



ANUAL REPORT OF SCIENTIFIC ACTIVITY 2021

INDEX

FOREWORD IP

■ LETTER FROM THE SCIENTIFIC DIRECTOR	6
■ MEMBERS OF THE INSTITUTE	8
■ ORGANIZATIONAL CHART	9
■ SCIENTIFIC PLATFORMS	16
■ RESEARCH AREAS	23
■ SCIENTIFIC OUTPUT	28
■ COMMUNICATION AND DISSEMINATION	58

CELLULAR AND MOLECULAR ETIOPATHOGENIC MECHANISMS IN INFLAMMATORY AND AUTOIMMUNE DISEASES

■ LINE 1.1 INTERCELLULAR COMMUNICATION IN THE INFLAMMATORY RESPONSE	68
■ LINE 1.2 CELLULAR AND MOLECULAR RESPONSES TO HYPOXIA	75
■ LINE 1.3 ANIMAL MODELS OF INFLAMMATORY DISEASES AND INTERCELLULAR SIGNALLING	81
■ LINE 1.5 CELLULAR MECHANISMS AND MOLECULAR DETERMINANTS OF ALLERGY BASED DISEASES	92
■ LINE 1.6 INFLAMMATORY PROCESSES IN NEPHROLOGICAL DISEASES	97
■ LINE 1.7 INFLAMMATORY MECHANISMS IN PULMONARY DISEASES	100
■ LINE 1.8 INFLAMMATORY RESPONSE IN HEPATIC DISEASES	108
■ LINE 1.9 MECHANISMS AND MEDIATORS OF ENDOCRINE DISEASES	114
■ LINE 1.10 CHILDREN'S DEVELOPMENT (OBESITY AND GROWTH)	119
■ LINE 1.11 METABOLIC SYNDROME AND VASCULAR RISK	123

TRANSLATIONAL NEUROSCIENCE

■ LINE 2.1	NEUROPHARMACOLOGY AND NEUROPROTECTION	130
■ LINE 2.3	CLINICAL PHARMACOLOGY AND PHARMACOGENETICS	136
■ LINE 2.4	DIAGNOSTIC AND THERAPEUTIC ADVANCES IN AFFECTIVE DISORDERS	141
■ LINE 2.5	NEUROSURGERY OF EPILEPSY	148
■ LINE 2.6	CEREBROVASCULAR DISEASES	150

ADVANCED THERAPIES AND INDIVIDUALIZED MEDICINE

■ LINE 3.1	PROGNOSTIC AND PREDICTOR MARKERS IN AUTOIMMUNE DISEASES	160
■ LINE 3.2	ESOPHAGOGASTROINTESTINAL INFLAMMATORY DISEASES	174
■ LINE 3.3	PROGENITORS AND CELL THERAPY	182
■ LINE 3.4	ADVANCED THERAPIES IN ONCOHEMATOLOGY	186
■ LINE 3.5	BIOLOGICAL, CELLULAR AND MOLECULAR MONITORING IN ONCOHEMATOLOGY	189
■ LINE 3.6	NEW DIAGNOSTIC AND THERAPEUTIC ADVANCES IN CARDIOVASCULAR DISEASES	193
■ LINE 3.7	NEW THERAPIES IN INFECTIOUS PATHOLOGIES	213
■ LINE 3.8	INDIVIDUALIZED MEDICINE IN SOLID TUMORS	224

ANNUAL
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ACTIVITY

2021

FOREWORD IP

IIS-PRINCESA 2020



■ LETTER FROM THE SCIENTIFIC DIRECTOR

■ MEMBERS OF THE INSTITUTE

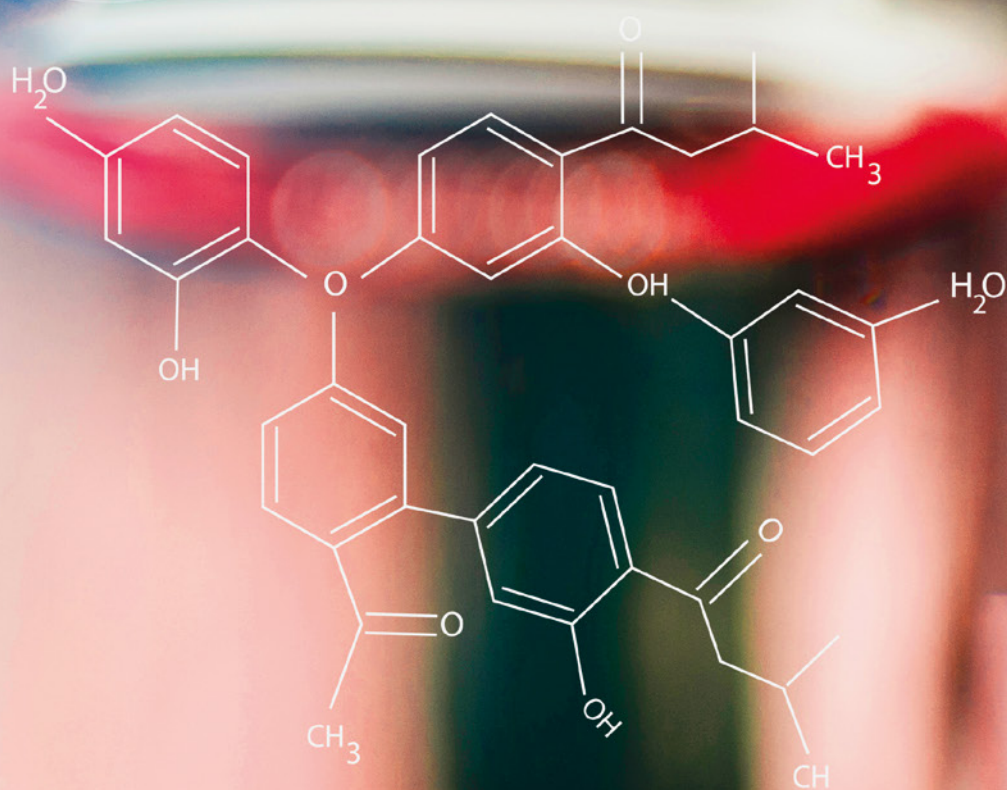
■ ORGANIZATIONAL CHART

■ SCIENTIFIC PLATFORMS

■ RESEARCH AREAS

■ SCIENTIFIC OUTPUT

■ COMMUNICATION AND DISSEMINATION



LETTER FROM THE SCIENTIFIC DIRECTOR



Francisco Sánchez Madrid
SCIENTIFIC DIRECTOR

In 2021, 12 years have passed since the first agreement for the creation of La Princesa Health Research Institute 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.

The year began with the audit for the renewal of our accreditation as a Health Research Institute by the Institute of Health Carlos III. Due to the preventive measures established because of the COVID-19 pandemic, the accreditation process had to be carried out online. Thanks to our IT skills and resources, we were able to successfully respond online to all the requirements of the audit team, including a virtual visit to the facilities. The

accreditation of our Institute was renewed in May until 2026.

The audit team interviewed more than 100 members of our Institute, including consolidated and emerging researchers, researchers in training, directors and personnel of research platforms, directors and management staff. Among their conclusions, they highlighted that all the professionals of the IIS Princesa had a positive and satisfactory vision of the actions carried out by the Institute, as well as a high pride of belonging to our Institution.

Focusing on the scientific output of 2021, the number of articles, monographic reviews and editorials, has decreased compared to 2020, likely due to the exceptionally high output of this year. This high number of publications in 2020 was due, on the one hand, to the large number of articles on the pandemic and its effects and, on the other hand, to the fact that online working favoured dedicating more time to expedite the publication of pending works. Most likely, this downward trend will continue in 2022, although we expect that the annual growth that the Institute experienced in past years will soon be consolidated. The number of articles published in 2021 was



Thanks to our IT skills and resources, we were able to successfully respond online to all the requirements of the audit team, including a virtual visit to the facilities. The accreditation of our Institute was renewed in May until 2026

636, 10% less than in 2020. On the contrary, the accumulated impact factor has maintained a value very similar to that shown last year, reaching a figure of 3917.951 (assessed with the 2019 Journal of Citations Report), thus increasing the relative impact per article.

As in previous years, the IIS Princesa has implemented different initiatives to encourage Open Access publication. As a result, 65% of our articles were published in Open Access format. In addition, 45% of the total number of our publications were led by researcher of IIS Princesa, which shows the scientific leadership of the members of our Institute.

The number of contracts signed for clinical studies this year has been 121, of which 80 correspond to clinical trials and 41 to observational studies.

Regarding academic output, it should be noted that 27 doctoral theses have been defended, more than twice as many as during 2020. Of note, 6 of them obtained and European Doctorate mention. During this year, four patents have been registered, and two applications of previous years have been granted.

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

In 2022, the Institute will continue with its efforts to address, above all, generational renewal, but also the new requirements of open science, data management plans, as well as the improvement of our participation in projects of the Horizon Europe programme.

Like every year, I would not like to finish without thanking the work carried out by all members of the Institute. Their effort and dedication has been crucial to achieve the milestone of the renewal of the accreditation, as well as the very positive data that we offer below. I would also like 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 continue doing a professional and dedicated work. ■

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. ■



 **Hospital Universitario
de La Princesa**

 **Hospital Universitario
Santa Cristina**

 **Hospital Universitario
Niño Jesús**



Dirección General de Investigación,
Docencia y Documentación
CONSEJERÍA DE SANIDAD

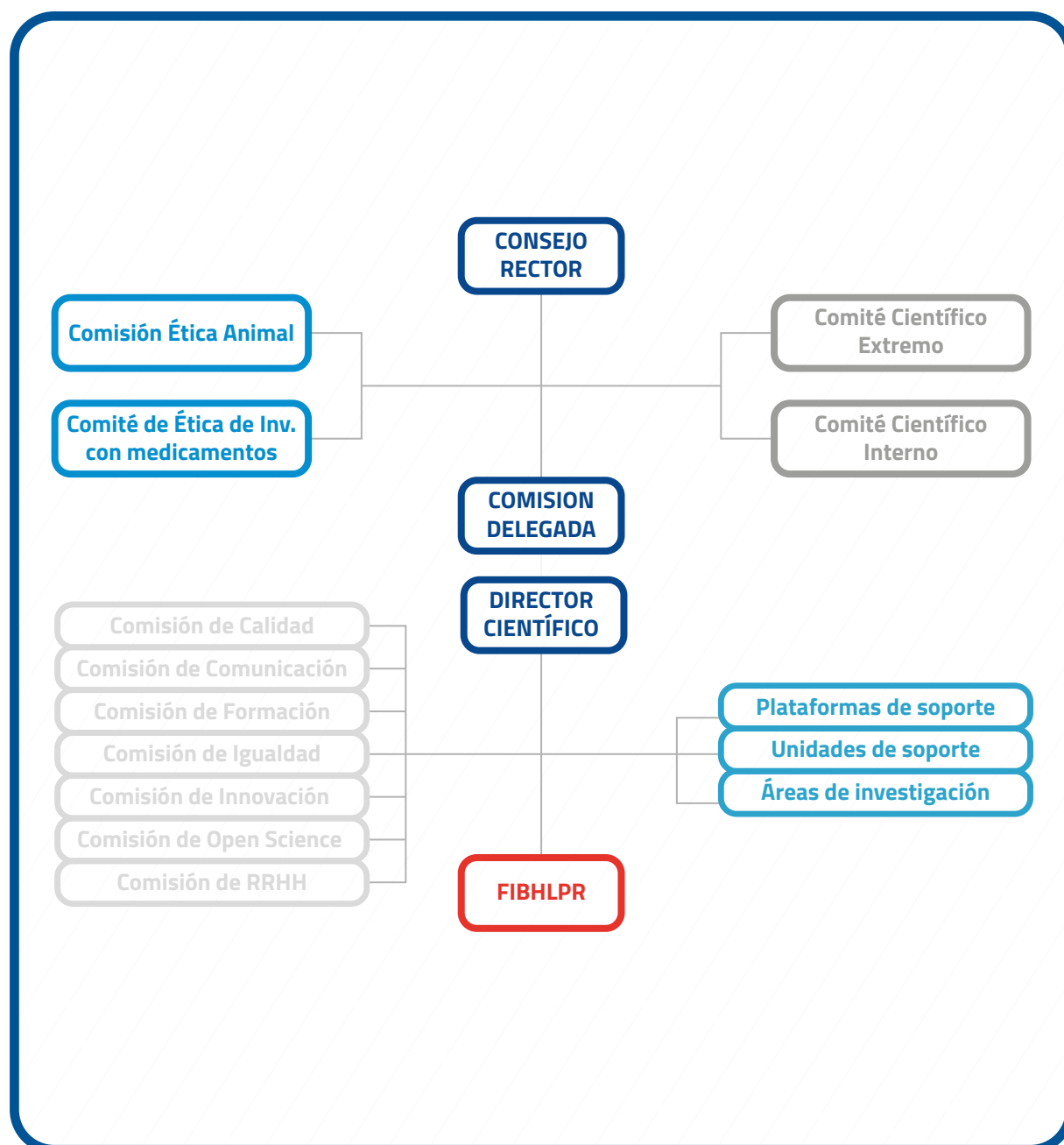


**Universidad Autónoma
de Madrid**





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Centro de Biología Molecular Severo Ochoa, Madrid

