tras someterse a una cirugía cardiaca a corazón abierto"**. Sponsored's protocol code: AKITA - 21-ROS-05.

Ochoa Mazarro, Dolores. **ESTUDIO DE FASE 2/3, ALEATORIZADO, CON OBSERVADOR CIEGO Y CONTROLADO CON PLACEBO PARA EVALUAR LA SEGURIDAD Y LA EFICACIA DE MRNA-1345, UNA VACUNA DE ARNM CONTRA EL VIRUS RESPIRATORIO SINCITIAL (VRS), EN ADULTOS A**

PARTIR DE 60 AÑOS DE EDAD.". Sponsored by: Moderna TX. Sponsored's protocol code: mRNA- 1345-P301.

Donnay Candil, Olga. **"Estudio observacional retrospectivo para evaluar la efectividad, seguridad y tolerabilidad en la vida real en españa de ecorafenib más cetuximab en el tratamiento de segunda línea del cáncer colorrectal metastásico con mutación BRAF.** Sponsored by: GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS TTD. Sponsored's protocol code: TTD-21-01.

Sanchez Pérez, Javier. **Ensayo de fase 3, aleatorizado, controlado con principio activo, de 2 grupos paralelos, con enmascaramiento para el evaluador**

y 24 semanas de duración, para comparar la eficacia y la seguridad de degocitinib, crema de 20mg/g dos veces al día, frente a alitrtinoína, cápsulas una vez al día, en participantes adultos con eczema de manos crónicos severos. Sponsored by: LEO PHARMA S.A.U. Sponsored's protocol code: LP0133-1528.

Reig Roselló, Gemma. **"ESTUDIO DE FASE II, CONTROLADO CON PLACEBO Y MULTICÉNTRICO PARA EVALUAR LA SEGURIDAD Y LA EFICACIA DE BALOVAPTÁN EN PACIENTES CON ICTUS ISQUÉMICO AGUDO Y ALTO RIESGO DE PRESENTAR EDEMA CEREBRAL MALIGNO"**.

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de los Santos Gil, Ignacio. **"Infecciones recientes, agudas y reinfecciones, por VHC en hombres que tienen sexo con hombres con y sin infección por VIH. (Estudio ATHENS)"**. Sponsored's protocol code: ATHENS.

Aurea Keough Delgado, Elena. **"Estudio de fase III con doble enmascaramiento y comparado con un placebo, de la seguridad y la eficacia del AR-301 como tratamiento complementario de los antibióticos en el tratamiento de la neumonía asociada al respirador (NAR) causada por S. aureus.".** Sponsored by: Aridis Pharmaceuticals, Inc. Sponsored's protocol code: AR-301-002.

Alfonso Manterola, Fernando. **"Globo con revestimiento de sirolimus frente a stent con liberación de fármaco en vasos coronarios nativos".** Sponsored by: Fondazione Ricerta e Innovazione Cardiovascolare ETS. Sponsored's protocol code: TRANSFORM II.

Loscertales Pueyo, Javier. **"Estudio de fase Iib para evaluar la eficacia y la seguridad de NS-018 administrado por vía oral frente al mejor tratamiento disponible en sujetos con mielofibrosis primaria, mielofibrosis post-policitemia vera o mielofibrosis post-trombocitemia esencial con trombocitopenia grave (recuento plaquetario <50000 micralitros".** Sponsored by: NS Pharma, Inc. Sponsored's protocol code: NS-018-201.

Sáez Bejar, Carmen. **"Estudio clínico y microbiológico sobre el impacto de la multirresistencia en la virulencia y en la respuesta del huésped a la infección por Pseudomonas aeruginosa".** Sponsored by: FUNDACIÓ INSTITUT HOSPITAL DEL MAR D'INVESTIGACIONS MÈDIQUES. Sponsored's protocol code: ESTUDIO IRVIPA.

de Toledo Heras, Maria. **"Estudio controlado con placebo para evaluar la eficacia, la seguridad y la tolerabilidad de JNJ-40411813 como tratamiento complementario en sujetos con crisis epilépticas de inicio focal con respuesta subóptima a levetiracetam.".** Sponsored by: JANSSEN- CILAG INTERNATIONAL N.V. Sponsored's protocol code: 40411813EPY2001.

Marazuela Aspíroz, Mónica. **"Estudio controlado con placebo para evaluar la seguridad, farmacocinética y eficacia del linsitinib en pacientes con enfermedad ocular tiroidea (EOT) activa y de moderada a grave".** Sponsored by: VasaraGen, Inc. Sponsored's protocol code: VGEN-TED-301.

Navas García, Marta. **"Optimización, ajustes y gestión remotos para la estimulación cerecral profunda".** Sponsored by: Abbot. Sponsored's protocol code: ROAM.

García Fraile, Lucio. **Estudio abierto, multicéntrico y aleatorizado para investigar el tratamiento antirretroviral con inhibidor de la integrasa frente al inhibidor de la proteasa potenciado para pacientes con enfermedad por el VIH avanzada - Estudio Late Presenter Treatment Optimisation (Optimización del tratamiento para pacientes con infección avanzada, LAPTOP).** Sponsored by: NEAT ID Foundation. Sponsored's protocol code: LAPTOP.

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Castañeda , Santos. **Ensayo clínico aleatorizado, multicéntrico, doble ciego para evaluar la eficacia y seguridad de Montelukast en pacientes con artrosis erosiva/inflamatoria de manos.** Sponsored by: Farmalider S.A. Sponsored's protocol code: FMLD-ARSIDOS-48.

Alegre Amor, Adrián. **"Estudio en Fase III aleatorizado y de dos grupos de Elranatamab (PF- 06863135) frente a Lenalidomida en pacientes con mieloma múltiple de diágnostico reciente que presentan enfermedad residual mínima después de someterse a autotrasplante de células madre.** Sponsored by: Pfizer. Sponsored's protocol code: C1071007.

Ochoa Mazarro, Dolores. **"Ensayo clínico aleatorizado de biodisponibilidad relativa de amilmetacresol, alcohol diclorobencílico, lidocaína y vitamina c pastillas para chupar, tras su administración oral en dosis única a voluntarios sanos en ayunas con diseño cruzado replicado.".** Sponsored by: Geiser Pharma. Sponsored's protocol code: G17-06-03.

Ochoa Mazarro, Dolores. **"Ensayo clínico aleatorizado de biodisponibilidad relativa de bencidamina hidrocloruro - 2,4-diclorobencil alcohol 3 mg / 1.2 mg pastillas para chupar vs bencidamina hidrocloruro - 2,4-diclorobencil alcohol 3 mg / 1.2 mg comprimidos para chupar, tras su administración oral en dosis única a voluntarios sanos en ayunas con diseño cruzado replicado".** Sponsored by: Geiser Pharma. Sponsored's protocol code: G21-01.

García Castillo, Elena. **"Estudio observacional transversal sobre la caracterización del flujo inspiratorio subóptimo en pacientes con EPOC grave: estudio PANACEA".** Sponsored by: Chiesi españa SAU. Sponsored's protocol code: CHI-COR-2021-01 PANACEA.

Barrios Blandino, Ana. **"PREVALENCIA DE LA SOLEDAD/AISLAMIENTO SOCIAL EN PERSONAS INFECTADAS POR VIH MAYORES DE 50 AÑOS. ESTUDIO "NADIE SOLO".** Sponsored by: Fundación Seims Gesida. Sponsored's protocol code: GESIDA 12021.

Isabel Ballesteros, Ana. **Estudio de fase 111, multicéntrico y abierto de ribociclib en comparación con palbociclib en pacientes con cáncer de mama avanzado con receptores hormonales positivos/ HER2-negativo/HER2-Enriquecido -ensayo HARMONIA.** Sponsored by: GRUPO SOLTI. Sponsored's protocol code: HARMONIA.

Pérez Gisbert, Javier. **"Estudio de fase 2 de búsqueda de dosis, aleatorizado, doble ciego, controlado con placebo y multicéntrico para evaluar la seguridad y la eficacia del tratamiento de inducción con efavaleucina alfa en sujetos con colitis ulcerosa activa de moderada a grave.".** Sponsored by: Amgen. Sponsored's protocol code: 20170104.

Ochoa Mazarro, Dolores. **"Estudio en fase 1/2a, aleatorizado, doble ciego y controlado con placebo, para evaluar la seguridad y la inmunogenicidad de varias formulaciones de vacunas basadas en RSV.preF en adultos de 60 años en adelante".** Sponsored by: Janssen. Sponsored's protocol code: VAC18195RSV1001.

Meça Lallana, Virginia. **"ESTUDIO DE FASE III, MULTICÉNTRICO, ALEATORIZADO, DOBLE CIEGO, CON DOBLE ENMASCARAMIENTO Y DE GRUPOS PARALELOS PARA EVALUAR LA EFICACIA Y LA SEGURIDAD DE FENEBRUTINIB EN COMPARACIÓN CON TERIFLUNOMIDA EN PACIENTES**

ADULTOS CON ESCLEROSIS MÚLTIPLE RECURRENTE". Sponsored by: Roche. Sponsored's protocol code: GN41851.

García Fraile, Lucio. **"FOUR-YEAR EFFECTIVENESS OF COVID-19 VACCINES AGAINST SEVERE DISEASE AND ASYMPTOMATIC INFECTION: THE COVID-VAC@SPAIN STUDY".** Sponsored by: Hospital La Paz. Sponsored's protocol code: COVIDVAC@SPAIN.

Ochoa Mazarro, Dolores. **ENSAYO CLINICO ALEA TO RIZADO DE BIOEQUIVALENCIA DE SACUBITRILON ALSART AN 97 MG/103 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN AYUNAS CON DISEÑO CRUZADO REPLICADO.** Sponsored by: Alter. Sponsored's protocol code: UECHUP- SACVAL/22-4.

Chicharro Manso, Pablo. **"Estudio prospectivo y observacional de cohortes de 24 meses de duración para evaluar los tratamientos sistémicos orales en el tratamiento de pacientes adultos con dermatitis atópica en la vida real (AD-REAL)".** Sponsored by: Eli Lilly and Company. Sponsored's protocol code: I4V-MC-B026.

Alegre Amor, Adrian. **Estudio FIH en fase 1/11 de REGN5458 (anticuerpo biespecífico anti- BCMA y anti-CD3) en pacientes con mieloma múltiple recidivante o resistente al tratamiento.** Sponsored by: Regeneron Pharmaceuticals, Inc. Sponsored's protocol code: R5458-ONC-1826.

Ochoa Mazarro, Dolores. **"Estudio Fase I aleatorizado, con escalado de dosis, para evaluar la seguridad, reactogenicidad e inmunogenicidad de la vacuna candidata monovalente frente a la gripe derivada de ARN mensajero en adultos sanos jóvenes y adultos más mayores".** Sponsored by: GSK. Sponsored's protocol code: FLU SV MRNA-003.

Alegre Amor, Adrián. **"Estudio de fase 3, de dos etapas abierto, aleatorizado y multicéntrico para comparar iberdomida, daratumumab y dexametasona (IberDd) con daratumumab, bortezomib**

y dexametasona (DVd) en pacientes con mieloma múltiple recidivante o resistente (MMRR)". Sponsored by: Celgene. Sponsored's protocol code: CC-220-MM-002 EXCALIBER.

CISNEROS SERRANO, CAROLINA. **Efectos de la combinación fija de dipropionato de beclometasona/fumarato de formoterol administrada con NEXT(haler) en un estudio en condiciones reales sobre la probabilidad de mejora del estado de control del asma después de 6 meses de tratamiento.** Sponsored by: Chiesi Italia SPA. Sponsored's protocol code: CHIT-2101 NEWTON.

Casals Seoane, Fernando. **"Ácido ursodesoxicólico vs placebo para la Prevención de La pancreatitis aguda biliar Recidivante. Ensayo clínico aleatorizado, multicéntrico, doble ciego, controlado con placebo.".** Sponsored by: Dr. Enrique de Madaria Pascual (Digestivo, Hospital General de Alicante). Sponsored's protocol code: OSOPOLAR.

López Manzanares, Lydia. **Estudio de fase IIb, multicéntrico, aleatorizado, con doble enmascaramiento, controlado con placebo, de grupos paralelos y de 12 semanas de duración para evaluar la seguridad y la eficacia de CX-8998 en el tratamiento de adultos con temblor esencial entre moderado y grave.** Sponsored by: Jazz Pharmaceuticals, INC. Sponsored's protocol code: JZP385-201-01.

Loscertales Pueyo, Javier. **"IBROMICS: Estudio de los parámetros clínicos y biológicos determinantes de respuesta en pacientes con Leucemia Linfocítica Crónica tratados en primera línea con Ibrutinib".** Sponsored by: Janssen-Cilag, S.A. Sponsored's protocol code: 54179060CLL4028 IRBOMICS.

, Farmacología. **"ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE NAPROXENO SÓDICO 550 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN PRESENCIA DE ALIMENTOS.".** Sponsored by: Laboratorios Normon. Sponsored's protocol code: N-NAP-21-270.

Figuera Álvarez, Ángela. **"Estudio en fase III, aleatorizado, abierto, para evaluar la seguridad y la eficacia de magrolimab en combinación con azacitidina frente a la elección del médico de venetoclax más azacitidina o quimioterapia intensiva, en pacientes con leucemia mieloide aguda y TP53 mutado no tratados previamente".** Sponsored by: Gilead Sciences S.L.U. Sponsored's protocol code: GS-US-546-5857.

Ochoa Mazarro, Dolores. **"ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE PREGABALINA 300 MG COMPRIMIDOS VERSUS PREGABALINA 300 MG CÁPSULAS DURAS, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN AYUNAS.".** Sponsored by: Laboratorios Normon. Sponsored's protocol code: N-PRE-22-273.

Zamora García, Enrique. **Apoyo respiratorio con EPOC tras una exacerbación de la enfermedad, con seguimiento de la calidad del apoyo.** Sponsored by: Foundation du souffle. Sponsored's protocol code: RESCUE2.

Fernando Muñoz Guerra, Mario. **"Ensayo clínico aleatorizado para evaluar la utilidad del genotipado de CYP2D6 para mejorar la eficacia y la seguridad del tramadol en el tratamiento del dolor postoperatorio agudo".** Sponsored by: Fundación de Investigación Biomédica del Hospital Universitario de la Princesa. Sponsored's protocol code: TRADOLPRIME.

Casabona Francés, Sergio. **"ESTUDIO DE EXTENSIÓN DE FASE 3 EN RÉGIMEN ABIERTO, MULTICÉNTRICO E INTERNACIONAL PARA EVALUAR LA SEGURIDAD A LARGO PLAZO DE CC-93538 EN SUJETOS ADULTOS Y ADOLESCENTES CON ESOFAGITIS EOSINOFÍLICA".** Sponsored by: CELGENE INTERNATIONAL II S.A.R.L. Sponsored's protocol code: CC-93538-EE-002.

Ahijón Lana, María. **"Estudio exploratorio, controlado, transversal, multicéntrico, para comparar los cambios en la señal ecográfica musculoesquelética en pacientes con psoriasis bajo sospecha de artritis psoriásica y en pacientes con psoriasis, antes y después del esfuerzo físico con dinamómetro".** Sponsored by: Novartis Farmacéutica, S.A. Sponsored's protocol code: CAIN457FES08R.

Pérez Hernández, Concepción. **"Estudio clínico de fase III aleatorizado, comparativo con placebo, multicéntrico y con enmascaramiento doble para evaluar la eficacia y la seguridad de la pregabalina de liberación lenta y de la pregabalina de liberación inmediata administradas una vez al día en el dolor neuropático periférico".** Sponsored by: Laboratorios Lesvi, S.L. Sponsored's protocol code: RZAA9807_LESVIPREGA20P3-3.

Ochoa Mazarro, Dolores. **Estudio de fase 3, aleatorizado, doble ciego, controlado con comparador activo y de consistencia entre lotes, para evaluar la seguridad, la tolerabilidad y la inmunogenicidad de V116 en adultos de 18 a 49 años.** Sponsored by: Merck Sharp & Dohme LLC. Sponsored's protocol code: V116-004.

Gómez Soria, Valle. **"Estudio de extensión de asciminib, multicéntrico y abierto para evaluar la seguridad a largo plazo en pacientes que hayan completado un estudio de asciminib promocionado por Novartis y que el investigador considere que**

se están beneficiando del tratamiento continuado". Sponsored by: NOVARTIS FARMACÉUTICA S.A. Sponsored's protocol code: CABL001A2001B.

Alegre Amor, Adrián. **Estudio observacional prospectivo para evaluar el mantenimiento con bortezomib ydaratumumab (V-Dara) tras la inducción con bortezomib, melfalan, prednisona y daratumumab (VMP-Dara) en pacientes recién diagnosticados con mieloma múltiple (MM) que no son elegibles para trasplante autólogo de células madre (ASCT): datos de evidencia real Alcyone-optimizado.** Sponsored by: Fundación Pethema. Sponsored's protocol code: GEM- OPTIMAL.

Miguel Sánchez Torres, Jose. **Estudio de fase 111, abierto, aleatorizado, global y multicéntrico de sacituzumab govitecán frente a docetaxel en pacientes con cáncer de pulmón no microcítico (CPNM) avanzado o metastásico con progresión durante o después de la quimioterapia a base de platino e inmunoterapia anti-PD-1/PD-L 1".** Sponsored by: Gilead Sciences S.L.U. Sponsored's protocol code: GS-US-577-6153.

Meca Lallana, Virginia. **"Estudio de prolongación multicéntrico, de un solo grupo, abierto y de extensión para evaluar la seguridad y la eficacia a largo plazo de ocrelizumab en pacientes con esclerosis múltiple".** Sponsored by: HOFFMAN-LA ROCHE. Sponsored's protocol code: MN43964.

Pérez Gisbert, Javier. **Beneficio a largo plazo de ustekinumab en la colitis ulcerosa en la práctica clínica.** Sponsored by: Francisco Javier Pérez Gisbert. Sponsored's protocol code: GIS-2022- ULISES.

Ochoa Mazarro, Dolores. **"Ensayo clínico de Fase 1, de dosis única, abierto, en grupos paralelos para investigar la farmacocinética y la seguridad de rupatadina (10 mg) y sus metabolitos activos en sujetos con insuficiencia hepática en comparación con sujetos con función hepática normal".** Sponsored by: Biohorm SL. Sponsored's protocol code: DC08RUP/1/21.

José Casanova, María. **"Impacto en la calidad de vida en base a la intervención terapéutica realizada en pacientes con colitis ulcerosa según el grado de curación mucosa".** Sponsored by: Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa (GETECCU). Sponsored's protocol code: CAVI CU.

Ochoa Mazarro, Dolores. **"Ensayo clínico de Fase 1, de dosis única, abierto, en grupos paralelos para investigar la farmacocinética y la seguridad de rupatadina (10 mg) y sus metabolitos activos en sujetos con insuficiencia renal en comparación con sujetos con función renal normal".** Sponsored by: Biohorm SL. Sponsored's protocol code: DC09RUP/1/21.

López Manzanares, Lydia. **"ESTUDIO DE FASE II, ALEATORIZADO, DOBLE CIEGO Y CONTROLADO CON PLACEBO PARA EVALUAR LA EFICACIA, LA SEGURIDAD, LA TOLERABILIDAD, LA FARMACOCINÉTICA Y LA FARMACODINÁMICA DEL TAK-341 INTRAVENOSO EN SUJETOS CON ATROFIA MULTISISTÉMICA".** Sponsored by: Takeda. Sponsored's protocol code: TAK-341-2001.

de los Santos Gil, Ignacio. **"Estudio de fase 2, multicéntrico, aleatorizado, en doble ciego (dentro del nivel de dosis), controlado con placebo, de grupos paralelos y búsqueda de dosis, para evaluar la eficacia y seguridad de TF0023 frente a placebo en el tratamiento de la COVID- 19 en adultos hospitalizados".** Sponsored by: Techfields Inc. Sponsored's protocol code: TF- TF0023-201.

Ochoa Mazarro, Dolores. **Estudio clínico de fase 3, aleatorizado, doble ciego y controlado con comparador activo para evaluar la seguridad, tolerabilidad e inmunogenicidad de V116 en adultos de 50 años en adelante sin exposición previa a vacunas antineumocócicas.".** Sponsored by: Merck Sharp & Dohme LLC. Sponsored's protocol code: V116-010.

Sáez Bejar, Carmen. **"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)".** Sponsored by: Shionogi S.L.U. Sponsored's protocol code: 2020-266-4.

Pérez Hernández, Concepción. **"Estudio en fase III, aleatorizado, con enmascaramiento doble y comparativo con placebo para evaluar la eficacia y la seguridad de una sola inyección intrarticular de RTX-GRT7039 en pacientes adultos con dolor derivado de la gonartrosis".** Sponsored by: Grünenthal GmbH. Sponsored's protocol code: KF7039-02.

Rivero Crespo, Fernando. **Revascularización guiada por reserva fraccional de flujo o por RFF de vasos basada en coronariografía cuantitativa 3D: FAST III.** Sponsored by: Instituto Europeo de Investigación Cardiovascular. Sponsored's protocol code: ECRI15.

Ochoa Mazarro, Dolores. **Estudio Fase III, observador ciego, aleatorizado, controlado con placebo, para evaluar la no inferioridad de la respuesta inmune y la seguridad de la vacuna candidata de GSK (RSVPreF3 OA) en adultos de 50 a 59 años de edad, incluyendo adultos con mayor riesgo de enfermedad del tracto respiratorio inferior causada por el virus respiratorio sincitial, comparado con adultos de 60 años de edad o más.** Sponsored by: GlaxoSmithKline. Sponsored's protocol code: RSV OA=ADJ-018 (219238).

Ochoa Mazarro, Dolores. **Estudio clínico de fase 3 para evaluar la seguridad, tolerabilidad e inmunogenicidad de V116 en adultos de 50 años en adelante que ya han recibido una vacuna antineumocócica.** Sponsored by: Merck Sharp & Dohme LLC. Sponsored's protocol code: V116- 006.

Ochoa Mazarro, Dolores. **"ENSAYO CLÍNICO CRUZADO ALEATORIZADO DE BIOEQUIVALENCIA DE ROSUVASTATINA/EZETIMIBA 20 MG / 10 MG COMPRIMIDOS RECUBIERTOS CON PELICULA VERSUS ROSUVASTATINA/EZETIMIBA 20 MG / 10 MG CÁPSULAS DURAS, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANO.".** Sponsored by: Laboratorios Normon. Sponsored's protocol code: N-ROSEZE-22-274.

García de Vicuña, Rosario. **"Registro Multicéntrico de Vasculitis Asociadas a ANCA (granulomatosis con poliangeítis, granulomatosis eosinofílica con poliangeítis y poliangeítis microscópica)".** Sponsored by: Fundación Española de Reumatología. Sponsored's protocol code: RESER-NVAN.

Alfonso Manterola, Fernando. **"Combined Ischemia And Vulnerable Plaque Percutaneous Intervention to Reduce Cardiovascular Events: Combine- Intervene trial".** Sponsored by: Diagram B.V. Sponsored's protocol code: COMBINE.

Gómez Soria, Valle. **Ensayo prospectivo, aleatorizado, doble ciego, controlado con placebo y multicéntrico de fase IIb para evaluar la eficacia y seguridad del mocravimod como tratamiento adyuvante y de mantenimiento en la leucemia mieloide aguda (LMA) en pacientes adultos sometidos a un Trasplante alogénico de células madre hematopoyéticas (TCMH).** Sponsored by: Priothera. Sponsored's protocol code: PKRPC001.

Valero Martín, Cristina. **"Biomarkers of disease activity in Rheumatoid Arthritis Patients undergoing JAK inhibitors: The MEASURE study, a multicentre prospective cohort study. MEASURE Study".** Sponsored by: FUNDACIÓCLÍNIC PER A LA RECERCA BIOMÈDICA. Sponsored's protocol code: MEASURE.

Ochoa Mazarro, Dolores. **"ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE EDOXABAN 60 MG COMPRIMIDOS RECUBIERTOS CON PELÍCULA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN AYUNAS".** Sponsored by: Biohorm, S.L. Sponsored's protocol code: DC01EDO/1/22.

Zapatero Laborda, Almudena. **"Estudio de fase II abierto de extensión para sujetos con cáncer de próstata que han participado anteriormente en un estudio clínico con enzalutamida.".** Sponsored by: Astellas Pharma Global Development.

Valenzuela , Claudia. **Ensayo doble ciego, aleatorizado y controlado con placebo para evaluar la eficacia y seguridad del 81 1015550 durante al menos 52 semanas en pacientes con Fibrosis Pulmonar Idiopática (FPI).** Sponsored by: Biohorm, S.L. Sponsored's protocol code: 1305-0014.

Valenzuela , Claudia. **"Estudio doble ciego, aleatorizado y controlado con placebo que evalúa la eficacia y la seguridad de BI 1015550 durante al menos 52 semanas en pacientes con enfermedades pulmonares intersticiales fibrosantes progresivas (EPI-FP)".** Sponsored by: Biohorm, S.L. Sponsored's protocol code: 1305-0023.

Gutiérrez , Ángela. **"Clínica y Epidemiología del brote de infección por Monkeypox en España en el año 2022. Estudio CEME-22".** Sponsored by: GESIDA. Sponsored's protocol code: FSG 023- 22_MONKEYPOX.

Colomer Bosch, Ramón. **ESTUDIO DE FASE III MULTICÉNTRICO, ALEATORIZADO, DOBLE CIEGO, CONTROLADO CON PLACEBO PARA EVALUAR LA EFICACIA Y SEGURIDAD DE GDC-9545 EN COMBINACIÓN CON PALBOCICLIB, COMPARADO CON LETROZOL EN COMBINACIÓN CON PALBOCICLIB, EN PACIENTES CON CÁNCER DE MAMA POSITIVO PARA RECEPTORES DE ESTRÓGENOS Y HER2 NEGATIVO LOCALMENTE AVANZADO O METASTÁSICO.** Sponsored by: F. Hoffmann-La Roche Ltd. Sponsored's protocol code: BO41843.

María Gómez Punter, Rosa. **Estudio longitudinal del efecto del tratamiento con ELX/TEZ/IVA en pacientes con fibrosis quística en la vida real.** Sponsored by: Vertex Pharmaceuticals Incorporated. Sponsored's protocol code: VX20_CFD_005.

María Serra, Jose. **Resultado en vida real del uso de anticuerpos monoclonales para profilaxis de la migraña en hospitales españoles.** Sponsored by: Fundación Española de Farmacia Hospitalaria (FEFH). Sponsored's protocol code: MIGREALIFE.

García de Vicuña, Rosario. **"Estudio multicéntrico en fase IIIb aleatorizado, doble ciego y controlado con placebo para evaluar la eficacia y la seguridad de guselkumab administrado por vía subcutánea a pacientes con artritis psoriásica activa que presentaban una respuesta inadecuada y/o intolerancia al tratamiento previo con un agente contra el factor de necrosis tumoral .".** Sponsored by: JANSSEN-CILAG INTERNATIONAL N.V. Sponsored's protocol code: CNTO1959PSA3005.

Alegre Amor, Adrián. **"Estudio aleatorizado de fase III para comparar Talquetamab SC combinado con Daratumumab SC y Pomalidomida (Tal-DP) o Talquetamab SC combinado con**

Daratumumab SC (Tal-D) frente a Daratumumab SC combinado con Pomalidomida y Dexametasona (DPd) en pacientes con mieloma múltiple refractario o recidivante que han recibido al menos 1 línea de tratamiento.". Sponsored by: JANSSEN-CILAG S.A. Sponsored's protocol code: 64407564MMY3002.

Loscertales Pueyo, Javier. **Estudio de fase II abierto para evaluar la seguridad, tolerabilidad, farmacocinética y eficacia de KER-050 en monoterapia o en combinación con ruxolitinib en participantes con mielofibrosis.** Sponsored by: Keros Therapeutics Inc. Sponsored's protocol code: KER050-MF-301.

Ochoa Mazarro, Dolores. **Estudio de fase I, abierto, para evaluar el efecto de la insuficiencia renal y el tratamiento de diálisis en la farmacocinética de una dosis única de citisiniclina 3mg.** Sponsored by: Achieve Life Sciences, INC. Sponsored's protocol code: ACH-CYT-05.

Meca Lallana, Virginia. **"Estudio observacional retrospectivo para evaluar el uso de siponimod (MAyzent) en pacientes con Esclerosis Múltiple Secundaria Progresiva en la práctica clínica habitual en España. Estudio RESYZE".** Sponsored by: NOVARTIS FARMACÉUTICA S.A. Sponsored's protocol code: CBAF312AES06.

Santander Vaquero, Cecilio. **Ensayo de fase III aleatorizado, doble ciego, de grupos paralelos, controlados con placebo, para evaluar la eficacia y seguridad de tezepelumab en pacientes con esofagitis eosinofilica (crossin).** Sponsored by: Astrazenaca. Sponsored's protocol code: CROSSING (D5244C00001).

Rivero Crespo, Fernando. **Una propuesta de evalación coronaria integral en pacientes con dolor torácico sugestivo de isquemia miocárdica y arterias coronarias angiográficamente normales.** Sponsored by: CoreAalst BV. Sponsored's protocol code: EUROCRAFT.

Meca Lallana, Virginia. **Estudio de fase III, prospectivo, multicéntrico, randomizado, doble ciego, controlado con placebo, de 96 semanas para comparar la eficacia y seguridad del ajuste de dosis de masitinib a 4,5 mg/kg/día frente a placebo en el tratamiento de pacientes con esclerosis m´ltiple primaria progresiva sin recidivas.** Sponsored by: AB Science. Sponsored's protocol code: AB20009.

Alfonso Manterola, Fernando. **Evaluación de una terapia antiplaquetaria modificada asociada con el stent farmacoactivo Firehawk recubierto de dosis baja de rapamicina en pacientes con infarto agudo de miocardio tratados con revascularización percutánea completa (TARGET FIRST).** Sponsored by: Sorin CRM SAS (Microport CRM). Sponsored's protocol code: Target First.

RAMASCO RUEDA, FERNANDO. **"Reanimación del Shock Séptico precoz basada en Fenotipos Hemodinámicos y guiada por Tiempo de Rellene Capilar: Un Ensayo clínico, aleatorizado, abierto, y multicéntrico.".** Sponsored by: Universidad Católica de Chile. Sponsored's protocol code: ANDROMEDA-SHOCK-2.

Rosa María Girón, Dra. **"Estudio Observacional para valorar el impacto de la terapia moduladora CFTR en la composición corporal, parámetros de control glucémico y respiratorios en pacientes adultos con fibrosis quística".** Sponsored by: Alfonso Arranz Martín. Sponsored's protocol code: Nutdiafib.

Ochoa Mazarro, Dolores. **"Ensayo clínico aleatorizado de biodisponibilidad relativa de bencidamina hidrocloruro - cetilpiridinio cloruro 3 mg / 1 mg pastillas para chupar, tras su administración oral en dosis única a voluntarios sanos en ayunas con diseño cruzado replicado.".** Sponsored by: GEISER PHARMA S.L. Sponsored's protocol code: G20-04.

Caballero Sánchez-Robles, Paloma. **"Análisis de la evolución del daño anatómico pulmonar estudiado mediante la tomografía computarizada en pacientes con fibrosis quística tratados con Elezacaftor/Tezacaftor/Ivacaftor".** Sponsored by: María Paloma Caballero Sánchez-Robles. Sponsored's protocol code: Kaftrio.

Rodríguez Huerta, Dolores. **"EFICACIA DE LOS AGHO VS APÓSITOS HIDROCOLOIDES EN LA PREVENCIÓN DE UPP EN PACIENTES CRÍTICOS SOMETIDOS A DECÚBITO PRONO".** Sponsored by: Leire Maculet García. Sponsored's protocol code: NCT05198167.

José Casanova, María. **"Evolución clínica tras la suspensión del tratamiento anti-TNF en pacientes con enfermedad inflamatoria intestinal en remisión: estudio EXIT largo plazo".** Sponsored by: María José Casanova González. Sponsored's protocol code: GIS-2022-EXIT-LT.

Pérez Gisbert, Javier. **"Evidencia de vida real con upadacitinib en enfermedad inflamatoria intestinal. Estudio U-REAL".** Sponsored by: Javier Pérez Gisbert. Sponsored's protocol code: GIS- UREAL-2022.

Pérez Gisbert, Javier. **"Conocimientos sobre EII en la mujer en edad reproductiva: validación del cuestionario ICECCU".** Sponsored by: Unidad EII. Servicio de Digestivo. Complejo Hospitalario Universitario de Ferrol. Sponsored's protocol code: EntrenaMujer-EII.

BOOKS

Comorbilidades del asma grave. Mª Victoria Múgica y Paula Galvan. WebApp Asma grave: Manual Asma grave. Comité de la Sociedad Española de Alergología e Inmunología Clínica (SEAIC). ISBN de la obra: 978-84-09-43769-6. 26 de octubre de 2022

Azahara López Raigada, Francisco Vega, Carlos Blanco Guerra. **Tirita para un corazón partío**. Libro de las sesiones interhospitalarias de la Sociedad de Madrid Castilla La Mancha (SMCLM) de Alergología 2022. ISBN 978-84-09-45812-7.

Azahara López Raigada, Francisco Vega, Carlos Blanco Guerra. **Fallo multisistémico durante tratamiento antineoplásico**. Libro de las sesiones interhospitalarias de la Sociedad de Madrid Castilla La Mancha (SMCLM) de Alergología. 2022. ISBN 978-84-09-45812-7.

Mario Braier, Julio Ancochea. **Memorias de la COVID-19. La pandemia en las Américas**. Gráficas Andalusí. 2022. ISBN:978-84-09-38248-4.

Luisa García Buey. **Implicaciones y complicaciones del Virus de la Hepatitis C** (Capítulo 1). En GUÍA DE DETECCIÓN Y CRIBADO DEL VIRUS DE LA HEPATITIS C EN PERSONAS CON TRASTORNO MENTAL GRAVE. Editado por a Fundación Española de Psiquiatría y Salud Mental. 2022. pp. 9-12. ISBN: 978-84-09-39293-3.

Francisco Abas Santos, Pablo Zubiaur Precioso. **Association Studies in Clinical Pharmacogenetics**. Editores del número especial de Pharmaceutis. 2022. ISSN 1999-4923.

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.

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Courses

	Título	Ponente/Director
20 ene	CURSO BIG DATA	Gerencia Estratégica de Planificación
21 ene	CURSO BIG DATA	Gerencia Estratégica de Planificación
08 feb / 10 feb	Curso de Soporte Vital Avanzado	Mariano Aguilar Mulet
15 feb / 17 feb	Curso de Soporte Vital Avanzado	Mariano Aguilar Mulet
22 feb / 24 feb	Curso de Soporte Vital Avanzado	Mariano Aguilar Mulet
16 mar	Competencias en Ecografía Clínica para AP Ed3	Andrés von Wernitz Teleki
17 mar	Competencias en Ecografía Clínica para AP Ed3	Andrés von Wernitz Teleki
24 mar	Competencias en Ecografía Clínica para AP Ed3	Andrés von Wernitz Teleki
25 mar	Competencias en Ecografía Clínica para AP Ed3	Andrés von Wernitz Teleki
19 abr / 21 abr / 26 abr / 28 abr	Curso Bioetica Clinica ed-04	Jose Mª Galvan Roman
17 may	Curso Infección Paciente Grave	Fernando Ramasco Rueda
01 jun	Curso Mindfulness - Edición 02	Fernando Ramasco Rueda

	Título	Ponente/Director
08 jun	Curso Mindfulness - Edición 02	Fernando Ramasco Rueda
14 jun	Curso de Soporte Vital para Residentes	Mariano Aguilar Mulet
15 jun	Curso Mindfulness - Edición 02	Fernando Ramasco Rueda
16 jun	Curso de Soporte Vital para Residentes	Mariano Aguilar Mulet
17 jun	Curso ECOCARDIOGRAFIA transtoracica	Fernando Ramasco Rueda
18 jun	Curso ECOCARDIOGRAFIA transtoracica	Fernando Ramasco Rueda
20 jun	Competencias en Ecografía Clínica para AP Ed4	Andrés von Wernitz Teleki
21 jun	Competencias en Ecografía Clínica para AP Ed4	Andrés von Wernitz Teleki
22 jun	Curso Mindfulness - Edición 02	Fernando Ramasco Rueda
23 jun	Competencias en Ecografía Clínica para AP Ed4	Andrés von Wernitz Teleki
3 sep	Curso de Cefaleas para Residentes de Neurologia	Sonia Quintas Gutierrez
8 sep/ 12 sep / 15 sep	Curso Teórico-Práctico V.M.N.I para Enfermería	Carmen Pérez Garrote
29 sep	Curso OCTNetwork	Fernando Rivero Crespo
30 sep	Curso OCTNetwork	Fernando Rivero Crespo
1 oct	Curso de Cefaleas para Residentes de Neurologia	Sonia Quintas Gutierrez
4 oct	Curso de Soporte Vital Avanzado	Mariano Aguilar Mulet
5 oct	Curso de Soporte Vital Avanzado	Mariano Aguilar Mulet
6 oct	LATEST - International	Elena Martín
7 oct	LATEST - International	Elena Martín
7 oct	Curso Edicion Unidad Trastornos del Movimiento VI	Lydia Lopez Manzanares
17 oct - 19 oct	Curso: Trabajo en Equipo en Unidades Especiales	Fernando Ramasco
20 oct	Competencias en Ecografía Clínica para AP Ed5	Andrés von Wernitz Teleki

Workshops

	Título	Ponente/Director
7 nov	Dale un giro a tu dolor, aprende a manejarlo	
7 nov	Presente y futuro en Enfermería, Fisioterapia y Técnicos Superiores Especialistas: nuevos roles al servicio de todos	
8 nov	Taller práctico de Alergia	
8 nov	Investigación traslacional: línea directa entre el laboratorio y el paciente	

	Título	Ponente/Director
8 nov / 11 nov	DESARROLLO DE MEDICAMENTOS EN HUMANOS. UNIDAD DE ENSAYOS CLÍNICOS FASE I	
10 nov / 17 nov	Abróchense los cinturones	
10 nov / 17 nov	DIAGNÓSTICO MICROBIOLÓGICO DE LAS ENFERMEDADES INFECCIOSAS	
11 nov	Inmunología del tubo digestivo: del laboratorio a los pacientes	
14 nov	Pensando de otra manera	
14 nov / 15 nov	CIRUGÍA TORÁCICA DEL SIGLO XXI	
15 nov	Tatuajes y Piercing. Infecciones de Transmisión sexual	
16 nov	BIOBANCO, CONTAMOS CONTIGO	
16 nov	Investigación biomédica translacional: investigación básica a la búsqueda de la aplicación clínica	
18 nov	¿Qué significa Respirar? Se explica para que usamos los pulmones y como se alteran con el uso del tabaco	

Sessions

	Título	Ponente/Director
17 mar	Jornada Medicos Atencion Primaria	Rosario Garcia de Vicuña
31 mar	Jornada de Puertas Abiertas de Residentes	Fernando Ramasco Rueda
23 may	I Jornada de Residentes de Cooperación Internacional y Colaboración Humanitaria	Elena Martin Perez
19 oct	Jornada de Puertas Abiertas "TU DOLOR IMPORTA"	Dolores Ochoa Mazarro
04 nov	21º Congreso de La SONCAM (SOCIEDAD MADRILEÑA DE NEUROCIRUGÍA)	José Antonio Fernández Alen
18 nov	Jornada en Neuroplastica	Teresa Perez de la Fuente
21 nov	107ª Jornada FUINSA: El Acceso a Medicamentos en proceso de financiación: ¿Cómo actuar?	Alberto Morell Baladron
22 nov	I Jornada de Investigación	Dir. Enfermería
25 nov	IV Jornada de Neurogastro enterología y motilidad digestiva	Cecilio Santander Vaquero

Seminars

Fecha/s	Título	Ponente/Director
20 ene	Mitochondrial function as a gatekeeper of redox homeostasis	Eduardo Balsa
27 ene	Perivascular Oxygen Sensors	Andrés Urrutia
3 feb	Natural killer (NK) cell-derived extracellular-vesicle shuttled microRNAs control T cell responses	Sara G. Dosil
10 feb	To Stop Blood Cancer, Target the Bone. Subversion of serotonin-receptor signaling in osteoblasts by kynurenine drives Acute Myeloid Leukemia	Marta Galán-Díez
17 feb	Impact of immune system and tumor heterogeneity on response to immune checkpoint inhibition in non-small cell lung cancer	Santiago Sánchez Alonso
24 feb	Papel de la chaperonina CCT en la dinámica de orgánulos	Amelia Rojas-Gómez
3 mar	Reconocimiento innato y generación de monocitos inflamatorios en respuesta a SARSCoV2. Implicaciones funcionales en patología del COVID-19	Ilya Tsukalov
10 mar	Cigarette smoke impact on the pulmonary artery: implications on COPD-related pulmonary hypertension	Javier Sevilla
24 mar	A Differential Signature of Circulating miRNAs and Cytokines between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19	Paula Vera
7 abr	HIF-1α as a regulator of colonic Innate Lymphoid Cells 3 during Citrobacter rodentium colitis	Aranzazu Cruz Adalia
28 abr	Metabolismo de las Células T durante la inflamación y el envejecimiento	María Mittelbrunn
5 may	Nuevos avances en el conocimiento de la patología isquémica cerebral y desarrollo de estrategias farmacológicas con potencial terapéutico en el ictus isquémico	Emma Martínez Alonso
19 may	ISG15 at crossroads of immune synapse, dendritic cells and contact hypersensitivity	Irene Fernández-Gallego
26 may	Funciones adicionales del intercambiador mitocondrial de sodio/calcio NCLX: efectos en HIF y efectos del litio	Carmen Choyas Foces
2 jun	CD69-oxLDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in T lymphocytes	María Jiménez Fernández
16 jun	ISG20L2: una exoribonucleasa regulando la activación de células T	Ana Rodríguez Galán
23 jun	Nuevo modelo animal de Miocarditis inducida por Tratamiento con Inhibidores de Punto de Control Inmunitario	Rosa Jiménez Alejandre
30 jun	Caracterización del efecto de ibrutinib en la expresión y funcionalidad del receptor CCR7 en leucemia linfocítica crónica y en la actividad antitumoral de CAP-100, el primer anticuerpo terapéutico contra CCR7	Tamara Mateu Albero
15 sep	Alteraciones en el sistema inmune y su relación con el desarrollo de comorbilidades en pacientes con apnea obstructiva del sueño	Elena Díaz García

Fecha/s	Título	Ponente/Director
29 sep	Estudio de la farmacocinética y la farmacodinámica de Natalizumab: Hacia la individualización del tratamiento en pacientes con esclerosis múltiple	José María Serra López-Matencio
13 oct	Terapias de combinación basadas en microRNAs para el tratamiento de linfomas B	Virginia García de Yébenes
20 oct	Papel de las proteínas morfogenéticas óseas en la fisiopatología hepática	Patricia Marañón Barnusell
27 oct	Implication of TFAM expression in γδ T cells and psoriasis development	Amelia Rojas
3 nov	Infiltración en el sistema nervioso central y biomarcadores en la leucemia linfoblástica aguda	Lidia Martínez Fernández de Sevilla
24 nov	Modulation of dendritic cell to boost NK cell-mediated immunity against HIV-1	Ildefonso Sánchez Cerillo
1 dic	Identificación de biomarcadores y estudio de las bases moleculares en anafilaxia: proteínas circulantes, vesículas extracelulares y microARNs	Emilio Núñez Borque
17 mar	Papel del sistema VIP/Receptores y su uso como marcadores de pronóstico en enfermedades inflamatorias y autoinmunes	Amalia Lamana
24 mar	A Differential Signature of Circulating miRNAs and Cytokines between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19	Paula Vera
7 abr	HIF-1***α*** as a regulator of colonic Innate Lymphoid Cells 3 during Citrobacter rodentium colitis	Aranzazu Cruz Adalia
28 abr	Metabolismo de las Células T durante la inflamación y el envejecimiento	María Mittelbrunn
5 may	Nuevos avances en el conocimiento de la patología isquémica cerebral y desarrollo de estrategias farmacológicas con potencial terapéutico en el ictus isquémico	Emma Martínez Alonso
19 may	ISG15 at crossroads of immune synapse, dendritic cells and contact hypersensitivity	Irene Fernández-Gallego
26 may	Funciones adicionales del intercambiador mitocondrial de sodio/calcio NCLX: efectos en HIF y efectos del litio	Carmen Choyas Foces
2 jun	CD69-oxLDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in T lymphocytes	María Jiménez Fernández
16 jun	ISG20L2: una exoribonucleasa regulando la activación de células T	Ana Rodríguez Galán
23 jun	Nuevo modelo animal de Miocarditis inducida por Tratamiento con Inhibidores de Punto de Control Inmunitario	Rosa Jiménez Alejandre
30 jun	Caracterización del efecto de ibrutinib en la expresión y funcionalidad del receptor CCR7 en leucemia linfocítica crónica y en la actividad antitumoral de CAP-100, el primer anticuerpo terapéutico contra CCR7	Tamara Mateu Albero
15 sep	Alteraciones en el sistema inmune y su relación con el desarrollo de comorbilidades en pacientes con apnea obstructiva del sueño	Elena Díaz García
29 sep	Estudio de la farmacocinética y la farmacodinámica de Natalizumab: Hacia la individualización del tratamiento en pacientes con esclerosis múltiple	José María Serra López-Matencio

Fecha/s	Título	Ponente/Director
13 oct	Terapias de combinación basadas en microRNAs para el tratamiento de linfomas B	Virginia García de Yébenes
20 oct	Papel de las proteínas morfogenéticas óseas en la fisiopatología hepática	Patricia Marañón Barnusell
27 oct	Implication of TFAM expression in γδ T cells and psoriasis development	Amelia Rojas
3 nov	Infiltración en el sistema nervioso central y biomarcadores en la leucemia linfoblástica aguda	Lidia Martínez Fernández de Sevilla
24 nov	Modulation of dendritic cell to boost NK cell-mediated immunity against HIV-1	Ildefonso Sánchez Cerillo
1 dic	Identificación de biomarcadores y estudio de las bases moleculares en anafilaxia: proteínas circulantes, vesículas extracelulares y microARNs	Emilio Núñez Borque
15 dic	The impact of allergic inflammation in atherosclerosis	Nieves Gallego Fernández

Training carried out on the Plataforma Conocimiento Princesa

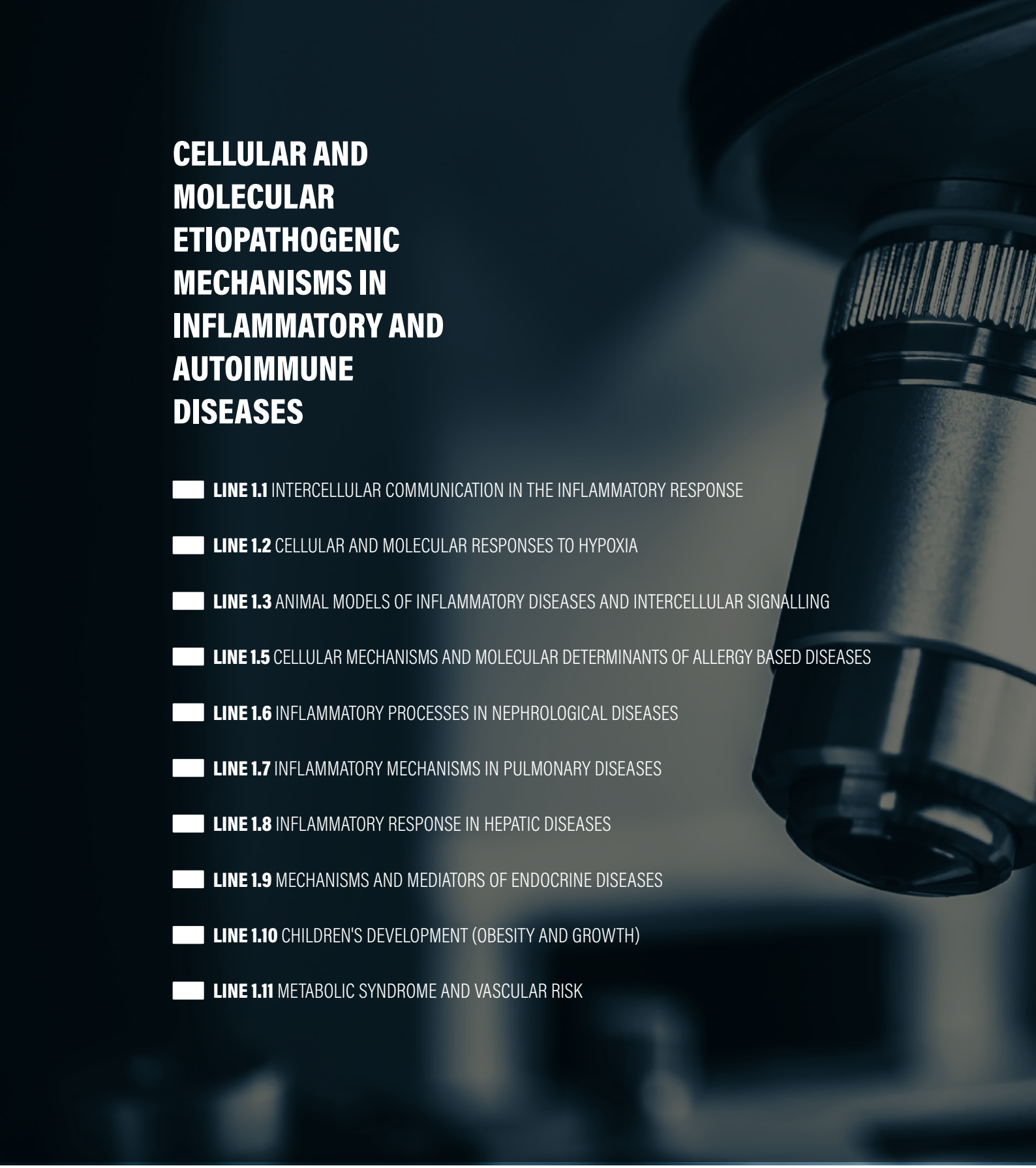
Fecha/s	Título	Ponente/Director
24 may	Eutanasia: Conceptos, Ley de Eutanasia, Aplicación de la Ley	Jose Mª Galvan Roman
2 jun	Grupo Trastorno del Movimiento	Lydia Lopez Manzanares
29 nov	Buenas Prácticas Clínicas en los Ensayos Clíncios Ed. 9	Dolores Ochoa Mazarro
30 nov	Buenas Prácticas Clínicas en los Ensayos Clíncios Ed. 9	Dolores Ochoa Mazarro
16 dic	25 años de la Unidad de Ensayos Clínicos Fase I en el Hospital Universitario de La Princesa (UECHUP)	Francisco Abad Santos

Continuing education La Princesa

Título	Ponente/Director
Competencias en Ecografía Clínica Urgencias Princesa	Juan Mariano Aguilar Mulet, Sonia González Del Val, Ana María Martínez Molina, Jorge Sorando Ortín, Francisco Javier Val de Santos, Andrés von Wernitz, Iñigo Guerra Molina, Fernando Alfageme Roldan, Emilia Roy Vallejo y Jose Ignacio Alonso González
Taller de suturas de heridas 2022	Mar de Castro Marinas
Competencias en Ecografía Clínica para Atención Primaria: Edición III	Juan Mariano Aguilar Mulet, Sonia González Del Val, Ana María Martínez Molina, Jorge Sorando Ortín, Francisco Javier Val de Santos, Andrés von Wernitz, Iñigo Guerra Molina, Fernando Alfageme Roldan, Emilia Roy Vallejo y Jose Ignacio Alonso González

Título	Ponente/Director
Código Sepsis Princesa (EDICIÓN 06)	Fernando Ramasco Rueda, Azucena Bautista Hernández, Andrés von Wernitz, SARA NAVARRO AUSERE, Rosa Mendez Hernandez, Marta Chicot Llano, Iñigo Garcia Sanz, Carmen Saez Bejar, Natalia Pascual Gomez, Maria Jose Rubio Perez, Nelly Zurita Cruz, Maria Semiglia, David Jiménez Jiménez y Ana Barrios Blandino
Competencias en Ecografía Clínica: Modelos	Andrés von Wernitz
Soporte Vital Básico para personal sanitario 6ª Edición 2022	Juan Mariano Aguilar Mulet, María Cristina Santiago Poveda, Francisco Javier Val De Santos, Diana Parrado, Noemí Díaz Velasco Y Elena Rojo Rodriguez
Soporte Vital Básico para personal sanitario 7ª Edición 2022	Juan Mariano Aguilar Mulet, María Cristina Santiago Poveda, Francisco Javier Val De Santos, Diana Parrado, Noemí Díaz Velasco Y Elena Rojo Rodriguez
CURSO SOBRE RETOS EN ANTIBIOTERAPIA EN EL PACIENTE CRÍTICO – 2ª ED.	Fernando Ramasco Rueda, Diana Parrado, Mar Orts Rodríguez, Rosa Mendez Hernandez, Nelly Zurita Cruz, Maria Semiglia, Sheila Santidrián, Carmen Vallejo Lantero, David Arribas Mendez, Sonia Exposito Carazo, Julia Hernando Santos, Carlos Figueroa Yusta, Rafael González De Castro Y Beatriz Lozano
Cuidados críticos postoperatorios para enfermería	Raquel Fernández Leal, Maria Garcia Franco, Yolanda Lopez Gonzalez, Celia Martin Almazan, Alba Martinez Camara, Rosa Mendez Hernandez, Mar Puente Cepeda, Fernando Ramasco Rueda, Diego Saiz Blázquez, Laura Torrent Iglesias, Cristina Yepes Temiño Y Beatriz Yuste Lozano
Soporte Vital Avanzado para personal sanitario 5ª Ed. 2022	Juan Mariano Aguilar Mulet, Elvira Contreras Murillo, Noemí Díaz Velasco, Diana Parrado, Elena Rojo Rodríguez, María Cristina Santiago Poveda y Francisco Javier Val de Santos
Soporte Vital Avanzado para personal sanitario 6ª Ed. 2022	Juan Mariano Aguilar Mulet, Elvira Contreras Murillo, Noemí Díaz Velasco, Diana Parrado, Elena Rojo Rodríguez, María Cristina Santiago Poveda y Francisco Javier Val de Santos
Curso de Bienvenida a los nuevos Residentes 2022	Juan Mariano Aguilar Mulet
Curso de Historia Clínica Electrónica - 2022	Juan Mariano Aguilar Mulet
Soporte Vital Inmediato para Residentes Del 2022	Juan Mariano Aguilar Mulet, Raquel Caminero García, Marta Caño Hortoneda, Lydia Chao Ricoy, Teresa Coco, Elvira Contreras Murillo, Maria Cruzate Aparicio, Ana Del Rey Ubago, Noemí Díaz Velasco, Verónica Espiga Prieto, Beatriz González Chesa, Sonia González Val, JAVIER MARTIN RUIZ, Ana María Martínez Molina, Mónica Negro Rua, Diana Parrado, Luis Picazo Garcia, Bárbara Retana Fernández, Elena Rojo Rodríguez, Jorge Sorando Ortín, Francisco Javier Val de Santos y Andrés von Wernitz

Título	Ponente/Director
Curso de Traumatología para nuevos residentes - 2022	Juan Mariano Aguilar Mulet
Cirugía para nuevos Residentes - 2022	Juan Mariano Aguilar Mulet y Iñigo García Sanz
ELECTROCARDIOGRAFÍA - 2022	Juan Mariano Aguilar Mulet
Curso de interpretación básica de radiología simple - 2022	Juan Mariano Aguilar Mulet
Curso Avanzado de eLearning: Creación de Minivideos Docentes – 4ª Edición	Elena Fernández Martínez
eLearning en Sanidad – 5ª Edición	Elena Fernández Martínez
Competencias en Ecografía Clínica para Atención Primaria: Edición IV	Juan Mariano Aguilar Mulet, Sonia González Del Val, Ana María Martínez Molina, Jorge Sorando Ortín, Francisco Javier Val de Santos, Andrés von Wernitz, Iñigo Guerra Molina, Fernando Alfageme Roldan y Jose Ignacio Alonso González
Cuidados críticos postoperatorios para enfermería – 3ª Edición	Raquel Fernández Leal, María Mercedes García Franco, Yolanda Lopez Gonzalez, Celia Martin Almazan, Alba Martinez Camara, Rosa Mendez Hernandez, Mar Puente Cepeda, Fernando Ramasco Rueda, Diego Saiz Blázquez, Laura Torrent, Cristina Yepes Temiño Y Beatriz Yuste Lozano
Simulación en el manejo de la vía aérea 5ª Ed. (2022)	Noemí Díaz Velasco, Jesús Nieves, Diana Parrado, Elena Rojo Rodríguez y Sheila Santidrián
Simulación en el manejo de la vía aérea 6ª Ed. (2022)	Noemí Díaz Velasco, Jesús Nieves, Diana Parrado, Elena Rojo Rodríguez y Sheila Santidrián
Código Sepsis Princesa (EDICIÓN 07)	Ana Barrios Blandino, Azucena Bautista Hernández, Marta Chicot Llano, Iñigo Garcia Sanz, David Jiménez Jiménez, Rosa Mendez Hernandez, SARA NAVARRO AUSERE, Natalia Pascual Gomez, Fernando Ramasco Rueda, Maria Jose Rubio Perez, Carmen Saez Bejar, MARIA DEL PILAR SANZ MARTIN, Maria Semiglia, Andrés von Wernitz y Nelly Zurita Cruz
Actualización en medicamentos biológicos y biosimilares. Ed. II	Carolina Aguilar Guisado, Maria Isabel Barcia Martin, Maria Mercedes Garcia Gimeno y Susana Sanchez Suarez
Competencias en Ecografía Clínica para Atención Primaria: Edición V	Juan Mariano Aguilar Mulet, Fernando Alfageme Roldan, Jose Ignacio Alonso González, Sonia González Del Val, Iñigo Guerra Molina, Ana María Martínez Molina, Jorge Sorando Ortín, Francisco Javier Val de Santos y Andrés von Wernitz
Neurorestauración: estimulación cerebral profunda para los trastornos psiquiátricos refractarios	Mónica Lara Almunia, Marta Navas García, Rodrigo Rodriguez Rodriguez, Alejandra Roldan, Purificación Salgado Serrano, Cristina Torres Díaz y Gloria Villalba
Competencias en Ecografía Clínica para Atención Primaria: Edición VI	Andrés von Wernitz teleki



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 ALLERGY BASED 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

ANNUAL REPORT OF SCIENTIFIC ACTIVITY

2022

AREA 1

INSTITUTO DE INVESTIGACIÓN SANITARIA
HOSPITAL UNIVERSITARIO DE LA PRINCESA

LINE 1.1 ›› INTERCELLULAR COMMUNICATION IN THE INFLAMMATORY RESPONSE.

GROUP 1

Head of laboratory: Sánchez Madrid, Francisco

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

Line 1.1 Intercellular communication in the inflammatory response.

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.

GROUP MEMBERS

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- Enrique Martín Gayo
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MAJOR GRANTS

Sánchez Madrid, Francisco. La sinapsis inmune como mecanismo educativo de linfocitos y células innatas para la regulación de procesos infecciosos e inflamatorios (ISEDINF). PID2020-120412RB-I00. Agencia Estatal de Investigación. 2021-2024.

Sánchez Madrid, Francisco. Transferencia de exosomas de células inmunes para para potenciar la inmunidad. PDC2021- 21797-I00. Agencia Estatal de Investigación. 2021-2023.

Sánchez Madrid, Francisco. Microscopio óptico de fluorescencia para la observación de muestras gruesas y tejidos: Mesoscopia. IFEQ21/00085. ISCIII 2022.

Sánchez Madrid, Francisco. Readying immune cells prior to disease- inducing encounters. HR17- 00016. Fundación La Caixa. 2019-2022.

Alfranca González, Arantza. Endothelial PD-L1 as a regulator of angiogenesis and response to immunotherapy. PI19/00549. ISCIII. 2020- 2022.

Sánchez Madrid, Francisco. INMUNOVACTER_REACT_EU. 2020-2022.

PUBLICATIONS

Dosil SG, Rodríguez Galán A, Sánchez Madrid F, Fernández Messina L. **MicroRNAs in T Cell-Immunotherapy.** Int J Mol Sci 24 (1). 2022. PMID: 36613706. IF: 6,21. DOI: 10.3390/ijms24010250.

Martin Gayo E, Gao C, Calvet Mirabent M, Ouyang Z, Lichterfeld M, Yu XG. **Cooperation between cGAS and RIG-I sensing pathways enables improved innate recognition of HIV-1 by myeloid dendritic cells in elite controllers.** Front Immunol 13. 2022. PMID: 36569826. IF: 8,79. DOI:10.3389/fimmu.2022.1017164.

Russo A, Schürmann H, Brandt M, Scholz K, Matos ALL, Grill D, Revenstorff J, Rembrink M, von Wulffen M, Fischer Riepe L, Hanley PJ, Häcker H, Prünster M, Sánchez Madrid F, Hermann S, Klotz L, Gerke V, Betz T, Vogl T, Roth J. **Alarming and Calming: Opposing Roles of S100A8/S100A9 Dimers and Tetramers on Monocytes.** Adv Sci 9 (36). 2022. PMID: 36310133. IF: 17,52. DOI: 10.1002/advs.202201505.

Delgado Arévalo C, Calvet Mirabent M, Triguero Martinez A, Vázquez de Luis E, Benguría Filippini A, Largo R, Calzada Fraile D, Popova O, Sánchez Cerrillo I, Tsukalov I, Moreno Vellisca R, de la Fuente H, Herrero Beaumont G, Ramiro AR, Sánchez Madrid F, Castañeda S, Dopazo A, González Álvaro I, Martin Gayo E. **NLRC4 -mediated activation of CD1c+ dendritic cells contributes to perpetuation of synovitis in rheumatoid arthritis.** JCI Insight 7 (22). 2022. PMID: 36194479. IF: 9,48. DOI: 10.1172/jci.insight.152886.

Fernández Gallego N, Castillo González R, Méndez Barbero N, López Sanz C, Obeso D, Villaseñor A, Escribese MM, López Melgar B, Salamanca J, Benedicto Buendía A, Jiménez Borreguero LJ, Ibañez B, Sastre J, Belver MT, Vega F, Blanco C, Barber D, Sánchez Madrid F, de la Fuente H, Martín P, Esteban V, Jiménez Saiz R. **The impact of type 2 immunity and allergic diseases in atherosclerosis.** Allergy 77 (11). 2022. PMID: 35781885. IF: 14,71. DOI: 10.1111/all.15426.

Blanco Domínguez R, de la Fuente H, Rodríguez C, Martín Aguado L, Sánchez Díaz R, Jiménez Alejandre R, Rodríguez Arabaolaza I, Curtabbi A, García Guimaraes MM, Vera A, Rivero F, Cuesta J, Jiménez Borreguero LJ, Cecconi A, Duran Cambra A, Taurón M, Alonso J, Bueno H, Villalba Orero M, Enríquez JA, Robson SC, Alfonso F, Sánchez Madrid F, Martínez González J, Martín P. **CD69 expression on regulatory T cells protects from immune damage after myocardial infarction.** J Clin Invest 132 (21). 2022. PMID: 36066993. IF: 19,46. DOI: 10.1172/JCI152418.

Izquierdo Serrano R, Fernández Delgado I, Moreno Gonzalo O, Martín Gayo E, Calzada Fraile D, Ramírez Huesca M, Jorge I, Camafeita E, Abián J, Vicente Manzanares M, Veiga E, Vázquez J, Sánchez Madrid F. **Extracellular vesicles from Listeria monocytogenes-infected dendritic cells alert the innate immune response.** Front Immunol 13. 2022. PMID: 36131943. IF: 8,79. DOI: 10.3389/fimmu.2022.946358.

Calvet Mirabent,M,Martin Gayo,E. **Effective innate immune response in natural HIV-1 controllers. Can mimicking lead to novel preventive and cure strategies against HIV-1?** Curr Opin HIV AIDS 17 (5): 2022. PMID: 35938465. IF: 4,06. DOI: 10.1097/COH.0000000000000750.

Jiménez Fernández M, Rodríguez Sinovas C, Cañes L, Ballester Servera C, Vara A, Requena S, de la Fuente H, Martínez González J, Sánchez Madrid F. **CD69-oxLDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in human CD4 + T lymphocytes.** Cell Mol Life Sci 79 (8). 2022. PMID: 35930205. IF: 9,21. DOI: 10.1007/s00018-022-04481-1.

Dosil SG, Lopez Cobo S, Rodriguez Galan A, Fernandez Delgado I, Ramirez Huesca M, Milan Rois P, Castellanos M, Somoza A, Gómez MJ, Reyburn HT, Vales Gomez M, Sánchez Madrid F, Fernandez Messina L. **Natural killer (NK) cell-derived extracellular-vesicle shuttled microRNAs control T cell responses.** ELIFE 11. 2022. PMID: 35904241. IF: 8,71. DOI: 10.7554/eLife.76319.

Uriarte Ecenarro M, Useros D, Alfranca A, Tejedor R, González Alvaro I, García Vicuña R. **Anti-Citrullinated Protein Antibody Titers Are Independently Modulated by Both Disease Activity and Conventional or Biologic Anti-Rheumatic Drugs.** Diagn 12 (7). 2022. PMID: 35885675. IF: 3,99. DOI: 10.3390/diagnostics12071773.

Calvet Mirabent M, Sánchez Cerrillo I, Martín Cófreces N, Martínez Fleta P, de la Fuente H, Tsukalov I,

Delgado Arévalo C, Calzada MJ, de los Santos I, Sanz J, García Fraile L, Sánchez Madrid F, Alfranca A, Muñoz Fernández MÁ, Buzón MJ, Martín Gayo E. **Antiretroviral therapy duration and immunometabolic state determine efficacy of ex vivo dendritic cell-based treatment restoring functional HIV-specific CD8+ T cells in people living with HIV.** EBioMedicine 81. 2022. PMID: 35665682. IF: 11,21. DOI: 10.1016/j.ebiom.2022.104090

Céspedes PF, Jainarayanan A, Fernández Messina L, Valvo S, Saliba DG, Kurz E, Kvalvaag A, Chen L, Ganskow C, Colin York H, Fritzsche M, Peng Y, Dong T, Johnson E, Siller Farfán JA, Dushek O, Sezgin E, Peacock B, Law A, Aubert D, Engledow S, Attar M, Hester S, Fischer R, Sánchez Madrid F, Dustin ML. **T-cell trans-synaptic vesicles are distinct and carry greater effector content than constitutive extracellular vesicles.** Nat Commun 13 (1). 2022. PMID: 35710644. IF: 17,69. DOI: 10.1038/s41467-022-31160-3

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

García Cuesta EM, Rodríguez Frade JM, Gardeta SR, D'Agostino G, Martínez P, Soler Palacios B, Cascio G, Wolf T, Mateos N, Ayala Bueno R, Santiago CA, Lucas P, Llorente L, Allende LM, González Granado LI, Martín Cófreces N, Roda Navarro P, Sallusto F, Sánchez Madrid F, García Parajo MF, Martínez Muñoz L, Mellado M. **Altered CXCR4 dynamics at the cell membrane impairs directed cell migration in WHIM syndrome patients.** Proc Natl Acad Sci U S A 119 (21). 2022. PMID: 35588454. IF: 12,78. DOI: 10.1073/pnas.2119483119

Fernando Garcia Jimenez Alvaro, Caceres Martell Yaiza, Fernandez Soto Daniel, Martinez Fleta Pedro, Casasnovas Jose M, Sanchez Madrid Francisco, Rodriguez Frade Jose Miguel, Vales Gomez Mar, Reyburn Hugh T. **Cross-reactive cellular, but not humoral, immunity is detected between OC43 and SARS-CoV-2 NPs in people not infected with SARS-CoV-2: Possible role of cT(FH) cells**. J Leukocyte Biol 112 (2). 2022. PMID: 35384035. IF: 6,01. DOI: 10.1002/JLB.4COVCRA0721-356RRR

Cecconi Alberto, Navarrete Gonzalo, Garcia Guimaraes Marcos, Vera Alberto, Blanco Dominguez Rafael, Sanz Garcia Ancor, Lozano Prieto Marta, Lopez Melgar Beatriz, Rivero Fernando, Martin Pilar, Sanchez Madrid Francisco, de la Fuente Hortensia, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Influence of air pollutants on circulating inflammatory cells and microRNA expression in acute myocardial infarction**. Sci Rep 12 (1). 2022. PMID: 35354890. IF: 5,00. DOI: 10.1038/s41598-022-09383-7

García Vicuña R, Rodriguez García SC, Abad Santos F, Bautista Hernández A, García Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso Pérez T, Cardeñoso L, Alfranca A, Mejía Abril G, Sanz J, González Alvaro I. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621

Esparcia Pinedo L, Martinez Fleta P, Ropero Noelia, Vera Tome P, Reyburn Hugh T, Casasnovas Jose M, Frade Jose M Rodriguez, Vales Gomez M, Vilches Carlos, Martin Gayo E, Munoz Calleja C, Sanchez Madrid F, Alfranca Arantzazu. **CD4+T Cell Immune Specificity Changes After Vaccination in Healthy And COVID-19 Convalescent Subjects**. Front Immunol 12. 2022. PMID: 35126347. IF: 8,79. DOI: 10.3389/fimmu.2021.755891

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

Calvet Mirabent Marta, Claiborne Daniel T, Deruaz Maud, Tanno Serah, Serra Carla, Delgado Arevalo Cristina, Sanchez Cerrillo Ildefonso, de Los Santos Ignacio, Sanz Jesus, Garcia Fraile Lucio, Sanchez Madrid Francisco, Alfranca Arantzazu, Munoz Fernandez Maria Angeles, Allen Todd M, Buzon Maria J, Balazs Alejandro, Vrbanac Vladimir, Martin Gayo Enrique. **Poly I:C and STING agonist-primed DC increase lymphoid tissue polyfunctional HIV-1-specific CD8(+) T cells and limit CD4(+) T-cell loss in BLT mice**. Eur J Immunol 52 (3). 2022. PMID: 34935145. IF: 6,69. DOI: 10.1002/eji.202149502

GROUP 3

Head of laboratory: Yáñez Mó, María

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

Line 1.1 Intercellular communication in the inflammatory response.

RESEARCH INTEREST

Our group is focused on the functional characterization of membrane microdomains based on tetraspanin proteins, which are involved in cell-cell adhesion and migration as well as in the biogenesis and cargo selection of extracellular vesicles (EVs). EVs represent a novel mechanism of intercellular communication and have a great potential as carriers of therapeutics or biomarkers for diagnosis in the liquid biopsy. Our translational efforts aim at exploiting the tools against tetraspanin molecules to develop new isolation, detection and quantification devices, as well as to develop synthetic exosome mimetics as reference materials or vaccination strategies.

In addition, tetraspanin enriched microdomains are connected to different cytoskeletal components and signalling pathways and have been shown to regulate different steps of the infectious cycle of several viruses, ranging from viral entry to budding, but also including other aspects that are not so evidently linked to cell membranes such as viral replication. Therefore, a parallel research line in our group aims at establishing the anti-viral potential of tetraspanin-targeted reagents as broad-spectrum therapeutics.

GROUP MEMBERS

- Soraya López Martín
- Miguel Palma Cobo
- Beatriz Benayas López
- Victor Toribio Serrano

MAJOR GRANTS

Yáñez Mó, María. Validación clínica de un sistema para detectar translocaciones de alk en vesículas extracelulares en plasma. DTS21/00134. ISCIII. 2022-2023.

Yáñez Mó, María. Microdominios de membrana, exosomas, virus y vacunas. PID2020-119627GB-I00. Agencia Estatal de Investigación. 2021- 2024.

Yáñez Mó, María. Vacunas basadas en exosomas miméticos. PDC2021- 121052. 2022-2023.

PUBLICATIONS

Toribio Victor, Yanez Mo Maria. **Tetraspanins interweave EV secretion, endosomal network dynamics and cellular metabolism**. Eur J Cell Biol 101 (3). 2022. PMID: 35500468. IF: 6,02. DOI:10.1016/j.ejcb.2022.151229.

Cardenes Beatriz, Clares Irene, Bezos Tamara, Toribio Victor, Lopez Martin Soraya, Rocha Almudena, Peinado Hector, Yanez Mo Maria, Cabanas Carlos. **ALCAM/CD166 Is Involved in the Binding and Uptake of Cancer- Derived Extracellular Vesicles**. Int J Mol Sci 23 (10). 2022. PMID: 35628559. IF: 6,21. DOI: 10.3390/ijms23105753.

Campos Silva Carmen, Caceres Martell Yaiza, Sanchez Herrero Estela, Sandua Amaia, Beneitez Martinez Alexandra, Gonzalez Alvaro, Provencio Mariano, Romero Atocha, Jara Acevedo Ricardo, Yanez Mo Maria, Vales Gomez Mar. **A simple immunoassay for extracellular vesicle liquid biopsy in microliters of non-processed plasma**. J Nanobiotechnology 20 (1). 2022. PMID: 35135541. IF: 9,43. DOI: 10.1186/s12951-022-01256-5.

GROUP 56

Head of laboratory: Urzainqui Mayayo, Ana Carmen

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

Line 1.1 Intercellular communication in the inflammatory response.

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 described 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. We described 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). In addition, we observed that the absence of P-Selectin, the main PSGL-1 ligand, causes an autoimmune syndrome similar to human systemic lupus erythematosus (SLE), with generation of anti-dsDNA autoantibodies, immune complex deposits in skin and kidney and hypersensitivity to UV light, characteristics that could match those of SLE (González- Tajuelo et al., Sci Reports 2017). Interestingly, we have recently described that aged P- Selectin and PSGL-1 female KO mice develop pulmonary arterial hypertension (PAH), the most severe form of connective tissue-related autoimmune disease, due to increased levels of Angiotensin II and endothelial dysfunction, with low production of NO (González-Tajuelo et al., Arthritis and Rhumatol. 2020). Remarkably, clinical studies with patients indicate that PSGL- 1 and P-Selectin expression is altered in both diseases. SSc patients have reduced PSGL-1 expression in B cells and increased expression in monocytes, dendritic cells and T cells. In addition, our data show the association of high PSGL-1 expression with the presence of interstitial lung disease (ILD) in SSc patients and that 75% or more circulating pDCs expressing ADAM8 associate with the presence of SSc. (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 correlating with disease activity. Given all these findings, our main goal is to study the molecular and cellular alterations that underlie the pathology of these diseases. Moreover, we have described that PSGL-1 expression is regulated during B cell development and that the absence of PSGL-1 leads to alterations in B cell differentiation and activation. In humans, PSGL-1 signaling controls the production of IgG. Remarkably, patients with PAH present altered PSGL-1 expression in B cells and plasma cells (González-Tajuelo et al., Frontiers in Immunol. 2020).

Main Research Lines:

- Study of interstitial pneumonia (ILD) and pulmonary arterial hypertension (PAH), idiopathic or associated to scleroderma (SSc) and lupus (SLE), which are main causes of death in these diseases.
- Analysis of the cells and molecular components implicated in the development of these pathologies to find molecular alterations that could be potential treatment targets.
- Targeted therapy for ILD treatment using PSGL-1 KO mice and P-Selectin KO mice as models of SSc-ILD and SLE-ILD, respectively.
- Analysis of PSGL-1 as possible regulator of cellular proteostasis and its contribution to scleroderma and SLE pathology

GROUP MEMBERS

- Ana Carmen Urzainqui Mayayo
- María Esther San Antonio Sánchez
- Antonio Muñoz Callejas
- Alejandra Isabel Ramos Manzano
- Inés Sánchez Abad
- Javier Silván Montoya

MAJOR GRANTS

Urzainqui Mayayo, Ana Carmen. Estudio de la relevancia de la interacción PSGL-1/P- selectina en la proteostasis celular y generación de NETS y su posible implicación en la patogénesis de esclerodermia y lupus. PI20/01690. ISCIII. 2021-2023.

Urzainqui Mayayo, Ana Carmen. Estudio de la relevancia de lainteracción PSGL-1/P- selectina en la proteostasis celular ygeneración de NETS y su posible implicación en la patogénesis deesclerodermia y lupus. PI20/01690. ISCIII. 2021-2023.

PUBLICATIONS

González Sánchez E, Muñoz Callejas A, Gómez Román J, San Antonio E, Marengo A, Tsapis N, Bohne Japiassu K, González Tajuelo R, Pereda S, García Pérez J, Cavagna L, González Gay MÁ, Vicente Rabaneda EF, Meloni F, Fattal E, Castañeda S, Urzainqui A. **Targeted nanotherapy with everolimus reduces inflammation and fibrosis in scleroderma-related interstitial lung disease developed by PSGL-1 deficient mice.** Br J Pharmacol 179 (18). 2022. PMID: 35726496. IF: 9,47. DOI: 10.1111/bph.15898.

LINE 1.2 ›› CELLULAR AND MOLECULAR RESPONSES TO HYPOXIA.

GROUP 9

Head of laboratory: Aragonés López, Julián

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

Line 1.2 Cellular and molecular responses to hypoxia

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 obesity. 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 current research interest is focused on the role of the HIF oxygen sensing pathways in cancer, pulmonary disease and obesity. In particular, we are mainly interested in cellular metabolic reprogramming, which is one the central biological functions executed by HIF factors. 1) HIF factors and renal cell carcinoma: HIF factors are induced in hypoxic areas in the inner core of the solid tumors but clear cell renal cell carcinomas (ccRCC) - which lose Vhl (the main repressor of HIFs in normoxia) - show constitutive HIF expression irrespective of the oxygen levels of the tumor. In these tumors HIF1 shows its cell autonomous anti- proliferative capability, whereas HIF2 acts as an oncoprotein. Therefore, ccRCC are being studied extensively to understand the role of HIF in cancer biology. Our studies have shown that the HIF2a isoform acts as an mTORC1 activator through the amino acid carrier SLC7A5, which is essential to sustain ccRCC tumor growth. We have recently found a novel link between glucose and lipid metabolism and HIF factors, which impacts remarkably on ccRCC progression. Independently of these projects on ccRCC tumor metabolism, we have recently initiated a project identifying unanticipated molecular links between HIF pathways and cancer immunology. 2) HIF factors and airway dysfunction in pulmonary disease: Pulmonary diseases such as COPD and sleep-apnea hypoapnea syndrome (SAHS) are the most common respiratory diseases causing illness and death, and are being anticipated 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 COPD and intermittent in 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 - is a first barrier encountered by oxygen, the role of the HIF oxygen-sensing responses in lung pathophysiology remains largely unknown. Based on (i) our recent studies about the HIF pathways as activators of proliferative markers in bronchial epithelium including mTORC1, we are currently studying, in collaboration with other researchers including pneumologists in Hospital de la Princesa IIS-IP (Dr. Julio Ancochea), the role of HIF oxygen sensing pathways in bronchial epithelium physiopathology.

GROUP MEMBERS

- Lucía Fernández-Arroyo Camacho
- Andrea Guajardo Grence
- Antonio Bouthelier de Pedro
- Claudia Mesa Ciller
- Andrés Amalio Urrutia Elorduy
- Esther Fuertes Yebra
- Florinda del Coral Meléndez Rodríguez
- Ana María Pacheco Aguado

MAJOR GRANTS

Aragonés López, Julián. Papel de los factores de respuesta a hipoxia HIF1/2 en la regulación del metabolismo de aminoácidos y su impacto en fisiopatología. PID2019- 106371RB-100. Agencia Estatal de Investigación. 2020-2023.

Aragonés López, Julián. Secuenciación ARN de última generación para identificar biomarcadores diagnóstico y pronostico en carcinoma renal.DTS21/00032. INSTITUTO SALUD CARLOS III.

Aragonés López, Julián. Identificación de Mecanismos, Biomarcadores e Intervenciones en comorbilidad en Enfermedades Respiratorias Hipoxémicas mediante abordajes preclínicos, clínicos y computacionales. P2022/BMD-7224. Comunidad Autónoma de Madrid. 2023 – 2026.

PUBLICATIONS

Latorre J, Martínez C, Ortega F, Oliveras Cañellas N, Díaz Sáez F, Aragonés J, Camps M, Gumà A, Ricart W, Fernández Real JM, Moreno Navarrete JM. **The relevance of EGFR, ErbB receptors and neuregulins in human adipocytes and adipose tissue in obesity.** Biomed Pharmacother 156. 2022. PMID: 36411648. IF: 7,42. DOI:10.1016/j.biopha.2022.113972

Martínez C, Latorre J, Ortega F, Arnoriaga Rodríguez M, Lluch A, Oliveras Cañellas N, Díaz Sáez F, Aragonés J, Camps M, Gumà A, Ricart W, Fernández Real JM, Moreno Navarrete JM. **Serum neuregulin 4 is negatively correlated with insulin sensitivity in humans and impairs mitochondrial respiration in HepG2 cells.** Front. Physiol 13. 2022. PMID: 36187779. IF: 4,76. DOI: 10.3389/fphys.2022.950791.

Bea C, Vela S, García Blas S, Perez Rivera JA, Díez Villanueva P, de Gracia AI, Fuertes E, Oltra MR, Ferrer A, Belmonte A, Santas E, Pellicer M, Colomina J, Doménech A, Bodi V, Forner MJ, Chorro FJ, Bonanad C. **Infective Endocarditis in the Elderly: Challenges and Strategies.** J Cardiovasc Dev Dis 9 (6). 2022. PMID: 35735821. IF: 4,42. DOI:10.3390/jcdd9060192.

Fernandez Cuadros Marcos E, Perez Moro Olga S, Albaladejo Florin Maria J, Tobar Izquierdo Maria M, Magana Sanchez Amelia, Jimenez Cuevas Patricia, Rodriguez Cia Javier. **Intra Articular Ozone Modulates Inflammation and Has Anabolic Effect on Knee Osteoarthritis: IL-6 and IGF-1 as Pro-Inflammatory and Anabolic Biomarkers**. Process 10 (1). 2022. IF: 3,35. DOI: 10.3390/pr10010138.

Bouthelier A, Fernández-Arroyo L, Mesa-Ciller C, Cibrian D, Martín-Cófreces NB, Castillo-González R, Calero M, Herráez-Aguilar D, Guajardo-Grence A, Pacheco AM, Marcos-Jiménez A, Quiroga B, Morado M, Monroy F, Muñoz- Calleja C, Sánchez-Madrid F, Urrutia AA, Aragonés J. **Erythroid SLC7A5/SLC3A2 amino acid carrier controls red blood cell size and maturation**. iScience 5: 26 (1): 105739. 2022. PMID: 36582828. IF: 6, 10. doi: 10.1016/j.isci.2022.105739.

Latorre J, Martínez C, Ortega F, Oliveras-Cañellas N, Díaz-Sáez F, Aragonés J, Camps M, Gumà A, Ricart W, Fernández-Real JM, Moreno-Navarrete JM. **The relevance of EGFR, ErbB receptors and neuregulins in human adipocytes and adipose tissue in obesity**. Biomed Pharmacother 156: 113972. 2022. PMID: 36411648. IF: 7, 41. Doi: 10.1016/j.biopha.2022.113972.

Martínez C, Latorre J, Ortega F, Arnoriaga-Rodríguez M, Lluch A, Oliveras- Cañellas N, Díaz-Sáez F, Aragonés J, Camps M, Gumà A, Ricart W, Fernández-Real JM, Moreno-Navarrete JM. **Serum neuregulin 4 is negatively correlated with insulin sensitivity in humans and impairs mitochondrial respiration in HepG2 cells**. Front Physiol 15: 13: 950791. 2022. PMID: 36187779. IF: 4, 75. doi: 10.3389/fphys.2022.950791.

Aboouf MA, Guscetti F, von Büren N, Armbruster J, Ademi H, Ruetten M, Meléndez-Rodríguez F, Rülicke T, Seymer A, Jacobs RA, Schneider Gasser EM, Aragones J, Neumann D, Gassmann M, Thiersch M. **Erythropoietin receptor regulates tumor mitochondrial biogenesis through iNOS and pAKT**. Front Oncol 16: 12: 976961. 2022. PMID: 36052260. IF: 5, 73. doi: 10.3389/fonc.2022.976961.

GROUP 7

Head of laboratory: Martínez Ruiz, Antonio

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

Line 1.2 Cellular and molecular responses to hypoxia

RESEARCH INTEREST

1. Redox signalling and damage mediated by the mitochondrial sodium/calcium exchanger NCLX. We have unveiled the molecular mechanism driving superoxide production and redox signalling in the acute response to hypoxia. The mitochondrial sodium/calcium exchanger NCLX is a key element in this mechanism, as hypoxia induces its activation, which drives mitochondrial sodium (Na+) import. The increase in matrix Na+ alters the inner mitochondrial membrane fluidity, regulating oxidative phosphorylatWWion and the mitochondrial production of reactive oxygen species (ROS). We are currently investigating the role of NCLX in different pathophysiological settings, such as inflammation or ischemia-reperfusion injury (IRI). In IRI, NCLX seems to take part in ROS production, not only during ischemia, but also during reperfusion. We are studying the molecular mechanism operating in this context, using cellular and animal models of ischemia-reperfusion, as well as its potential clinical application, mainly focused on diminishing brain damage after ischemic stroke.

2. Oxidative post-translational modifications and redox proteomics. Some time ago we studied the functional role of S-nitrosylation and other cysteine reversible oxidations, developing methods for detecting these modifications using thiol redox proteomics. In an international collaboration, we now seek to study the role of protein sulfhydration, an oxidative modification of cysteines with sulfhydric acid (H2S), in neurogenesis in Down syndrome.

GROUP MEMBERS

- Susana Delgado Martín
- Carmen Choya Foces

MAJOR GRANTS

Martínez Ruiz, Antonio. El intercambiador mitocondrial de sodio/calcio NCLX como diana farmacológica en ictus isquémico (NCLXtroke). PDC2022-133246-I00. Agencia Estatal de Investigación. 2022-2024.

Martínez Ruiz,Antonio.Análisis del papel del transportador mitocondrial de Na+/Ca2+/Li+ NCLX y especies reactivas de oxígeno en ictus e inflamación // Dissecting the role of mitochondrial Na+/Ca2+/Li+ exchanger NCLX and reactive oxygen species in stroke and inflammation. PID2021-124688OB- I00.AGENCIA ESTATAL DE INVESTIGACION.2022.

PUBLICATIONS

Sevilla Montero J, Munar Rubert O, Pino Fadon J, Aguilar Latorre C, Villegas Esguevillas M, Climent B, Agro M, Choya Foces C, Martinez Ruiz A, Balsa E, Munoz Calleja C, Gomez Punter RM, Vazquez Espinosa E, Cogolludo A, Calzada MJ. **Cigarette smoke induces pulmonary arterial dysfunction through an imbalance in the redox status of the soluble guanylyl cyclase**. Free Radic Biol Med 193 (Pt 1). 2022. PMID: 36174878. IF: 8,10. DOI: 10.1016/j.freeradbiomed.2022.09.026.

Terrile Maria Cecilia, Tebez Nuria Malena, Colman Silvana Lorena, Mateos Julieta Lisa, Morato Lopez Esperanza, Sanchez Lopez Nuria, Izquierdo Alvarez Alicia, Marina Anabel, Villalobos Luz Irina A Calderon, Estelle Mark, Martinez Ruiz Antonio, Fiol Diego Fernando, Casalongue Claudia Anahi, Iglesias Maria Jose. **S-Nitrosation of E3 Ubiquitin Ligase Complex Components Regulates Hormonal Signalings in Arabidopsis**. Front Plant Sci 12. 2022. PMID: 35185952. IF: 6,63. DOI: 10.3389/fpls.2021.794582.

GROUP 8

Head of laboratory: Calzada García, María Josefa

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

Line 1.2 Cellular and molecular responses to hypoxia

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 on the diagnosis and treatment of these pathologies. Our group has studied the role of hypoxia in pathological processes, such as cancer and pulmonary hypertension. Currently, our main line of research is focused on studying the involvement of hypoxia and tobacco smoke in chronic and inflammatory lung diseases. Some of our more recent publications have contributed to identify early markers involved in the development of lung diseases such as COPD, identifying relevant molecular mechanisms related to early stages of the development of vascular dysfunction. Dr. Calzada has participated in numerous national and international competitive projects as PI and currently belongs to CIBERES (EPOC GROUP).

GROUP MEMBERS

- María Josefa Calzada García
- Javier Sevilla Montero

MAJOR GRANTS

Calzada García, María José. Efectos del humo de tabaco en la vasculatura pulmonar. Mecanismos moleculares subyacentes al desarrollo de hipertensión pulmonar secundaria a EPOC. Agencia Estatal de Investigación. PID2019-104406RB-100. 2020- 2023.

Calzada García, María José. **Identificación de Mecanismos, Biomarcadores e Intervenciones en comorbilidad en Enfermedades Respiratorias Hipoxémicas mediante abordajes preclínicos, clínicos y computacionales**. Redes de Investigación en Biomedicina 2022. CAM. S2022/BMD-7224- INSPIRA-CM. 2023-2026.

PUBLICATIONS

Sevilla-Montero J, Munar-Rubert O, Pino-Fadón J, Aguilar-Latorre C, Villegas-Esguevillas M, Climent B, Agrò M, Choya-Foces C, Martínez- Ruiz A, Balsa E, Muñoz-Calleja C, Gómez-Punter RM, Vázquez- Espinosa E, Cogolludo A, Calzada MJ (AC). **Cigarette smoke induces pulmonary arterial dysfunction through an imbalance in the redox status of the soluble guanylyl cyclase.** Free Radic Biol Med 26: 193 (Pt 1): 9-22. 2022. PMID: 36174878. IF: 8,1. doi: 10.1016/j.freeradbiomed.2022.09.026.

Calvet-Mirabent M, et al., Calzada MJ, de Los Santos I, Sanz J, García-Fraile L, Sánchez-Madrid F, Alfranca A, Muñoz-Fernández MÁ, Buzón MJ, Martín- Gayo E. EBioMedicine. 2022 81:104090. IF: 8,14. doi: 10.1016/j.ebiom.2022.104090. https://pubmed.ncbi.nlm.nih.gov/3566568 2/ IF: 8,14 D1

Palomino-Antolin A, Narros-Fernández P, Farré-Alins V, Sevilla-Montero J, Decouty-Pérez C, Lopez-Rodriguez AB, Fernández N, Monge L, Casas AI, Calzada MJ, Egea J**. Time-dependent dual effect of NLRP3 inflammasome in brain ischaemia**. Br J Pharmacol 179 (7): 1395-1410. 2022. PMID: 34773639. IF: 8,7. doi: 10.1111/bph.15732.

Neves KB,- Rios FJ, **Sevilla-Montero J**, Montezano AC,Touyz RM. **Exosomes and the cardiovascular system: role in cardiovascular health and disease**. J Physiol. 2022. PMID: 35306667. IF: 6,23**.** DOI: 10.1113/JP282054.

GROUP 10

Head of laboratory: Cadenas Álvarez, Susana

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

Line 1.2 Cellular and molecular responses to hypoxia

RESEARCH INTEREST

Our group studies the function of mitochondria within cells and their implication in the development of pathological conditions. Uncoupling proteins (UCPs) have been involved in the control of mitochondrial reactive oxygen species (ROS) production and the protection against oxidative stress. Since oxidative stress underlies a wide variety of pathophysiological processes, UCPs are potentially important drug targets. The elucidation of the molecular pathways that control their expression and activity is essential to develop strategies for modulating their function. An efficient response to oxidative damage is crucial for cell survival, and Nrf2 (nuclear factor erythroid 2-related factor 2) is an essential transcription factor that regulates the expression of several antioxidant genes via binding to the antioxidant response element (ARE), and plays a pivotal role in cellular defense against oxidative stress. Among several pathologies related to oxidative stress, we are particularly interested in cardiac ischemia- reperfusion (IR) injury. Reperfusion of ischemic myocardium results in an excessive production of ROS that may cause tissue damage. Our group pursues three main lines of research. 1) The regulation of the expression and function of UCP3 in response to oxidative stress. We have previously found that the treatment with hydrogen peroxide (H2O2) or 4- hydroxy-2-nonenal induces UCP3 expression in cells from mouse heart and skeletal muscle. This effect is mediated by the transcription factor Nrf2. Moreover, we have shown that UCP3 upregulation is accompanied by an increase in the proton conductance of the inner mitochondrial membrane, which results in a decreased production of mitochondrial ROS and, consequently, in an increased cell survival. We are currently investigating the effects of low oxygen concentrations on UCP3 expression and their functional consequences. 2) The protective role of UCP3 against IR injury and its involvement in ischemic preconditioning (IPC). We have detected Nrf2 nuclear accumulation and increased UCP3 protein in intact mouse hearts subjected to IR, a condition known to increase ROS generation. We are currently studying the potential protective role of UCP3 against IR injury and its involvement in IPC in the isolated perfused mouse heart and in vivo.

3) The implication of Nrf2 in IPC. There is experimental evidence showing that Nrf2 activation protects against IR injury. By using Nrf2 activators and Nrf2 knockout mice, we will study the role of this factor in IPC and the molecular mechanisms involved. In addition, we have established a collaboration with cardiac surgeons to study the molecular and cellular alterations taking place in the ischemic human heart.

GROUP MEMBERS

- Susana Cadenas Álvarez
- Ana Mata Villanueva

MAJOR GRANTS

Cadenas Álvarez, Susana. Mecanismos de cardioprotección sensibles al estado redox en el daño por isquemia-reperfusión. ISCIII. PI19/01030. 2020-2022.

PUBLICATIONS

Jiménez Villegas J, Kirby J, Mata A, Cadenas S, Turner MR, Malaspina A, Shaw PJ, Cuadrado A, Rojo AI. **Dipeptide Repeat Pathology in C9orf72-ALS Is Associated with Redox, Mitochondrial and NRF2 Pathway Imbalance.** Antioxidants 11 (10). 2022. PMID: 36290620. IF: 7,68. DOI: 10.3390/antiox11101897.

Cadenas S. **Mitochondria rescue cells from ischemic injury.** Sci 377 (6606). 2022. PMID: 35926037. IF: 63,71. DOI: 10.1126/science.add4629.

LINE 1.3 ›› ANIMAL MODELS OF INFLAMMATORY DISEASES AND INTERCELLULAR SIGNALLING

GROUP **11**

Head of laboratory: Mayor Menéndez, Federico

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

Line 1.3 Animal models of inflammatory diseases and intercellular signalling

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 Galphaq interactome on autophagy and nutrient sensing and on oxidative stress processes and its impact on endothelial cell function and cardiovascular disease.

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:

GROUP MEMBERS

- Cristina Delgado Arévalo
- Irene García Higuera
- Inmaculada Navarro Lérida
- Alba Ortega Giménez
- Alejandro Asensio López
- María Sanz Flores
- María Margarida Martins Neves
- Catalina Ribas Núñez

MAJOR GRANTS

Mayor Menéndez, Federico / Murga Montesinos, Cristina. Redes de señalización de GRK2 y mecanismos moleculares de procesos patológicos. PID2020-117218RB-I00. Agencia Estatal de Investigación. 2021-2024.

Mayor Menéndez, Federico. COVTRAVI-19 CM. Comunidad de Madrid. 2021-2022.

Ribas Núñez,Catalina.Un nuevo interactoma de Gq implicado en la modulación de autofagia y estrés oxidativo: repercusión en disfunción endotelial y patalogías relacionadas.FIS.18/01662. INSTITUTO SALUD CARLOS III. 2019-Ribas Núñez, Catalina."Redes de señalización de Gaq en la homeostasis y comunicación celular: repercusión en disfunción endotelial e inflamación". FIS.22/00966. INSTITUTO SALUD CARLOS III.

Mayor Menéndez, Federico. European Union: H2020-MSCA Programme, Grant agreement 860229- ONCORNET2.0 (ONCOgenic Receptor Network of Excellence and Training). Coordinator: Martine Smit, Amsterdam. 2020-2024.

Mayor Menéndez, Federico. Group CB16/11/00278 (PI, F Mayor). CIBER CARDIOVASCULAR. Instituto de Salud Carlos III. 2017-2023.

Mayor Menéndez, Federico. New molecular and cellular mechanisms in immune physiopathology and inflammatory diseases. Programa de Actividades I+D en BIOMEDICINA INFLAMUNE-B2017/BMD-3671 Comunidad de Madrid. 2018 -2022.

Ribas Nuñez, Catalina. Miembro en ERNEST (European Research Network on Signal Transduction) COST ACTION (European cooperation in Science and Technology). 2019-2023.

PUBLICATIONS

Mayor FJr, Murga C. **G Protein-Coupled Receptor Kinases Take Central Stage.** Cells 12 (1): 2022. PMID: 36611817. IF: 7, 67. DOI: 10.3390/cells12010023.

Delgado Arévalo C, Calvet Mirabent M, Triguero Martinez A, Vázquez de Luis E, Benguría Filippini A, Largo R, Calzada Fraile D, Popova O, Sánchez Cerrillo I, Tsukalov I, Moreno Vellisca R, de la Fuente H, Herrero Beaumont G, Ramiro AR, Sánchez Madrid F, Castañeda S, Dopazo A, González Álvaro I, Martin Gayo E. **NLRC4 -mediated activation of CD1c+ dendritic cells contributes to perpetuation of synovitis in rheumatoid arthritis.** JCI Insight. 7 (22). 2022. PMID: 36194479. IF: 9,48. DOI:10.1172/jci.insight.152886.

Neves M, Marolda V, Mayor FJr, Penela P. **Crosstalk between CXCR4/ACKR3 and EGFR Signaling in Breast Cancer Cells.** Int J Mol. Sci 23 (19). 2022. PMID: 36233192. IF: 6,21. DOI: 10.3390/ijms231911887.

Navarro Lérida I, Aragay AM, Asensio A, Ribas C. **Gq Signaling in Autophagy Control: Between Chemical and Mechanical Cues.** Antioxidants 11 (8). 2022. PMID: 36009317. IF: 7,68. DOI: 10.3390/antiox11081599.

Calvet Mirabent M, Sánchez Cerrillo I, Martín Cófreces N, Martínez Fleta P, de la Fuente H, Tsukalov I, Delgado Arévalo C, Calzada MJ, de los Santos I, Sanz J, García Fraile L, Sánchez Madrid F, Alfranca A, Muñoz Fernández MÁ, Buzón MJ, Martín Gayo E. **Antiretroviral therapy duration and immunometabolic state determine efficacy of ex vivo dendritic cell-based treatment restoring functional HIV- specific CD8+ T cells in people living with HIV.** EBioMedicine 81 2022. PMID: 35665682. IF: 11,21. DOI: 10.1016/j.ebiom.2022.104090.

Cuadrado, M, Garzón, J, Moreno, S, García-Higuera, I. **Efficient terminal erythroid differentiation requires the APC/C cofactor Cdh1 to limit replicative stress in erythroblasts**. Sci Rep., 12(1):10489. 2022. PMID: 35729193. IF: 4.997. doi: 10.1038/s41598-022-14331-6.

Perdices-Lopez C, Avendaño MS, Barroso A, Gaytán F, Ruiz-Pino F, Vázquez MJ, Leon S, Song YB, Sobrino V, Heras V, Romero-Ruiz A, Roa J, Mayor F Jr, Murga C, Pinilla L, Kaiser UB, Tena-Sempere M. **Connecting nutritional deprivation and pubertal inhibition via GRK2-mediated repression of kisspeptin actions in GnRH neurons**. Metabolism. 129:155141. 2022. IF: 13.934. PMID: 35074314. doi: 10.1016/j.metabol.2022.155141.

Cacho-Navas C, Reglero-Real N, Colás-Algora N, Barroso S, de Rivas G, Stamatakis K, Feito J, Andrés G, Fresno M, Kremer L, Correas I, Alonso MA, Millán J. **Plasmolipin regulates basolateral-to-apical transcytosis of ICAM-1 and leukocyte adhesion in polarized hepatic epithelial cells**. Cell Mol Life Sci. 2022. 9;79(1):61.IF: 9.234. PMID: 34999972. doi: 10.1007/s00018-021-04095-z.

GROUP 12

Head of laboratory: Fresno Escudero, Manuel

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

Line 1.3 Animal models of inflammatory diseases and intercellular signalling

RESEARCH INTEREST

We are analyzing the involvement of Pathogen recognition receptors, such as Toll-like receptors (TLRs) or galectin, and Cyclooxygenase (Cox)- 2/ prostaglandins (PGs) in the immune system and inflammatory pathologies. We have found that PGF2a negatively regulates adipocyte differentiation through the transcription factor NFAT. Moreover, NFATc4 deficiency induces obesity in mice indicating a key role in obesity. We have also found that galectin-1 (Gal-1) deficiency abolishes diet induced obesity and insulin resistance in mice. Gal-1 is needed for the differentiation of pre- adipocytes by regulation of the key pro-adipogenic transcription factor PPAR-gamma and in the differentiation of brown adipocytes.

TLRs play a crucial role in pathogen recognition. However, signaling via TLR4 and TLR2 is different, as TLR2 ligands activate NF-κB and MAPKs earlier and exhibit a higher IL-10 /IL-12 ratio compared to TLR4 ligands. Furthermore, p38 MAPK is critical for IL-10 expression in response to TLR2 ligands, which triggers the macrophage change to an M2 and regulatory phenotype in contrast to the M1 phenotype induced by TLR4 activation. TRIF is required for IFN-beta induction and consequent expression of IL-12 in response to TLR2. Moreover, in vivo administration of TLR2 ligands exert a modulatory effect on cytokines with beneficial effects on the prevention of Listeria dissemination in a murine model of neonatal listeriosis.

TLR4 is considered the major receptor to recognize all LPSs. However, some atypical LPSs are derived from the well-studied E. coli LPS and induce a TLR2-dependent inflammatory response in immune cells. Molecular docking analysis of O. intermedium LPS predicts a favorable formation of a TLR2/TLR4/MD-2 heterodimer, further confirmed by FRET. This implies that atypical LPSs may induce TLR4/TLR2 heterodimerization to decrease bacterial activation of the innate immune system.

On the other hand, TCFL5 is a member of the bHLH transcription factor family with multiple isoforms in both humans and mice. Deletion of TCFL5, a bHLH transcription factor, drastically reduces the tumor properties of colon cancer cells. Interestingly, the two major isoforms TCFL5_E1/E8 and TCFL5_E2b/E8 (CHA), had a different promoter and opposite functions, being the function of TCFL5_E2b/E8 protumoral. TCFL5_E1/E8 is essential for NFKB2 activity regulating the expression of anti-apoptotic genes such as BCL2, whereas TCFL5_E2b/E8 controls the expression of the pluripotency markers SOX2, NANOG and KLF4. We have identified some genes regulated by TCFL5_E1/E8 and TCFL5_E2b/E8 and established their role in some leukemias and in normal lymphopoiesis. TCFL5_E2b/E8 expression in samples from lymphoma and myeloma patients was associated with greater disease severity. Using Tcfl5 deficient mice, we found Tcfl5 is required for the formation of germinal centers and differentiation of pro-B to pre-B cells by affecting the levels of SYK and BCR signaling, resulting in an inability to respond to stimuli and an increase in cell death. TCFL5 is also expressed during early mouse embryonic development, the preimplantation period, and plays a role in the differentiation of embryonic cells to germline precursors by controlling the expression of genes important in their differentiation, as shown in Tcfl5 deficient mice.

We are working on the infection by the protozoan parasite T. cruzi, focusing on the impact of T. cruzi genetic variability on the clinical outcome and immunopathology of Chagas' disease as well as on drug susceptibility. All intended for improved understanding and prevention of Chagas' disease. Different genetic lineages have been defined in Trypanosoma cruzi, the causative agent of Chagas´

disease. However, understanding of their comparative biology and pathogenesis is fragmentary. We have identified different T dependent immune responses both in patients and mouse models, which differ depending on the infecting strain. Besides, we are studying how the parasite enters, infects and escapes destruction by myeloid cells, defining Slamf1 (CD150) as a new T. cruzi receptor. In contrast, we found that Slamf8 (CD353) is a cell surface receptor that is expressed upon activation of macrophages by IFN-gamma and plays a negative role in the infection through repression of NADPH oxidase. We have studied the role that CD4+ T cell subsets and myeloid subclasses including myeloid-derived suppressor cells (MDSC) may play in the immunopathogenesis of Chagas´ disease, with special focus on myocarditis in animal models and in patients. Different heart immunopathogenic responses depend on host genetics. Nonetheless, Systems Biology approaches have allowed us defining immunopathogenic markers independent of host and parasite genetics. We have found many metabolic alterations in T. cruzi infection suggesting a stressful condition in the heart, some of which can be used as biomarkers.

Serum miRNAs are also excellent biomarkers of Chagas' disease progression.

Finally, we were also interested in pathogenic mechanisms and complications derived from SARS-CoV-2 infection, especially inflammatory, metabolic, cardiovascular and reproductive in acute or persistent COVID-19. We found a mechanistic association between the severity of SARS-CoV- 2 infection and the differential expression of its receptor protein ACE2 which downregulates the inflammatory peptides of the Angiotensin- Bradykinin system, whose upregulation in aging, chronic inflammation and SARS-CoV-2 infection may play a key role in infection severity. We showed that the expression of ACE2 influences the probability of avoiding infection despite exposure to the virus, and the outcome of infections. We studied the immune response in exposed but not infected children and we are currently investigating the role of the renin-angiotensin system (RAS) and autoimmunity in patients with long Covid.

GROUP MEMBERS

- Cristina Delgado Arévalo
- Irene García Higuera
- Inmaculada Navarro Lérida
- Alba Ortega Giménez
- Alejandro Asensio López
- María Sanz Flores
- María Margarida Martins Neves
- Catalina Ribas Núñez

MAJOR GRANTS

Fresno Escudero, Manuel. Plataforma y modelos preclínicos para el abordaje multidisciplinar en covid19 y en respuestas a futuras pandemias. Contracovid-19. Comunidad de Madrid. 2021-2022

Manuel Fresno (Coordinador). Inflamune-cm. Nuevos mecanismos moleculares y celulares implicados en la fisiopatología inmune y enfermedades inflamatorias. B2017/BMD-3671. Comunidad de Madrid. 2018-2022.

Fresno Escudero, Manuel. TCFL5/CHA en la diferenciación y activación de linfocitos b y t y en la generación de leucemias. PIB2019-104760RB-100. Ministerio de Ciencia e Innovación. 2020-2023.

PUBLICATIONS

Cacheiro Llaguno C, Hernández Subirá E, Díaz Muñoz MD, Fresno M, Serrador JM, Iñiguez MA. **Regulation of Cyclooxygenase-2 Expression in Human T Cells by Glucocorticoid Receptor-Mediated Transrepression of Nuclear Factor of Activated T Cells.** Int J Mol Sci 23 (21). 2022. PMID: 36362060. IF: 6,21. DOI: 10.3390/ijms232113275.

Maza Maria del Carmen, Ubeda Maria, Delgado Pilar, Horndler Lydia, Llamas Miguel A, van Santen Hisse M, Alarcon Balbino, Abia David, Garcia Bermejo Laura, Serrano Villar Sergio, Bastolla Ugo, Fresno Manuel. **ACE2 Serum Levels as Predictor of Infectability and Outcome in COVID-19**. Front Immunol 13. 2022. PMID: 35401548. IF: 8,79. DOI: 10.3389/fimmu.2022.836516.

Stamatakis K, Torres Gérica P, Jiménez Segovia A, Ramos Muñoz E, Crespo Toro L, Fuentes P, Toribio ML, Callejas Hernández F, Carrato A, García Bermejo ML, Fresno M. **Cyclooxygenase 2 Effector Genes as Potential Inflammation-Related Biomarkers for Colorectal Cancer Circulating Tumor Cells Detection by Liquid Biopsy.** Front. Pharmacol 12. 2022. PMID: 35153760. IF: 5,99. DOI: 10.3389/fphar.2021.806395.

Galán-Martínez J, Berenguer I, Del Carmen Maza M, Stamatakis K, Gironès N, Fresno M. **TCFL5 deficiency impairs the pachytene to diplotene transition during spermatogenesis in the mouse**. Sci Rep. 2022 (1): 10956. 2022. IF: 4.997 doi: 10.1038/s41598-022-15167-w.

Cacho-Navas C, Reglero-Real N, Colás-Algora N, Barroso S, de Rivas G, Stamatakis K, Feito J, Andrés G, Fresno M, Kremer L, Correas I, Alonso MA, Millán J. **Plasmolipin regulates basolateral-to-apical transcytosis of ICAM- 1 and leukocyte adhesion in polarized hepatic epithelial cells**. Cell Mol Life Sci (1):

61. 2022. PMID: 34999972. IF: 9.234. doi: 10.1007/s00018-021- 04095-z.

Galán-Martínez J, Stamatakis K, Sánchez-Gómez I, Vázquez-Cuesta S, Gironés N, Fresno M. **Isoform-specific effects of transcription factor TCFL5 on the pluripotency-related genes SOX2 and KLF4 in colorectal cancer development**. Mol Oncol. (9):1876-1890. 2022. PMID: 34623757. IF: 7.449. doi: 10.1002/1878-0261.13085.

Bastolla U, Chambers P, Abia D, Garcia-Bermejo M-L, Fresno M. **Is Covid-19 Severity Associated With ACE2 Degradation?** Frontiers in Drug Discovery. 2022. PMID: 36936972. DOI: 10.3389/fddsv.2021.789710

Pérez-Regidor L, Guzmán-Caldentey J, Oberhauser N, Punzón C, Balogh B, Pedro JR, Falomir E, Nurisso A, Mátyus P, Menéndez JC, de Andrés B, Fresno M, Martín-Santamaría S**. Small Molecules as Toll-like Receptor 4 Modulators Drug and In- House Computational Repurposing**. Biomedicines. (9):2326. 2022. PMID: 36140427. doi: 10.3390/biomedicines10092326.

Pérez-Regidor L, Guzmán-Caldentey J, Oberhauser N, Punzón C, Balogh B, Pedro JR, Falomir E, Nurisso A, Mátyus P, Menéndez JC, de Andrés B, Fresno

M, Martín-Santamaría S. **Small Molecules as Toll-like Receptor 4 Modulators Drug and *In-House* Computational Repurposing**. Biomedicines. 19: 10 (9): 2326. 2022. PMID: 36140427. IF: 4.757. doi: 10.3390/biomedicines10092326.

Cuesta N, Fernández-Veledo S, Punzón C, Moreno C, Barrocal B, Sreeramkumar V, Desco M, Fresno M. **Opposing Actions of TLR2 and TLR4 in Adipocyte Differentiation and Mature-Onset Obesity**. Int J Mol Sci 10: 23 (24): 15682. 2022. PMID: 36555322. IF: 6.208 doi: 10.3390/ijms232415682

Francisco S, Billod JM, Merino J, Punzón C, Gallego A, Arranz A, Martin- Santamaria S, Fresno M. **Induction of TLR4/TLR2 Interaction and Heterodimer Formation by Low Endotoxic Atypical LPS**. Front Immunol. 12:748303. 2022. PMID: 35140704. IF: 8.787. doi: 10.3389/fimmu.2021.748303

GROUP 13

Head of laboratory: Penela Márquez, Petronila

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

Line 1.3 Animal models of inflammatory diseases and intercellular signalling

RESEARCH INTEREST

Breast cancer is a heterogeneous disease at the molecular and histopathological level with different clinical outcomes that make it challenging to identify and raise targeted therapies. Its incidence is much higher in the developed world, suggesting that the western lifestyle with unhealthy dietary habits (excessive caloric intake, imbalanced diets, obesity) and chronic stress states (adrenergic overstimulation) may influence the onset and progression of this disease by progressively weakening the processes that preserve genome stability. In breast cancer, the main altered proteins responsible for genomic instability and tumour cell heterogeneity are ATM kinase, Brca1 ligase and the tumour suppressor transcription factor p53. Notably, in ~ 80% of ductal breast carcinomas p53 is restrained by activation or amplification of the ligase Mdm2, but therapies based on these targets are not yet satisfactory. In addition, adaptive mechanisms involving dynamic rewiring of cell signalling networks can contribute to fostering cellular instability and malignancy. Another important problem is the emergence of resistances amongst all breast cancer subtypes, paralleled by enhanced genomic instability and tumour metabolic reprogramming. All this complexity highlights the need for a deeper understanding of the pathways leading to breast cancer development and progression.

The objective of our group is to identify regulatory nodes that integrate multiple cellular inputs and environmental cues for modifying tumour hallmarks such as genomic instability, cellular dissemination or chemoresistance. Understanding how dynamic signalling nodes interact with breast cancer susceptibility genes to strengthen these malignant features will pave the way for new therapeutic approaches. Our laboratory is addressing the role of the regulatory feedback loop involving serine- threonine kinase GRK2 and the Mdm2 ligase in cell-autonomous malignant transformation, as well as in the interplay of the transformed cell with the tumour micro-environment and the systemic condition of the patient. Our results indicate that these proteins modulate each other differently in normal epithelial cells and in tumour cells, responding in different ways to signals that stimulate adrenergic receptors and other G-protein coupled receptors (GPCR) or growth factor tyrosine kinase receptors (RTK). We aim at understanding the role of phosphorylated and ubiquitinated proteins modified by the interplay between GRK2 and Mdm2 in diverse cellular processes such as cell cycle control and cell division, differentiation, energy metabolism or senescence, which are key in maintaining a normal cell behaviour. We also aim to gain insight into the connection of these molecules with hormonal (adrenergic, estrogenic) and metabolic stress, by analysing its impact on the functionality of BRCA1, and other proteins related to genomic stability, as well as on stromal remodelling processes such as tumour angiogenesis, which together will promote tumour progression.

GROUP MEMBERS

- Ángela Albitre Sanz
- Belén Ortiz del Castillo

MAJOR GRANTS

Penela Márquez, Petronila. Papel de GRK2 en la disfunción de BRCA1 y en la resistencia a inhibidores PARP en modelos tumorales de mama más allá del estatus de BRCA. PI21/01834. ISCIII. 2022-2024.

Penela Márquez, Petronila. Análisis de la regulación post-traduccional de los procesos relacionados con angiogénesis e inflamación durante la progresión y recurrencia diferencial del cáncer colorectal. Fundación Ramón Areces. 2021-2024.

Platforms and preclinical models for a multidisciplinary approach in COVID- 19 and in response to future pandemics. Proyecto Coordinado. Proyectos de I+D REACT-UE Investigación Madrid. 2022.

H2020-MSCA-ITN-2019. ONCOgenic Receptor Network of Excellence and Training 2.0 (Oncornet2.0). Innovative Training Networks (ITN). MSC- ACTIONS (ERC). 2021-2024.

PUBLICATIONS

Jiménez-Reinoso A, Tirado N, Martinez-Moreno A, Díaz VM, García-Peydró M, Hangiu O, Díez-Alonso L, Albitre Á, Penela P, Toribio ML, Menéndez P, Álvarez-Vallina L, Sánchez Martínez D. **Efficient preclinical treatment of cortical T cell acute lymphoblastic leukemia with T lymphocytes secreting anti-CD1a T cell engagers.** J Immunother Cancer 10 (12): 2022. PMID: 36564128. IF: 12,47. DOI: 10.1136/jitc-2022-005333.

Neves M, Marolda V, Mayor F Jr, Penela P. **Crosstalk between CXCR4/ACKR3 and EGFR Signaling in Breast Cancer Cells.** Int J Mol Sci 23 (19): 11887. 2022. PMID: 36233192. IF: 6,21. DOI: 10.3390/ijms231911887.

GROUP 17

Head of laboratory: Murga Montesinos, Cristina

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

Line 1.3 Animal models of inflammatory diseases and intercellular signalling

RESEARCH INTEREST

Pathological insults and metabolic cues are increasingly being regarded as key modulators of immunological responses and inflammatory processes. Thus, metabolic signals that affect inflammatory routes are a strategic focus of research to unveil the mechanistic basis of human physiology, but also of different pathologies, in particular those with an inflammatory or metabolic component such as insulin resistance, obesity, metabolic dysregulation and cardiovascular conditions.

An important point of control in the metabolic, stress and inflammatory network of routes is the signaling hub of the G protein-coupled receptor kinase 2 (GRK2), that emerges as a pivotal control point in the onset and/or progression of these diseases.

In this line, our group focuses its research efforts on the following lines:

Analysis of the phenotypic 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 different metabolically-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 metabolic situations or even serve as biomarkers of disease. We have recently published research that describes the influence of GRK2 on the control of pancreatic insulin secretion and on glucagon-induced hepatic glucose production.

Changes in the levels of GRK2 protein in macrophages and other inflammatory cells contribute to the control of insulin sensitivity, adiposity and obesity in animal models of disease. We have published how myeloid

GRK2 affects whole body responses such as glycaemic control and hepatic inflammation. Furthermore, we described the influence of the perivascular adipose tissue of animals with low GRK2 levels in myeloid cells on the response of vessels to different vasoconstrictor and vasodilator stimuli in the face of vascular dysfunction and vascular insulin resistance developed by a high fat diet.

Finally, we have recently reported that the expression of GRK2 in different tissues shows sexual dimorphism, and we have also published that changes in the amount of this kinase in cardiac and skeletal muscle with age do not follow the same pattern in male and female mice. This is particularly important since the dynamics of GRK2 appears to parallel the increase in cardiovascular risk that is observed in females after menopause. We are therefore investigating whether these gender-specific changes in the amount of GRK2 may reflect or, additionally, can impact the sexual dimorphism observed for cardiovascular risk with age using models of pre and post-menopausal female mice.

GROUP MEMBERS

- María del Carmen Vida Rueda

PUBLICATIONS

Mayor FJr, Murga C. **G Protein-Coupled Receptor Kinases Take Central Stage.** Cells 12 (1): 2022. PMID: 36611817. IF: 7,67. DOI: 10.3390/cells12010023.

Perdices-Lopez C, Avendaño MS, Barroso A, Gaytán F, Ruiz-Pino F, Vázquez MJ, Leon S, Song YB, Sobrino V, Heras V, Romero-Ruiz A, Roa J, Mayor F Jr, Murga C, Pinilla L, Kaiser UB, Tena-Sempere M. **Connecting nutritional deprivation and pubertal inhibition via GRK2-mediated repression of kisspeptin actions in GnRH neurons**. Metabolism 129:155141. 2022. PMID: 35074314. DOI:10.1016/j.metabol.2022.155141

GROUP 18

Head of laboratory: Iñiguez Peña, Miguel Ángel

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

Line 1.3 Animal models of inflammatory diseases and intercellular signalling

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 (LNO2 and OA-NO2). 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.

GROUP MEMBERS

- Miguel Ángel Iñiguez Peña
- Ángel Bago Plaza
- Ana Renshaw Calderón

PUBLICATIONS

Cacheiro Llaguno C, Hernández Subirá E, Díaz Muñoz MD, Fresno M, Serrador JM, Iñiguez MA. **Regulation of Cyclooxygenase-2 Expression in Human T Cells by Glucocorticoid Receptor-Mediated Transrepression of Nuclear Factor of Activated T Cells.** Int J Mol Sci 23 (21). 2022. PMID: 36362060. IF: 6,21. DOI: 10.3390/ijms232113275.

LINE 1.5 ›› CELLULAR MECHANISMS AND MOLECULAR DETERMINANTS OF ALLERGY BASED DISEASES

GROUP 20

Head of laboratory: Blanco Guerra, Carlos Alberto

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

Line 1.5 Cellular mechanisms and molecular determinants of allergy based diseases

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:

- Searching for biomarkers of allergy severity: multicentric BIOGRIAL study led by Dr. Barber from San Pablo CEU University and funded by FIS from ISCIII, including patients with respiratory- food- and drug-allergies, is ongoing.
- Immunotherapy for respiratory allergy: a 2-yr placebo controlled clinical trial has been finished, assessing 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, coordinated by Dra. Escribese from San Pablo CEU University, and funded by FIS from ISCIII, is ongoing, results are expected in 2023.
- Cross-reactivity between Cupressus arizonica and Cryptomeria japonica has been assessed in collaboration with ALK-Abello. A related article is in its writing phase.
- A study on adverse reactions to iodinated- and gadolinium-contrasts led by Dr. Vega, which is ongoing, assesses tolerance to alternative contrasts by means of a protocol of fast challenge tests at full dose. Results have been already published and a doctoral thesis has been presented in UAM by Dr. Vega in 2022.
- A multicentric study on perioperative drug adverse reactions started in 2022, funded by FIS from ISCIII, and led in our Hospital by Dr. Vega (from Allergy Dept.) and Dr. Planas (from Anaesthesiology Dept.).
- We have participated in a research project (Retos Investigación: Proyectos I+D+i 2017, MINECO) with Dra. Cuadrado from INIA (The National Institute for Agricultural and Food Research and Technology), focused on nut allergy. Results have already been submitted for publication.
- Possible cross-reactivity between peanut and the new food called miracle berry has been assessed in collaboration with the biotechnology Dept. of Madrid Polytechnic University. Results have been recently published.
- Flaxseed allergy has been characterized in collaboration with the Complutense University of Madrid, and an article focused on this item has been published.
- Dra. Múgica and Dra. Ramos are collaborating with the Spanish Allergy Society in the Allergodata study, recording patients treated with biological drugs.

- Finally, Dr. Rodrigo Jiménez-Saiz has joined our group as Miguel Servet Investigator. He is interested in understanding immunological principles of Th2 immunity in the context of allergic disease, particularly as it pertains to acute allergic reactions (anaphylaxis) and their modulation by the microbiota, but also related to the mast cell neuron axis during allergen immunotherapy, and the impact of allergic disease on the development of atherosclerosis. (https://www.jimenezsaizlab.com/).

GROUP MEMBERS

- Carlos Alberto Blanco Guerra
- Carlos Rodrigo Jimenez Saiz
- María Teresa Belver González
- María Victoria Múgica García
- Álvaro Daschner
- María Consolación de Frutos Moreno
- María Paloma las Heras Almazán
- Tania María Ramos García
- Ana María Valls Sánchez
- Francisco Félix Vega de la Osada

MAJOR GRANTS

Jiménez Saiz, Rodrigo. Prevention of peanut-induced anaphylaxis through bacterial metabolism. NFR-FE-2019-00083. New Frontiers in Research Fund – Exploration Grant (Canada). 2020-2022.

Jiménez Saiz, Rodrigo. Prevention and immunomodulation of peanut induced anaphylaxis through bacterial metabolism. FRF2021-13. Nutricia Research Foundation (The Netherlandas). 2020-2022.

Jiménez Saiz, Rodrigo. Identification of atherogenic mechanisms of food allergy and anaphylaxis. CP20/00043. ISCIII. 2021-2026.

Jiménez Saiz, Rodrigo. Neuroinmunomodulación de mastocitos durante inmunoterapia a alérgenos. BECA20A9. Fundación de la Sociedad Española de Alergología e Inmunología Clínica (SEAIC). 2021-2023.

Jiménez-Saiz, Rodrigo. Integrative study of acute and chronic inflammation in allergic disease and its association with dy slipidemia and atherosclerosis. PI22/00236. ISCIII. 2023 – 2025.

PUBLICATIONS

Menendez Rey A, Jerez Arroyo F, Alegria Aravena N, Quiroz Troncoso J, Gonzalez Martos R, Sanchez Diez M, Blanco c, Unturbe CM, Bensadon Naeder L, Ramirez Castillejo C. **Discarded cross-allergy between miracle berry (Synsepalum dulcificum) and peanut**. Int J Food Sci Technol 57 (12). 2022. IF: 3,61. DOI: 10.1111/ijfs.16114.

Fernández Gallego N, Castillo González R, Méndez Barbero N, López Sanz C, Obeso D, Villaseñor A, Escribese MM, López Melgar B, Salamanca J, Benedicto Buendía A, Jiménez Borreguero LJ, Ibañez B, Sastre J, Belver MT, Vega F, Blanco C, Barber D, Sánchez Madrid F, de la Fuente H, Martín P, Esteban V, Jiménez Saiz R. **The impact of type 2 immunity and allergic diseases in atherosclerosis.** Allergy 77 (11). 2022. PMID: 35781885. IF:14,71. DOI:10.1111/all.15426.

Vega F, Lopez Raigada A, Mugica MV, Blanco C. **Fast challenge tests with gadolinium-based contrast agents to search for an alternative contrast media in allergic patients**. Allergy 77 (10): 2022. PMID: 35775416. IF: 14,71. DOI: 10.1111/all.15420.

McGrath JJC, Vanderstocken G, Dvorkin Gheva A, Cass SP, Afkhami S, Fantauzzi MF, Thayaparan D, Reihani A, Wang P, Beaulieu A, Shen P, Morissette M, Jiménez Saiz R, Revill SD, Tabuchi A, Zabini D, Lee WL, Richards CD, Miller MS, Ask K, Kuebler WM, Simpson JA, Stämpfli MR. **Cigarette smoke augments CSF3 expression in neutrophils to compromise alveolar-capillary barrier function during influenza infection.** Eur Respir J60 (2). 2022. PMID: 35058252. IF: 33,80. DOI: 10.1183/13993003.02049-2021.

Mena Alicia Habernau, Garcia Moguel Ismael, de la Torre Gaspar Maria Vazquez, Mugica Victoria, Alvarado Izquierdo Maria Isabel, Jimenez Blanco Maria Aranzazu, Gandolfo Cano Mar, Jimenez Lara Mar, Gonzalez Moreno Ana, Saura Foix Pilar,

Navarro Pulido Ana, Martin Arriscado Arroba Cristina, Delgado Romero Julio, Dominguez Ortega Javier. **COVID-19 Course in Allergic Asthma Patients: A Spanish Cohort Analysis**. J Asthma Allerg 15. 2022. PMID: 35228805. IF: 3,03. DOI:10.2147/JAA.S344934.

Vega F, Blanco C. **A Reply to "Spanish Society of Allergology and Clinical Immunology (SEAIC) Vision of Drug Provocation Tests"**. J Invest Allergol Clin Immunol 32 (3): 2022. PMID: 35723207. IF: 8,19. DOI: 10.18176/jiaci.0787.

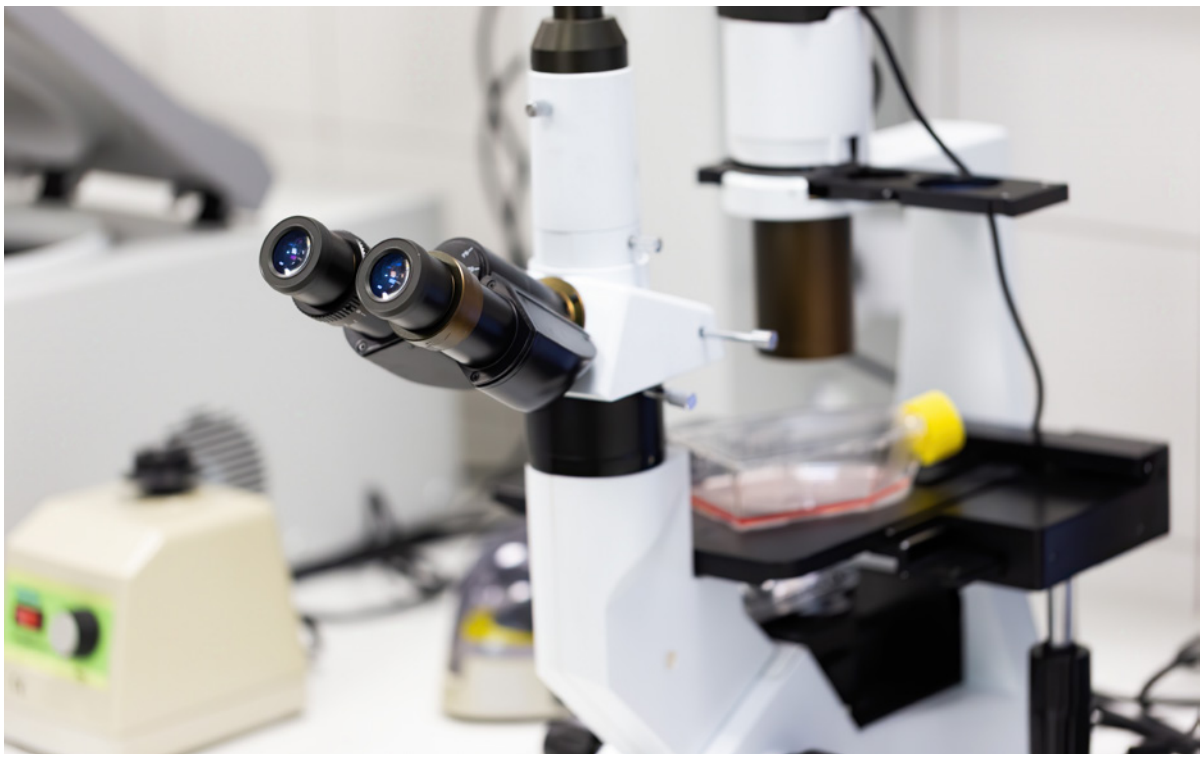
Sánchez-Hernández MC, Dordal MT, Navarro AM, et al. **Severity and duration of allergic conjunctivitis: are they associated with severity and duration of allergic rhinitis and asthma?** Eur Ann Allergy Clin Immunol. 2022: 54 (6): 277-283. doi:10.23822/EurAnnACI.1764-1489.231

Habernau Mena A, García-Moguel I, María Vazquez de la Torre Gaspar M, Mugica V, Alvarado Izquierdo MI, Jimenez Blanco MA, Gandolfo-Cano M, Jiménez Lara M, Gonzalez Moreno A, Saura Foix P, Navarro-Pulido A, Martin-Arriscado Arroba C, Delgado Romero J, Dominguez. **COVID-19 Course in Allergic Asthma patients. A Spanish Cohort Analysis**. Journal of Asthma and Allergy. 2022. 257–264. PMID: 35228805. IF: 3.027. DOI:

10.2147/JAA.S344934. Sánchez-Martínez E, Garrido-Romero M, Moreno FJ. **Functional role of ST-6GALNAC1-mediated sialylation of mucins in preserving intestinal barrier integrity and ameliorating inflammation**. Allergy. (12)3697-3698. 2022. PMID: 35993845. IF: 14,7. doi: 10.1111/all.15489.

Lee AJ, Feng E, Chew MV, Balint E, Poznanski SM, Giles E, Zhang A, Marzok A, Revill SD, Vahedi F, Dubey A, Ayaub E, Jimenez-Saiz R, McGrath JJC, Ritchie TM, Jordana M, Jonigk DD, Ackermann M, Ask K, Miller M, Richards CD, Ashkar AA. **Type I interferon regulates proteolysis by macrophages to prevent immunopathology following viral infection**. PLoS Pathog. 2022. PMID: 35512020. IF: 7,4. doi: 10.1371/journal.ppat.1010471.

Angelina A, Jiménez-Saiz R, Pérez-Diego M, Maldonado A, Rückert B, Akdis M, Martín-Fontecha M, Akdis CA, Palomares O. **Cannabinoid WIN55212-2 impairs peanut-allergic sensitization and promotes the generation of allergen-specific regulatory T cells**. Clin Exp Allergy (4): 540-549. 2022. PMID: 34995385. IF: 5,4. doi: 10.1111/cea.14092.



GROUP 15

Head of laboratory: Ibáñez Sandín, María Dolores

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

Line 1.5 Cellular mechanisms and molecular determinants of allergy based diseases

RESEARCH INTEREST

Study of the intestinal microbiota.

Microbiota in the development of cow's milk allergy in infants as a longitudinal epigenetic influence (infants, their mothers and their grandmothers) from a genomic and metabolomic point of view.

Microbiota and biomarkers as predictors of allergic diseases and in newborns: asthma, atopic dermatitis, food allergy. Study of anaphylaxis markers. Characterization of the human miRNA profile and other markers during anaphylaxis and assessment of their capacity as diagnostic markers and their participation in the molecular mechanisms of this event.Food immunotherapy for food allergy.

Milk allergy. Evaluation of the impact of sublingual immunotherapy (SLIT) pretreatment on the safety and efficacy of subsequent oral immunotherapy (ITO) in children with persistent cow milk protein allergy (CMPA). Evaluation of immunological, dietary and quality of life changes associated with milk immunotherapy.

Peanut allergy. Long-term efficacy and safety of AR-101 characterized oral desensitization immunotherapy in subjects with peanut allergy.

LTP immunotherapy for the treatment of patients with allergy to plant foods: Efficacy and mechanisms involved in specific sublingual immunotherapy with Prup3 (Pru p3-ITSL) in patients with allergy to nsLTPs with severe symptoms in their response to peach, peanut, mugwort and olive.

Severe asthma in children and adolescents: control and management in a multidisciplinary Severe Asthma Unit.

Translational study in anaphylaxis: search for biomarkers and investigation of its etiopathogenesis for a personalized and precise clinical approach.

GROUP MEMBERS

- Raphaëlle Bazire Batiz
- Carmelo Escudero Díez
- Pablo Rodríguez del Rio
- Silvia Sánchez García

PUBLICATIONS

Bernaola Marta, Rodriguez del Rio Pablo. **De-labelling of beta-lactam allergy in children**. Clin Exp Allergy 52 (4): 2022. PMID: 35307905. IF: 5,40. DOI: 10.1111/cea.14125.

Gómez-López A, Fernández-Bravo S, Nuñez-Borque E, Betancor Pérez D, Bernaola Abraira M, Esteban Vázquez V, Pastor-Vargas C, Cuesta-Herranz J, Ibáñez Sandín MD, Escudero Díez C. **11S globulin identified as a new bean allergen.** J Investig Allergol Clin Immunol. 2022 Dec 1:0. PMID: 36515650. FI: 8,185. doi: 10.18176/jiaci.0873.

Mera-Berriatua L, Zubeldia-Varela E, Martín-Antoniano IA, López de Maturana E, Rojo D, Bazire R, Cabrera-Freitag P, Barker-Tejeda TC, Ubeda C, Barber D, Francino MP, Ibáñez-Sandín MD, Pérez-Gordo M. **Unravelling the Gut Microbiota of Cow's Milk-Allergic Infants, Their Mothers, and Their Grandmothers.** J Investig Allergol Clin Immunol. 32 (5): 395-398. 2022. PMID: 36219548. FI: 8,185. doi: 10.18176/jiaci.0781.

Bartha I, Bernaola M, Escudero C, Rodríguez Del Río P, Bazire R, Ibáñez Sandín MD. **COVID-19 and childhood asthma: Analysis of a pediatric ferral hospital**. Pediatr Allergy Immunol. 33 (3): e13757. 2022. PMID: 35338727. FI: 5.401. DOI: 10.1111/pai.13757.

Turner PJ, Duca B, Chastell SA, Alvarez O, Bazire R, Vazquez-Ortiz M, Rodríguez Del Río P. **IgEsensitization predicts threshold but not anaphylaxis during oral food challenges to cow's milk.Allergy**. 77 (4): 1291-1293. 2022. PMID: 34874567. FI: 13,146. DOI: 10.1111/all.15195.

Ibáñez-Sandin MD*, Rodríguez Del Río P*, Alvarado MI, García BE, Garriga- Baraut T, Reche Frutos M, Escudero C, Ramirez Jiménez A, Vila L, Lasa EM, Blasco C, Marchán-Martin E, Martorell A, Sanchez- García S, Rodríguez- Álvarez M, Infante S, Rodríguez Vazquez V, Olaguibel JM, Labrador-Horrillo M, Carrillo T. **AFRUSEN Task Force, Pediatric Allergy Committee, Spanish Society of Allergy and Clinical Immunology (SEAIC). Onset of Nut Allergy in a Pediatric Cohort: Clinical and Molecular Patterns in the AFRUSEN Study**. J Investig Allergol Clin Immunol. 22: 32 (4): 270-281. 2022. PMID: 33884956. FI: 8,185. doi: 10.18176/jiaci.0696.

Bernaola M,Rodriguez del Rio P. **De-labelling of betalactam allergy in children**. Clin Exp Allergy 52 (4): 485-488. 2022. PMID: 35307905. FI: 5,40. DOI: 10.1111/cea.14125.

LINE 1.6 ›› INFLAMMATORY PROCESSES IN NEPHROLOGICAL DISEASES

GROUP 21

Head of laboratory: Barril Cuadrado, Guillermina

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

Line 1.6 Inflammatory processes in nephrological diseases

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, Roxiglitazona) 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 biocompatible 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 importance 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.

GROUP MEMBERS

- Borja Quiroga Gili
- Almudena Núñez Sánchez
- Vicente Álvarez Chiva
- Antonio Carlos Fernández Perpén
- Martin Giovanni Giorgi González
- Isabel Herráez Jiménez
- Pablo Ruano Suárez
- Laura Salanova Villanueva
- María Carmen Sánchez González

PUBLICATIONS

Montomoli M, Roca L, Rivera M, Fernandez Prado R, Redondo B, Camacho R, Moyano C, Pampa S, Gonzalez A, Casas J, Kislikova M, Sanchez Horrillo A, Cabrera Cárdena A, Quiroga B, Rabasco C, Piqueras S, Suso A, Reque J, Villa J, Ojeda R, Arroyo D. **Oral Anticoagulation in Patients with Chronic Kidney Disease and Non-Valvular Atrial Fibrillation: The FAERC Study.** Healthcare (Basel) 10 (12). 2022. PMID: 36554089. IF: 3,16. DOI: 10.3390/healthcare10122566.

Quiroga B, Soler MJ, Ortiz A, Sequera P, SENCOVAC collaborative network. **Lessons from SENCOVAC: a prospective study evaluating the response to SARS-CoV-2 vaccination in the CKD spectrum.** Nefrologia. 2022. PMID:36540904. IF: 3,08. DOI: 10.1016/j.nefro.2022.12.006.

Horrillo AS, Villanueva LS, Cardenas AC, Ramos PM, Ortiz A, Quiroga B. **Infectious consequences of the AKI-to-CKD transition**. Clin Kidney J 15 (12). 2022. PMID: 36381366. IF: 5,86. DOI: 10.1093/ckj/sfac178.

Ortega Junco E, Quiroga B. **Kidney-vascular-bone axis in down syndrome.** Nefrologia 42 (4). 2022. PMID: 36396571. IF: 3,08. DOI: 10.1016/j.nefroe.2021.09.006.

Nogueira Á, Álvarez G, Barril G. **Impact of the Nutrition-Inflammation Status on the Functionality of Patients with Chronic Kidney Disease.** NUTRIENTS 14 (22). 2022. PMID: 36432432. IF: 6,71. DOI: 10.3390/nu14224745.

Quiroga,B,Torra,R. **Dietary Aspects and Drug-Related Side Effects in Autosomal Dominant Polycystic Kidney Disease Progression**. NUTRIENTS14 (21):2022. PMID: 36364911. IF: 6,71. DOI: 10.3390/nu14214651.

de Sequera P, Quiroga B, Goicoechea M, en representación de la Junta Directiva de la Sociedad Española de Nefrología (. **Actualización de las recomendaciones de medidas de prevención y aislamiento frente al SARS- CoV-2 en las unidades de diálisis: un posicionamiento de la Sociedad Española de Nefrología.** Nefrologia 42 (6). 2022. PMID: 36247494. IF: 3,08. DOI: 10.1016/j.nefro.2022.10.001.

Sanchez Gonzalez,C,Calvo,JAH. **Nonvalvular atrial fibrillation in patients undergoing chronic hemodialysis. Should dialysis patients with atrial fibrillation receive oral anticoagulation?** Nefrologia 42 (6):2022. IF: 3,08. DOI: 10.1016/j.nefro.2022.01.005.

Quiroga B, Soler MJ, Ortiz A, Gansevoort RT, Leyva A, Rojas J, de Sequera P, SENCOVAC Collaborative Network. **Long-Term Dynamic Humoral Response to SARS-CoV-2 mRNA Vaccines in Patients on Peritoneal Dialysis.** Vaccines 10 (10). 2022. PMID: 36298603. IF: 4,96. DOI: 10.3390/vaccines10101738.

Quiroga B, Soler MJ, Ortiz A, Jaravaca Mantecón CJ, Nava Pérez N, Serra Martín M, Sato Y, Marin Franco AJ, Pazmiño Zambrano DF, Lucena Valverde R, Ortega Diaz M, Calderón González C, Cazorla López JM, Pereira M, González Parra E, Sánchez Horrillo A, Sánchez González C, Toapanta N, Cigarrán Guldris S, Sánchez Hernández R, Pizarro Sánchez S, Muñiz Rincón M, Garcia Fernández N, Blanco Castro N, Collantes Mateo R, Quiroz Morales MA, Escamilla Cabrera B, Berdud Godoy I, Gil Casares Casanova B, Leyva A et al. **Anti-Spike antibodies 3 months after SARS-CoV-2 mRNA vaccine booster dose in patients on hemodialysis: the prospective SENCOVAC study.** Clin Kidney J 15 (10). 2022. PMID: 36147708. IF: 5,86. DOI: 10.1093/ckj/sfac169.

Quiroga B, Soler MJ, Ortiz A, Martínez Vaquera S, Jarava Mantecón CJ, Useche G, Sánchez Márquez MG, Carnerero M, Jaldo Rodríguez MT, Muñoz Ramos P, Ruiz San Millán JC, Toapanta N, Gracia Iguacel C, Aguilar Cervera MC, Balibrea Lara N, Leyva A, Rojas J, Gansevoort RT, de Sequera P, SENCOVAC Collaborative Network. **Safety and immediate humoral response of COVID-19 vaccines in chronic kidney disease patients: the SENCOVAC study.** Nephrol Dial

Transplant 37 (10). 2022. PMID: 34788858. IF: 7,19. DOI: 10.1093/ndt/gfab313.

Barril G, Nogueira A, Alvarez García G, Núñez A, Sánchez González C, Ruperto M. **Nutritional Predictors of Mortality after 10 Years of Follow- Up in Patients with Chronic Kidney Disease at a Multidisciplinary Unit of Advanced Chronic Kidney Disease.** NUTRIENTS 14 (18). 2022. PMID: 36145223. IF: 6,71. DOI: 10.3390/nu14183848.

Barril G, Nogueira A. **Bioimpedance as a useful tool for the study of hydration and body composition in patients with chronic kidney disease**. Nutr Hosp 39 (5):2022. PMID: 36173199. IF: 1,17. DOI: 10.20960/nh.04469.

Ruperto M, Barril G. **Nutritional Status, Body Composition, and Inflammation Profile in Older Patients with Advanced Chronic Kidney Disease Stage 4-5: A Case-Control Study**. NUTRIENTS 14 (17). 2022. PMID: 36079906. IF: 6,71. DOI: 10.3390/nu14173650.

Quiroga B, Ortiz A, Cabezas Reina CJ, Ruiz Fuentes MC, López Jiménez V, Zárraga Larrondo S, Toapanta N, Molina Gómez M, de Sequera P, Sánchez Álvarez E, Spanish COVID 19 Registry collaborative group KRT. **Evolving spectrum but persistent high mortality of COVID-19 among patients on kidney replacement therapy in the vaccine era: the Spanish COVID-19 KRT Registry.** Clin Kidney J 15 (9). 2022. PMID: 35999961. IF: 5,86. DOI: 10.1093/ckj/sfac135

Junco,EO,Quiroga,B. **Kidney-vascular-bone axis in down syndrome**. Nefrologia 42 (4):2022. IF: 3,08. DOI: 10.1016/j.nefro.2021.09.019.

Quiroga B, Ortiz A, Sánchez Álvarez E, Goicoechea M, de Sequera P, Spanish Society of Nephrology Council. **SARS-CoV-2 Infection Evolution Among Nephrologists During the Pandemic: Clinical Features and Impact of Vaccination.** Kidney Intl Rep 7 (7). 2022. PMID:35529248. IF:6,23. DOI: 10.1016/j.ekir.2022.04.093.

Goicoechea M, Álvarez V, Segarra A, Polaina M, Martín Reyes G, Robles NR, Escudero V, Orellana C, Bea Granell S, de Juan Ribera J, Fernández Lucas M, Graña JM, Reque J, Sánchez Hernández R, Villamayor S, Górriz JL. **Lipid profile of patients treated with evolocumab in Spanish hospital nephrology units (RETOSS NEFRO).** Nefrologia 42 (3). 2022. PMID: 36210619. IF: 3,08. DOI: 10.1016/j.nefroe.2022.05.005.

Quiroga Borja, Sanz Sainz Marta, Santos Sanchez Rey Begona, Munoz Ramos Patricia, Ortiz Alberto, Ruano Pablo. **Persistent kidney dysfunction after acute kidney injury predicts short-term outpatient mortality**. Intern Med J 52 (5). 2022. PMID: 33342021. IF: 2,61. DOI: 10.1111/imj.15166.

Goicoechea Marian, Alvarez Vicente, Segarra Alfonso, Polaina Manuel, Martin Reyes Guillermo, Roberto Robles Nicolas, Escudero Veronica, Orellana Cristhian, Bea Granell Sergio, de Juan Ribera Joaquin, Fernandez Lucas Milagros, Maria Grana Jose, Reque Javier, Sanchez Hernandez Rosa, Villamayor Santiago, Luis Gorriz Jose. **Lipid profile of patients treated with evolocumab in Spanish hospital nephrology units (RETOSS NEFRO)**. Nefrologia 42 (3). 2022. PMID: 34389184. IF: 3,08. DOI: 10.1016/j.nefro.2021.06.004.

Ruperto Mar, Barril Guillermina. **The Extracellular Mass to Body Cell Mass Ratio as a Predictor of Mortality Risk in Hemodialysis Patients**. NUTRIENTS 14 (8). 2022. PMID: 35458220. IF: 6,71. DOI: 10.3390/nu14081659.

Quiroga Borja, Munoz Ramos Patricia, Sanchez Horrillo Ana, Ortiz Alberto, Manuel Valdivieso Jose, Carrero Juan Jesus. **Triglycerides-glucose index and the risk of cardiovascular events in persons with non-diabetic chronic kidney disease**. Clin Kidney J 15 (9). 2022. PMID: 36003671. IF: 5,86. DOI: 10.1093/ckj/sfac073.

Quiroga Borja, Soler Maria Jose, Ortiz Alberto, Bernat Amparo, Munoz Diaz Ana Beatriz, Jarava Mantecon Carlos Jesus, Gomez Perez Virginia Olinda, Calderon Gonzalez Carmen, Cervienka Michal, Mazuecos Auxiliadora, Cazorla Juan Manuel, Carnerero Di Riso Manuel, Martinez Shaira, Diaz Mayra Ortega, Valverde Rafael Lucena, Sanchez Marquez Maria Gabriela, Lancho Novillo Carolina, Gonzalez Parra Emilio, Gracia Iguacel Carolina, Rodrigo De Tomas Maria Teresa, Aguilar Cervera Maria Cinta, Giorgi Martin, Munoz Ramos Patricia, Carmona Nicolas Macias, Toapanta Nestor, Cigarran Secundino, Ruiz San Millan Juan Carlos, Santana Estupinan Raquel, Crespo Marta, Villacorta Linaza Blanca et al. **Loss of humoral response 3 months after SARS-CoV-2 vaccination in the CKD spectrum: the multicentric SENCOVAC study**. Nephrol Dial Transplant 37 (5). 2022. PMID: 35022757. IF: 7,19. DOI: 10.1093/ndt/gfac007.

Valdivia Mazeyra MF, Muñoz Ramos P, Serrano R, Alonso Riaño M, Gil Giraldo Y, Quiroga B. **Mesoamerican nephropathy: A not so unknown chronic kidney disease.** Nefrologia 41 (6). 2022. PMID: 36165150. IF: 3,08. DOI: 10.1016/j.nefroe.2021.12.009.

Roger Marta, Hernandez Gallego Roman, Martinez Jimenez Victor, Rodriguez Perez Jose Carlos, Furlano Monica, Sans Atxer Laia, Gallego Zurro Daniel, Romeo Casabona Carlos Maria, Gomez Clemente, Perez Bermudez Pilar, Arellano Armisen Manuel, Albaladejo Lopez Santiago, Gutierrez Porras Inmaculada, Gomez Ruiz Josefa, Martin Orgaz Jose Manuel, Moreno Baron Marta, de Sequera Ortiz Patricia, de Arriba de la Fuente Gabriel, Quiroga Gili Borja, Fernandez Fresnedo Gema, Soriano Cabrera Sagrario, Perez Contreras Javier, Blasco Pelicano Miquel, Mazuecos Blanca Auxiliadora, Rodriguez Portillo Mariano, Sanchez Alvarez J Emilio, Soler Romeo Maria Jose, Gorostidi Perez Manuel, Goicoechea Diezhandino Marian, Hernandez Marrero Domingo et al. **CKD: The burden of disease invisible to research funders**. Nefrologia 42 (1). 2022. PMID: 34803202. IF: 3,08. DOI: 10.1016/j.nefro.2021.09.004.