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Quality Coordinator, Hospital Universitario La Princesa

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Directress of Fundación de Investigación Biomédica Hospital Universitario La Princesa

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General Director, Hospital Universitario La Princesa

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Universidad Autónoma de Madrid

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Francisco Sánchez Madrid

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Purificación Muñoz Cánoves

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Clinical Pharmacology Department, Hospital Universitario La Princesa

VICE-CHAIRMAN**Enrique Alday Muñoz**

Anesthesiology Department, Hospital Universitario La Princesa

MEMBERS**Ángel Carlos Abanades Cuenca**

Patient representative

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Gynecology and Obstetrics Department, Hospital Universitario Santa Cristina.

Carmen del Arco Galán

Emergency Department, Hospital Universitario La Princesa

Sara Cardenal Rodríguez

Clinical Trials Department, FIB, Hospital Universitario La Princesa

José María Galván Román

Internal Medicine Department, Hospital Universitario La Princesa

Andrés López Romero

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Pablo Montalvo Rebuelta

Lawyer, ASJUSA

Carolina Pozuelo González

Pharmacy Department, Primary Care

Amelia Rodríguez Nogueiras

Nurse, Hospital Universitario La Princesa

Nuria Romero Laorden

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Eduardo Sánchez Sánchez

Internal Medicine Department, Hospital Universitario La Princesa

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Biobank, Hospital Universitario La Princesa

ADMINISTRATIVE SECRETARY**Raquel Moguer González****Ángel Núñez Pagán****FOUNDATION FOR BIOMEDICAL RESEARCH (FIBHLPR)****DIRECTRESS**

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PROJECTS MANAGEMENT DEPARTMENT

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Silvia González Herráez

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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:

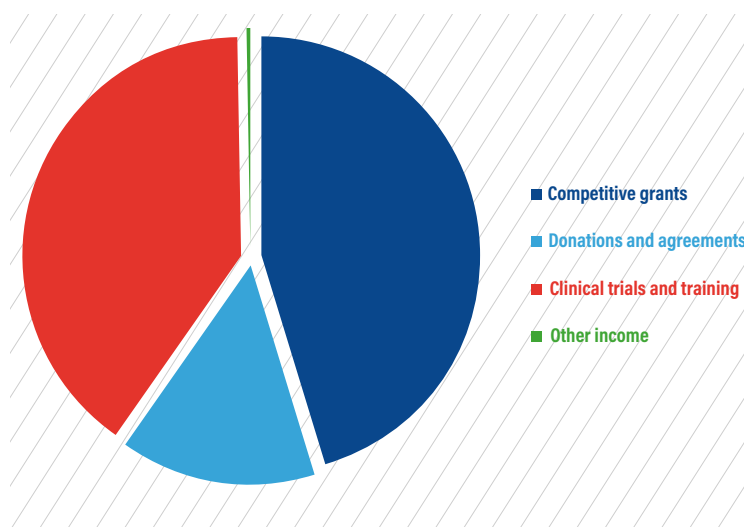
	2021	2020
Income	10.431.539	8.005.466
Expenses	10.416.006	7.990.091

ACTIVE ASSETS	
<i>Non-current active assest</i>	
Intangible fixed assets	59.693
Material fixed assets	423.884
<i>Current active assets</i>	
Debtors and Client to collect	1.068.391
Financial short term investments	0
Cash	17.424.174
Total Active Assets	18.976.142

PASSIVE ASSETS	
<i>Net Worth</i>	
Own funds	2.435.964
Non-refundable grants	622.261
<i>Non-current Passive Assets</i>	
Long term debts	0
<i>Current Passive Assets</i>	
Short term provisions	7.596.238
Refundable grants	7.342.432
Creditors to pay	491.012
Short term accruals	488.235
Total Passive Assets	18.976.142

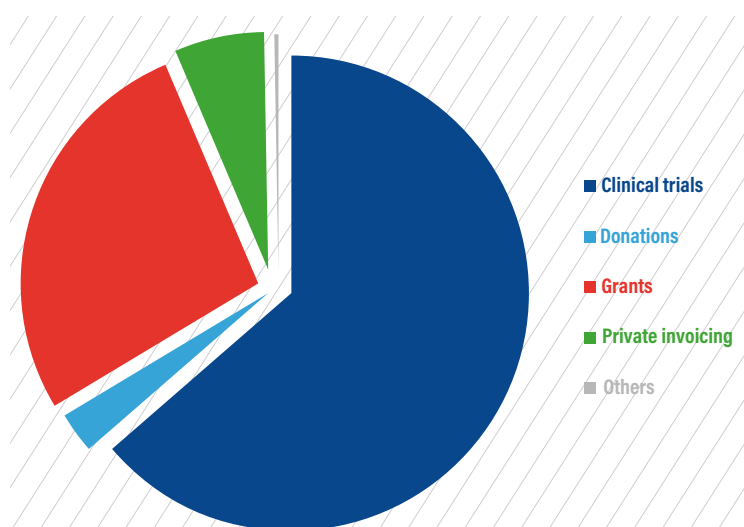
Below is shown the information on the income obtained by the Foundation for Biomedical Research, with the income sources grouped as obtained through competitive grants, clinical trials, private invoicing, donations, or other income.

Competitive grants	Donations and agreements	Clinical trials and training	Other income
2.897.979	1.066.828	6.466.730	2.000



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

PLATFORM SUPPORT

BIOBANK

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

SCIENTIFIC COORDINATOR

Mara Ortega Gómez

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Scientific Management Support Unit

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Isidoro González Álvaro

Rheumatology Department

José A. Jiménez Heffernan

Pathology Department

Carlos Manuel Olivier Gómez

Urology Department

TECHNICAL STAFF

Laura Gómez Cabañas

Ángel Lancho Sánchez

Plataforma ISCIII.



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

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 Ramirez

HIGH DEFINITION VIDEOMICROSCOPY

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

COORDINATOR

Noa B. Martín Cofreces

TECHNICIAN

Francisca Molina Jiménez

ANIMAL FACILITY

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

DIRECTOR

David Muñoz Valverde

DATA ANALYSIS UNIT

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

COORDINATOR**Guillermo J. Ortega Rabbione****BIOINFORMATICIAN****Jorge García Martínez****UNITS****BIOLOGICAL AND TARGETED
THERAPIES UNIT**

Biological therapies are the result of the large parallel progress in understanding the pathogenesis of chronic inflammatory and autoimmune diseases and in biotechnology. Their development is one of the most significant changes in recent decades. This Unit coordinates effective treatments (with high cost) ensuring their sustainability. The main idea is to contribute to the better use of biological therapies based on criteria of scientific thoroughness, safety, efficiency and cost-effectiveness.

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

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Alberto Morell Baladrón

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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

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**

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Marta de los Ríos Rodríguez

Marina Aldama Martin

Samuel Martin Vílchez

Alejandro de Miguel Cáceres

Soledad Rubio Domínguez

Jaime Pérez Calvo

María Eugenia Flores Ruiz

Yao Yuan Chang

SECRETARY-CTA

Ana del Río Moreno

Irene Román Martínez

Rebeca Manzanares López

Roberto Rodríguez Domínguez

PLATAFORMA ISCIII.



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

INNOVATION COMMITTEE

EMERGENCY DEPARTMENT

María Concepción Alonso Cerezo

Carmen del Arco Galán

CLINICAL ANALYSIS DEPARTMENT

Gustavo Casero Balboa

Management and general services Director

Elena Español Pueyo

Communication Department

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Fidel Illana Robles

General Manager, Hospital Universitario La Princesa

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María Elena Martín Pérez

General and Gastrointestinal Surgery

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Hospital Pharmacy Department Ramón Moreno Balsalobre

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Ancor Sanz García
Data Analysis Unit

Carmen Suarez Fernández
Internal Medicine Department

María Mercedes Vinuesa Sebastián
Quality Coordinator

SECRETARY INNOVATION COMMITTEE AND INNOVACION STAFF

Lara Pérez Martínez

PLATAFORMA ISCIII.



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

M^a Angels Figuerola Tejerina
Preventive Medicine Department

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 Management

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

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Elena Martín Pérez

Head of studies Resident Doctor

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Thoracic Surgery Service

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Jesús Capa Algara

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HUMAN RESOURCES COMMITTEE COORDINATOR

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HUMAN RESOURCES COMMITTEE

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Clinical Trial Department

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Gastroenterology Department,

Elena Español Pueyo

Communication Cabinet

Jorge Gómez Zamora

Humanization Director,
Hospital Universitario de
La Princesa

Sergio Luquero Bueno

Clinical Trial Unit

Noa Beatriz Martín Cofreces

Immunology Department

María del Rosario Ortiz de Urbina Barba

Directora Fundación para la
Investigación Biomédica
Hospital Universitario de
La Princesa

María Pilar Prieto Alaguero

Nursing Department

Nuria Romero Laorden

Medical Oncology Department

SECRETARY

Jesús Capa Algara

Research Management

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

Immunology Department

María del Mar Martín Cuenca

Human Resources Department

María del Rosario Ortiz de Urbina Barba

Directora Fundación para la Investigación
Biomédica Hospital Universitario de La Princesa

Nuria Romero Laorden

Medical Oncology Department

SECRETARY

Jesús Capa Algara

Research Management

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

Immunology Department

María del Mar Martín Cuenca

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Biomédica Hospital Universitario de La Princesa

Nuria Romero Laorden

Medical Oncology Department

SECRETARY

Jesús Capa Algara

Research Management



Research Areas

AREA 1:

CELLULAR AND MOLECULAR ETIOPATHOGENIC MECHANISMS IN INFLAMMATORY AND AUTOIMMUNE DISEASES

COORDINATOR

Francisco Sánchez Madrid

DEPUTY DIRECTRESS

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 2 – María Yáñez Mó

Suarez H, Andreu Z, Mazzeo C, Toribio V, Perez AE, Lopez S, Garcia S, Hurtado B, Morato E, Peñalaz L, Arribas EA, Tolentino T, Barreda G, Marina AI, Peinado H, Yanez M. **CD9 inhibition reveals a functional connection of extracellular vesicle secretion with mitophagy in melanoma cells.** J Extracell Vesicles. 2021. 10. (7):e12082. IF:25,841. (1).

Grupo 8 – María Josefa Calzada García

Sevilla J, Labrousse D, Fernandez C, Fernandez L, Barreira B, Mondejar G, Alfaro E, Lopez IP,

Perez S, Peces G, Pichel JG, Peinado VI, Cogol-ludo A, Calzada MJ. **Cigarette Smoke Directly Promotes Pulmonary Arterial Remodeling and Kv7.4 Channel Dysfunction.** Am J Respir Crit Care Med. 2021. 203. (10):p. 1290-1305. IF:21,405. (1).

Grupo 1 – Francisco Sánchez Madrid

Alcaraz A, Bustos E, Fernández I, Calzada D, Torralba D, Marina E, Lorenzo E, Vázquez E, de Albuquerque JB, Ruef N, Gómez MJ, Sánchez F, Dopazo A, Stein JV, Ramiro A, Sánchez F. **Immune synapse instructs epigenomic and transcriptomic functional reprogramming in dendritic cells.** Sci Adv. 2021. 7. (6):eabb9965. IF:14,143. (1).

Grupo 11 – Federico Mayor Menéndez

Cabezudo S, Sanz M, Caballero A, Tasset I, Rebollo E, Diaz A, Aragay AM, Cuervo AM, Mayor F, Ribas C. **G alpha q activation modulates autophagy by promoting mTORC1 signaling.** Nat Commun. 2021. 12. (1):4540. IF:14,919. (1).

Grupo 22 – Julio Ancochea Bermudez

Izquierdo JL, Almonacid C, González Y, Del Rio C, Ancochea J, Cárdenas R, Lumbreras S, Soriano JB. **The Impact of COVID-19 on Patients with Asthma.** Eur. Resp. J. 2021. 57. (3):2003142. IF:16,671. (1).

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**



Areas:

3



Research lines:

23



Research groups:

48



Personnel dedicated to research: 505



Men:

200



Women:

305

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 allergy-based 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 Gonzalez Rodríguez**

**AREA 2:
TRANSLATIONAL NEUROSCIENCE
COORDINATOR**

José Luis Ayuso Mateos

DEPUTY DIRECTRESS

María Dolores Ochoa Mazarro

General objectives:

1. Design, synthesis and characterization of new compounds with potential neuroprotective

effect on neurodegenerative diseases and stroke.

2. Search for biomarkers for early diagnosis, study of progression and response to treatment in these diseases.
3. Drug characterization in preclinical studies in animal models and in clinical trials in humans
4. Expand the knowledge about affective disorders in the population, studying risk factors, clinical evolution and response to treatment, in order to improve the mental health of the population.

Five most relevant publications of each area:

Grupo 16 - Manuela García López

Fernandez C, Luengo E, Trigo P, Garcia N, Negredo P, Lopez MG. **Protective role of microglial HO-1 blockade in aging: Implication of iron metabolism.** Redox Biol. 2021. 38. p. 101789-101789. IF:11,799. (1).

Grupo 35 – José Aurelio Vivancos Mora

Gonzalez A, Fanjul V, Ramos C, Serrano J, Bustamante M, Villa A, Alvarez C, Garcia del Alamo Y, Vivancos J, Gago AB. **Headache during SARS-CoV-2 infection as an early symptom associated with a more benign course of disease: a case-control study.** Eur J Neurol. 2021. 28. (10):p. 3426- 3436. IF:6,089. (1).

Grupo 33 – José Luis Ayuso Mateos

Cabello M, Rico LA, Martinez JC, Sanchez A, Caballero FF, Borges G, Mellor B, Haro JM, Prina M, Koskinen S, Ayuso JL. **The role of ageing in the wish to be dead: disentangling age, period and cohort effects in suicide ideation in European population.** Epidemiol Psychiatr Sci. 2021. 30. e17. IF:6,892. (1).

Grupo 41 – Javier Egea Maiquez

Rosa JM, Farre V, Ortega MC, Navarrete M, Lopez AB, Palomino A, Fernandez E, Vila V, Decouty C, Narros P, Clemente D, Egea J. **TLR4-pathway impairs synaptic number and cerebrovascular functions through astrocyte activation following traumatic brain injury.** Br J Pharmacol. 2021. 178. (17):p. 3395-3413. IF:8,740. (1).

Grupo 32 – Francisco Abad Santos

Zubiaur P, Soria P, Koller D, Navares M, Ochoa D, Almenara S, Saiz M, Mejia G, Villapalos G, Roman

M, Martin S, Abad F. **Impact of polymorphisms in transporter and metabolizing enzyme genes on olanzapine pharmacokinetics and safety in healthy volunteers.** BIOMED PHARMACOTHER. 2021. 133. p. 111087-111087. IF:6,530. (1).

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 DIRECTRESS

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 37 – Esteban Dauden Tello

Lozano M, Adlam D, García M, Sanz A, Vera P, Rivero F, Cuesta J, Bastante T, Baranowska AA, Vara A, Martin E, Vicente M, Martin P, Samani NJ, Sanchez F, Alfonso F, de la Fuente H. **Differential miRNAs in acute spontaneous coronary artery dissection: Pathophysiological insights from a potential biomarker.** EBioMedicine. 2021. 66. p. 103338-103338. IF:8,143. (1).

Grupo 48 – Jesús Jimenez Borreguero

Martin F, Lopez R, del Pozo C, Delgado JF, Ortega GJ, Castro MA, Sanz A. **Association of Prehospital Oxygen Saturation to Inspired Oxygen Ratio With 1-, 2-, and 7-Day Mortality.** JAMA Netw Open. 2021. 4. (4):e215700. IF:8,485. (1).

Grupo 38 – Javier Pérez Gisbert

Chaparro M, Garre A, Mesonero F, Rodríguez C, Barreiro M, Martínez J, Arroyo MT, Manceñido N, Sierra M, Vera I, Casanova MJ, Nos P, González C, Martínez T, Boscá M, Calafat M, Busquets D, Girona E, Llaó J, Martín MD, Piqueras M, Ramos L, Surís G, Bermejo F, Carbajo AY, Casas D, Fernández A, García MJ, Ginard D, Gutiérrez A, Hernández L, Lucendo AJ, Márquez L, Merino O, Rancel FJ, Taxonera C, López A, Rubio S, Domènech E, Gisbert JP. **Tofacitinib in Ulcerative Colitis: Real-world Evidence From the ENEIDA Registry.** J Crohns Colitis. 2021. 15. (1):p. 35-42. IF:9,071. (1).

Grupo 36 – Isidoro González Álvaro

Galván JM, Rodríguez SC, Roy E, Marcos A, Sánchez S, Fernández C, Alcaraz A, Mateu T, Rodríguez P, Sánchez I, Esparcia L, Martínez P, López C, Gabriele L, Del Campo L, Suárez C, Ancochea J, Canabal A, Albert P, Rodríguez DA, Aguilar JM, Del Arco C, de los Santos I, García L, de la Cámara R, Serra JM, Ramírez E, Alonso T, Landete P, Soriano JB, Martín E, Fraile A, Zurita ND, García R, Cardeñoso L, Sánchez F,

Alfranca A, Muñoz C, González I, REINMUN G. IL-6 serum levels predict severity and response to tocilizumab in COVID-19: An observational study. J Allergy Clin Immunol. 2021. 147. (1):p. 72-72. IF:10,793. (1).

Grupo 58 – Fernando Alfonso Manterola

Gatzov P, Monsuez JJ, Agoston G, Aschermann M, Badran HM, Cohen A, Huber K, Shlyakhto E, Ural D, Ferreira I, Alfonso F. Heart Failure 2019. Eur. Heart J. 2021. 42. (6):p. 557-559. IF:29,983. (1).

Line 1 Prognostic and predictor markers in autoimmune diseases.

Group 36 **Isidoro González Álvaro**

Group 37 **Esteban Daudén Tello**

Line 2 Esophagogastrintestinal 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 ²
Publications	636	3917,951	6,16	19	54	9	39	65	45
Articles	568	3466,192	6,10	20	54	8	39	65	42
Editorial	26	253,452	9,05	35	50	31	42	38	85
Review	42	216,307	5,15	5	57	5	36	83	64

New Projects:

New Research projects in 2021: 24.

New Human Resources grants in 2021: 9.

Clinical Trials:

Ongoing Clinical Trials during the year 2021: 420

Clinical Trial agreements signed in 2021: 121

Clinical Practice Guidelines:

Clinical practice guidelines: 15

Patents:

NATIONAL APPLICATIONS	NATIONAL PATENTS GRANTED	ROYALTY APPLICATIONS
2	1	2

Number of innovations generated by IIS (2021):

13 projects enrolled in the year and 36 in development phase in 2021.

*Total number innovation projects generated by IIS: 102.**Number of patents or useful models during 2021: 7* applications, 2 granted.*Total number of patents or useful models:*

70 applications, 14 granted and 5 licensed / transferred.

Number of spin-offs and start-ups created and active:

1 start-up created in 2018 and active as of December 31, 2020.

Theses:

Number of theses defended: 27

Number of theses with European mention: 6

Communication:

Number of sessions / communication conferences held: 38

Number of press releases: 31

Number of news published in printed press: 17

News in other audiovisual media (Radio TV): 25 (15 in TV, 10 in Radio)

Number of news in specialised and non-specialised digital media: 52

Number of Research Bulletin "Factor de Impacto" with the last scientific news with wide dissemination among patients, researchers and media: 2

Number of visitors to the website: 94.524

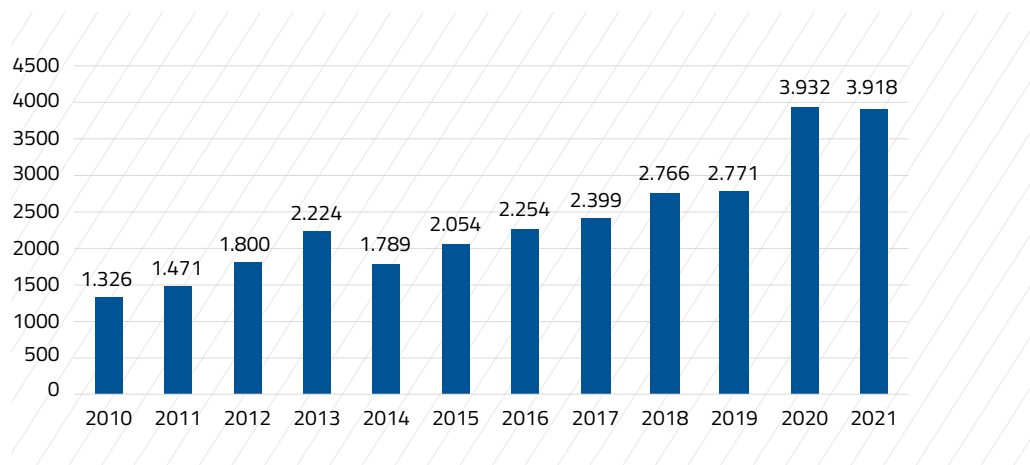
Evolution of staff according to their profile in the European Research Career:

	01/01/2021	31/12/2021
First Stage Researcher (R1):	53	61
Recognised Researcher (R2)	163	198
Established Researcher (R3)	31	37
Leading Researcher (R4)	70	70

PUBLICATIONS

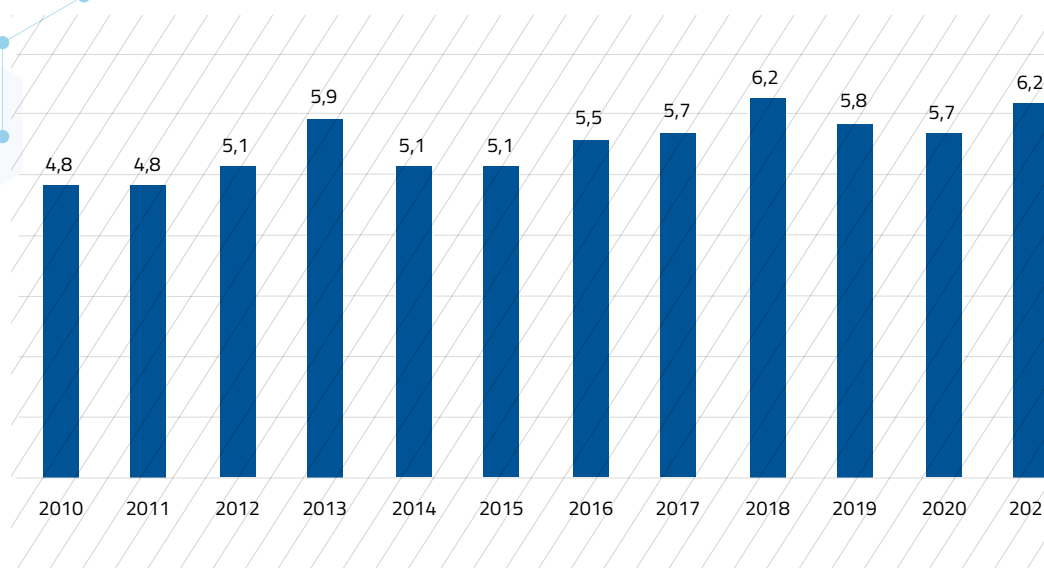
After the increase in the number of publications in the year 2020, due to the number of articles published on COVID-19, in 2021, 636 publications have been registered by members of the Institute, which represents a decrease of 10%. However, this decrease has not affected the cumulative impact factor, which remains stable compared to last year, once again close to 4,000 points. This figure indicates the high quality of the journals in which our work has been published.