Pérez Fontán M, Moreiras Plaza M, Prieto Velasco M, Quereda Rodriguez Navarro C, Bajo Rubio MA, Borràs Sans M, de la Espada Piña V, Pérez Contreras J, del Peso Gilsanz G, Ponz Clemente E, Quirós Ganga P, Remón Rodríguez C, Rodríguez Carmona A, Sánchez Alvarez E, Vega Díaz N, Vera Rivera M, Aresté Fosalba N, Bordes Benítez A, Castro Notario MJ, Fernández Perpén A, Fernández Reyes MJ, Gasch Blasi O, Gil Cunquero JM, Julián Mauro JC, Minguela Pesquera JI, Munar Vila MA, Núñez del Moral M, Pérez López T, Portolés Pérez J, Rivera Gorrín M et al. **Clinical guide of the Spanish Society of Nephrology on the prevention and treatment of peritoneal infection in peritoneal dialysis**. Nefrologia 42. 2022. IF: 3,08. DOI: 10.1016/j.nefroe.2022.07.005.

Ortiz A, Roger M, Jiménez VM, Perez JCR, Furlano M, Atxer LS, Zurro DG, Casabona CMR, Gómez CG, Bermúdez PP, Armisen MA, López SA, Porras IG, Ruiz JG, Orgaz JMM, Barón MM, Ortiz PDS, De La Fuente GDA, Gili BQ, Fresnedo GF, Cabrera SS, Contreras JP, Pelicano MB, Blanca AM, Portillo MR, Alvarez JES, Romeo MJS, Pérez MG, Diezhandino MG, Marrero DH et al. **RICORS2040: The need for collaborative research in chronic kidney disease**. Clin Kidney J 15 (3). 2022. IF:5,86. PMID: 35211298. DOI:10.1093/ckj/sfab170.

LINE 1.7 ›› INFLAMMATORY MECHANISMS IN PULMONARY DISEASES

GROUP 22

Head of laboratory: Ancochea Bermúdez, Julio

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

Line 1.7 Inflammatory mechanisms in pulmonary diseases

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.

GROUP MEMBERS

- Julio Ancochea Bermúdez
- Carlos Melero Moreno
- Adrián Martínez Vergara
- Jonathan James Reid McFarland
- María del Mar Barrio Mayo
- Francisco Javier García Pérez
- María Celeste Marcos
- Marta Chicot Llano
- Emma Vázquez Espinosa
- Elena García Castillo
- Tamara Alonso Pérez
- Claudia Valenzuela
- María Patricia Pérez González
- Pilar Rubio Bueno
- Rosa Mar Gómez Punter
- Joan Bautista Soriano Ortiz
- Carolina Victoria Cisneros Serrano
- Rosa María Girón Moreno
- Enrique Domingo Zamora García
- Adrián Peláez Laderas

MAJOR GRANTS

García Monzón, Carmelo / Landete Rodríguez, Pedro. **Caracterización de los mediadores moleculares clave de la enfermedad hepática grasa metabólica asociada al síndrome de apnea obstructiva del sueño: Implicaciones diagnósticas y terapéuticas**. PI20/00837. ISCIII. 2021-2023.

Soriano Ortiz, Joan B. **unCoVer: Unravelling Data for Rapid Evidence-Based Response to COVID-19**. unCoVer: 101016216. Comisión Europea. 2020- 2022.

Melero Moreno, Carlos. **Estudio COVasma: components volátiles orgánicos en el asma**. SEPAR. 2015-2022.

Soriano, Joan B. **COVID Persistente y fumadores: magnitud del problema y ensayo clínico de deshabituación**. Sociedad Española de Neumología y Cirugía Torácica.

Soriano, Joan B**. unCoVer: Unravelling Data for Rapid Evidence-Based Response to COVID-19**. SOCIETAL CHALLENGES - Health, demographic change and well-being (Horizonte 2020).

Ramírez González, Noelia / Soriano, Joan B. **On-BREATHE: Monitorización personal de la calidad del aire y digitalización de datos para el seguimiento de enfermedades crónicas respiratorias**.

Fernández Muñoz, Esteve / García Castillo, Elena. **Efectividad de una intervención basada en la evidencia para promover hogares libres del humo de tabaco: ensayo controlado aleatorizado**. Beca SEPAR 2022.

López Padilla, Daniel / García Castillo, Elena. **Valor Pronóstico del Índice de Masa Libre de Grasa en una Escala Multidimensional en la Enfermedad Pulmonar Obstructiva Crónica – Estudio FODEP-OC.** Beca SEPAR 2019.

Girón, Rosa Mª. **Influencia del ciclo menstrual en las mujeres con fibrosis quística**. Estudio multicéntrico. Beca Separ. 2020-2023.

Girón, Rosa Mª. **Asociación de la proteína Alfa Klotho con la condición física, la función pulmonar y la morbilidad en pacientes con fibrosis quística (proyecto FQ - Klotho).** Beca Separ. 2020-2023.

PUBLICATIONS

Delgado Romero J, Blanco Aparicio M, Cisneros Serrano C, Díaz Pérez D, Ferrando Piqueres R, López Carrasco V, Merino Bohórquez V, Soto Retes L, Domínguez Ortega J. **Biological therapy at-home administration support for patients with severe asthma BioCart©.** J Invest Allergol Clin Immunol 32 (6): 482-484. 2022. PMID: 35088761. IF: 8,19. DOI: 10.18176/jiaci.0786.

Lazarus JV, Ortiz A, Tyrovolas S, Fernández E, Guy D, White TM, Ma R, Hay SI, Naghavi M, Soriano JB, Spain Collaborators GBD2019. **A GBD 2019 study of health and Sustainable Development Goal gains and forecasts to 2030 in Spain.** Sci Rep 12 (1): 21154-21154. 2022. PMID: 36477107. IF: 5,00. DOI: 10.1038/s41598-022-24719-z.

Sevilla Montero J, Munar Rubert O, Pino Fadon J, Aguilar Latorre C, Villegas Esguevillas M, Climent B, Agro M, Choya Foces C, Martinez Ruiz A, Balsa E, Munoz Calleja C, Gomez Punter RM, Vazquez Espinosa E, Cogolludo A, Calzada MJ. **Cigarette smoke induces pulmonary arterial dysfunction through an imbalance in the redox status of the soluble guanylyl cyclase**. Free Radic Biol Med 193 (Pt 1): 9-22. 2022. PMID: 36174878. IF: 8,10. DOI: 10.1016/j.freeradbiomed.2022.09.026.

Girón RM, Peláez A, Ibáñez A, Martínez Besteiro E, Gómez Punter RM, Martínez Vergara A, Ancochea J, Morell A. **Longitudinal Study of Therapeutic Adherence in a Cystic Fibrosis Unit: Identifying Potential Factors Associated with Medication Possession Ratio.** Antibiotics 11 (11): 1637. 2022. PMID: 36421281. IF: 5,22. DOI: 10.3390/antibiotics11111637.

Miravitlles M, Soler Cataluña JJ, Soriano JB, García Río F, de Lucas P, Alfageme I, Casanova C, Rodríguez González Moro JM, Sánchez G, Ancochea J, Cosío BG. **Respiratory symptoms and their determinants in the general Spanish population: changes over 20 years.** ERJ Open Res 8 (4):

00067-2022. 2022. PMID: 36382234. IF: 4,24. DOI: 10.1183/23120541.00067-2022.

Soler Cataluña JJ, Puente Maestu L, Román Rodríguez M, Esteban C, Gea J, Bernabeu Mora R, Pleguezuelos Cobo E, Ancochea J, García Río F. **Validation of the Spanish Activity Questionnaire in COPD (SAQ-COPD) in Patients with Chronic Obstructive Pulmonary Disease.** Int J COPD 17. 2835-2846. 2022. PMID: 36381995. IF: 2,89. DOI: 10.2147/COPD.S381427.

Domingo LC, Vallejo ER, Cruz NDZ, Llano MC, Perez Urria EA, Barrios A, Santos JH, Ortiz J, Garcia SCR, Ramirez AM, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Garcia AS, Villa A, Azofra AS, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martinez AT, Arevalo C, Roman JMG, Garcia Vicuna R et al. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol 94 (11): 5260-5270. 2022. PMID: 35811284. IF: 20,69. DOI: 10.1002/jmv.27989.

Global Burden of Disease Long COVID Collaborators, Wulf Hanson S, Abbafati C, Aerts JG, Al Aly Z, Ashbaugh C, Ballouz T, Blyuss O, Bobkova P, Bonsel G, Borzakova S, Buonsenso D, Butnaru D, Carter A, Chu H, De Rose C, Diab MM, Ekbom E, El Tantawi M, Fomin V, Frithiof R, Gamirova A, Glybochko PV, Haagsma JA, Haghjooy Javanmard S, Hamilton EB, Harris G, Heijenbrok Kal MH, Helbok R, Hellemons ME et al. **Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021.** JAMA 328 (16): 1604-1615. 2022. PMID: 36215063. IF: 157,34. DOI: 10.1001/jama.2022.18931.

Cottin V, Valenzuela C. **Progressive pulmonary fibrosis: all roads lead to Rome (but not all at the same speed).** Eur Respir J 60 (4): 2201449. 2022. PMID: 36202405. IF: 33,80. DOI: 10.1183/13993003.01449-2022.

Martinez García MÁ, Olveira C, Girón R, García Clemente M, Máiz Carro L, Sibila O, Golpe R, Méndez R, Rodríguez Hermosa JL, Barreiro E, Prados C, Rodríguez López J, de la Rosa D. **Peripheral Neutrophil-to-Lymphocyte Ratio in Bronchiectasis: A Marker of Disease Severity.** Biomolecules 12 (10): 1399. 2022. PMID: 36291608. IF: 6,06. DOI: 10.3390/biom12101399.

García Castillo E, Alonso Pérez T, Peláez A, Pérez González P, Soriano JB, Ancochea J. **Prevalence of Chronic Obstructive Pulmonary Disease in an Urban Area. Changes in COPD Ten Years on.** Int J COPD 1. 2431-2441. 2022. PMID: 36199759. IF: 2,89. DOI: 10.2147/COPD.S377140.

Soriano JB. **Planetary respiratory health for asthma, rhinoconjunctivitis and eczema.** Eur Respir J 60 (3): 2200440. 2022. PMID: 36109045. IF: 33,80. DOI: 10.1183/13993003.00440-2022.

Tarraso J, Safont B, Carbonell Asins JA, Fernandez Fabrellas E, Sancho Chust JN, Naval E, Amat B, Herrera S, Ros JA, Soler Cataluña JJ, Rodriguez Portal JA, Andreu AL, Marín M, Rodriguez Hermosa JL, Gonzalez Villaescusa C, Soriano JB, Signes Costa J, COVID FIBROTIC study team. **Lung function and radiological findings 1 year after COVID-19: a prospective follow-up.** Respir Res 23 (1): 242-242. 2022. PMID: 36096801. IF: 7,16. DOI: 10.1186/s12931-022-02166-8.

Valenzuela C, Cottin V. **Epidemiology and real-life experience in progressive pulmonary fibrosis**. Curr Opin Pulm Med 28 (5): 407-413. 2022. PMID: 35938201. IF: 2,87. DOI: 10.1097/MCP.0000000000000908.

Cottin V, Si Mohamed S, Diesler R, Bonniaud P, Valenzuela C. **Pleuroparenchymal fibroelastosis.** Curr Opin Pulm Med 28 (5): 432-440. 2022. PMID: 35855575. IF: 2,87. DOI: 10.1097/MCP.0000000000000907.

González Sánchez E, Muñoz Callejas A, Gómez Román J, San Antonio E, Marengo A, Tsapis N, Bohne Japiassu K, González Tajuelo R, Pereda S, García Pérez J, Cavagna L, González Gay MÁ, Vicente Rabaneda EF, Meloni F, Fattal E, Castañeda S, Urzainqui A. **Targeted nanotherapy with everolimus reduces inflammation and fibrosis in scleroderma-related interstitial lung disease developed by PSGL-1 deficient mice.** Br J Pharmacol 179 (18): 4534-4548. 2022. PMID: 35726496. IF: 9,47. DOI: 10.1111/bph.15898.

Carrasco L, Girón RM, Peláez A, Gómez A, Gómez B, Diab L, Tejedor MT, García M, Solís M, González L, Blanco M, Olveira C, Girón MV, Zamarrón de Lucas E, Prados C, Quintana E. **Real Life With Tezacaftor and Ivacaftor in Adult Patients With Cystic Fibrosis: Spanish Multicenter Study.** Arch Bronconeumol 58 (9): 672-674. 2022. PMID: 35781398. IF: 6,33. DOI: 10.1016/j.arbres.2022.06.003.

Martínez M, Prados C, García F, Quintana E, Castillo S, Salcedo A, Girón R, Martínez MT, Máiz L, de Vicente CM, Costa J,Álvarez R, Spanish Working Group Atelectasis in CF. **The Relation of CFTR-Genotype and Associated Comorbidities to Development of Pulmonary Atelectasis in Cystic Fibrosis Patients.** Arch Bronconeumol 58 (9): 666-668. 2022. PMID: 35644710. IF: 6,33. DOI: 10.1016/j.arbres.2022.02.009.

Louis R, Satia I, Ojanguren I, Schleich F, Bonini M, Tonia T, Rigau D, Ten Brinke A, Buhl R, Loukides S,

Kocks JWH, Boulet LP, Bourdin A, Coleman C, Needham K, Thomas M, Idzko M, Papi A, Porsbjerg C, Schuermans D, Soriano JB, Usmani OS. **European Respiratory Society Guidelines for the Diagnosis of Asthma in Adults.** Eur Respir J 60 (3): 2101585. 2022. PMID: 35169025. IF: 33,80. DOI: 10.1183/13993003.01585-2021.

León Román F, Valenzuela C, Molina M. **Idiopathic pulmonary fibrosis.** Med Clin 159 (4): 189-194. 2022. PMID: 35659420. IF: 3,20. DOI: 10.1016/j.medcli.2022.02.020.

Martínez Vergara A, Girón Moreno RM, Olveira C, Victoria Girón M, Peláez A, Ancochea J, Oscullo G, Martínez García MÁ. **Impact of the SARS-CoV-2 Virus Pandemic on Patients with Bronchiectasis: A Multicenter Study.** Antibiotics 11 (8): 1096. 2022. PMID: 36009967. IF: 5,22. DOI: 10.3390/antibiotics11081096.

Marcos MC, Erro M, Cisneros C. **Effectiveness of omalizumab as treatment of allergic pulmonary aspergillosis in patients with cystic fibrosis and asthma.** Med Clin 159 (3): 21-22. 2022. PMID: 35644627. IF: 3,20. DOI: 10.1016/j.medcli.2022.02.008.

Molina M, Castellví I, Valenzuela C, Ramirez J, Rodríguez Portal JA, Franquet T, Narváez J. **Management of progressive pulmonary fibrosis associated with connective tissue disease.** Expert Rev Respir Med 16 (7): 765-774. 2022. PMID: 35912842. IF: 4,30. DOI: 10.1080/17476348.2022.2107508.

Stival C, Lugo A, Odone A, van den Brandt PA, Fernandez E, Tigova O, Soriano JB, José López M, Scaglioni S, Gallus S, TackSHS Project Investigators. **Prevalence and Correlates of Overweight and Obesity in 12 European Countries in 2017-2018.** Obes Facts 15 (5): 655-665. 2022. PMID: 35917801. IF: 4,81. DOI: 10.1159/000525792.

Soriano JB, Dai X, Ancochea J. **An Euler Proportional Venn Diagram of Obstructive Lung Disease.** Arch Bronconeumol 58 (8): 627-628. 2022. PMID: 35312496. IF: 6,33. DOI: 10.1016/j.arbres.2022.01.013.

Cottin V, Tomassetti S, Valenzuela C, Walsh SLF, Antoniou KM, Bonella F, Brown KK, Collard HR, Corte TJ, Flaherty KR, Johannson KA, Kolb M, Kreuter M, Inoue Y, Jenkins RG, Lee JS, Lynch DA, Maher TM, Martinez FJ, Molina M, Myers JL, Nathan SD, Poletti V, Quadrelli S, Raghu G, Rajan SK, Ravaglia C, Remy Jardin M, Renzoni E, Richeldi LK et al. **Integrating Clinical Probability into the Diagnostic Approach to Idiopathic Pulmonary Fibrosis An International Working Group Perspective**. Am J Respir Crit Care Med 206 (3): 247-259. 2022. PMID: 35353660. IF: 30,53. DOI: 10.1164/rccm.202111-2607PP.

García Clemente M, Olveira C, Girón R, Máiz L, Sibila O, Golpe R, Menéndez R, Rodríguez J, Barreiro E, Rodríguez Hermosa JL, Prados C, De la Rosa D, Carbajal CM, Solís M, Martínez García MÁ. **Impact of Chronic Bronchial Infection by Staphylococcus aureus on Bronchiectasis.** J Clin Med 11 (14): 3960. 2022. PMID: 35887723. IF: 4,96. DOI: 10.3390/jcm11143960.

Carr SB, McClenaghan E, Elbert A, Faro A, Cosgriff R, Abdrakhmanov O, Brownlee K, Burgel PR, Byrnes CA, Cheng SY, Colombo C, Corvol H, Daneau G, Goss CH, Gulmans V, Gutierrez H, Harutyunyan S, Helmick M, Jung A, Kashirskaya N, McKone E, Melo J, Middleton PG, Mondejar Lopez P, de Monestrol I, Nährlich L, Padoan R, Parker M, Pastor Vivero MD, Rizvi S et al. **Factors associated with clinical progression to severe COVID-19 in people with cystic fibrosis: A global observational study.** J Cyst Fibrosis 21 (4): 221-231. 2022. PMID: 35753987. IF: 5,53. DOI: 10.1016/j.jcf.2022.06.006.

Merino M, Martín Lorenzo T, Maravilla Herrera P, Ancochea J, Gómez Sáenz JT, Hass N, Molina J, Peces Barba G, Trapero Bertran M, Trigueros Carrero JA, Hidalgo Vega Á. **A Social Return on Investment Analysis of Improving the Management of Chronic Obstructive Pulmonary Disease Within the Spanish National Healthcare System.** Int J COPD 17. 1431-1442. 2022. PMID: 35761956. IF: 2,89. DOI: 10.2147/COPD.S361700.

Martínez García MÁ, Soriano JB. **Asthma, bronchiectasis, and chronic obstructive pulmonary disease: the Bermuda Triangle of the airways.** Chin Med J 135 (12): 1390-1393. 2022. PMID: 35869863. IF: 6,13. DOI: 10.1097/CM9.0000000000002225.Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos

E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 855639-855639. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro,

Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1): 9208-9208. 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Richeldi Luca, Azuma Arata, Cottin Vincent, Hesslinger Christian, Stowasser Susanne, Valenzuela Claudia, Wijsenbeek Marlies S, Zoz Donald F, Voss Florian, Maher Toby M, Trial Investigators 1305-0013. **Trial of a Preferential Phosphodiesterase 4B Inhibitor for Idiopathic Pulmonary Fibrosis**. N Engl J Med 386 (23): 2178-2187. 2022. PMID: 35569036. IF: 176,08. DOI: 10.1056/NEJMoa2201737.

Bonella Francesco, Cottin Vincent, Valenzuela Claudia, Wijsenbeek Marlies, Voss Florian, Rohr Klaus B, Stowasser Susanne, Maher Toby M. **Meta- Analysis of Effect of Nintedanib on Reducing FVC Decline Across Interstitial Lung Diseases**. Adv Ther 39 (7): 3392-3402. 2022. PMID: 35576048. IF: 4,07. DOI: 10.1007/s12325-022-02145-x.

Wang Xuejie, Olveira Casilda, Giron Rosa, Garcia Clemente Marta, Maiz Luis, Sibila Oriol, Golpe Rafael, Menendez Rosario, Rodriguez Lopez Juan, Prados Concepcion, Angel Martinez Garcia Miguel, Luis Rodriguez Juan, de la Rosa David, Qin Liyun, Duran Xavier, Garcia Ojalvo Jordi, Barreiro Esther. **Blood Neutrophil Counts Define Specific Clusters of Bronchiectasis Patients: A Hint to Differential Clinical Phenotypes**. Biomedicines 10 (5): 1044. 2022. PMID: 35625780. IF: 4,76. DOI: 10.3390/biomedicines10051044.

Martinez MA, Bekki A, Vergara AM. **Is bronchiectasis associated with cardiovascular disease?** Res Med Res 81. 100912-100912. 2022. PMID: 35568020. IF: 3,15. DOI: 10.1016/j.resmer.2022.100912.

Soriano JB, Hopkinson NS. **Sing out for COPD!**. Eur Respir J 59 (5): 2102961. 2022. PMID: 35589115. IF: 33,80. DOI: 10.1183/13993003.02961-2021.

Molina M, Buendia Roldan I, Castillo D, Caro F, Valenzuela C, Selman M. **Diagnostic and Therapeutic Developments in Progressive Pulmonary Fibrosis.** Arch Bronconeumol 58 (5): 418-424. 2022. PMID: 35312511. IF: 6,33. DOI: 10.1016/j.arbres.2021.12.006.

Tejada S, Ramirez Estrada S, Tejo AM, Forero CG, Pomares X, Gallego M, Soriano JB, Chalmers JD, Rello J. **Critical appraisal of international adult bronchiectasis guidelines using the AGREE II tool**. Eur J Intern Med 98. 4-

11. 2022. PMID: 35074245. IF: 7,75. DOI: 10.1016/j.ejim.2022.01.023.

Girón RM, Ibáñez A, Gómez Punter RM, Alarcón T. **New evidence in severe pneumonia: imipenem/cilastatin/relebactam.** Rev Esp Quimioter 35 (Suppl 1): 46-49. 2022. PMID: 35488826. IF: 2,52. DOI: 10.37201/req/s01.11.2022.

Varona Jose F, Landete Pedro, Lopez Martin Jose A, Estrada Vicente, Paredes Roger, Guisado Vasco Pablo, Fernandez de Orueta Lucia, Torralba Miguel, Fortun Jesus, Vates Roberto, Barberan Jose, Clotet Bonaventura, Ancochea Julio, Carnevali Daniel, Cabello Noemi, Porras Lourdes, Gijon Paloma, Monereo Alfonso, Abad Daniel, Zuniga Sonia, Sola Isabel, Rodon Jordi, Vergara Alert Julia, Izquierdo Useros Nuria, Fudio Salvador, Jose Pontes Maria, de Rivas Beatriz, Giron de Velasco Patricia, Nieto Antonio, Gomez Javier et al. **Preclinical and randomized phase I studies of plitidepsin in adults with COVID-19**. Life Sci Alliance 5 (4): 202101200. 2022. PMID: 35012962. IF: 5,78. DOI: 10.26508/lsa.202101200.

Soriano Joan B, Pelaez Adrian, Fernandez Esteve, Moreno Laura, Ancochea Julio. **The Emergence of COVID-19 as a Cause of Death in 2020 and its** Effect on Mortality by Diseases of the Respiratory System in Spain: Trends and Their Determinants Compared to 2019. Arch Bronconeumol 58. 13-21. 2022. PMID: 35340748. IF: 6,33. DOI: 10.1016/j.arbres.2022.03.001.

Buendia I, Valenzuela C, Selmana M. **Pulmonary Fibrosis in the Time of COVID-19**. Arch Bronconeumol 58. 6-7. 2022. PMID: 35491285. IF: 6,33. DOI: 10.1016/j.arbres.2022.03.007.

Miravitlles Marc, Jose Soler Cataluna Juan, Soriano Joan B, Garcia Rio Francisco, de Lucas Pilar, Alfageme Inmaculada, Casanova Ciro, Rodriguez Gonzalez Moro Jose Miguel, Guadalupe Sanchez Herrero M, Ancochea Julio, Cosio Borja G. **Determinants of blood eosinophil levels in the general population and patients with COPD: a population-based, epidemiological study**. Respir Res 23 (1): 49-49. 2022. PMID: 35248041. IF: 7,16. DOI: 10.1186/s12931-022-01965-3.

Balandin Barbara, Ballesteros Daniel, Pintado Vicente, Soriano Cuesta Cruz, Cid Tovar Irene, Sancho Gonzalez Milagros, Jose Perez Pedrero Maria, Chicot Marta, Jose Asensio Martin Maria, Alberto Silva Jose, Ruiz de Luna Rafael, Martin Dal Gesso Cristina, Anibal Rodriguez Serrano Diego, Martinez Sagasti Fernando, Royuela Ana. **Multicentre study of ceftazidime/avibactam for Gram-negative bacteria infections**

in critically ill patients. Int J Antimicrob Agents 59 (3): 106536-106536. 2022. PMID: 35091054. IF: 15,44. DOI: 10.1016/j.ijantimicag.2022.106536.

Soriano JB, Villagrasa JR, Ancochea J. **COVID-19 in Youth and the Fifth Wave**. Arch Bronconeumol 58 (3): 213-214. 2022. PMID: 35194292. IF: 6,33. DOI: 10.1016/j.arbres.2021.08.021.

Landete Pedro, Fernandez Garcia Carlos Ernesto, Aldave Orzaiz Beatriz, Hernandez Olivo Marta, Acosta Gutierrez Carmen M, Zamora Garcia Enrique, Ancochea Julio, Gonzalez Rodriguez Agueda, Garcia Monzon Carmelo. **Increased Oxygen Desaturation Time During Sleep Is a Risk Factor for NASH in Patients With Obstructive Sleep Apnea: A Prospective Cohort Study**. Front Med 9. 808417-808417. 2022. PMID: 35280896. IF: 5,06. DOI: 10.3389/fmed.2022.808417.

García Vicuña R, Rodriguez García SC, Abad Santos F, Bautista Hernández A, García Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso Pérez T, Cardeñoso L, Alfranca A, Mejía Abril G, Sanz J, González Alvaro I. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9. 819621-819621. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621.

Ferrari Alize J, Santomauro Damian F, Herrera Ana M Mantilla, Shadid Jamileh, Ashbaugh Charlie, Erskine Holly E, Charlson Fiona J, Degenhardt Louisa, Scott James G, McGrath John J, Allebeck Peter, Benjet Corina, Breitborde Nicholas J K, Brugha Traolach, Dai Xiaochen, Dandona Lalit, Dandona Rakhi, Fischer Florian, Haagsma Juanita A, Maria Haro Josep, Kieling Christian, Knudsen Ann Kristin Skrindo, Kumar G Anil, Leung Janni, Majeed Azeem, Mitchell Philip B, Moitra Modhurima, Mokdad Ali H, Molokhia Mariam, Patten Scott B et al. **Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019**. Lancet Psychiatry 9 (2): 137-150. 2022. PMID: 35026139. IF: 77,06. DOI: 10.1016/S2215-0366(21)00395-3.

Tejada S, Ramirez S, Forero CG, Gallego M, Soriano JB, Cardinal PA, Ehrmann S, Rello J. **Safety and Efficacy of Devices Delivering Inhaled Antibiotics among Adults with Non-Cystic Fibrosis Bronchiectasis: A Systematic Review and a Network Meta-Analysis**. Antibiotics 11 (2): 275. 2022. PMID: 35203878. IF: 5,22. DOI: 10.3390/antibiotics11020275.

Soler Cataluna Juan Jose, Pinera Pascual, Antonio Trigueros Juan, Calle Myriam, Casanova Ciro, Cosio Borja G, Lopez Campos Jose Luis, Molina Jesus, Almagro Pere, Gomez Jose-Tomas, Antonio Riesco Juan, Simonet Pere, Rigau David, Soriano Joan B, Ancochea Julio, Miravitlles Marc, GesEPOC Working 2021Grp. **Spanish COPD Guidelines (GesEPOC) 2021 Update. Diagnosis and Treatment of COPD Exacerbation Syndrome**. Arch. Bronconeumol 58 (2): 159-170. 2022. PMID: 35971815. IF: 6,33. DOI: 10.1016/j.arbres.2021.05.033.

Cavagna L, Meloni F, Meyer A, Sambataro G, Belliato M, De Langhe E, Cavazzana I, Pipitone N, Triantafyllias K, Mosca M, Barsotti S, Zampogna G, Biglia A, Emmi G, de Visser M, van der Kooi A, Parronchi P, Hirschi S, da Silva JAP, Scire CA, Furini F, Giannini M, Martinez Gonzalez O, Damian L, Piette Y, Smith V, Mera Varela A, Bachiller Corral J, Cabezas Rodriguez I, Brandy Garcia AM et al. **Clinical spectrum time course in non-Asian patients positive for anti-MDA5 antibodies**. Clin Exp Rheumatol 40 (2): 274-283. 2022. PMID: 35200123. IF: 4,86. DOI: 10.55563/clinexprheumatol/di1083.

Lopez Padilla Daniel, Teran Tinedo Jose, Cerezo Lajas Alicia, Ramirez Garcia Laura, Ojeda Castillejo Elena, Lopez Martin Soledad, Diaz Cambriles Trinidad, Gonzalez Virseda Sonia, Arias Melgar Begona, Candel Pizarro Ana, Lozano Alcocer Hector, Fernanda Troncoso Acevedo Maria, Gomez Garcia Teresa, Lopez Yeste Pablo, Cano Pumarega Irene, Garcia Sanchez Aldara, Arias Arcos Beatriz, Zamora Garcia Enrique, Landete Rodriguez Pedro, Iturricastillo Gorane, Lores Gutierrez Vanesa, Rodriguez Alonso Carlos, Vidal Ortola Martha, Lopez Riolobos Cristina, Garcia Prieto Fernando, Abad Fernandez Araceli, Manas Baena Eva. **Moderate obstructive sleep apnea and cardiovascular outcomes in older adults: a propensity score-matched multicenter study (CPAGE-MODE study)**. J Clin Sleep Med 18 (2): 553-561. 2022. PMID: 34534075. IF: 4,32. DOI: 10.5664/jcsm.9656.

Wang X, Villa C, Dobarganes Y, Olveira C, Girón R, García Clemente M, Máiz L, Sibila O, Golpe R, Menéndez R, Rodríguez López J, Prados C, Martinez García MA, Rodriguez JL, de la Rosa D, Duran X, Garcia Ojalvo J, Barreiro E. **Systemic Inflammatory Biomarkers Define Specific Clusters in Patients with Bronchiectasis: A Large-Cohort Study.** Biomedicines 10 (2): 225. 2022. PMID: 35203435. IF: 4,76. DOI: 10.3390/biomedicines10020225.

Luis Izquierdo Jose, Soriano Joan B, Gonzalez Yolanda, Lumbreras Sara, Ancochea Julio, Echeverry Christian, Miguel Rodriguez Jose. **Use of N- Acetylcysteine at high doses as an oral treatment for patients hospitalized with COVID-19**. Sci Prog 105 (1): 00368504221074574. 2022. PMID: 35084258. IF: 1,51. DOI: 10.1177/00368504221074574.

Perez de Llano Luis, Dacal Rivas David, Marina Malanda Nuria, Plaza Moral Vicente, Gullon Blanco Jose Antonio, Munoz Esquerre Mariana, Garcia Moguel

Ismael, Diaz Campos Rocio M, Martinez Moragon Eva, Harbenau Mena Alicia, Cosio Borja G, Padilla Galo Alicia, Cisneros Serrano Carolina. **The Response to Biologics is Better in Patients with Severe Asthma Than in Patients with Asthma-COPD Overlap Syndrome**. J Asthma Allerg 15. 363-369. 2022. PMID: 35330786. IF: 3,03. DOI: 10.2147/JAA.S338467.

Farre Xavier, Espin Roderic, Baiges Alexandra, Blommaert Eline, Kim Wonji, Giannikou Krinio, Herranz Carmen, Roman Antonio, Saez Berta, Casanova Alvaro, Ancochea Julio, Valenzuela Claudia, Ussetti Piedad, Laporta Rosalia, Rodriguez Portal Jose A, van Moorsel Coline H M, van der Vis Joanne J, Quanjel Marian J R, Tena Garitaonaindia Mireia, Sanchez de Medina Fermin, Mateo Francesca, Molina Maria, Won Sungho, Kwiatkowski David J, de Cid Rafael, Angel Pujana Miquel. **Evidence for shared genetic risk factors between lymphangioleiomyomatosis and pulmonary function**. ERJ Open Res 8 (1): 00375. 2022. PMID: 35083324. IF: 4,24. DOI: 10.1183/23120541.00375-2021.

Marinero Martínez Lázaro A, Girón Moreno RM, Casals Seoane F, Cano Valderrama Ó, García Buey L. **Cystic fibrosis with liver involvement in adults has a benign course. Results from a tertiary referral centre cohort.** Rev Esp Enferm Dig 114. 2022. PMID: 36353964. IF: 2,39. DOI: 10.17235/reed.2022.9289/2022.

Agustí A, Alcázar B, Ancochea J, Casanova C, Celli B, Cosio B, Echave- Sustaeta JM, Fernandez Villar A, Garcia Rivero JL, González C, Izquierdo JL, Lopez-Campos JL, Marín Trigo JM, Martín Sánchez J, Miravitlles M, Molina J, Peces-Barba G, Roman M, Soler Cataluña JJ, Villar-Alvarez F. **The ANTES program in COPD: First year**. Arch Bronconeumol 58(4):291-294. 2022. PMID: 35312529. IF: 6.33. doi: 10.1016/j.arbres.2021.10.009.

Soriano JB, Gerli AG, Centanni S, Ancochea J. **Forecasting COVID-19 Infection Trends and New Hospital Admissions in Spain due to SARS-CoV- 2 Variant of Concern Omicron**. Arch Bronconeumol 58 (2): 200-202. 2022. PMID: 35035025. IF: 6.33. doi: 10.1016/j.arbres.2022.01.001.

Vicente-Rabaneda EF, Serra López-Matencio JM, Ancochea J, Blanco R, González-Gay MÁ, Castañeda S. **Efficacy and safety of biological drugs in interstitial lung disease associated with connective tissue diseases**. Expert Opin Drug Saf 21 (3): 311-333. 2022. PMID: 34433372. IF: 4.01. doi: 10.1080/14740338.2021.1973428.

Teran-Tinedo JR, Gonzalez-Rubio J, Najera A, Castany-Faro A, Contreras MLN, Garcia IM, Lopez-Mellado L, Lorente-Gonzalez M, Perez-Garvin P, Sacristan-Crespo G, Suarez-Ortiz M, Navarro-Lopez JD, Jimenez-Diaz L, Landete P. **Clinical characteristics and respiratory care in hospitalized vaccinated SARS-CoV-2 patients**. EClinicalMedicine 48: 101453. 2022. PMID: 35611064. doi: 10.1016/j.eclinm.2022.101453.

Landete P, Prieto Romo JI, Giacomini F. **Experience on the Management of Patients with Asthma or Chronic Obstructive Pulmonary Disease During the COVID-19 Pandemic: the NEUMOBIAL Study**. Adv Ther 39 (11): 5216- 5228. 2022. PMID: 36114950. IF: 4.07. doi: 10.1007/s12325-022-02313-z.

Madurka I, Vishnevsky A, Soriano JB, Gans SJ, Ore DJS, Rendon A, Ulrik CS, Bhatnagar S, Krishnamurthy S, Mc Harry K, Welte T, Fernandez AA, Mehes B, Meiser K, Gatlik E, Sommer U, Junge G, Rezende E; Study group. **DFV890: a new oral NLRP3 inhibitor-tested in an early phase 2a randomised clinical trial in patients with COVID-19 pneumonia and impaired respiratory function**. Infection. 2022. 14:1–14. PMID: 36104613. IF: 7.455. doi: 10.1007/s15010-022-01904-w.

Domínguez-Ortega J, Sánchez-García S, Melero Moreno C. **COVID-19 and Severe Asthma: Reflections and Future Solutions [Letter]**. J Asthma Allergy.15:525-527. 2022. PMID: 35495875. IF: 3.027. doi: 10.2147/JAA.S356234

Casas-Maldonado F, Álvarez-Gutiérrez FJ, Blanco-Aparicio M, Domingo- Ribas C, Cisneros-Serrano C, Soto-Campos G, Román-Bernal B, González- Barcala FJ. **Monoclonal antibody treatment for severe uncontrolled asthma in Spain: analytical map**. J Asthma 59 (10): 1997-2007. 2022. PMID: 34503370. IF: 2.00. doi: 10.1080/02770903.2021.1978483.

Rudilla D, Beceiro MJ, Alonso T, Oliver A, Soriano J, Valenzuela C, Ancochea J. **Psychological Profile of Patients Diagnosed With Idiopathic Pulmonary Fibrosis**. Arch Bronconeumol. 58(2):191-193. 2022. PMID: 34045108. IF: 6.33. doi: 10.1016/j.arbres.2021.04.025.

LINE 1.8 ›› INFLAMMATORY RESPONSE IN HEPATIC DISEASES

GROUP 24

Head of laboratory: Majano Rodríguez, Pedro Lorenzo

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

Line 1.8 Inflammatory response in hepatic diseases

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.

GROUP MEMBERS

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MAJOR GRANTS

Laserna Mendieta, Emilio José. Identificación de polimorfismos genéticos en sangre predictivos de la respuesta al tratamiento con inhibidores de la bomba de protones en pacientes con esofagitis eosinofílica. PI21/00579. ISCIII. 2022-2024.

PUBLICATIONS

Prieto Aparicio JF, Caldas Álvarez M, Herranz Pérez R, Gordillo Vélez CH, Santander Vaquero C. **Intestinal amyloidosis: a diagnostic challenge.** Rev Esp Enferm Dig 114 (12). 2022. PMID: 35638766. IF: 2,39. DOI: 10.17235/reed.2022.8934/2022.

Santander C, FACME. **Recertification model of the Spanish scientific- medical societies. FACME.** Rev Esp Enferm Dig 114 (10):2022. PMID: 35770537. IF: 2,39. DOI: 10.17235/reed.2022.9029/2022.

Resina E, Donday MG, Martínez Domínguez SJ, Laserna Mendieta EJ, Lanas Á, Lucendo AJ, Sánchez Luengo M, Alcaide N, Fernández Salazar L, De La Peña Negro L, Bujanda L, Arbulo MG, Alcedo J, Pérez Aísa A, Rodríguez R, Hermida S, Brenes Y, Nyssen OP, Gisbert JP. **Evaluation of a New Monoclonal Chemiluminescent Immunoassay Stool Antigen Test for the Diagnosis of Helicobacter pylori Infection: A Spanish Multicentre Study.** J Clin Med 11 (17) 2022. PMID: 36079007. IF: 4,96. DOI: 10.3390/jcm11175077.

Soleto I, Fernández Tomé S, Mora Gutiérrez I, Baldan Martin M, Ramírez C, Santander C, Moreno Monteagudo JA, Casanova MJ, Casals F, Casabona S, Becerro I, Chaparro M, Bernardo D, Gisbert JP. **Differential Effects of Anti-TNFa and Anti-a4ß7 Drugs on Circulating Dendritic Cells Migratory Capacity in Inflammatory Bowel Disease.** Biomedicines 10 (8). 2022. PMID: 36009431. IF: 4,76. DOI: 10.3390/biomedicines10081885.

Resina Sierra E, García Gil JC, Rosell Alayza A,Ezquerra Durán A, Muñoz González R, González Moreno L, Caldas M, Santander Vaquero C. **From metastasis to the primary tumor: Giant liver metastasis from a pancreatic neuroendocrine tumor.** Rev Esp Enferm Dig 114 (8): 2022. PMID: 35255705. IF: 2,39. DOI: 10.17235/reed.2022.8758/2022.

Santander Vaquero C. **Recertification of the specialty. Recognition of the professional prestige of the doctor.** Rev Esp Enferm Dig. PMID: 35770583. IF: 2, 38. DOI: 10.17235/reed.2022.9022/2022.

Navarro Pilar, Laserna Mendieta Emilio J, Casabona Sergio, Savarino Edoardo, Perez Fernandez Maria Teresa, Ghisa Matteo, Perez Martinez Isabel, Guagnozzi Danila, Perello Antonia, Guardiola Arevalo Antonio, Racca Francesca, Betore Elena, Blas Jhon Leonardo, Krarup Anne Lund, Martin Dominguez Veronica, Maniero Daria, Suarez Adolfo, Llerena Castro Ronald, de la Pena negro Luisa, Navacerrada Alicia Granja, Pellegatta Gaia, Alcedo Javier, de Hurtado Mendoza Guena Lonore, Feo Ortega Sara, Barrio Jesus, Gutierrez Junquera Carolina, Fernandez Sonia, de la Riva Susana, Naves Juan, Carrion Silvia et al. **Accurate and timely diagnosis of Eosinophilic Esophagitis improves over time in Europe. An analysis of the EoE CONNECT Registry**. United European Gastroenterol J 10 (5). 2022. PMID: 35578565. IF: 6,87. DOI: 10.1002/ueg2.12240.

Miehlke Stephan, Schlag Christoph, Lucendo Alfredo J, Biedermann Luc, Vaquero Cecilio Santander, Schmoecker Christoph, Hayat Jamal, Hruz Petr, Ciriza de los Rios Constanza, Jan Bredenoord Albert, Vieth Michael, Schoepfer Alain, Attwood Stephen, Mueller Ralph, Burrack Sarah, Greinwald Roland, Straumann Alex, Int EOS 2 Study Grp. **Budesonide orodispersible tablets for induction of remission in patients with active eosinophilic oesophagitis: A 6-week open-label trial of the EOS-2 Programme**. United European Gastroenterol J 10 (3). 2022. PMID: 35412032. IF: 6,87. DOI: 10.1002/ueg2.12220.

Lucendo Alfredo J, Santander Cecilio, Savarino Edoardo, Guagnozzi Danila, Perez Martinez Isabel, Perello Antonia, Guardiola Arevalo Antonio, Barrio Jesus, Elena Betore Glaria Maria, Gutierrez Junquera Carolina, Ciriza de los Rios Constanza, Racca Francesca, Fernandez Sonia, Blas Jhon Leonardo, Lund Krarup Anne, de la Riva Susana, Naves Juan E, Carrion Silvia, Rodriguez Oballe Juan Armando, Garcia Morales Natalia, Tamarit Sebastian Sonsoles, Navarro Pilar, Arias Angel, Laserna Mendieta Emilio J, EUREOS EoE CONNECT Grp. **EoE CONNECT, the European Registry of Clinical, Environmental, and Genetic Determinants in Eosinophilic Esophagitis: rationale, design, and study protocol of a large-scale epidemiological study in Europe**. Therap Adv Gastroenterol 15. 2022. PMID: 35126668. IF: 4,80. DOI: 10.1177/17562848221074204.

GROUP 23

Head of laboratory: García Buey, Luisa Consuelo

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

Line 1.8 Inflammatory response in hepatic diseases

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 immune 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.

GROUP MEMBERS

- Felipe de la Morena López
- Yolanda Real Martínez
- Leticia González Moreno
- Jorge Mendoza Jiménez-Ridruejo
- María Caldas Álvarez

PUBLICATIONS

Prieto Aparicio JF, Caldas Álvarez M, Herranz Pérez R, Gordillo Vélez CH, Santander Vaquero C. **Intestinal amyloidosis: a diagnostic challenge.** Rev Esp Enferm Dig 114 (12). 2022. PMID: 35638766. IF: 2,39. DOI:10.17235/reed.2022.8934/2022.

Ezquerra Durán A, Gutiérrez Cobos A, García Buey L. **Healing of chronic hepatitis delta relapsing to pegylated interferon with tenofovir.** Med Clin 159 (5): 2022. PMID: 35659423. IF: 3,20. DOI: 10.1016/j.medcli.2022.02.017.

Resina Sierra E, García Gil JC, Rosell Alayza A, Ezquerra Durán A, Muñoz González R, González Moreno L, Caldas M, Santander Vaquero C. **From metastasis to the primary tumor: Giant liver metastasis from a pancreatic neuroendocrine tumor.** Rev Esp Enferm Dig 114 (8): 2022. PMID: 35255705. IF: 2,39. DOI: 10.17235/reed.2022.8758/2022.

Gutiérrez Rojas L, de la Gándara Martín JJ, García Buey L, Uriz Otano JI, Mena A, Roncero C. **Patients with severe mental illness and hepatitis C virus infection benefit from new pangenotypic direct-acting antivirals: Results of a literature review.** Gastroenterol Hepatol. PMID: 35718017. DOI: 10.1016/j.gastrohep.2022.06.001.

Nyssen Olga P, Vaira Dino, Saracino Ilaria Maria, Fiorini Giulia, Caldas Maria, Bujanda Luis, Pellicano Rinaldo, Keco Huerga Alma, Pabon Carrasco Manuel, Susanibar Elida Oblitas, Di Leo Alfredo, Losurdo Giuseppe, Perez Aisa Angeles, Gasbarrini Antonio, Boltin Doron, Smith Sinead, Phull Perminder, Rokkas Theodore, Lamarque Dominique, Cano Catala Anna, Puig Ignasi, Megraud Francis, O'Morain Colm, Gisbert Javier P. **Experience with Rifabutin-Containing Therapy in 500 Patients from the European Registry on Helicobacter pylori Management (Hp-EuReg)**. J Clin Med 11 (6). 2022. PMID: 35329984. IF: 4,96. DOI: 10.3390/jcm11061658.

Marinero Martínez Lázaro A, Girón Moreno RM, Casals Seoane F, Cano Valderrama Ó, García Buey L. **Cystic fibrosis with liver involvement in adults has a benign course. Results from a tertiary referral centre cohort.** Rev Esp Enferm Dig 114. 2022. PMID: 36353964. IF: 2,39.

García-Fraile LJ, García-Buey L, Alonso Cerezo C, Sanz Sanz J, de Los Santos Gil I. **Evolution of HCV associated porphyria cutanea tarda after HCV sustained virologic response by direct acting antivirals.** Gastroenterol Hepatol 45 (4): 249-255. 2022. PMID: 34562521. IF: 5,8672. doi: 10.1016/j.gastrohep.2021.09.001.

Marinero Martínez-Lázaro A, Girón Moreno RM, Casals Seoane F, Cano- Valderrama Ó, García-Buey L. **Cystic fibrosis with liver involvement in adults has a benign course. Results from a tertiary referral centre cohort**. Rev Esp Enferm Dig 10: 114. 2022. PMID: 36353964. IF: 2,393. doi: 10.17235/reed.2022.9289/2022.

Ezquerra A, Martínez B, García-Buey L**. Invasive listeriosis in a patient with autoimmune hepatitis on glucocorticosteroid therapy**. Med Clin (Barc) 7: 158 (1): 39. 2022. PMID: 34074475. IF: 3,20. doi: 10.1016/j.medcli.2021.03.015.

Ezquerra-Durán A, Gutiérrez-Cobos A, García-Buey L. **Healing of chronic hepatitis delta relapsing to pegylated interferon with tenofovir**. Med Clin (Barc). 9: 159(5): e32. 2022. PMID: 35659423. IF: 3,205. doi: 10.1016/j.medcli.2022.02.017.

Gutiérrez-Rojas L, de la Gándara Martín JJ, García Buey L, Uriz Otano JI, Mena Á, Roncero C. **Patients with severe mental illness and hepatitis C virus infection benefit from new pangenotypic direct- acting antivirals: Results of a literature review**. Gastroenterol Hepatol 17: S0210-5705(22)00164-9. 2022. PMID: 36464081. IF: 5,867. doi: 10.1016/j.gastrohep.2022.11.007.

Pardilla Moraleda FJ, Serrano Pardo R, Del Campo Del Val L, García-Buey L. **An unusual cause of fulminant hepatic failure: Metastatic infiltration by infiltrating ductal carcinoma of the breast.** Gastroenterol Hepatol. 1: S0210-5705(22)00279-5. 2022. PMID: 36464081. IF: 5,867. doi: 10.1016/j.gastrohep.2022.11.007.

Nyssen OP, Vaira D, Pérez Aísa Á, Rodrigo L, Castro-Fernandez M, Jonaitis L, Tepes B, Vologzhanina L, Caldas M, Lanas A, Lucendo AJ, Bujanda L, Ortuño J, Barrio J, Huguet JM, Voynovan I, Lasala JP, Sarsenbaeva AS, Fernandez-Salazar L, Molina-Infante J, Jurecic NB, Areia M, Gasbarrini A, Kupčinskas J, Bordin D, Marcos-Pinto R, Lerang F, Leja M, Buzas GM, Niv Y, Rokkas T, Phull P, Smith S, Shvets O, Venerito M, Milivojevic V, Simsek I, Lamy V, Bytzer P, Boyanova L, Kunovský L, Beglinger C, Doulberis M, Marlicz W, Goldis A, Tonkić A, Capelle L, Puig I, Megraud F, Morain CO, Gisbert JP; European Registry on Helicobacter pylori Management Hp-EuReg Investigators. **Empirical Second-Line Therapy in 5000 Patients of the European Registry on Helicobacter pylori Management (Hp-EuReg)**. Clin Gastroenterol Hepatol 20 (10): 2243-2257. 2022. PMID: 34954341. IF: 11,382. doi: 10.1016/j.cgh.2021.12.025

Jiménez-Heffernan JA, Gordillo CH, Caldas M, Valdivia-Mazeyra M, Adrados M**. Cytological features in ascitic fluid of well-differentiated papillary mesothelial tumour**. Cytopathology 33 (2): 253-256. 2022. PMID: 34806791. IF: 1,376. doi: 10.1111/cyt.13078.

Resina Sierra E, García-Gil JC, Rosell Alayza A, Ezquerra Durán A, Muñoz González R, González Moreno L, Caldas M, Santander Vaquero C. **From metastasis to the primary tumor: Giant liver metastasis from a pancreatic neuroendocrine tumor**. Rev Esp Enferm Dig 114 (8): 498-499. 2022. PMID: 35255705. IF: 2,39. doi: 10.17235/reed.2022.8758/2022

Nyssen OP, Vaira D, Saracino IM, Fiorini G, Caldas M, Bujanda L, Pellicano R, Keco-Huerga A, Pabón-Carrasco M, Oblitas Susanibar E, Di Leo A, Losurdo G, Pérez-Aísa Á, Gasbarrini A, Boltin D, Smith S, Phull P, Rokkas T, Lamarque D, Cano-Català A, Puig I, Mégraud F, O'Morain C, Gisbert JP. **Experience with Rifabutin-Containing Therapy in 500 Patients from the European Registry on Helicobacter pylori Management (Hp-EuReg).** J Clin Med 16: 11 (6): 1658. 2022. PMID: 35329984. IF: 4,9611. doi: 10.3390/jcm11061658

Prieto Aparicio JF, Caldas Álvarez M, Herranz Pérez R, Gordillo Vélez CH, Santander Vaquero C. **Intestinal amyloidosis: a diagnostic challenge**. Rev Esp Enferm Dig 114 (12): 752. 2022. PMID: 35638766. IF: 2,39. doi: 10.17235/reed.2022.8934/2022.

LINE 1.9 ›› MECHANISMS AND MEDIATORS OF ENDOCRINE DISEASES

GROUP **25**

Head of laboratory: Marazuela Azpíroz, Mónica

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

Line 1.9 Mechanisms and mediators of endocrine diseases.

RESEARCH INTEREST

Our current and future work involve different research fields in endocrine diseases. We are studying the role of immunoregulatory molecules in patients with autoimmune thyroid diseases (AITD) including Hashimoto's thyroiditis (HT), Graves' disease (GD) and Graves' ophthalmopathy (GO). During the last years, we have discovered that patients with AITD have altered populations of regulatory T cells (Treg), augmented Th17 cells, a defective production of Tr1 regulatory cells and abnormalities in Natural Killer cell 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). We also studied additional regulatory molecules in these patients, such as VIP (Scientific Reports 2020; 10:13018). These abnormalities in immunoregulatory molecules may contribute to the pathogenesis and/or auto-perpetuation of AITD.

We have also studied the expression of miRNAs (miRNome) in thyroid samples from patients with AITD and healthy controls and the potential use of selected miRNAs as biomarkers in serum samples from AITD patients. Our results in this field included characterizing the role of microvesicles (MVs) and microRNAs in the pathogenesis of AITD. We have demonstrated that MVs 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, 100:12). Furthermore, we have developed a 5-miRNA signature that could be an independent risk factor for developing AITD and for predisposition to a worse clinical picture in GD patients (J Clin Endocrinol Metab. 2018 Mar 1;103(3):1139-1150.)

We also participated in a collaborative project to study immunoregulatory molecules and miRNAs in different immune-mediated inflammatory diseases (IMID) including rheumatoid arthritis, psoriasis, inflammatory bowel disease and AITD, with the aim of trying to find new predictive biomarkers (immunoregulatory molecules) of IMID severity and responsiveness to biological therapies. We have identified a signature model that can contribute to an improvement in the detection of severe IMID forms, and also to reveal common events present in several IMIDs, thereby studying possible links between the different types of diseases (Journal of Autoimmunity 111 (2020) 102472).

In the last years, we have been integrating the power of omics in characterizing new clinical approaches and susceptibility pathways in AITD. We have carried out an integration study of miRNAs and mRNAs in order to search for new candidate genes and miRNAs to be used as potential biomarkers and / or therapeutic targets. The results of this project led to the study new susceptibility pathways in AITD such as ciliogenesis. We observed, for the first time, the important role in the etiopathogenesis of AITD played by genes involved in cilia regulation (EBioMedicine. 2019 Dec;50:329-342). Furthermore, we have discovered the important role of HDAC9 in the altered immune regulatory mechanisms observed in patients with AITD (J Clin Endocrinol Metab. 2021 Oct 21;106(11):3213-3227). Our next approach is to characterize the cell type specific transcriptomic heterogeneity and regulatory networks in thyrocytes

and infiltrating T lymphocytes in AITD thyroid tissue, taking advantage of digital pathology approaches such as Spatial Trancriptomics.

Another area of investigation of the group is the study of mechanisms resulting in evasion of immune attack in gastroentero-pancreatic neuroendocrine tumors (GEP-NETs). We have found that PD-1 expression is detected in a small but significant proportion of 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 specific mechanisms that increase nutrient uptake, such as LAT-1 and GLUT-1, are increased in GEP-NETs, which might be related to their proliferation and metastatic capacity (Cancers 2020, 12, 2968). Our group also leads the Spanish Molecular Registry of Pituitary Adenomas (REMAH) with 1,400 patients registered. 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 (Endocr Relat Cancer. 2020 Jun;27(6):375-389). Deepening into the knowledge of these molecular patterns will enable to better understand this condition and adopt more appropriate decisions on the treatment and follow-up of pituitary tumors. Furthermore, the identification of new molecules using Tissue Microarrays in these tumors will allow us testing the effect of new treatments, thus increasing the range of adenomas that can be treated pharmacologically.

In summary, our group has an extensive and relevant research trajectory and a high number of scientific publications in impact journals in the aforementioned areas of knowledge. Likewise, our research has an important basic-clinical translational component, based on a global approach to the study of the aforementioned endocrine disorders, covering not only their most basic aspects, but also those related to their pathophysiology, diagnosis and treatment.

GROUP MEMBERS

- Alicia Justel Enriquez
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- Ana María Ramos Levi
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MAJOR GRANTS

Marazuela Azpiroz, Mónica. Martínez Hernández, Rebeca. Integromics in Autoimmune Thyroid Diseases: Combining miRNome, transcriptome and single cell analysis to characterize new clinical approaches and susceptibility pathways in AITD. PI19/00584. ISCIII. 2020-2022.

Martínez Hernández, Rebeca. Marazuela Azpiroz, Mónica. Uncovering the molecular architecture of Autoimmune Thyroid Diseases by spatial transcriptomics. PI22/01404. Instituto de Salud Carlos III (ISCIII). 2023- 2025.

Marazuela Azpiroz, Mónica. Robledo, Mercedes. Al-Shahrour, Fátima. Valderrabano, Pablo. Estudio de la heterogeneidad celular, molecular y del entorno inmunológico en las patologías tiroideas: cáncer y enfermedad autoinmune-iTIRONET-CM. P2022/BMD-7379. Comunidad de Madrid. 2023-2026.

Marazuela Azpiroz, Mónica. Puig, Manel. ACROMICS: next-generation precision medicine in the diagnosis and treatment of Acromegaly. PMP22/00021. Instituto de Salud Carlos III (ISCIII). 2023-2025.

Martínez Hernández, Rebeca. El cilio primario en adenomas hipofisarios y su asociación con agresividad. IPI/2022/N5. SENDIMAD ("VI convocatoria de Beca a la investigación clínica y básica en Endocrinología y Nutrición"). 2022.

Martínez Hernández, Rebeca. D-Axoneme: Método in vitro para el diagnóstico y prognosis de tumores neuroendocrinos hipofisarios. 4033-22. Fundación para la innovación y la prospectiva en la salud en España (FIPSE). 2022.

Marazuela Azpiroz, Mónica. Integromics in Autoimmune Thyroid Diseases: Combining miRNome, transcriptome and single cell analysis to characterize new clinical approaches and susceptibility pathways in AITD. PI19/00584. Instituto de Salud Carlos III (ISCIII). 2020-2022.

PUBLICATIONS

Ramos Leví AM, Collado G, Marazuela M. **Seasonality of month of birth in patients with autoimmune endocrine diseases: A systematic review.** Endocrinol Diabetes Nutr 69 (10). 2022. PMID: 36526353. IF: 1,83. DOI: 10.1016/j.endien.2022.11.017

Ramos Leví AM, Fernández Pombo A, García Fontao C, Gómez Vázquez E, Cantón Blanco A, Martínez Olmos MÁ, Andújar Plata P, Mariño PB, Rodríguez Carnero MG, Villar Taibo R. **Gestational weight gain influences neonatal outcomes in women with**

obesity and gestational diabetes. Endocrinol Diabetes Nutr 69 (10). 2022. PMID: 36526355. IF: 1,83. DOI: 10.1016/j.endien.2022.11.018

Sebastian Valles F, Carrero NSD, Rodriguez Laval V, Martinez Hernandez R, Serrano Somavilla A, Knott Torcal C, de Nova JLM, Martin Perez E, Marazuela M, Sampedro Nunez MA. **Impact of Change in Body Composition during Follow-Up on the Survival of GEP-NET**. Cancers 14(21). 2022. PMID: 36358607. IF: 6,58. DOI: 10.3390/cancers14215189

Ramos Levi A, Barabash A, Valerio J, García de la Torre N, Mendizabal L, Zulueta M, de Miguel MP, Diaz A, Duran A, Familiar C, Jimenez I, Del Valle L, Melero V, Moraga I, Herraiz MA, Torrejon MJ, Arregi M, Simón L, Rubio MA, Calle Pascual AL. **Genetic variants for prediction of gestational diabetes mellitus and modulation of susceptibility by a nutritional intervention based on a Mediterranean diet.** Front Endocrinol 13. 2022. PMID: 36313769. IF: 6,06. DOI: 10.3389/fendo.2022.1036088.

Araujo Castro M, Marazuela M. **Cushing´s syndrome due to bilateral adrenal cortical disease: Bilateral macronodular adrenal cortical disease and bilateral micronodular adrenal cortical disease.** Front. Endocrinol 13. 2022. PMID: 35992106. IF: 6,06. DOI: 10.3389/fendo.2022.913253.

Lamana A, Castro Vazquez D, De La Fuente H, Trigueros Martinez A, Martinez Hernandez R, Revenga M, Villanueva Romero R, Llamas Velasco M, Chicharro P, Juarranz Y, Marazuela M, Sales Sanz M, Garcia Vicuna R, Tomero E, Gonzalez Alvaro I, Martinez C, Gomariz RP. **VIP/VPAC Axis Expression in Immune-Mediated Inflammatory Disorders: Associated miRNA Signatures**. Int J Mol Sci 23 (15). 2022. PMID: 35955723. IF: 6,21. DOI: 10.3390/ijms23158578

Guadalajara H, Yiasemidou M, Muñoz de Nova JL, Sedman P, Fernandez Gonzalez S, Maslekar S, Recarte Rico M, Egan R, Juez LD, Riyad K, García Septiem J, Lockwood S, Galindo Jara P, Giorga A, García Virosta M, Hance J, Lobo Martínez E, Martín Pérez E, Howitt A, Jayne D, Chetter I, García Olmo D, PIACO Collaboration Group. **The international PIACO study: pattern of surgical approaches for acute surgical pathologies in Spain versus UK. Was conservative treatment and open surgery during COVID-19 the way to go?** BJS Open 6 (4). 2022. PMID: 35939374. IF: 3,88. DOI: 10.1093/bjsopen/zrac089

Gil Joan, Marques Pamies Montserrat, Sampedro Miguel, Webb Susan M, Serra Guillermo, Salinas Isabel, Blanco Alberto, Valassi Elena, Carrato Cristina, Pico Antonio, Garcia Martinez Araceli, Martel Duguech Luciana, Sardon Teresa, Simo Servat Andreu, Biagetti Betina, Villabona Carles, Camara Rosa, Fajardo Montanana Carmen, Alvarez Escola Cristina, Lamas Cristina, Alvarez Clara V, Bernabeu Ignacio, Marazuela Monica, Jorda Mireia, Puig Domingo Manel. **Data mining analyses for precision medicine in acromegaly: a proof of concept**. Sci Rep 12 (1). 2022. PMID: 35643771. IF: 5,00. DOI: 10.1038/s41598-022-12955-2

Muñoz de Nova JL, Hernando J, Sampedro Núñez M, Vázquez Benítez GT, Triviño Ibáñez EM, Del Olmo García MI, Barriuso J, Capdevila J, Martín- Pérez E. **Management of incidentally discovered appendiceal neuroendocrine tumors after an appendicectomy**. World J. Gastroenterol.28. (13):2022. PMID: 35645544. IF: 5,37. DOI: 10.3748/wjg.v28.i13.1304

Araujo Castro Marta, Garcia Centeno Rogelio, Robles Lazaro Cristina, Parra Ramirez Paola, Gracia Gimeno Paola, Martin Rojas Marcos Patricia, Tome Fernandez Ladreda Mariana, Percovich Hualpa Juan Carlos, Sampedro Nunez Miguel, Lopez Garcia Maria-Carmen, Lamas Cristina, Alvarez Escola Cristina, Calatayud Gutierrez Maria, Blanco Carrera Concepcion, de Miguel Novoa Paz, Valdes Gallego Nuria, Hanzu Felicia, Marazuela Monica, Mora Porta Mireia, Minguez Ojeda Cesar, Gomez Muriel Isabel Garcia, Escobar Morreale Hector F, Valderrabano Pablo. **Predictive model of pheochromocytoma based on the imaging features of the adrenal tumours**. Sci Rep 12 (1). 2022. PMID: 35177692. IF: 5,00. DOI: 10.1038/s41598-022-06655-0

Gil Joan, Marques Pamies Montserrat, Valassi Elena, Garcia Martinez Araceli, Serra Guillermo, Hostalot Cristina, Fajardo Montanana Carmen, Carrato Cristina, Bernabeu Ignacio, Marazuela Monica, Rodriguez Lloveras Helena, Camara Rosa, Salinas Isabel, Lamas Cristina, Biagetti Betina, Simo Servat Andreu, Webb Susan M, Pico Antonio, Jorda Mireia, Puig Domingo Manel, REMAH Investigators. **Implications of Heterogeneity of Epithelial- Mesenchymal States in Acromegaly Therapeutic Pharmacologic Response**. Biomedicines 10 (2). 2022. PMID: 35203668. IF: 4,76. DOI: 10.3390/biomedicines10020460.

Pla Peris Begona, Arranz Martin Alfonso, Ballesteros Garcia Anabel, Sebastian Valles Fernando, Marazuela Azpiroz Monica. **Alpelisib-Induced Diabetes Mellitus: Case Report, Pharmacodynamics and Management Considerations**. Front Endocrinol 13. 2022. PMID: 35178031. IF: 6,06. DOI: 10.3389/fendo.2022.802612

GROUP 26

Head of laboratory: Argente Oliver, Jesús

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

Line 1.10 Children's development (obesity and growth)

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 outcome to weight gain. The implications of weight gain and abnormal circulating levels of leptin and insulin have also been implicated in increased susceptibility to neurodegenerative diseases, with this susceptibility 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.

GROUP MEMBERS

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MAJOR GRANTS

Chowen, Julie Ann / Frago Fernández, Laura María. Cross-talk entre los astrocitos hipotalámicos y el tejido adiposo perivascular en el metabolismo energético y la función cardiovascular: Impacto de las

modificaciones en la dieta. FFU2017-82565-C2-1-R. Ministerio de Ciencia, Innovación y Universidades. 2018-2022.

Argente Oliver, Jesús. Estudio de nuevos factores reguladores identificados en el sistema GH/IGF: Implicaciones en patología humana, análisis de los mecanismos involucrados y desarrollo de nuevas terapias potenciales. PI19/00166. ISCIII. 2020-2022.

Chowen Julie Ann/ Frago Fernández, Laura María. Astrocitos, exosomas y miRNAs en la respuesta diferencial de los machos y hembras a ácidos grasos específicos. Ministerio de Ciencia e Innovación. PID2021-122653OB- I00. 2022-2025.

PUBLICATIONS

Güemes M, Martín Rivada Á, Bascuas Arribas M, Andrés Esteban EM, Molina Angulo B, Pozo Román J, Argente J. **Endocrine Sequelae in 157 Pediatric Survivors of Hematopoietic Stem Cell Transplantation (HSCT).** J Endocr Soc 7 (2). 2022. PMID: 36532360. DOI: 10.1210/jendso/bvac183

Escudero García J, Martín Rivada Á, Uribe Posada A, Sanz Santiago V, Argente J, Martos Moreno GÁ. **Carbohydrate metabolism impairment in children and adolescents with cystic fibrosis.** Endocrinol Diabetes Nutr 69 (8). 2022. PMID: 36347795. IF: 1,83. DOI: 10.1016/j.endien.2021.08.009.

Martín Rivada Á, Guerra Cantera S, Campillo Calatayud A, Andrés Esteban EM, Sánchez Holgado M, Martos Moreno GÁ, Pozo J, Güemes M, Soriano Guillén L, Pellicer A, Oxvig C, FrystykJ, Chowen JA, Barrios V, Argente J. **Pappalysins and Stanniocalcins and Their Relationship With the Peripheral IGF Axis in Newborns and During Development.** J Clin Endocrinol Metab 107 (10). 2022. PMID: 35902207. IF: 6,13. DOI: 10.1210/clinem/dgac453.

Palomino OM, Giordani V, Chowen J, Alfonso SF, Goya L. **Physiological Doses of Oleic and Palmitic Acids Protect Human Endothelial Cells from Oxidative Stress.** MOLECULES 27 (16). 2022. PMID: 36014457. IF: 4,93. DOI: 10.3390/molecules27165217.

Freire Regatillo A, Diaz Pacheco S, Frago LM, Arévalo MÁ, Argente J, Garcia Segura LM, de Ceballos

ML, Chowen JA. **Sex Differences in Hypothalamic Changes and the Metabolic Response of TgAPP Mice to a High Fat Diet.** Front Neuroanat 16. 2022. PMID: 35958733. IF: 3,54. DOI:10.3389/fnana.2022.910477

Dahir KM, Seefried L, Kishnani PS, Petryk A, Högler W, Linglart A, Martos Moreno GÁ, Ozono K, Fang S, Rockman Greenberg C. **Clinical profiles of treated and untreated adults with hypophosphatasia in the Global HPP Registry.** Orphanet J Rare Dis 17 (1). 2022. PMID: 35854311. IF: 4,30. DOI: 10.1186/s13023-022-02393-8

Barrios V, Guerra Cantera S, Martín Rivada Á, Canelles S, Campillo Calatayud A, Arilla Ferreiro E, Frago LM, Chowen JA, Argente J. **Chronic Central Leptin Infusion Promotes an Anti-Inflammatory Cytokine Profile Related to the Activation of Insulin Signaling in the Gastrocnemius of Male Rats.** Biomedicines 10 (7). 2022. PMID: 35884769. IF: 4,76. DOI: 10.3390/biomedicines10071465

Teare H, **Argente J**, Dattani M, Leger J, Maghnie M, Sherlock M, Ali G-C, Francombe J, Marjanovic S. **Challenges and improvement needs in the care of patients with central diabetes insipidus**. Orphanet J Rare Dis 17 (1): 58-58. 2022. PMID: 35172866. IF: 4,30. DOI: 10.1186/s13023-022-02191-2.

Fernandez Felipe Jesus, Valencia Avezuela Maria, Merino Beatriz, Somoza Beatriz, Cano Victoria, Sanz Martos Ana B, Frago Laura M, Fernandez Alfonso Maria S, Ruiz Gayo Mariano, Chowen Julie A. **Effects of saturated versus unsaturated fatty acids on metabolism, gliosis, and hypothalamic leptin sensitivity in male mice**. Nutr Neurosci 26 (2). 2022. PMID: 35125071. IF: 4,06. DOI: 10.1080/1028415X.2022.2029294

Haqq AM, Chung WK, Dollfus H, Haws RM, Martos-Moreno GÁ, Poitou C, Yanovski JA, Mittleman RS, Yuan G, Forsythe E, Clément K, Argente J. **Efficacy and safety of setmelanotide, a melanocortin-4 receptor agonist, in patients with Bardet-Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial with an open-label period**. Lancet Diabetes Endocrinol. 2022. PMID: 36356613. IF: 44.867. DOI: 10.1016/S2213-8587(22)00277-7.

Grange LJ, Reynolds JJ, Ullah F, Isidor B, Shearer RF, Latypova X, Baxley RM, Oliver AW, Ganesh A, Cooke SL, Jhujh SS, McNee GS, Hollingworth R, Higgs MR, Natsume T, Khan T, Martos-Moreno GÁ, Chupp S, Mathew CG, Parry D, Simpson MA, Nahavandi N, Yüksel Z, Drasdo M, Kron A, Vogt P, Jonasson A, Seth SA, Gonzaga-Jauregui C, Brigatti KW, Stegmann APA, Kanemaki M, Josifova D, Uchiyama Y, Oh Y, Morimoto A, Osaka H, Ammous Z, Argente J, Matsumoto N, Stumpel CTRM, Taylor AMR, Jackson AP, Bielinsky AK, Mailand N, Le Caignec C, Davis EE, Stewart GS.**Pathogenic variants in SLF2 and SMC5 cause segmented chromosomes and mosaic variegated hyperploidy**.Nat Commun. 2022. PMID: 36333305. IF: 17.694. DOI: 10.1038/s41467-022-34349-8

Akin L, Rizzoti K, Gregory LC, Corredor B, Le Quesne Stabej P, Williams H, Buonocore F, Mouilleron S, Capra V, McGlacken-Byrne SM, Martos-Moreno GÁ, Azmanov DN, Kendirci M, Kurtoglu S, Suntharalingham JP, Galichet C, Gustincich S, Tasic V, Achermann JC, Accogli A, Filipovska A, Tuilpakov A, Maghnie M, Gucev Z, Gonen ZB, Pérez-Jurado LA, Robinson I, Lovell-Badge R, Argente J, Dattani MT. **Pathogenic variants in RNPC3 are associated with hypopituitarism and primary ovarian insufficiency**. Genet Med. 2022. PMID: 34906446. IF: 8.864. DOI: 10.1016/j.gim.2021.09.019

Soriano-Guillén L, Tena-Sempere M, Seraphim CE, Latronico AC, Argente J. **Precocious sexual maturation: Unravelling the mechanisms of pubertal onset through clinical observations**.J Neuroendocrinol. 2022. PMID: 33904190. IF: 3.870. DOI: 10.1111/jne.12979.

Rivera P, Guerra-Cantera S, Vargas A, Díaz F, García-Úbeda R, Tovar R, Ramírez-López MT, Argente J, de Fonseca FR, Suárez J, Chowen JA.**Maternal hypercaloric diet affects factors involved in lipid metabolism and the endogenous cannabinoid systems in the hypothalamus of adult offspring: sex-specific response of astrocytes to palmitic acid and anandamide**. Nutr Neurosci. 2022. PMID: 32954972. IF: 4.062. DOI: 10.1080/1028415X.2020.1821519.

LINE 1.11 ›› METABOLIC SYNDROME AND VASCULAR RISK

GROUP 5

Head of laboratory: García Monzón, Carmelo

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

Line 1.11 Metabolic syndrome and vascular risk

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 seek three main research lines for the next five years.

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.

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.

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 acions. 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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MAJOR GRANTS

García Monzón, Carmelo/ Landete Rodríguez, Pedro. Caracterización de los mediadores moleculares clave de la enfermedad hepática grasa metabólica asociada al síndrome de apnea obstructiva del sueño: Implicaciones diagnósticas y terapéuticas. PI20/00837. ISCIII. 2021-2023.

García Monzón, Carmelo. Plan estratégico multinivel para la microeliminación de la infección por el virus de la hepatitis C en un área sanitaria de la Comunidad de Madrid. Gilead. 2021-2023.

PUBLICATIONS

Patil NP, Gómez Hernández A, Zhang F, Cancel L, Feng X, Yan L, Xia K, Takematsu E, Yang EY, Le V, Fisher ME, Gonzalez Rodriguez A, Garcia Monzon C, Tunnell J, Tarbell J, Linhardt RJ, Baker AB. **Rhamnan sulfate reduces atherosclerotic plaque formation and vascular inflammation.** BIOMATERIALS 291. 2022. PMID: 36332287. IF: 15,30. DOI: 10.1016/j.biomaterials.2022.121865.

Landete P, Prieto Romo JI, Giacomini F. **Experience on the Management of Patients with Asthma or Chronic Obstructive Pulmonary Disease During the COVID-19 Pandemic: the NEUMOBIAL Study.** Adv Ther 39 (11). 2022. PMID: 36114950. IF: 4,07. DOI: 10.1007/s12325-022-02313-z.

Valencia Ines, Vallejo Susana, Dongil Pilar, Romero Alejandra, San Hipolito Luengo Alvaro, Shamoon Licia, Posada Maria, Garcia Olmo Damian, Carraro Raffaelle, Erusalimsky Jorge D, Romacho Tania, Peiro Concepcion, Sanchez Ferrer Carlos F. **DPP4 Promotes Human Endothelial Cell Senescence and Dysfunction via the PAR2-COX-2-TP Axis and NLRP3 Inflammasome Activation**. Hypertension 79 (7). 2022. PMID: 35477273. IF: 9,90. DOI: 10.1161/HYPERTENSIONAHA.121.18477.