The following graph shows the historical evolution from 2010 to 2020.



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 second highest in the history of our Institute, exceeding 6 points.

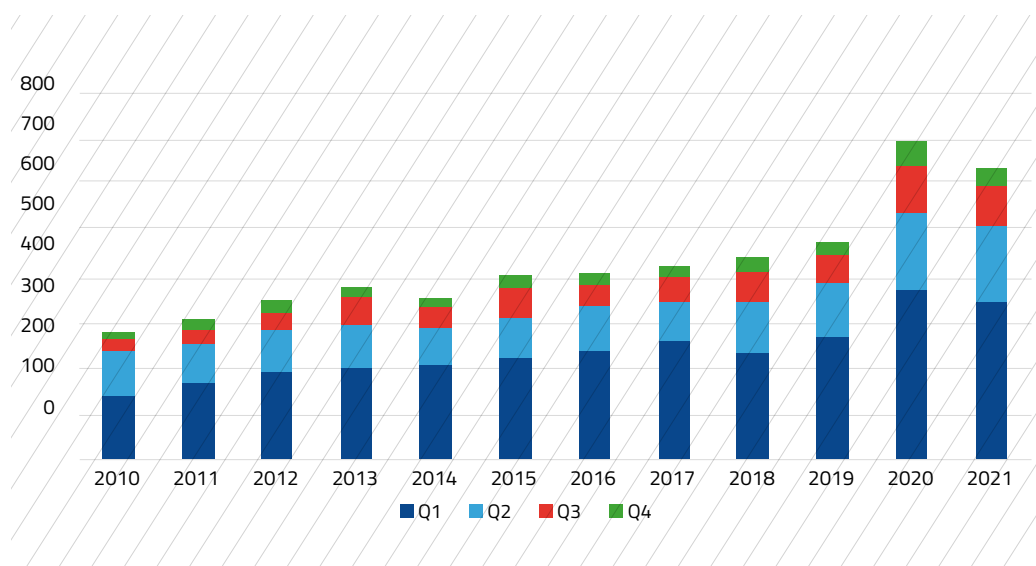
The following table shows the evolution of the mean impact factor from 2010 to 2021.



Regarding the distribution by quartiles, 54% of the all publications were published in first quartile journals and 80% of them were published in first and second quartile journals.

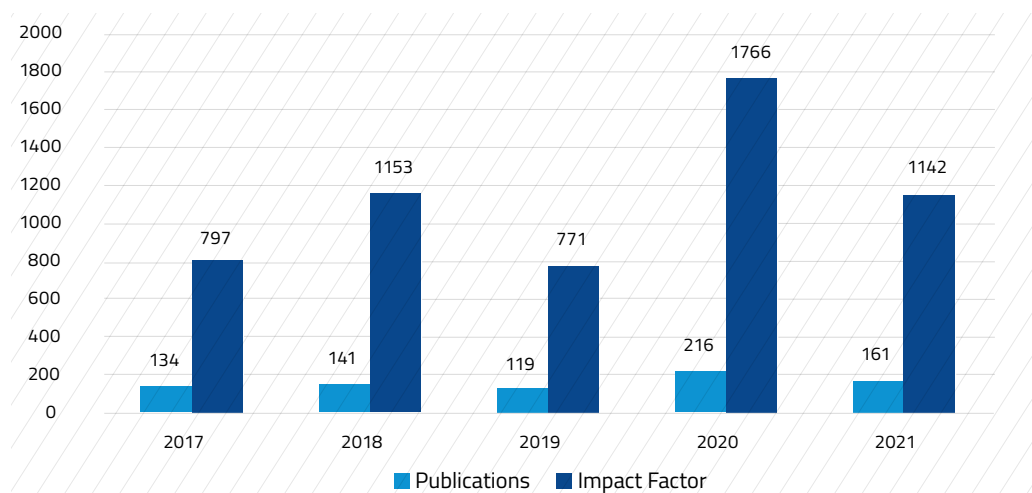
The following table shows a graph with the distribution of publications by quartile from 2010 to 2021.

A more detailed analysis relative to each area in the last 5 years shows that area 1 had the greatest increase of all areas in the number of publications during the year 2020 and the greatest decrease during 2021, while the scientific output of areas 2 and 3 in this year has remained fairly stable compared to the previous year. The lower number of publications in area 1 has also affected the cumulative impact factor of this area, while in area 2 and area 3 this parameter has increased considerably with respect to the previous year.



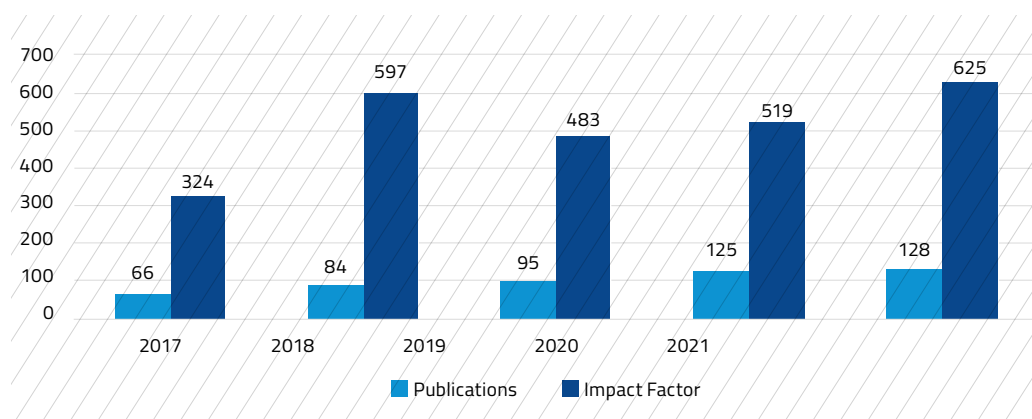
Area 1:

Cellular and molecular etiopathogenic mechanisms in inflammatory and autoimmune diseases



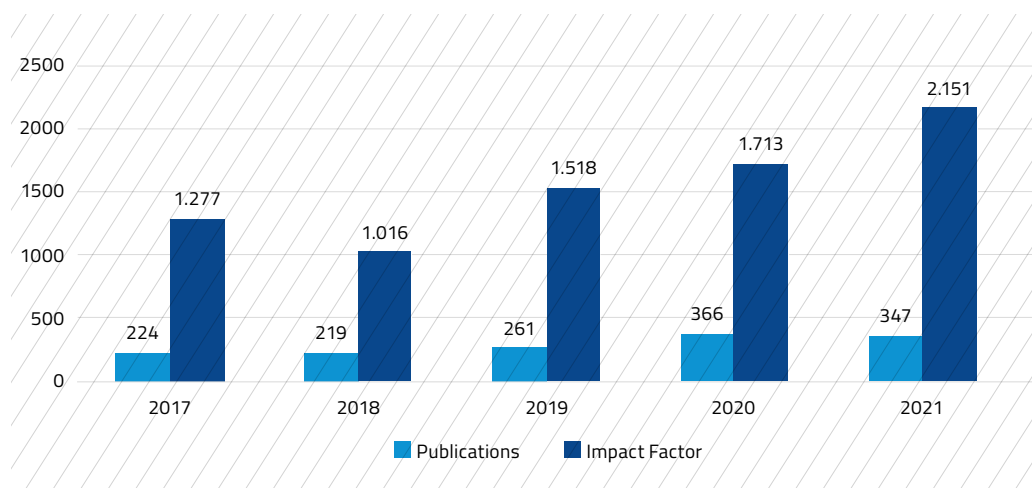
Area 2:

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	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
NEW ENGLAND JOURNAL OF MEDICINE	0028-4793	1	Q1	91,253
LANCET	0140-6736	1	Q1	79,323
JAMA-J AM MED ASSOC	0098-7484	1	Q1	56,274
JOURNAL OF CLINICAL ONCOLOGY	0732-183X	1	Q1	44,544
LANCET ONCOLOGY	1470-2045	1	Q1	41,316
LANCET RESPIRATORY MEDICINE	2213-2600	1	Q1	30,7
EUROPEAN HEART JOURNAL	0195-668X	6	Q1	29,983
JOURNAL OF EXTRACELLULAR VESICLES	2001-3078	1	Q1	25,841
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY	0735-1097	1	Q1	24,093
GUT	0017-5749	1	Q1	23,059
GASTROENTEROLOGY	0016-5085	1	Q1	22,682
AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	1073-449X	1	Q1	21,405
EUR UROL	0302-2838	1	Q1	20,096
ANNALS OF THE RHEUMATIC DISEASES	0003-4967	2	Q1	19,103
JOURNAL OF HEMATOLOGY & ONCOLOGY	1756-8722	1	Q1	17,388
ADVANCED SCIENCE	2198-3844	1	Q1	16,806
TRENDS IN IMMUNOLOGY	1471-4906	1	Q1	16,687
EUROPEAN RESPIRATORY JOURNAL	0903-1936	4	Q1	16,671
AUTOPHAGY	1554-8627	1	Q1	16,016
NATURE COMMUNICATIONS	2041-1723	2	Q1	14,919
JOURNAL OF CLINICAL INVESTIGATION	0021-9738	1	Q1	14,808
JACC-CARDIOVASCULAR IMAGING	1936-878X	1	Q1	14,805
SCIENCE ADVANCES	2375-2548	1	Q1	14,143
ANNU REV PHARMACOL	0362-1642	1	Q1	13,82
ALLERGY	0105-4538	4	Q1	13,146
TRENDS FOOD SCI TECH	0924-2244	1	Q1	12,563
EMBO MOLECULAR MEDICINE	1757-4676	2	Q1	12,137
REDOX BIOLOGY	2213-2317	2	Q1	11,799
LEUKEMIA	0887-6924	1	Q1	11,528
JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY	0190-9622	2	Q1	11,527
CLINICAL GASTROENTEROLOGY AND HEPATOLOGY	1542-3565	1	Q1	11,382
JACC-CARDIOVASCULAR INTERVENTIONS	1936-8798	1	Q1	11,195
J EXP CLIN CANC RES	1756-9966	1	Q1	11,161
BLOOD CANCER JOURNAL	2044-5385	1	Q1	11,037
ARTHRITIS & RHEUMATOLOGY	2326-5191	1	Q1	10,995
THE AMERICAN JOURNAL OF GASTROENTEROLOGY	0002-9270	1	Q1	10,864
JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY	0091-6749	2	Q1	10,793