Barahona Ines, Rada Patricia, Calero Perez Silvia, Grillo Risco Ruben, Pereira Laura, Carmen Soler Vazquez M, Maria Lalglesia Laura, Moreno Aliaga Maria J, Herrero Laura, Serra Dolors, Garcia Monzon Carmelo, Gonzalez Rodriguez Agueda, Balsinde Jesus, Garcia Francisco, Pilar Valdecantos M, Valverde Angela M. **Ptpn1 deletion protects oval cells against lipoapoptosis by favoring lipid droplet formation and dynamics**. Cell Death Differ 29 (12). 2022. PMID: 35681014. IF: 12,07. DOI: 10.1038/s41418-022-01023-x.

Maranon Patricia, Ernesto Fernandez Garcia Carlos, Isaza Stephania C, Rey Esther, Gallego Duran Rocio, Montero Vallejo Rocio, Rodriguez de Cia Javier, Ampuero Javier, Romero Gomez Manuel, Garcia Monzon Carmelo, Gonzalez Rodriguez Agueda. **Bone morphogenetic protein 2 is a new molecular target linked to non-alcoholic fatty liver disease with potential value as non-invasive screening tool**. Biomarker Res 10 (1). 2022. PMID: 35614516. IF: 8,63. DOI: 10.1186/s40364-022-00383-3.

Varona Jose F, Landete Pedro, Lopez Martin Jose A, Estrada Vicente, Paredes Roger, Guisado Vasco Pablo, Fernandez de Orueta Lucia, Torralba Miguel, Fortun Jesus, Vates Roberto, Barberan Jose, Clotet Bonaventura, Ancochea Julio, Carnevali Daniel, Cabello Noemi, Porras Lourdes, Gijon Paloma, Monereo Alfonso, Abad Daniel, Zuniga Sonia, Sola Isabel, Rodon Jordi, Vergara Alert Julia, Izquierdo Useros Nuria, Fudio Salvador, Jose Pontes Maria, de Rivas Beatriz, Giron de Velasco Patricia, Nieto Antonio, Gomez Javier et al. **Preclinical and randomized phase I studies of plitidepsin in adults with COVID-19**. Life Sci Alliance 5 (4). 2022. PMID: 35012962. IF: 5,78. DOI: 10.26508/lsa.202101200.

Gallego Duran Rocio, Ampuero Javier, Pastor Ramirez Helena, Alvarez Amor Leticia, Antonio del Campo Jose, Maya Miles Douglas, Montero Vallejo Rocio, Cardenas Garcia Antonio, Jesus Pareja Ma, Gato Zambrano Sheila, Millan Raquel, del Carmen Rico Maria, Luque Sierra Amparo, Gil Gomez Antonio, Rojas Angela, Munoz Hernandez Rocio, Garcia Lozano Maria, Aller Rocio, Andrade Raul J, Garcia Monzon Carmelo, Andreola Fausto, Martin Francisco, Jalan Rajiv, Romero Gomez Manuel. **Liver injury in non-alcoholic fatty liver disease is associated**

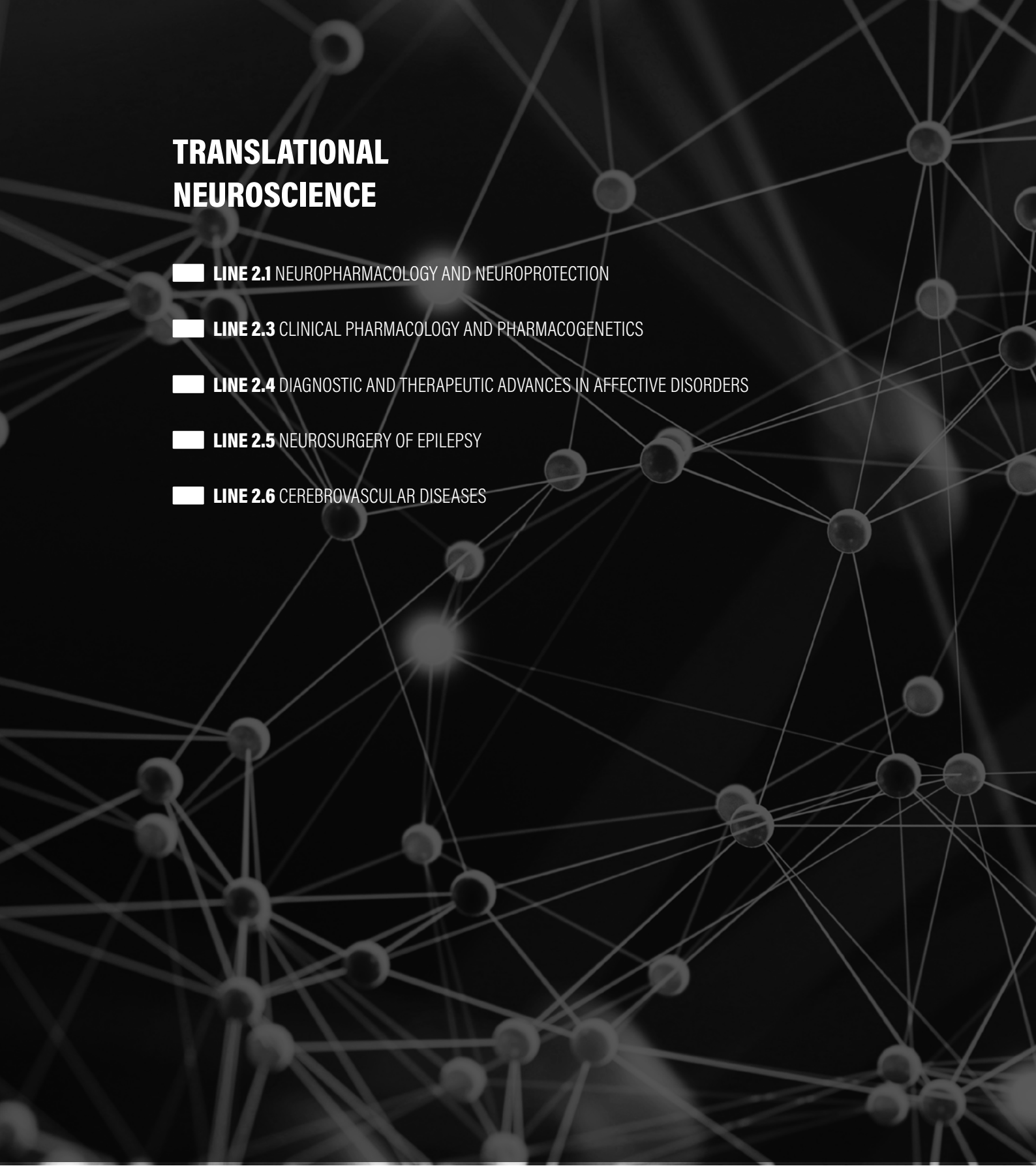
with urea cycle enzyme dysregulation. Sci Rep 12 (1). 2022. PMID: 35232986. IF: 5,00. DOI: 10.1038/s41598-022-06614-9.

Landete Pedro, Fernandez Garcia Carlos Ernesto, Aldave Orzaiz Beatriz, Hernandez Olivo Marta, Acosta Gutierrez Carmen M, Zamora Garcia Enrique, Ancochea Julio, Gonzalez Rodriguez Agueda, Garcia Monzon Carmelo. **Increased Oxygen Desaturation Time During Sleep Is a Risk Factor for NASH in Patients With Obstructive Sleep Apnea: A Prospective Cohort Study**. Front Med 9 2022. PMID: 35280896. IF: 5,06. DOI: 10.3389/fmed.2022.808417.

Lopez Padilla Daniel, Teran Tinedo Jose, Cerezo Lajas Alicia, Ramirez Garcia Laura, Ojeda Castillejo Elena, Lopez Martin Soledad, Diaz Cambriles Trinidad, Gonzalez Virseda Sonia, Arias Melgar Begona, Candel Pizarro Ana,

Lozano Alcocer Hector, Fernanda Troncoso Acevedo Maria, Gomez Garcia Teresa, Lopez Yeste Pablo, Cano Pumarega Irene, Garcia Sanchez Aldara, Arias Arcos Beatriz, Zamora Garcia Enrique, Landete Rodriguez Pedro, Iturricastillo Gorane, Lores Gutierrez Vanesa, Rodriguez Alonso Carlos, Vidal Ortola Martha, Lopez Riolobos Cristina, Garcia Prieto Fernando, Abad Fernandez Araceli, Manas Baena Eva. **Moderate obstructive sleep apnea and cardiovascular outcomes in older adults: a propensity score-matched multicenter study (CPAGE-MODE study)**. J Clin Sleep Med 18 (2). 2022. PMID: 34534075. IF: 4,32. DOI: 10.5664/jcsm.9656.

Fernandez Cuadros Marcos E, Perez Moro Olga S, Albaladejo Florin Maria J, Tobar Izquierdo Maria M, Magana Sanchez Amelia, Jimenez Cuevas Patricia, Rodriguez Cia Javier. **Intra Articular Ozone Modulates Inflammation and Has Anabolic Effect on Knee Osteoarthritis: IL-6 and IGF-1 as Pro-Inflammatory and Anabolic Biomarkers**. Process 10 (1). 2022. IF: 3,35. DOI: 10.3390/pr10010138.



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

ANNUAL REPORT OF SCIENTIFIC ACTIVITY

2022

AREA 2

INSTITUTO DE INVESTIGACIÓN SANITARIA
HOSPITAL UNIVERSITARIO DE LA PRINCESA

LINE 2.1 ›› NEUROPHARMACOLOGY AND NEUROPROTECTION

GROUP 5

Head of laboratory: García López, Manuela

Area 2 Translational neuroscience

Line 2.1 Neuropharmacology and neuroprotection

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.

GROUP MEMBERS

- Manuela García López
- Lucía Viqueira Díaz-Alejo
- Elsa Cortés Montero
- María de la Fuente Fernández
- Teresa Isabel Varela Jeraldo
- Paloma Pilar Mayo Mariscal de Gante
- Eric del Sastre López
- Paula Trigo Alonso
- Cristina Fernández Mendivil

MAJOR GRANTS

García López, Manuela. Bench to bedside transition for pharmacological regulation of NRF2 in noncommunicable diseases. CA20121. Acción COST. 2021-2025.

García López, Manuela. Implicación de la glía en taupatía: Nuevas dianas terapéuticas. PID2021-125986OB-I00. Ministerio de Ciencia e Innovación. 2022-2024.

García López, Manuela. Hacia un fármaco innovador para el tratamiento de las taupatías: prueba de concepto. PDC2022-133809-I00. Ministerio de Ciencia e Innovación. 2022-2024.

Tortosa Binacua, Elena. Between vesicles and microtubules: deciphering molecular mechanisms of axon degeneration. 2020-T1/BMD-19886. Comunidad de Madrid. 2022-2026.

PUBLICATIONS

Fernandez Albarral JA, Salobrar Garcia E, Matamoros JA, Fernandez Mendivil C, del Sastre E, Chen LJ, de Hoz R, Lopez Cuenca I, Sanchez Puebla L, Ramirez JM, Salazar JJ, Lopez MG, Ramirez AI. **Microglial Hemoxygenase- 1 Deletion Reduces Inflammation in the Retina of Old Mice with Tauopathy**. Antioxidants 11 (11). 2022. PMID: 36358522. IF: 7,68. DOI: 10.3390/antiox11112151.

Casas AI, Hassan AA, Manz Q, Wiwie C, Kleikers P, Egea J, Lopez MG, List M, Baumbach J, Schmidt HHHW. **Un-biased housekeeping gene panel selection for high-validity gene expression analysis**. Sci Rep 12 (1). 2022. PMID: 35853974. IF: 5,00. DOI: 10.1038/s41598-022-15989-8.

Herrera Arozamena Clara, Estrada Valencia Martin, Lopez Caballero Patricia, Perez Concepcion, Morales Garcia Jose A, Perez Castillo Ana, del Sastre Eric, Fernandez Mendivil Cristina, Duarte Pablo, Michalska Patrycja, Lombardia Jose, Senar Sergio, Leon Rafael, Lopez Manuela G, Isabel Rodriguez Franco Maria. **Resveratrol-Based MTDLs to Stimulate Defensive and Regenerative Pathways and Block Early Events in Neurodegenerative Cascades br**. J Med Chem 65 (6). 2022. PMID: 35245051. IF: 8,04. DOI: 10.1021/acs.jmedchem.1c01883.

E. Luengo, P. Trigo-Alonso, C.F Ernandez Mendivil, A. Nuñez, M. del Campo, C. Porrero, N. Garciamagro, P. Negredo, C. Sanchez, JA Bernal, A Rabano, J Hoozemans, AI Casas, Hhhw Schmidt, M G Lopez. **Implication of Type 4 NADPH Oxidase (NOX4) in Tauopathy**. Redox Biology 49: 102210. 2022. PMID: 34922273. IF: 10.787. DOI: 10.1016/j.redox.2021.102210.

Garzón-Niño J; Cortés-Montero E; Rodríguez-Muñoz M; Sánchez-Blázquez P.**αN-Acetyl β-Endorphin Is an Endogenous Ligand of σ1Rs That Regulates Mu-Opioid Receptor Signaling by Exchanging G Proteins for σ2Rs in σ1R Oligomers**. Int J Mol Sci 29: 24 (1): 582. 2022. PMID: 36614024. IF: 6.208. DOI:10.3390/ijms24010582.

Tortosa E, Sengupta Ghosh A, Li Q, Wong WR, Hinkle T, Sandoval W, Rose CM Hoogenraad CC. **Stress-induced vesicular assemblies of dual leucine zipper kinase are signaling hubs involved in kinase activation and neurodegeneration**. EMBO J 18: 41 (14): e110155. 2022. PMID: 35611591. IF: 13.783. DOI: 10.15252/embj.2021110155

GROUP 36

Head of laboratory: de los Ríos Salgado, Cristóbal

- Gabriel Martín Alcala
- Antonio Miguel García de Diego
- María Francisca Cano Abad
- Ricardo de Pascual y del Castillo
- Antonio García García
- María Bass Padilla

Area 2 Translational neuroscience

Line 2.1 Neuropharmacology and neuroprotection

RESEARCH INTEREST

My current work focuses on the validation of new therapeutic targets for thetreatment of the central nervous system. During the latest years, it has been stated that the most accepted hypotheses to explain the development of Alzheimer´s disease have not given the expected results. For this reason, new approaches have to be aimed.

Since I started my scientific career as an independent investigator, I have focused on drug discovery on alternative biological targets to treat neurodegenerative diseases, like the mitochondrial Na/Ca exchanger (NCLX) and the phosphoprotein phosphatase PP2A. In my lab, we are designing and synthesizing new compounds able to selectively act on these targets. Also, we have described a family of non-nucleotide purine derivatives that block the purinergic P2X7 ionotropic receptors, which are biological targets of increasing interest for the treatment of neuroinflammation-related pathologies.

Many of these compounds present promising outcomes in experiments assessing the neuroprotective effect, as they mitigate the neuronal death induced by toxic stimuli mimicking physiopathological events where the selected targets are implicated.

GROUP MEMBERS

- Cristóbal de los Ríos Salgado
- Lucía Viejo de Navas
- Ana Fernández Martín

MAJOR GRANTS

Ríos Salgado, Cristóbal de los. Therapeutic potential of the maintenance of protein phosphatase 2A activity: A pharmacological alternative for the treatment of neurodegenerative diseases and cancer. PI19/01724. ISCIII. 2020-2022.

PUBLICATIONS

Bisi A, Feoli A, Trezza A, Viejo L, Formaggio F, Bartolini M, Belluti F, Gobbi S, Spiga O, Caprini M, de los Rios C, Castellano S, Rampa A. **Targeting neuronal calcium channels and GSK3ß for Alzheimer's disease with naturally-inspired Diels-Alder adducts.** Bioorg Chem 129. 2022. PMID: 36155094. IF: 5,31. DOI: 10.1016/j.bioorg.2022.106152.

Martínez Gil N, Kutsyr O, Noailles A, Fernández Sánchez L, Vidal L, Sánchez Sáez X, Sánchez Castillo C, Lax P, Cuenca N, García AG, Maneu V. **Purinergic Receptors P2X7 and P2X4 as Markers of Disease Progression in the rd10 Mouse Model of Inherited Retinal Dystrophy.** Int J Mol Sci 23. (23). 2022. PMID: 36499084. IF: 6,21. DOI: 10.3390/ijms232314758.

Diez Iriepa D, Knez D, Gobec S, Iriepa I, de Los Ríos C, Bravo I, López Muñoz F, Marco Contelles J, Hadjipavlou Litina D. **Polyfunctionalized a-Phenyl-tert-butyl(benzyl)nitrones: Multifunctional Antioxidants for Stroke Treatment.** Antioxidants 11 (9). 2022. PMID: 36139811. IF: 7,68. DOI: 10.3390/antiox11091735.

Maneu V, Lax P, De Diego AMG, Cuenca N, García AG. **Combined drug triads for synergic neuroprotection in retinal degeneration**. Biomed. Pharmacother.149. 2022. PMID: 36068774. IF: 7,42. DOI: 10.1016/j.biopha.2022.112911.

Beamer Edward, Morgan James, Alves Mariana, Menendez Mendez Aida, Morris Gareth, Zimmer Bela, Conte Giorgia, de Diego Garcia Laura, Alarcon Vila Cristina, Yiu Ng Nico Ka, Madden Stephen, Calzaferri Francesco, de los Rios Cristobal, Garcia Antonio G, Hamacher Michael, Dinkel Klaus, Pelegrin Pablo, Henshall David C, Nicke Annette, Engel Tobias. **Increased expression of the ATP-gated P2X7 receptor reduces responsiveness to anti- convulsants during status epilepticus in mice**. Br J Pharmacol 179 (12). 2022. PMID: 34962289. IF: 9,47. DOI: 10.1111/bph.15785.

GROUP 41

Head of laboratory: Egea Máiquez, Francisco Javier

Area 2 Translational neuroscience

Line 2.1 Neuropharmacology and neuroprotection

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.

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- 1ß 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 ß-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.

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).

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.

GROUP MEMBERS

- Ana Belén López Rodríguez
- Paloma Narros Fernández
- Alejandra Palomino Antolín

MAJOR GRANTS

Egea Máiquez, Javier. Inflammasome proteins as new molecular targets for the diagnosis, prognosis and treatment of traumatic brain injury. PI19/00082. ISCIII. 2020-2022.

Egea Máiquez, Francisco Javier. Nuevas dianas moleculares relacionadas con angiogénesis e inflamación para el diagnóstico, pronóstico y tratamiento del traumatismo craneoencefálico. Mutua Madrileña. 2021- 2024.

PUBLICATIONS

Mesa Ciller C, Turiel G, Guajardo Grence A, Lopez Rodriguez AB, Egea J, De Bock K, Aragonés J, Urrutia AA. **Unique expression of the atypical mitochondrial subunit NDUFA4L2 in cerebral pericytes fine tunes HIF activity in response to hypoxia.** J Cereb Blood Flow Metab 43 (1). 2023. PMID: 35929074. IF: 6,96. DOI: 10.1177/0271678X221118236.

Padín JF, Maroto M, Entrena JM, Egea J, Montell E, Vergés J, López MG, Cobos EJ, García AG. **Small Synthetic Hyaluronan Disaccharide BIS014 Mitigates Neuropathic Pain in Mice.** J Pain 24 (1). 2023. PMID: 36087908. IF: 5,38. DOI: 10.1016/j.jpain.2022.07.014.

Lopez Rodriguez AB, Decouty Perez C, Farre Alins V, Palomino Antolin A, Narros Fernandez P, Egea J. **Activation of NLRP3 Is Required for a Functional and Beneficial Microglia Response after Brain Trauma**. Pharmaceutics 14 (8). 2022. PMID: 35893807. IF: 6,53. DOI: 10.3390/pharmaceutics14081550.

Casas AI, Hassan AA, Manz Q, Wiwie C, Kleikers P, Egea J, Lopez MG, List M, Baumbach J, Schmidt HHHW. **Un-biased housekeeping gene panel selection for high-validity gene expression analysis**. Sci Rep 12 (1). 2022. PMID: 35853974. IF: 5,00. DOI: 10.1038/s41598-022-15989-8.

Lopez Munoz,F,Reiter,RJ,Egea,J,Romero,A. **Editorial: Therapeutic Advances in Melatonin Research**. Front Pharmacol 13. 2022. PMID: 35774600. IF: 5,99. DOI: 10.3389/fphar.2022.947117.

Narros Fernandez Paloma, Chioua Mourad, Petcu Sonia A, Diez Iriepa Daniel, Cerrada Galvez Laura, Decouty Perez Celine, Palomino Antolin Alejandra, Ramos Eva, Farre Alins Victor, Belen Lopez Rodriguez Ana, Romero Alejandro, Marco Contelles Jose, Egea Javier. **Synthesis and Pharmacological Evaluation of New N-Sulfonylureasas NLRP3 Inflammasome Inhibitors: Identification of a HitCompound to Treat Gout**. J Med Chem 65 (8). 2022. PMID: 35403430. IF: 8,04. DOI: 10.1021/acs.jmedchem.2c00149.

Egea Javier, Lopez Munoz Francisco, Fernandez Capetillo Oscar, Reiter Russel J,Romero Alejandro. **Alkylating Agent-Induced Toxicity and Melatonin-Based Therapies**. Front Pharmacol 13. 2022. PMID: 35401215. IF: 5,99. DOI: 10.3389/fphar.2022.873197.

Palomino Antolin Alejandra, Narros Fernandez Paloma, Farre Alins Victor, Sevilla Montero Javier, Decouty Perez Celine, Belen Lopez Rodriguez Ana, Fernandez Nuria, Monge Luis, I, Jose Calzada Maria, Egea Javier. **Time- dependent dual effect of NLRP3 inflammasome in brain ischaemia**. Br J Pharmacol 179 (7). 2022. PMID: 34773639. IF: 9,47. DOI:10.1111/bph.15732.

GROUP 32

Head of laboratory: Abad Santos, Francisco

Area 2 Translational neuroscience

Line 2.3 Clinical pharmacology and pharmacogenetics

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 20 clinical trials each year, and this number is expected to increase due to demand from the pharmaceutical industry. In recent years, several clinical trials on the COVID-19 vaccine have been 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 2022, 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. Seven funded projects were active in 2022. In addition to projects funded in previous years, Francisco Abad Santos and Pablo Zubiaur were awarded with 4 new grants in 2022.

GROUP MEMBERS

- Francisco Abad Santos
- Houwaida Abbes
- Eva Bernardos González
- Ana Casajus Rey
- Antía Gómez Fernández
- Eva González Iglesias
- Diana María Campodónico
- Samuel Martín Vílchez Gina
- Paola Mejía Abril
- Marcos Navares Gómez
- Jesús Miguel Novalbos Reina
- María Dolores Ochoa Mazarro
- María del Carmen Ovejero Benito
- Raul Miguel Parra Garces
- Concepción Pérez Hernández
- Andrea Rodríguez López
- Manuel Román Martínez
- Irene Román Martínez
- Patricia Sánchez Jiménez
- Paula Soria Chacartegui
- Gonzalo Villapalos García
- Paula Vizcaíno Rodríguez
- Pablo Zubiaur Precioso

MAJOR GRANTS

Abad Santos, Francisco. Identificación de factores clínicos y farmacogenéticos predictores de respuesta a nuevos anticoagulantes orales en el tratamiento de la fibrilación auricular no valvular. PI19/00932. ISCIII. 2020-2022.

Ochoa Mazarro, Dolores. Evaluación del sexo y marcadores farmacogenéticos en el tratamiento del dolor PI19/01802. ISCIII. 2020- 2022.

Abad Santos, Francisco. ERA4TB: European Regimen accelerator for Tuberculosis 853989- 2. IMI 2. 2019-2025.

Abad Santos, Francisco. Ensayo clínico aleatorizado para evaluar la utilidad del genotipado de CYP2D6 para mejorar la eficacia y la seguridad del tramadol en el tratamiento del dolor postoperatorio agudo. ICI20/00131. ISCIII. 2021-2024.

Abad Santos,Francisco. Medicina personalizada de precisión: "evaluación de una propuesta de implementación de farmacogenética en el sistema nacional de salud para salud mental y cardiovascular [BIOfRAM22]".PMP22/00139. ISCIII.

Abad Santos,Francisco. TREATMENT: TRAINING EUROPEAN NETWORK: METABOLIC DYSFUNCTIONS ASSOCIATED WITH PHARMACOLOGICAL TREATMENT OF SCHIZOPHRENIA.UE.TREATMENT.674921. EUROPEAN COMMISSION.2017-2022.

Abad Santos, Francisco; Zubiaur Precioso, Pablo (participante). H2020-JTI- IMI2-2018-15. Monitorización terapéutica y estudio farmacogenético de ibrutinib en pacientes con leucemia linfocítica crónica. Gerencia Regional de Salud de Castilla y León-Sacyl (GRS 2202/A/2020). 2021-2023.

Abad Santos, Francisco. Medicina Genómica. IMP/00009. ISCIII-IMPaCT. 2021-2023.

Abad Santos, Francisco. Ensayo clínico aleatorizado para evaluar la utilidad del genotipado de CYP2D6 para mejorar la eficacia y la seguridad del tramadol en el tratamiento del dolor postoperatorio agudo. ICI20/00131. ISCIII. 2021-2024.

Ochoa Mazarro, Dolores. Evaluación del sexo y marcadores farmacogenéticos en el tratamiento del dolor PI19/01802. ISCIII. 2020- 2022 (prorroga junio 2024).

Abad Santos, Francisco. Utilidad la farmacogenética para mejorar la prescripción de estatinas en atención primaria y especializada. PI22/01647. ISCIII. 2023-2025.

Abad Santos, Francisco. Evaluación de una propuesta de implementación de Farmacogenética en el Sistema Nacional de Salud para Salud Mental y Cardiovascular [BIOfRAM22]. PMP22/00139. ISCIII. 2023-2025.

Zubiaur Precioso, Pablo. Proyecto iPHARMGx: Estudio colaborativo nacional para evaluar la efectividad y eficiencia de la implementación de biomarcadores farmacogenéticos mediante una estrategia de genotipado anticipado en el SNS. ISCIII. 2023-2026.

Zubiaur Precioso, Pablo. Utilidad de la farmacogenética para mejorar la prescripción de estatinas en atención primaria y especializada: percepciones y formación de médicos prescriptores. ISCIII. 2023-2025.

PUBLICATIONS

Marcos-Jiménez A, Claudino Carvoeiro D, Ruef N, Cuesta-Mateos C, Roy- Vallejo E, Gómez-García de Soria V, Laganá C, Del Campo L, Zubiaur P, Villapalos-García G, Abad-Santos F, Stein JV, Muñoz-Calleja C. **Dasatinib- induced spleen contraction leads to transient lymphocytosis**. Blood Adv. 2022. PMID: 36583674. IF:7.64. DOI: 10.1182/bloodadvances.2022009279.

Zubiaur P, Abad F**. Association Studies in Clinical Pharmacogenetics.** Pharmaceutics 15 (1). 2022. PMID: 36678742. IF: 6,53. DOI: 10.3390/pharmaceutics15010113.

Escobar Y, Margarit C, Pérez-Hernández C, Quintanar T, Virizuela JA. **Good practice recommendations to better coordinate the management of oncological pain: a Delphi survey.** Sci Rep 12 (1): 22459-22459. 2022. PMID: 36577791. IF: 5,00. DOI: 10.1038/s41598-022-26753-3.

Zubiaur P, Abad-Santos F. **Use of pharmacogenetics for benzodiazepine prescription: state of the art and expectations.** Pharmacogenomics 23 (18): 949-952. 2022. PMID: 36412207. IF: 2,64. DOI: 10.2217/pgs-2022-0161.

Ferreira V, Folgueira C, Guillén M, Zubiaur P, Navares M, Sarsenbayeva A, López-Larrubia P, Eriksson JW, Pereira MJ, Abad-Santos F, Sabio G, Rada P, Valverde ÁM. **Modulation of hypothalamic AMPK phosphorylation by olanzapine controls energy balance and body weight.** Metab Clin Exp 137: 155335-155335. 2022. PMID: 36272468. IF: 13,93. DOI: 10.1016/j.metabol.2022.155335.

Zubiaur P, Gaedigk A. **CYP2C18: the orphan in the CYP2C family**. Pharmacogenomics 23 (16) 913-916. 2022. PMID: 36331025. IF: 2,64. DOI: 10.2217/pgs-2022-0142.

Zubiaur P, Figueiredo-Tor L, Villapalos-García G, Soria-Chacartegui P, Navares-Gómez M, Novalbos J, Matas M, Calleja S, Mejía-Abril G, Román M, Ochoa D, Abad-Santos F. **Association between CYP2C19 and CYP2B6 phenotypes and the pharmacokinetics and safety of diazepam**. Biomed Pharmacother 155: 113747-113747.

2022. PMID: 36162369. IF: 7,42. DOI: 10.1016/j.biopha.2022.113747.

de Toledo M, de la Fuente E, Ramos C, Ferreiros-Martinez R, Muro I, Vieira Campos A, de Toledo MP, Lagares A, Sobrado M, Ovejero-Benito MC. **Extensive pharmacokinetic variability of Levetiracetam. ¿Are doctors aware?**. Epilepsy Res 187: 107029-107029. 2022. PMID: 36272308. IF: 2,99. DOI: 10.1016/j.eplepsyres.2022.107029.

Campodónico DM, Zubiaur P, Soria-Chacartegui P, Casajús A, Villapalos- García G, Navares-Gómez M, Gómez-Fernández A, Parra-Garcés R, Mejía- Abril G, Román M, Martín-Vílchez S, Ochoa D, Abad-Santos F. **CYP2C83 and 4 define CYP2C8 phenotype: An approach with the substrate cinitapride**. Clin Transl Sci 15 (11): 2613-2624. 2022. PMID: 36065758. IF: 4,44. DOI: 10.1111/cts.13386.

Villapalos-García G, Zubiaur P, Rivas-Durán R, Campos-Norte P, Arévalo- Román C, Fernández-Rico M, García-Fraile Fraile L, Fernández-Campos P, Soria-Chacartegui P, Fernández de Córdoba-Oñate S, Delgado-Wicke P, Fernández-Ruiz E, González-Álvaro I, Sanz J, Abad-Santos F, de Los Santos I. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity and sex are the primary predictors of Covid-19 severity (vol 5, e202201396, 2022)**. Life Sci Alliance 5 (10): 1-2. 2022. PMID: 35680409. IF: 5,78. DOI: 10.26508/lsa.202201545.

Zubiaur P, Matas M, Martín-Vílchez S, Soria-Chacartegui P, Villapalos- García G, Figueiredo-Tor L, Calleja S, Navares-Gómez M, de Miguel A, Novalbos J, Mejía-Abril G, Luquero-Bueno S, Román M, Ochoa D, Abad- Santos F. **Polymorphism of Drug Transporters, Rather Than Metabolizing Enzymes, Conditions the Pharmacokinetics of Rasagiline**. Pharmaceutics 14 (10): 2001. 2022. PMID: 36297437. IF: 6,53. DOI: 10.3390/pharmaceutics14102001.

Reolid A, Sahuquillo-Torralba A, Sanz-García A, Botella-Estrada R, Muñoz- Aceituno E, Llamas-Velasco M, García-Martínez J, Daudén E, Abad-Santos F, Ovejero-Benito MC. **CNVs Associated with Different Clinical Phenotypes of Psoriasis and Anti-TNF-Induced Palmoplantar Pustulosis.** J Pers Med 12 (9): 1452. 2022. PMID: 36143237. IF: 3,51. DOI: 10.3390/jpm12091452.

Román Martinez M, García Aguilar E, Martin Vílchez S, González García J, Luquero-Bueno S, Camargo-Mamani P, Mejia-Abril G, García-Castro L, de Miguel-Cáceres A, Saz-Leal P, Abad-Santos F, Nieto Magro C, Ochoa Mazarro D.. **Bioavailability of Oniria (R), a Melatonin Prolonged-Release Formulation, Versus Immediate-Release Melatonin in Healthy Volunteers**. Drugs R D 22 (3): 235-243. 2022. PMID: 35918587. IF: 3,20. DOI: 10.1007/s40268-022-00394-3.

Li H, Zhang Z, Weng H, Qiu Y, Zubiaur P, Zhang Y, Fan G, Yang P, Vuorinen AL, Zuo X, Zhai Z, Wang C. **Association between CES1 rs2244613 and the pharmacokinetics and safety of dabigatran: Meta-analysis and quantitative trait loci analysis.** Front Cardiovasc Med 9: 959916-959916. 2022. PMID: 35990949. IF: 5,85. DOI: 10.3389/fcvm.2022.959916.

Pérez-Hernández C, Cánovas ML, Carmona-Bayonas A, Escobar Y, Margarit C, Mulero Cervantes JF, Quintanar T, Serrano Alfonso A, Virizuela J. **A Delphi Study on the Management of Neuropathic Cancer Pain in Spain: The DOLNEO Study.** J Pain Res 15: 2181-2196. 2022. PMID: 35942117. IF: 2,83. DOI: 10.2147/JPR.S365351.

Chien YH, Würthwein G, Zubiaur P, Posocco B, Pena MÁ, Borobia AM, Gagno S, Abad-Santos F, Hempel G. **Population pharmacokinetic modelling of imatinib in healthy subjects receiving a single dose of 400 mg.** Cancer Chemother Pharmacol 90 (2): 125-136. 2022. PMID: 35831644. IF: 3,29. DOI: 10.1007/s00280-022-04454-y.

Valdés-Garicano M, Mejía-Abril G, Campodónico D, Parra-Garcés R, Abad- Santos F. **Utility of a Laboratory Alert System for Detecting Adverse Drug Reactions in Hospitalised Patients: Hyponatremia and Rhabdomyolysis.** Front Pharmacol 13: 937045-937045. 2022. PMID: 35873584. IF: 5,99. DOI: 10.3389/fphar.2022.937045.

Hernández-Jiménez M, Martín-Vílchez S, Ochoa D, Mejía-Abril G, Román M, Camargo-Mamani P, Luquero-Bueno S, Jilma B, Moro MA, Fernández G, Piñeiro D, Ribó M, González VM, Lizasoain I, Abad-Santos F. **First-in-human phase I clinical trial of a TLR4-binding DNA aptamer, ApTOLL: Safety and pharmacokinetics in healthy volunteers**. Mol Ther Nucl Acids 28: 124-135. 2022. PMID: 35402075. IF: 10,18. DOI: 10.1016/j.omtn.2022.03.005.

Serra López-Matencio JM, Gago-Veiga AB, Gómez M, Alañón Plaza E, Mejía GP, González-Gay MÁ, Castañeda S. **Treatment of migraine with monoclonal antibodies**. Expert Opin Biol Ther 22 (6): 707-716. 2022. PMID: 35502612. IF: 5,59. DOI: 10.1080/14712598.2022.2072207.

Ovejero-Benito MC, Ochoa D, Enrique-Benedito T, Del Peso-Casado M, Zubiaur P, Navares M, Román M, Abad-Santos F.**Pharmacogenetics of Donepezil and Memantine in Healthy Subjects**. J Pers Med 12 (5): 788. 2022. PMID: 35629210. IF: 3,51. DOI: 10.3390/jpm12050788.

Serrano-Afonso A, Gálvez R, Paramés E, Navarro A, Ochoa D, Pérez- Hernández C.**Update on Interventional Management of Neuropathic Pain: A Delphi Consensus of the Spanish Pain Society Neuropathic Pain Task Force**. Medicina 58 (5): 627. 2022. PMID: 35630044. IF: 2,95. DOI: 10.3390/medicina58050627.

Pinto-Merino Á, Labrador J, Zubiaur P, Alcaraz R, Herrero MJ, Montesinos P, Abad-Santos F, Saiz-Rodríguez M. **Role of Pharmacogenetics in the Treatment of Acute Myeloid Leukemia: Systematic Review and Future Perspectives**. Pharmaceutics 14 (3): 559. 2022. PMID: 35335935. IF: 6,53. DOI: 10.3390/pharmaceutics14030559.

García-Vicuña R, Rodriguez-García SC, Abad-Santos F, Bautista Hernández A, García-Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso-Pérez T, Cardeñoso L, Alfranca A, Mejía-Abril G, Sanz Sanz J, González-Alvaro I.. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9: 819621-819621. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621.

Casajús A, Zubiaur P, Méndez M, Campodónico D, Gómez A, Navares- Gómez M, Villapalos-García G, Soria-Chacartegui P, Novalbos J, Román M, Mejía-Abril G, Ochoa D, Abad-Santos F. **Genotype-Guided Prescription of Azathioprine Reduces the Incidence of Adverse Drug Reactions in TPMT Intermediate Metabolizers to a Similar Incidence as Normal Metabolizers**. Adv Ther 39 (4): 1743-1753. 2022. PMID: 35192152. IF: 4,07. DOI: 10.1007/s12325-022-02067-8.

Zubiaur P, Prósper-Cuesta DN, Novalbos J, Mejía-Abril G, Navares-Gómez M, Villapalos-García G, Soria-Chacartegui P, Abad-Santos F. **Patients' Perceptions of Pharmacogenetic Testing and Access to Their Results: State of the Art in Spain and Systematic Review**. J Pers Med 12 (2): 270. 2022. PMID: 35207758. IF: 3,51. DOI: 10.3390/jpm12020270.

Monserrat Villatoro J, Mejía-Abril G, Díaz García L, Zubiaur P, Jiménez González M, Fernandez Jimenez G, Cancio I, Arribas JR, Suarez Fernández C, Mingorance J, García Rodríguez J, Villagrasa Ferrer JR, Carcas AJ, Frías J, Abad-Santos F, Borobia AM, Ramírez E, On Behalf Of The Covid Hulp Working Group And Other Collaborators From Hospital Universitario de la Princesa. **A Case-Control of Patients with COVID-19 to Explore the Association of Previous Hospitalisation Use of Medication on the Mortality of COVID-19 Disease: A Propensity Score Matching Analysis**. Pharmaceuticals 15 (1): 78. 2022. PMID: 35056135. IF: 5,22. DOI: 10.3390/ph15010078.

Grajales D, Vázquez P, Ruíz-Rosario M, Tudurí E, Mirasierra M, Ferreira V, Hitos AB, Koller D, Zubiaur P, Cigudosa JC, Abad-Santos F, Vallejo M, Quesada I, Tirosh B, Leibowitz G, Valverde ÁM. **The second-generation antipsychotic drug aripiprazole modulates the serotonergic system in pancreatic islets and induces beta cell dysfunction in female mice**. Diabetologia 65 (3): 490-505. 2022. PMID: 34932133. IF: 10,46. doi: 10.1007/s00125-021-05630-0.

Rey AC, Precioso PZ, Alday EA, Aragones C, Campodonico D, Martinez MH, Gomez MN, Garcia GV, Chacartegui PS, Abril GM, Gutierrez L, Mazarro DO, Rodriguez MS, Santos FA. **Influence of CYP2D6 phenotype and polymorphisms in other genes on the response and tolerability to tramadol in patients with acute postsurgical pain**. Basic Clin Pharmacol Toxicol 130: 38-38. 2022. IF: 3,69.

Rey AC, Zubiaur P, Alday E, Aragones C, Campodonico D, Gomez A, Gomez MN, Villapalos G, Chacartegui PS, Novalbos J, Mejia G, Ochoa D, Abad F. **INFLUENCE OF CYP2D6 AND OTHER GENES' PHENOTYPE ON THE SAFETY AND EFFICACY OF TRAMADOL IN PATIENTS WITH ACUTE POSTSURGICAL PAIN**. Eur J Clin Pharmacol 78 (SUPPL 1): 102-102. 2022. IF: 3,06.

GROUP 33

Head of laboratory: Ayuso Mateos, José Luis

Area 2 Translational neuroscience

Line 2.4 Diagnostic and therapeutic advances in affective disorders

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 populations 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:

"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.

"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.

"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.

"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.

"Peripheral oxidative stress and inflammatory markers in Major Depressive Disorder", focuses on finding biological markers in Major Depressive Disorder.

"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.

"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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- Itziar Leal Leturia
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- Iosune Torio Palmero
- María Cabello Salmerón

MAJOR GRANTS

Ayuso Mateos, José Luis. Understanding mental health and disease in Spain: determinants and trajectory patterns in a population-based cohort over 9 years. PI19/00150. ISCIII. 2020- 2022.

Ayuso Mateos, José Luis. EMPOWER: European platform to promote wellbeing and health in the workplace. EMPOWER: 848180. 2020-2024.

Ayuso Mateos, José Luis. RESPOND: Improving the preparedness of health systems to reduce mental health and psychosocial concerns resulting from the COVID-19 Pandemic. RESPOND: 101016127. 2020-2023.

José Luis Ayuso Mateos Psychiatric Ratings using Intermediate Stratified Markers -2 (PRISM-2) CIBERSAM / Unión Europea H2020 Duración: 3 años

PUBLICATIONS

Lazarus JV, Ortiz A, Tyrovolas S, Fernández E, Guy D, White TM, Ma R, Hay SI, Naghavi M, Soriano JB, Spain Collaborators GBD2019. **A GBD 2019 study of health and Sustainable Development Goal gains and forecasts to 2030 in Spain.** Sci Rep 12 (1). 2022. PMID: 36477107. IF: 5,00. DOI: 10.1038/s41598-022-24719-z.

Hecker I, El Aarbaoui T, Wallez S, Andersen AJ, Ayuso Mateos JL, Bryant R, Corrao G, McDaid D, Mediavilla R, Mittendorfer Rutz E, Compagnoni MM, Park AL, Riepenhausen A, Rigotti T, Seeber K, Sijbrandij M, Smith P, Tüscher O, Walter H, Witteveen A, Mary Krause M, Melchior M. **Impact of work arrangements during the COVID-19 pandemic on mental health in France.** SSM Popul Health 20. 2022. PMID: 36415675. IF: 4,09. DOI: 10.1016/j.ssmph.2022.101285

Witteveen AB, Young S, Cuijpers P, Ayuso Mateos JL, Barbui C, Bertolini F, Cabello M, Cadorin C, Downes N, Franzoi D, Gasior M, John A, Melchior M, McDaid D, Palantza C, Purgato M, Van der Waerden J, Wang S, Sijbrandij

M. **Remote mental health care interventions during the COVID-19 pandemic: An umbrella review.** Behav Res Ther 159. 2022. PMID: 36410111. IF: 5,32. DOI: 10.1016/j.brat.2022.104226

Braak S, Su T, Krudop W, Pijnenburg YAL, Reus LM, van der Wee N, Bilderbeck AC, Dawson GR, van Rossum IW, Campos AV, Arango C, Saris IMJ, Kas MJ, Penninx BWJH. **Theory of Mind and social functioning among neuropsychiatric disorders: A transdiagnostic study.** Eur Neuropsychopharmacol 64. 2022. PMID: 36070667. IF: 5,42. DOI: 10.1016/j.euroneuro.2022.08.005.

de Toledo M, de la Fuente E, Ramos C, Ferreiros Martinez R, Muro I, Vieira Campos A, de Toledo MP, Lagares A, Sobrado M, Ovejero Benito MC.

Extensive pharmacokinetic variability of Levetiracetam. ¿Are doctors aware? Epilepsy Res 187. 2022. PMID: 36272308. IF: 2,99. DOI: 10.1016/j.eplepsyres.2022.107029.

Garcia Lopez M, Alonso Sanchez M, Leal I, Martin Hernandez D, Caso JR, Diaz Caneja CM, Andreu Bernabeu A, Arango C, Rodriguez Jimenez R, Sanchez Pastor L, Diaz Marsa M, Mellor Marsa B, Ibanez A, Malpica N, Bravo Ortiz MF, Baca Garcia E, Ayuso Mateos JL, Izquierdo A, AGES CM Grp. **The relationship between negative symptoms, social cognition, and social functioning in patients with first episode psychosis**. J Psychiatr Res 155. 2022. PMID: 36041260. IF: 5,25. DOI: 10.1016/j.jpsychires.2022.08.004.

Mediavilla R, McGreevy KR, Felez Nobrega M, Monistrol Mula A, Bravo Ortiz MF, Bayón C, Rodríguez Vega B, Nicaise P, Delaire A, Sijbrandij M, Witteveen AB, Purgato M, Barbui C, Tedeschi F, Melchior M, van der Waerden J, McDaid D, Park AL, Kalisch R, Petri Romão P, Underhill J, Bryant RA, Haro JM, Ayuso Mateos JL,

RESPOND Consortium. **Effectiveness of a stepped-care programme of internet-based psychological interventions for healthcare workers with psychological distress: Study protocol for the RESPOND healthcare workers randomised controlled trial.** Digit Health 8. 2022. PMID: 36211795. IF: 4,69. DOI: 10.1177/20552076221129084

Rico Uribe LA, Morillo Cuadrado D, Rodríguez Laso A, Vorstenbosch E, Weser AJ, Fincias L, Marcon Y, Rodriguez Mañas L, Haro JM, Ayuso Mateos JL. **Worldwide mapping of initiatives that integrate population cohorts.** Front Public Health 10. 2022. PMID: 36262229. IF: 6,46. DOI: 10.3389/fpubh.2022.964086.

Lara E, Miret M, Olaya B, Caballero FF, Morillo D, Moneta MV, Haro JM, Ayuso Mateos JL. **Cohort Profile: The Spanish Longitudinal Study on Ageing and Health (Edad Con Salud)**. Int J Epidemiol 51 (4). 2022. PMID: 35712861. IF: 9,69. DOI: 10.1093/ije/dyac118

Delgado Parada E, Alonso Sanchez M, Ayuso Mateos JL, Robles Camacho M, Izquierdo A. **Liaison psychiatry before and after the COVID-19 pandemic**. Psychiatry Res 314. 2022. PMID: 35640325. IF: 11,23. DOI: 10.1016/j.psychres.2022.114651

Mediavilla R, Monistrol Mula A, McGreevy KR, Felez Nobrega M, Delaire A, Nicaise P, Palomo Conti S, Bayón C, Bravo Ortiz MF, Rodríguez Vega B, Witteveen A, Sijbrandij M, Turrini G, Purgato M, Vuillermoz C, Melchior M, Petri Romão P, Stoffers Winterling J, Bryant RA, McDaid D, Park AL, Ayuso Mateos JL, RESPOND Consortium. **Mental health problems and needs of frontline healthcare workers during the COVID-19 pandemic in Spain: A qualitative analysis.** Front Public Health 10. 2022. PMID: 35968478. IF: 6,46. DOI: 10.3389/fpubh.2022.956403

Delgado Parada E, Morillo Cuadrado D, Saiz Ruiz J, Cebollada Gracia A, Ayuso Mateos JL, Cruz Jentoft AJ. **Diagnostic accuracy of the Spanish version of the 4AT scale (4AT-ES) for delirium screening in older inpatients**. Eur J Psychiatry 36 (3). 2022. IF: 1,29. DOI: 10.1016/j.ejpsy.2022.01.003

Mediavilla R, Fernández Jiménez E, Martinez Morata I, Jaramillo F, Andreo Jover J, Morán Sánchez I, Mascayano F, Moreno Küstner B, Minué S, Ayuso Mateos JL, Bryant RA, Bravo Ortiz MF, Martínez Alés G. **Sustained Negative Mental Health Outcomes Among Healthcare Workers Over the First Year of the COVID-19 Pandemic: A Prospective Cohort Study.** Int J Public Health 67. 2022. PMID: 35814735. IF: 5,10. DOI: 10.3389/ijph.2022.1604553

Villarejo Galende Alberto, Garcia Arcelay Elena, Pinol Ripoll Gerard, del Olmo Rodriguez Antonio, Vinuela Felix, Boada Merce, Franco Macias Emilio, Ibanez de la Pena Almudena, Riverol Mario, Puig Pijoan Albert, Abizanda Soler Pedro, Arroyo Rafael, Baquero Toledo Miquel, Feria Vilar Inmaculada, Balasa Mircea, Berbel Angel, Rodriguez Eloy, Vieira Campos Alba, Garcia Ribas Guillermo, Rodrigo Herrero Silvia, Lleo Albert, Maurino Jorge. **Awareness of Diagnosis in Persons with Early-Stage Alzheimer's Disease: An Observational Study in Spain**. Neurol Ther 11 (3). 2022. PMID: 35648383. IF: 4,45. DOI: 10.1007/s40120-022-00367-3.

Haagsma Juanita A, Charalampous Periklis, Ariani Filippo, Gallay Anne, Moesgaard Iburg Kim, Nena Evangelia, Ngwa Che Henry, Rommel Alexander, Zelviene Ausra, Abegaz Kedir Hussein, Al Hamad Hanadi, Albano Luciana, Liliana Andrei Catalina, Andrei Tudorel, Antonazzo Ippazio Cosimo, Aremu Olatunde, Arumugam Ashokan, Atreya Alok, Aujayeb Avinash, Ayuso Mateos Jose Luis, Engelbert Bain Luchuo, Banach Maciej, Winfried Baernighausen Till, Barone Adesi Francesco, Beghi Massimiliano, Bennett Derrick A, Bhagavathula Akshaya S, Carvalho Felix, Castelpietra Giulio, Caterina Ledda et al. **The burden of injury in Central, Eastern, and Western European sub-region: a systematic analysis from the Global Burden of Disease 2019 Study**. Arch Public Health 80 (1). 2022. PMID: 35590340. IF: 2,74. DOI: 10.1186/s13690-022-00891-6

Rodriguez Gomez I, Sanchez Martin C, Garcia FJ, Garcia Esquinas E, Miret M, Jimenez Pavon D, Guadalupe Grau A, Manas A, Carnicero JA, Casajus JA, Ayuso Mateos JL, Rodriguez Artalejo F, Rodriguez Manas L, Ara I. **The Medium-Term Changes in Health-Related Behaviours among Spanish Older People Lifestyles during Covid-19 Lockdown**. J Nutr Health Aging 26 (5). 2022. PMID: 35587761. IF: 5,29. DOI: 10.1007/s12603-022-1781-0

Barmpas Petros, Tasoulis Sotiris, Vrahatis Aristidis G, V, Anagnostou Panagiotis, Prina Matthew, Ayuso Mateos Jose Luis, Bickenbach Jerome, Bayes Ivet, Bobak Martin, Caballero Francisco Felix, Chatterji Somnath, Egea Cortes Laia, Garcia Esquinas Esther, Leonardi Matilde, Koskinen Seppo, Koupil Ilona, Pajak Andrzej, Prince Martin, Sanderson Warren, Scherbov Sergei, Tamosiunas Abdonas, Galas Aleksander, Haro Josep Maria, Sanchez Niubo Albert, Plagianakos Vassilis P, Panagiotakos Demosthenes. **A divisive hierarchical clustering methodology for enhancing the ensemble prediction power in large scale population studies: the ATHLOS project**. Health Inf Sci Syst 10 (1). 2022. PMID: 35529251. IF: 5,02. DOI: 10.1007/s13755-022-00171-1

Kogan Cary S, Rebello Tahilia J, Sadowska Karolina, Garcia Pacheco Jose A, Khoury Brigitte, Kulygina Maya, Matsumoto Chihiro, Robles Rebeca, Huang Jingjing, Andrews Howard F, Ayuso Mateos Jose Luis,

Denny Keith, Gaebel Wolfgang, Gureje Oye, Kanba Shigenobu, Mare Karen, Medina Mora Maria Elena, Pike Kathleen M, Roberts Michael C, Sharan Pratap, Stein Dan J, Stroup T Scott, Zhao Min, Reed Geoffrey M. **An international survey examining the impact of the COVID-19 pandemic on telehealth use among mental health professionals**. J Psychiatr Res 148. 2022. PMID: 35131587. IF: 5,25. DOI: 10.1016/j.jpsychires.2022.01.050

Riepenhausen Antje, Veer Ilya M, Wackerhagen Carolin, Reppmann Zala C, Koeber Goeran, Luis Ayuso Mateos Jose, Boegemann Sophie A, Corrao Giovanni, Felez Nobrega Mireia, Haro Abad Josep Maria, Hermans Erno, van Leeuwen Judith, Lieb Klaus, Lorant Vincent, Mary Krause Murielle, Mediavilla Roberto, Melchior Maria, Mittendorfer Rutz Ellenor, Compagnoni Matteo Monzio, Pan Kuan-Yu, Puhlmann Lara, Roelofs Karin, Sijbrandij Marit, Smith Pierre, Tuescher Oliver, Witteveen Anke, Zerban Matthias, Kalisch Raffael, Kroeger Hannes, Walter Henrik. **Coping with COVID: risk and resilience factors for mental health in a German representative panel study**. Psychol Med. 2022. PMID: 35301966. IF: 10,59. DOI: 10.1017/S0033291722000563

Martín Ávila G, Vieira Campos A, Labrador Marcos S, Zheng X, Méndez Burgos A, Thuissard I, Andreu Vázquez C, Ordieres Meré J, Aladro Y. **Patients' self-assessment of essential tremor severity by a validated scale: A useful tool in telemedicine?** Parkinsonism Relat Disord 96. 2022. PMID: 35124409. IF: 4,40. DOI: 10.1016/j.parkreldis.2022.01.021

Rodríguez Gómez I, Sánchez Martín C, García FJ, García Esquinas E, Miret M, Vicente Rodriguez G, Gusi N, Mañas A, Carnicero JA, Gonzalez Gross M, Ayuso Mateos JL, Rodríguez Artalejo F, Rodríguez Mañas L, Ara I. **The medium-term consequences of a COVID-19 lockdown on lifestyle among Spanish older people with hypertension, pulmonary disease, cardiovascular disease, musculoskeletal disease, depression, and cancer.** Epidemiol Health 44. 2022. PMID: 35209708. IF: 5,92. DOI: 10.4178/epih.e2022026.

Gabarrell Pascuet Aina, V, Ayuso Mateos Jose L, Miret Marta, Lara Elvira, Haro Josep M, Olaya Beatriz, Domenech Abella Joan. **The effect of loneliness and social support on the course of major depressive disorder among adults aged 50 years and older: A longitudinal study**. Depression Anxiety 39 (2). 2022. PMID: 35029840. IF: 8,13. DOI: 10.1002/da.23236

Saris Ilja M J, Aghajani Moji, Jongs Niels, Reus Lianne M, van der Wee Nic J A, Bilderbeck Amy C, van Rossum Inge Winter, Arango Celso, de la Torre Luque Alejandro, Malik Asad, Raslescu Andreea, Dawson Gerard R, Ayuso Mateos Jose L, Kas Martien J, Penninx Brenda W J H. **Cross-disorder and disorder-specific deficits in social functioning among schizophrenia and alzheimer's disease patients**. PLoS One 17 (4). 2022. PMID: 35421108. IF: 3,75. DOI: 10.1371/journal.pone.0263769

Villarejo Galende A, García Arcelay E, Piñol Ripoll G, Del Olmo Rodríguez A, Viñuela F, Boada M, Franco Macías E, Ibañez de la Peña A, Riverol M, Puig Pijoan A, Abizanda Soler P, Arroyo R, Baquero Toledo M, Feria Vilar I, Balasa M, Berbel A, Rodríguez E, Vieira Campos A, García Ribas G, Rodrigo Herrero S, Terrancle A, Prefasi D, Lleó A, Maurino J. **Quality of Life and the Experience of Living with Early-Stage Alzheimer's Disease.** J Alzheimer's Dis 90 (2). 2022. PMID: 36155523. IF: 4,16. DOI: 10.3233/JAD-220696

Armocida B, Monasta L, Sawyer S, Bustreo F, Segafredo G, Castelpietra G et al. **Burden of non-communicable diseases among adolescents aged 10-24 years in the EU, 1990-2019: a systematic analysis of the Global Burden of Diseases Study 2019**. The Lancet Child & adolescent health. 2022. PMID: 35339209. IF: 37.746. DOI: 10.1016/S2352-4642(22)00073-6.

GBD 2019 Dementia Forecasting Collaborators. **Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019**. Lancet Public Health 7 (2): 105-125. 2022. PMID: 34998485. IF: 72.427. doi: 10.1016/S2468-2667(21)00249-8

Jorid Kalseth, Valeria Donisi, Marta Miret, Anna K Forsman, Johanna Cresswell-Smith. **Exploring the Association between Welfare State and Mental Wellbeing in Europe: Does Age Matter?** International journal of environmental research and public health. 2022. PMID: 36078694. IF: 4.614**.** DOI:10.3390/ijerph191710985

Javier-David Lopez-Morinigo, Hilario Blasco-Fontecilla, Philippe Courtet, José-Luis Ayuso-Mateos. **Investigating the relationship between cross-national suicide rates and COVID-19 first and second waves spread across the world: an exploratory study**. Revista de Psiquiatria y Salud Mental. 2022. PMID: 35251385. IF: 6.795. DOI:10.1016/j.rpsm.2022.02.002

Akin Ojagbemi, Eduardo Estrada, Alejandro de la Torre-Luque, Dario Moreno-Agostino, Elvira Lara, Francisco Felix Caballero, Toyin Bello, Beatriz Olaya, Josep Maria Haro, Oye Gureje, Jose Luis Ayuso-Mateos. **Late-life disability trajectories in Yoruba Nigerians and the Spanish population: a state space model in continuous time**. Aging and mental health. 2022. PMID: 34842009. IF: 3.520. DOI:10.1080/13607863.2021.2008307.

GBD 2020 Alcohol Collaborators. **Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020 Prostate Cancer**. The lancet. 2022. PMID: 35843246. IF: 202.731. DOI: 10.1016/S0140-6736(22)00847-9.

Alejandro de la Torre-Luque , Alba Viera-Campos, Amy C Bilderbeck, Maria Teresa Carreras, Jose Vivancos, Covadonga M Diaz-Caneja, Moji Aghajani, Ilja M J Saris, Andreea Raslescu, Asad Malik, Jenna Clark, Brenda W J H Penninx, Nic van der Wee, Inge Winter-van Rossum, Bernd Sommer, Hugh Marston, Gerard R Dawson, Martien J Kas, Jose Luis Ayuso-Mateos, Celso Arango. **Relationships between social withdrawal and facial emotion recognition in neuropsychiatric disorders.** Progress in Neuro- Psychopharmacology and Biological Psychiatry. 2022. PMID: 34718073. IF: 5.201. DOI: 10.1016/j.pnpbp.2021.110463

Renaldo M Bernard, Claudia Toppo, Alberto Raggi, Marleen de Mul, Carlota de Miquel, Maria Teresa Pugliese, Christina M van der Feltz-Cornelis, Ana Ortiz-Tallo, Luis Salvador-Carulla, Sue Lukersmith, Leona Hakkaart-van Roijen, Dorota Merecz-Kot, Kaja Staszewska , Carla Sabariego. **Strategies for Implementing Occupational eMental Health Interventions: Scoping Review**. Journal of Medical Internet Research. 2022. PMID: 35648457. IF: 7.077. DOI 10.2196/34479

Alejandro de la Torre-Luque, Andres Pemau, Victor Perez-Sola, Jose Luis Ayuso-Mateos. **Suicide mortality in Spain in 2020: The impact of the COVID-19 pandemic**. Revista de Psiquiatria y Salud Mental. 2022. PMID: 35132342. IF: 6.795. DOI: 10.1016/j.rpsm.2022.01.003

Irene Rodríguez-Gómez, Coral Sánchez-Martín, Francisco J García-García, Esther García-Esquinas, Marta Miret, Germán Vicente-Rodriguez, Narcís Gusi, Asier Mañas, José A Carnicero, Marcela Gonzalez-Gross, José L Ayuso- Mateos, Fernando Rodríguez-Artalejo, Leocadio Rodríguez-Mañas, Ignacio Ara. **The medium-term consequences of a COVID-19 lockdown on lifestyle among Spanish older people with hypertension, pulmonary disease, cardiovascular disease, musculoskeletal disease, depression, and cáncer**. Epidemiology and health. 2022. PMID: 35209708. IF: 5.919. DOI: 10.4178/epih.e2022026.

LINE 2.5 ›› NEUROSURGERY OF EPILEPSY

GROUP 34

Head of laboratory: Pastor Gómez, Jesús

Area 2 Translational neuroscience

Line 2.5 Neurosurgery of epilepsy

RESEARCH INTEREST

My current work focuses on the validation of 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 electrophisiological 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.

GROUP MEMBERS

- Jesús Pastor Gómez
- Esmeralda Rocío Martín
- Cecilia Luque Cárdenas
- Pilar Martín Plasencia
- Fernando Carvajal Molina
- Miguel Pintor Zamora
- Marta Navas García
- Cristina Virginia Torres Díaz
- Lorena Carolina Vega Zelaya
- Eva de Dios Tomás
- Eduardo García Navarrete
- María Luisa Meilan Paz
- Paloma Pulido Rivas
- Rybel Wix Ramos

Torres Díaz,Cristina Virginia;Ovejero Benito,María del Carmen. CARACTERIZACIÓN PROFUNDA DE LA ZONA EPILEPTÓGENA DE PACIENTES CON EPILEPSIA FÁRMACORRESISTENTE: DESCIFRANDO EL PAPEL DE LAS CÉLULAS TETRAPLOIDES NEURALES.FIS.20/01391.INSTITUTO SALUD CARLOS III.2021-2023.

★ MAJOR GRANTS

Pastor J, Vega Zelaya L, Torres CV, Navas García M, López Manzanares L. **Hacia una definición fisiológica positiva de los núcleos cerebrales profundos en humanos.** Rev Neurol 75 (12). 2022. PMID: 36514203. IF: 1,24. DOI: 10.33588/rn.7512.2022187.

Rivas EA, Giannetti R, Garcia CRM, Domingo JM, Frias JDM, Scandurra G, Ciofi C, Vega Zelaya L, Pastor J. **A Quasi-Wireless Intraoperatory Neurophysiological Monitoring System**. Electronics (Switzerland) 11 (23). 2022. IF: 2,69. DOI: 10.3390/electronics11233918.

Nava Cedeño DJ, Alonso Cerezo MC, Sanz García A, Vega Zelaya L, Gordillo Perdomo JJ, Toledo Heras M, Pastor Gómez J, Torres Díaz C, Pulido Rivas P, García Sola R. **Asociación entre los polimorfismos genéticos de nucleótido único en genes transportadores ABC con la epilepsia farmacorresistente en la población española.** Rev Neurol 75 (9). 2022. PMID: 36285445. IF: 1,24. DOI: 10.33588/rn.7509.2022133.

Wix Ramos R, Rocio Martín E, Luque Cárdenas C, López Viñas L, Gago Veiga A. **Greater occipital nerve (GON) blocks for treating of hypnic headache: A case report.** Sleep Med 97. 2022. PMID: 35679776. IF: 4,84. DOI: 10.1016/j.sleep.2022.05.012.

Castaño Leon AM, Paredes I, Lagares A, Gomez PA, González Leon P, Perez Nuñez A, Jiménez Roldán L, Delgado Fernández J, Eiriz Fernández C, García Pérez D, Moreno Gómez LM, Esteban Sinovas O, Delgado López PD, Martín Alonso J, Kaen A, Tirado Caballero J, Ordóñez Carmona M, Arteaga Romero F, González Pombo M, Alén FJ, Gil Simoes R, Torres CV, Navas García M, Blasco García de Andoain G, Frade Porto N, González Tarno P, Martin Segura A, Gelabert González M, Menéndez Cortezón B, Rodríguez Botana B et al. **Patients awaiting surgery for neurosurgical diseases during the first wave of the COVID-19 pandemic in Spain: a multicentre cohort study.** BMJ OPEN 12 (8). 2022. PMID: 35977759. IF: 3,01. DOI: 10.1136/bmjopen-2022-061208.

López Viñas L, Vega Villar J, Rocío Martín E, García P, De La Rosa Santiago E, Galván Román JM, Wix Ramos R. **Diaphragm impairment in patients admitted for severe COVID-19.** Eur J Trans Mylogy 32 (2). 2022. PMID: 35727218. DOI: 10.4081/ejtm.2022.10460.

Martínez Álvarez R, Torres Diaz C. **Surgery of autism: Is it possible?** Prog Brain Res 272 (1). 2022. PMID: 35667807. IF: 2,62. DOI: 10.1016/bs.pbr.2022.03.001.

Pastor J, Vega Zelaya L, Martín Abad E. **Atypical Extracellular Action Potentials from Posteromedial Hypothalamus in Anesthetized Humans.** Front Biosci Landmark 27 (5). 2022. PMID: 35638422. IF: 3,12. DOI: 10.31083/j.fbl2705155.

Pérez Sánchez JR, Martínez Álvarez R, Martínez Moreno NE, Torres Diaz C, Rey G, Pareés I, Del Barrio A, Álvarez Linera J, Kurtis MM. **Gamma Knife® stereotactic radiosurgery as a treatment for essential and parkinsonian tremor: long-term experience.** Neurologia (Engl Ed). PMID: 35305964. IF: 5, 48. DOI: 10.1016/j.nrleng.2020.05.025.

Arevalo Saenz Alejandra, Lopez Manzanares Lydia, Navas Garcia Marta, Pastor Jesus, Vega Zelaya Lorena, V. **Deep brain stimulation in Parkinson's disease: analysis of brain fractional anisotropy differences in operated patients**. Rev Neurol 74 (4). 2022. PMID: 35148421. IF: 1,24. DOI:10.33588/rn.7404.2021196.

Martínez Álvarez R, Torres Diaz C. **Modern Gamma Knife radiosurgery for management of psychiatric disorders.** Prog Brain Res 270. (1). 2022. PMID: 35396026. IF: 2,62. DOI: 10.1016/bs.pbr.2021.12.002.

Yan H, Elkaim LM, Venetucci Gouveia F, Huber JF, Germann J, Loh A, Benedetti-Isaac JC, Doshi PK, Torres CV, Segar DJ, Elias GJB, Boutet A, Cosgrove GR, Fasano A, Lozano AM, Kulkarni AV, Ibrahim GM. **Deep brain stimulation for extreme behaviors associated with autism spectrum disorder converges on a common pathway: a systematic review and connectomic analysis**. J Neurosurg. 21:1-10. 2022. PMID: 35061980. IF: 5, doi: 10.3171/2021.11.JNS21928.

LINE 2.6 ›› CEREBROVASCULAR DISEASES

GROUP 35

Head of laboratory: Vivancos Mora, José Aurelio

Area 2 Translational neuroscience

Line 2.6 Cerebrovascular diseases

RESEARCH INTEREST

Stroke and Cerebrovascular Diseases

1. 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.
2. Acute phase treatments: Interventional neuroradiology and emerging therapies. Strategies to improve the selection of patient candidates.
3. Neuroprotection: Biomolecular markers of ischemia and new therapeutic targets and strategies
4. Primary and secondary stroke prevention: Detection of atrial fibrillation using a new ECG monitoring device based on biomedical textiles (wearables). Identification of risk profiles.
5. Population-based health services delivery / stroke code system
6. Telemedicine Movement Disorders

- Parkinson disease in young patients
- Parkinson disease. Follow-up and control helped by new technologies Cephaleas
- Study of the response variables to botulinum toxin and anti- CGRP monoclonal antibodies.
- Glutamate and headaches
- Non-invasive outpatient monitoring of biometric and biophysical variables as a method for prediction of migraine crises. 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

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 Epilepsy
- Drug-refractory epilepsy
- Genetic alterations in refractory epilepsy
- Non-convulsive epileptic status
- Neuroimaging in the emergency epileptic patient. Neuromuscular diseases
- Immunopathogenesis of myasthenia gravis

GROUP MEMBERS

- Alicia González Martínez
- José Antonio Fernández Alén
- Clara Aguirre Hernández
- Carmen Ramos Martín

- Beatriz González García
- Santiago Trillo Senin
- Gustavo Enrique Zapata
- Wainberg Aránzazu Vázquez Doce
- María de Toledo Heras
- Ana Beatriz Gago Veiga
- Álvaro Ximenez-Carrillo Rico
- Teresa Carreras Rodríguez
- Mónica Sobrado Sanz
- Lydia López Manzanares
- Virginia Meca Lallana
- Florentino Nombela Merchán
- Gemma Reig Roselló
- Noemí Mora Pérez

MAJOR GRANTS

Vivancos Mora, José Aurelio. RICORS-ICTUS: Enfermedades vasculares cerebrales. RD21/0006/0009. ISCIII. 2022-2024.

Gago Veiga,Ana Beatriz.PMP22/00158 - MEDICINA PERSONALIZADA DE PRECISIÓN: PREDIMIGRAINE: Medicina de precisión para prevenir la cronificación de la migraña a través de la predicción de las crisis de dolor y de la respuesta al tratamiento con anticuerpos anti-CGRP utilizando estrategias multi-ómicas. PMP22/00158. ISCIII. 2023-2025.

Reig-Roselló, Gemma. Vivancos, José. Modelo de predicción con técnicas de aprendizaje automático (Machine Learning) del pronóstico y de las complicaciones intrahospitalarias del ictus en su fase aguda. PI22/01454. ISCIII.2023-2025.

PUBLICATIONS

Pastor J, Vega-Zelaya L, Torres CV, Navas-García M, López-Manzanares L. **Hacia una definición fisiológica positiva de los núcleos cerebrales profundos en humanos.** Rev Neurol 75 (12): 369-376. 2022. PMID: 36514203. IF: 1,24. DOI: 10.33588/rn.7512.2022187.

Vera A, Cecconi A, Ximénez-Carrillo Á, Ramos C, Martínez-Vives P, Lopez- Melgar B, Sanz-García A, Ortega G, Aguirre C, Vivancos J, Jiménez- Borreguero LJ, Alfonso F, DECRYTORING Study Investigators. **Advanced Echocardiography With Left Atrial Strain and Indexed Left Atrial Three- Dimensional Volume for Predicting Underlying Atrial Fibrillation After Cryptogenic Stroke.** Am J Cardiol 185: 87-93. 2022. PMID: 36307348. IF: 3,13. DOI: 10.1016/j.amjcard.2022.09.004.

Meca-Lallana V, García Domínguez JM, López Ruiz R, Martín-Martínez J, Arés Luque A, Hernández Pérez MA, Prieto González JM, Landete Pascual L, Sastre-Garriga J. **Expert-Agreed Practical Recommendations on the Use of Cladribine.** Neurol Ther 11 (4): 1475-1488. 2022. PMID: 36068429. IF: 4,45. DOI: 10.1007/s40120-022-00394-0.

Villanueva V, García-Ron A, Smeyers P, Arias E, Soto V, García-Peñas JJ, González-Álguacil E, Sayas D, Serrano-Castro P, Garces M, Hampel K, Tomás M, Lara J, de Toledo M, Barceló I, Aledo-Serrano A, Gil-Nagel A, Iacampo L, Falip M, Saiz-Diaz RA, Gómez-Ibañez A, Sopelana D, Sanchez-Larsen A, López-González FJ. **Outcomes from a Spanish Expanded Access Program on cannabidiol treatment in pediatric and adult patients with epilepsy.** Epilepsy Behav 137 (Pt A): 108958-108958. 2022. PMID: 36327646. IF: 3,34. DOI: 10.1016/j.yebeh.2022.108958.

Gonzalez-Martinez A, Guerrero-Peral ÁL, Arias-Rivas S, Silva L, Sierra Á, Gago-Veiga AB, García-Azorín D. **Amitriptyline for post-COVID headache: effectiveness, tolerability, and response predictors.** J Neurol 269 (11): 5702-5709. 2022. PMID: 35829760. IF: 6,68. DOI: 10.1007/s00415-022-11225-5.

de Toledo M, de la Fuente E, Ramos C, Ferreiros-Martinez R, Muro I, Vieira Campos A, de Toledo MP, Lagares A, Sobrado M, Ovejero-Benito MC. **Extensive pharmacokinetic variability of Levetiracetam. ¿Are doctors aware?**. Epilepsy Res 187: 107029-107029. 2022. PMID: 36272308. IF: 2,99. DOI: 10.1016/j.eplepsyres.2022.107029.

Máñez-Miró JU, Vivancos-Matellano F, Alonso-Frech F, Vela-Desojo L, López-Ariztegui N, López-Manzanares L, Balaguer E, Martínez-Castrillo JC, Herrero-Infante Y, Gasca-Salas C, Morales-Casado MI, Casas E, Hernández A, Pareés I, Tegel-Ayuela I, Martínez-Fernández R, Martinez-Martin P. **Validation of the OPTIMIPARK Questionnaire: A Tool to Optimize Treatment in Parkinson's Disease.** MOV DISORD CLIN PRACT 9 (8): 1085- 1093. 2022. PMID: 36339297. IF: 4,51. DOI: 10.1002/mdc3.13581.

Nava-Cedeño DJ, Alonso-Cerezo MC, Sanz-García A, Vega-Zelaya L, Gordillo-Perdomo JJ, Toledo-Heras M, Pastor-Gómez J, Torres-Díaz C, Pulido-Rivas P, García-Sola R. **Asociación entre los polimorfismos genéticos de nucleótido único en genes transportadores ABC con la epilepsia farmacorresistente en la población española.** Rev Neurol 75 (9): 251-259. 2022. PMID: 36285445. IF: 1,24. DOI: 10.33588/rn.7509.2022133.

Basterra PP, Nombela F, Iriarte P, Del Rincon CR, Maroto JA, Quintas S. **Proprioceptive Stimuli as a New Type of Trigger for Epilepsy in Stiff Person Syndrome**. NEUROLOGY 99 (16): 711-712. 2022. PMID: 36240096. IF: 11,80. DOI: 10.1212/WNL.0000000000201196.

Gonzalez-Martinez A, Pagán J, Sanz-García A, García-Azorín D, Rodríguez- Vico JS, Jaimes A, García AG, de Terán JD, González-García N, Quintas S, Belascoaín R, Casas Limón J, Latorre G, Calle de Miguel C, Sierra Á, Guerrero-Peral ÁL, Trevino-Peinado C, Gago-Veiga AB. **Machine-learning- based approach for predicting response to anti-calcitonin gene-related peptide (CGRP) receptor or ligand antibody treatment in patients with migraine: A multicenter Spanish study.** Eur J Neurol 29 (10): 3102-3111. 2022. PMID: 35726393. IF: 6,29. DOI: 10.1111/ene.15458.

Alonso-Singer P, Aguilar-Amat Prior MJ, Oliva-Navarro J, Massot-Tarrús A, Giráldez BG, Bermejo P, DeToledo-Heras M, Aledo-Serrano Á, Martínez- Cayuelas E, Tirado-Requero P, Velázquez-Fragua R, López-Sobrino G, Ojeda J. **Perampanel as adjuvant treatment in epileptic encephalopathies: A multicenter study in routine clinical practice.** Epilepsy Behav 134: 108836-108836. 2022. PMID: 35870432. IF: 3,34. DOI: 10.1016/j.yebeh.2022.108836.

Wix Ramos R, Rocio Martín E, Luque Cárdenas C, López Viñas L, Gago Veiga A.. **Greater occipital nerve (GON) blocks for treating of hypnic headache: A case report.** Sleep Med 97: 10-12. 2022. PMID: 35679776. IF: 4,84. DOI: 10.1016/j.sleep.2022.05.012.

Ximénez-Carrillo Á, Zapata-Wainberg G, Sastre R, Álvarez-Pasquín MJ, Javierre AP, Lozano T, Samir E, Perosanz L, González B, Sobrado M, Vivancos J. **Detection of hidden atrial fibrillation in primary care using a long-term band-based ECG registration system: The DESCUUBRE-FA study.** J Stroke Cerebrovasc Dis 31 (9): 106642-106642. 2022. PMID: 35863263. IF: 2,68. DOI: 10.1016/j.jstrokecerebrovasdis.2022.106642.

Garcia-Pastor A, Gil-Núñez A, Ramirez-Moreno JM, González-Nafría N, Tejada J, Moniche F, Portilla-Cuenca JC, Martínez-Sánchez P, Fuentes B, Gamero-García MA, de Leciñana MA, Masjuan J, Verge DC, Aladro Y, Parkhutik V, Lago A, de Arce-Borda AM, Usero-Ruiz M, Delgado-Mederos R, Pampliega A, Ximenez-Carrillo A, Bártulos-Iglesias M, Castro-Reyes E, Stroke Project of the Spanish Cerebrovascular Diseases Study Group. **Endarterectomy, Stenting, or Medical Treatment for Symptomatic Carotid Near-Occlusion: Results from CAOS, a Multicenter Registry Study.** Am J Neuroradiol 43 (9): 1304-1310. 2022. PMID: 35981762. IF: 4,97. DOI: 10.3174/ajnr.A7617.

Castaño-Leon AM, Paredes I, Lagares A, Gomez PA, González-Leon P, Perez- Nuñez A, Jiménez-Roldán L, Delgado-Fernández J, Eiriz Fernández C, García- Pérez D, Moreno-Gómez LM, Esteban-Sinovas O, Delgado-López PD, Martín-Alonso J, Kaen A, Tirado-Caballero J, Ordóñez-Carmona M, Arteaga- Romero F, González-Pombo M, F Alén J, Gil-Simoes R, Torres CV, Navas-García M, Blasco García de Andoain G, Frade-Porto N, González-Tarno P, Martin Segura A, Gelabert-González M, Menéndez-Cortezón B, Rodríguez- Botana Bet al. **Patients awaiting surgery for neurosurgical diseases during the first wave of the COVID-19 pandemic in Spain: a multicentre cohort study.** BMJ OPEN 12 (8): 061208. 2022. PMID: 35977759. IF: 3,01. DOI: 10.1136/bmjopen-2022-061208.

Aledo-Serrano A, Hariramani R, Gonzalez-Martinez A, Álvarez-Troncoso J, Toledano R, Bayat A, Garcia-Morales I, Becerra JL, Villegas-Martínez I, Beltran-Corbellini A, Gil-Nagel A. **Anakinra and tocilizumab in the chronic phase of febrile infection-related epilepsy syndrome (FIRES): Effectiveness and safety from a case-series.** Seizure 100: 51-55. 2022. PMID: 35759951. IF: 3,41. DOI: 10.1016/j.seizure.2022.06.012.

Brieva L, Estruch BC, Merino JAG, Meca-Lallana V, Río J, Rodríguez- Antigüedad A, Agüera E, Ara JR, Luque AA, Garcia CA, Blanco Y, Castillo- Triviño T, Costa-Frossard L, González Platas M, Pascual LL, Llaneza-González M, Ginés MLM, Matías-Guiu J, Meca-Lallana JE, Bilbao MM, Sempere AP, Romero-Pinel L, Saiz A, Moral E. **Disease modifying therapy switching in relapsing multiple sclerosis: A Delphi consensus of the demyelinating expert group of the Spanish society of neurology**. Mult Scler Relat Disord 63: 103805-103805. 2022. PMID: 35512501. IF: 4,81. DOI: 10.1016/j.msard.2022.103805.

Santos-García D, de Deus Fonticoba T, Cores Bartolomé C, Íñiguez Alvarado MC, Feal Panceiras MJ, Suárez Castro E, Canfield H, Martínez Miró C, Jesús S, Aguilar M, Pastor P, Planellas L, Cosgaya M, García Caldentey J, Caballol N, Legarda I, Hernández Vara J, Cabo I, López Manzanares L, González Aramburu I, Ávila Rivera MA, Gómez Mayordomo V, Nogueira V, Puente V, Dotor García-Soto J, Borrué C, Solano Vila B, Álvarez Sauco M, Vela L, Escalante S et al. **Predictors of the change in burden, strain, mood, and quality of life among caregivers of Parkinson's disease patients.** Int J Geriatr Psychiatry 37 (6): GPS5761. 2022. PMID: 35633051. IF: 3,85. DOI: 10.1002/gps.5761.

Pérez-López C, Hernández-Vara J, Caballol N, Bayes À, Buongiorno M, Lopez-Ariztegui N, Gironell A, López-Sánchez J, Martínez-Castrillo JC, Sauco M A, López-Manzanares L, Escalante-Arroyo S, Pérez-Martínez DA, Rodríguez-Molinero A, MoMoPa-EC Research Group. **Comparison of the Results of a Parkinson's Holter Monitor With Patient Diaries, in Real Conditions of Use: A Sub-analysis of the MoMoPa-EC Clinical Trial.** Front Neurol 13: 835249-835249. 2022. PMID: 35651347. IF: 4,09. DOI: 10.3389/fneur.2022.835249.

Serra López-Matencio JM, Gago-Veiga AB, Gómez M, Alañón Plaza E, Mejía GP, González-Gay MÁ, Castañeda S. **Treatment of migraine with monoclonal antibodies**. Expert Opin Biol Ther 22. (6): 707-716. 2022. PMID: 35502612. IF: 5,59. DOI: 10.1080/14712598.2022.2072207.

Meca-Lallana JE, Gómez-Ballesteros R, Pérez-Miralles F, Forero L, Sepúlveda M, Calles C, Martínez-Ginés ML, González-Suárez I, Boyero S, Romero-Pinel L, Sempere ÁP, Meca-Lallana V, Querol L, Costa-Frossard L, Prefasi D, Maurino J. **Impact of Neuromyelitis Optica Spectrum Disorder on Quality of Life from the Patients' Perspective: An Observational Cross- Sectional Study**. Neurol Ther 11 (3): 1101-1116. 2022. PMID: 35524037. IF: 4,45. DOI: 10.1007/s40120-022-00356-6.

Galvez-Goicurla J, Pagan J, Gago-Veiga AB, Moya JM, Ayala JL. **Cluster- Then-Classify Methodology for the Identification of Pain Episodes in Chronic Diseases**. IEEE J Biomedical Health Informat 26 (5): 2339-2350. 2022. PMID: 34813482. IF: 7,02. DOI: 10.1109/JBHI.2021.3129779.

Lopez-Soley E, Meca-Lallana JE, Llufriu S, Blanco Y, Gómez-Ballesteros R, Maurino J, Pérez-Miralles F, Forero L, Calles C, Martinez-Gines ML, Gonzalez-Suarez I, Boyero S, Romero-Pinel L, Sempere ÁP, Meca-Lallana V, Querol L, Costa-Frossard L, Sepulveda M, Solana E. **Cognitive Performance and Health-Related Quality of Life in Patients with Neuromyelitis Optica Spectrum Disorder**. J Pers Med 12 (5): 743. 2022. PMID: 35629165. IF: 3,51. DOI: 10.3390/jpm12050743.

Santos-García D, de Deus Fonticoba T, Bartolomé CC, Painceiras MJF, Castro ES, Canfield H, Miró CM, Jesús S, Aguilar M, Pastor P, Planellas L, Cosgaya M, Caldentey JG, Caballol N, Legarda I, Hernández-Vara J, Cabo I, Manzanares LL, Aramburu IG, Rivera MAÁ, Mayordomo VG, Nogueira V, Puente V, García-Soto JD, Borrué C, Vila BS, Sauco MÁ, Vela L, Escalante S, Cubo E et al. **Motor Fluctuations Development Is Associated with Non- Motor Symptoms Burden Progression in Parkinson's Disease Patients: A 2-Year Follow-Up Study**. Diagn 12 (5): 1147. 2022. PMID: 35626303. IF: 3,99. DOI: 10.3390/diagnostics12051147.

Monteiro C, Miarka L, Perea-García M, Priego N, García-Gómez P, Álvaro- Espinosa L, de Pablos-Aragoneses A, Yebra N, Retana D, Baena P, Fustero- Torre C, Graña-Castro O, Troulé K, Caleiras E, Tezanos P, Muela P, Cintado E, Trejo JL, Sepúlveda JM, González-León P, Jiménez-Roldán L, Moreno LM, Esteban O, Pérez-Núñez Á, Hernández-Lain A, Mazarico Gallego J, Ferrer I, Suárez R, Garrido-Martín EM, Paz-Ares L et al. **Stratification of radiosensitive brain metastases based on an actionable S100A9/RAGE resistance mechanism**. Nat Med 28 (4): 752-765. 2022. PMID: 35411077. IF: 87,24. DOI: 10.1038/s41591-022-01749-8.

Fernández-Velasco JI, Monreal E, Kuhle J, Meca-Lallana V, Meca-Lallana J, Izquierdo G, Oreja-Guevara C, Gascón-Giménez F, Sainz de la Maza S, Walo-Delgado PE, Lapuente-Suanzes P, Maceski A, Rodríguez-Martín E, Roldán E, Villarrubia N, Saiz A, Blanco Y, Diaz-Pérez C, Valero-López G, Diaz-Diaz J, Aladro Y, Brieva L, Íñiguez C, González-Suárez I, Rodríguez de Antonio LA, García-Domínguez JM, Sabin J, Llufriu S, Masjuan J, Costa-Frossard L et al. **Baseline Inflammatory Status Reveals Dichotomic Immune Mechanisms Involved In Primary-Progressive Multiple Sclerosis Pathology.** Front Immunol 13: 842354-842354. 2022. PMID: 35386690. IF: 8,79. DOI: 10.3389/fimmu.2022.842354.

Rueda Vega M, Martínez-Fernández A, Quintas S, Díaz de Terán J, Latorre González G, Trabajos García O, Vivancos Mora J, Gago-Veiga AB. **"The Triptan's Hangover": A Multicentric Cross-sectional Observational Study of the Adverse Events of Triptans in Patients With Migraine**. Clin Neuropharmacol 45 (2): 21-26. 2022. PMID: 35185146. IF: 1,38. DOI: 10.1097/WNF.0000000000000498.

Zhu L, Retana D, García-Gómez P, Álvaro-Espinosa L, Priego N, Masmudi- Martín M, Yebra N, Miarka L, Hernández-Encinas E, Blanco-Aparicio C, Martínez S, Sobrino C, Ajenjo N, Artiga MJ, Ortega-Paino E, Torres-Ruiz R, Rodríguez-Perales S; RENACER; Soffietti R, Bertero L, Cassoni P, Weiss T, Muñoz J, Sepúlveda JM, González-León P, Jiménez-Roldán L, Moreno LM, Esteban O, Pérez-Núñez Á, Hernández-Laín A, Toldos O et al. **A clinically compatible drug-screening platform based on organotypic cultures identifies vulnerabilities to prevent and treat brain metastasis**. EMBO Mol Med 14 (3): 14552. 2022. PMID: 35174975. IF: 14,26. DOI: 10.15252/emmm.202114552.

Arévalo-Sáenz A, López-Manzanares L, Navas-García M, Pastor J, Vega- Zelaya L, Torres CV. **Deep brain stimulation in Parkinson's disease: analysis of brain fractional anisotropy differences in operated patients**. Rev Neurol 74 (4): 125-133. 2022. PMID: 35148421. IF: 1,24. DOI: 10.33588/rn.7404.2021196.

Garcia-Azorin D, Layos-Romero A, Porta-Etessam J, Membrilla JA, Caronna E, Gonzalez-Martinez A, Mencia ÁS, Segura T, Gonzalez-García N, Díaz-de- Terán J, Gallardo VJ, Gago-Veiga AB, Ballvé A, Trigo López J, Sastre-Real M, Llauradó A, Cornejo A, de Lorenzo I, Guerrero-Peral Á, Pozo-Rosich P. **Post- COVID-19 persistent headache: A multicentric 9-months follow-up study of 905 patients**. CEPHALALGIA 42 (8): 804-809. 2022. PMID: 35166156. IF: 6,08. DOI: 10.1177/03331024211068074.

Santos García D, García Roca L, de Deus Fonticoba T, Cores Bartolomé C, Naya Ríos L, Canfield H, Paz González JM, Martínez Miró C, Jesús S, Aguilar M, Pastor P, Planellas L, Cosgaya M, García Caldentey J, Caballol N, Legarda I, Hernández Vara J, Cabo I, López Manzanares L, González Aramburu I, Ávila Rivera MA, Gómez Mayordomo V, Nogueira V, Puente V, Dotor García-Soto J, Borrué C, Solano Vila B, Álvarez Sauco M, Vela L, Escalante S et al. **Constipation Predicts Cognitive Decline in Parkinson's Disease: Results from the COPPADIS Cohort at 2-Year Follow-up and Comparison with a Control Group**. J Parkinson's Dis 12 (1): 315-331. 2022. PMID: 34602501. IF: 5,52. DOI: 10.3233/JPD-212868.

Palacio-Portilla EJ, Roquer J, Amaro S, Arenillas JF, Ayo-Martín O, Castellanos M, Freijo MM, Fuentes B, García-Pastor A, Gomis M, Gómez-Choco M, López-Cancio E, Martínez-Sánchez P, Morales A, Rodríguez-Yáñez M, Segura T, Serena J, Vivancos-Mora J, de Leciñana MA, Comité ad hoc del Grupo de Estudio de Enfermedades Cerebrovasculares de la Sociedad Española de Neurología. **Dyslipidemias and stroke prevention: recommendations of the Study Group of Cerebrovascular Diseases of the Spanish Society of Neurology**. Neurologia 37 (1): 61-72. 2022. PMID: 33160722. IF: 5,49. DOI: 10.1016/j.nrl.2020.07.027.

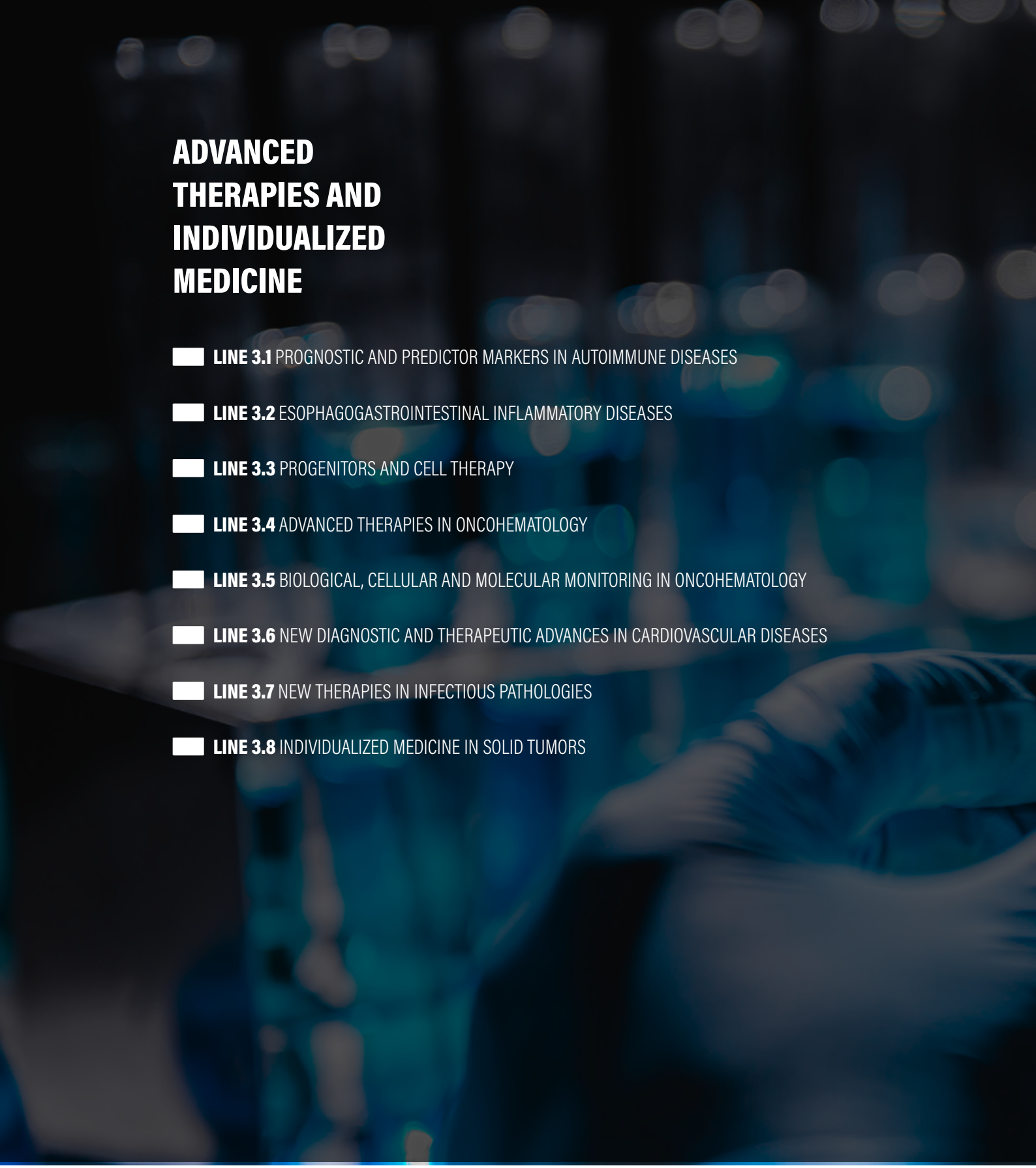
Higueras Y, Salas E, Meca-Lallana V, Carrascal Rueda P, Rodríguez De la Fuente O, Cabello-Moruno R, Maurino J, Ruiz Díaz MÁ. **Information- Seeking Strategies of People with Multiple Sclerosis in Spain: The INFOSEEK-MS Study**. Patient Preference Adherence 16: 51-60. 2022. PMID: 35046641. IF: 2,31. DOI: 10.2147/PPA.S344690.

Santos García D, Canfield H, de Deus Fonticoba T, Cores Bartolomé C, Naya Ríos L, García Roca L, Martínez Miró C, Jesús S, Aguilar M, Pastor P, Cosgaya M, García Caldentey J, Caballol N, Legarda I, Hernández Vara J, Cabo I, López Manzanares L, González Aramburu I, Ávila Rivera MA, Gómez Mayordomo V, Nogueira V, Puente V, Dotor J, Borrué C, Solano Vila B, Álvarez Sauco M, Vela L, Escalante S, Cubo E, Carrillo Padilla F et al. **Parkinson's Disease Motor Subtypes Change with the Progression of the Disease: Results from the COPPADIS Cohort at 2-Year Follow-Up**. J Parkinson's Dis 12 (3): 935-955. 2022. PMID: 34957949. IF: 5,52. DOI: 10.3233/JPD-213004.

Pagano G, Taylor KI, Anzures-Cabrera J, Marchesi M, Simuni T, Marek K, Postuma RB, Pavese N, Stocchi F, Azulay JP, Mollenhauer B, López- Manzanares L, Russell DS, Boyd JT, Nicholas AP, Luquin MR, Hauser RA, Gasser T, Poewe W, Ricci B, Boulay A, Vogt A, Boess FG, Dukart J, D'Urso G, Finch R, Zanigni S, Monnet A, Pross N, Hahn A et al. **Trial of Prasinezumab in Early-Stage Parkinson's Disease**. N Engl J Med 387 (5): 421-432. 2022. PMID: 35921451. IF: 176,08. DOI: 10.1056/NEJMoa2202867.

Gonzalez A, De la Cruz RG, Quintas S, Gomez RB, Heredia P, Vivancos J, Gago A. **Efficacy and safety of Fremanezumab in patients with episodic and chronic migraine in a real-life setting**. Eur J Neurol 29: 737-737. 2022. IF: 6,29.

Martinez AG, Galvez J, Pagan J, Quintas S, Vieira A, Rodrigo J, Sanz A, Sobrado M, Vivancos J. **Semiology characteristics of a migraine crisis according to the pain curve**. CEPHALALGIA. 42. (1_SUPPL):p. 124-124. 2022. IF: 6,08.



ADVANCED THERAPIES AND INDIVIDUALIZED MEDICINE

- **LINE 3.1** PROGNOSTIC AND PREDICTOR MARKERS IN AUTOIMMUNE DISEASES
- **LINE 3.2** ESOPHAGOGASTROINTESTINAL 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

ANNUAL REPORT OF SCIENTIFIC ACTIVITY

2022

AREA 3

INSTITUTO DE INVESTIGACIÓN SANITARIA
HOSPITAL UNIVERSITARIO DE LA PRINCESA

LINE 3.1 ›› PROGNOSTIC AND PREDICTOR MARKERS IN AUTOIMMUNE DISEASES

GROUP 36

Head of laboratory: González Álvaro, Isidoro

Area 3 Advanced therapies and individualized medicine

Line 3.1 Prognostic and predictor markers in autoimmune diseases

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 erythematous, 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 and at national level.

Regarding the first, in 2013 we were involved in the development of BioIMID 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 finished in 2018, our group will continue including patients in the IIS-IP Biobank, and we are expanding the sample collection to JAK-inhibitors.

On the other hand, we maintain an intense collaborative effort with groups of the Network of Inflamatory Disorders (REI), 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. During the las two years, and especially during 2020, we have collaborated with Dr Amaya Puig Kröguer to deepen in the understanding of their mechanism of action, resulting in the possible development of efficient biomarkers to predict response to these drugs. 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.

Obviously, the COVID-19 outbreak has conditioned the research of our group and several members have been involved in collaborative efforts with many other groups of IIS-IP and other Institutions, such as Universidad Complutense de Madrid and Centro Nacional de Biotecnología, to develop different research lines that have led not only to several publications, but also to interesting observations. Results from these studies have helped to select patients that can benefit most from being treated with IL-6 receptor blockade, or have established the relevance of detecting SARS-Cov-2 viremia in serum samples as a predictor of severity. This information has been already transmitted to physicians involved in treating COVID-19 patients, allowing to improve the management of these patients.

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. In addition, we will also focus on how to improve response to COVID-19 vaccination in a population (patients treated with immune-modulatory drugs) that usually presents a decreased response to vaccines.

GROUP MEMBERS

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- Juan Carlos López Robledillo
- Irene María Llorente Cubas
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- María de las Nieves Gómez León
- Ana María Ortiz García
- Eva Gloria Tomero Muriel
- Esther Francisca Vicente Rabaneda
- María Ahijón Lana

MAJOR GRANTS

Covid-19 en pacientes con artritis reumatoide. Estudio aleatorizado. PI21/01474. ISCIII. 2022-2024.

González Álvaro, Isidoro. Inflamación e inmunopatología de órganos y sistemas. Enfermedades inflamatorias. RD21/0002/0027. ISCIII. 2022- 2024.

González Álvaro,Isidoro. Predicción en la evolución de la Artritis Reumatoide mediante técnicas de "machine learning".FIS.18/00371. INSTITUTO SALUD CARLOS III. 2019-2022.

González Álvaro, Isidoro. PREDIRA: PREDICTION MEDICAL DEVICE FOR RHEUMATOID ARTHRITIS. UE.PREDIRA.EITHEALTH.19577. ASOCIACIÓN EIT HEALTH SPAIN. 2019-2022.

González Alvaro, Isidoro. Biomarcadores que contribuyen a optimizar la ventana de oportunidad en pacientes con artritis de reciente comienzo. PI21/00526. ISCIII. 2022-2024.

Castañeda Sanz, Santos. Impacto de la suspensión temporal del metotrexato sobre la respuesta inmune humoral y celular a la vacuna.

PUBLICATIONS

Rueda Gotor J, Ferraz Amaro I, Genre F, González Mazón I, Corrales A, Portilla V, Llorca J, Agudo Bilbao M, Aurrecoechea E, Expósito R, Hernández V, Quevedo Abeledo JC, Rodríguez Lozano C, Lopez Medina C, Ladehesa Pineda ML, Castañeda S, Vicente EF, Fernández Carballido C, Martínez Vidal MP, Castro Corredor D, Anino Fernández J, Peiteado D, Plasencia Rodríguez C, Vivar MLG, Galíndez Agirregoikoa E, Perez EM, Fernández Díaz C, Blanco R, González Gay MÁ. **Cardiovascular and disease-related features associated with extra-articular manifestations in axial spondyloarthritis. A multicenter study of 888 patients.** Semin Arthritis Rheum 57. 2022. PMID: 36150319. IF: 5,43. DOI: 10.1016/j.semarthrit.2022.152096

Delgado Arévalo C, Calvet Mirabent M, Triguero Martinez A, Vázquez de Luis E, Benguría Filippini A, Largo R, Calzada Fraile D, Popova O, Sánchez Cerrillo I, Tsukalov I, Moreno Vellisca R, de la Fuente H, Herrero Beaumont G, Ramiro AR, Sánchez Madrid F, Castañeda S, Dopazo A, González Álvaro I, Martin Gayo E. **NLRC4 -mediated activation of CD1c+ dendritic cells contributes to perpetuation of synovitis in rheumatoid arthritis.** JCI Insight 7 (22). 2022. PMID: 36194479. IF: 9,48. DOI: 10.1172/jci.insight.152886.

Calvo Río V, Sánchez Bilbao L, Álvarez Reguera C, Castañeda S, González Mazón I, Demetrio Pablo R, González Gay MA, Blanco R. **Baricitinib in severe and refractory peripheral ulcerative keratitis: a case report and literature review.** Ther. Adv. Musculoskelet. Dis.14. 2022. PMID: 36419482. IF: 3,63. DOI: 10.1177/1759720X221137126.

Domingo LC, Vallejo ER, Cruz NDZ, Llano MC, Perez Urria EA, Barrios A, Santos JH, Ortiz J, Garcia SCR, Ramirez AM, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Garcia AS, Villa A, Azofra AS, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martinez AT, Arevalo C, Roman JMG, Garcia Vicuna R et al. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol 94 (11). 2022. PMID: 35811284. IF: 20,69. DOI: 10.1002/jmv.27989

Castañeda S, Casas A, González Alba A, Martínez Guerra G, Nogués X, Ojeda Thies C, Torregrosa Suau Ó, Rodríguez Lescure Á. **Bone loss induced by cancer treatments in breast and prostate cancer patients.** Clin. Transl. Oncol. 24. (11). 2022. PMID: 35779210. IF: 3,34. DOI: 10.1007/s12094-022-02872-1

Castañeda S, Casas A, González Alba A, Martínez Guerra G, Nogués X, Ojeda Thies C, Torregrosa Suau Ó, Rodríguez Lescure Á. **Correction to: Bone loss induced by cancer treatments in breast and prostate cancer patients.** Clin Transl Oncol 24 (11): 2022. PMID: 35932363. IF: 3,34. DOI: 10.1007/s12094-022-02905-9

Triguero Martinez A, Roy Vallejo E, Tomero EG, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Lamana A, Gonzalez Alvaro I. **Galectin-1: A Potential Biomarker Differentiating between Early Rheumatoid Arthritis and Spondyloarthritis**. J Clin Med 11 (21). 2022. PMID: 36362537. IF: 4,96. DOI: 10.3390/jcm11216313.

Villapalos-García G, Zubiaur P, Rivas-Durán R, Campos-Norte P, Arévalo- Román C, Fernández-Rico M, García-Fraile Fraile L, Fernández-Campos P, Soria-Chacartegui P, Fernández de Córdoba-Oñate S,

Delgado-Wicke P, Fernández-Ruiz E, González-Álvaro I, Sanz J, Abad-Santos F, de Los Santos I. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity and sex are the primary predictors of Covid-19 severity (vol 5, e202201396, 2022)**. Life Sci Alliance 5 (10): 1-2. 2022. PMID: 35680409. IF: 5,78. DOI: 10.26508/lsa.202201545.

Villapalos-García G, Zubiaur P, Rivas-Durán R, Campos-Norte P, Arévalo- Román C, Fernández-Rico M, García-Fraile Fraile L, Fernández-Campos P, Soria-Chacartegui P, Fernández de Córdoba-Oñate S, Delgado-Wicke P, Fernández-Ruiz E, González-Álvaro I, Sanz J, Abad-Santos F, de Los Santos I. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity, and sex are the primary predictors of COVID-19 severity**. Life Sci Alliance 5 (10): e202201396. 2022. PMID: 35636966. IF: 5,78. DOI: 10.26508/lsa.202201396.

Batista Liz JC, Genre F, Pulito Cueto V, Remuzgo Martínez S, Prieto Peña D, Márquez A, Ortego Centeno N, Leonardo MT, Peñalba A, Narváez J, Martín Penagos L, Belmar Vega L, Gómez Fernández C, Miranda Filloy JA, Caminal Montero L, Collado P, De Argila D, Quiroga Colina P, Vicente Rabaneda EF, Triguero Martínez A, Rubio E, León Luque M, Blanco Madrigal JM, Galíndez Agirregoikoa E, Martín J, Gualillo O, Blanco R, Castañeda S, González Gay MA, López Mejías R. **IgA Vasculitis: Influence of CD40, BLK and BANK1 Gene Polymorphisms.** J Clin Med 11 (19). 2022. PMID: 36233442. IF: 4,96. DOI: 10.3390/jcm11195577

González Sánchez E, Muñoz Callejas A, Gómez Román J, San Antonio E, Marengo A, Tsapis N, Bohne Japiassu K, González Tajuelo R, Pereda S, García Pérez J, Cavagna L, González Gay MÁ, Vicente Rabaneda EF, Meloni F, Fattal E, Castañeda S, Urzainqui A. **Targeted nanotherapy with everolimus reduces inflammation and fibrosis in scleroderma-related interstitial lung disease developed by PSGL-1 deficient mice.** Br J Pharmacol 179 (18). 2022. PMID: 35726496. IF: 9,47. DOI: 10.1111/bph.15898.

Castaneda S, Moro Alvarez MJ. **Update of the osteoporosis guidelines of SEIOMM**. Rev Clin Esp 222 (7): 412-413. 2022. PMID: 35908819. IF: 3,06. DOI: 10.1016/j.rce.2022.06.001.

Lamana A, Castro Vazquez D, De La Fuente H, Triguero Martinez A, Martinez Hernandez R, Revenga M, Villanueva Romero R, Llamas Velasco M, Chicharro P, Juarranz Y, Marazuela M, Sales Sanz M, Garcia Vicuna R, Tomero E, Gonzalez Alvaro I, Martinez C, Gomariz RP. **VIP/VPAC Axis Expression in Immune-Mediated Inflammatory Disorders: Associated miRNA Signatures**. Int J Mol Sci 23 (15). 2022. PMID: 35955723. IF: 6,21. DOI: 10.3390/ijms23158578.

Rueda Gotor J, Ferraz Amaro I, Genre F, González Mazón I, Corrales A, Calvo Rio V, Portilla V, Llorca J, Expósito R, Hernández V, Quevedo Abeledo JC, Rodríguez Lozano C, Lopez Medina C, Ladehesa Pineda ML, Castañeda S, Vicente EF, Fernández Carballido C, Martínez Vidal MP, Castro Corredor D, Anino Fernández J, Peiteado D, Plasencia Rodríguez C, García Vivar ML, Galíndez Agirregoikoa E, Montes Perez E, Fernández Díaz C, Blanco R, González Gay MÁ. **Factors associated with atherosclerosis in radiographic and non-radiographic axial spondyloarthritis. A multicenter study on 838 patients.** Semin Arthritis Rheum 55. 2022. PMID: 35689912. IF: 5,43. DOI: 10.1016/j.semarthrit.2022.152037.

Mazzucchelli R, Rodríguez Martín S, Crespí Villarías N, García Vadillo A, Gil M, Izquierdo Esteban L, Rodríguez Miguel A, Barreira Hernández D, Fernández Antón E, García Lledó A, Pascual A, Vitaloni M, Vergés J, de Abajo FJ. **Risk of ischaemic stroke among new users of glucosamine and chondroitin sulphate: a nested case-control study.** Ther Adv Musculoskelet Dis 14. 2022. PMID: 35923649. IF: 3,63. DOI: 10.1177/1759720X221113937

Loricera J, Castañeda S, Moriano C, Narváez J, Aldasoro V, Maiz O, Melero R, Villa I, Vela P, Romero Yuste S, Callejas JL, de Miguel E, Galíndez Agirregoikoa E, Sivera F, Fernández López JC, Galisteo C, Ferraz Amaro I, Sánchez Martín J, Sánchez Bilbao L, Calderón Goercke M, Casado A, Hernández JL, González Gay MA, Blanco R. **Tocilizumab in visual involvement of giant cell arteritis: a multicenter study of 471 patients.** Ther Adv Musculoskelet Dis 14. 2022. PMID: 35898567. IF: 3,63. DOI: 10.1177/1759720X221113747

Uriarte Ecenarro M, Useros D, Alfranca A, Tejedor R, González Alvaro I, García Vicuña R. **Anti-Citrullinated Protein Antibody Titers Are Independently Modulated by Both Disease Activity and Conventional or Biologic Anti-Rheumatic Drugs.** Diagn 12 (7). 2022. PMID: 35885675. IF: 3,99. DOI: 10.3390/diagnostics12071773

Remuzgo Martínez S, Rueda Gotor J, Pulito Cueto V, López Mejías R, Corrales A, Lera Gómez L, Pérez Fernández R, Portilla V, González Mazón I, Blanco R, Expósito R, Mata C, Llorca J, Hernández V, Rodríguez Lozano C, Barbarroja N, Ortega Castro R, Vicente E, Fernández Carballido C, Martínez Vidal MP, Castro Corredor D, Anino Fernández J, Peiteado D, Plasencia Rodríguez C, Galíndez Agirregoikoa E, García Vivar ML, Vegas Revenga N, Urionaguena I, Gualillo O, Quevedo Abeledo JC et al. **Irisin as a Novel Biomarker of Subclinical Atherosclerosis, Cardiovascular Risk and Severe Disease in Axial Spondyloarthritis.** Front Immunol 13. 2022. PMID: 35898516. IF: 8,79. DOI: 10.3389/fimmu.2022.894171

Zurita-Cruz ND, Martín-Ramírez A, Rodríguez-Serrano DA, González-Álvaro I, Roy-Vallejo E, De la Cámara R, Fontán García-Rodrigo L, Cardeñoso- Domingo L. **Usefulness of real-time RT-PCR to understand the kinetics of SARS-CoV-2 in blood: A prospective study**. J Clin

Virol 152: 105166-105166. 2022. PMID: 35594784. IF: 14,48. DOI: 10.1016/j.jcv.2022.105166.

Triguero Martinez A, Roy Vallejo E, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Gonzalez Alvaro I, Lamana A. **Genetic LGALS1 Variants Are Associated with Heterogeneity in Galectin-1 Serum Levels in Patients with Early Arthritis**. Int J Mol Sci 23 (13). 2022. PMID: 35806182. IF: 6,21. DOI: 10.3390/ijms23137181

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639

Valero C, Baldivieso-Achá JP, Uriarte M, Vicente-Rabaneda EF, Castañeda S, García-Vicuña R. **Vasculitis flare after COVID-19: report of two cases in patients with preexistent controlled IgA vasculitis and review of the literature**. Rheumatol. Int. 42. (9):p. 1643-1652. 2022. PMID: 35691980. IF: 3,58. DOI: 10.1007/s00296-022-05153-w.

Julià A, Gómez A, López Lasanta M, Blanco F, Erra A, Fernández Nebro A, Mas AJ, Pérez García C, Vivar MLG, Sánchez Fernández S, Alperi López M, Sanmartí R, Ortiz AM, Fernandez Cid CM, Díaz Torné C, Moreno E, Li T, Martínez Mateu SH, Absher DM, Myers RM, Molina JT, Marsal S. **Longitudinal analysis of blood DNA methylation identifies mechanisms of response to tumor necrosis factor inhibitor therapy in rheumatoid arthritis.** EBioMedicine 80. 2022. PMID: 35576644. IF: 11,21. DOI: 10.1016/j.ebiom.2022.104053.

Martín-López M, Galindo M, Pego-Reigosa JM, Jiménez N, Olivé Marqués A, Tomero E, Freire M, Martínez-Barrio J, Boteanu A, Salgado-Perez E, Fernández-Nebro A, Calvo J, Menor-Almagro R, Rúa-Figueroa I. **Clinical characteristics and risk factors associated with lymphoma in patients with systemic lupus erythematosus: a nationwide cohort study**. Rheumatology 62 (1): 217-224. 2022. PMID: 35482477. IF: 7,05. DOI: 10.1093/rheumatology/keac258.

Serra López-Matencio JM, Gago-Veiga AB, Gómez M, Alañón Plaza E, Mejía GP, González-Gay MÁ, Castañeda S. **Treatment of migraine with monoclonal antibodies**. Expert Opin Biol Ther 22 (6): 707-716. 2022. PMID: 35502612. IF: 5,59. DOI: 10.1080/14712598.2022.2072207.

González-Gay MA, Prieto-Peña D, Castañeda S. **The role of PET/CT in the evaluation of patients with large-vessel vasculitis: useful for diagnosis but with potential limitations for follow-up**. Rheumatology 61 (12): 4587-4589. 2022. PMID: 35536166. IF: 7,05. DOI: 10.1093/rheumatology/keac251.

Atienza-Mateo B, Prieto-Peña D, Vicente-Rabaneda EF, Blanco R, González- Gay MA, Castañeda S. **Utility of tocilizumab in autoimmune eye diseases**. Expert Opin Biol Ther 22 (6): 789-799. 2022. PMID: 35422184. IF: 5,59. DOI: 10.1080/14712598.2022.2066971.

Prieto Pena D, Remuzgo Martinez S, Genre F, Ocejo Vinyals J Gonzalo, Atienza Mateo B, Munoz Jimenez A, Ortiz Sanjuan F, Romero Yuste S, Moriano C, Galindez Agirregoikoa E, Calvo I, Ortego Centeno N, Alvarez Rivas N, Miranda Filloy JA, Llorente I, Blanco R, Gualillo O, Martin J, Marquez A, Castaneda S, Ferraz Amaro I, Lopez Mejias R, Gonzalez Gay MA. **Vascular endothelial growth factor haplotypes are associated with severe ischaemic complications in giant cell arteritis regardless of the disease phenotype**. Clin Exp Rheumatol 40 (4). 2022. PMID: 35349405. IF: 4,86. DOI: 10.55563/clinexprheumatol/8mku9c.

Castañeda S, Prieto-Peña D, Vicente-Rabaneda EF, Triguero-Martínez A, Roy-Vallejo E, Atienza-Mateo B, Blanco R, González-Gay MA. **Advances in the Treatment of Giant Cell Arteritis**. J Clin Med 11 (6): 1588. 2022. PMID: 35329914. IF: 4,96. DOI: 10.3390/jcm11061588.

Urruticoechea-Arana A, Castañeda S, Otón T, Benavent D, Loza E, Martín- Martínez MA, González-Gay MÁ. **Prevalence of Metabolic Syndrome in Psoriatic Arthritis Systematic Literature Review and Results From the CARMA Cohort**. J Clin Rheumatol 28 (2): 388-396. 2022. PMID: 35192593. IF: 3,90. DOI: 10.1097/RHU.0000000000001738.

Mazzucchelli R, Almodóvar R, Turrado-Crespí P, Crespí-Villarías N, Pérez- Fernández E, García-Zamora E, García-Vadillo A. **Trends in orthopaedic surgery for spondyloarthritis: outcomes from a National Hospitalised Patient Registry (MBDS) over a 17-year period (1999-2015).TREND-EspA study**. RMD Open 8 (1): e002107. 2022. PMID: 35296531. IF: 5,81. DOI: 10.1136/rmdopen-2021-002107.

García Vicuña R, Rodriguez García SC, Abad Santos F, Bautista Hernández A, García Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso Pérez T, Cardeñoso L, Alfranca A, Mejía Abril G, Sanz J, González Alvaro I. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621.

Herrero-Morant A, Martín-Varillas JL, Castañeda S, Maíz O, Sánchez J, Ortego N, Raya E, Prior-Español Á, Moriano C, Melero-González RB,

Graña- Gil J, Urruticoechea-Arana A, Ramos-Calvo Á, Loredo-Martínez M, Salgado- Pérez E, Sivera F, Torre I, Narváez J, Andreu JL, Martínez-González O, Torre RG, Fernández-Aguado S, Romero-Yuste S, González-Mazón I, Álvarez- Reguera C, Hernández JL, González-Gay MÁ, Blanco R; Neurobehçet Spanish Collaborative Group. **Biologic therapy in refractory neurobehcet's disease: a multicentre study of 41 patients and literature review**. Rheumatology 61 (11): 4427-4436. 2022. PMID: 35166821. IF: 7,05. DOI: 10.1093/rheumatology/keac097.

Cavagna L, Meloni F, Meyer A, Sambataro G, Belliato M, De Langhe E, Cavazzana I, Pipitone N, Triantafyllias K, Mosca M, Barsotti S, Zampogna G, Biglia A, Emmi G, de Visser M, van der Kooi A, Parronchi P, Hirschi S, da Silva JAP, Scire CA, Furini F, Giannini M, Martinez Gonzalez O, Damian L, Piette Y, Smith V, Mera Varela A, Bachiller Corral J, Cabezas Rodriguez I, Brandy Garcia AM et al. **Clinical spectrum time course in non-Asian patients positive for anti-MDA5 antibodies**. Clin Exp Rheumatol 40 (2). 2022. PMID: 35200123. IF: 4,86. DOI: 10.55563/clinexprheumatol/di1083.

Rúa Figueroa I, Rúa Figueroa D, Pérez Veiga N, Anzola AM, Galindo Izquierdo M, Calvo Alén J, Fernández Nebro A, Sangüesa C, Menor Almagro R, Tomero E, Del Val N, Uriarte Isazelaya E, Blanco R, Andreu JL, Boteanu A, Narváez J, Cobo T, Bohórquez C, Montilla C, Salas E, Toyos FJ, Bernal JA, Salgado E, Freire M, Mas AJ, Expósito L, Hernández Beriain JA, Ibarguengoitia O, Velloso Feijoo ML, Lozano Rivas N et al. **Antimalarials exert a cardioprotective effect in lupus patients: Insights from the Spanish Society of Rheumatology Lupus Register (RELESSER) analysis of factors associated with heart failure.** Semin Arthritis Rheum 52. 2022. PMID: 35033377. IF: 5,43. DOI: 10.1016/j.semarthrit.2021.11.012

Valero C, Baldivieso JP, Gonzalez-Alvaro I, Tomero E, Castañeda S, García- Vicuña R.. **Effectiveness and safety of combined biological therapy in patients with refractory multidomain spondyloarthritis**. Ann Rheum Dis 81 (6): 899-901. 2022. PMID: 35086814. IF: 27,97. DOI: 10.1136/annrheumdis-2021-221812.

Hernández-Cruz B, Rosas J, Díaz-Torné C, Belzunegui J, García-Vicuña R, Inciarte-Mundo J, Pons A, Millán AM, Jeria-Navarro S, Valero JA, García- Castañeda N, Valero C, Llorente I, Calvo A, Díaz-Cerezo S, Núñez M. **Real- World Treatment Patterns and Clinical Outcomes of Baricitinib in Rheumatoid Arthritis Patients in Spain: Results of a Multicenter, Observational Study in Routine Clinical Practice (The ORBIT-RA Study)**. Rheumatol Ther 9 (2): 589-608. 2022. PMID: 35041155. IF: 4,08. DOI: 10.1007/s40744-021-00423-8.

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651

Tornero-Molina J, Alperi-López M, Castellví I, de Agustín-de Oro JJ, Escudero A, García-Vicuña R, González-Gay MA, Hidalgo C, Rubio E, Sanmartí R, Casamira N, Calvo-Alén J. **Experts document on methotrexate use in combined therapy with biological or targeted synthetic disease modifying drugs in patients with rheumatoid arthritis**. Reumatol Clin (Engl Ed) 18(1): 33-41. 2022. PMID: 35090610. doi: 10.1016/j.reumae.2020.08.009

Garcia-Giralt N, Roca-Ayats N, Abril JF, Martinez-Gil N, Ovejero D, Castañeda S, Nogues X, Grinberg D, Balcells S, Rabionet R. **Gene Network of Susceptibility to Atypical Femoral Fractures Related to Bisphosphonate Treatment**. Genes 13 (1): 146. 2022. PMID: 35052486. IF: 4,14. DOI: 10.3390/genes13010146.

- Vegas N, Martin JL, Calvo V, Gonzalez I, Sanchez L,Beltran E,Fonollosa A, Maiz O, Blanco A, Cordero M, Ortego N, Torre I, Hernandez FF, Munoz S, Ortega MME, Diaz M, Canal J, Ventosa JA, Demetrio R, Agudo M, Dominguez L, Hernandez JL, **Castaneda S**, Gonzalez MA, Blanco R. **Intravenous methylprednisolone induces rapid improvement in non-infectious uveitis: a multicentre study of 112 patients**. Clin. Exp. Rheumatol. 40. (1):p. 142-149. 2022. PMID: 33666160. IF: 4,86.

Vegas-Revenga N, Martín-Varillas JL, Calvo-Río V, González-Mazón I, Sánchez-Bilbao L, Beltrán E, Fonollosa A, Maíz O, Blanco A, Cordero-Coma M, Ortego N, Torre I, Francisco Hernández F, Muñoz-Fernández S, Esteban Ortega MM, Diaz-Llopis M, Cañal J, Ventosa JA, Demetrio-Pablo R, Agudo- Bilbao M, Domínguez-Casas L, Hernández JL, Castañeda S, González-Gay MA, Blanco R. **Intravenous methylprednisolone induces rapid improvement in non-infectious uveitis: a multicentre study of 112 patients**. Clin Exp Rheumatol 40 (1): 142-149. 2022. PMID: 33666160. IF: 4,86. doi: 10.55563/clinexprheumatol/imrgo2.

Baldivieso JP, Ramirez E, Uriarte Ecenarro M, Valero C, Velasco E, Llorente I, Morell A, Solas O, Garcia Vicuna R. **PATIENT-REPORTED EXPERIENCE IN IMMUNE MEDIATED INFLAMMATORY DISEASES (IMID) IN THECONTEXT OF THE COVID-19 PANDEMIC: ACCESSIBILITY AND CONTINUITY OF CARE.** Ann Rheum Dis 81. 2022. IF: 27,97. DOI: 10.1136/annrheumdis-2022- eular.5203.

Baldivieso JP, Tato EM, Valero C, Gutierrez Rodriguez F, Gonzalez CA, Serrano DR, Garcia Vadillo A. **CHARACTERISTICS AND MORTALITY OF PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES ADMITTED TO THE INTENSIVE CARE UNIT.** Ann Rheum Dis 81. 2022. IF: 27,97. DOI: 10.1136/annrheumdis-2022-eular.5052.

Delgado-Arévalo C, Calvet-Mirabent M, Triguero-Martínez A, Vázquez de Luis E, Benguría-Filippini A, Largo R, Calzada-Fraile D, Popova O, Sánchez-Cerrillo I, Tsukalov I, Moreno-Vellisca R, de la Fuente H, Herrero-Beaumont G, Ramiro A, Sánchez-Madrid F, Castañeda S, Dopazo A, González Álvaro I, Martin-Gayo E. **NLRC4-mediated activation of CD1c+ DC contributes to perpetuation of synovitis in rheumatoid arthritis**. JCI Insight. 2022. PMID: 36194479.IF: 9.496. doi: 10.1172/jci.insight.152886

Martín Ramírez A, Zurita Cruz ND, Gutiérrez-Cobos A, Rodríguez Serrano DA, González Álvaro I, Roy Vallejo E, Gómez de Frutos S, Fontán García- Rodrigo L, Cardeñoso Domingo L. **Evaluation of two RT-PCR techniques for SARS-CoV-2 RNA detection in serum for microbiological diagnosis**. J Virol Methods. 2022. PMID: 34910983. IF: 2.623. doi: 10.1016/j.jviromet.2021.114411.

Calderón-Goercke M, Loricera J, Moriano C, Castañeda S, Narváez J, Aldasoro V, Maiz O, Melero R, Villa JI, Vela P, Romero-Yuste S, Callejas JL, de Miguel E, Galíndez-Agirregoikoa E, Sivera F, Fernández-López JC, Galisteo C, Ferraz-Amaro I, Sanchéz-Martín J, Sánchez-Bilbao L, González- Gay MA, Hernández JL, Blanco R; Tocilizumab in Giant Cell Arteritis Spanish Collaborative Group. **Optimisation of tocilizumab therapy in giant cell arteritis. A multicentre real-life study of 471 patients**. Clin Exp Rheumatol. 2022. PMID: 36377586.IF: 4.473. doi: 10.55563/clinexprheumatol/oqs8u9

Vertui V, Zanframundo G, Castañeda S, Biglia A, Palermo BL, Cavazzana I, Meloni F, Cavagna L. **Clinical evolution of antisynthetase syndrome after SARS-CoV2 infection: a 6-month follow-up analysis. Clin Rheumatol**. 2022. (8):2601-2604. PMID: 35612768. IF: 3.650. doi: 10.1007/s10067-022- 06216-w.

Martínez-López D, Sánchez-Bilbao L, De Cos-Gómez M, González-Mazón I, Rodrigo-Calabia E, Ruiz-San Millán JC, Gómez Román J, Castañeda S, González-Gay MA, Hernández JL, Blanco R. **Long-term survival of renal transplantation in patients with lupus nephritis: experience from a single university centre**. Clin Exp Rheumatol. 2022. (3):581-588. PMID: 34665698.IF: 4.862. doi: 10.55563/clinexprheumatol/ri873i

Serra López-Matencio JM, Gómez Garcia de Soria V, Gómez M, Alañón- Plaza E, Muñoz-Calleja C, Castañeda S**. Monitoring and safety of CAR-T therapy in clinical practice**. Expert Opin Drug Saf. 2022. (3):363-371. PMID: 34519234.IF: 4.011. doi: 10.1080/14740338.2021.1979958

Vicente-Rabaneda EF, Serra López-Matencio JM, Ancochea J, Blanco R, González-Gay MÁ, Castañeda S. **Efficacy and safety of biological drugs in interstitial lung disease associated with connective tissue diseases**. Expert Opin Drug Saf. 2022. (3):311-333. PMID: 34433372. IF: 4.011. doi: 10.1080/14740338.2021.1973428.

Pulito-Cueto V, Remuzgo-Martínez S, Genre F, Calvo-Alén J, Aurrecoechea E, Llorente I, Triguero-Martinez A, Blanco R, Llorca J, Ruiz-Lucea E, Rivera-García N, Gualillo O, López-Mejías R, Castañeda S, González-Gay MA. **Role of adiponectin in non-diabetic patients with rheumatoid arthritis undergoing anti-IL-6 therapy**. Clin Exp Rheumatol. 2022. (5):988-992. PMID: 34251326. IF: 4.862. doi: 10.55563/clinexprheumatol/p8nx80.

Valero-Martínez C, Butrón Bris B, Castañeda S. **Dermatomyositis associated with anti-MDA5 antibodies: A heterogenous clinical picture**. Med Clin (Barc). 2022. (4):186-187. PMID: 34074482. doi: 10.1016/j.medcli.2021.03.013

Carmona EG, García-Giménez JA, López-Mejías R, Khor CC, Lee JK, Taskiran E, Ozen S, Hocevar A, Liu L, Gorenjak M, Potočnik U, Kiryluk K, Ortego- Centeno N, Cid MC, Hernández-Rodríguez J, Castañeda S, González-Gay MA, Burgner D, Martín J, Márquez A; Spanish IgA Vasculitis Consortium;* International Kawasaki Disease Genetics Consortium. **Identification of a shared genetic risk locus for Kawasaki disease and immunoglobulin A vasculitis by a cross-phenotype meta-analysis**. Rheumatology (Oxford). 2022.(3):1204-1210. PMID: 33993232. doi: 10.1093/rheumatology/keab443

Baldivieso Achá JP, Valero Martínez C, García Vadillo JA. **How much bone growth can occur in Paget's disease?** Med Clin (Barc). 2022. (1):46. PMID: 34247864. doi: 10.1016/j.medcli.2021.03.012.

Loarce-Martos J, Larena C, Blázquez MÁ, Joven BE, Carreira PE, Martínez- Barrio J, Monteagudo I, López-Longo FJ, Ruiz L, López-Robledillo JC, Almodóvar R, Llorente I, Tomero E, García-de la Peña P, Moruno H, Pérez A, Cobo-Ibáñez T, Lojo Oliveira L, Barbadillo MC, García-De Yébenes MJ, Nuño-Nuño L. **Clinical Characteristics of Juvenile Idiopathic Inflammatory Myopathy and Comparison With Adult Patients: Analysis From a Multicentric Cohort in Spain**. J Clin Rheumatol. 2022. (1):e195-e202. PMID: 33492027. IF: 3.902. doi: 10.1097/RHU.0000000000001696.

GROUP 37

Head of laboratory: Daudén Tello, Esteban

Area 3 Advanced therapies and individualized medicine

Line 3.1 Prognostic and predictor markers in autoimmune diseases

RESEARCH INTEREST

The research 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 biological 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. 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.

d. Survival analysis of conventional systemic therapies and biologics in psoriasis.

e. Study of optimization strategies (dose reduction, increase of the administration interval) in the treatment of moderate-to-severe psoriasis with systemic agents.

f. Regulation of CXCL12 and RAPTOR by novel miRNAs and their role during the inflammatory process in psoriasis.

g. Integrative study of systemic inflammation in chronic inflammatory skin diseases and its association with cardiovascular disease.

h. Big data-driven study to describe the proportion and patient journey of patients with psoriasis, chronic urticaria, hidradenitis suppurativa and atopic dermatitis.

2. Eczematous dermatitis.

- Study on the prevalence of allergens responsible for allergic contact dermatitis in the Spanish population.
- Development of an artificial intelligence model based on convolutional networks with the purpose of diagnosing inflammation intensity when applying epicutaneous tests.
- Pharmacogenetics in atopic dermatitis to predict therapeutic response after the administration of biological drugs.

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 urticarial

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MAJOR GRANTS

de la Fuente Flores, Hortensia / Daudén Tello, Esteban. Estudio integrativo de la inflamación sistémica en Dermatitis Atópica e Hidradenitis Supurativa y su asociación con la enfermedad cardiovascular. PI21/01583. ISCIII. 2022- 2024.

Cibrian Vera, Danay / Llamas Velasco, María del mar. Amino acids transporters as novel targets of inflammatory skin diseases. ISCIII. 2022- 2024.

PUBLICATIONS

Seguí M, Llamas Velasco M. **A comprehensive review on pathogenesis, associations, clinical findings, and treatment of livedoid vasculopathy.** Front Med 9. 2022. PMID: 36569162. IF: 5,06. DOI: 10.3389/fmed.2022.993515

Chicharro P, Llamas Velasco M, Armesto S, Herrera Acosta E, Vidal D, Vilarrasa E, Rivera Diaz R, De Cueva P, Martorell Calatayud A, Ballescà F, Belinchon I, Carretero G, Rodriguez L, Romero Maté A, Pujol Montcusí J, Salgado L, Sahuquillo Torralba A, Coto Segura P, Baniandrés Rodríguez O, Feltes R, Riera Monroig J, Dauden E. **Secukinumab is effective and safe in the long-term treatment of plaque psoriasis in a daily practice setting: Multicenter study in 384 Spanish patients.** Dermatol Ther 35 (12). 2022. PMID: 36223184. IF: 3,86. DOI: 10.1111/dth.15929.

Delgado Arévalo C, Calvet Mirabent M, Triguero Martinez A, Vázquez de Luis E, Benguría Filippini A, Largo R, Calzada Fraile D, Popova O, Sánchez Cerrillo I, Tsukalov I, Moreno Vellisca R, de la Fuente H, Herrero Beaumont G, Ramiro AR, Sánchez Madrid F, Castañeda S, Dopazo A, González Álvaro I, Martin Gayo E. **NLRC4 -mediated activation of CD1c+ dendritic cells contributes to perpetuation of synovitis in rheumatoid arthritis.** JCI Insight 7 (22). 2022. PMID: 36194479. IF: 9,48. DOI: 10.1172/jci.insight.152886

Rocamora V, Crespi L, Ferran M, Llamas Velasco M, Del Alcázar E, Carrascosa JM, Beltran E, Urruticoechea Arana A, Estebaranz JLL, Vidal D, Riera J, Rodríguez L, Armesto S, Fernández JM, Aparicio G, Pérez S, Porcar S, Montesinos E, Gallardo F. **Guselkumab effectiveness and survival in patients with psoriasis and psoriatic arthritis: Multicenter analysis in daily clinical practice by the Spanish Psoriasis Group.** Dermatol Ther 35 (11). 2022. PMID: 36175141. IF: 3,86. DOI: 10.1111/dth.15865.

López Ferrer A, Vilarrasa E, Armesto S, Santos Juanes J, Galache C, Carretero G, Sahuquillo A, Salgado Boquete L, Del Alcázar E, González Cantero A, Martorell A, Rivera Díaz R, Mitxelena Ezeiza J, Mateu A, Belinchón I, Llamas Velasco M, Riera Monroig J, Lázaro A, López Estebaranz JL, Gich I, Puig L. **Drug survival of adalimumab biosimilars in real-world treatment of psoriasis: A Spanish multicenter study.** Dermatol Ther 35 (11): 2022. PMID: 36109488. IF: 3,86. DOI: 10.1111/dth.15831.

Ruiz Genao DP, Carretero G, Rivera Diaz R, Carrascosa JM, Sahuquillo Torralba A, Herrera Acosta E, García FJG, Daudén E, Estebaranz JLL, Garcia Doval I, BIOBADADERM Study Group. **Differences in epidemiology, comorbidities and treatment choice between plaque psoriasis and pustular psoriasis: results from the BIOBADADERM registry.** Br J Dermatol 187 (5): 2022. PMID: 35819180. IF: 11,11. DOI: 10.1111/bjd.21763.

Fernández Gallego N, Castillo González R, Méndez Barbero N, López Sanz C, Obeso D, Villaseñor A, Escribese MM, López Melgar B, Salamanca J, Benedicto Buendía A, Jiménez Borreguero LJ, Ibañez B, Sastre J, Belver MT, Vega F, Blanco C, Barber D, Sánchez Madrid F, de la Fuente H, Martín P, Esteban V, Jiménez Saiz R. **The impact of type 2 immunity and allergic diseases in atherosclerosis.** Allergy 77 (11). 2022. PMID: 35781885. IF: 14,71. DOI: 10.1111/all.15426.

Blanco Domínguez R, de la Fuente H, Rodríguez C, Martín Aguado L, Sánchez Díaz R, Jiménez Alejandre R, Rodríguez Arabaolaza I, Curtabbi A, García Guimaraes MM, Vera A, Rivero F, Cuesta J, Jiménez Borreguero LJ, Cecconi A, Duran Cambra A, Taurón M, Alonso J, Bueno H, Villalba Orero M, Enríquez JA, Robson SC, Alfonso F, Sánchez Madrid F, Martínez González J, Martín P. **CD69 expression on regulatory T cells protects from immune damage after**

myocardial infarction. J Clin Invest 132 (21). 2022. PMID: 36066993. IF: 19,46. DOI: 10.1172/JCI152418

Torres T, Puig L, Vender R, Yeung J, Carrascosa JM, Piaserico S, Gisondi P, Lynde C, Ferreira P, Bastos PM, Dauden E, Leite L, Valerio J, Del Alcázar Viladomiu E, Rull EV, Llamas Velasco M, Pirro F, Messina F, Bruni M, Licata G, Ricceri F, Nidegger A, Hugo J, Mufti A, Daponte AI, Teixeira L, Balato A, Romanelli M, Prignano F, Gkalpakiotis S et al. **Drug Survival of Interleukin (IL)-17 and IL-23 Inhibitors for the Treatment of Psoriasis: A Retrospective Multi-country, Multicentric Cohort Study.** Am J Clin Dermatol 23 (6). 2022. PMID: 35976568. IF: 6,23. DOI: 10.1007/s40257-022-00722-y

Triguero Martinez A, Roy Vallejo E, Tomero EG, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Lamana A, Gonzalez Alvaro I. **Galectin-1: A Potential Biomarker Differentiating between Early Rheumatoid Arthritis and Spondyloarthritis**. J Clin Med 11 (21). 2022. PMID: 36362537. IF: 4,96. DOI: 10.3390/jcm11216313.

Reymundo A, Vilarrasa E, Baniandres O, Rodriguez Freire L, Feltes R, Llamas Velasco M, Dauden E. **Effectiveness and safety profile of secukinumab for the treatment of patients with generalized pustular psoriasis in daily practice**. J Eur Acad Dermatol Venereol 36. (10): 2022. PMID: 35689497. IF: 9,23. DOI: 10.1111/jdv.18317.

Berenguer Ruiz S, Rivera R, Herranz P, De la Cueva P, Hospital M, Ruiz Genao D, Roustan G, Daudén E, Llamas Velasco M. **Ustekinumab to guselkumab transitions: A series of 54 patients emulating the navigate trial in real life.** Dermatol Ther 35 (10). 2022. PMID: 36190008. IF: 3,86. DOI: 10.1111/dth.15757

Fernandez AP, Dauden E, Gerdes S, Lebwohl MG, Menter MA, Leonardi CL, Gooderham M, Gebauer K, Tada Y, Lacour JP, Bianchi L, Egeberg A, Pau Charles I, Mendelsohn AM, Rozzo SJ, Mehta NN. **Tildrakizumab efficacy and safety in patients with psoriasis and concomitant metabolic syndrome: post hoc analysis of 5-year data from reSURFACE 1 and reSURFACE 2.** J Eur Acad Dermatol Venereol 36 (10). 2022. PMID: 35460287. IF: 9,23. DOI: 10.1111/jdv.18167

Reolid A, Sahuquillo Torralba A, Sanz García A, Botella Estrada R, Muñoz Aceituno E, Llamas Velasco M, García Martínez J, Daudén E, Abad Santos F, Ovejero Benito MC. **CNVs Associated with Different Clinical Phenotypes of Psoriasis and Anti-TNF-Induced Palmoplantar Pustulosis.** J Pers Med 12 (9). 2022. PMID: 36143237. IF: 3,51. DOI: 10.3390/jpm12091452

Castillo Gazquez,L,Vera Díaz,EC,Muñoz Hernández,P,Jiménez Heffernan,JA. **Curschmann's spiral in a voided urine sample.** CYTOPATHOLOGY33 (5): 2022. PMID: 35699383. IF: 1,29. DOI: 10.1111/cyt.13155

Reolid A, Armesto S, Sahuquillo Torralba A, Torres T, Feltes R, Vilarrasa E, Belinchón I, Cueva P, Rodríguez L, Romero Maté A, Vidal D, Coto Segura P, Herrera Acosta E, Riera Monroig J, Salgado L, Llamas Velasco M, Daudén E. **Secukinumab is effective in the treatment of recalcitrant palmoplantar psoriasis and palmoplantar pustular psoriasis in a daily practice setting.** J Am Acad Dermatol 87 (3). 2022. PMID: 35640798. IF: 15,49. DOI: 10.1016/j.jaad.2022.05.047

Jiménez Fernández M, Rodríguez Sinovas C, Cañes L, Ballester Servera C, Vara A, Requena S, de la Fuente H, Martínez González J, Sánchez Madrid F. **CD69-oxLDL ligand engagement induces Programmed Cell Death 1 (PD-1) expression in human CD4 + T lymphocytes.** Cell Mol Life Sci 79 (8). 2022. PMID: 35930205. IF: 9,21. DOI: 10.1007/s00018-022-04481-1.

- Lamana A, Castro Vazquez D, De La Fuente H, Triguero Martinez A, Martinez Hernandez R, Revenga M, Villanueva Romero R, Llamas Velasco M, Chicharro P, Juarranz Y, Marazuela M, Sales Sanz M, Garcia Vicuna R, Tomero E, Gonzalez Alvaro I, Martinez C, Gomariz RP. **VIP/VPAC Axis Expression in Immune-Mediated Inflammatory Disorders: Associated miRNA Signatures**. Int J Mol Sci 23 (15). 2022. PMID: 35955723. IF: 6,21. DOI: 10.3390/ijms23158578

Chicharro P, Llamas Velasco M, Armesto S, Herrera Acosta E, Vidal D, Vilarrasa E, Rivera R, De la Cueva P, Martorell Calatayud A, Ballescà F, Belinchón I, Carretero G, Rodríguez L, Romero Maté A, Pujol Montcusí J, Salgado L, Sahuquillo Torralba A, Coto Segura P, Baniandrés Rodríguez O, Feltes R, Alsina M, Daudén E. **Fast and sustained improvement of patient- reported outcomes in psoriatic patients treated with secukinumab in a daily practice setting.** Dermatol Ther 35 (8). 2022. PMID: 35731640. IF: 3,86. DOI: 10.1111/dth.15653

Triguero Martinez A, Roy Vallejo E, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Gonzalez Alvaro I, Lamana A. **Genetic LGALS1 Variants Are Associated with Heterogeneity in Galectin-1 Serum Levels in Patients with Early Arthritis**. Int J Mol Sci 23 (13). 2022. PMID: 35806182. IF: 6,21. DOI: 10.3390/ijms23137181

Calvet Mirabent M, Sánchez Cerrillo I, Martín Cófreces N, Martínez Fleta P, de la Fuente H, Tsukalov I, Delgado Arévalo C, Calzada MJ, de los Santos I, Sanz J, García Fraile L, Sánchez Madrid F, Alfranca A, Muñoz Fernández MÁ, Buzón MJ,

Martín Gayo E. **Antiretroviral therapy duration and immunometabolic state determine efficacy of ex vivo dendritic cell-based treatment restoring functional HIV-specific CD8+ T cells in people living with HIV.** EBioMedicine 81 2022. PMID: 35665682. IF: 11,21. DOI: 10.1016/j.ebiom.2022.104090

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

van Huizen AM, Menting SP, Gyulai R, Iversen L, van der Kraaij GE, Middelkamp Hup MA, Warren RB, Spuls PI, SPIN Consensus Survey Study Group MTX, Schejtman AA, Egeberg A, Firooz A, Kumar AS, Oakley A, Foulkes A, Ramos AMC, Fougerousse AC, Carija A, Akman Karakas A, Horváth B, Fábos B, Matlock BH, Claréus BW, Castro C, Ferrándiz C, Correa CC, Marchesi C, Goujon C, Gonzalez C, Maldonado García C et al. **International eDelphi Study to Reach Consensus on the Methotrexate Dosing Regimen in Patients With Psoriasis.** JAMA Dermatol 158 (5). 2022. PMID: 35353175. IF: 11,82. DOI: 10.1001/jamadermatol.2022.0434

Reolid Alejandra, Martinez Palazuelo Maria, Rodriguez Jimenez Pedro, Munoz Aceituno Ester, Llamas Velasco Mar, Fraga Javier, Dauden Esteban. **Cutaneous vascular calcification. Perieccrine calcification as a diagnostic key for calciphylaxis**. J Cutaneous Pathol 49 (8). 2022. PMID: 35357702. IF: 1,46. DOI: 10.1111/cup.14234

Cecconi Alberto, Navarrete Gonzalo, Garcia Guimaraes Marcos, Vera Alberto, Blanco Dominguez Rafael, Sanz Garcia Ancor, Lozano Prieto Marta, Lopez Melgar Beatriz, Rivero Fernando, Martin Pilar, Sanchez Madrid Francisco, de la Fuente Hortensia, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Influence of air pollutants on circulating inflammatory cells and microRNA expression in acute myocardial infarction**. Sci Rep 12 (1). 2022. PMID: 35354890. IF: 5,00. DOI: 10.1038/s41598-022-09383-7.

Llamas Velasco Mar, Itlinger Monshi Babak, Flucke Uta, Mentzel Thomas. **Dermal lipofibromatosis-like neural tumor**. J. Cutaneous Pathol 49 (6). 2022. PMID: 35195930. IF: 1,46. DOI: 10.1111/cup.14216

Rivero Fernando, Marco Valeria, Biccire Flavio Giuseppe, Budassi Simone, Cuesta Javier, Del Val David, Bastante Teresa, de la Fuente Hortensia, Prati Francesco, Alfonso Fernando. **The double injection technique to improve visualization of severe coronary lesions with optical coherence tomography**. Catheter Cardiovasc Interventions 99 (5). 2022. PMID: 35238444. IF: 2,59. DOI: 10.1002/ccd.30138

Jose Caston Juan, Cano Angela, Perez Camacho Ines, Aguado Jose M, Carratala Jordi, Ramasco Fernando, Soriano Alex, Pintado Vicente, Castelo Corral Laura, Sousa Adrian, Carmen Farinas Maria, Munoz Patricia, Lopez De Medrano Vicente Abril, Sanz Pelaez Oscar, Los Arcos Ibai, Gracia Ahufinger Irene, Perez Nadales Elena, Vidal Elisa, Doblas Antonio, Natera Clara, Martinez Luis, Torre Cisneros Julian. **Impact of ceftazidime/avibactam versus best available therapy on mortality from infections caused by carbapenemase-producing Enterobacterales (CAVICOR study)**. J Antimicrob Chemother 77 (5). 2022. PMID: 35187577. IF: 5,76. DOI: 10.1093/jac/dkac049

Duarte Pablo, Michalska Patrycja, Crisman Enrique, Cuadrado Antonio, Leon Rafael. **Novel Series of Dual NRF2 Inducers and Selective MAO-B Inhibitors for the Treatment of Parkinson's Disease**. Antioxidants 11 (2). 2022. PMID: 35204129. IF: 7,68. DOI: 10.3390/antiox11020247

Lopez Castillo D, Descalzo MA, Olmos Alpiste F, Armario Hita J, Fernández Redondo V, García Gavín J, Ruiz Gonzalez I, Mercader García P, Sanchez Perez J, Silvestre JF, Gimenez Arnau AM. **Chronic hand eczema: clinical characterization, aetiology, concomitant foot eczema and polysensitization.** Eur J Dermatol 32 (1). 2022. PMID: 35200142. IF: 2,81.

DOI: 10.1684/ejd.2022.4234

del Alcazar Elena, Lopez Ferrer Anna, Martinez Domenech Alvaro, Ruiz Villaverde Ricardo, Llamas Velasco Ma del Mar, Rocamora Vicenc, Julia Marc, Notario Jaime, Fernandez Freire Lourdes Rodriguez, Sahuquillo Torralba Antonio, Vidal David, Rivera Raquel, Carretero Gregorio, Mateu Almudena, de la Cueva Pablo, Carrascosa Jose Manuel. **Effectiveness and safety of guselkumab for the treatment of psoriasis in real-world settings at 24 weeks: A retrospective, observational, multicentre study by the Spanish Psoriasis Group**. Dermatol Ther 35 (2). 2022. PMID: 34820971. IF: 3,86. DOI: 10.1111/dth.15231

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

Cores Angel, Michalska Patrycja, Perez Jose Miguel, Crisman Enrique, Gomez Clara, Villacampa Mercedes, Menendez Jose Carlos, Leon Rafael. **Enantioselective Synthesis and Pharmacological Evaluation of Aza- CGP37157-Lipoic Acid Hybrids for the Treatment of Alzheimer's Disease**. Antioxidants 11 (1). 2022. PMID: 35052616. IF: 7,68. DOI: 10.3390/antiox11010112.

Blanco Dominguez R, Martin Aguado L, De la Fuente H, Rodriguez C, Jimenez Alejandre R, Rodriguez Arabaolaza I, Garcia Guimaraes MM, Vera A, Cuesta J, Cecconi A, Alfonso F, Sanchez Madrid F, Martinez Gonzalez J, Martin P. **CD69 expression on Treg cells prevents chronic heart damage after myocardial infarction**. Cardiovasc Res 118 (SUPPL 1): 2022. IF: 13,08. DOI: 10.1093/cvr/cvac066.149.

Ruiz-Salas V, Sanmartin-Jiménez O, Garcés JR, Vilarrasa E, Miñano- Medrano R, Escutia-Muñoz B, Flórez-Menéndez Á, Artola-Igarza JL, Alfaro- Rubio A, Redondo P, **Delgado-Jiménez Y**, Sánchez-Schmidt J, Allende- Markixana I, García Bracamonte B, de la Cueva-Dobao P, Ciudad C, Carnero-González L, Vázquez-Veiga H, Sánchez- Sambucety P, Estebaranz JL, Botella- Estrada R, González-Sixto B, Martorell A, Morales-Gordillo V, Toll-Abelló A, Mayor-Arenal M, Suárez-Fernández R, Sainz- Gaspar L, Descalzo MA, Garcia-Doval I; REGESMOHS (Registro Español de Cirugía de Mohs). **Complications Associated with Mohs Micrographic Surgery: Data from the Nationwide Prospective Cohort REGESMOHS.** Dermatology. *238(2):320-328.* 2022. PMID: 34380138. IF: 5.197. doi: 10.1159/000517010.

Navarro R, Delgado-Jiménez Y, Guinea-Viniegra J,Llamas-Velasco M, Daudén E. **Expression of microRNA-21 and TIMP-3 in paradoxical psoriasiform reactions during treatment with antitumor necrosis factor agents.** J Cutan Pathol. 49(2):116-122. 2022. PMID: 34322902. IF: 1.458. doi: 10.1111/cup.14113.

Oro-Ayude M, González-Sixto B, Sanmartin-Jiménez O, Garcés JR, Rodríguez-Prieto MA, Ruiz-Salas V, de Eusebio-Murillo E, Miñano-Medrano R, Escutia-Muñoz B, Feal Cortizas C, Artola-Igarza JL, Alfaro-Rubio A, Redondo P, Delgado-Jiménez Y, Sánchez-Schmidt JM, Allende-Markixana I, Alonso-Pacheco ML, García-Bracamonte B, de la Cueva-Dobao P, Navarro- Tejedor R, Ciudad-Blanco C, Carnero-González L, Vázquez-Veiga H, Cano-Martínez N, Vilarrasa-Rull E, Sánchez-Sambucety P, López- Estebaranz JL, Botella-Estrada R, Martorell-Calatayud A, Gil P, Morales-Gordillo V, Toll- Abelló A, Ocerin-Guerra I, Mayor-Arenal M, Suárez-Fernández R, Sainz- Gaspar L, Descalzo MA, Garcia-Doval I, Flórez Á; REGESMOHS (Registro Español de Cirugía de Mohs). **Incomplete Mohs surgery: a long-term, nationwide prospective cohort to describe recurrence rate and risk factors (REGESMOHS, Spanish Registry of Mohs Surgery).** J Eur Acad Dermatol Venereol 36(1): 35-37. 2022. PMID: 34374137. IF: 9.228. doi: 10.1111/jdv.17597.