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
ANNALS OF NEUROLOGY	0364-5134	1	Q1	10,422
MOVEMENT DISORD	0885-3185	1	Q1	10,338
NEW PHYTOL	1469-8137	1	Q1	10,152
DIABETOLOGIA	0012-186X	1	Q1	10,122
CARDIOVASCULAR DIABETOLOGY	1475-2840	1	Q1	9,951
HAEMATOLOGICA	0390-6078	1	Q1	9,941
ADVANCED HEALTHCARE MATERIALS	2192-2640	1	Q1	9,933
NEUROLOGY	0028-3878	1	Q1	9,91
AUTOIMMUNITY REVIEWS	1568-9972	1	Q1	9,754
ENVIRONMENT INTERNATIONAL	0160-4120	2	Q1	9,621
J CLIN ANESTH	0952-8180	1	Q1	9,452
CHEST	0012-3692	2	Q1	9,41
BRITISH JOURNAL OF DERMATOLOGY	0007-963	1	Q1	9,302
EUROPEAN JOURNAL OF CANCER	0959-8049	5	Q1	9,162
CRITICAL CARE	1364-8535	1	Q1	9,097
CLINICAL INFECTIOUS DISEASES	1058-4838	4	Q1	9,079
JOURNAL OF CROHNS & COLITIS	1873-9946	2	Q1	9,071
J CHILD PSYCHOL PSYC	0021-9630	1	Q1	8,982
EUROPEAN RESPIRATORY REVIEW	0905-9180	2	Q1	8,839
BMC MEDICINE	1741-7015	1	Q1	8,775
BRITISH JOURNAL OF PHARMACOLOGY	0007-1188	1	Q1	8,74
JOURNAL OF INVESTIGATIVE DERMATOLOGY	0022-202X	1	Q1	8,551
JAMA NETWORK OPEN	2574-3805	1	Q1	8,485
NEUROLOGY-NEUROIMMUNOLOGY & NEUROINFLAMMATION	2332-7812	2	Q1	8,485
CAN MED ASSOC J	0820-3946	1	Q1	8,262
ALIMENTARY PHARMACOLOGY & THERAPEUTICS	0269-2813	4	Q1	8,171
EBIOMEDICINE	2352-3964	2	Q1	8,143
CLINICAL MICROBIOLOGY AND INFECTION	1198-743X	3	Q1	8,067
STROKE	0039-2499	1	Q1	7,914
NEUROPSYCHOPHARMACOL	0893-133X	1	Q1	7,855
ACTA NEUROPATHOLOGICA COMMUNICATIONS	2051-5960	1	Q1	7,801
CLINICAL NUCLEAR MEDICINE	0363-9762	1	Q1	7,794
NEUROTHERAPEUTICS	1933-7213	1	Q1	7,62
RHEUMATOLOGY	1462-324	3	Q1	7,58
FRONTIERS IN IMMUNOLOGY	1664-3224	5	Q1	7,561
TOB CONTROL	0964-4563	1	Q1	7,552
JOURNAL OF MEDICINAL CHEMISTRY	0022-2623	1	Q1	7,446
BMC BIOL	1741-7007	1	Q1	7,431

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
AMERICAN JOURNAL OF CLINICAL DERMATOLOGY	1175-561	1	Q1	7,403
J HEADACHE PAIN	1129-2369	1	Q1	7,277
INT J EPIDEMIOL	0300-5771	1	Q1	7,196
JOURNAL OF INVESTIGATIONAL ALLERGOLOGY & CLINICAL IMMUNOLOGY	1018-9068	3	Q1	7,033
BRITISH JOURNAL OF HAEMATOLOGY	0007-1048	2	Q1	6,998
CANCER IMMUNOLOGY IMMUNOTHERAPY	0340-7004	1	Q1	6,968
BRITISH JOURNAL OF SURGERY	0007-1323	2	Q1	6,939
EPIDEMIOLOGY AND PSYCHIATRIC SCIENCES	2045-7960	2	Q1	6,892
EUROPEAN HEART JOURNAL-CARDIOVASCULAR IMAGING	2047-2404	1	Q1	6,875
BLOOD ADVANCES	2473-9529	1	Q1	6,799
FRONTIERS IN CELL AND DEVELOPMENTAL BIOLOGY	2296-634X	2	Q1	6,684
EUROPEAN JOURNAL OF ENDOCRINOLOGY	0804-4643	1	Q1	6,664
CANCERS	2072-6694	5	Q1	6,639
MOLECULAR ONCOLOGY	1574-7891	2	Q1	6,603
CELLS	2073-4409	7	Q2	6,6
CONTACT DERMATITIS	0105-1873	3	Q1	6,6
FRONTIERS IN NUTRITION	2296-861X	1	Q1	6,576
EUROINTERVENTION	1774-024X	5	Q1	6,534
BIOMED PHARMACOTHER	0753-3322	3	Q1	6,53
REVIEWS IN ENDOCRINE & METABOLIC DISORDERS	1389-9155	1	Q1	6,514
ENVIRON RES	0013-9351	1	Q1	6,498
TRANSLATIONAL LUNG CANCER RESEARCH	2218-6751	1	Q1	6,498
BREAST CANCER RES	1465-5411	1	Q1	6,488
CLIN PHARMACOKINET	0312-5963	1	Q1	6,447
PEDIATRIC ALLERGY AND IMMUNOLOGY	0905-6157	3	Q1	6,377
PHARMACEUTICS	1999-4923	2	Q1	6,321
ANTIOXIDANTS	2076-3921	6	Q1	6,312
ACTA PHYSIOLOGICA	1748-1708	1	Q1	6,311
RADIOTHERAPY AND ONCOLOGY	0167-8140	1	Q1	6,28
FRONTIERS IN ONCOLOGY	2234-943X	2	Q2	6,244
EUROPEAN JOURNAL OF NEUROLOGY	1351-5101	4	Q1	6,089
BIOMEDICINES	2227-9059	5	Q1	6,081
EUROPEAN UROLOGY FOCUS	2405-4569	1	Q1	5,996
NEUROBIOL DIS	0969-9961	1	Q1	5,996
HEART	1355-6037	3	Q1	5,994
JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM	0021-972X	3	Q1	5,958
INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	1422-67	12	Q1	5,923
HEADACHE	0017-8748	1	Q1	5,887

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
PHARMACEUTICALS	1424-8247	4	Q1	5,863
MABS-AUSTIN	1942-862	1	Q1	5,857
MOL CANCER RES	1541-7786	1	Q2	5,852
LIVER INTERNATIONAL	1478-3223	2	Q2	5,828
MOLECULAR NUTRITION & FOOD RESEARCH	1613-4125	1	Q1	5,82
FRONTIERS IN PHARMACOLOGY	1663-9812	4	Q1	5,811
JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY	0305-7453	2	Q1	5,79
ALLERGY ASTHMA IMMUN	2092-7355	1	Q2	5,764
DISEASE MODELS & MECHANISMS	1754-8403	1	Q1	5,758
NUTRIENTS	2072-6643	6	Q1	5,717
LUNG CANCER	0169-5002	1	Q1	5,705
ANNALS OF THE NEW YORK ACADEMY OF SCIENCES	0077-8923	1	Q1	5,691
AGING-US	1945-4589	1	Q1	5,682
DIABETES RESEARCH AND CLINICAL PRACTICE	0168-8227	1	Q1	5,602
BMJ GLOBAL HEALTH	2059-7908	1	Q1	5,558
FRONTIERS IN ENDOCRINOLOGY	1664-2392	2	Q1	5,555
EUROPEAN JOURNAL OF IMMUNOLOGY	0014-2980	2	Q2	5,532
SEMINARS IN ARTHRITIS AND RHEUMATISM	0049-172	2	Q1	5,532
JOURNAL OF THE AMERICAN HEART ASSOCIATION	2047-9980	2	Q1	5,501
BONE MARROW TRANSPLANTATION	0268-3369	6	Q1	5,483
ISCIENCE	2589-42	2	Q1	5,458
MECH AGEING DEV	0047-6374	2	Q1	5,432
BIOCHEMICAL SOCIETY TRANSACTIONS	0300-5127	1	Q2	5,407
DERMATOLOGY	1018-8665	1	Q1	5,366
THERAPEUTIC ADVANCES IN MUSCULOSKELETAL DISEASE	1759-720X	2	Q1	5,346
INFLAMMATORY BOWEL DISEASES	1078-998	2	Q2	5,325
FRONTIERS IN CELLULAR AND INFECTION MICROBIOLOGY	2235-2988	2	Q1	5,293
NEUROPHARMACOLOGY	0028-3908	1	Q1	5,251
JOURNAL OF INFECTIOUS DISEASES	0022-1899	1	Q1	5,226
ARTHRITIS RESEARCH & THERAPY	1478-6354	1	Q2	5,156
RMD OPEN	2056-5933	2	Q2	5,117
JOURNAL OF NEUROSURGERY	0022-3085	2	Q1	5,115
FRONTIERS IN MEDICINE	2296-858X	5	Q1	5,091
REVISTA ESPANOLA DE CARDIOLOGIA	0300-8932	3	Q1	5,078
PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY	0278-5846	1	Q1	5,067
PAIN PHYSICIAN	1533-3159	1	Q1	4,97
JOURNAL OF PERSONALIZED MEDICINE	2075-4426	5	Q1	4,945
JOINT BONE SPINE	1297-319X	1	Q2	4,929
NEUROENDOCRINOLOGY	0028-3835	1	Q2	4,914
PSYCHONEUROENDOCRINOLOGY	0306-4530	2	Q1	4,905

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
BIOMOLECULES	2218-273X	3	Q2	4,879
ARCHIVOS DE BRONCONEUMOLOGIA	0300-2896	10	Q2	4,872
INT J EAT DISORDER	0276-3478	1	Q1	4,861
JOURNAL OF AFFECTIVE DISORDERS	0165-327	3	Q1	4,839
J PSYCHIATR RES	0022-3956	2	Q1	4,791
REVISTA ESPANOLA DE CARDIOLOGIA	0300-8932	8	Q2	4,753
AMERICAN HEART JOURNAL	0002-8703	1	Q2	4,749
ANNALS OF MEDICINE	0785-3890	2	Q1	4,709
EUROPEAN HEART JOURNAL-ACUTE CARDIOVASCULAR CARE	2048-8734	1	Q2	4,696
EUROPEAN JOURNAL OF CLINICAL INVESTIGATION	0014-2972	2	Q1	4,686
JOURNAL OF RHEUMATOLOGY	0315-162X	2	Q2	4,666
ANTIBIOTICS	2079-6382	5	Q2	4,639
EUROPEAN JOURNAL OF INTERNAL MEDICINE	0953-6205	2	Q1	4,624
UNITED EUROPEAN GASTROENTEROLOGY JOURNAL	2050-6406	2	Q2	4,623
FRONTIERS IN PHYSIOLOGY	1664-042X	2	Q1	4,566
OSTEOPOROSIS INTERNATIONAL	0937-941X	2	Q2	4,507
CLINICAL AND EXPERIMENTAL RHEUMATOLOGY	0392-856X	6	Q2	4,473
EXPERT REVIEW OF CLINICAL IMMUNOLOGY	1744-666X	2	Q2	4,473
JOURNAL OF ALZHEIMERS DISEASE	1387-2877	1	Q2	4,472
CANCER MEDICINE	2045-7634	1	Q2	4,452
CKJ: CLINICAL KIDNEY JOURNAL	2048-8505	1	Q1	4,452
CLINICAL GENETICS	0009-9163	1	Q2	4,438
ACTA DERMATO-VENEREOLÓGICA	0001-5555	3	Q1	4,437
EUROPEAN JOURNAL OF PHARMACOLOGY	0014-2999	1	Q2	4,432
VACCINES	2076-393X	1	Q2	4,422
ACS CHEMICAL NEUROSCIENCE	1948-7193	1	Q2	4,418
MOLECULES	1420-3049	2	Q2	4,411
THERAPEUTIC ADVANCES IN GASTROENTEROLOGY	1756-283X	1	Q2	4,409
SCIENTIFIC REPORTS	2045-2322	10	Q1	4,38
BRITISH JOURNAL OF CLINICAL PHARMACOLOGY	0306-5251	1	Q2	4,34
MULTIPLE SCLEROSIS AND RELATED DISORDERS	2211-348	1	Q2	4,339
EUROPEAN JOURNAL OF ANAESTHESIOLOGY	0265-215	2	Q2	4,33
CLINICAL ORTHOPAEDICS AND RELATED RESEARCH	0009-921X	1	Q1	4,291
COMMUN NONLINEAR SCI	1007-5704	1	Q1	4,26
JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION	0391-4097	1	Q2	4,256
EXPERT OPINION ON DRUG SAFETY	1474-338	2	Q2	4,25
JOURNAL OF CLINICAL MEDICINE	2077-383	20	Q1	4,241
INTERNATIONAL JOURNAL OF CARDIOLOGY	0167-5273	6	Q2	4,164