Llamas-Velasco M, Muñoz-Aceituno E, Sánchez -Pérez J, Camarero-Mulas C, Fraga J, Aragüés M. **Graft-versus-host disease-associated angiomatosis with striking lipomatous metaplasia**. J Cutan Pathol 49(4): 373-376. 2022. PMID: 34743349.IF: 1.458. doi: 10.1111/cup.14162. PMID: 34743349.

Chicharro P, **Llamas-Velasco M**, Armesto S, Herrera-Acosta E, Vidal D, Vilarrasa E, Rivera R, De la Cueva P, Martorell-Calatayud A, Ballescà F, Belinchón I, Carretero G, Rodríguez L, Romero-Maté A, Pujol-Montcusí J, Salgado L, Sahuquillo-Torralba A, Coto-Segura P, Baniandrés-Rodríguez O, Feltes R, Alsina M, **Daudén E**. **Fast and sustained improvement of patient- reported outcomes in psoriatic patients treated with secukinumab in a daily practice setting**. Dermatol Ther 35 (8): 15653. 2022. PMID: 35731640.IF: 3.858. doi: 10.1111/dth.15653.

Belinchón Romero I, **Dauden E**, Ferrándiz Foraster C, González-Cantero Á, Carrascosa Carrillo JM; Psoriasis Group of the Spanish Academy of Dermatology and Venereology. **PASI 100 response rates in moderate to severe psoriasis: a systematic literature review and analysis of clinical practice guidelines.** J Dermatolog Treat 33 (3): 1661-1669. 2022. PMID: 33615959.IF: 3.230. doi: 10.1080/09546634.2021.1890683.

Munera-Campos M, Vilar-Alejo J, Rivera R, Carrascosa JM, **Daudén E**, Herrera-Acosta E, Sahuquillo-Torralba A, Gómez-García FJ, Baniandrés- Rodríguez O, de la Cueva P, López-Estebaranz JL, Belinchón I, Ferran M, Riera-Monroig J, Rodriguez L, Carretero G, García-Donoso C, Ballescá F, **Llamas-Velasco M**, Herrera-Ceballos E, Pujol-Marco C, Nieto-Benito LM, Ruiz-Genao DP, Alsina M, Descalzo MA, García-Doval I; BIOBADADERM Study Group. **The risk of hepatic adverse events of systemic medications for psoriasis: a prospective cohort study using the BIOBADADERM registry.** J Dermatolog Treat 33 (4): 2110-2117. 2022. PMID: 33913796. IF: 3.230. doi: 10.1080/09546634.2021.1922572.

GROUP 38

Head of laboratory: Pérez Gisbert, Francisco Javier

Area 3 Advanced therapies and individualized medicine

Line 3.2 Esophagogastrointestinal inflammatory diseases

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 more than 100 Spanish and 250 European hospitals.

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.), Organic Chemistry Department at the Complutense University, Cooperative Biosciences Research Centre from Euskadi (CIC BioGUNE), the Galician Genomics Foundation, the National Center for Cardiovascular Research (CNIC), the National Center for Oncology Research (CNIO), the Asturian Institute of Dairy Products (IPLA-CSIC), the Institute of Food Science Research (CIAL-CSIC), the Institute of Molecular Biology and Genetics (IBGM, University of Valladolid- CSIC), Metagenomics Platform (CIBER- IBIMA) and Coagulopathies and Haemostasis Disorders research group of the Hospital Universitario La Paz. Internationally, the group leads projects with the National Institutes of Health of U.S.A. (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 transference 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 with: 1) National scientific societies: Asociación Española de Gastroenterología (AEG), Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa (GETECCU), Sociedad 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.
- Analysis of the metabolome in serum and urine.

- Metagenomic analysis of fecal microbiota.
- Analysis of the effect of immunomodulatory peptides secreted by the gut microbiota on mucosal dendritic cells in IBD patients.
- Transcriptomics from biopsies and plasma-derived extracellular vesicles as markers.

1.2. Epidemiology in IBD.

- Evaluation of the incidence of IBD in Spain.
- 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 with anti-TNF drugs in patients with IBD.

- Identification of candidate genes to predict clinical response to anti-TNF drugs.
- Correlation between serological levels of TNFa and response to anti-TNF therapy.
- Identification of the mechanism of antibody production against anti-TNF drugs, in order to identify patients at higher risk of immunogenicity.
- Evaluation of the influence of serum levels of anti-TNF drugs and anti-TNF antibodies on short- and long-term response, loss of response and response to intensification of anti-TNF therapy.
- Switching to biosimilar drugs.
- Immunomodulatory effect of the combination of biologic drugs in IBD patients.
- Identification of biomarkers of response to treatment with biological drugs and tofacitinib in IBD using a proteomic and cytometry approach, both in blood and intestinal tissue (PI18/00622).

1.5. Strategies for advanced therapies cycling.

- 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

- 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. H. 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 250 hospitals of 29 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.
- Effect of eradication treatment on intestinal microbiota.
- Validation of new diagnostic methods.

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- María García Donday

MAJOR GRANTS

Chaparro Sánchez, María. Comprehensive study of mechanisms underlying inflammatory bowel disease: a multi-omic approach of a newly diagnosed cohort. PI19/01034. ISCIII. 2020-2022.

Chaparro Sánchez, María. Seguridad de los tratamientos para la enfermedad inflamatoria intestinal durante el embarazo y la lactancia: impacto en las madres y en los niños (registro DUMBO). ICI19/00083. 2020- 2023.

Pérez Gisbert, Javier. Predictive biomarkers for response to JAK-inhibitors and biologic therapies in

ulcerative colitis by a multi-omic approach. Pfizer. 2019-2023.

Chaparro Sánchez, María. Estudio mecanístico e identificación de biomarcadores de respuesta al tratamiento con fármacos biológicos y tofacitinib en la enfermedad inflamatoria intestinal mediante abordaje multi-ómico. Convocatoria de proyectos de investigación Intramurales CIBERHD, ISCIII. 2021-2023.

Pérez Gisbert, Francisco Javier. Riesgo trombótico en pacientes con colitis ulcerosa en tratamiento con inhibidores JAK: efecto sobre la función plaquetaria y la cascada de coagulación. PI21/01086. ISCIII. 2022-2024.

Palomino Pérez, Laura María. Estudio de la microbiota y afectación de intestino delgado con videocápsula endoscópica (VCE) en pacientes con enfermedad injerto contra huésped (EICH). Implicación en el pronóstico y estudio de viabilidad y rentabilidad. Mutua Madrileña. 2021-2024.

Pérez Gisbert, Francisco Javier. Comparative study of the immunomodulatory effect of the combination of biologic drugs in inflammatory bowel disease (COMBINE). Janssen-Fundación Encuentros Médico-Quirúrgicos para el estudio de la EII. 2022.

Pérez Gisbert, Francisco Javier. Long-term trends in targeted therapies (biologics and tofacitinib) usage in inflammatory bowel disease: TRENDY study. Galapagos Investigator Initiated Sponsored Research. 2022.

Pérez Gisbert, Francisco Javier. Long-term benefit of ustekinumab in ulcerative colitis in clinical practice (ULISES study). Janssen Investigator Initiated Sponsored Research. 2022.

PUBLICATIONS

Zabana Y, Marín-Jiménez I, Rodríguez-Lago I, Vera I, Martín-Arranz MD, Guerra I, P Gisbert J, Mesonero F, Benítez O, Taxonera C, Ponferrada-Díaz Á, Piqueras M, J Lucendo A, Caballol B, Mañosa M, Martínez-Montiel P, Bosca-Watts M, Gordillo J, Bujanda L, Manceñido N, Martínez-Pérez T, López A, Rodríguez-Gutiérrez C, García-López S, Vega P, Rivero M, Melcarne L, Calvo M, Iborra M, Barreiro de Acosta M et al. **Risk Factors for COVID-19 in Inflammatory Bowel Disease: A National, ENEIDA-Based Case-Control Study (COVID-19-EII).** J Clin Med 11 (24): 7540. 2022. PMID: 36556155. IF: 4,96. DOI: 10.3390/jcm11247540.

Iborra M, Moret I, Busó E, García-Giménez JL, Ricart E, Gisbert JP, Cabré E, Esteve M, Márquez-Mosquera L, García-Planella E, Guardiola J, Pallardó FV, Serena C, Algaba-Chueca F, Domenech E, Nos P, Beltrán B. **The Genetic Diversity and Dysfunctionality of Catalase Associated with a Worse Outcome in Crohn's Disease.** Int J Mol Sci 23 (24): 15881. 2022. PMID: 36555526. IF: 6,21. DOI: 10.3390/ijms232415881.

Yanai H, Kagramanova A, Knyazev O, Sabino J, Haenen S, Mantzaris GJ, Mountaki K, Armuzzi A, Pugliese D, Furfaro F, Fiorino G, Drobne D, Kurent T, Yassin S, Maharshak N, Castiglione F, de Sire R, Nardone OM, Farkas K, Molnar T, Krznaric Z, Brinar M, Chashkova E, Livne Margolin M, Kopylov U, Bezzio C, Bar-Gil Shitrit A, Lukas M, Chaparro M, Truyens M et al. **Endoscopic Postoperative Recurrence In Crohn's Disease After Curative Ileocecal Resection With Early Prophylaxis By Anti-Tnf, Vedolizumab Or Ustekinumab: A Real-World Multicenter European Study.** J Crohn's Colitis 16 (12): 1882-1892. 2022. PMID: 35895074. IF: 10,02. DOI: 10.1093/ecco-jcc/jjac100.

Chaparro M, Garre A, Núñez Ortiz A, Diz-Lois Palomares MT, Rodríguez C, Riestra S, Vela M, Benítez JM, Fernández Salgado E, Sánchez Rodríguez E, Hernández V, Ferreiro-Iglesias R, Ponferrada Díaz Á, Barrio J, Huguet JM, Sicilia B, Martín-Arranz MD, Calvet X, Ginard D, Alonso-Abreu I, Fernández- Salazar L, Varela Trastoy P, Rivero M, Vera-Mendoza I, Vega P, Navarro P, Sierra M, Cabriada JL, Aguas M, Vicente R et al. **Correction: Chaparro et al. Incidence, Clinical Characteristics and Management of Inflammatory Bowel Disease in Spain: Large-Scale Epidemiological Study. J. Clin. Med. 2021, 10, 2885.** J Clin Med 11 (19): 5816. 2022. PMID: 36233844. IF: 4,96. DOI: 10.3390/jcm11195816.

Casadó-Llombart S, Velasco-de Andrés M, Català C, Leyton-Pereira A, Gutiérrez-Cózar R, Suárez B, Armiger N, Carreras E, Esteller M, Ricart E, Ordás I, Gisbert JP, Chaparro M, Esteve M, Márquez L, Busquets D, Iglesias E, García-Planella E, Martín-Arranz MD, Lohmann J, Ayata CK, Niess JH, Engel P, Panés J, Salas A, Domènech E, Lozano F; ENEIDA Project of GETECCU. **Experimental and genetic evidence for the impact of CD5 and CD6 expression and variation in inflammatory bowel disease.** Front. Immunol 13: 966184-966184. 2022. PMID: 36211446. IF: 8,79. DOI: 10.3389/fimmu.2022.966184.

Montoro M, Cucala M, Lanas Á, Villanueva C, Hervás AJ, Alcedo J, Gisbert JP, Aisa ÁP, Bujanda L, Calvet X, Mearin F, Murcia Ó, Canelles P, García López S, Martín de Argila C, Planella M, Quintana M, Jericó C, García Erce JA. **Indications and hemoglobin thresholds for red blood cell transfusion and iron replacement in adults with gastrointestinal bleeding: An algorithm proposed by gastroenterologists and patient blood management experts.** Front Med 9: 903739-903739. 2022. PMID: 36186804. IF: 5,06. DOI: 10.3389/fmed.2022.903739.

Gisbert JP, Hunt RH. **Editorial: slow progress to optimising H. pylori eradication treatment with antisecretory drugs.** Aliment Pharmacol Ther 56 (6): 1074-1075. 2022. PMID: 35995738. IF: 9,52. DOI: 10.1111/apt.17142.

Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, Gasbarrini A, Hunt RH, Leja M, O'Morain C, Rugge M, Suerbaum S, Tilg H, Sugano K, El-Omar EM; European Helicobacter and Microbiota Study group. **Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report.** Gut 71 (9): 1724-1762. 2022. PMID: 35944925. IF: 31,79. DOI: 10.1136/gutjnl-2022-327745.

Resina E, Donday MG, Martínez-Domínguez SJ, Laserna-Mendieta EJ, Lanas Á, Lucendo AJ, Sánchez-Luengo M, Alcaide N, Fernández-Salazar L, De La Peña-Negro L, Bujanda L, Arbulo MG, Alcedo J, Pérez-Aísa Á, Rodríguez R, Hermida S, Brenes Y, Nyssen OP, Gisbert JP. **Evaluation of a New Monoclonal Chemiluminescent Immunoassay Stool Antigen Test for the Diagnosis of Helicobacter pylori Infection: A Spanish Multicentre Study.** J Clin Med 11 (17): 5077. 2022. PMID: 36079007. IF: 4,96. DOI: 10.3390/jcm11175077.

Soleto I, Fernández-Tomé S, Mora-Gutiérrez I, Baldan-Martin M, Ramírez C, Santander C, Moreno-Monteagudo JA, Casanova MJ, Casals F, Casabona S, Becerro I, Chaparro M, Bernardo D, Gisbert JP. **Differential Effects of Anti- TNFa and Anti-a4ß7 Drugs on Circulating Dendritic Cells Migratory Capacity in Inflammatory Bowel Disease.** Biomedicines 10 (8): 1885. 2022. PMID: 36009431. IF: 4,76. DOI: 10.3390/biomedicines10081885.

Chaparro M, Baston-Rey I, Fernández Salgado E, González García J, Ramos L, Diz-Lois Palomares MT, Argüelles-Arias F, Iglesias Flores E, Cabello M, Rubio Iturria S, Núñez Ortiz A, Charro M, Ginard D, Dueñas Sadornil C, Merino Ochoa O, Busquets D, Iyo E, Gutiérrez Casbas A, Ramírez de la Piscina P, Boscá-Watts MM, Arroyo M, García MJ, Hinojosa E, Gordillo J, Martínez Montiel P, Velayos Jiménez B, Quílez Ivorra C, Vázquez Morón JM, Huguet JM, González-Lama Y et al. **Using Interpretable Machine Learning to Identify Baseline Predictive Factors of Remission and Drug Durability in Crohn's Disease Patients on Ustekinumab.** J Clin Med 11 (15): 4518. 2022. PMID: 35956133. IF: 4,96. DOI: 10.3390/jcm11154518.

Rubín de Célix C, Chaparro M, Gisbert JP. **Real-World Evidence of the Effectiveness and Safety of Ustekinumab for the Treatment of Crohn's Disease: Systematic Review and Meta-Analysis of Observational Studies.** J Clin Med 11 (14): 4202. 2022. PMID: 35887966. IF: 4,96. DOI: 10.3390/jcm11144202.

Riestra S, Taxonera C, Zabana Y, Carpio D, Chaparro M, Barrio J, Rivero M, López-Sanroman A, Esteve M, de Francisco R, Bastida G, García-López S, Mañosa M, Martin-Arranz MD, Pérez-Calle JL, Guardiola J, Muñoz F, Arranz L, Cabriada JL, García-Sepulcre MF, Navarro M, Montoro-Huguet MÁ, Ricart E, Bermejo F, Calvet X, Piqueras M, Garcia-Planella E, Márquez L, Mínguez M, Van Domselar M et al. **Performance of Screening Strategies for Latent Tuberculosis Infection in Patients with Inflammatory Bowel Disease: Results from the ENEIDA Registry of GETECCU.** J Clin Med 11 (13): 3915. 2022. PMID: 35807201. IF: 4,96. DOI: 10.3390/jcm11133915.

Fernández-Salazar L, Campillo A, Rodrigo L, Pérez-Aisa Á, González- Santiago JM, Segarra Ortega X, Denkovski M, Brglez Jurecic N, Bujanda L, Gómez Rodríguez BJ, Ortuño J, Georgopoulos S, Jonaitis L, Puig I, Nyssen OP, Megraud F, O'Morain C, Gisbert JP.. **Effectiveness and Safety of High- Dose Dual Therapy: Results of the European Registry on the Management of Helicobacterpylori Infection (Hp-EuReg).** J Clin Med 11 (12): 3544. 2022. PMID: 35743627. IF: 4,96. DOI: 10.3390/jcm11123544.

Nyssen OP, Espada M, Gisbert JP. **Empirical vs. Susceptibility-Guided Treatment of Helicobacter pylori Infection: A Systematic Review and Meta-Analysis.** Front Microbiol 13: 913436-913436. 2022. PMID: 35774456. IF: 6,06. DOI: 10.3389/fmicb.2022.913436.

Chaparro M, Kunovský L, Aguas M, Livne M, Rivière P, Bar-Gil Shitrit A, Myrelid P, Arroyo M, Barreiro-de Acosta M, Bautista M, Biancone L, Biron IA, Boysen T, Carpio D, Castro B, Dragoni G, Ellul P, Holubar SD, de Jorge MÁ, Leo E, Manceñido N, Moens A, Molnár T, Ramírez de la Piscina P, Ricanek P, Sebkova L, Sempere L, Teich N, Gisbert JP, Julsgaard M. **Surgery due to Inflammatory Bowel Disease During Pregnancy: Mothers and Offspring Outcomes From an ECCO Confer Multicentre Case Series [Scar Study]**. J Crohn's Colitis 16 (9): 1428-1435. 2022. PMID: 35380641. IF: 10,02. DOI: 10.1093/ecco-jcc/jjac050.

Gomollón F, Gisbert JP, Guerra I, Plaza R, Pajares Villarroya R, Moreno Almazán L, López Martín MC, Domínguez Antonaya M, Vera Mendoza MI, Aparicio J, Martínez V, Tagarro I, Fernández-Nistal A, Lumbreras S, Maté C, Montoto C; Premonition-CD Study Group. **Clinical characteristics and prognostic factors for Crohn's disease relapses using natural language processing and machine learning: a pilot study.** Eur J Gastroenterol Hepatol 34 (4): 389-397. 2022. PMID: 34882644. IF: 2,59. DOI: 10.1097/MEG.0000000000002317.

Panaccione R, Abreu MT, Lazariciu I, Mundayat R, Lawendy N, Salese L, Woolcott JC, Sands BE, Chaparro M. **Persistence of treatment in patients with**

ulcerative colitis who responded to tofacitinib therapy: Data from the open-label, long-term extension study, OCTAVE open. Aliment Pharmacol Ther 55 (12): 1534-1544. 2022. PMID: 35246988. IF: 9,52. DOI: 10.1111/apt.16848.

Guijarro LG, Cano-Martínez D, Toledo-Lobo MV, Ruiz-Llorente L, Chaparro M, Guerra I, Iborra M, Cabriada JL, Bujanda L, Taxonera C, García-Sánchez V, Marín-Jiménez I, Barreiro-de Acosta M, Vera I, Martín-Arranz MD, Mesonero F, Sempere L, Gomollón F, Hinojosa J, Zoullas S, Monserrat J, Menor-Salvan C, Alvarez-Mon M, Gisbert JP, Ortega MA, Hernández-Breijo B. **Evaluation of AIF-1 (Allograft Inflammatory Factor-1) as a Biomarker of Crohn's Disease Severity**. Biomedicines 10 (3): 727. 2022. PMID: 35327530. IF: 4,76. DOI: 10.3390/biomedicines10030727.

Nyssen OP, Vaira D, Saracino IM, Fiorini G, Caldas M, Bujanda L, Pellicano R, Keco-Huerga A, Pabón-Carrasco M, Oblitas Susanibar E, Di Leo A, Losurdo G, Pérez-Aísa Á, Gasbarrini A, Boltin D, Smith S, Phull P, Rokkas T, Lamarque D, Cano-Català A, Puig I, Mégraud F, O'Morain C, Gisbert JP.. **Experience with Rifabutin-Containing Therapy in 500 Patients from the European Registry on Helicobacter pylori Management (Hp-EuReg)**. J Clin Med 11 (6): 1658. 2022. PMID: 35329984. IF: 4,96. DOI: 10.3390/jcm11061658.

Chaparro M, Baston-Rey I, Fernández-Salgado E, González García J, Ramos L, Diz-Lois Palomares MT, Argüelles-Arias F, Iglesias Flores E, Cabello M, Rubio Iturria S, Núñez Ortiz A, Charro M, Ginard D, Dueñas Sadornil C, Merino Ochoa O, Busquets D, Iyo E, Gutiérrez Casbas A, Ramírez de la Piscina P, Boscá-Watts MM, Arroyo M, García MJ, Hinojosa E, Gordillo J, Martínez Montiel P, Velayos Jiménez B, Quílez Ivorra C, Vázquez Morón JM, María Huguet J, González-Lama Y et al. **Long-Term Real-World Effectiveness and Safety of Ustekinumab in Crohn's Disease Patients: The SUSTAIN Study**. Inflamm Bowel Dis 28 (11): 1725-1736. 2022. PMID: 35166347. IF: 7,29. DOI: 10.1093/ibd/izab357.

Gutiérrez A, Zapater P, Ricart E, González-Vivó M, Gordillo J, Olivares D, Vera I, Mañosa M, Gisbert JP, Aguas M, Sánchez-Rodríguez E, Bosca-Watts M, Laredo V, Camps B, Marín-Jiménez I, Zabana Y, Martín-Arranz MD, Muñoz R, Navarro M, Sierra E, Madero L, Vela M, Pérez-Calle JL, Sainz E, Calvet X, Arias L, Morales V, Bermejo F, Fernández-Salazar L, Van Domselaar M et al. **Immigrant IBD Patients in Spain Are Younger, Have More Extraintestinal Manifestations and Use More Biologics Than Native Patients**. Front Med 9: 823900-823900. 2022. PMID: 35178413. IF: 5,06. DOI: 10.3389/fmed.2022.823900.

Barreiro-de Acosta M, Riestra S, Calafat M, Soto MP, Calvo M, Sánchez Rodríguez E, Caballol B, Vela M, Rivero M, Muñoz F, de Castro L, Calvet X, García-Alonso FJ, Utrilla Fornals A, Ferreiro-Iglesias R, González-Muñoza C, Chaparro M, Bujanda L, Sicilia B, Alfambra E, Rodríguez A, Pérez Fernández R, Rodríguez C, Almela P, Argüelles F, Busquets D, Tamarit-Sebastián S, Reygosa Castro C, Jiménez L, Marín-Jiménez I et al. **Management and Long- term Outcomes of Crohn's Disease Complicated with Enterocutaneous Fistula: ECUFIT Study from GETECCU**. J Crohn's Colitis 16 (7): 1049-1058. 2022. PMID: 35104314. IF: 10,02. DOI: 10.1093/ecco-jcc/jjac016.

Montoto C, Gisbert JP, Guerra I, Plaza R, Pajares Villarroya R, Moreno Almazán L, López Martín MDC, Domínguez Antonaya M, Vera Mendoza I, Aparicio J, Martínez V, Tagarro I, Fernandez-Nistal A, Canales L, Menke S, Gomollón F, PREMONITION-CD Study Group. **Evaluation of Natural Language Processing for the Identification of Crohn Disease-Related Variables in Spanish Electronic Health Records: A Validation Study for the PREMONITION-CD Project**. JMIR Med Inform 10 (2): 30345. 2022. PMID: 35179507. IF: 3,23. DOI: 10.2196/30345.

Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, Bachmann O, Bettenworth D, Chaparro M, Czuber-Dochan W, Eder P, Ellul P, Fidalgo C, Fiorino G, Gionchetti P, Gisbert JP, Gordon H, Hedin C, Holubar S, Iacucci M, Karmiris K, Katsanos K, Kopylov U, Lakatos PL, Lytras T, Lyutakov I, Noor N, Pellino G, Piovani D, Savarino E et al. **ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment**. J Crohn's Colitis 16 (1): 2-17. 2022. PMID: 34635919. IF: 10,02. DOI: 10.1093/ecco-jcc/jjab178.

Ellul P, Revés J, Abreu B, Chaparro M, Gisbert JP, Allocca M, Fiorino G, Barberio B, Zingone F, Pisani A, Cassar D, Michalopoulos G, Mantzaris G, Koutroubakis I, Karmiris K, Katsanos K, Ďuricova D, Burisch J, Madsen GR, Maaser C, Naila A, Orfanoudaki E, Milivojevic V, Buisson A, Avedano L, Leone S, Torres J. **Implementation and Short-term Adverse Events of Anti- SARS-CoV-2 Vaccines in Inflammatory Bowel Disease Patients: An International Web-based Survey**. J Crohn's Colitis 16 (7): 558-558. 2022. PMID: 35037033. IF: 10,02. DOI: 10.1093/ecco-jcc/jjac010.

Gisbert JP, Gaffney K, Young D, Ebbers HC, Girolomoni G.**Current evidence on the use of the adalimumab biosimilar SB5 (Imraldi (TM)): multidisciplinary perspective**. Expert Opin Biol Ther 22 (2): 109-121. 2022. PMID: 34918591. IF: 5,59. DOI: 10.1080/14712598.2022.2012146.

Zabana Y, Marín-Jiménez I, Rodríguez-Lago I, Vera I, Martín-Arranz MD, Guerra I, Gisbert JP, Mesonero F, Benítez O, Taxonera C, Ponferrada-Díaz Á, Piqueras M, Lucendo AJ, Caballol B, Mañosa M,

Martínez-Montiel P, Bosca-Watts M, Gordillo J, Bujanda L, Manceñido N, Martínez-Pérez T, López A, Rodríguez-Gutiérrez C, García-López S, Vega P, Rivero M, Melcarne L, Calvo M, Iborra M, Barreiro de-Acosta M et al. **Nationwide COVID-19-EII Study: Incidence, Environmental Risk Factors and Long-Term Follow-Up of Patients with Inflammatory Bowel Disease and COVID-19 of the ENEIDA Registry**. J Clin Med 11 (2): 421. 2022. PMID: 35054116. IF: 4,96. DOI: 10.3390/jcm11020421.

Moreno LO, Sánchez PN, Abalo R. **Lipidomics as Tools for Finding Biomarkers of Intestinal Pathology: From Irritable Bowel Syndrome to Colorectal Cancer.** Curr Drug Targets 23 (6): 636-655. 2022. PMID: 34238154. IF: 2,94. DOI: 10.2174/1389450122666210707122151.

Rokkas T, Georgopoulos S, Michopoulos S, Ntouli V, Liatsos C, Puig I, Nyssen OP, Mégraud F, O'Morain C, Gisbert JP; Hp-EuReg Investigators. **Assessment of first-line eradication treatment in Greece: data from the European Registry on *Helicobacter pylori* management (Hp-EuReg)**. Ann Gastroenterol 35 (1): 42-47. 2022. PMID: 34987287.IF: doi: 10.20524/aog.2021.0670.

Danese S, Colombel JF, Lukas M, Gisbert JP, D'Haens G, Hayee B, Panaccione R, Kim HS, Reinisch W, Tyrrell H, Oh YS, Tole S, Chai A, Chamberlain-James K, Tang MT, Schreiber S; GARDENIA Study Group. **Etrolizumab versus infliximab for the treatment of moderately to severely active ulcerative colitis (GARDENIA): a randomised, double-blind, double- dummy, phase 3 study**. Lancet Gastroenterol Hepatol 7 (2): 118-127. 2022. PMID: 34798038. IF: doi: 10.1016/S2468-1253(21)00294-6.

Nyssen OP, Vaira D, Tepes B, Kupcinskas L, Bordin D, Pérez-Aisa Á, Gasbarrini A, Castro-Fernández M, Bujanda L, Garre A, Lucendo A, Vologzhanina L, Jurecic NB, Rodrigo-Sáez L, Huguet JM, Voynovan I, Perez-Lasala J, Romero PM, Vujasinovic M, Abdulkhakov R, Barrio J, Fernandez- Salazar L, Mégraud F, O'Morain C, Gisbert JP; Hp-EuReg Investigators. **Room for Improvement in the Treatment of Helicobacter pylori Infection: Lessons from the European Registry on H. pylori Management (Hp- EuReg)**. J Clin Gastroenterol 56 (2): 98-108. 2022. PMID: 33405435. IF: 3.17. doi: 10.1097/MCG.0000000000001482.

Spinelli A, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, Bachmann O, Bettenworth D, Chaparro M, Czuber-Dochan W, Eder P, Ellul P, Fidalgo C, Fiorino G, Gionchetti P, Gisbert JP, Gordon H, Hedin C, Holubar S, Iacucci M, Karmiris K, Katsanos K, Kopylov U, Lakatos PL, Lytras T, Lyutakov I, Noor N, Pellino G, Piovani D, Savarino E, Selvaggi F, Verstockt B, Doherty G, Raine T, Panis Y. **ECCO Guidelines on Therapeutics in Ulcerative Colitis: Surgical Treatment**. J Crohns Colitis. 2022 16 (2):179-189. 2022. PMID: 34635910. IF: 9.17. doi: 10.1093/ecco-jcc/jjab177.

Almeida JI, Tenreiro MF, Martinez-Santamaria L, Guerrero-Aspizua S, Gisbert JP, Alves PM, Serra M, Baptista PM. **Hallmarks of the human intestinal microbiome on liver maturation and function**. J Hepatol. 2022 76 (3):694-725. 2022. PMID: 34715263. IF: 30.08. doi: 10.1016/j.jhep.2021.10.015.

Calafat M, Mañosa M, Ricart E, Nos P, Iglesias-Flores E, Vera I, López- Sanromán A, Guardiola J, Taxonera C, Mínguez M, Martín-Arranz MD, de Castro L, de Francisco R, Rivero M, Garcia-Planella E, Calvet X, García-López S, Márquez L, Gomollón F, Barrio J, Esteve M, Muñoz F, Gisbert JP, Gutiérrez A, Hinojosa J, Argüelles-Arias F, Busquets D, Bujanda L, Pérez-Calle JL, Sicilia B et al. **Risk of Immunomediated Adverse Events and Loss of Response to Infliximab in Elderly Patients with Inflammatory Bowel Disease: A Cohort Study of the ENEIDA Registry**. J Crohns Colitis 16 (6): 946-953. 2022. PMID: 34864947. IF: 10.02. doi: 10.1093/ecco-jcc/jjab213.

Festa S, Zerboni G, Derikx LAAP, Ribaldone DG, Dragoni G, Buskens C, van Dijkum EN, Pugliese D, Panzuto F, Krela-Kaźmierczak I, Mintz HR, Shitrit AB, Chaparro M, Gisbert JP, Kopylov U, Teich N, Vainer E, Nagtegaal I, Hoentjen F, Garcia MJ, Filip R, Foteinogiannopoulou K, Koutroubakis IE, Argollo M, van Wanrooij RLJ, Laja H, Lobaton T, Truyens M, Molnar T, Savarino E ET AL. **Gastroenteropancreatic Neuroendocrine Neoplasms in Patients with Inflammatory Bowel Disease: An ECCO CONFER Multicentre Case Series**. J Crohns Colitis 16 (6): 940-945. 2022. PMID: 34864927.IF: 9.17. doi: 10.1093/ecco-jcc/jjab217.

Pauwels RWM, van der Woude CJ, Nieboer D, Steyerberg EW, Casanova MJ, Gisbert JP, Kennedy NA, Lees CW, Louis E, Molnár T, Szántó K, Leo E, Bots S, Downey R, Lukas M, Lin WC, Amiot A, Lu C, Roblin X, Farkas K, Seidelin JB, Duijvestein M, D'Haens GR, de Vries AC, CEASE Study Group. **Prediction of Relapse After Anti-Tumor Necrosis Factor Cessation in Crohn's Disease: Individual Participant Data Meta-analysis of 1317 Patients From 14 Studies**. Clin Gastroenterol Hepatol 20 (8): 1671-1686.e16. 2022. PMID: 33933376. IF: 10.02. doi: 10.1016/j.cgh.2021.03.037.

Calvet X, Panés J, Gallardo-Escudero J, de la Cuadra-Grande A, Bartolomé E, Marín L, de la Portilla F, Navarro-Correal E, Gutiérrez A, Nos P, Serrano R, Casado MÁ, Barreiro-de Acosta M, Consensus Group. **Multicriteria Decision Analysis for Updating of Quality Indicators for Inflammatory Bowel Disease Comprehensive Care Units in Spain**. J Crohns Colitis 16 (11): 1663-1675. 2022. PMID: 35551380. IF: 9.17. doi: 10.1093/ecco-jcc/jjac068.

Iborra M, Moret I, Busó E, García-Giménez JL, Ricart E, Gisbert JP, Cabré E, Esteve M, Márquez-Mosquera L, García-Planella E, Guardiola J, Pallardó FV, Serena C, Algaba-Chueca F, Domenech E, Nos P, Beltrán B. **The Genetic Diversity and Dysfunctionality of Catalase Associated with a Worse Outcome in Crohn's Disease**. Int J Mol Sci 23 (24): 15881. 2022. PMID: 36555526. IF: 6.20. doi: 10.3390/ijms232415881.

Zabana Y, Marín-Jiménez I, Rodríguez-Lago I, Vera I, Martín-Arranz MD, Guerra I, P Gisbert J, Mesonero F, Benítez O, Taxonera C, Ponferrada-Díaz A, Piqueras M, J Lucendo A, Caballol B, Mañosa M, Martínez-Montiel P, Bosca-Watts M, Gordillo J, Bujanda L, Manceñido N, Martínez-Pérez T, López A, Rodríguez-Gutiérrez C, García-López S, Vega P, Rivero M, Melcarne L, Calvo M, Iborra M, Barreiro de Acosta M et al. **Risk Factors for COVID-19 in Inflammatory Bowel Disease: A National, ENEIDA-Based Case-Control Study (COVID-19-EII)**. J Clin Med 11 (24): 7540. 2022. PMID: 36556155. IF: 4.96. doi: 10.3390/jcm11247540.

Yanai H, Kagramanova A, Knyazev O, Sabino J, Haenen S, Mantzaris GJ, Mountaki K, Armuzzi A, Pugliese D, Furfaro F, Fiorino G, Drobne D, Kurent T, Yassin S, Maharshak N, Castiglione F, de Sire R, Nardone OM, Farkas K, Molnar T, Krznaric Z, Brinar M, Chashkova E, Livne Margolin M, Kopylov U, Bezzio C, Bar-Gil Shitrit A, Lukas M, Chaparro M et al. **Endoscopic Postoperative Recurrence in Crohn's Disease After Curative Ileocecal Resection with Early Prophylaxis by Anti-TNF, Vedolizumab or Ustekinumab: A Real-World Multicentre European Study**. J Crohns Colitis 16 (12): 1882-1892. 2022. PMID: 35895074. IF: 9.17. doi: 10.1093/ecco-jcc/jjac100.

LINE 3.3 ›› PROGENITORS AND CELL THERAPY

GROUP 39

Head of laboratory: Madero López, Luis

Area 3 Advanced therapies and individualized medicine

Line 3.3 Progenitors and cell therapy

RESEARCH INTEREST

Although more than half of children diagnosed with cancer survive, yet cancer remains the leading cause of death by disease in children under 14 years. The reality for patients with metastasis at diagnosis or those who have genetic markers of poor prognosis or in cases of relapsed / refractory tumors, is very negative. Therefore, new treatment options are much needed to bail out all these patients. Our interest is trying to develop treatment strategies for children with poor prognosis, based on strategies of immunotherapy against cancer.

We propose to develop treatment strategies for children with malignant tumors of poor prognosis, based on the use of immune cells, able to attack and kill the cancer cells. This is a project that has both a clinical aspect and a preclinical one, and which is oriented both towards hematological malignancies and solid tumors. For children with leukemia, we aim to evaluate the administration of NK cells from the donor 1 month after receiving a haploidentical transplantation. Our current experience has allowed us to identify that the reconstitution of an insufficient number of NK cells 1 month after transplant is a factor significantly associated with leukemic relapse, so that administration of NK cells in this group of children may increase the clinical benefit of transplantation. In the case of solid tumors, we aim at evaluating a treatment that is not experienced in childhood cancer, but it has proven antitumor capacity especially in melanomas. It is the use of tumor infiltrating lymphocytes (TILs) as an anti- tumor therapy.

This clinical investigation plan is accompanied by a parallel experimental research plan, which aims to prepare a product of cellular immunotherapy able to overcome the barriers imposed by the tumor on the effector cells, known as tolerance. Of the various mechanisms known to produce tolerance, we will begin to address the soluble molecules that induce a decrease in the cytotoxic capacity of both NK cells and TILs. We aim at making effector cells resistant to the action of these immunoregulatory molecules, and also setting up protocols that may have immediate clinical translation. These strategies of cell manipulation want to be a proof of concept, and therefore will be evaluated in preclinical models, serving as a "master protocol" to apply to other known molecules or from which new knowledge is generated. The results should serve for the design of new clinical trials for the continuation of the project. The team is a multidisciplinary group, with proven experience in the diagnosis and treatment of childhood cancer, and in developing research projects in advanced therapies applied to refractory pediatric cancer, and the development of clinical trials in pediatric oncology. It also has all the technical means and infrastructure for the development of the project, ensuring their implementation to the patients who tries to deal with potential impact for all children Advanced therapies and individualized medicine being treated in any of the pediatric oncology units in Spain. The group is focused in:

Pediatric Oncology. Immunotherapies strategies:

1. Celyvir.
2. Nanoimmune medicine.
3. Adoptive Celular Immunotherapy. Tumor-infiltrating lymphocytes (TILs). Childhood leukemias.

Haematopoietic progenitor cell transplantation.

GROUP MEMBERS

- Isabel Vicuña Andrés
- Maitane Andion Catalán
- Ana Isabel Benito Bernal
- David Ruano Domínguez
- Blanca Herrero Velasco
- Blanca Molina Angulo

- Beatriz Aguado Bueno
- Ana María Gómez García
- Manuel Ramírez Orellana

MAJOR GRANTS

Sevilla Navarro, Julián. Efecto del agonista no peptídico del receptor de trombopoyetina (Eltrombopag) en la hematopoyesis de los pacientes con Anemia de Fanconi. PI19/00782. ISCIII. 2020-2022.

Ramirez Orellana, Manuel. Combination of nanomedicine and immunotherapy for the treatment of neuroblastoma. PI19/01758. ISCIII. 2020-2022.

Ramirez Orellana, Manuel. Phase I trial to assess the safety and clinical response of intra- arterial infusion of repeated doses of autologous mesenchymal cells in children and adolescents with autoimmune refractory epilepsies. ICI20/00120. ISCIII. 2021-2024.

Ramirez Orellana, Manuel. Identification and functional analyses of germline and somatic mutations predisposing children in Spain to acute lymphoblastic leukemia. CUNINA. Fundación uno entre Cienmil. 2020-2022.

Madero López, Luis. Viabilidad clínica de la combinación de AloCelyvir con quimioterapia y radioterapia para el tratamiento de niños y adolescentes con tumores sólidos extracraneales en recaída o refractarios. ICI21/00021. 2022-2025.

Ramírez Orellana, Manuel. Red de Investigación Cooperativa Orientadas a Resultados en Salud en Terapias Avanzadas (RICORS TERAV). RD21/0017/0005. ISCIII. 2022-2024.

Ramírez Orellana, Manuel. Celómica integrativa para la medicina de precisión: en leucemia infantil: una acción eHealth coordinada para biodigitalización del cáncer (LEUKODOMICS). TED2021-132296B-51. ISCIII. 2022-2024.

Sánchez García, Isidoro. Infectious triggers and novel therapeutic opportunities in childhood B cell leukemia (PREVENT). Agencia Asociación Española Contra El Cáncer, referencia Proyectos Coordinados 2021. 2021- 2026.

Moreno Martín-Retortillo, Lucas. Estrategia nacional para la implementación de la medicina personalizada en niños y adolescentes con cáncer. PMP21/00088. ISCIII. 2022-2024.

Rosa Durán, Ana. Identificación temprana de recidiva y optimización de tratamientos en LLA mediante modelización y análisis discriminante. ITI- 0038-2019. Universidad de Cádiz. 2020-2023.

PUBLICATIONS

Fernández-Sevilla LM, Valencia J, Ortiz-Sánchez P, Fraile-Ramos A, Zuluaga P, Jiménez E, Sacedón R, Martínez-Sánchez MV, Jazbec J, Debeljak M, Fedders B, Stanulla M, Schewe D, Cario G, Minguela A, Ramírez M, Varas A, Vicente Á. **High BMP4 expression in low/intermediate risk BCP-ALL identifies children with poor outcomes**. Blood 2; 139 (22): 3303-3313. 2022. PMID: 35313334. IF: 25,48. doi: 10.1182/blood.2021013506. PMID: 35313334.

Lopez-Millan B, Costales P, Gutiérrez-Agüera F, Díaz de la Guardia R, Roca- Ho H, Vinyoles M, Rubio-Gayarre A, Safi R, Castaño J, Romecín PA, Ramírez- Orellana M, Anguita E, Jeremias I, Zamora L, Rodríguez-Manzaneque JC, Bueno C, Morís F, Menendez P. **The Multi-Kinase Inhibitor EC-70124 Is a Promising Candidate for the Treatment of FLT3-ITD-Positive Acute Myeloid Leukemia**. Cancers 14 (6): 1593. 2022. PMID: 35326743. IF: 6,58. DOI: 10.3390/cancers14061593.

Madrazo E, González-Novo R, Ortiz-Placín C, García de Lacoba M, González- Murillo Á, Ramírez M, Redondo-Muñoz J. **Fast H3K9 methylation promoted by CXCL12 contributes to nuclear changes and invasiveness of T-acute lymphoblastic leukemia cells**. Oncogene 41 (9): 1324-1336. 2022. PMID: 34999734. IF: 8,76. doi: 10.1038/s41388-021-02168-8.

García-Salido A, García-Teresa MÁ, Leoz-Gordillo I, Martínez de Azagra- Garde A, Cabrero-Hernández M, Ramirez-Orellana M. **Innate cell response in severe SARS-CoV-2 infection in children: Expression analysis of CD64, CD18 and CD11a**. Med Intensiva 46 (1): 50-53. 2022. PMID: 33994613. IF: 2.799. doi: 10.1016/j.medin.2020.09.003.

Casado-García A, Isidro-Hernández M, Oak N, Mayado A, Mann-Ran C, Raboso-Gallego J, Alemán-Arteaga S, Buhles A, Sterker D, Sánchez EG, Martínez-Cano J, Blanco O, Orfao A, Alonso-López D, De Las Rivas J, Riesco S, Prieto-Matos P, González-Murillo Á, García Criado FJ, García Cenador MB, Radimerski T, Ramírez-Orellana M, Cobaleda C, Yang JJ, Vicente-Dueñas C, Weiss A, Nichols KE, Sánchez-García I. **Transient Inhibition of the JAK/STAT Pathway Prevents B-ALL Development in Genetically Predisposed Mice**. Cancer Res 15 ; 82 (6): 1098-1109. 2022. PMID: 35131871. IF: 13.312. doi: 10.1158/0008-5472.CAN-21-3386.

Fernández-Sevilla LM, Belenguer G, Martí-Prado B, Ortiz-Sánchez P, Ramírez M, Varas A, Fariñas I, Vicente Á. **Acute lymphoblastic leukemia cells are able to infiltrate the brain subventricular zone stem cell niche and impair neurogenesis**. Haematologica 1; 107 (4): 1004-1007. 2022. PMID: 35045691. IF: 11.049. doi: 10.3324/haematol.2021.279383.

García-Salido A, Leoz-Gordillo I, González Brabin A, García-Teresa MÁ, Martínez-de-Azagra-Garde A, Iglesias-Bouzas MI, Cabrero-Hernández M, De Lama Caro-Patón G, Unzueta-Roch JL, Castillo-Robleda A, Ramirez- Orellana M, Nieto-Moro M. **PIMS-TS immunophenotype: description and comparison with healthy children, Kawasaki disease and severe viral and bacterial infections.** Infect Dis 54 (9): 687-691. 2022. PMID: 35394410. IF: 5.838. doi: 10.1080/23744235.2022.2059561.

Iriondo J, Zubicaray J, Sebastián E, González de Pablo J, González-Vicent M, Molina B, López-Torija I, Castillo A, Ramírez M, Madero L, Díaz MÁ, Sevilla J. **Mobilization with high-dose granulocyte colony-stimulating factor alone at 12 µg/kg twice a day in high-risk pediatric patients: A retrospective analysis of the experience in a single center**. J Clin Apher 37 (5): 420-429. 2022. PMID: 35662241. IF: 2.605. doi: 10.1002/jca.21994.

Ramos-Muntada M, Trincado JL, Blanco J, Bueno C, Rodríguez-Cortez VC, Bataller A, López-Millán B, Schwab C, Ortega M, Velasco P, Blanco ML, Nomdedeu J, Ramírez-Orellana M, Minguela A, Fuster JL, Cuatrecasas E, Camós M, Ballerini P, Escherich G, Boer J, DenBoer M, Hernández-Rivas JM, Calasanz MJ, Cazzaniga G, Harrison CJ, Menéndez P, Molina O. **Clonal heterogeneity and rates of specific chromosome gains are risk predictors in childhood high-hyperdiploid B-cell acute lymphoblastic leukemia**. Mol Oncol 16 (16): 2899-2919. 2022. PMID: 35726693. IF: 7.449. doi: 10.1002/1878-0261.13276.

Gonzalez-Vicent M, Molina B, Lopez I, Zubicaray J, Ruiz J, Vicario JL, Sebastián E, Iriondo J, Castillo A, Abad L, Ramirez M, Sevilla J, Diaz MA. **T- Cell Depleted Haploidentical Transplantation in Children With Hematological Malignancies: A Comparison Between CD3+/CD19+ and TCRαβ+/CD19+ Depletion Platforms**. Front Oncol 20; 12: 884397. 2022. PMID: 35795036. IF: 5.738. doi: 10.3389/fonc.2022.884397.

Cobaleda C, Vicente-Dueñas C, Ramírez-Orellana M, Sanchez-Garcia I. **Revisiting the concept of childhood preleukemia**. Trends Cancer 8 (11): 887-889. 2022. PMID: 35871053.IF: 19.161. doi: 10.1016/j.trecan.2022.06.012.

Sebastián E, Andrés Esteban EM, González-Vicent M, González de Pablo J, Zubicaray J, Gálvez E, Guillén M, Ruiz Pato J, Molina B, Albi G, Ramírez M, Castillo A, Pérez Maroto F, Madero L, Díaz MÁ, Sevilla J. **Extracorporeal photopheresis in paediatric patients: A retrospective comparison between different 'off-line' protocols**. Vox Sang 117 (10): 1220-1229. 2022. PMID: 36102135. IF: 2.996. doi: 10.1111/vox.13346

Molina B, González-Vicent M, Lopez I, Pereto A, Ruiz J, Ramirez M, Díaz MA. **Long-term transplant outcomes after allogeneic hematopoietic transplant in pediatric patients with hematological malignancies are influenced by severe chronic graft vs. host disease and immune reconstitution**. Front Pediatr 12; 10: 947531.2022. PMID: 36034564. IF: 3.569. doi: 10.3389/fped.2022.947531.

GROUP 44

Head of laboratory: Steegmann Olmedillas, Juan Luis

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.4 Advanced therapies in oncohematology

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 variegate 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.

GROUP MEMBERS

- Juan Luis Steegmann Olmedillas
- Luis Miguel Juárez Salcedo
- Javier Ortiz Martín
- Carlota Mayor Bastida
- Ana Puchol Crespo
- Gonzalo Benzo Callejo
- Eva María Arranz Muñoz
- María Ángeles Sanz de Benito
- Adrián Alegre Amor
- María Reyes Arranz Sáez
- María Jimena Cannata Ortiz
- Ángela Figuera Álvarez
- Ana María García-Noblejas Moya
- Valle Gómez García de Soria
- Jimena Jiménez Braña
- Javier Loscertales Pueyo

PUBLICATIONS

Marcos Jiménez A, Claudino Carvoeiro D, Ruef N, Cuesta Mateos C, Roy Vallejo E, Gómez García de Soria V, Laganá C, Del Campo L, Zubiaur P, Villapalos García G, Abad Santos F, Stein JV, Muñoz Calleja C. **Dasatinib- induced spleen contraction leads to transient lymphocytosis.** Blood Adv. 2022.PMID: 36583674. IF: 7,64. DOI: 10.1182/bloodadvances.2022009279.

Hernández Boluda JC, Pastor Galán I, Arellano Rodrigo E, Raya JM, Pérez Encinas M, Ayala R, Ferrer Marín F,

Velez P, Mora E, Fox ML, Hernández Rivas JM, Xicoy B, Mata Vázquez MI, García Fortes M, Pérez López R, Angona A, Cuevas B, Senín A, Ramírez MJ, Ramírez Payer Á, Gómez Casares MT, Martínez Valverde C, Magro E, Steegmann JL, Durán MA, García Hernández C, Gasior M, de Villambrosia SG, Alvarez Larrán A, Pereira A et al. **Predictors of thrombosis and bleeding in 1613 myelofibrosis patients from the Spanish Registry of Myelofibrosis.** Br J Haematol 199 (4). 2022. PMID: 36089912. IF: 8,62. DOI: 10.1111/bjh.18440.

García Sancho AM, Bellei M, López Parra M, Gritti G, Cortés M, Novelli S, Panizo C, Petrucci L, Gutiérrez A, Dlouhy I, Bastos Oreiro M, Sancho JM, Ramírez MJ, Moraleda JM, Carrillo E, Jiménez Ubieto AI, Jarque I, Orsucci L, García Torres E, Montalbán C, Dodero A, Arranz R, De Las Heras N, Pascual MJ, López Jiménez J, Spina M, Re A, De Villambrosia SG, Bobillo S, Federico M et al. **Autologous stem-cell transplantation as consolidation of first-line chemotherapy in patients with peripheral T-cell lymphoma: a multicenter GELTAMO/FIL study.** Haematologica 107 (11). 2022. PMID: 35320921. IF: 11,05. DOI: 10.3324/haematol.2021.279426.

Termini R, Z ihala D, Terpos E, Perez Montaña A, Jelínek T, Raab M, Weinhold N, Mai EK, Grab AL, Corre J, Vergez F, Sacco A, Chiarini M, Giustini V, Tucci A, Rodriguez S, Moreno C, Perez C, Maia C, Martín Sánchez E, Guerrero C, Botta C, Garces JJ, Lopez A, Tamariz Amador LE, Prosper F, Bargay J, Cabezudo ME, Ocio EM, Hájek R et al. **Circulating Tumor and Immune Cells for Minimally Invasive Risk Stratification of Smoldering Multiple Myeloma.** Clin Cancer Res 28 (21). 2022. PMID: 36074126. IF: 13,80. DOI: 10.1158/1078-0432.CCR-22-1594.

Luna A, Pérez Lamas L, Boque C, Giraldo P, Xicoy B, Ruiz Nuño C, Vega MM, Alvarez Larrán A, Salamanca A, García Noblejas A, Vall Llovera F, Villalon L, De Las Heras N, Ramila E, Pérez Encinas M, Cuevas B, Perez Lopez R, Sanchez Guijo F, Jiménez Velasco A, Lakhwani S, Casado LF, Rosell A, Escola A, Fernández MJ, Garcia Hernandez C, Cervero C, Mora E, Sagüés M, Suarez Varela S, Vélez P et al. **Real-life analysis on safety and efficacy of asciminib for ponatinib pretreated patients with chronic myeloid leukemia.** Ann Hematol 101 (10). 2022. PMID: 35997804. IF: 4,03. DOI: 10.1007/s00277-022-04932-6.

Antic D, Milic N, Chatzikonstantinou T, Scarfò L, Otasevic V, Rajovic N, Allsup D, Alonso Cabrero A, Andres M, Baile Gonzales M, Capasso A, Collado R, Cordoba R, Cuéllar García C, Correa JG, De Paoli L, De Paolis MR, Del Poeta G, Dimou M, Doubek M, Efstathopoulou M, El Ashwah S, Enrico A, Espinet B, Farina L, Ferrari A, Foglietta M, Lopez Garcia A, García Marco JA, García Serra R et al. **Thrombotic and bleeding complications in patients with chronic lymphocytic leukemia and severe COVID-19: a study of ERIC, the European Research Initiative on CLL.** J Hematol Oncol 15 (1). 2022. PMID: 36028857. IF: 23,17. DOI: 10.1186/s13045-022-01333-0.

Sanchez R, Dorado S, Ruiz Heredia Y, Martin Munoz A, Rosa JM, Ribera J, Garcia O, Jimenez Ubieto A, Carreno Tarragona G, Linares M, Rufian L, Juarez A, Carrillo J, Espino MJ, Caceres M, Exposito S, Cuevas B, Vanegas R, Casado LF, Torrent A, Zamora L, Mercadal S, Coll R, Cervera M, Morgades M, Hernandez Rivas JA, Bravo P, Seri C, Anguita E, Barragan E et al. **Detection of kinase domain mutations in BCR::ABL1 leukemia by ultra- deep sequencing of genomic DNA**. Sci Rep 12 (1). 2022. PMID: 35906470. IF: 5,00. DOI: 10.1038/s41598-022-17271-3.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Mateu Albero Tamara, Marcos Jimenez Ana, Wissmann Stefanie, Loscertales Javier, Terron Fernando, V, Munoz Calleja Cecilia, Cuesta Mateos Carlos. **Ibrutinib Does Not Impact CCR7-Mediated Homeostatic Migration in T-Cells from Chronic Lymphocytic Leukemia Patients**. Cancers 14 (11). 2022. PMID: 35681706. IF: 6,58. DOI: 10.3390/cancers14112729.

Sancho Juan-Manuel, Marin Niebla Ana, Fernandez Silvia, Capote Francisco-Javier, Canigral Carolina, Grande Carlos, Donato Eva, Zeberio Izaskun, Puerta Jose-Manuel, Rivas Alfredo, Perez

Ceballos Elena, Vale Ana, Martin Garcia Sancho Alejandro, Salar Antonio, Gonzalez Barca Eva, Teruel Anabel, Pastoriza Carmen, Conde Royo Diego, Sanchez Garcia Joaquin, Barrenetxea Cristina, Arranz Reyes, Hernandez Rivas Jose-Angel, Ramirez Maria-Jose, Jimenez Aroa, Rubio Azpeitia Eva. **IBRORS-MCL study: a Spanish retrospective and observational study of relapsed/refractory mantle-cell lymphoma treated with ibrutinib in routine clinical practice**. Int J Hematol 116 (3). 2022. PMID: 35551632. IF: 2,32. DOI: 10.1007/s12185-022-03367-z.

Encinas Cristina, Hernandez Rivas Jose-Angel, Oriol Albert, Rosinol Laura, Blanchard Maria-Jesus, Bellon Jose-Maria, Garcia Sanz Ramon, de la Rubia Javier, Lopez de la Guia Ana, Jimenez Ubieto Ana, Jarque Isidro, Inigo Belen, Dourdil Victoria, de Arriba Felipe, Cuellar Perez Avila Clara, Gonzalez Yolanda, Hernandez Miguel-Teodoro, Bargay Joan, Granell Miguel, Rodriguez Otero Paula, Silvent Maialen, Cabrera Carmen, Rios Rafael, Alegre Adrian, Gironella Mercedes, Gonzalez Marta-Sonia, Sureda Anna, Sampol Antonia, Ocio Enrique M, Krsnik Isabel et al. **A simple score to predict early severe infections in patients with newly diagnosed multiple myeloma**. Blood Cancer J 12 (4). 2022. PMID: 35440057. IF: 9,81. DOI: 10.1038/s41408-022-00652-2.

Labrador Jorge, Saiz Rodriguez Miriam, de Miguel Dunia, de Laiglesia Almudena, Rodriguez Medina Carlos, Vidriales Maria Belen, Perez Encinas Manuel, Jose Sanchez Sanchez Maria, Cuello Rebeca, Roldan Perez Alicia, Vives Susana, Benzo Callejo Gonzalo, Colorado Mercedes, Garcia Fortes Maria, Jose Sayas Maria, Olivier Carmen, Recio Isabel, Conde Royo Diego, Bienert Garcia Alvaro, Vahi Maria, Munoz Garcia Carmen, Seri Merino Cristina, Tormo Mar, Vall Ilovera Ferran, Foncillas Maria-Angeles, Martinez Cuadron David, Sanz Miguel Angel, Montesinos Pau. **Use of Venetoclax in Patients with Relapsed or Refractory Acute Myeloid Leukemia: The PETHEMA Registry Experience**. Cancers 14 (7). 2022. PMID: 35406512. IF: 6,58. DOI: 10.3390/cancers14071734.

Schjesvold F, Richardson PG, Facon T, Alegre A, Spencer A, Jurczyszyn A, Sunami K, Frenzel L, Min CK, Guillonneau S, Lin PL, Le Guennec S, Campana F, Van de Velde H, Bensfia S, Bringhen S. **Isatuximab plus pomalidomide and dexamethasone in elderly patients with relapsed/refractory multiple myeloma: ICARIA-MM subgroup analysis.** Haematologica. 107 (3). 2022. PMID: 35229573. IF: 11,05. DOI: 10.3324/haematol.2021.279160.

LINE 3.5 ›› BIOLOGICAL, CELLULAR AND MOLECULAR MONITORING IN ONCOHEMATOLOGY

GROUP 45

Head of laboratory: Fernández Ruiz, Elena

Area 3 Advanced therapies and individualized medicine

Line 3.5 Biological, cellular and molecular monitoring in oncohematology

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.

GROUP MEMBERS

- Estíbaliz Alegría Carrasco
- María Rosa Carracedo Rodríguez
- Ana Nicolao Gómez
- Santa Matilde Santos Roncero

MAJOR GRANTS

Fernández Ruíz, Elena. Effect of TYK2 deficiency in B Cell function: impact in lymphoproliferative diseases. PI19/00096. ISCIII. 2020-2022.

PUBLICATIONS

Villapalos Garcia Gonzalo, Zubiaur Pablo, Rivas Duran Rebeca, Campos Norte Pilar, Arevalo Roman Cristina, Fernandez Rico Marta, Garcia Fraile Fraile Lucio, Fernandez Campos Paula, Soria Chacartegui Paula, Fernandez de Cordoba Onate Sara, Delgado Wicke Pablo, Fernandez Ruiz Elena, Gonzalez Alvaro Isidoro, Sanz Jesus, Abad Santos Francisco, de Los Santos Ignacio. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity, and sex are the primary predictors of COVID-19 severity**. Life

Sci Alliance 5 (10). 2022. PMID: 35636966. IF: 5,78. DOI: 10.26508/lsa.202201396.

Roy-Vallejo E, Cardeñoso L, Triguero-Martínez A, Marta Chicot Llano M,Zurita N, Ávalos E, Barrios A, Hernando J, Ortiz J, Rodriguez-García S.C, Ciudad Sañudo M, Marcos C, García Castillo E, Fontán L, González B, Méndez R, Iturrate I, Sanz-García A, Villa A, Sánchez-Azofra A, Quicios B, Arribas D, Álvarez Rodríguez J, Patiño P, Trigueros M, Uriarte M, Martín- Ramírez A, Arévalo Román C, Galván-Román JM, García-Vicuña R, Ancochea J, Muñoz-Calleja C, Fernández-Ruiz E, de la Cámara R, Suárez Fernández C, González-Álvaro I, Rodríguez-Serrano DA and the PREDINMUN-COVID Group. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9: 855639. 2022. PMID: 35783606. IF: 5,091. DOI: 10.3389/fmed.2022.855639

GROUP 46

Head of laboratory: Muñoz Calleja, Cecilia

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.5 Biological, cellular and molecular monitoring in oncohematology

RESEARCH INTEREST

Testing Antibodies in Multiple Sclerosis: This project stems from an urgent need of novel therapies in Multiple Sclerosis (MS) and aims to address the following main objectives:

- To find novel therapeutic targets in MS - To provide novel therapeutic tools against novel targets in the field. The project is carried out by the company IMMED as the leader and two participant research centres LEITAT and IISP.

-FIBHLPR, the latter represented by the researcher Dr. Cecilia Muñoz Calleja. Overall, this project aims to reinforce the knowledge on the deleterious role of immune receptors in MS and to provide novel, specific, target-directed therapeutic monoclonal antibodies in a field with high medical need of novel drugs. Likewise, results might provide enough pre- clinical evidence to evaluate an eventual clinical development of the different therapeutic monoclonal antibody candidates in the setting of MS and related syndromes. If successful, novel therapies from this project would certainly benefit MS patients, their families, and their clinicians, which could provide additional tools to assist the patients.

GROUP MEMBERS

- Cecilia Muñoz Calleja
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- Noelia López García
- Ana María Marcos Jiménez
- Carlos Cuesta Mateos

MAJOR GRANTS

Muñoz Calleja, Cecilia. Disección del papel de las distintas subpoblaciones leucocitarias CCR7+ en la patogénesis de la leucemia linfocítica crónica y la enfermedad de injerto contra huésped: utilidad diagnóstica y terapéutica. PI21/01803. ISCIII. 2022-2024.

Muñoz Calleja, Cecilia. Impact of the tyrosine kinase inihibitor disatinib on lymphoid tissue microenvironment and tumor cell niche. Fundación San Salvatore. 2021-2023.

Muñoz Calleja, Cecilia. Testing Antibodies in Multiple Sclerosis.

Ministerio de Ciencia e Innovacion. 2022-2025.

PUBLICATIONS

Marcos Jiménez A, Claudino Carvoeiro D, Ruef N, Cuesta Mateos C, Roy Vallejo E, Gómez García de Soria V, Laganá C, Del Campo L, Zubiaur P, Villapalos García G, Abad Santos F, Stein JV, Muñoz Calleja C. **Dasatinib- induced spleen contraction leads to transient lymphocytosis.** Blood Adv. PMID: 36583674. IF: 7.64. DOI: V10.1182/bloodadvances.2022009279.

Sevilla Montero J, Munar Rubert O, Pino Fadon J, Aguilar Latorre C, Villegas Esguevillas M, Climent B, Agro M, Choya Foces C, Martinez Ruiz A, Balsa E, Munoz Calleja C, Gomez Punter RM, Vazquez Espinosa E, Cogolludo A, Calzada MJ. **Cigarette smoke induces pulmonary arterial dysfunction through an imbalance in the redox status of the soluble guanylyl cyclase**. Free Radic Biol Med 193 (Pt 1). 2022. PMID: 36174878. IF: 8,10. DOI: 10.1016/j.freeradbiomed.2022.09.026.

Wissmann S, Stolp B, Jímenez AM, Stein JV. **DOCK2 and phosphoinositide- 3 kinase d mediate two complementary signaling pathways for CXCR5-dependent B cell migration.** Front Immunol 13. 2022. PMID: 36341455. IF: 8,79. DOI: 10.3389/fimmu.2022.982383.

Santamaria S, Delgado M, Botas M, Castellano E, Corraliza Gorjon I, Lafuente P, Muñoz Calleja C, Toribio ML, Kremer L, Garcia Sanz JA. **Therapeutic potential of an anti-CCR9 mAb evidenced in xenografts of human CCR9(+) tumors.** Front Immunol 13. 2022. PMID: 35967322. IF: 8,79. DOI: 10.3389/fimmu.2022.825635.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Mateu Albero Tamara, Marcos Jimenez Ana, Wissmann Stefanie, Loscertales Javier, Terron Fernando, V, Munoz Calleja Cecilia, Cuesta Mateos Carlos. **Ibrutinib Does Not Impact CCR7-Mediated Homeostatic Migration in T-Cells from Chronic Lymphocytic Leukemia Patients**. Cancers 14 (11). 2022. PMID: 35681706. IF: 6,58. DOI: 10.3390/cancers14112729.

Esparcia Pinedo Laura, Martinez Fleta Pedro, Ropero Noelia, Vera Tome Paula, Reyburn Hugh T, Casasnovas Jose M, Frade Jose M Rodriguez, Vales Gomez Mar, Vilches Carlos, Martin Gayo Enrique, Munoz Calleja Cecilia, Sanchez Madrid Francisco, Alfranca Arantzazu. **CD4+T Cell Immune Specificity Changes After Vaccination in Healthy And COVID-19 Convalescent Subjects**. Front Immunol 12. 2022. PMID: 35126347. IF: 8,79. DOI: 10.3389/fimmu.2021.755891.

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

GROUP 58

Head of laboratory: Alfonso Manterola, Fernando

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.6 New diagnostic and therapeutic advances in cardiovascular diseases

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.

GROUP MEMBERS

- Fernando Alfonso Manterola
- Teresa Bastante Valiente
- Francisco Javier Cuesta Cuesta
- Stephanía Chavez Isaza
- David del Val Martín
- Fernando Suárez Sipmann
- Pablo Díez Villanueva
- Marcos Manuel García Guimaraes
- Amparo Benedicto Buendía
- Guillermo Reyes Copa
- Fernando Rivero Crespo

MAJOR GRANTS

Rivero Crespo, Fernando / Alfonso Manterola, Fernando. In vivo detection of activated coronary endothelium using optical coherence tomography (OCT) combined with functionalized optical contrast nanocomposites. PI19/00565. ISCIII. 2020-2022.

Alfonso Manterola, Fernando. Modelo integral de predicción de fibrilación auricular en pacientes con ictus criptogénico. Sociedad Española de Cardiología. 2019-2023.

Suarez Sipmann, Fernando. Validación clínica de un método capnodinámico para la monitorización continúa del volumen y perfusión pulmonar efectivos en pacientes en ventilación mecánica. PI20/01548. ISCIII. 2021-2023.

Alfonso Manterola, Fernando. The Betablockers and Antiplatelet agents in patients with Spontaneous Coronary Artery Dissection, randomized clinical trial (BA-SCAD RCT). Sociedad Española de Cardiología. 2021-2024.

Suárez Sipmann, Fernando. IINTELLILUNG: INTELLIGENT LUNG SUPPORT FOR MECHANICALLY VENTILATED PATIENTS IN THE INTENSIVE CARE UNIT. UE. INTELLILUNG. 101057434. EUROPEAN COMMISSION.2022-

Ecografía 3D carotidea y femoral en pacientes con cardiopatía isquémica precoz: caracterización y búsqueda de marcadores para pacientes y familiares. "CArotid and FEmoral atherosclerosis burden in Early CORonary heart disease: the CAFEECOR study". López Melgar, Beatriz. Alfonoso Manterola, Fernando. Proyectos de Investigación en Salud. Ministerio de Ciencia e Innovación. ISCIII. PI22/01414. 2022-2025.

PUBLICATIONS

Ortega Paz L, Arévalos V, Fernández Rodríguez D, Jiménez Díaz V, Bañeras J, Campo G, Rodríguez Santamarta M, Díaz JF, Scardino C, Gómez Álvarez Z, Pernigotti A, Alfonso F, Amat Santos IJ, Silvestro A, Rampa L, de la Torre Hernández JM, Bastidas G, Gómez Lara J, Bikdeli B, García HM, Angiolillo DJ, Rodés Cabau J, Sabaté M, Brugaletta S, COVID 19 registry investigators CV. **One-year cardiovascular outcomes after coronavirus disease 2019: The cardiovascular COVID-19 registry.** PLoS One 17 (12). 2022. PMID: 36583998. IF: 3,75. DOI: 10.1371/journal.pone.0279333.

Alfonso F, Aguilar R, Reyes G. **Management of Post-Infarction Ventricular Septal Defects: Are We Moving Forward?** Eur Heart J 43 (48). 2022. PMID: 36124726. IF: 35,86. DOI: 10.1093/eurheartj/ehac532.

Vera A, Cecconi A, Ximénez Carrillo Á, Ramos C, Martínez Vives P, Lopez Melgar B, Sanz García A, Ortega G, Aguirre C, Vivancos J, Jiménez Borreguero LJ, Alfonso F, DECRYTORING Study Investigators. **Advanced Echocardiography With Left Atrial Strain and Indexed Left Atrial Three- Dimensional Volume for Predicting Underlying Atrial Fibrillation After Cryptogenic Stroke.** Am J Cardiol 185. 2022. PMID: 36307348. IF: 3,13. DOI: 10.1016/j.amjcard.2022.09.004.

Alfonso F, Sanz Ruiz R, Sabate M, Macaya F, Roura G, Jimenez Kockar M, Nogales JM, Velazquez M, Veiga G, Camacho Freire S, Moreu J, Peláez JAF, Pérez Espejo P, Amat Santos IJ, Diez Villanueva P, Bastante T, Del Val D, Rivero F, García Guimaraes M. **Clinical Implications of the "Broken Line" Angiographic Pattern in Patients With Spontaneous Coronary Artery Dissection.** Am J Cardiol 185. 2022. PMID: 36244863. IF: 3,13. DOI: 10.1016/j.amjcard.2022.09.017.

McInerney A, Salazar C, Pérez Vizcayno MJ, Jimenez Quevedo P, Jiménez Valero S, Brugaletta S, Romaguera R, Nombela Franco L, Travieso Gonzalez A, Jerónimo Baza A, Tirado Conte G, Fernández Ortiz A, Escaned J, Alfonso F, Macaya C, Gonzalo N. **Vascular healing responses to paclitaxel coated balloons or everolimus eluting stents for the treatment of in-stent restenosis. Insights from optical coherence tomography.** Coron Artery Dis 33 (8). 2022. PMID: 36238983. IF: 1,72. DOI: 10.1097/MCA.0000000000001189.

Hernández G, Paredes I, Moran F, Buj M, Colinas L, Rodríguez ML, Velasco A, Rodríguez P, Pérez Pedrero MJ, Suarez Sipmann F, Canabal A, Cuena R, Blanch L, Roca O. **Effect of postextubation noninvasive ventilation with active humidification vs high-flow nasal cannula on reintubation in patients at very high risk for extubation failure: a randomized trial.** Intensive Care Med 48 (12). 2022. PMID: 36400984. IF: 41,79. DOI: 10.1007/s00134-022-06919-3.

Jiménez Méndez C, Díez Villanueva P, Bonanad C, Ortiz Cortés C, Barge Caballero E, Goirigolzarri J, Esteban Fernández A, Pérez Rivera Á, Cobo M, López J, Sanz García A, Guerrero C, Pardo HG, Robles C, Iglesias D, Pinilla JMG, Rodríguez LL, Formiga F, Martín Sánchez FJ, Vidán MT, Ariza A, Martínez Sellés M, Alfonso F, en representación de los investigadores del registro FRAGIC. **Frailty and prognosis of older patients with chronic heart failure.** Rev Esp Cardiol 75 (12). 2022. PMID: 35718066. IF: 6,98. DOI: 10.1016/j.rec.2022.04.016.

Lorenzo,N,Hernandez,V,Montes,A,Rivero, F, Reyes, G, Aguilar, R. **Left Ventricular Thrombosis and**

Pulmonary Thromboembolism in an Asymptomatic Covid-19 Patient. Arq Bras Cardiol 119 (6): 2022. PMID: 36541997. IF: 2,67. DOI: 10.36660/abc.20210590.

Alfonso F, Fernández Pérez C, Del Prado N, García Guimaraes M, Bernal JL, Bastante T, Del Val D, García Márquez M, Elola J. **Characteristics and outcomes of percutaneous coronary interventions in patients with spontaneous coronary artery dissection. A study from the administrative minimum data set of the Spanish National Health System.** Front Cardiovasc Med 9. 2022. PMID: 36531730. IF: 5,85. DOI: 10.3389/fcvm.2022.1054413.

González Colaço Harmand M, García Sanz MDM, Agustí A, Prada Arrondo PC, Domínguez Rodríguez A, Grandal Leirós B, Peña Otero D, Negrín Mena N, López Hernández JJ, Díez Villanueva P. **Review on the management of cardiovascular risk factors in the elderly.** J Geriatr Cardiol 19 (11). 2022. PMID: 36561061. IF: 3,19. DOI: 10.11909/j.issn.1671-5411.2022.11.008.

Mollar A, Bonanad C, Diez Villanueva P, Segarra D, Civera J, Sastre C, Conesa A, Villaescusa A, Fernández J, Miñana G, Navarro J, Sanchis J, Núñez J. **Frailty and Hospitalization Burden in Patients With Chronic Heart Failure.** Am J Cardiol 183. 2022. PMID: 36153181. IF: 3,13. DOI: 10.1016/j.amjcard.2022.08.013.

Roleder Dylewska M, Gasior P, Hommels TM, Roleder T, Berta B, Ang HY, NgJCK, Hermanides RS, Fabris E, IJsselmuiden AJJ, Kauer F, Alfonso F, von Birgelen C, Escaned J, Camaro C, Kennedy MW, Pereira B, Magro M, Nef H, Reith S, Malinowski K, De Luca G, Garcia HM, Granada JF, Wojakowski W, Kedhi E. **Morphological characteristics of lesions with thin cap fibroatheroma-a substudy from the COMBINE (OCT-FFR) trial.** Eur Heart J Cardiovasc. Imaging. IF: 9,13. PMID: 36342269. DOI: 10.1093/ehjci/jeac218.

Vera A, Rojas González A, López Melgar B, Cecconi A, Olivera MJ, Jiménez Borreguero LJ, Alfonso F. **One for All and All for One.** Can J Cardiol 38 (11). 2022. PMID: 35933065. IF: 6,61. DOI: 10.1016/j.cjca.2022.07.015.

Del Val D, Cuesta J, Roquero P, Alfonso F. **Lithotripsy for calcified in-stent restenosis. The "rock strata peeling pattern": A novel fracture pattern detected by optical coherence tomography.** Catheter Cardiovasc Interventions 100 (6): 2022. PMID: 36229940. IF: 2,59. DOI: 10.1002/ccd.30420.

Fernández Gallego N, Castillo González R, Méndez Barbero N, López Sanz C, Obeso D, Villaseñor A, Escribese MM, López Melgar B, Salamanca J, Benedicto Buendía A, Jiménez Borreguero LJ, Ibañez B, Sastre J, Belver MT, Vega F, Blanco C, Barber D, Sánchez Madrid F, de la Fuente H, Martín P, Esteban V, Jiménez Saiz R. **The impact of type 2 immunity and allergic diseases in atherosclerosis.** Allergy 77 (11). 2022. PMID: 35781885. IF:

14,71. DOI: 10.1111/all.15426.

Blanco Domínguez R, de la Fuente H, Rodríguez C, Martín Aguado L, Sánchez Díaz R, Jiménez Alejandre R, Rodríguez Arabaolaza I, Curtabbi A, García Guimaraes MM, Vera A, Rivero F, Cuesta J, Jiménez Borreguero LJ, Cecconi A, Duran Cambra A, Taurón M, Alonso J, Bueno H, Villalba Orero M, Enríquez JA, Robson SC, Alfonso F, Sánchez Madrid F, Martínez González J, Martín P. **CD69 expression on regulatory T cells protects from immune damage after myocardial infarction.** J Clin Invest 132 (21). 2022. PMID: 36066993. IF: 19,46. DOI: 10.1172/JCI152418.

Rodriguez Leor O, de la Torre Hernández JM, García Camarero T, García Del Blanco B, López Palop R, Fernández Nofrerías E, Cuellas Ramón C, Jiménez Kockar M, Jiménez Mazuecos J, Fernández Salinas F, Gómez Lara J, Brugaletta S, Alfonso F, Palma R, Gómez Menchero AE, Millán R, Tejada Ponce D, Linares Vicente JA, Ojeda S, Pinar E, Fernández Pelegrina E, Morales Ponce FJ, Cid Álvarez AB, Rama Merchan JC, Molina Navarro E, Escaned J, Pérez de Prado A. **Instantaneous Wave-Free Ratio for the Assessment of Intermediate Left Main Coronary Artery Stenosis: Correlations With Fractional Flow Reserve/Intravascular Ultrasound and Prognostic Implications: The iLITRO-EPIC07 Study.** Circ Cardiovasc Interventions 15 (11). 2022. PMID: 36111801. IF: 7,51. DOI: 10.1161/CIRCINTERVENTIONS.122.012328.

Alfonso F, Bastante T. **Spontaneous Coronary Artery Dissection in Men: So Rare? So Different?** JACC Cardiovasc Interventions 15 (20): 2022. PMID: 36265937. IF: 11,08. DOI: 10.1016/j.jcin.2022.09.020.

Prati F, Arbustini E, Alfonso F. **Skating on thin ice: searching for vulnerable plaques.** EuroIntervention 18 (9). 2022. PMID: 36269207. IF: 7,73. DOI: 10.4244/EIJ-D-22-00397.

Greco A, Sciahbasi A, Abizaid A, Mehran R, Rigattieri S, de la Torre Hernandez JM, Alfonso F, Cortese B. **Sirolimus-coated balloon versus everolimus-eluting stent in de novo coronary artery disease: Rationale and design of the TRANSFORM II randomized clinical trial.** Catheter Cardiovasc Interventions 100 (4). 2022. PMID: 36054266. IF: 2,59. DOI: 10.1002/ccd.30358.

Romagnoli E, Ramazzotti V, Burzotta F, Gatto L, Marco V, Paoletti G, Biondi Zoccai G, Alfonso F, Crea F, Trani C, Prati F, CLI OPCI Project Investigators*.

Definition of Optimal Optical Coherence Tomography-Based Stent Expansion Criteria: In-Stent Minimum Lumen Area Versus Residual Stent Underexpansion. Circ Cardiovasc Interventions 15 (9). 2022. PMID: 36126136. IF: 7,51. DOI: 10.1161/CIRCINTERVENTIONS.121.011496.

Diez Villanueva P, Jimenez Mendez C, Bonanad C, Ortiz Cortes C, Barge Caballero E, Goirigolzarri J, Esteban Fernandez A, Perez Rivera A, Cobo M, Sanz Garcia A, Formiga F, Ariza Sole A, Martinez Selles M, Alfonso F. **Sex differences in the impact of frailty in elderly outpatients with heart failure**. Front Cardiovasc Med 9 2022. PMID: 36172583. IF: 5,85. DOI:10.3389/fcvm.2022.1000700.

Hernández G, Vaquero C, Ortiz R, Colinas L, de Pablo R, Segovia L, Rodriguez ML, Villasclaras A, Muñoz Moreno JF, Suarez Sipmann F, Canabal A, Cuena R, Roca O. **Benefit with preventive noninvasive ventilation in subgroups of patients at high-risk for reintubation: a post hoc analysis.** J Intensive Care 10 (1). 2022. PMID: 36089625. IF: 7,52. DOI: 10.1186/s40560-022-00635-2.

García Guimarães,M,Gutiérrez Barrios,A,Gómez Lara,J,Aparisi,Á,Salvatella,N,Rivero,F. **Microvascular dysfunction and invasive absolute coronary flow after percutaneous coronary intervention for a chronic total occlusion. The FLOW-CTO study.** Rev Esp Cardiol 75 (9): 2022. PMID: 35662521. IF: 6,98. DOI: 10.1016/j.rec.2022.03.008.

Ortega Paz L, Brugaletta S, Gomez Lara J, Alfonso F, Cequier A, Romaní S, Bordes P, Serra A, Iñiguez A, Salinas P, García Del Blanco B, Goicolea J, Hernández Antolín R, Cuesta J, Gómez Hospital JA, Sabaté M. **Magnesium- based resorbable scaffold vs permanent metallic sirolimus-eluting stent in patients with ST-segment elevation myocardial infarction: 3-year results of the MAGSTEMI randomised controlled trial.** EuroIntervention 18 (5). 2022. PMID: 35225793. IF: 7,73. DOI: 10.4244/EIJ-D-21-00651.

McInerney A, Rodés Cabau J, Veiga G, López Otero D, Muñoz García E, Campelo Parada F, Oteo JF, Carnero M, Tafur Soto JD, Amat Santos IJ, Travieso A, Mohammadi S, Barbanti M, Cheema AN, Toggweiler S, Saia F, Dabrowski M, Serra V, Alfonso F, Ribeiro HB, Regueiro A, Alpieri A, Gil Ongay A, Martinez Cereijo JM, Muñoz García A, Matta A, Arellano Serrano C, Barrero A, Tirado Conte G, Gonzalo N et al. **Transcatheter versus surgical aortic valve replacement in patients with morbid obesity: a multicentre propensity score-matched analysis.** EuroIntervention 18 (5). 2022. PMID: 35321860. IF: 7,73. DOI: 10.4244/EIJ-D-21-00891.

Cuesta J, Rivero F, Bastante T, Antuña P, Jiménez C, García Guimares M, Alfonso F. **Treatment of in-stent restenosis with sirolimus-eluting magnesium bioresorbable scaffolds: optical coherence tomography insights.** Coron Artery Dis 33 (5). 2022. PMID: 35170552. IF: 1,72. DOIGonzalez ME, Suarez Sipmann F. **Perioperative Continuous Noninvasive Cardiac Output Monitoring in Cardiac Surgery Patients by a Novel Capnodynamic Method.** J Cardiothorac Vasc Anesth 36 (8 Pt B). 2022. PMID: 35283043. IF: 2,89. DOI: 10.1053/j.jvca.2022.02.002.

Munoz Ortiz Tamara, Hu Jie, Sanz Rodriguez Francisco, Ortgies Dirk H, Jaque Daniel, Mendez Gonzalez Diego, Aguilar Rio, Alfonso Fernando, Rivero Fernando, Rodriguez Emma Martin, Sole Jose Garcia. **Optical detection of atherosclerosis at molecular level by optical coherence tomography: An in vitro study**. Nanomed Nanotechnol Biol Med 43. 2022. PMID: 35390527. IF: 6,46. DOI: 10.1016/j.nano.2022.102556.

Martínez Vives P, Cecconi A, Vera A, Fernández C, López Melgar B, Sanz García A, Rojas González A, Nogales Romo MT, Hernandez Muñiz S, Olivera MJ, Caballero P, Jiménez Borreguero LJ, Alfonso F. **Usefulness of Tissue Tracking by Cardiac Magnetic Resonance to Predict Events in Patients With Hypertrophic Cardiomyopathy.** Am J Cardiol 174. 2022. PMID: 35525624. IF: 3,13. DOI: 10.1016/j.amjcard.2022.03.024.

Torres A, Motos A, Cillóniz C, Ceccato A, Fernández Barat L, Gabarrús A, Bermejo Martin J, Ferrer R, Riera J, Pérez Arnal R, García Gasulla D, Peñuelas O, Lorente JÁ, de Gonzalo Calvo D, Almansa R, Menéndez R, Palomeque A, Villar RA, Añón JM, Balan Mariño A, Barberà C, Barberán J, Blandino Ortiz A, Boado MV, Bustamante Munguira E, Caballero J, Cantón Bulnes ML, Carbajales Pérez C, Carbonell N, Catalán González M et al. **Major candidate variables to guide personalised treatment with steroids in critically ill patients with COVID-19: CIBERESUCICOVID study.** Intensive Care Med 48 (7). 2022. PMID: 35727348. IF: 41,79. DOI: 10.1007/s00134- 022-06726-w.

Alfonso F, Byrne RA. **Limus-Coated Balloons in "de Novo" Coronary Lesions: Quo Vadis?** JACC Cardiovasc Interventions 15 (12): 2022. PMID: 35637127. IF: 11,08. DOI: 10.1016/j.jcin.2022.04.011.

Bea C, Vela S, García Blas S, Perez Rivera JA, Díez Villanueva P, de Gracia AI, Fuertes E, Oltra MR, Ferrer A, Belmonte A, Santas E, Pellicer M, Colomina J, Doménech A, Bodi V, Forner MJ, Chorro FJ, Bonanad C. **Infective Endocarditis in the Elderly: Challenges and Strategies.** J Cardiovasc Dev Dis 9 (6). 2022. PMID: 35735821. IF: 4,42. DOI: 10.3390/jcdd9060192.

Alfonso F, Fernández Pérez C, García Márquez M, García Guimaraes M, Bernal JL, Bastante T, Del Val D,

Del Prado N, Elola J. **Spontaneous coronary artery dissection in Spain: a study using the minimum data set of the Spanish National Health System.** Rev. Esp. Cardiol. IF: 7,05. PMID: 35716909. DOI: 10.1016/j.rec.2022.04.017.

Vera Alberto, Cecconi Alberto, Martinez Vives Pablo, Jose Olivera Maria, Hernandez Susana, Lopez Melgar Beatriz, Rojas Gonzalez Antonio, Diez Villanueva Pablo, Salamanca Jorge, Tejelo Julio, Caballero Paloma, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Electrocardiogram and CMR to differentiate tachycardia-induced cardiomyopathy from dilated cardiomyopathy in patients admitted for heart failure**. HEART VESSELS 37 (11). 2022. PMID: 35657427. IF: 1,81. DOI: 10.1007/s00380-022-02102-2.

Alfonso F, Coughlan JJ, Giacoppo D, Kastrati A, Byrne RA. **Management of in-stent restenosis.** EuroIntervention 18 (2). 2022. PMID: 35656726. IF: 7,73. DOI: 10.4244/EIJ-D-21-01034.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Bonanad C, Esteve-Claramunt F, García-Blas S, Ayesta A, Díez-Villanueva P, Pérez-Rivera JÁ, Ferreiro JL, Cánoves J, López-Fornás F, Ariza Solé A, Raposerias S, Vivas D, Blanco R, Bompart Berroterán D, Cordero A, Núñez J, Fácila L, Núñez-Gil IJ, Górriz JL, Bodí V, Martínez-Selles M, Ruiz Nodar JM, Chorro FJ. **Antithrombotic Therapy in Elderly Patients with Acute Coronary Syndromes**. J Clin Med 11 (11): 2022. PMID: 35683397. IF: 4,96. DOI: 10.3390/jcm11113008.

Alfonso F, Cortese B. **Drug-Coated Balloons for Unselected Real World Patients: Are We There Yet?**. Korean Circ J 52. (6): 2022. PMID: 35656903. IF: 3,10. DOI: 10.4070/kcj.2022.0108.

Panagides V, Del Val D, Abdel Wahab M, Mangner N, Durand E, Ihlemann N, Urena M, Pellegrini C, Giannini F, Scislo P, Huczek Z, Landt M, Auffret V, Sinning JM, Cheema AN, Nombela Franco L, Chamandi C, Campelo Parada F, Munoz Garcia E, Herrmann HC, Testa L, Kim WK, Castillo JC, Alperi A, Tchetche D, Bartorelli AL, Kapadia S, Stortecky S, Amat Santos I, Wijeysundera HC et al. **Mitral Valve Infective Endocarditis after Trans- Catheter Aortic Valve Implantation**. Am J Cardiol 172. 2022. PMID: 35387738. IF: 3,13. DOI: 10.1016/j.amjcard.2022.02.034.

Bonanad C, Fernández Olmo R, García Blas S, Alarcon JA, Díez Villanueva P, Mansilla CR, García Pardo H, Toledo P, Ayesta A, Pereira E, Carol A, Castro Conde A, de Pablo Zarzoso C, Martínez Sellés M, Arrarte V, Campuzano R, Ariza Solé A. **Cardiovascular prevention in elderly patients.** J. Geriatr. Cardiol. 19. (5). 2022. PMID: 35722032. IF: 3,19. DOI: 10.11909/j.issn.1671-5411.2022.05.004.

Collet Jean-Philippe, Van Belle Eric, Thiele Holger, Berti Sergio, Lhermusier Thibault, Manigold Thibault, Neumann Franz-Josef, Gilard Martine, Attias David, Beygui Farzin, Cequier Angel, Alfonso Fernando, Aubry Pierre, Baronnet Flore, Ederhy Stephane, El Kasty Mohamad, Kerneis Mathieu, Barthelemy Olivier, Lefevre Thierry, Leprince Pascal, Redheuil Alban, Henry Patrick, Portal Jean-Jacques, Vicaut Eric, Montalescot Gilles, ACTION Grp. **Apixaban vs. standard of care after transcatheter aortic valve implantation: the ATLANTIS trial**. Eur Heart J 43 (29). 2022. PMID: 35583186. IF: 35,86. DOI: 10.1093/eurheartj/ehac242.

García-Guimarães M, Fuertes-Ferre G, Jiménez-Valero S, Lozano I, Cruz- González I, Cortés C, Portero-Portaz JJ, Valero E, Bastante T, Alfonso F; Spanish Registry on SCAD investigators. **Characteristics, Acute Results, and Prognostic Impact of Percutaneous Coronary Interventions in Spontaneous Coronary Artery Dissection (from the Prospective Spanish Registry on SCAD [SR-SCAD]).** Am J Cardiol 171. 2022. PMID: 35321804. IF: 3,13. DOI: 10.1016/j.amjcard.2022.02.008.

Rai Himanshu, Harzer Fiona, Otsuka Tatsuhiko, Abdelwahed Youssef S, Antuna Paula, Blachutzik Florian, Koppara Tobias, Raber Lorenz, Leistner David M, Alfonso Fernando, Nef Holger, Seguchi Masaru, Aytekin Alp, Xhepa Erion, Kufner Sebastian, Cassese Salvatore, Laugwitz Karl-Ludwig, Byrne Robert A, Kastrati Adnan, Joner Michael. **Stent Optimization Using Optical Coherence Tomography and Its Prognostic Implications After Percutaneous Coronary Intervention**. J Am Heart Assoc 11 (9). 2022. PMID: 35470682. IF: 6,11. DOI:10.1161/JAHA.121.023493.

Fabris Enrico, Berta Balasz, Roleder Tomasz, Hermanides Renicus S, IJsselmuiden Alexander J J, Kauer Floris, Alfonso Fernando, von Birgelen Clemens, Escaned Javier, Camaro Cyril, Kennedy

Mark W, Pereira Bruno, Magro Michael, Nef Holger, Reith Sebastian, Roleder Dylewska Magda, Gasior Pawel, Malinowski Krzysztof, De Luca Giuseppe, Garcia Hector M, Granada Juan F, Wojakowski Wojciech, Kedhi Elvin. **Thin-Cap Fibroatheroma Rather Than Any Lipid Plaques Increases the Risk of Cardiovascular Events in Diabetic Patients: Insights From the COMBINE OCT-FFR Trial**. Circ Cardiovasc Interventions 15 (5). 2022. PMID: 35485232. IF: 7,51. DOI:10.1161/CIRCINTERVENTIONS.121.011728.

Araki M, Park SJ, Dauerman HL, Uemura S, Kim JS, Di Mario C, Johnson TW, Guagliumi G, Kastrati A, Joner M, Holm NR, Alfonso F, Wijns W, Adriaenssens T, Nef H, Rioufol G, Amabile N, Souteyrand G, Meneveau N, Gerbaud E, Opolski MP, Gonzalo N, Tearney GJ, Bouma B, Aguirre AD, Mintz GS, Stone GW, Bourantas CV, Räber L, Gili S et al. **Optical coherence tomography in coronary atherosclerosis assessment and intervention**. Nat Rev Cardiol 19 (10): 2022. PMID: 35449407. IF: 49,42. DOI: 10.1038/s41569-022-00687-9.

Budassi Simone, Biccire Flavio Giuseppe, Paoletti Giulia, Marco Valeria, Boi Alberto, Romagnoli Enrico, Fabbiocchi Franco, Fineschi Massimo, Di Pietro Riccardo, Versaci Francesco, Calligaris Giuseppe, Gatto Laura, Albertucci Mario, Ramazzotti Vito, Burzotta Francesco, Ozaki Yukio, Arbustini Eloisa, Alfonso Fernando, Prati Francesco. **The Role of the Association Between Serum C-Reactive Protein Levels and Coronary Plaque Macrophage Accumulation in Predicting Clinical Events - Results from the CLIMA Registry**. J Cardiovasc Transl Res 15 (6). 2022. PMID: 35437619. IF: 3,22. DOI: 10.1007/s12265-022-10250-z.

- Jurado Román A, Miñana G, Salinas P, Regueiro A, Caballero Borrego J, Martín Moreiras J, Rivero F, Lacunza J, Rondán J, Amat Santos IJ, Sanchís J, Gonzalo N, Sabaté M, Astorga JC, Mohandes M, Gómez Menchero A, Fernández Díaz JA, Ojeda S, Paredes E, Vaquerizo B, Vinhas H, López M, Rodríguez S, Rúmiz E, Jiménez Mazuecos J, Lee DH, Robles J, Gutiérrez A, Morales FJ, Consuegra L et al. **Overlapping versus single long stents in long chronic total occlusions: insights of the Iberian CTO Registry.** Minerva Cardiol Angiol. PMID: 35420282. DOI:10.23736/S2724-5683.22.06046-X.

Ammirati Enrico, Lupi Laura, Palazzini Matteo, Hendren Nicholas S, Grodin Justin L, V, Schmidt Matthieu, Hekimian Guillaume, Peretto Giovanni, Bochaton Thomas, Hayek Ahmad, Piriou Nicolas, Leonardi Sergio, Guida Stefania, Turco Annalisa, Sala Simone, Uribarri Aitor, Van de Heyning Caroline M, Mapelli Massimo, Campodonico Jeness, Pedrotti Patrizia, Sanchez Maria Isabel Barrionuevo, Sole Albert Ariza, Marini Marco, Matassini Maria Vittoria, Vourc'h Mickael, Cannata Antonio, I, Briguglia Daniele, Salamanca Jorge et al. **Prevalence, Characteristics, and Outcomes of COVID-19-Associated Acute Myocarditis**. Circulation 145 (15). 2022. PMID: 35404682. IF: 39,92. DOI:10.1161/CIRCULATIONAHA.121.056817.

Circulation.

Garcia Guimaraes Marcos, Masotti Monica, Sanz Ruiz Ricardo, Macaya Fernando, Roura Gerard, Nogales Juan Manuel, Tizon Marcos Helena, Velazquez Martin Maite, Veiga Gabriela, Flores Rios Xacobe, Altisent Omar Abdul-Jawad, Jimenez Kockar Marcelo, Camacho Freire Santiago, Moreu Jose, Ojeda Soledad, Santos Martinez Sandra, Sanz Garcia Ancor, Del Val David, Bastante Teresa, Alfonso Fernando, Spanish Registry SCAD Investigator. **Clinical outcomes in spontaneous coronary artery dissection**. Heart 108 (19). 2022. PMID: 35410894. IF: 7,37. DOI: 10.1136/heartjnl-2022-320830.

Loughlin Gerard, Pachon Marta, Luis Martinez Sande Jose, Luis Ibanez Jose, Bastante Teresa, Osca Asensi Joaquin, Gonzalez Melchor Laila, Gabriel Martinez Martinez Juan, Cuesta Javier, Arias Miguel A. **Outcomes of leadless pacemaker implantation in patients with mechanical heart valves**. J Cardiovasc Electrophysiol 33 (5). 2022. PMID: 35322490. IF: 2,94. DOI: 10.1111/jce.15462.

- Torres Antoni, Motos Anna, Ceccato Adrian, Bermejo Martin Jesus, de Gonzalo Calvo David, Perez Raquel, Barroso Marta, Zubizarreta Pascual Ion, Gonzalez Jessica, Fernandez Barat Laia, Ferrer Ricard, Riera Jordi, Garcia Gasulla Dario, Penuelas Oscar, Angel Lorente Jose, Almansa Raquel, Menendez Rosario, Kiarostami Kasra, Canseco Joan, Amaya Villar Rosario, Anon Jose M, Balan Marino Ana, Barbera Carme, Barberan Jose, Blandino Ortiz Aaron, Victoria Boado Maria, Bustamante Munguira Elena, Caballero Jesus, Luisa Canton Bulnes Maria, Carbajales Perez Cristina et al. **Methodology of a Large Multicenter Observational Study of Patients with COVID-19 in Spanish Intensive Care Units**. Arch Bronconeumol 58. 2022. PMID: 35491287. IF: 6,33. DOI: 10.1016/j.arbres.2022.03.010.

Nunez Gil IJ, Cerrato E, Bollati M, Nombela Franco L, Terol B, Alfonso Rodriguez E, Camacho Freire SJ, Villablanca PA, Santos IJA, de la Torre Hernandez JM, Pascual I, Liebetrau C, Camacho B, Pavani M, Latini RA, Varbella F, Diaz VAJ, Piraino D, Mancone M, Alfonso F, Linares JA, Jimenez Mazuecos JM, Palazuelos Molinero J, Lozano I, Fernandez Ortiz A, CAAR Registry Investigators. **Stent-grafts versus drug-eluting stents in arterial aneurysms, insights from the International Coronary Artery Aneurysm Registry (CAAR)**. REC-Interv Cardiol 4 (2). 2022. DOI:10.24875/RECICE.M21000241.

Cecconi Alberto, Navarrete Gonzalo, Garcia Guimaraes Marcos, Vera Alberto, Blanco Dominguez Rafael, Sanz Garcia Ancor, Lozano Prieto Marta, Lopez Melgar Beatriz, Rivero Fernando, Martin Pilar, Sanchez Madrid Francisco, de la Fuente Hortensia, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Influence of air pollutants on circulating inflammatory cells and microRNA expression in acute myocardial infarction**. Sci Rep 12 (1). 2022. PMID: 35354890. IF: 5,00. DOI: 10.1038/s41598-022-09383-7.

Reyes Guillermo, Munoz Daniel, Monguio Emilio, Berastegui Elisabet, Camara Maria Luisa, de Antonio Nieves, Julia Ignasi, Aguirre Maria Fernanda, Fernandez Claudio, Badia Sara, Munoz Guijosa Christian. **Long- term outcomes with the On-X bileaflet mitral valve: clinical events up to 17 years in 661 patients**. Eur J Cardio-thorac Surg 62 (5). 2022. PMID: 35348660. IF: 4,53. DOI: 10.1093/ejcts/ezac157.

de Rueda C, Díez-Villanueva P, Bonanad C, Alfonso F. **Circadian Rhythms and Acute Coronary Syndrome in the Elderly**. Front Biosci Landmark 27 (3): 2022. PMID: 35345314. IF: 3,12. DOI: 10.31083/j.fbl2703082.

- Rivero Fernando, Marco Valeria, Biccire Flavio Giuseppe, Budassi Simone, Cuesta Javier, Del Val David, Bastante Teresa, de la Fuente Hortensia, Prati Francesco, Alfonso Fernando. **The double injection technique to improve visualization of severe coronary lesions with optical coherence tomography**. Catheter Cardiovasc Interventions 99 (5). 2022. PMID: 35238444. IF: 2,59. DOI: 10.1002/ccd.30138.

Alfonso F, Del Val D, Prati F. **Comprehensive clinical assessment of coronary plaque phenotype: integrating optical coherence tomography and intravascular ultrasound co-registration.** Coron Artery Dis 33 (2). 2022. PMID: 34657096. IF: 1,72. DOI: 10.1097/MCA.0000000000001104.

Del Val D, López Melgar B, Rivero F, Valdivia Mazeyra MF, Bastante T, Cuesta J, Roquero P, Alfonso F. **Anterior Mitral Leaflet Dissection and Pseudoaneurysm Late After Transcatheter Aortic Valve Replacement: Look Beyond the Obvious.** Circ Cardiovasc Imaging 15 (3). 2022. PMID: 35184573. IF: 8,59. DOI: 10.1161/CIRCIMAGING.121.013724.

Salamanca J, Diez Villanueva P, Canabal A, Reyes G, Ramasco F, Alfonso F. **Outcomes of a multidisciplinary mechanical circulatory support network in cardiogenic shock in a centre without heart transplant program: A successful interprofessional coordination model**. Rev Esp Anestesiol Reanim 69 (3). 2022. PMID: 35279416. doi: 10.1016/j.redare.2021.09.002.

Delgado Arana Jose R, Rumoroso Jose R, Regueiro Ander, Martin Moreiras Javier, Minana Gema, Mohandes Mohsen, Pan Manuel, Salinas Pablo, Caballero Borrego Juan, Fernandez Diaz Jose A, Jurado Roman Alfonso, Lacunza Javier, Vaquerizo Beatriz, Rivero Fernando, Abellan Huerta Jose, Rondan Juan, Gomez Menchero Antonio, Santos Martinez Sandra, Subinas Asier, Arevalos Victor, Diego Nieto Alejandro, Sanchis Juan, Rojas Sergio, Ojeda Soledad, Gonzalo Nieves, Lopez Perez Manuel, Goicolea Javier, Sadaba Mario, Gomez Salvador Itziar, Sabate Manel et al. **Plaque modification in calcified chronic total occlusions: the PLACCTON study**. Rev Esp Cardiol 75 (3). 2022. PMID: 34301507. IF: 4,75. DOI: 10.1016/j.rec.2021.06.011.

Mangner Norman, Del Val David, Abdel Wahab Mohamed, Crusius Lisa, Durand Eric, Ihlemann Nikolaj, Urena Marina, Pellegrini Costanza, Giannini Francesco, Gasior Tomasz, Wojakowski Wojtek, Landt Martin, Auffret Vincent, Sinning Jan Malte, Cheema Asim N, Nombela Franco Luis, Chamandi Chekrallah, Campelo Parada Francisco, Munoz Garcia Erika, Herrmann Howard C, Testa Luca, Kim Won-Keun, Castillo Juan Carlos, Alperi Alberto, Tchetche Didier, Bartorelli Antonio L, Kapadia Samir, Stortecky Stefan, Amat Santos Ignacio, Wijeysundera Harindra C et al. **Surgical Treatment of Patients With Infective Endocarditis After Transcatheter Aortic Valve Implantation**. J Am Coll Cardiol 79 (8). 2022. PMID: 35210032. IF: 27,20. DOI: 10.1016/j.jacc.2021.11.056.

- Bonanad Clara, Raposeiras Roubin Sergio, Garcia Blas Sergio, Nunez Gil Ivan, Vergara Uzcategui Carlos, Diez Villanueva Pablo, Baneras Jordi, Badia Molins Clara, Aboal Jaime, Carreras Jose, Bodi Vicente, Gabaldon Perez Ana, Mateus Porta Gemma, Parada Barcia Jose Antonio, Martinez Selles Manuel, Javier Chorro Francisco, Ariza Sole Albert. **Evaluation of the Use of Dual Antiplatelet Therapy beyond the First Year after Acute Coronary Syndrome**. J Clin Med 11 (6). 2022. PMID: 35330004. IF: 4,96. DOI: 10.3390/jcm11061680.

Rivero F, Cuesta J, Jiménez-Valero S, Bastante T, Del Val D, Alfonso F. Balloon-assisted tracking deployment of a coronary sinus reducer **through a Vieussens valve**. Cardiol J 29 (2): 2022. PMID: 35411932. IF: 3,49. DOI: 10.5603/CJ.2022.0017.

Ayesta A, Bonanad C, Díez-Villanueva P, García-Blas S, Ariza-Solé A, Martínez-Sellés M. **Ethical considerations in elderly patients with acute coronary syndrome**. Rev Cardiovasc Med 23. (2): 2022. PMID: 35229546. IF: 4,43. DOI: 10.31083/j.rcm2302055.

Roldan Rollin, Rodriguez Shalim, Barriga Fernando, Tucci Mauro, Victor Marcus, Alcala Glasiele, Villamonte Renan, Suarez Sipmann Fernando, Amato Marcelo, Brochard Laurent, Tusman Gerardo. **Sequential**

lateral positioning as a new lung recruitment maneuver: an exploratory study in early mechanically ventilated Covid-19 ARDS patients. Ann Intensive Care 12 (1). 2022. PMID: 35150355. IF: 10,32. DOI: 10.1186/s13613-022-00988-9.

Tonet Elisabetta, Ariza Sole Albert, Serenelli Matteo, Formiga Francesc, Sanchis Juan, Pavasini Rita, Diez Villanueva Pablo, Vitali Francesco, Bonanad Clara, Grazzi Giovanni, Carol Antoni, Chiaranda Giorgio, Pompei Graziella, Cardelli Laura Sofia, Caglioni Serena, Gibiino Federico, Volpato Stefano, Campo Gianluca. **The impact of sex and physical** performance **on long-term mortality in older patients with myocardial infarction**. BMC Med 20 (1). 2022. PMID: 35045843. IF: 11,15. DOI: 10.1186/s12916-021-02211-1.

Del Val D, Rivero F, Cuesta J, Bastante T, Alfonso F. **Coronary perforation after intravascular lithotripsy for severe stent underexpansion in a heavily calcified lesion**. Coron Artery Dis 31 (1): 2022. PMID: 34866131. IF: 1,72. DOI: 10.1097/MCA.0000000000001078.

Blanco Dominguez R, Martin Aguado L, De la Fuente H, Rodriguez C, Jimenez Alejandre R, Rodriguez Arabaolaza I, Garcia Guimaraes MM, Vera A ,Cuesta J,Cecconi A, Alfonso F,Sanchez Madrid F,Martinez Gonzalez J, Martin P. **CD69 expression on Treg cells prevents chronic heart damage after myocardial infarction**. Cardiovasc. Res.118. (SUPPL 1):2022. IF: 13,08. DOI: 10.1093/cvr/cvac066.149.

Biccirè FG, Debelak C, Varricchione G, Budassi S, Gatto L, Romagnoli E, Di Pietro R, Sammartini E, Marco V, Paoletti G, Burzotta F, Ozaki Y, Pastori D, Alfonso F, Arbustini E, Prati F. **Sex-specific features of optical coherence tomography detected plaque vulnerability related to clinical outcomes: insights from the CLIMA study.** Int J Cardiovasc Imaging. 2022. PMID: 36534217. IF: 16.051. doi: 10.1007/s10554-022-02775-w.

Zhou Y, Liu E, Yang Y, Alfonso FS, Ahmed B, Nakasone K, Forró C, Müller H, Cui B. **Dual-Color Optical Recording of Bioelectric Potentials by Polymer Electrochromism**.J Am Chem Soc. 28; 144 (51): 23505-23515. 2022. PMID: 36525312. IF: 16.383. doi: 10.1021/jacs.2c10198.

García-Guimarães M, Sanz-Ruiz R, Sabaté M, Velázquez-Martín M, Veiga G, Ojeda S, Avanzas P, Cortés C, Trillo-Nouche R, Pérez-Guerrero A, Gutiérrez-Barrios A, Becerra-Muñoz V, Lozano-Ruiz-Poveda F, Pérez de Prado A, Del Val D, Bastante T, **Alfonso F**. **Spontaneous coronary artery dissection and ST-segment elevation myocardial infarction: Does clinical presentation matter?**.Int J Cardiol 15; 373: 1-6. 2022. PMID: 36435331. doi: 10.1016/j.ijcard.2022.11.033.

Panei CJ, Bravi ME, Moré G, De Felice L, Unzaga JM, Salina M, **Rivero FD**, Di Lullo D, Pecoraro M, Alvarez D, Castro E, Fuentealba NA. **Serological evidence of SARS-CoV-2 infection in pets naturally exposed during the COVID-19 outbreak in Argentina**.Vet Immunol Immunopathol. 254: 110519. 2022. PMID: 36434944. IF: 1.943. doi:

10.1016/j.vetimm.2022.110519.

Muñiz ÁM, Cecconi A, Avial MCM, Rico PF, Muñiz SH, Santin EM, Jimenez- Borreguero LJ, Alfonso F**. Calretinin stain for the accurate diagnosis of atypical Cardiac Myxoma.** Int J Cardiovasc Imaging. 39(2):461-462. 2022. PMID: 36394681. IF: 16.051. doi: 10.1007/s10554-022-02725-6.

Fumero A, Marrero RJ, Olivares T, Rivero F, Alvarez-Pérez Y, Pitti C, Peñate

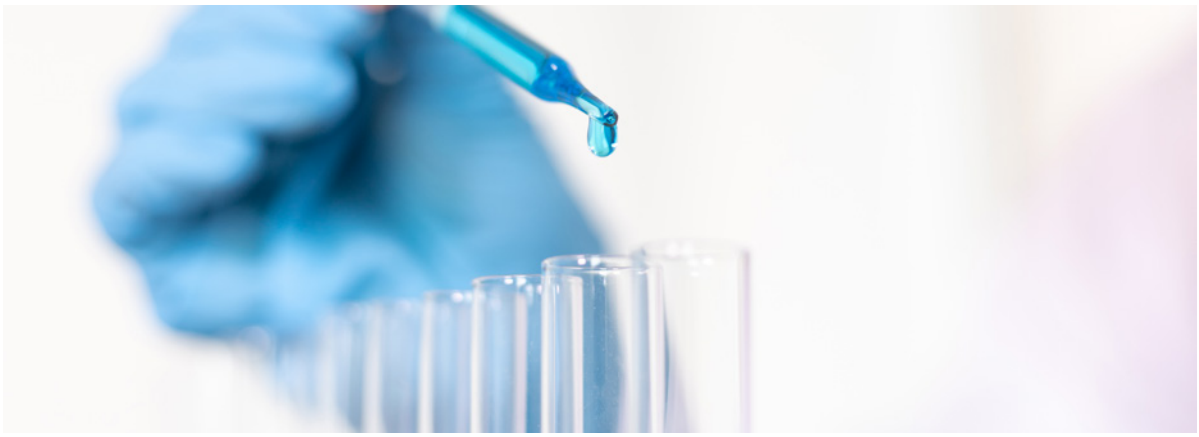
W. **Neuronal Activity during Exposure to Specific Phobia through fMRI: Comparing Therapeutic Components of Cognitive Behavioral Therapy.** Life (Basel) 27; 12(8): 1132. 2022. PMID: 36013311.IF: 3.253. doi: 10.3390/life12081132.

Saldanha PA, Bolanle IO, Palmer TM, Nikitenko LL, Rivero F**. Complex Transcriptional Profiles of the *PPP1R12A* Gene in Cells of the Circulatory System as Revealed by In Silico Analysis and Reverse Transcription PCR.** Cells 11 (15): 2315. 2022. PMID: 35954160. IF: 7.666. doi: 10.3390/cells11152315.

Moreno-Fernandez J, Chico A, Martínez-Brocca MA, Beato-Víbora PI, Vidal M, Piedra M, Quirós C, Muñoz-Rodríguez JR. **Continuous Subcutaneous Insulin Infusion in Type 1 Diabetes Mellitus Patients: Results from the Spanish National Registry.** Diabetes Technol Ther 24 (12): 898-906. 2022. PMID: 35947087. IF: 7.337. doi: 10.1089/dia.2022.0207.

Chan N, Premawardhana D, Al-Hussaini A, Wood A, Bountziouka V, Kotecha D, Swahn E, Palmefors H, Pagonis C, Lawesson SS, Kądziela J, Garcia- Guimarães M, Alfonso F, Escaned J, Macaya F, Santás M, Cerrato E, Maas AHEM, Hlinomaz O, Bogale N, Cortese B, Cheng M, Bolger A, Hussain ST, Samani NJ, Knight M, Cauldwell M, Adlam D. **Pregnancy and Spontaneous Coronary Artery Dissection: Lessons From Survivors and Nonsurvivors**. Circulation 146 (1): 69-72. 2022. PMID: 35656808. IF: 39.92. doi: 10.1161/CIRCULATIONAHA.122.059635.

Alfonso F, Cuesta J, Ojeda S, Camacho-Freire S, García Del Blanco B, Vaquerizo B, Zueco J, Trillo R, Mauri J, Velázquez M, Córdoba-Soriano JG, Serra A, Navarro F, Pan M, Díaz J, Otaegui I, Salvatella N, De la TorreHernandez JM, Val DD, Bastante T, Rivero F, Under the auspices of the Association of Interventional Cardiology of the Spanish Society of Cardiology.



Procedural Results and One-Year Clinical Outcomes of Treatment of Bioresorbable Vascular Scaffolds Restenosis (from the RIBS VII Prospective Study). Am J Cardiol 162: 31-40. 2022. PMID: 34903344. IF: 3.13. doi: 10.1016/j.amjcard.2021.09.027.

Alfonso F, Rivero F, Cortese B. **Excimer laser prior to drug-coated balloon treatment of in-stent restenosis**. Int J Cardiol 348: 47-49. 2022. PMID: 34864077. IF: 4.03. doi: 10.1016/j.ijcard.2021.11.082

Jimenez-Quevedo P, Bernardo E, Del Trigo M, Otsuki S, Nombela-Franco L, Brugaletta S, Ortega-Pozi A, Herrera R, Salinas P, Nuñez-Gil I, Mejía- Rentería H, Alfonso F, Fernandez-Perez C, Fernandez-Ortiz A, Macaya C, Escaned J, Sabate M, Gonzalo N. **Vascular Injury After Stenting - Insights of Systemic Mechanisms of Vascular Repair**. Circ J 86 (6): 966-974. 2022. PMID: 34853277. IF: 3.35. doi: 10.1253/circj.CJ-21-0649. Epub 2021 Dec 2. PMID: 34853277.

Prati F, Romagnoli E, Biccirè FG, Burzotta F, La Manna A, Budassi S, Ramazzotti V, Albertucci M, Fabbiocchi F, Sticchi A, Trani C, Calligaris G, Fineschi M, Versaci F, Tamburino C, Ozaki Y, Alfonso F, Mintz GS. **Clinical outcomes of suboptimal stent deployment as assessed by optical coherence tomography: long-term results of the CLI-OPCI registry**. EuroIntervention. 2022 18 (2): 150-157. 2022. PMID: 34825652. IF: 7.72. doi: 10.4244/EIJ-D-21-00627.

Bocchino PP, Franchin L, Angelini F, D'Ascenzo F, De Ferrari GM, Alfonso F. **Outcomes during the first year following spontaneous coronary artery dissection: A systematic timeframe pooled analysis**. Catheter Cardiovasc Interv 99 (2): 472-479. 2022. PMID: 34773431. IF: 2.58. doi: 10.1002/ccd.30016.

Vera A, Cecconi A, Ximénez-Carrillo Á, Ramos C, Martínez-Vives P, Lopez- Melgar B, Sanz-García A, Ortega G, Aguirre C, Vivancos J, Jiménez- Borreguero LJ, Alfonso F, Decryptoring Study Investigators. **A Comprehensive Model to Predict Atrial Fibrillation in Cryptogenic Stroke: The Decryptoring Score**. J Stroke Cerebrovasc Dis 31 (1): 106161. 2022. PMID: 34689053. IF: 2.67. doi: 10.1016/j.jstrokecerebrovasdis.2021.106161.

Bastante T, Rivero F, Cuesta J, Del Val D, Roquero P, Alfonso F. **Treatment of spontaneous coronary artery dissection with fenestration: clinical and angiographic follow-up**. Rev Esp Cardiol (Engl Ed) 75 (2): 177-179. 2022. PMID: 34635468. IF: 1.42. doi: 10.1016/j.rec.2021.07.018.

Alfonso F, de la Torre Hernández JM, Ibáñez B, Sabaté M, Pan M, Gulati R, Saw J, Angiolillo DJ, Adlam D, Sánchez-Madrid F. **Rationale and design of the BA-SCAD (Beta-blockers and Antiplatelet agents in patients with Spontaneous Coronary Artery Dissection) randomized clinical trial**. Rev Esp Cardiol (Engl Ed) 75(6):515-522. 2022. PMID: 34561195. IF: 1.42. doi: 10.1016/j.rec.2021.08.003.

Pascual I, Almendárez M, Avanzas P, Álvarez R, Arboine LA, Del Valle R, Hernández-Vaquero D, Alfonso F, Morís C. **Cusp-overlapping TAVI technique with a self-expanding device optimizes implantation depth and reduces permanent pacemaker requirement.** Rev Esp Cardiol (Engl Ed) 75(5):412-420. 2022. PMID: 34226165. IF: 1.42. doi: 10.1016/j.rec.2021.05.009.

Alfonso F, García-Guimaraes M, Alvarado T, Sanz-Ruiz R, Roura G, Amat- Santos IJ, Abdul-Jawad Altisent O, Tizón-Marcos H, Flores-Ríos X, Masotti M, Pérez-de Prado A, Ferre GF, Ruiz-Poveda FL, Valero E, Portero-Portaz JJ, Diez-Villanueva P, Salamanca J, Bastante T, Rivero F. **Clinical implications of arterial hypertension in patients with spontaneous coronary artery dissection**. Coron Artery Dis 33 (2): 75-80. 2022. PMID: 33878074. IF: 1.71, doi: 10.1097/MCA.0000000000001043.

GROUP 48

Head of laboratory: Jiménez Borreguero, Luis Jesús

Area 3 Advanced therapies and individualized medicine

Line 3.6 New diagnostic and therapeutic advances in cardiovascular diseases

RESEARCH INTEREST

Our research work is developed in cardiovascular diagnostics technologies for clinical research, in coordination with physicists and basic scientists at La Princesa Hospital.

We are carrying out a research line in collaboration with physicist scientists at La Princesa Hospital focusing in machine learning of big data for the prediction of heart disease, based on an in-deep analysis of more than 250.000 ECGs raw data.

Another line of clinical research focuses on the characterization of the heart phenotype in patients with hypertrophic cardiomyopathy and its association with prognosis, by identifying new targets in cardiovascular imaging technology.

GROUP MEMBERS

- Luis Jesús Jiménez Borreguero
- Guillermo José Ortega Rabbione
- Miriam Pérez Romero
- Ancor Sanz García
- Beatriz López Melgar
- Alberto Cecconi Duca
- María José Olivera Serrano

MAJOR GRANTS

Ortega Rabbione, Guillermo / Jiménez Borreguero, Jesús. 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. PI20/00792. ISCIII. 2021- 2023.

Ortega Rabbione, Guillermo José. Proyecto de I+D "Modelo numérico de predicción de propagación de la infección por COVID-19" - Proyecto healthstart Plus fi nanciado con fondos REACT-UE. Fundación para el Conocimiento madrimasd. 2022.

PUBLICATIONS

Martin Rodriguez Francisco, Sanz Garcia Ancor, Ortega Guillermo J, Delgado Benito Juan F, Garcia Villena Eduardo, Mazas Perez Oleaga Cristina, Lopez Izquierdo Raul, Castro Villamor Miguel A. **One-on-one comparison between qCSI and NEWS scores for mortality risk assessment in patients with COVID-19**. Ann Med 54 (1). 2022. PMID: 35193439. IF: 5,35. DOI: 10.1080/07853890.2022.2042590.

Vera A, Cecconi A, Ximénez Carrillo Á, Ramos C, Martínez Vives P, Lopez Melgar B, Sanz García A, Ortega G, Aguirre C, Vivancos J, Jiménez Borreguero LJ, Alfonso F, DECRYTORING Study Investigators. **Advanced Echocardiography With Left Atrial Strain and Indexed Left Atrial Three- Dimensional Volume for Predicting Underlying Atrial Fibrillation After Cryptogenic Stroke.** Am J Cardiol 185. 2022. PMID: 36307348. IF: 3,13. DOI: 10.1016/j.amjcard.2022.09.004.

Muñoz Guerra MF, Rodríguez Campo FJ, Escorial Hernández V, Sanz García A, Brabyn PJ, Fernández Domínguez M. **Temporomandibular joint arthroscopy in advanced stages of internal derangement: a retrospective cohort study on the influence of age.** Int J Oral Maxillofac Surg 51 (12). 2022. PMID: 35654642. IF: 2,99. DOI: 10.1016/j.ijom.2021.12.009.

Bañeras J, Iglesies Grau J, Téllez Plaza M, Arrarte V, Báez Ferrer N, Benito B, Campuzano Ruiz R, Cecconi A, Domínguez Rodríguez A, Rodríguez Sinovas A, Ujueta F, Vozzi C, Lamas GA, Navas Acién A.

Environment and cardiovascular health: causes, consequences and opportunities in prevention and treatment. Rev Esp Cardiol 75. (12). 2022. PMID: 35931285. IF: 6,98. DOI: 10.1016/j.rec.2022.05.030.

Jiménez Méndez C, Díez Villanueva P, Bonanad C, Ortiz Cortés C, Barge Caballero E, Goirigolzarri J, Esteban Fernández A, Pérez Rivera Á, Cobo M, López J, Sanz García A, Guerrero C, Pardo HG, Robles C, Iglesias D, Pinilla JMG, Rodríguez LL, Formiga F, Martín Sánchez FJ, Vidán MT, Ariza A, Martínez Sellés M, Alfonso F, en representación de los investigadores del registro FRAGIC. **Frailty and prognosis of older patients with chronic heart failure.** Rev Esp Cardiol 75. (12). 2022. PMID: 35718066. IF: 6,98. DOI: 10.1016/j.rec.2022.04.016.

Bañeras J, Iglesies Grau J, Téllez Plaza M, Arrarte V, Báez Ferrer N, Benito B, Campuzano Ruiz R, Cecconi A, Domínguez Rodríguez A, Rodríguez Sinovas A, Ujueta F, Vozzi C, Lamas GA, Navas Acién A. **Medio ambiente y salud cardiovascular: causas, consecuencias y oportunidades en prevención y tratamiento.** Rev Esp Cardiol 75. (12). 2022. PMID: 36570815. IF: 6,98. DOI: 10.1016/j.recesp.2022.05.022.

Vera A, Rojas González A, López Melgar B, Cecconi A, Olivera MJ, Jiménez Borreguero LJ, Alfonso F. **One for All and All for One.** Can J Cardiol 38 (11). 2022. PMID: 35933065. IF: 6,61. DOI: 10.1016/j.cjca.2022.07.015.

Fernández Gallego N, Castillo González R, Méndez Barbero N, López Sanz C, Obeso D, Villaseñor A, Escribese MM, López Melgar B, Salamanca J, Benedicto Buendía A, Jiménez Borreguero LJ, Ibañez B, Sastre J, Belver MT, Vega F, Blanco C, Barber D, Sánchez Madrid F, de la Fuente H, Martín P, Esteban V, Jiménez Saiz R. **The impact of type 2 immunity and allergic diseases in atherosclerosis.** Allergy 77 (11). 2022. PMID: 35781885. IF: 14,71. DOI: 10.1111/all.15426.

Blanco Domínguez R, de la Fuente H, Rodríguez C, Martín Aguado L, Sánchez Díaz R, Jiménez Alejandre R, Rodríguez Arabaolaza I, Curtabbi A, García Guimaraes MM, Vera A, Rivero F, Cuesta J, Jiménez Borreguero LJ, Cecconi A, Duran Cambra A, Taurón M, Alonso J, Bueno H, Villalba Orero M, Enríquez JA, Robson SC, Alfonso F, Sánchez Madrid F, Martínez González J, Martín P. **CD69 expression on regulatory T cells protects from immune damage after myocardial infarction.** J Clin Invest 132 (21). 2022. PMID: 36066993. IF: 19,46. DOI: 10.1172/JCI152418.

Gonzalez Martinez A, Pagán J, Sanz García A, García Azorín D, Rodríguez Vico JS, Jaimes A, García AG, de Terán JD, González García N, Quintas S, Belascoaín R, Casas Limón J, Latorre G, Calle de Miguel C, Sierra Á, Guerrero Peral ÁL, Trevino Peinado C, Gago Veiga AB. **Machine-learning-based approach for predicting response to anti-calcitonin gene-related peptide (CGRP) receptor or ligand antibody treatment in patients with migraine: A multicenter Spanish study.** Eur J Neurol 29 (10). 2022. PMID: 35726393. IF: 6,29. DOI: 10.1111/ene.15458.

Castro Portillo E, López Izquierdo R, Sanz García A, Ortega GJ, Delgado Benito JF, Castro Villamor MA, Sánchez Soberón I, Del Pozo Vegas C, Martín Rodríguez F. **Role of prehospital point-of-care N-terminal pro-brain natriuretic peptide in acute life-threatening cardiovascular disease.** Int J Cardiol 364. 2022. PMID: 35716940. IF: 4,04. DOI: 10.1016/j.ijcard.2022.06.025.

Diez Villanueva P, Jimenez Mendez C, Bonanad C, Ortiz Cortes C, Barge Caballero E, Goirigolzarri J, Esteban Fernandez A, Perez Rivera A, Cobo M, Sanz Garcia A, Formiga F, Ariza Sole A, Martinez Selles M, Alfonso F. **Sex differences in the impact of frailty in elderly outpatients with heart failure**. Front Cardiovasc Med 9. 2022. PMID: 36172583. IF: 5,85. DOI: 10.3389/fcvm.2022.1000700.

Reolid A, Sahuquillo Torralba A, Sanz García A, Botella Estrada R, Muñoz Aceituno E, Llamas Velasco M, García Martínez J, Daudén E, Abad Santos F, Ovejero Benito MC. **CNVs Associated with Different Clinical Phenotypes of Psoriasis and Anti-TNF-Induced Palmoplantar Pustulosis.** J Pers Med 12 (9). 2022. PMID: 36143237. IF: 3,51. DOI: 10.3390/jpm12091452.

Monteagudo Vela M, Alayza AR, Santin EM, Cecconi A, Copa GR. **Pulmonary artery sarcoma with extensive leiomyosarcoma differentiation and heterologous osteosarcomatous elements**. Cardiovasc Pathol 60. 2022. PMID: 35597407. IF: 3,98. DOI: 10.1016/j.carpath.2022.107436.

Martínez Vives P, Cecconi A, Vera A, Fernández C, López Melgar B, Sanz García A, Rojas González A, Nogales Romo MT, Hernandez Muñiz S, Olivera MJ, Caballero P, Jiménez Borreguero LJ, Alfonso F. **Usefulness of Tissue Tracking by Cardiac Magnetic Resonance to Predict Events in Patients With Hypertrophic Cardiomyopathy.** Am J Cardiol 174. 2022. PMID: 35525624. IF: 3,13. DOI: 10.1016/j.amjcard.2022.03.024.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Vera Alberto, Cecconi Alberto, Martinez Vives Pablo, Jose Olivera Maria, Hernandez Susana, Lopez Melgar

Beatriz, Rojas Gonzalez Antonio, Diez Villanueva Pablo, Salamanca Jorge, Tejelo Julio, Caballero Paloma, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Electrocardiogram and CMR to differentiate tachycardia-induced cardiomyopathy from dilated cardiomyopathy in patients admitted for heart failure**. HEART VESSELS 37 (11). 2022. PMID: 35657427. IF: 1,81. DOI: 10.1007/s00380-022-02102-2.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Lopez Melgar B, Mass V, Nogales P, Sanchez Gonzalez J, Entrekin R, Collet Billon A, Rossello X, Fernandez Friera L, Fernandez Ortiz A, Sanz J, Bentzon JF, Bueno H, Ibanez B, Fuster V. **New 3-Dimensional Volumetric Ultrasound Method for Accurate Quantification of Atherosclerotic Plaque Volume**. JACC Cardiovasc Imaging 15 (6). 2022. PMID: 35680220. IF: 16,05. DOI: 10.1016/j.jcmg.2022.01.005.

Martin Rodriguez Francisco, Lopez Izquierdo Raul, Sanz Garcia Ancor, del Pozo Vegas Carlos, Castro Villamor Miguel Angel, Mayo Iscar Agustin, Martin Conty Jose L, Jose Ortega Guillermo. **Novel Prehospital Phenotypes and Outcomes in Adult-Patients with Acute Disease**. J Med Syst 46 (7). 2022. PMID: 35596887. IF: 4,92. DOI: 10.1007/s10916-022-01825-z.

Garcia Guimaraes Marcos, Masotti Monica, Sanz Ruiz Ricardo, Macaya Fernando, Roura Gerard, Nogales Juan Manuel, Tizon Marcos Helena, Velazquez Martin Maite, Veiga Gabriela, Flores Rios Xacobe, Altisent Omar Abdul-Jawad, Jimenez Kockar Marcelo, Camacho Freire Santiago, Moreu Jose, Ojeda Soledad, Santos Martinez Sandra, Sanz Garcia Ancor, Del Val David, Bastante Teresa, Alfonso Fernando, Spanish Registry SCAD Investigator. **Clinical outcomes in spontaneous coronary artery dissection**.Heart 108 (19). 2022. PMID: 35410894. IF: 7,37. DOI: 10.1136/heartjnl-2022-320830.

Sanz Garcia Ancor, Perez Romero Miriam, Ortega Guillermo J. **Spectral and network characterization of focal seizure types and phases**. Comput. Methods Programs Biomed 217. 2022. PMID: 35220198. IF: 7,03. DOI: 10.1016/j.cmpb.2022.106704.

Cecconi Alberto, Navarrete Gonzalo, Garcia Guimaraes Marcos, Vera Alberto, Blanco Dominguez Rafael, Sanz Garcia Ancor, Lozano Prieto Marta, Lopez Melgar Beatriz, Rivero Fernando, Martin Pilar, Sanchez Madrid Francisco, de la Fuente Hortensia, Jesus Jimenez Borreguero Luis, Alfonso Fernando. **Influence of air pollutants on circulating inflammatory cells and microRNA expression in acute myocardial infarction**. Sci Rep 12 (1). 2022. PMID: 35354890. IF: 5,00. DOI: 10.1038/s41598-022-09383-7.

Martin Rodriguez Francisco, Melero Guijarro Laura, Ortega Guillermo J, Sanz Garcia Ancor, de la Torre de Dios Teresa, Manzanares Jesus Alvarez, Martin Conty Jose L, Castro Villamor Miguel A, Delgado Benito Juan F, Lopez Izquierdo Raul. **Combination of Prehospital NT-proBNP with qSOFA and NEWS to Predict Sepsis and Sepsis-Related Mortality**. Dis Markers. 2022. PMID: 35242244. IF: 3,46. DOI: 10.1155/2022/5351137.

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

Cruz González I, Estévez Loureiro R, Barreiro Pérez M, Aguilera Saborido A, Olmos Blanco C, Rincón LM, Gómez Polo JC, Arzamendi D, Borreguero L, Vilacosta I, Gámez JM, Martínez Monzonis A. **Mitral and tricuspid valve disease: diagnosis and management. Consensus document of the Section on Valvular Heart Disease and the Cardiovascular Imaging, Clinical Cardiology, and Interventional Cardiology Associations of the Spanish Society of Cardiology.** Rev Esp Cardiol 75 (11). 2022. PMID: 35926720. IF: 6,98. DOI: 10.1016/j.rec.2022.05.031.

Barreiro Pérez M, Cabeza B, Calvo D, Reyes Juárez JL, Datino T, Vañó Galván E, Maceira González AM, Delgado Sánchez Gracián C, Prat González S, Perea RJ, Bastarrika G, Sánchez M, Jiménez Borreguero LJ, Fernández Golfín Lobán C, Rodríguez Palomares JF, Tolosana JM, Hidalgo Pérez JA, Pérez David E, Bertomeu González V, Cuéllar H, Revisores expertos:. **Magnetic resonance in patients with cardiovascular devices. SEC-GT CRMTC/SEC- Heart Rhythm Association/SERAM/ SEICAT consensus document**. Rev. Esp. Cardiol. IF: 7,05. DOI: 10.1016/j.recesp.2022.09.010.

GROUP 57

Head of laboratory: Suárez Fernández, Carmen

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.6 New diagnostic and therapeutic advances in cardiovascular diseases

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 venoues 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).

GROUP MEMBERS

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- Mercedes de la Torre Espi
- Jara Gaitero Tristán
- Francesco Giuseppe Ecclesia
- David Andina Martínez
- María Pilar Storch de Gracia Calvo
- José Antonio Alonso Cadenas
- Beatriz Sánchez Moreno
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- María del Pilar González Molina
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- Fernando Moldenhauer Díaz
- Nuria Ruiz-Giménez Arrieta
- Pedro Pablo Casado Escribano

MAJOR GRANTS

Real de Asua Cruzat, Diego / Suarez Fernández, Carmen. Estudio de los mecanismos protectores frente al desarrollo de hipertensión arterial en adultos con síndrome de Down. PI19/00634. ISCIII. 2020-2022.

Real de Asua Cruzat, Diego. ICOD: Improving Cognition in Down syndrome. ICOD: 899986. Comisión Europea. 2021-2025.

Real de Asúa Cruzat, Diego. Analysis of the immune response before and after vaccination against SARS-CoV-2 in adults with Down syndrome. Fundación Jerome Lejeune. 2021- 2023.

Sánchez Moreno, Beatriz. The utility of brain computed tomography for the diagnosis and tracking of Alzheimer's disease in adults with down syndrome. Fundación Jerome Lejeune. 2021-2023

PUBLICATIONS

Rabes L, Adán Lirola L, González Molina MDP, Galván Román JM, Moldenhauer F, Roy Vallejo E, Real de Asúa D. **Evaluation of congenital and acquired heart diseases in a Spanish cohort of adults with Down syndrome.** Sci Rep 12 (1): 22461-22461. 2022. PMID: 36577781. IF: 5,00. DOI: 10.1038/s41598-022-26918-0.

Antequera A, Cuadrado Conde MA, Roy Vallejo E, Montoya Martínez M, León García M, Madrid Pascual O, Calderón Larrañaga S, Research for gender equity collaboration. **Lack of sex-related analysis and reporting in Cochrane Reviews: a cross-sectional study.** Syst Rev 11 (1): 281-281. 2022. PMID: 36572932. IF: 3,14. DOI: 10.1186/s13643-021-01867-3.

Mostaza JM, Suárez Fernández C, Cosín Sales J, Gómez Huelgas R, Brotons C, Araujo FP, Borrayo G, Ruiz E, VULCANO investigators. **Safety and efficacy of a cardiovascular polypill in people at high and very high risk without a previous cardiovascular event: the international VULCANO randomised clinical trial.** BMC Cardiovasc Disord 22 (1): 560-560. 2022. PMID: 36550424. IF: 2,17. DOI: 10.1186/s12872-022-03013-w.

Bonanad C, Formiga F, Anguita M, Petidier R, Gullón A. **Oral Anticoagulant Use and Appropriateness in Elderly Patients with Atrial Fibrillation in Complex Clinical Conditions: ACONVENIENCE Study.** J Clin Med 11 (24): 7423. 2022. PMID: 36556039. IF: 4,96. DOI: 10.3390/jcm11247423.

Domingo LC, Vallejo ER, Cruz NDZ, Llano MC, Perez Urria EA, Barrios A, Santos JH, Ortiz J, Garcia SCR, Ramirez AM, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Garcia AS, Villa A, Azofra AS, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martinez AT, Arevalo C, Roman JMG, Garcia Vicuna R et al. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol 94 (11): 5260-5270. 2022. PMID: 35811284. IF: 20,69. DOI: 10.1002/jmv.27989.

Moraleda C, Domínguez Rodríguez S, Mesa JM, García Sánchez P, de la Serna M, Alonso Cadenas JA, Bermejo A, Sabrido G, Martínez Campos L, González Posada AF, Illán Ramos M, Cobos Carrascosa E, Ballesteros Á, Galán JC, Llorente F, Aguilera Alonso D, Jiménez AB, Catalán P, Dahdouh E, Navarro I, Fernández Garoz B, Mendoza P, Pérez Jorge C, Cabezas Fernández T, Blázquez Gamero D, Rivas G, Gonzalez Donapetry P, Sáez E, Fernández Pinero J, Lucas Fernández J et al. **Oral saliva swab reverse transcription PCR for Covid-19 in the paediatric population.** Arch Dis Child 107 (11): 1051-1058. 2022. PMID: 35688603. IF: 4,92. DOI: 10.1136/archdischild-2021-323712.

Triguero Martinez A, Roy Vallejo E, Tomero EG, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Lamana A, Gonzalez Alvaro I. **Galectin-1: A Potential Biomarker Differentiating between Early Rheumatoid Arthritis and Spondyloarthritis**. J Clin Med 11 (21): 6313. 2022. PMID: 36362537. IF: 4,96. DOI: 10.3390/jcm11216313.

Fernández A, Ramírez Toraño F, Bruña R, Zuluaga P, Esteba Castillo S, Abásolo D, Moldenhauer F, Shumbayawonda E, Maestú F, García Alba J. **Brain signal complexity in adults with Down syndrome: Potential application in the detection of mild cognitive impairment.** Front Aging Neurosci 14. 988540-988540. 2022. PMID: 36337705. IF: 5,70. DOI: 10.3389/fnagi.2022.988540.

Villén Villegas T, Campo Linares R, Alonso Viladot JR, Martínez Mas R, Luque Hernández MJ, Ruiz Durán M, Oviedo García A, Álvarez Gregori JA, Aguilar Mulet M, Campos Caubet L, Cárdenas Bravo L, Chaparro Pardo D, Chehayeb Morán J, Esteban Velasco JV, Ferreiro Gómez M, García Martín D, García Suárez I, Martínez Hernández A, Hernández Galán Á, Millán Soria J, Martínez López JF, Rodríguez García JF, Ruano Peña I, Salvador Suárez FJ, Simó Meléndez S, Zafra Sánchez JJ, Nogué Bou R. **Description of basic competencies in clinical ultrasound imaging for emergency departments.** Emerg 34 (5): 377-387. 2022. PMID: 36217933. IF: 5,35.

Santoro JD, Patel L, Kammeyer R, Filipink RA, Gombolay GY, Cardinale KM, **Real de Asua D**, Zaman S, Santoro SL, Marzouk SM, Khoshnood M, Vogel BN, Tanna R, Pagarkar D, Dhanani S, Ortega MDC, Partridge R, Stanley MA, Sanders JS, Christy A, Sannar EM, Brown R, McCormick AA, Van H, Franklin C, Worley G, Quinn EA, Capone GT, Chicoine B, Skotko BG, et al. **Assessment and Diagnosis of Down Syndrome Regression Disorder: International Expert Consensus.** Front Neurol 13. 940175-940175. 2022. PMID: 35911905. IF: 4,09. DOI: 10.3389/fneur.2022.940175.

Zurita Cruz Nelly Daniela, Martin Ramirez Alexandra, Rodriguez Serrano Diego Anibal, Gonzalez Alvaro Isidoro, Roy Vallejo Emilia, de la Camara Rafael, Garcia Rodrigo Leticia Fontan. **Usefulness of real-time RT-PCR to understand the kinetics of SARS-CoV-2 in blood: A prospective study**. J Clin Virol 152. 105166-105166. 2022. PMID: 35594784. IF: 14,48. DOI: 10.1016/j.jcv.2022.105166.

Triguero Martinez A, Roy Vallejo E, Montes N, De La Fuente H, Ortiz AM, Castaneda S, Gonzalez Alvaro I, Lamana A. **Genetic LGALS1 Variants Are Associated with Heterogeneity in Galectin-1 Serum**

Levels in Patients with Early Arthritis. Int J Mol Sci 23 (13): 7181. 2022. PMID: 35806182. IF: 6,21. DOI: 10.3390/ijms23137181.

Martínez Vives P, Cecconi A, Vera A, Fernández C, López Melgar B, Sanz García A, Rojas González A, Nogales Romo MT, Hernandez Muñiz S, Olivera MJ, Caballero P, Jiménez Borreguero LJ, Alfonso F. **Usefulness of Tissue Tracking by Cardiac Magnetic Resonance to Predict Events in Patients With Hypertrophic Cardiomyopathy.** Am J Cardiol 174. 126-135. 2022. PMID: 35525624. IF: 3,13. DOI: 10.1016/j.amjcard.2022.03.024.

Barrios V, Escobar C, Suarez C, Garcia Moll X, Lozano F. **Clinical Profile and Management of Patient Patients with Ischemic Heart Disease and/or Peripheral Artery Disease in Clinical Practice: The APALUSA Study.** J Clin Med 11 (12): 3554. 2022. PMID: 35743622. IF: 4,96. DOI: 10.3390/jcm11123554.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 855639-855639. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Vera A, **Cecconi A**, Martinez P, **Jose M**, Hernandez S, **Lopez B**, Rojas A, **Diez P**, Salamanca J, Tejelo J, **Caballero P**, **Jesus Jimenez L**, **Alfonso F**. **Electrocardiogram and CMR to differentiate tachycardia-induced cardiomyopathy from dilated cardiomyopathy in patients admitted for heart failure**. HEART VESSELS 37 (11): 1850-1858. 2022. PMID: 35657427. IF: 1,81. DOI: 10.1007/s00380-022-02102-2.

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1): 9208-9208. 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6.

Fernandez Simon Amparo, Martin Alfonso, Suero Coral, Sanchez Juan, Varona Mercedes, Sanchez Susana, Cancio Manuel, Carbajosa Jose, Tamargo Juan, del Arco Carmen, Javier Medrano Francisco, Coll Vinent Blanca, Investigadores Estudio HERMES-A. **Emergency department prescription of sinus rhythm maintenance therapy for patients treated for atrial fibrillation: a secondary analysis of the HERMES-AF study**. Emerg 34 (2): 111-118. 2022. PMID: 35275461. IF: 5,35.

Huls Anke, Feany Patrick T, Zisman Sophia Isabella, Costa Alberto C S, Dierssen Mara, Balogh Robert, Bargagna Stefania, Baumer Nicole T, Brandao Ana Claudia, Carfi Angelo, Chicoine Brian Allen, Ghosh Sujay, Lakhanpaul Monica, Levin Johannes, Lunsky Yona, Manso Coral, Okun Eitan, Real De Asua Diego, Rebillat Anne-Sophie, Rohrer Tilman R, Sgandurra Giuseppina, Valentini Diletta, Sherman Stephanie L, Strydom Andre, Trisomy Res Soc COVID 19 Initia 21. **COVID-19 Vaccination of Individuals with Down Syndrome-Data from the Trisomy 21 Research Society Survey on Safety, Efficacy, and Factors Associated with the Decision to Be Vaccinated**. Vaccines 10 (4): 530. 2022. PMID: 35455279. IF: 4,96. DOI: 10.3390/vaccines10040530.

Castaneda Santos, Prieto Pena Diana, Vicente Rabaneda Esther F, Triguero Martinez Ana, Roy Vallejo Emilia, Atienza Mateo Belen, Blanco Ricardo, Gonzalez Gay Miguel A. **Advances in the Treatment of Giant Cell Arteritis**.

J. Clin. Med. 11. (6):1588. 2022. PMID: 35329914. IF: 4,96. DOI: 10.3390/jcm11061588.

Bikdeli B, Moustafa F, Nieto JA, Lee AI, Ruíz Giménez N, Lorenzo A, Schellong S, Soler S, Ortíz S, Morales MDV, Bosevski M, Gavín O, Lip GYH, Monreal M, RIETE Investigators. **Clinical characteristics, time course, and outcomes of major bleeding according to bleeding site in patients with venous thromboembolism.** Thromb Res 211. 10-18. 2022. PMID: 35051831. IF: 10,41. DOI: 10.1016/j.thromres.2022.01.007.

Barrio Cortes J, Cuevas MM, Reguillo AC, Bandeira de Oliveira M, Martín MM, Fernández CS. **Use of hospital care services by chronic patients according to their characteristics and risk levels by adjusted morbidity groups.** PLoS One 17 (2): 0262666. 2022. PMID: 35113882. IF: 3,75. DOI: 10.1371/journal.pone.0262666.

de Asua Diego Real, Dague Karmele Olaciregui, Arriaga Andres, Herreros Benjamin. **Animating**

Clinical Ethics: A Structured Method to Teach Ethical Analysis Through Movies. HEC Forum. 2022. PMID: 35092518. IF: 1,20. DOI: 10.1007/s10730-022-09470-2.

Collazos Julio, Domingo Pere, Fernandez Araujo Nerio, Asensi Diaz Elia, Vilchez Rueda Helem, Lalueza Antonio, Roy Vallejo Emilia, Blanes Rosa, Raya Cruz Manuel, Sanz Canovas Jaime, Artero Arturo, Ramos Rincon Jose- Manuel, Duenas Gutierrez Carlos, Luis Lamas Ferreiro Jose, Asensi Victor, Valproic Acid COVID 19 Study Grp. **Exposure to valproic acid is associated with less pulmonary infiltrates and improvements in diverse clinical outcomes and laboratory parameters in patients hospitalized with COVID-19**. PLoS One 17 (1): 0262777. 2022. PMID: 35085321. IF: 3,75. DOI: 10.1371/journal.pone.0262777.

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 815651-815651. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

Monserrat Villatoro Jaime, Mejia Abril Gina, Diaz Garcia Lucia, Zubiaur Pablo, Jimenez Gonzalez Maria, Jimenez Guillermo Fernandez, Cancio Ines, Arribas Jose Ramon, Suarez Fernandez Carmen, Mingorance Jesus, Rodriguez Julio Garcia, Villagrasa Ferrer Jose Ramon, Carcas Antonio J J, Frias Jesus, Abad Santos Francisco, Borobia Alberto M M, Ramirez Elena, COVID HULP Working Grp, Hosp Univ de la Princesa. **A Case-Control of Patients with COVID-19 to Explore the Association of Previous Hospitalisation Use of Medication on the Mortality of COVID-19 Disease: A Propensity Score Matching Analysis**. Pharmaceuticals 15 (1): 78. 2022. PMID: 35056135. IF: 5,22. DOI: 10.3390/ph15010078.

Ruiz Hornillos J, Albert M, Real de Asua D, Herrera Abián M, de Miguel Beriain Í, Guillén Navarro E. **Priorización de recursos sanitarios en contextos de escasez. Informe SESPAS 2022.** Gaceta Sanit 36 Suppl 1. 51-55. 2022. PMID: 35781149. IF: 2,48. DOI: 10.1016/j.gaceta.2022.04.003.

Bellenguez C, Küçükali F, Jansen IE, Kleineidam L, Moreno Grau S, Amin N, Naj AC, Campos Martin R, Grenier Boley B, Andrade V, Holmans PA, Boland A, Damotte V, van der Lee SJ, Costa MR, Kuulasmaa T, Yang Q, de Rojas I, Bis JC, Yaqub A, Prokic I, Chapuis J, Ahmad S, Giedraitis V, Aarsland D, Garcia Gonzalez P, Abdelnour C, Alarcón Martín E, Alcolea D, Alegret M et al. **New insights into the genetic etiology of Alzheimer's disease and related dementias**. Nat Genet 54 (4): 412-436. 2022. PMID: 35379992. IF: 41,31. DOI: 10.1038/s41588-022-01024-z.

GROUP 49

Head of laboratory: Novella Arribas, Blanca

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.6 New diagnostic and therapeutic advances in cardiovascular diseases

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 Diabetes 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.

GROUP MEMBERS

- Marta Ruiz López
- Rosa María Sánchez Alcalde
- Ana Cubillo Serna
- María Jesús Fernández Luque
- Ángela Gallego Arenas
- Amelia González Gamarra
- María del Pilar Loeches Belinchón
- Javier López González
- María Soledad Mayayo Vicente
- Francisco José Rodríguez Salvanés
- María Lourdes Ruiz Díaz
- Luis María Sánchez Gómez
- María Belén Sierra García

MAJOR GRANTS

Novella Arribas, Blanca. Utilización de un modelo innovador basado en comunidad, para el manejo y el seguimiento por personal de salud no médico (PSNM) para mejorar la conciencia, el tratamiento y el control de la Hipertensión Arterial (HTA). AC19/00112. ISCIII. 2020-2022.

LINE 3.7 ›› NEW THERAPIES IN INFECTIOUS PATHOLOGIES

GROUP 50

Head of laboratory: de los Santos Gil, Ignacio

Area 3 Advanced therapies and individualized medicine

Line 3.7 New therapies in infectious pathologies

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.

We are also involved in clinical trials of new drugs and new therapeutic strategies for HIV, including the combination of two drugs Dolutegravir and lamivudine for naive and experienced patients, and the new maturation inhibitor in a very early phase. These trials began in 2019 and will last two years.

We expect to start a new clinical trial this year 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. This aspect of HIV infection is currently having a major projection, due to the appearance of new drugs to treat hepatitis C, i.e direct antiviral agents. These drugs have revolutionized treatment achieving the greatest effectiveness until now (more than 95%) with few side effects. 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.

GROUP MEMBERS

- Ignacio de los Santos Gil
- Carmen María Sáez Béjar
- Ángela Gutiérrez Liarte
- Ana María Barrios Blandino
- Lucio Jesús García-Fraile Fraile
- Azucena Bautista Hernández
- Rafael de la Cámara de Llanza
- Jesús Sanz Sanz

MAJOR GRANTS

Fernández Ruíz, Elena. Effect of TYK2 deficiency in B Cell function: impact in lymphoproliferative diseases. PI19/00096. ISCIII. 2020-2022.

PUBLICATIONS

Cabezón G, López J, Vilacosta I, Sáez C, García Granja PE, Olmos C, Jerónimo A, Gutiérrez Á, Pulido P, de Miguel M, Gómez I, San Román JA. **Response to Letter to the Editor.** J Am Soc Echocardiogr 35 (12):2022. PMID: 35948262. IF: 7,72. DOI: 10.1016/j.echo.2022.07.016.