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
JOURNAL OF CARDIOVASCULAR TRANSLATIONAL RESEARCH	1937-5387	2	Q2	4,132
OBESITY SURGERY	0960-8923	1	Q1	4,129
MICROORGANISMS	2076-2607	3	Q2	4,128
DIGESTIVE AND LIVER DISEASE	1590-8658	1	Q2	4,088
HEALTH PLACE	1353-8292	1	Q1	4,078
MOLECULAR DIAGNOSIS & THERAPY	1177-1062	2	Q2	4,074
J BONE ONCOL	2212-1374	1	Q3	4,072
J GLOB ANTIMICROB RE	2213-7165	1	Q2	4,035
PREVENTIVE MEDICINE	0091-7435	1	Q1	4,018
EUR J CLIN NUTR	0954-3007	1	Q2	4,016
NUTRITION	0899-9007	1	Q2	4,008
FRONTIERS IN NEUROLOGY	1664-2295	2	Q2	4,003
SURGERY	0039-6060	1	Q1	3,982
EXPERIMENTAL DERMATOLOGY	0906-6705	1	Q2	3,96
WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY	1562-2975	1	Q2	3,941
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS	0731-7085	1	Q2	3,935
ADDICTIVE BEHAVIORS	0306-4603	1	Q1	3,913
EMERGENCIAS	1137-6821	1	Q1	3,881
ADVANCES IN THERAPY	0741-238X	2	Q2	3,847
LIFE	0024-3019	3	Q2	3,817
TECH COLOPROCTOL	1123-6337	1	Q1	3,781
EXPERT REVIEW OF RESPIRATORY MEDICINE	1747-6348	1	Q2	3,772
PAIN MEDICINE	1526-2375	2	Q2	3,75
CHEM RES TOXICOL	0893-228X	1	Q2	3,739
JOURNAL OF VIRAL HEPATITIS	1352-504	1	Q2	3,728
FRONTIERS IN PUBLIC HEALTH	2296-2565	1	Q1	3,709
DIAGNOSTICS	2075-4418	2	Q2	3,706
EUR J TRAUMA EMERG S	1863-9933	1	Q1	3,693
ANNALS OF HEMATOLOGY	0939-5555	1	Q2	3,673
AGING & MENTAL HEALTH	1360-7863	2	Q1	3,658
PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY	0031-6768	1	Q2	3,657
HPB	1365-182X	2	Q1	3,647
ENDOCRINE	1355-008X	4	Q3	3,633
JOURNAL OF NEUROENDOCRINOLOGY	0953-8194	1	Q3	3,627
RHEUMATOLOGY AND THERAPY	2198-6576	2	Q3	3,494
PATHOGENS	2076-817	1	Q2	3,492
SLEEP MEDICINE	1389-9457	1	Q2	3,492
CLINICAL ENDOCRINOLOGY	0300-664	2	Q3	3,478
CLINICAL AND EXPERIMENTAL DERMATOLOGY	0307-6938	1	Q2	3,47
JOURNAL OF GASTROINTESTINAL SURGERY	1091-255X	1	Q2	3,452
NURS EDUC TODAY	0260-6917	1	Q1	3,442
FRONTIERS IN PEDIATRICS	2296-2360	1	Q1	3,418
CLINICAL & TRANSLATIONAL ONCOLOGY	1699-048X	6	Q3	3,405
CLINICAL THERAPEUTICS	0149-2918	1	Q3	3,396

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
BRAIN SCIENCES	2076-3425	2	Q3	3,394
INTERNATIONAL JOURNAL OF ENVIRONMENTAL	1661-7827	3	Q1	3,39
RESEARCH AND PUBLIC HEALTH				
JOURNAL OF DERMATOLOGICAL TREATMENT	0954-6634	1	Q2	3,359
CANCER CHEMOTH PHARM	0344-5704	1	Q3	3,333
JOURNAL OF GERIATRIC CARDIOLOGY	1671-5411	1	Q2	3,327
LARYNGOSCOPE	0023-852X	1	Q1	3,325
REVISTA DE PSIQUIATRIA Y SALUD MENTAL	1888-9891	2	Q2	3,318
NEUROLOGICAL SCIENCES	1590-1874	3	Q2	3,307
LEUKEMIA & LYMPHOMA	1042-8194	3	Q3	3,28
EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES	0934-9723	1	Q3	3,267
DERMATOLOGY AND THERAPY	2193-8210	2	Q2	3,264
PLOS ONE	1932-6203	6	Q2	3,24
CLINICAL LYMPHOMA MYELOMA & LEUKEMIA	2152-2650	1	Q3	3,231
J EPIDEMIOL	0917-5040	1	Q2	3,211
ACTA NEUROLOGICA SCANDINAVICA	0001-6314	1	Q3	3,209
J ADV NURS	0309-2402	1	Q1	3,187
HEALTH AND QUALITY OF LIFE OUTCOMES	1477-7525	1	Q2	3,186
EUROPEAN JOURNAL OF PEDIATRICS	0340-6199	2	Q1	3,183
HIV MEDICINE	1464-2662	1	Q3	3,18
JOURNAL OF PAIN RESEARCH	1178-7090	1	Q3	3,133
NEUROLOGIA (BARCELONA, SPAIN)	0213-4853	8	Q3	3,109
BMC INFECTIOUS DISEASES	1471-2334	1	Q3	3,09
PREHOSP EMERG CARE	1090-3127	1	Q1	3,077
PSYCHOLOGY & HEALTH	0887-446	2	Q2	3,073
NEUROSCIENCE LETTERS	0304-3940	1	Q3	3,046
JOURNAL OF HUMAN HYPERTENSION	0950-9240	1	Q3	3,012
CIRCULATION JOURNAL	1346-9843	1	Q3	2,993
FRONTIERS IN PSYCHOLOGY	1664-1078	1	Q2	2,988
CLINICAL RHEUMATOLOGY	0770-3198	1	Q3	2,98
EPILEPSY & BEHAVIOR	1525-5050	1	Q2	2,937
REVIEWS IN CARDIOVASCULAR MEDICINE	1530-6550	1	Q3	2,93
J MED ETHICS	0306-6800	1	Q1	2,916
JOURNAL OF THORACIC DISEASE	2072-1439	1	Q3	2,895
J INT NEUROPSYCH SOC	1355-6177	1	Q2	2,892
HORM-INT J ENDOCRINO	1109-3099	2	Q3	2,885
NPI PRIMARY CARE RESPIRATORY MEDICINE	2055-1010	1	Q2	2,871
HORMONE RESEARCH IN PAEDIATRICS	1663-2818	1	Q2	2,852
HEALTH SOC CARE COMM	0966-410	1	Q1	2,821
J CLIN APHERESIS	0733-2459	1	Q3	2,821
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE	0732-8893	1	Q3	2,803
EUROPEAN JOURNAL OF EMERGENCY MEDICINE	0969-9546	2	Q2	2,799
UPDATES IN SURGERY	2038-131X	1	Q2	2,797

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
BMC MED INFORM DECIS	1472-6947	1	Q3	2,796
AGEING SOC	0144-686X	2	Q2	2,786
AMERICAN JOURNAL OF CARDIOLOGY	0002-9149	2	Q3	2,778
PATIENT PREFERENCE AND ADHERENCE	1177-889X	1	Q2	2,711
BRAIN BEHAV	2162-3279	1	Q3	2,708
PARKINSONS DIS-US	2090-8083	1	Q3	2,704
OPERATIVE NEUROSURGERY	2332-4252	1	Q2	2,703
J APPL RES INTELLECT	1360-2322	1	Q1	2,7
BMJ OPEN	2044-6055	2	Q2	2,692
CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS	1522-1946	2	Q3	2,692
J THEOR BIOL	0022-5193	1	Q2	2,691
RHEUMATOLOGY INTERNATIONAL	0172-8172	1	Q4	2,631
JOURNAL OF CLINICAL DENSITOMETRY	1094-6950	1	Q4	2,617
J ANAT	0021-8782	1	Q2	2,61
MED BIOL ENG COMPUT	0140-118	1	Q2	2,602
EUR J OPHTHALMOL	1120-6721	2	Q3	2,597
INJURY-INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED	0020-1383	2	Q2	2,586
AM J SURG	0002-9610	1	Q2	2,565
PHARMACOGENOMICS	1462-2416	1	Q3	2,533
JOURNAL OF ASTHMA	0277-903	1	Q3	2,515
INTERNATIONAL JOURNAL OF CLINICAL PRACTICE	1368-5031	1	Q2	2,503
J CLIN MONIT COMPUT	1387-1307	1	Q3	2,502
CLINICAL, COSMETIC AND INVESTIGATIONAL DERMATOLOGY	1178-7015	1	Q3	2,489
BMC NEUROLOGY	1471-2377	1	Q3	2,474
AMERICAN JOURNAL OF EMERGENCY MEDICINE	0735-6757	2	Q2	2,469
CHRONIC RESPIRATORY DISEASE	1479-9723	1	Q4	2,444
MEDICINA-LITHUANIA	1010-660X	1	Q2	2,43
SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY	0036-5521	1	Q4	2,425
DIGEST DIS	0257-2753	1	Q4	2,404
ACTA NEUROL BELG	0300-9009	1	Q3	2,396
SURG-J R COLL SURG E	1479-666X	1	Q3	2,392
GROWTH HORMONE & IGF RESEARCH	1096-6374	1	Q4	2,372
BMC MUSCULOSKEL DIS	1471-2474	1	Q2	2,362
INTERNATIONAL JOURNAL OF CARDIOVASCULAR IMAGING	1569-5794	3	Q3	2,357
ACTA CYTOLOGICA	0001-5547	1	Q3	2,319
BMC CARDIOVASCULAR DISORDERS	1471-2261	1	Q3	2,298
TRIALS	1745-6215	1	Q4	2,279
APPL NEUROPSYCH-ADUL	2327-9095	1	Q3	2,248
TRANSPLANT INFECTIOUS DISEASE	1398-2273	1	Q3	2,228
BMC ANESTHESIOLOG	1471-2253	1	Q4	2,217
INT J TECHNOL ASSESS	0266-4623	1	Q3	2,188
JOURNAL OF CARDIOVASCULAR MEDICINE	1558-2027	1	Q3	2,16
SURGICAL INFECTIONS	1096-2964	1	Q3	2,15
ACTA ANAESTH SCAND	0001-5172	1	Q4	2,105

JOURNAL	ISSN	TOTAL OF PUBLICATION	QUARTIL	IMPACT FACTOR
WORLD NEUROSURGERY	1878-8750	1	Q3	2,104
GASTROENTEROLOGIA Y HEPATOLOGIA	0210-5705	5	Q4	2,102
PHARMACOGENETICS AND GENOMICS	1744-6872	1	Q4	2,089
UROLOGIA INTERNATIONALIS	0042-1138	1	Q3	2,089
REVISTA ESPAÑOLA DE ENFERMEDADES DIGESTIVAS	1130-108	4	Q4	2,086
CYTOPATHOLOGY	0956-5507	2	Q3	2,073
SURG INNOV	1553-3506	1	Q3	2,058
NEFROLOGIA	0211-6995	6	Q4	2,033
JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY	0278-2391	1	Q3	1,895
MEDICINE	0025-7974	1	Q3	1,889
CLIN NEUROL NEUROSUR	0303-8467	1	Q3	1,876
THERAPEUTIC APHERESIS AND DIALYSIS	1744-9979	1	Q4	1,762
CIRUGIA ESPAÑOLA	0009-739X	3	Q3	1,653
JOURNAL OF CUTANEOUS PATHOLOGY	0303-6987	2	Q4	1,587
DIAGNOSTIC CYTOPATHOLOGY	8755-1039	2	Q4	1,582
APPL ARTIF INTELL	0883-9514	1	Q3	1,58
JOURNAL OF STOMATOLOGY ORAL AND MAXILLOFACIAL SURGERY	2468-8509	1	Q4	1,569
REVISTA CLINICA ESPAÑOLA	0014-2565	3	Q3	1,556
ANALES DE PEDIATRIA	1695-4033	2	Q4	1,5
CORONARY ARTERY DISEASE	0954-6928	4	Q4	1,439
JOURNAL OF ELECTROCARDIOLOGY	0022-736	1	Q4	1,438
INT J CLIN PHARM TH	0946-1965	1	Q4	1,366
REVISTA IBEROAMERICANA DE MICOLOGIA	1130-1406	1	Q4	1,044

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.