Cabello Ubeda A, de Quirós JCLB, Martín Carbonero L, Sanz J, Vergas J, Mena Á, Torralba M, Hernández Segurado M, Pinto A, Tejerina F, Palmier E, Gutiérrez Á,

Vázquez P, Pulido F, Górgolas M. **48-Week effectiveness and tolerability of dolutegravir (DTG) + lamivudine (3TC) in antiretroviral-**naïve adults living with HIV: A multicenter real-life cohort. PLoS One 17 (11). 2022. PMID: 36409695. IF: 3,75. DOI: 10.1371/journal.pone.0277606

Domingo LC, Vallejo ER, Cruz NDZ, Llano MC, Perez Urria EA, Barrios A, Santos JH, Ortiz J, Garcia SCR, Ramirez AM, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Garcia AS, Villa A, Azofra AS, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martinez AT, Arevalo C, Roman JMG, Garcia Vicuna R et al. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol 94. (11). 2022. PMID: 35811284. IF: 20,69. DOI: 10.1002/jmv.27989.

Villapalos-García G, Zubiaur P, Rivas-Durán R, Campos-Norte P, Arévalo- Román C, Fernández-Rico M, García-Fraile Fraile L, Fernández-Campos P, Soria-Chacartegui P, Fernández de Córdoba-Oñate S, Delgado-Wicke P, Fernández-Ruiz E, González-Álvaro I, Sanz J, Abad-Santos F, de Los Santos I. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity and sex are the primary predictors of Covid-19 severity (vol 5, e202201396, 2022)**. Life Sci Alliance 5 (10): 2022. PMID: 35680409. IF: 5,78. DOI: 10.26508/lsa.202201545.

Villapalos Garcia Gonzalo, Zubiaur Pablo, Rivas Duran Rebeca, Campos Norte Pilar, Arevalo Roman Cristina, Fernandez Rico Marta, Garcia Fraile Fraile Lucio, Fernandez Campos Paula, Soria Chacartegui Paula, Fernandez de Cordoba Onate Sara, Delgado Wicke Pablo, Fernandez Ruiz Elena, Gonzalez Alvaro Isidoro, Sanz Jesus, Abad Santos Francisco, de Los Santos Ignacio. **Transmembrane protease serine 2 (TMPRSS2) rs75603675, comorbidity, and sex are the primary predictors of COVID-19 severity**. Life Sci Alliance 5 (10). 2022. PMID: 35636966. IF: 5,78. DOI: 10.26508/lsa.202201396

Zurita Cruz Nelly Daniela, Martin Ramirez Alexandra, Rodriguez Serrano Diego Anibal, Gonzalez Alvaro Isidoro, Roy Vallejo Emilia, de la Camara Rafael, Garcia Rodrigo Leticia Fontan. **Usefulness of real-time RT-PCR to understand the kinetics of SARS-CoV-2 in blood: A prospective study**. J Clin Virol 152. 2022. PMID: 35594784. IF: 14,48. DOI: 10.1016/j.jcv.2022.105166.

Calvet Mirabent M, Sánchez Cerrillo I, Martín Cófreces N, Martínez Fleta P, de la Fuente H, Tsukalov I, Delgado Arévalo C, Calzada MJ, de los Santos I, Sanz J, García Fraile L, Sánchez Madrid F, Alfranca A, Muñoz Fernández MA, Buzón MJ, Martín Gayo E. **Antiretroviral therapy duration and immunometabolic state determine efficacy of ex vivo dendritic cell-based treatment restoring functional HIV-specific CD8+ T cells in people living with HIV.** EBioMedicine 81.

2022. PMID: 35665682. IF: 11,21. DOI: 10.1016/j.ebiom.2022.104090.

Martínez Román P, Crespo Bermejo C, Valle Millares D, Lara Aguilar V, Arca Lafuente S, Martín Carbonero L, Ryan P, de Los Santos I, López Huertas MR, Palladino C, Muñoz M, Fernández Rodríguez A, Coiras M, Briz V, On Behalf Of The Covihep Network. **Dynamics of HIV Reservoir and HIV-1 Viral Splicing in HCV-Exposed Individuals after Elimination with DAAs or Spontaneous Clearance.** J Clin Med 11 (13). 2022. PMID: 35806864. IF: 4,96. DOI: 10.3390/jcm11133579

Troya J, Dueñas C, Irazola I, de los Santos I, de la Fuente S, Gil D, Hernández C, Galindo MJ, Gómez J, Delgado E, Moreno García E, Posada G, Aldámiz T, Iribarren JA, Guerra JM, Morán MÁ, Galera C, Fuente J, Peláez A, Cervero M, Garcinuño M, Montero M, Ceballos F, Buzón L, on behalf of the DORIPEX Study Group. **Dolutegravir plus rilpivirine: benefits beyond viral suppression: DORIPEX retrospective study.** Medicine 101 (24). 2022. PMID: 35713430. IF: 1,82. DOI: 10.1097/MD.0000000000029252

Arca Lafuente S, Casanueva Benitez C, Crespo Bermejo C, Lara Aguilar V, Martin Carbonero L, De los Santos I, Madrid R, Briz V. **903 Protein Saver cards: the best alternative for dried blood spot storage at room temperature for HCV RNA**. Sci. Rep. 12. (1). 2022. PMID:35710721. IF:5,00. DOI:10.1038/s41598-022-14375-8.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front. Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639

Cecconi Alberto, Martinez Vives Pablo, Vera Alberto, Lavilla Olleros Cristina, Barrios Ana, Fonseca Aizpuru Eva, Roquero Pilar, Hernandez Muniz Susana, Jose Olivera Maria, Ciudad Marianela, Pampin Sanchez Ruben, Fernandez Madera Martinez Rosa, Bautista Hernandez Azucena, Garcia Castillo Elena, Iturricastillo Gorane, Avalos Elena, Prada Cotado Diana, Alejandre de Ona Alvaro, Fernandez Carracedo Eduardo, Marcos Jimenez Ana, Sanz Garcia Ancor, Alfranca Aranzazu, Cecconi Maurizio, de la Fuente Hortensia, Sanz de Benito Maria Angeles, Caballero Paloma, Sanchez Madrid Francisco, Ancochea Julio, Suarez Carmen, Jesus Jimenez Borreguero Luis et al. **Efficacy of short-course colchicine treatment in hospitalized patients with moderate to severe COVID-19 pneumonia and hyperinflammation: a randomized clinical trial**. Sci Rep 12 (1). 2022. PMID: 35654818. IF: 5,00. DOI: 10.1038/s41598-022-13424-6

Lopez Melgar B, Mass V, Nogales P, Sanchez Gonzalez J, Entrekin R, Collet Billon A, Rossello X, Fernandez Friera L, Fernandez Ortiz A, Sanz J, Bentzon JF, Bueno H, Ibanez B, Fuster V. **New 3-Dimensional Volumetric Ultrasound Method for Accurate Quantification of Atherosclerotic Plaque Volume**. JACC Cardiovasc Imaging 15 (6). 2022. PMID: 35680220. IF: 16,05. DOI: 10.1016/j.jcmg.2022.01.005

Snowden John A, Sanchez Ortega Isabel, Corbacioglu Selim, Basak Grzegorz W, Chabannon Christian, de la Camara Rafael, Dolstra Harry, Duarte Rafael F, Glass Bertram, Greco Raffaella, Lankester Arjan C, Mohty Mohamad, Neven Benedicte, de Latour Regis Peffault, Pedrazzoli Paolo, Peric Zinaida, Yakoub Agha Ibrahim, Sureda Anna, Kroeger Nicolaus, European Soc Blood Marrow Transpla. **Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2022**. Bone Marrow Transplant 57 (8). 2022. PMID: 35589997. IF: 5,17. DOI: 10.1038/s41409-022-01691-w

Jeronimo Adrian, Olmos Carmen, Vilacosta Isidre, Saez Carmen, Lopez Javier, Sanz Marta, Cabezon Gonzalo, Perez Serrano Javier B, Zulet Pablo, San Roman J Alberto. **Contemporary comparison of infective endocarditis caused by Candida albicans and Candida parapsilosis: a cohort study**. Eur J Clin Microbiol Infect Dis 41 (6): 2022. PMID: 35568743. IF: 5,10. DOI: 10.1007/s10096-022-04456-x

Cesaro S, Ljungman P, Mikulska M, Hirsch HH, von Lilienfeld-Toal M, Cordonnier C, Meylan S, Mehra V, Styczynski J, Marchesi F, Besson C, Baldanti F, Masculano RC, Beutel G, Einsele H, Azoulay E, Maertens J, de la Camara R; ECIL 9 Pagano L. **Recommendations for the management of COVID-19 in patients with haematological malignancies or haematopoietic cell transplantation, from the 2021 European Conference on Infections in Leukaemia (ECIL 9)**. Leukemia 36 (6): 1467-1480. 2022. PMID: 35488021. IF: 12,88. DOI: 10.1038/s41375-022-01578-1.

Escudero Sanchez Rosa, Muriel Garcia Alfonso, Garcia Fernandez Sergio, Valencia Alijo Angela, Tasias Pitarch Mariona, Merino De Lucas Esperanza, Gutierrez Rojas Angela, Ramos Martinez Antonio, Salavert Lleti Miguel, Giner Livia, Ruiz Ruigomez Maria, Garcia Basas Lorena, Fernandez Fradejas Jorge, Olmedo Sampedrio Maria, Cano Yuste Angela, Diaz Pollan Beatriz, Rodriguez Hernandez Maria Jesus, Martin Segarra Oriol, Saez Bejar Carmen, Arminanzas

Castillo Carlos, Gutierrez Belen, Rodriguez Pardo Dolors, De La Torre Cisneros Julian, Lopez Medrano Francisco, Cobo Reinoso Javier. **Fidaxomicin monotherapy versus standard therapy combined with bezlotoxumab for treating patients with Clostridioides difficile infection at high risk of recurrence: a matched cohort study**. J Antimicrob Chemother 77 (7). 2022. PMID: 35403189. IF: 5,76. DOI: 10.1093/jac/dkac106

Bautista Hernández A, de Vega Ríos E, Serrano Ballesteros J, Useros Braña D, Cardeñoso Domingo L, Figuerola Tejerina A, Jiménez D, De Los Santos Gil I, Sáez Béjar C. **Impact of the implementation of a Sepsis Code Program in medical patient management: a cohort study in an Internal Medicine ward.** Rev Esp Quimioter 35 (2). 2022. PMID: 35099161. IF: 2,52. DOI: 10.37201/req/132.2021

Serrano Villar Sergio, Lopez Huertas Maria Rosa, Jimenez Daniel, Galera Carlos, Martinez Sanz Javier, Moreno Elena, Muriel Alfonso, Gutierrez Felix, Busca Carmen, Portilla Joaquin, Bisbal Otilia, Iribarren Jose Antonio, Tejerina Francisco, de Los Santos Ignacio, Moreno Santiago, CoRIS. **Long- Term Changes of Inflammatory Biomarkers in Individuals on Suppressive Three-Drug or Two-Drug Antiretroviral Regimens**. Front Immunol 13. 2022. PMID: 35359950. IF: 8,79. DOI: 10.3389/fimmu.2022.848630.

Podzamczer D, Mican R, Tiraboschi J, Portilla J, Domingo P, Llibre JM, Ribera E, Vivancos MJ, Morano L, Masia M, Gomez C, Fanjul F, Payeras A, Inciarte A, Estrada V, Rivero A, Castro A, Bernal E, Vinuesa D, Knobel H, Troya J, Macias J, Montero M, Sanz J, Navarro Alcaraz A, Caicedo A, Fernandez G, Martinez E, Moreno S, SYMTRI Study Investigators. **Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir/Abacavir/Lamivudine in Antiretroviral-Naive Adults (SYMTRI): A Multicenter Randomized Open-Label Study (PReEC/RIS-57)**. Open Forum Infect Dis 9 (3). 2022. PMID: 35237700. IF: 4,42. DOI: 10.1093/ofid/ofab595

García Vicuña R, Rodriguez García SC, Abad Santos F, Bautista Hernández A, García Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso Pérez T, Cardeñoso L, Alfranca A, Mejía Abril G, Sanz J, González Alvaro I. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621

Montoto S, Snowden JA, Chabannon C, Corbacioglu S, de la Camara R, Dolstra H, Greco R, Gusi A, Hamad N, Kenyon M, Kroeger N, Mohty M, Murray J, Mueller A, Neven B, de Latour R Peffault, Peric Z, Sanchez Ortega I, Sureda A, Verhoeven B, Villar A, Yakoub Agha I. **The first steps towards a diverse and inclusive EBMT: a position paper**. Bone Marrow Transplant 57 (3). 2022. PMID: 35121807. IF: 5,17. DOI: 10.1038/s41409-022-01586-w

Styczynski Jan, Cesaro Simone, von Lilienfeld Toal Marie, Marchesi Francesco, Gil Lidia, Mikulska Malgorzata, Knelange Nina, Wendel Lotus, Averbuch Diana, de la Camara Rafael. **Current attitude to deferral of cellular therapy or nontransplant chemotherapy due to SARS-CoV-2 asymptomatic infection: Survey of Infectious Diseases Working Party EBMT**. Transplant Infect Dis 24 (2). 2022. PMID: 34918856. IF: 2,23. DOI: 10.1111/tid.13773

Resino Salvador, Jimenez Sousa Maria Angeles, Blanco Julia, Pacheco Yolanda M, del Romero Jorge, Peraire Joaquim, Virseda Berdices Ana, Munoz Gomez Maria Jose, Galera Penaranda Carlos, Garcia Fraile Lucio Jesus, Benito Jose M, Rallon Norma, Epiclin SARNPR. **DBP rs7041 and DHCR7 rs3829251 are Linked to CD4(+) Recovery in HIV Patients on Antiretroviral Therapy**. Front Pharmacol 12. 2022. PMID: 35115928. IF: 5,99. DOI:10.3389/fphar.2021.773848.

Fanciulli Chiara, Berenguer Juan, Busca Carmen, Vivancos Maria J, Tellez Maria J, Dominguez Lourdes, Domingo Pere, Navarro Jordi, Santos Jesus, Iribarren Jose A, Morano Luis, Artero Arturo, Moreno Javier, Rivero Roman Antonio, Santos Ignacio, Giner Livia, Arminanzas Carlos, Montero Marta, Manzardo Christian, Cifuentes Carmen, Garcia Coral, Galindo Maria J, Ferrero Oscar L, Sanz Jose, de la Fuente Belen, Rodriguez Carmen, Gaspar Gabriel, Perez Laura, Losa Juan E, Force Luis et al. **Epidemiological trends of HIV/HCV coinfection in Spain, 2015-2019**. HIV Med 23 (7). 2022. PMID: 35037379. IF: 3,09. DOI: 10.1111/hiv.13229

Calvet Mirabent Marta, Claiborne Daniel T, Deruaz Maud, Tanno Serah, Serra Carla, Delgado Arevalo Cristina, Sanchez Cerrillo Ildefonso, de Los Santos Ignacio, Sanz Jesus, Garcia Fraile Lucio, Sanchez Madrid Francisco, Alfranca Arantzazu, Munoz Fernandez Maria Angeles, Allen Todd M, Buzon Maria J, Balazs Alejandro, Vrbanac Vladimir, Martin Gayo Enrique. **Poly I:C and STING agonist-primed DC increase lymphoid tissue polyfunctional HIV-1-specific CD8(+) T cells and limit CD4(+) T-cell loss in BLT mice**. Eur J Immunol 52 (3). 2022. PMID: 34935145. IF: 6,69. DOI: 10.1002/eji.202149502

Martinez Sanz J, Serrano Villar S, Muriel A, Fraile LG, Orviz E, de Cea AM, Campins A, Guillen SM. **Metabolic-related outcomes after switching from tenofovir disoproxil fumarate to tenofovir alafenamide in adults living with HIV: a multicentre prospective cohort study**. J. Int. AIDS Soc.25. 2022. IF: 6,71.

GROUP 51

Head of laboratory: Aspa Marco, Francisco Javier

Area 3 Advanced therapies and individualized medicine

Line 3.7 New therapies in infectious pathologies

RESEARCH INTEREST

MicroRNAs (miRNAs) are a family of endogenous, small, noncoding RNA molecules that modulate physiological and pathological processes by post-transcriptional inhibition of gene expression. Recent studies have also begun to reveal that altered miRNA expression profiles may be associated with pathological processes within the lung and lead to the development of various pulmonary diseases, ranging from inflammatory diseases to lung cancers. Also miRNAs are pivotal to both adaptive and innate immunity, with regulatory effects on cell differentiation and immunological function.

miRNAs and community acquired pneumonia: Community acquired pneumonia (CAP) is an infectious disease with high prevalence and great morbimortality rate. Numerous strategies have been studied to improve the prediction of CAP prognosis, and thus help in decision-making for the management of these patients. Regarding CAP pathophysiology, miRNAs can influence the development and function of immune cells by blocking the translation of key proteins such as transcription factors or intermediate molecules in cell receptor signalling cascades. In addition, some miRNAs have been identified as key players in modulating the immune response to severe bacterial infection, by controlling neutrophil activation and recruitment and the chemotactic signal that initiates the inflammatory process. Moreover, several studies have established the utility of circulating miRNAs in the diagnosis of sepsis and in various specific infections (e.g. HIV, viral hepatitis or tuberculosis). However, there is limited scientific literature on the usefulness of these molecules as prognosis markers in CAP.

We aim to explore the role of different miRNAs in CAP and their role in the regulation of the inflammatory response in CAP patients.

miRNAs and Lung cancer: The search for a biomarker that enables optimizing the early diagnosis of lung cancer is a pending challenge. The adequate management of a potentially malignant solitary pulmonary nodule in early stages is especially important in fragile and elderly patients. It is also important to use non-aggressive techniques to obtain good quality samples of deep breath. Exhaled breath condensate (EBC) is a simple, non- aggressive technique that provides a biological sample where different markers can be determined.

Recent promising studies have analysed miRNA profiles in EBC as potential biomarkers for early diagnosis in lung cancer patients. We will focus our efforts on establishing the utility of miRNA determination in EBC samples as a first step in the building process of a molecular signature for EBC in lung cancer patients.

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- Sergio Luquero Bueno
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- Olga Rajas Naranjo

MAJOR GRANTS

Convocatoria Becas SEPAR. Sociedad Española de Neumología y Cirugía Torácica. 2022.

Ayuda a la investigación. Proyecto Análisis molecular del condensado del aire exhalado en el manejo del nódulo pulmonar solitario.

PUBLICATIONS

Rabes L, Adán Lirola L, González Molina MDP, Galván Román JM, Moldenhauer F, Roy Vallejo E, Real de Asúa D. **Evaluation of congenital and acquired heart diseases in a Spanish cohort of adults with Down syndrome.** Sci Rep 12 (1). 2022. PMID: 36577781. IF: 5,00. DOI: 10.1038/s41598-022-26918-0.

López Urrutia E, Sancha A, Useros D, Galván Román JM, García Sanz I, Casals F, Fernández Bueno J, Real de Asúa D, en representación del Comité de Ética para la Asistencia Sanitaria del Hospital. **Description of the experience of a clinical ethics consultation service from 2019-2021.** Rev Clin Esp (Barc) 222 (10). 2022. PMID: 36427658. DOI: 10.1016/j.rceng.2022.09.004.

Domingo LC, Vallejo ER, Cruz NDZ, Llano MC, Perez Urria EA, Barrios A, Santos JH, Ortiz J, Garcia SCR, Ramirez AM, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Garcia AS, Villa A, Azofra AS, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martinez AT, Arevalo C, Roman JMG, Garcia Vicuna R et al. **Relevant SARS-CoV-2 viremia is associated with COVID-19 severity: Prospective cohort study and validation cohort**. J Med Virol 94 (11). 2022. PMID: 35811284. IF: 20,69. DOI: 10.1002/jmv.27989.

Zubiaur P, Matas M, Martin Vilchez S, Soria Chacartegui P, Villapalos Garcia G, Figueiredo Tor L, Calleja S, Navares Gomez M, de Miguel A, Novalbos J, Mejia Abril G, Luquero Bueno S, Roman M, Ochoa D, Abad Santos F. **Polymorphism of Drug Transporters, Rather Than Metabolizing Enzymes, Conditions the Pharmacokinetics of Rasagiline**. Pharmaceutics 14 (10). 2022. PMID: 36297437. IF: 6,53. DOI: 10.3390/pharmaceutics14102001.

Martinez MR, Aguilar EG, Vilchez SM, Garcia JG, Luquero Bueno S, Camargo Mamani P, Mejia Abril G, Garcia Castro L, de Miguel Caceres A, Saz Leal P, Abad Santos F, Magro CN, Mazarro DO. **Bioavailability of Oniria (R), a Melatonin Prolonged-Release Formulation, Versus Immediate-Release Melatonin in Healthy Volunteers**. Drugs R D 22 (3). 2022. PMID: 35918587. IF: 3,20. DOI: 10.1007/s40268-022-00394-3.

López Viñas L, Vega Villar J, Rocío Martín E, García P, De La Rosa Santiago E, Galván Román JM, Wix Ramos R. **Diaphragm impairment in patients admitted for severe COVID-19.** Eur. J Trans Mylogy 32 (2). 2022. PMID: 35727218. DOI: 10.4081/ejtm.2022.10460.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Hernandez Jimenez Macarena, Martin Vilchez Samuel, Ochoa Dolores, Mejia Abril Gina, Roman Manuel, Camargo Mamani Paola, Luquero Bueno Sergio, Jilma Bernd, Moro Maria A, Fernandez Geronimo, Pineiro David, Ribo Marc, Gonzalez Victor M, Lizasoain Ignacio, Abad Santos Francisco. **First-in-human phase I clinical trial of a TLR4-binding DNA aptamer, ApTOLL: Safety and pharmacokinetics in healthy volunteers**. Mol Ther Nucl Acids 28. 2022. PMID: 35402075. IF: 10,18. DOI: 10.1016/j.omtn.2022.03.005.

Serra Lopez-Matencio, Jose Maria, Gago Veiga, Ana Beatriz, Gomez, Manuel, Alanon Plaza, Estefania, Paola Mejia, Gina, Ángel González-Gay, Miguel, Castaneda, Santos. **Treatment of migraine with monoclonal antibodies**. Expert Opin Biol Ther 22 (6):2022. PMID: 35502612. IF: 5,59. DOI: 10.1080/14712598.2022.2072207.

Martínez Fleta P, Vera Tomé P, Jiménez Fernández M, Requena S, Roy Vallejo E, Sanz García A, Lozano Prieto M, López Sanz C, Vara A, Lancho Sánchez Á, Martín Gayo E, Muñoz Calleja C, Alfranca A, González Álvaro I, Galván Román JM, Aspa J, de la Fuente H, Sánchez Madrid F. **A Differential Signature of Circulating miRNAs and Cytokines Between COVID-19 and Community-Acquired Pneumonia Uncovers Novel Physiopathological Mechanisms of COVID-19.** Front Immunol 12. 2022. PMID: 35087533. IF: 8,79. DOI: 10.3389/fimmu.2021.815651.

Monserrat Villatoro Jaime, Mejia Abril Gina, Diaz Garcia Lucia, Zubiaur Pablo, Jimenez Gonzalez Maria, Jimenez Guillermo Fernandez, Cancio Ines, Arribas Jose Ramon, Suarez Fernandez Carmen, Mingorance Jesus, Rodriguez Julio Garcia, Villagrasa Ferrer Jose Ramon, Carcas Antonio J J, Frias Jesus, Abad Santos Francisco, Borobia Alberto M M, Ramirez Elena, COVID HULP Working Grp, Hosp Univ de la Princesa. **A Case-Control of Patients with COVID-19 to Explore the Association of Previous Hospitalisation Use of Medication on the Mortality of COVID-19 Disease: A Propensity Score Matching Analysis**. Pharmaceuticals 15 (1). 2022. PMID: 35056135. IF: 5,22. DOI: 10.3390/ph15010078.

GROUP 52

Head of laboratory: Alarcón Cavero, Teresa

Area 3 Advanced therapies and individualized medicine

Line 3.7 New therapies in infectious pathologies

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.

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PUBLICATIONS

Díaz García J, Gómez A, Machado M, Alcalá L, Reigadas E, Sánchez Carrillo C, Pérez Ayala A, de la Pedrosa EG, González Romo F, Cuétara MS, García Esteban C, Quiles Melero I, Zurita ND, Algarra MM, Durán Valle MT, Sánchez García A, Muñoz P, Escribano P, Guinea J, On Behalf Of The Candimad Study Group. **Candida Genotyping of Blood Culture Isolates from Patients Admitted to 16 Hospitals in Madrid: Genotype Spreading during the COVID-19 Pandemic Driven by Fluconazole-Resistant C. parapsilosis.** J Fungi 8 (11). 2022. PMID: 36422050. IF: 5,72. DOI: 10.3390/jof8111228.

Thorpe HA, Tourrette E, Yahara K, Vale FF, Liu S, Oleastro M, Alarcon T, Perets TT, Latifi Navid S, Yamaoka Y, Martinez Gonzalez B, Karayiannis I, Karamitros T, Sgouras DN, Elamin W, Pascoe B, Sheppard SK, Ronkainen J, Aro P, Engstrand L, Agreus L, Suerbaum S, Thorell K, Falush D. **Repeated out-of-Africa expansions of Helicobacter pylori driven by replacement of deleterious mutations.** Nat Commun 13 (1). 2022. PMID: 36369175. IF: 17,69. DOI: 10.1038/s41467-022-34475-3.

Díaz García J, Gómez A, Machado M, Alcalá L, Reigadas E, Sánchez Carrillo C, Pérez Ayala A, Gómez García De La Pedrosa E, González Romo F, Cuétara MS, García Esteban C, Quiles Melero I, Zurita ND, Muñoz Algarra M, Durán Valle MT, Sánchez García A, Muñoz P, Escribano P, Guinea J, CANDIMAD Study Group. **Blood and intra-abdominal Candida spp. from a multicentre study conducted in Madrid using EUCAST: emergence of fluconazole resistance in Candida parapsilosis, low echinocandin resistance and absence of Candida auris.** J Antimicrob Chemother 77 (11). 2022. PMID: 36031723. IF: 5,76. DOI: 10.1093/jac/dkac288.

Villalva M, Silvan JM, Alarcón Cavero T, Villanueva Bermejo D, Jaime L, Santoyo S, Martinez Rodriguez AJ. **Antioxidant, Anti-Inflammatory, and Antibacterial Properties of an Achillea millefolium L. Extract and Its Fractions Obtained by Supercritical Anti-Solvent Fractionation against Helicobacter pylori.** Antioxidants 11 (10). 2022. PMID: 36290572. IF: 7,68. DOI: 10.3390/antiox11101849.

Ezquerra Durán,A,Gutiérrez Cobos,A,García Buey,L. **Healing of chronic hepatitis delta relapsing to pegylated interferon with tenofovir.** Med Clin 159 (5): 2022. PMID: 35659423. IF: 3,20. DOI: 10.1016/j.medcli.2022.02.017.

Díaz García J, Gómez A, Alcalá L, Reigadas E, Sánchez Carrillo C, Pérez Ayala A, Gómez García de la Pedrosa E, González Romo F, Merino Amador P, Cuétara MS, García Esteban C, Quiles Melero I, Zurita ND, Muñoz Algarra M, Sánchez Romero I, Durán Valle MT, Sánchez García A, Alcoceba E, Muñoz P, Escribano P, Guinea J, CANDIMAD study group. **Evidence of Fluconazole-Resistant Candida parapsilosis Genotypes Spreading across Hospitals Located in Madrid, Spain and Harboring the Y132F ERG11p Substitution.** Antimicrob Agents Chemother 66 (8). 2022. PMID: 35852369. IF: 5,94. DOI: 10.1128/aac.00710-22.

Fernandez Caso B, Miqueleiz A, Valdez VB, Alarcón T. **Are molecular methods helpful for the diagnosis of Helicobacter pylori infection and for the prediction of its antimicrobial resistance?** Front Microbiol 13. 2022. PMID: 36016780. IF: 6,06. DOI: 10.3389/fmicb.2022.962063.

Esparcia Pinedo L, Yarci Carrión A, Mateo Jiménez G, Ropero N, Gómez Cabañas L, Lancho Sánchez A, Almendro Vázquez P, Martín Gayo E, Paz Artal E, Sanchez Madrid F, Moldenhauer F, Gutiérrez Cobos A, de Asúa DR, Alfranca A. **Development of an effective immune response in adults with Down Syndrome after SARS-CoV-2 vaccination.** Clin Infect Dis PMID: 35869848. IF: 20, 99. DOI: 10.1093/cid/ciac590.

Zurita Cruz Nelly Daniela, Martin Ramirez Alexandra, Rodriguez Serrano Diego Anibal, Gonzalez Alvaro Isidoro, Roy Vallejo Emilia, de la Camara Rafael, Garcia Rodrigo Leticia Fontan. **Usefulness of real-time RT-PCR to understand the kinetics of SARS-CoV-2 in blood: A prospective study**. J Clin Virol 152. 2022. PMID: 35594784. IF: 14,48. DOI: 10.1016/j.jcv.2022.105166.

Villalva M, Silvan JM, Guerrero Hurtado E, Gutierrez Docio A, Navarro Del Hierro J, Alarcón Cavero T, Prodanov M, Martin D, Martinez Rodriguez AJ. **Influence of In Vitro Gastric Digestion of Olive Leaf Extracts on Their Bioactive Properties against H. pylori.** Foods 11 (13). 2022. PMID: 35804647. IF: 5,56. DOI: 10.3390/foods11131832.

Roy Vallejo E, Cardenoso L, Triguero Martinez A, Llano MC, Zurita N, Avalos E, Barrios A, Hernando J, Ortiz J, Rodriguez Garcia SC, Sanudo MC, Marcos C, Castillo EG, Garcia Rodrigo LF, Gonzalez B, Mendez R, Iturrate I, Sanz Garcia A, Villa A, Sanchez Azofra A, Quicios B, Arribas D, Rodriguez JA, Patino P, Trigueros M, Uriarte M, Martin Ramirez A, Roman CA, Galvan Roman JM, Garcia Vicuna R et al. **SARS-CoV-2 Viremia Precedes an IL6 Response in Severe COVID-19 Patients: Results of a Longitudinal Prospective Cohort**. Front Med 9. 2022. PMID: 35783606. IF: 5,06. DOI: 10.3389/fmed.2022.855639.

Girón RM, Ibáñez A, Gómez Punter RM, Alarcón T. **New evidence in severe pneumonia: imipenem/cilastatin/relebactam.** Rev Esp Quimioter 35 (Suppl 1). 2022. PMID: 35488826. IF: 2,52. DOI: 10.37201/req/s01.11.2022.

Bautista Hernández A, de Vega Ríos E, Serrano Ballesteros J, Useros Braña D, Cardeñoso Domingo L, Figuerola Tejerina A, Jiménez D, De Los Santos Gil

I, Sáez Béjar C. **Impact of the implementation of a Sepsis Code Program in medical patient management: a cohort study in an Internal Medicine ward.** Rev Esp Quimioter 35 (2). 2022. PMID: 35099161. IF: 2,52. DOI:10.37201/req/132.2021.

García Vicuña R, Rodriguez García SC, Abad Santos F, Bautista Hernández A, García Fraile L, Barrios Blandino A, Gutiérrez Liarte A, Alonso Pérez T, Cardeñoso L, Alfranca A, Mejía Abril G, Sanz J, González Alvaro I. **Subcutaneous IL-6 Inhibitor Sarilumab vs. Standard Care in Hospitalized Patients With Moderate-To-Severe COVID-19: An Open Label Randomized Clinical Trial.** Front Med 9. 2022. PMID: 35280907. IF: 5,06. DOI: 10.3389/fmed.2022.819621.

GROUP 40

Head of laboratory: Colomer Bosch, Ramón

Area 3 Advanced therapies and individualized medicine

Line 3.7 New therapies in infectious pathologies

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 CCDN1 in breast cancer. By using a systems biology approach, we are clustering breast cancer into subtypes defined by biologic features that constitute therapeutic targets.

GROUP MEMBERS

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- Eugenia Jareño Dorrego
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- José Miguel Sánchez Torres
- Natalia Torres Waldhaus

- Erich Alberto Vargas Díez
- Francisco Eduardo Viamontes Ugalde
- Verónica Jiménez Renard

MAJOR GRANTS

Colomer Bosch, Ramón. Un nuevo papel tumorogenico de la Sintasa de Acidos Grasos relacionado con el compartimiento de células T tumorales. PI20/01458. ISCIII. 2021-2023.

Romero Laorden, Nuria. Caracterización evolutiva del fenotipo inmune en cáncer de próstata metastásico. PI21/01111 ISCIII. 2022-2024.

Romero Laorden, Nuria. Biomarcadores asociados al huésped en cáncer de próstata: estudio multi-cohorte en 3 etapas. Mutua Madrileña. 2021-2024.

Romero Laorden, Nuria. CARACTERIZACIÓN EVOLUTIVA DEL FENOTIPO INMUNE EN CÁNCER DE PRÓSTATA METASTÁSICO.

PUBLICATIONS

Marcos Jiménez A, Claudino Carvoeiro D, Ruef N, Cuesta Mateos C, Roy Vallejo E, Gómez García de Soria V, Laganá C, Del Campo L, Zubiaur P, Villapalos García G, Abad Santos F, Stein JV, Muñoz Calleja C. **Dasatinib- induced spleen contraction leads to transient lymphocytosis.** Blood Adv. 2022. PMID: 36583674. IF: 7,64. DOI: 10.1182/bloodadvances.2022009279.

Mouron S, Bueno MJ, Lluch A, Manso L, Calvo I, Cortes J, Garcia Saenz JA, Gil M, Martinez Janez N, Apala JV, Caleiras E, Ximénez Embún P, Muñoz J, Gonzalez Cortijo L, Murillo R, Sánchez Bayona R, Cejalvo JM, Gómez López G, Fustero Torre C, Sabroso Lasa S, Malats N, Martinez M, Moreno A, Megias D, Malumbres M, Colomer R, Quintela Fandino M. **Phosphoproteomic analysis of neoadjuvant breast cancer suggests that increased sensitivity to paclitaxel is driven by CDK4 and filamin A.** Nat Commun 13 (1). 2022. PMID: 36477027. IF: 17,69. DOI: 10.1038/s41467- 022-35065-z.

Ramírez E, Romero Jiménez R, Hernández Muniesa B, Fernández Pacheco M, Calvo A, Chamorro Vega E, Herrero N, Úbeda B, Morell A, Ais Larisgoitia A, Lobato Matilla E, Muñoz Á, Casado A, Casado MÁ, Escudero Vilaplana V. **Evaluation of the hospital care quality perceived by patients with immune-mediated inflammatory diseases from the pharmacy service. SACVINFA study.** J Clin Pharm Ther 47 (12). 2022. PMID: 35929568. IF: 2,15. DOI:10.1111/jcpt.13742.

López Urrutia E, Sancha A, Useros D, Galván Román JM, García Sanz I, Casals F, Fernández Bueno J, Real de Asúa D, en representación del Comité de Ética para la Asistencia Sanitaria del Hospital. **Description of the experience of a clinical ethics consultation service from 2019-2021.** Rev Clin Esp (Barc) 222 (10). 2022. PMID: 36427658. IF: 3,06. DOI:10.1016/j.rceng.2022.09.004.

Araujo Castro M, Mínguez Ojeda C, García Centeno R, López García MC, Lamas C, Hanzu FA, Mora M, Del Castillo Tous M, Rodríguez de Vera Gómez P, Parra Ramírez P, Alvarez Escola C, Blanco Carrera C, Barahona San Millán R, Recasens M, Valdés N, Gracia Gimeno P, de Miguel Novoa P, Vicente A, Manjón L, García Sanz I, Michalopoulou T, Calatayud M. **Glycemic disorders in patients with pheochromocytomas and sympathetic paragangliomas.** Endocr Relat Cancer 29 (12). 2022. PMID: 36069783. IF: 5,90. DOI: 10.1530/ERC-22-0218.

Araujo Castro M, Paja Fano M, González Boillos M, Pla Peris B, Pascual Corrales E, García Cano AM, Parra Ramírez P, Martín Rojas Marcos P, Ruiz Sanchez JG, Vicente Delgado A, Gómez Hoyos E, Ferreira R, García Sanz I, Recasens Sala M, Barahona San Millan R, Picón César MJ, Díaz Guardiola P, García González JJ, Perdomo CM, Manjón Miguélez L, García Centeno R, Percovich JC, Rebollo Román Á, Gracia Gimeno P, Robles Lázaro C, Morales Ruiz M, Hanzu FA. **Predictive model of hypertension resolution after adrenalectomy in primary aldosteronism: the SPAIN-ALDO score.** J Hypertens 40 (12). 2022. PMID: 36018220. IF: 4,78. DOI: 10.1097/HJH.0000000000003284.

Pardilla Moraleda,FJ,Serrano Pardo,R,del Campo Del Val,L,García Buey,L. An unusual cause of fulminant hepatic failure: Metastatic infiltration by **infiltrating ductal carcinoma of the breast.** Gastroenterol Hepatol. PMID: 36464081. IF: 5,86. DOI: 10.1016/j.gastrohep.2022.11.007.

Girón RM, Peláez A, Ibáñez A, Martínez Besteiro E, Gómez Punter RM, Martínez Vergara A, Ancochea J, Morell A. **Longitudinal Study of Therapeutic Adherence in a Cystic Fibrosis Unit: Identifying Potential Factors Associated with Medication Possession Ratio.** Antibiotics 11 (11). 2022. PMID: 36421281. IF: 5,22. DOI: 10.3390/antibiotics11111637.

Mollar A, Bonanad C, Diez Villanueva P, Segarra D, Civera J, Sastre C, Conesa A, Villaescusa A, Fernández J, Miñana G, Navarro J, Sanchis J, Núñez J. **Frailty and Hospitalization Burden in Patients With Chronic Heart Failure.** Am J Cardiol 183. 2022. PMID: 36153181. IF: 3,13. DOI: 10.1016/j.amjcard.2022.08.013.

Sebastian Valles F, Carrero NSD, Rodriguez Laval V, Martinez Hernandez R, Serrano Somavilla A, Knott Torcal C, de Nova JLM, Martin Perez E, Marazuela M, Sampedro Nunez MA. **Impact of**

Change in Body Composition during Follow-Up on the Survival of GEP-NET. Cancers 14 (21). 2022. PMID: 36358607. IF: 6,58. DOI: 10.3390/cancers14215189.

Rogado J, Pozo F, Troule K, Sanchez Torres JM, Romero Laorden N, Mondejar R, Donnay O, Ballesteros A, Pacheco Barcia V, Aspa J, Al Shahrour F, Alfranca A, Colomer R. **Excess weight and anti-PD-1 immune checkpoint inhibitor's outcomes in non-small cell lung cancer**. Clin Transl Oncol 24 (11). 2022. PMID: 35870091. IF: 3,34. DOI: 10.1007/s12094-022-02887-8.

Gordillo CH, Jiménez Heffernan JA. **Melamed-Wolinska bodies in a pleural effusion.** Diagn Cytopathol 50 (11). 2022. PMID: 36040844. IF: 1,39. DOI:10.1002/dc.25049.

Vera R, Ibarrola Andrés C, Adeva J, Pérez Rojas J, García Alfonso P, Rodríguez Gil Y, Macarulla T, Serrano Piñol T, Mondéjar R, Madrigal Rubiales B. **Expert consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology on the determination of biomarkers in pancreatic and biliary tract cancer.** Clin Transl Oncol 24 (11). 2022. PMID: 36008616. IF: 3,34. DOI: 10.1007/s12094-022-02873-0.

Araujo Castro M, Paja Fano M, González Boillos M, Pla Peris B, Pascual Corrales E, García Cano AM, Parra Ramírez P, Rojas Marcos PM, Ruiz Sanchez JG, Vicente Delgado A, Gómez Hoyos E, Ferreira R, García Sanz I, Recasens Sala M, Barahona San Millan R, Picón César MJ, Díaz Guardiola P, García González JJ, Perdomo CM, Manjón Miguélez L, García Centeno R, Percovich JC, Rebollo Román Á, Gracia Gimeno P, Robles Lázaro C, Morales Ruiz M, Hanzu FA. **Adrenal venous sampling in primary aldosteronism: Experience of a Spanish multicentric study (Results from the SPAIN-ALDO Register).** Endocrine 78 (2) 2022. PMID: 35751774. IF: 3,93. DOI: 10.1007/s12020-022-03122-8.

Nava Cedeño DJ, Alonso Cerezo MC, Sanz García A, Vega Zelaya L, Gordillo Perdomo JJ, Toledo Heras M, Pastor Gómez J, Torres Díaz C, Pulido Rivas P, García Sola R. **Asociación entre los polimorfismos genéticos de nucleótido único en genes transportadores ABC con la epilepsia farmacorresistente en la población española.** Rev Neurol 75 (9). 2022. PMID: 36285445. IF: 1,24. DOI: 10.33588/rn.7509.2022133.

Jiménez Heffernan JA, Rosell A, Vázquez Espinosa E, Idoate Ortueta C, Solís García M, Pacios E. **Cytologic features of a pleural effusion after silicone breast implant rupture.** Virchows Arch. PMID: 36227351. IF: 4,54. DOI: 10.1007/s00428-022-03425-1.

Ramia JM, Aparicio López D, Asencio Pascual JM, Blanco Fernández G, Cugat Andorrá E, Gómez Bravo MÁ, López Ben S, Martín Pérez E, Sabater L, Serradilla Martín M. **Applicability and reproducibility of the validated intraoperative bleeding severity scale (VIBe scale) in liver surgery: A multicenter study.** SURGERY 172 (4). 2022. PMID: 35871850. IF: 4,35. DOI: 10.1016/j.surg.2022.05.022.

Di Martino M, Primavesi F, SynN, Dorcaratto D, de la Hoz Rodríguez Á, Dupré A, Piardi T, Rhaiem R, Blanco Fernández G, de Armas Conde N, Rodríguez Sanjuán JC, Fernández Santiago R, Fernández Moreno MC, Ferret G, López Ben S, Suárez Muñóz MÁ, Perez Alonso AJ, Koh YX, Jones R, Martín Pérez E. **ASO Visual Abstract: Long-Term Outcomes of Perioperative versus Neoadjuvant Chemotherapy for Resectable Colorectal Liver Metastases-An International Multicenter Propensity-Score Matched Analysis with Stratification by Contemporary Risk Scoring.** Ann Surg Oncol 29 (11). 2022. PMID: 35810229. IF: 4,34. DOI: 10.1245/s10434-022-12077-z.

Di Martino M, Primavesi F, SynN, Dorcaratto D, de la Hoz Rodríguez Á, Dupré A, Piardi T, Rhaiem R, Blanco Fernández G, de Armas Conde N, Rodríguez Sanjuán JC, Fernández Santiago R, Fernández Moreno MC, Ferret G, López Ben S, Suárez Muñoz MÁ, Perez Alonso AJ, Koh YX, Jones R, Martín Pérez E. **Long-Term Outcomes of Perioperative Versus Neoadjuvant Chemotherapy for Resectable Colorectal Liver Metastases: An International Multicentre Propensity-Score Matched Analysis with Stratification by Contemporary Risk-Scoring.** Ann Surg Oncol 29 (11). 2022. PMID: 35849284. IF: 4,34. DOI: 10.1245/s10434-022-12027-9.

Castillo Gazquez,L,Vera Díaz,EC,Muñoz Hernández,P,Jiménez Heffernan,JA. **Curschmann's spiral in a voided urine sample.** CYTOPATHOLOGY33 (5): 2022. PMID: 35699383. IF: 1,29. DOI: 10.1111/cyt.13155.

Cabañero Sánchez A, Muñoz Molina GM, Fra Fernández S, Muriel García A, Cilleruelo Ramos A, Martínez Hernández N, Hernando Trancho F, Moreno Mata N, GE-VATS. **Impact of neoadjuvant therapy on postoperative complications in non-small-cell lung cancer patients subjected to anatomic lung resection.** Eur J Surg Oncol 48 (9). 2022. PMID: 35379545. IF: 4,04. DOI: 10.1016/j.ejso.2022.03.008.

Guadalajara H, Yiasemidou M, Muñoz de Nova JL, Sedman P, Fernandez Gonzalez S, Maslekar S, Recarte Rico M, Egan R, Juez LD, Riyad K, García Septiem J, Lockwood S, Galindo Jara P, Giorga A, García Virosta M, Hance J, Lobo Martínez E, Martín Pérez E, Howitt A, Jayne D, Chetter I, García Olmo D, PIACO Collaboration Group. **The international PIACO study: pattern of surgical approaches for acute surgical**

pathologies in Spain versus UK. Was conservative treatment and open surgery during COVID-19 the way to go?. BJS Open 6 (4). 2022. PMID: 35939374. IF: 3,88. DOI: 10.1093/bjsopen/zrac089.

Parra Ramírez P, Rojas Marcos PM, Paja Fano M, González Boillos M, Pascual Corrales E, García Cano A, Ruiz Sanchez JG, Vicente A, Gómez Hoyos E, Ferreira R, García Sanz I, Recasens M, Pla Peris B, Barahona San Millan R, Picón César MJ, Díaz Guardiola P, Jesús García González J, Perdomo C, Manjón L, García Centeno R, Percovich JC, Rebollo Román Á, Gracia Gimeno P, Robles Lázaro C, Morales M, Hanzu F, Araujo Castro M. **Differences in the presentation and evolution of primary aldosteronism in elderly (=65 years) and young patients.** Endocr Connect 11 (6). 2022. PMID: 35583179. IF: 3,22. DOI: 10.1530/EC-22-0169.

Pacheco Barcia V, Muñoz A, Castro E, Ballesteros AI, Marquina G, González Díaz I, Colomer R, Romero Laorden N. **The Homologous Recombination Deficiency Scar in Advanced Cancer: Agnostic Targeting of Damaged DNA Repair.** Cancers 14 (12). 2022. PMID: 35740616. IF: 6,58. DOI: 10.3390/cancers14122950.

Bernabé Caro R, Garrido P, García Campelo R, Palmero R, Artal Á, Bayona C, Rodríguez Abreu D, López Brea M, Paredes A, Vicente D, Sánchez Torres JM, Majem M, Diz P, Gordo R, Coca M, de Castro J. **Alectinib after failure to crizotinib in patients with ALK-positive non-small cell lung cancer: results from the Spanish early access program.** ONCOTARGET 13 (1). 2022. PMID: 35720977. IF: 5,17. DOI: 10.18632/oncotarget.28244.

Rogado J, Pozo F, Troule K, Sanchez Torres JM, Romero Laorden N, Mondejar R, Donnay O, Ballesteros A, Pacheco Barcia V, Aspa J, Al Shahrour F, Alfranca A, Colomer R. **Peripheral Blood Mononuclear Cells Predict Therapeutic Efficacy of Immunotherapy in NSCLC**. Cancers 14 (12). 2022. PMID: 35740564. IF: 6,58. DOI: 10.3390/cancers14122898.

Maqueda Gonzalez Rocio, Di Martino Marcello, Galan Gonzalez Itxaso, Rodriguez Carnero Pablo, Martin Perez Elena. **Development of a prediction model of pancreatic fistula after duodenopancreatectomy and soft pancreas by assessing the preoperative image**. Langenbeck's Arch. Surg. 407 (6). 2022. PMID: 35643803. IF: 2,90. DOI: 10.1007/s00423-022-02564-y.

Dang C, Ewer MS, Delaloge S, Ferrero JM, Colomer R, de la Cruz Merino L, Werner TL, Dadswell K, Verrill M, Eiger D, Sarkar S, de Haas SL, Restuccia E, Swain SM. **BERENICE Final Analysis: Cardiac Safety Study of Neoadjuvant Pertuzumab, Trastuzumab, and Chemotherapy Followed by Adjuvant Pertuzumab and Trastuzumab in HER2-Positive Early Breast Cancer.** Cancers 14 (11). 2022. PMID: 35681574. IF: 6,58. DOI: 10.3390/cancers14112596.

Escudero Vilaplana V, Bernal E, Casado G, Collado Borrell R, Diez Fernández R, Fernández Román AB, Folguera C, González Cortijo L, Herrero Fernández M, Marquina G, Martínez Nieto C, Rodríguez MA, Rubio AR, Sanmartin Fenollera P, Vazquez Castillo MJ, Comellas M, Guerra EM. **Defining a Standard Set of Patient-Reported Outcomes for Patients With Advanced Ovarian Cancer.** Front Oncol 12. 2022. PMID: 35664764. IF: 5,74. DOI: 10.3389/fonc.2022.885910.

Adamina Michel, Ademuyiwa Adesoji, Adisa Adewale, Bhangu Aneel A, Bravo Ana Minaya, Cunha Miguel F, Emile Sameh, Ghosh Dhruva, Glasbey James C, Harris Benjamin, Keller Debby, Lawday Samuel, Lederhuber Hans, Leventoglu Sezai, Li Elizabeth, Modolo Maria Marta, Mittal Rohin, Mohan Helen M, Nepogodiev Dmitri, Parreno Sacdalan Marie Dione, Pata Francesco, Pockney Peter, Rutegard Martin, Simoes Joana F F, Smart Neil, Varghese Chris, Siaw Acheampong Kwabena, Benson Ruth A, Bywater Edward, Chaudhry Daoud et al. **The impact of surgical delay on resectability of colorectal cancer: An international prospective cohort study**. Colorectal Dis 24 (6). 2022. PMID: 35286766. IF: 3,92. DOI: 10.1111/codi.16117.

Majem Margarita, de las Penas Ramon, Antonio Virizuela Juan, Cabezon Gutierrez Luis, Cruz Patricia, Lopez Castro Rafael, Mendez Miriam, Mondejar Rebeca, del Mar Munoz Maria, Escobar Yolanda. **SEOM clinical guideline emesis (2021)**. Clin Transl Oncol 24 (4). 2022. PMID: 35347571. IF: 3,34. DOI: 10.1007/s12094-022-02802-1.

Araujo Castro Marta, Paja Fano Miguel, Gonzalez Boillos Marga, Pla Peris Begona, Pascual Corrales Eider, Garcia Cano Ana Maria, Parra Ramirez Paola, Martin Rojas Marcos Patricia, Gabriel Ruiz Sanchez Jorge, Vicente Delgado Almudena, Gomez Hoyos Emilia, Ferreira Rui, Garcia Sanz Inigo, Diaz Guardiola Patricia, Garcia Gonzalez Juan Jesus, Perdomo Carolina M, Morales Manuel, Hanzu Felicia A. **Evolution of the cardiometabolic profile of primary hyperaldosteronism patients treated with adrenalectomy and with mineralocorticoid receptor antagonists: results from the SPAIN- ALDO Registry**. Endocrine 76 (3). 2022. PMID: 35275344. IF: 3,93. DOI: 10.1007/s12020-022-03029-4.

Di Martino Marcello, Gancedo Quintana Alvaro, Vaello Jodra Victor, Sanjuanbenito Dehesa Alfonso, Morales Garcia Dieter, Caina Ruiz Ruben, Garcia Moreno Nisa Francisca, Mendoza Moreno Fernando, Alonso Batanero Sara, Quinones Sampedro Jose Edecio, Lora Cumplido Paola, Arango Bravo Altea, Rubio Perez

Ines, Asensio Gomez Luis, Pardo Aranda Fernando, Senti Farrarons Sara, Ruiz Moreno Cristina, Martinez Moreno Clara Maria, Sarriugarte Lasarte Aingeru, Prieto Calvo Mikel, Aparicio Sanchez Daniel, Perea del Pozo Eduardo Perea, Pellino Gianluca, Martin Perez Elena. **Early laparoscopic cholecystectomy in oldest-old patients: a propensity score matched analysis of a nationwide registry**. Updates Surg 74 (3). 2022. PMID: 35253094. IF: 2,69. DOI: 10.1007/s13304-022-01254-0.

Lopez Campos Fernando, Gajate Pablo, Romero Laorden Nuria, Zafra Martin Juan, Juan Manel, Hernando Polo Susana, Conde Moreno Antonio, Counago Felipe. **Immunotherapy in Advanced Prostate Cancer: Current Knowledge and Future Directions**. Biomedicines 10 (3). 2022. PMID: 35327339. IF: 4,76. DOI: 10.3390/biomedicines10030537.

Tovar Pérez R, Di Martino M, Blanco Terés L, Martín Pérez E. **Cystic artery pseudoaneurism secondary to acute cholecystitis.** Cir Esp (Engl Ed) 100 (3). 2022. PMID: 35216912. DOI: 10.1016/j.cireng.2022.02.009.

Jimenez Heffernan Jose A, Diaz del Arco Cristina, Adrados Magdalena. **A Cytological Review of Follicular Dendritic Cell-Derived Tumors with Emphasis on Follicular Dendritic Cell Sarcoma and Unicentric Castleman Disease**. Diagn 12 (2). 2022. PMID: 35204497. IF: 3,99. DOI: 10.3390/diagnostics12020406.

Pla Peris Begona, Arranz Martin Alfonso, Ballesteros Garcia Anabel, Sebastian Valles Fernando, Marazuela Azpiroz Monica. **Alpelisib-Induced Diabetes Mellitus: Case Report, Pharmacodynamics and Management Considerations**. Front Endocrinol 13. 2022. PMID: 35178031. IF: 6,06. DOI: 10.3389/fendo.2022.802612.

Valdivia Mazeyra MF, Muñoz Ramos P, Serrano R, Alonso Riaño M, Gil Giraldo Y, Quiroga B. **Mesoamerican nephropathy: A not so unknown chronic kidney disease.** Nefrologia 41 (6). 2022. PMID: 36165150. DOI: 10.1016/j.nefroe.2021.12.009.

Ortiz A, Roger M, Jiménez VM, Perez JCR, Furlano M, Atxer LS, Zurro DG, Casabona CMR, Gómez CG, Bermúdez PP, Armisen MA, López SA, Porras IG, Ruiz JG, Orgaz JMM, Barón MM, Ortiz PDS, De La Fuente GDA, Gili BQ, Fresnedo GF, Cabrera SS, Contreras JP, Pelicano MB, Blanca AM, Portillo MR, Álvarez JES, Romeo MJS, Pérez MG, Diezhandino MG, Marrero DH et al. **RICORS2040: The need for collaborative research in chronic kidney disease**. Clin Kidney J 15 (3). 2022. IF: 5,86. DOI: 10.1093/ckj/sfab170.

GROUP 49

Head of laboratory: Zapatero Laborda, Almudena

Area 3 Prognostic and predictor markers in autoimmune diseases

Line 3.8 Individualized medicine in solid tumors

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.

a. 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).

b. 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.

c. IRONMAN-ES: "Estudio prospectivo observacional de parámetros clínicos y biomarcadores en cáncer de próstata avanzado en hospitales de España"; in colaboration with CNIO (co-sponsor).

d. Collection of biological markers within the EORTC research project platform 1822 E2-RADIatE- OligoCare: A pragmatic observational cohort study to evaluate radical radiotherapy for oligo-metastatic cancer patients.

2. Advances in Prostate Cancer Treatment:

a. 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. Sub-study analysis of prognostic and predictive value of Testosterone nadir is ongoing.

b. 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:

a. Over the last 10 years we have actively worked in Intensity Modulated Radiation Treatment - Image Guided Radiotherapy (IMRT-IGRT) versus three-dimensional con-formal 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.

b. 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).PROMOTER: 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-RADIatE - OligoCare: A pragmatic observational cohort study to evaluate radical radiotherapy for oligo- metastatic cancer patients. Activation phase.

5. BLADDER CANCER-BLADDER SPARING PROGRAM

a. 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.

b. 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

6. 3D PRINTING TECHNOLOGY FOR THE DEVELOPMENT OF IMMOBILIZATION DEVICES IN RADIOTHERAPY:

Two projects are being developed investigating the manufacture of immobilizers using additive technology for the skull and extremities and its implications in the radiotherapy process: it would allow a complete customization of the immobilizer, minimize errors due to the automation and simplification of the process, and achieve a higher degree of precision. It might mean a paradigm shift in the field of immobilization used in radiotherapy treatments.

GROUP MEMBERS

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- José Alfonso Cruz Conde
- María del Carmen Martin de Vidales Cervantes
- Pablo Castro Tejero

MAJOR GRANTS

Romero Laorden, Nuria. **Immune phenotype of metastatic prostate cáncer: Immuno-PROfiling**. ISCIII. PI21/01111. 2021-2023.

Romero Laorden, Nuria. **BIOMARCADORES ASOCIADOS AL HUÉSPED EN CÁNCER DE PRÓSTATA: ESTUDIO MULTI-COHORTE EN 3 ETAPAS**. MM. 2022-2024.

Hernández González, David. Desarrollo de inmovilizadores personalizados basados en impresión 3D para tratamientos de radioterapia externa de **lesiones localizadas en extremidades**. Sociedad Española de Física Médica. 2022-2023.

PUBLICATIONS

Romero Laorden, Nuria. **Immune phenotype of metastatic prostate cáncer: Immuno-PROfiling**. ISCIII. PI21/01111. 2021-2023.

Romero Laorden, Nuria. **BIOMARCADORES ASOCIADOS AL HUÉSPED EN CÁNCER DE PRÓSTATA: ESTUDIO MULTI-COHORTE EN 3 ETAPAS**. MM. 2022-2024.

Hernández González, David. Desarrollo de inmovilizadores personalizados basados en impresión 3D para tratamientos de radioterapia externa de **lesiones localizadas en extremidades**. Sociedad Española de Física Médica. 2022-2023.

PUBLICATIONS

Zapatero A, Calvo FA, Gonzalez San-Segundo C, Alvarez A. Reply to Leonard

P. Bokhorst and Berdine L. Bokhorst and Berdine L**. Heesterman's Words of Wisdom re: High-dose Radiotherapy and Risk-adapted Androgen Deprivation in Localised Prostate Cancer (DART 01/05): 10-Year Results of a Phase 3 Randomised, Controlled Trial. Eur Urol. 2022;82:441.** Eur Urol 82 (6): 177-178. 2022. PMID: 36115773. IF: 24,27. DOI: 10.1016/j.eururo.2022.08.033.

Zilli T, Achard V, Dal Pra A, Schmidt-Hegemann N, Jereczek-Fossa BA, Lancia A, Ingrosso G, Alongi F, Aluwini S, Arcangeli S, Blanchard P, Conde Moreno A, Couñago F, Créhange G, Dirix P, Gomez Iturriaga A, Guckenberger M, Pasquier D, Sargos P, Scorsetti M, Supiot S, Tree AC, Zapatero A, Le Guevelou J, Ost P, Belka C. **Recommendations for radiation therapy in oligometastatic prostate cancer: An ESTRO-ACROP Delphi consensus.** Radiother Oncol 176. 199-207. 2022. PMID: 36228761. IF: 6,90. DOI: 10.1016/j.radonc.2022.10.005.

Garrido Siles M, López-Beltran A, Pelechano P, García Vicente AM, Gironés Sarrió R, González-Haba Peña E, Rodríguez Antolín A, Zapatero A, Arranz JÁ, Climent MÁ, Spanish Oncology Genitourinary Multidisciplinary Working Group. **Advances in Transversal Topics Applicable to the Care of Bladder Cancer Patients in the Real-World Setting.** Cancers 14 (16): 3968. 2022. PMID: 36010964. IF: 6,58. DOI: 10.3390/cancers14163968.

Achard V, Jaccard M, Vanhoutte F, Siva S, Heikkilä R, Dirix P, Liefhooghe N, Otte FX, Gomez-Iturriaga A, Berghen C, Shelan M, Conde-Moreno A, López Campos F, Papachristofilou A, Guckenberger M, Meersschout S, Putora PM, Zwahlen D, Couñago F, Scorsetti M, Eito C, Barrado M, Zapatero A, Muto P, Van De Voorde L, Lamanna G, Koutsouvelis N, Dipasquale G, Ost P, Zilli T. **Oligorecurrent nodal prostate cancer: Radiotherapy quality assurance of the randomized PEACE V-STORM phase II trial.** Radiother Oncol 172. 1-9. 2022. PMID: 35476942. IF: 6,90. DOI: 10.1016/j.radonc.2022.04.020.

Kishan AU, Wang X, Sun Y, Romero T, Michalski JM, Ma TM, Feng FY, Sandler HM, Bolla M, Maingon P, De Reijke T, Neven A, Steigler A, Denham JW, Joseph D, Nabid A, Carrier N, Souhami L, Sydes MR, Dearnaley DP, Syndikus I, Tree AC, Incrocci L, Heemsbergen WD, Pos FJ, Zapatero A, Efstathiou JA, Guerrero A, Alvarez A, San-Segundo CG et al. **High-dose Radiotherapy or Androgen Deprivation Therapy (HEAT) as Treatment Intensification for Localized Prostate Cancer: An Individual Patient-data Network Meta-analysis from the MARCAP Consortium.** Eur Urol 82 (1): 106-114. 2022. PMID: 35469702. IF: 24,27. DOI: 10.1016/j.eururo.2022.04.003.

Turco F, Armstrong A, Attard G, Beer TM, Beltran H, Bjartell A, Bossi A, Briganti A, Bristow RG, Bulbul M, Caffo O, Chi KN, Clarke C, Clarke N, Davis ID, de Bono J, Duran I, Eeles R, Efstathiou E, Efstathiou J, Evans CP, Fanti S, Feng FY, Fizazi K, Frydenberg M, George D, Gleave M, Halabi S, Heinrich D, Higano C et al. **Corrigendum to "What Experts Think About Prostate Cancer Management During the COVID-19 Pandemic: Report from the Advanced Prostate Cancer Consensus Conference 2021" [Eur Urol 82(1):6-11].** Eur Urol 82 (1):18-19. 2022. PMID: 35440417. IF: 24,27. DOI: 10.1016/j.eururo.2022.04.004.

Gillessen S, Armstrong A, Attard G, Beer TM, Beltran H, Bjartell A, Bossi A, Briganti A, Bristow RG, Bulbul M, Caffo O, Chi KN, Clarke CS, Clarke N, Davis ID, de Bono JS, Duran I, Eeles R, Efstathiou E, Efstathiou J, Ekeke ON, Evans CP, Fanti S, Feng FY, Fizazi K, Frydenberg M, George D, Gleave M, Halabi S, Heinrich D et al. **Management of Patients with Advanced Prostate Cancer: Report from the Advanced Prostate Cancer Consensus Conference 2021.** Eur Urol 82 (1): 115-141. 2022. PMID: 35450732. IF: 24,27. DOI: 10.1016/j.eururo.2022.04.002.

Zapatero A, Guerrero A, Maldonado X, Álvarez A, San-Segundo CG, Rodríguez MÁC, Solé JM, Olivé AP, Casas F, Boladeras A, de Vidales CM, de la Torre MLV, Vara S, Sanz JL, Calvo FA. **High-dose radiotherapy and risk- adapted androgen deprivation in localised prostate cancer (DART 01/05): 10-year results of a phase 3 randomised, controlled trial.** Lancet Oncol 23 (5): 671-681. 2022. PMID: 35427469. IF: 54,43. DOI: 10.1016/S1470-2045(22)00190-5.

Zapatero A. **Testosterone levels and testosterone kinetics: The importance of its clinical significance**. Radiother Oncol 169. 148-149. 2022. PMID: 35101463. IF: 6,90. DOI: 10.1016/j.radonc.2022.01.027.

Kishan AU, Sun Y, Hartman H, Pisansky TM, Bolla M, Neven A, Steigler A, Denham JW, Feng FY, Zapatero A, Armstrong JG, Nabid A, Carrier N, Souhami L, Dunne MT, Efstathiou JA, Sandler HM, Guerrero A, Joseph D, Maingon P, de Reijke TM, Maldonado X, Ma TM, Romero T, Wang X, Rettig MB, Reiter RE, Zaorsky NG, Steinberg ML, Nickols NG et al. **Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis**. Lancet Oncol 23

(2): 304-316. 2022. PMID: 35051385. IF: 54,43. DOI: 10.1016/S1470-2045(21)00705-1.

Jiménez-Heffernan JA, Díaz Del Arco C, Adrados M. **A Cytological Review of Follicular Dendritic Cell-Derived Tumors with Emphasis on Follicular Dendritic Cell Sarcoma and Unicentric Castleman Disease**. Diagn 12 (2): 406. 2022. PMID: 35204497. IF: 3,99. DOI: 10.3390/diagnostics12020406.

Kishan AU, Steigler A, Denham JW, Zapatero A, Guerrero A, Joseph D, Maldonado X, Wong JK, Stish BJ, Dess RT, Pilar A, Reddy C, Wedde TB, Lilleby WA, Fiano R, Merrick GS, Stock RG, Demanes DJ, Moran BJ, Tran PT, Martin S, Martinez-Monge R, Krauss DJ, Abu-Isa EI, Pisansky TM, Choo CR, Song DY, Greco S, Deville C, McNutt T et al. **Interplay Between Duration of Androgen Deprivation Therapy and External Beam Radiotherapy With or Without a Brachytherapy Boost for Optimal Treatment of High-risk Prostate Cancer A Patient-Level Data Analysis of 3 Cohorts**. JAMA Oncol 8 (3): 216871. 2022. PMID: 35050303. IF: 33,01. DOI: 10.1001/jamaoncol.2021.6871.

Angulo JC, Ciria Santos JP, Gómez-Caamaño A, Poza de Celis R, González Sala JL, García Garzón JM, Galán-Llopis JA, Pérez Sampietro M, Perrot V, Planas Morin J, ANARESISTANCE study group. **Development of castration resistance in prostate cancer patients treated with luteinizing hormone- releasing hormone analogues (LHRHa): results of the ANARESISTANCE study.** World J Urol 40 (10): 2459-2466. 2022. PMID: 36057895. IF: 3.66. doi: 10.1007/s00345-022-04108-x.

GROUP 54

Head of laboratory: Laura Cerezo Padellano

Area 3 Advanced therapies and individualized medicine

Line 3.8 Individualized medicine in solid tumors.

RESEARCH INTEREST

Advances in head and neck cancer include new knowledge on etiology and progress on organ preservation treatments modalities. Head and neck cancer (HNC) is mainly related to smoking, however, another risk factor, the human papillomavirus (HPV), has emerged in recent years. HPV related carcinoma constitutes a distint entity which presents in young adults, not heavy smokers, usually presenting as regionally advanced disease and with better prognosis, probably due to their different molecular profile. In the other hand, organ preservation with chemoradiation is feasible in locally advanced head and neck cancer without compromising survival.

Our group pursues four lines of investigation:

Monitor the evolving incidence of HPV-induced OPSCC in our region and identify new molecular mechanisms in these tumors, related to increased radiosensitivity. For the next years we are planning to expand this research, analyzing all patients with oropharyngeal cancer treated from 2011 to 2015 from six large hospitals in Madrid and studying the percentage of HPV positive. Thus, we will have a clear picture of the incidence of oropharyngeal cancer related to HPV infection in our region. We have applied for a grant to study the gene expression profile of HPV positive and HPV negative oropharyngeal cancer, with potential implications on treatment choices.

Advance in organ preservation treatment in locally advanced head and neck within a multidisciplinary approach of chemotherapy, radiotherapy and inmunotherapy. We will participate in phase III, randomized, study of the effects of leukocyte interleukin injection plus radiotherapy in patients with advanced squamous cell carcinoma of the oral cavity.

Test new drugs that can reduce acute and late toxicity derived from chemoradiation, such as mucositis and xerostomia. Our multicentric phase III study on the benefit of Clonidine for the prevention of oral mucositis in head and neck cancer patients has completed accrual now and statistical analysis is planned for

this year. Also, the study on intranasal Fentanyl for the treatment of pain associated with oral mucositis, has completed its accrual now.

We are also working in surgical rehabilitation, including dental implants and mandibular reconstruction in order to improve quality of life of head and neck cancer patients. A review on neck dissection after chemoradiation for head and neck cancer has been done, in collaboration with the E.N.T. department, and the Radiology department to establish which patients undergoing a conservative treatment need to be operated.

GROUP MEMBERS

- Laura Cerezo Padellano
- Pablo Rodríguez Carnero
- Francisco José Rodríguez Campo
- Mario Fernando Muñoz Guerra
- Alicia Marín Palomo
- Consuelo López Elzaurdía
- Mario López Rodríguez
- Luis Naval Gías
- Eduardo Raboso García-Baquero

PUBLICATIONS

Muñoz Guerra MF, Rodríguez Campo FJ, Escorial Hernández V, Sanz García A, Brabyn PJ, Fernández Domínguez M. **Temporomandibular joint arthroscopy in advanced stages of internal derangement: a retrospective cohort study on the influence of age.** Int J Oral Maxillofac Surg 51 (12). 2022. PMID: 35654642. IF: 2,99. DOI: 10.1016/j.ijom.2021.12.009.

Tarraso J, Safont B, Carbonell Asins JA, Fernandez Fabrellas E, Sancho Chust JN, Naval E, Amat B, Herrera S, Ros JA, Soler Cataluña JJ, Rodriguez Portal JA, Andreu AL, Marín M, Rodriguez Hermosa JL, Gonzalez Villaescusa C, Soriano JB, Signes Costa J, COVID FIBROTIC study team. **Lung function and radiological findings 1 year after COVID-19: a prospective follow-up.** Respir Res 23 (1). 2022. PMID: 36096801. IF: 7,16. DOI: 10.1186/s12931-022-02166-8.

GROUP 59

Head of laboratory: Olivier Gómez, Carlos Manuel

Area 3 Advanced therapies and individualized medicine

Line 3.8 Individualized medicine in solid tumors.

RESEARCH INTEREST

Our group focused on different research areas:

Urothelial cancer:

A comprehensive characterization of cell subpopulations involved in the immune response against bladder cancer has not been performed. In addition, due to the high prevalence, recurrence, and progression capacity of non-muscle-invasive bladder cancer (NMIBC), identifying novel biomarkers of tumor progression and response to therapy is of utmost importance. The detailed analysis of the immune landscape in these patients is highly relevant to anticipating tumor behavior and optimizing diagnosis methods and tumor management. We present the results of the first detailed characterization of immune cell populations in the normal bladder, tumor samples, and peripheral blood from patients with NMIBC. We have found specific immune cell subsets differentially expressed in these samples and identified potential markers of tumor progression and patient outcome in peripheral blood. These findings provide relevant information about the host immune response against bladder cancer and set the basis for novel non-invasive patient stratification and monitoring procedures.

Exosomal extracellular vesicles are potent intercellular mediators containing membrane and cytosolic

proteins, mRNA, and specific miRNA, which can be obtained from fluids such as urine. We have analyzed urinary exosomes, miRNA, and protein content to find diagnostic markers for bladder urothelial carcinoma. Some of the miRNAs 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 helpful as non- invasive diagnostic biomarkers in bladder cancer. Concerning surgical techniques, we have optimized the diagnosis and therapeutic endourologic approach to upper urothelial tract cancer.

Prostate cancer: Impact of intraoperative Neurophysiologic Monitoring of Periprostatic Neurovascular Bundles in Laparoscopic Radical Prostatectomy on the incidence of positive margins. Radical Prostatectomy is associated with significant adverse effects such as urinary incontinence and erectile dysfunction. Preservation of neurovascular bundles to mitigate these risks may be related to an increase in the rate of positive margins in the RP specimen and, therefore, to having a local relapse of the disease during follow-up leading to salvage treatments such as Radiotherapy, which in turn perpetuates the aforementioned adverse effects due to damage to the intervened tissues. Intraoperative neurophysiological monitoring of the neurovascular bundles can provide the surgeon with a map of the structures to be preserved to have an optimal safety margin without the need to violate the neurovascular structures, thereby maintaining the functionality of these patients to create harmony between the desired oncological results and good postoperative quality of life.

Functional Urology: Genitourinary tract symptoms in patients admitted with coronavirus disease 2019 (COVID-19): Exploring changes in frequency by determinants and pandemic waves. Urothelial cells exhibit increased expression of angiotensin-converting enzyme-2 receptor, which is the binding site of severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2) to cells. The frequency and distribution of genitourinary tract symptoms in patients diagnosed with COVID-19 are unknown. We explored trends in genitourinary tract symptoms by gender and each of the six pandemic waves in patients admitted for COVID-19 and related them with severity, death, and length of hospitalization. A retrospective study was conducted in our institution with COVID-19 admitted patients. Only patients with RT-PCR or antigen test-confirmed SARS-CoV-2 infection were included. Demographic, clinical, and genitourinary symptoms were explored. COVID- 19 patients with genitourinary tract symptoms were compared with those without them. Statistical comparisons were conducted by parametric and nonparametric tests for quantitative variables and $\chi 2$ test for qualitative variables. Out of 4,661 COVID-19 patients, genitourinary symptoms were found in 21.1%. These symptoms were more frequent in patients admitted for longer than 30 days, except for urinary incontinence (UI) and erectile dysfunction (ED). Acute kidney injury (AKI) and urinary tract infections (UTI)

had a higher presence in the 5th (16.7% and 12.8%, respectively) and 3rd wave (13.3% and 12.6%, respectively). Genitourinary symptoms were higher for those patients admitted to critical care units. Frequency of AKI, UI, UTI and acute urinary retention (AUR) were higher for patients who were finally deceased (26.2%, 3.5%, 13.6%, and 3.6%, respectively). A high frequency of genitourinary symptoms in patients admitted for COVID-19 was observed, whose frequency and distribution varied according to pandemic waves. Specific genitourinary conditions were associated with worse outcomes and poorer prognoses.

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 characterized by advanced inflammatory and oxidative state. Vardenafil is one of the most effective 5- phosphodiesterase inhibitors in patients with ED and DM. We have determined the plasma proteome of patients with DM and the effect of Vardenafil administration on the expression of proteins related to inflammatory oxidative stress and cellular homeostasis. We have observed a significant negative correlation between plasma levels of beta- tropomyosin and IIEF-EF score. Elevated levels of beta-tropomyosin in plasma indicate cell damage and loss of cellular regenerative capacity.

GROUP MEMBERS

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- María José Galán Sánchez-Heredero

PUBLICATIONS

Pablo Valdevenito J, Mercado Campero A, Lopez Fando L, Ignacio Calvo C, Manriquez V, Medina L. **Dropped abdominal pressure at void in women**. Int Urogynecol J 33 (11): 3275-3281. 2022. PMID: 35445356. IF: 1,93. DOI: 10.1007/s00192-022-05202-9.

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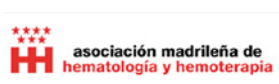
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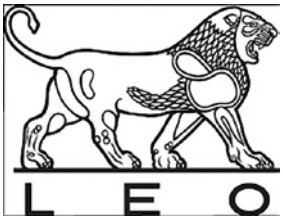
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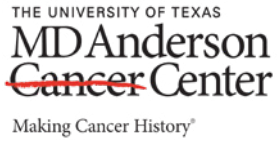
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