EUROPEAN PATENT APPLICATIONS

Título: Treatment of NRF2-related diseases

Number: EP21382025.1

Date of applicant: 15/01/2021

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (5%), CSIC (42,5%), UAM (37,5%), Universidad Miguel Hernández de Elche (15%)

Inventors: Antonio Cuadrado Pastor, Raquel Fernández Ginés, Jose Antonio Encinar, Rafael León Martínez, Juan Felipe Franco González, Manuela García López, Maria Isabel Rodríguez Franco, Ana Isabel Rojo Sanchís.

NATIONAL PATENT APPLICATIONS

Title: Método de detección temprano de daño hepático me-diante la proteína morfogenética ósea 2 (BMP2) EN BIOPSIA LÍ-QUIDA

Number: P202130777

Date of applicant: 10/08/2021

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (100%) **Inventors:** Patricia Maraño Barnusell, Paloma Narros Fer-Nández, Esther Rey Fernández, Carmelo García Monzón, Javier Egea Máiquez, Águeda González Rodríguez

Title: Derivados de n-sulfonilureas y su uso terapéutico

Number: P202130839

Date of applicant: 08/09/2021

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (90%), Consejo Superior de Investigaciones Científicas (CSIC) (10%)

Inventors: Francisco Javier Egea Máiquez, Paloma Narros Fernández, Lau-ra Cerrada Gálvez, Alejandra Palomino Antolín, Víctor Farré Alins, Celine Decouty Pérez, Ana Belén López Rodríguez, José Luis Marco Contelles.

NATIONAL PATENT GRANTED

Title: Compuestos derivados de 2-iodo-7-(((2-(5-metoxi-1h-indol-3-il)etil)amino)metil)-1-alquil/aril-6,7,7a,8-tetrahidro-3h-pirrol[2,1-j]quinolina-3,9(5h)-diona como agentes antioxidantes, inductores de nrf2 y moduladores nicotínicos para el tratamiento de enfermedades neurodegenerativas.

Number: P201930190

Grant date: 02/02/2021

Owners/s: Universidad Complutense de Madrid (3%), Universidad Autónoma de Madrid (12%) Fundación de Investigación Hospital Universitario de La Princesa (85%).

Inventors: Rafael León Martínez, Sheila Abril Comesaña, Patrycja Michalska, Izaskun Buendia Abaitua, Mercedes Salaces Sánchez, Jose Carlos Menéndez Ramos y Manuela García López.

Title: Compuestos agonistas nicotínicos y antioxidantes para el tratamiento de enfermedades neurodegenerativas.

Number: P201930908

Grant date: 03/11/2021

Owners/s: Fundación de Investigación Hospital Universitario de La Princesa (79%) Universidad Autónoma de Madrid (16%) y Universidad Complutense de Madrid (5%)

Inventors: Rafael León Martínez, Sheila Abril Comesaña, Pablo Duarte Florez, Enrique Crisman Vigil, Patrycja Michalska, Mercedes Salaces Sánchez y José Carlos Menéndez Ramos.



COMPETITIVE PROJECTS

GRANTS:

Funding Institution	Call	Calls Granted
Instituto de Salud Carlos III	Proyectos de Investigación	8
	Investigación Clínica Independiente	2
	Proyecto de Desarrollo Tecnológico	1
	Proyectos asociados Contrato Miguel Servet	1
	RICORS	3
	Infraestructura de Investigación	1
Mutua Madrileña	Proyectos de Investigación	3
Fundación Jerome Lejeune	Proyectos de Investigación	1
Agencia Estatal de Investigación	Prueba de Concepto	1
	PROYECTOS DE I+D+i	1
Gilead	Proyectos Hepatitis	1
H2020		1

*Research staff fully or partially funded
through competitive calls in 2021:*

Funding Institution	Call	Calls Granted
Agencia Estatal de Investigación	Contratos predoctorales para la formación de doctores 2021	1
	Retos Colaboración	1
	Promoción de empleo joven	2
	Juan de la Cierva-Formación	1
	Plataformas	2
Comunidad de Madrid	Garantía Juvenil	9
	Programas de actividades de I+D	2
ISCIII	Personal técnico bioinformático	1
	Ayudas Sara Borrell	3
	Miguel Servet	1
	Miguel Servet II	1
	Contratos Predoctorales	4
	Gestión en investigación en salud en los IIS	1
	Investigación Clínica Independiente	4
	Proyectos de Investigación	7
	Redes de Investigación	3
	Rio Hortega	3
	Juan Rodes	3
	Intensificación	2
Ministerio de Educación	Formación de Profesorado Universitario	2
H2020	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 2021, a total of 27 theses have been defended by member of the IIS. Six of them was a European thesis.

THESES

Doctoral Candidate	Title	Director/s	Defense date
Caballero Lombrana, Álvaro	Nuevo interactoma de la proteína Gq y su implicación en la homeostasis vascular	Ribas Núñez, Catalina / Mayor Menéndez, Federico	17/3/21
Alba Rubio, Claudio	Estudio bioinformático de muestras clínicas en la infección de helicobacter pylori: importancia del microbioma	Alarcón Caverio, Teresa	19/2/21
Rodríguez Galán, Ana	Mirna dynamics in T cell activation	Sánchez Madrid, Francisco	18/6/21
Castillo González, Raquel Ana	Gal-1 and LAT1 as regulatory molecules in skin inflammatory diseases	Sánchez Madrid, Francisco / Cibrián Vera, Danay	15/7/21
Sánchez Gómez, Inés	The role of the transcription factor TCFL5 in the physiopathology of B lymphocytes	Fresno Escudero, Manuel / Gironès Pujol, Nuria	18/3/21
Molejón García, Adolfo Javier	G Protein Coupled Receptor Kinase (GRK)-2: Involvement in DNA Damage Response and Functional Repercussions in Senescence	Penela Márquez, Petronila	9/6/21
Fernández Mendiola, Cristina	Microglial heme oxygenase I (HO-1) modulation for the treatment of age-related diseases	García López, Manuela	1/7/21
Rojo Aldama, Eukene	Estudio de las características epidemiológicas, clínicas y de la respuesta al tratamiento en una cohorte de pacientes con colitis microscópica	Pérez Gisbert, Francisco Javier / Casanova González, María José	17/5/21
Ramascó Rueda, Fernando	Utilidad de la determinación preoperatoria de los niveles séricos de MR-Proadrenomedulina para predecir la necesidad de soporte orgánico postoperatorio en cirugía oncológica abdominal	Gilsanz Rodríguez, Fernando / Planas Roca, Antonio	23/4/21
Pacheco Barcia, Vilma Emilia	Índice de Respuesta Inflamatoria Sistémica (IRIS): Factor Pronóstico en el Cáncer de Páncreas	Mondejar Solis, Rebeca / Colomer Bosch, Ramón	28/1/21
Galván Román, José María	Capacidad pronóstica de los microRNAs circulantes en la neumonía adquirida en la comunidad	Aspa Marco, Francisco Javier	24/9/21
Andino Ruiz, Ricardo	Oxigenoterapia de alto flujo en pacientes con insuficiencia respiratoria aguda severa	Vega González, María Gema / Suárez Fernández, Carmen	7/4/21
Cuesta Cuesta, Francisco Javier	Uso de dispositivos vasculares bioabsorbibles en el tratamiento de la reestenosis intrastent	Alfonso Manterola, Fernando	9/4/21
Sanz Martín, María del Pilar	Evaluación de la reconstitución inmunitaria postrasplante autólogo de progenitores hematopoyéticos en pacientes con mieloma múltiple	Muñoz Calleja, Cecilia	23/6/21

Doctoral Candidate	Title	Director/s	Defense date
Miqueleiz Zapatero, Ana	Detección de <i>Helicobacter pylori</i> y su resistencia antibiótica: métodos fenotípicos, genotípicos, y secuenciación del genoma completo	Alarcón Cavero, Teresa	26/11/21
Ferrer Barcelo, Luis	Tratamiento de la anemia ferropénica posthemorragia digestiva aguda: ferroterapia oral vs. intravenosa	Canelles Gamir, Pilar / Medina Chuliá, Enrique / Pérez Gisbert, Francisco Javier	20/4/21
Zorzo, Cristina	Importancia de la progresión del daño estructural pulmonar en adultos con fibrosis quística mediante tomografía computarizada y su relación con la evolución clínica y espirométrica	Girón Moreno, Rosa María / Caballero Sánchez-Robles, María Paloma	27/1/21
Peláez Laderas, Adrián	Characterisation of the virome of an agricultural ecosystem to understand virus ecology and evolution in a heterogeneous environment	García-Arenal Rodríguez, Fernando / John McLeish, Michael	13/12/21
Bouthelie de Pedro, Antonio	Papel del transportador de aminoácidos LAT1 en eritropoyesis y su regulación por el factor de respuesta a hipoxia HIF2a	Aragón López, Julián	12/11/21
Chicharro Manso, Pablo	Identificación de MicroARNs como biomarcadores de gravedad y respuesta al tratamiento en pacientes con psoriasis	de la Fuente Flores, Hortensia / Llamas Velasco, María del Mar	28/5/21
Nogueira Pérez, Ángel	Importancia de la capacidad funcional en el paciente con enfermedad renal crónica avanzada (ERCA) y la relación con el binomio nutrición-inflamación	Barril Cuadrado, Guillermina	16/12/21

EUROPEAN THESES:

Doctoral Candidate	Title	Director/s	Defense date
Marcos Jiménez, Ana María	Effect of the tyrosine kinase inhibitor dasatinib on lymphocyte trafficking	Cecilia Muñoz Calleja / Stein, Jens	2/7/21
Calzaferri, Francesco	Design, synthesis and pharmacological evaluation of novel blood-brain barrier-permeable non- nucleotide purine derivatives as P2X7 antagonists for the treatment of neurodegenerative diseases	García García, Antonio / Ríos Salgado, Cristóbal de los	25/2/21
Farré Alins, Victor	Validación de biomarcadores y dianas terapéuticas de origen inflamatorio en traumatismo craneoencefálico	Egea Máiquez, Francisco Javier	18/6/21
Martins Neves, María Margarida	Mecanismos moleculares subyacentes al papel del GRK2 en la progresión del cancer de mama	Mayor Menéndez, Federico / Penela Márquez, Petronila	3/5/21
Jeronimo Dos Santos, Tiago	An equity-oriented analysis on using diabetes-related technology in children and adolescents with type 1 diabetes mellitus	Argente Oliver, Jesús	4/11/21
Palomino Antolín, Alejandra	Estrategias antiinflamatorias para la protección de la unidad neurovascular en modelos de isquemia cerebral	Egea Máiquez, Francisco Javier	20/12/21

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 2021, IIS Princesa researchers have participated in the development of 15 clinical guidelines.

García Pastor, A., López-Cancio Martínez, E., Rodríguez-Yañez, M., de Lecinana, M. Alonso, Amaro, S., Arenillas, J. F., Ayo-Martin, O., Castellanos, M., Fuentes, B., Freijo, M. M., Gomis, M., Gómez Choco, M., Martínez Sánchez, P., Morales, A., Palacio-Portilla, E. J., Segura, T., Serena, J., Vivancos-Mora, J., Roquer, J., Soc Espanola Neurologia. **Recommendations of the Spanish Society of Neurology for the prevention of stroke. Interventions on lifestyle and air pollution.** Neurologia 36 (5): 377-387. 2021. PMID: 32917433. IF: 3,109. DOI: 10.1016/j.nrl.2020.05.018.

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Abad Santos, Francisco. **Guía clínica para la atención al paciente long covid/ covid persistente.**

Fernández de Misa Cabrera, Ricardo, Novelli Canales, Silvana, Calzado Villareal, Leticia, García Herrera, Adriana, López Lerma, Ingrid, Marín Niebla, Ana, Marín Palomo, Alicia, Muniesa Montserrat, Cristina, Rodríguez Pinilla, Socorro María, Zapatero Laborda, Almudena. **Linfoma cutáneo primario. Guía multidisciplinar para el abordaje diagnóstico y terapéutico del paciente con linfoma cutáneo primario.**

Zapatero Laborda, Almudena, González, Emma, Aldave, Diego. **Moderate Hypofractionation in radical and postoperative prostate cancer. Prostate Cancer Controversies IV.**

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 2021, 121 new agreements have been signed for clinical trials led by IIS members.

OCHOA MAZARRO, DOLORES. **"ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE DESVENLAFAXINA 100 mg COMPRIMIDOS DE LIBERACIÓN PROLONGADA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS MÚLTIPLE A VOLUNTARIOS SANOS EN AYUNAS."** Sponsored by: Laboratorios Normon, S.A. Sponsored's protocol code: N-DEV-19-252. Eudra CT: 2019-003272-39.

OCHOA MAZARRO, DOLORES. **"Ensayo clínico cruzado, replicado, aleatorizado de bioequivalencia de atorvastatina 80 mg comprimidos recubiertos con película, tras su administración oral en dosis única a voluntarios sanos en ayunas"**. Sponsored by: Laboratorios Normon, S.A. Sponsored's protocol code: N-ATO-20-261. Eudra CT: 2020-004750-29.

CARRERAS RODRIGUEZ, MARÍA TERESA. **"Estudio DETCOG-COVID: Estudio observacional para evaluar la repercusión del confinamiento en el contexto de la pandemia por COVID-19 en pacientes con diagnóstico de Deterioro Cognitivo. Versión 3.0"**. Sponsored by: Dra. María Teresa Carreras Rodríguez. Sponsored's protocol code: Estudio DETCOG-COVID.

PASTOR GÓMEZ, JESÚS. **"RESPUESTA CEREBRAL A LA MÚSICA EN PACIENTES EN COMA O CON SEDO-ANALGESIA"**. Sponsored by: Dr. Jesús Pastor Gómez.

VALDÉS ANCA, ÁLVARO. **"ESTUDIO OBSERVACIONAL SOBRE LA IMPLANTACIÓN DE UN PROGRAMA DE CIRUGÍA LAPAROSCÓPICA EXTRAPERITONEAL DE LA HERNIA INGUINAL: RESULTADOS DURANTE LA CURVA DE APRENDIZAJE"**. Sponsored by: Dr. Álvaro Valdés Anca.

ROCÍO MARTÍN, ESMERALDA. **"Valor diagnóstico de los potenciales evocados miogénicos vestibulares en el vértigo posicional paroxístico benigno"**. Sponsored by: Dra. Esmeralda Rocío Martín.

MAQUEDA GONZÁLEZ, ROCÍO Y DI MARTINO, MARCELO. **"Utilidad de la tomografía computarizada multicorte preoperatoria con volumetría pancreática como predictor de fístula pancreática tras la duodenopancreatectomía cefálica"**. Sponsored by: Dra. Rocío Maqueda y Dr. Marcelo di Martino.

CORREA BENITO, ALBA. **"INTERNATIONAL, PROSPECTIVE SNAPSHOT COLLABORATIVE AUDIT OF ACUTE DIVERTICULITIS (AUDITORÍA INTERNACIONAL PROSPECTIVA DE LA DIVERTICULITIS AGUDA)"**. Sponsored by: Birmingham Surgical Trials Consortium (Bowel Disease Research Foundation in the United Kingdom). Sponsored's protocol code: DAMASCUS.

SAMPEDRO NÚÑEZ, MIGUEL ANTONIO. **"Cuidado nutricional en pacientes críticos hospitalizados por el COVID 19: estudio observacional de seguimiento de 1 año"**. Sponsored by: SOCIEDAD DE ENDOCRINOLOGÍA, NUTRICIÓN Y DIABETES DE LA COMUNIDAD DE MADRID. Sponsored's protocol code: NUTRICOVID.

SÁNCHEZ TORRES, JOSÉ MIGUEL. **"Estudio aleatorizado de fase III de sitravatinib en combinación con nivolumab frente a docetaxel en pacientes con cáncer de pulmón no microcítico no escamoso avanzado con progresión de la enfermedad durante o después de la quimioterapia con platino y el"**. Sponsored by: Mirati Therapeutics INC. Sponsored's protocol code: 516-005. Eudra CT: 2019-001043-41.

MIRANDA, PABLO. **"RME-FRÍA VS RME-ESTÁNDAR PARA EL TRATAMIENTO DE LESIONES COLÓNICAS NO PEDICULADAS HOMOGÉNEAS DE GRAN TAMAÑO. ENSAYO CLÍNICO ALEATORIZADO Y MULTICÉNTRICO"**. Sponsored by: GRUPO DE RESECCIÓN DE LA SOCIEDAD ESPAÑOLA DE ENDOSCOPIA DIGESTIVA (GRSEED). Sponsored's protocol code: RMEFRÍA.2019.

ABAD SANTOS, FRANCISCO y LOSCERTALES PUEYO, JAVIER. **"Monitorización terapéutica y estudio farmacogenético de ibrutinib en pacientes con leucemia linfocítica crónica"**. Sponsored by: Dr. Jorge Labrador (Hospital Universitario de Burgos). Sponsored's protocol code: JLG-IBRU-2020-01.

MARAZUELA AZPIROZ, MÓNICA. **"Ensayo de 78 semanas para comparar el efecto y la seguridad de la insulina icodec una vez a la semana y de insulina glargina 100 unidades/ml una vez al día, ambas en combinación con tratamiento antidiabético no insulínico, en pacientes con diabetes tipo"**. Sponsored by: Novo Nordisk Pharma SA. Sponsored's protocol code: NN1436-4477. Eudra CT: 2020-000442-34.

COLOMER I BOSCH, RAMÓN. **"Primer ensayo en humanos, abierto, de aumento escalonado de la dosis con cohortes de ampliación para evaluar la seguridad de GEN1046 en sujetos con tumores sólidos malignos"**. Sponsored by: Genmab A/S.

Sponsored's protocol code: GCT1046-01. Eudra CT: 2018-003402-63.

LÓPEZ MANZANARES, LYDIA. **"Ensayo abierto de 58 semanas de Tavapadón en la enfermedad de Parkinson (ensayo TEMPO-4)".** Sponsored by: Cerevel Therapeutics LLC. Sponsored's protocol code: CVL-751-PD-004.

CASADO ESCRIBANO, PEDRO PABLO. **"Efectos de semaglutida sobre la capacidad funcional en pacientes con diabetes tipo 2 y arteriopatía periférica."** Sponsored by: Novo Nordisk Pharma S.A. Sponsored's protocol code: NN9535-4533. Eudra CT: 2019-003399-38.

GONZÁLEZ MARTÍNEZ, ALICIA; MECA LALLANA, VIRGINIA; MUÑOZ CALLEJA, CECILIA; SÁNCHEZ MADRID, FRANCISCO. **"Papel de los miRNA como biomarcadores en patología inmunome-diada: Esclerosis Múltiple"**. Sponsored by: Dra. Alicia González. Sponsored's protocol code: AGM-ALE-2019-01.

MURILLO GONZÁLEZ, MARÍA TERESA. **"Radioterapia antiinflamatoria a dosis bajas para el tratamiento de la neumonía por covid-19: estudio prospectivo multicéntrico"**. Sponsored by: GRUPO DE INVESTIGACIÓN CLÍNICA EN ONCOLOGÍA RADIOTERÁPICA (GICOR). Sponsored's protocol code: IPACOVID.

IBÁÑEZ ZURRIAGA, AMPARO. **"Estudio de Prevalencia y Adecuación del Uso Hospitalario de Antimicrobianos en España"**. Sponsored by: Grupo de Atención Farmacéutica al Paciente con Enfermedad Infecciosa de la Sociedad Española de Farmacia Hospitalaria (SEFH). Sponsored's protocol code: AFI-AMO-2019-01.

CASTRO TEJERO, PABLO. **"E²-RADlatE - OligoCare: A pragmatic observational cohort study to evaluate radical radiotherapy for oligo-metastatic cancer patients (Un estudio de cohorte observacional pragmático para evaluar la radioterapia radical en pacientes con cáncer oligo-metast. Sponsored by: European Organisation for Research and Treatment of Cancer (EORTC). Sponsored's protocol code: E2-RADlatE (1811) - oligocare (1822).**

CISNEROS SERRANO, CAROLINA. **"A non-interventional, cross-sectional, observational cohort study to evaluate health-related quality of life (HRQoL) and utility measure in patients with severe uncontrolled asthma in Spain"**. Sponsored by: Astrazeneca Farmacéutica Spain, S.A. Sponsored's protocol code: Estudio UTILITY.

PÉREZ GISBERT, JAVIER. **"Estudio clínico fase 2a aleatorizado, doble ciego, controlado con placebo, de grupos paralelos, multicéntrico y de prueba de concepto para evaluar la seguridad y eficacia de JNJ-64304500 como terapia complementaria a la terapia biológica estándar con ant."** Sponsored by: Janssen-Cilag S.A. Sponsored's protocol code: 64304500CRD2002. Eudra CT: 2020-002701-26.

COLOMER I BOSCH, RAMÓN. **"Ensayo clínico de fase IB de palbociclib y binimetinib en cáncer de mama triple negativo avanzado con hiperactivación de ERK y/o CDK4/6"**. Sponsored by: Fundación Oncosur. Sponsored's protocol code: PAL-BOBIN. Eudra CT: 2020-000930-16.

ALEGRE AMOR, ADRIÁN. **"Estudio aleatorizado de fase III, multicéntrico, abierto, para evaluar la eficacia y seguridad de Belantamab Mafodotin en combinación con Pomalidomida y Dexametasona (B-Pd) versus Pomalidomida más Bortezomib y Dexametasona (PVd) en participantes con miel."** Sponsored by: GlaxoSmithKline Research & Development Limited. Sponsored's protocol code: 207499 / DREAMM 8 / GSK2857916. Eudra CT: 2018-004354-21.

DÍEZ VILLANUEVA, PABLO. **"Comportamiento de Edoxabán en pacientes con fibrilación auricular no valvular e insuficiencia cardíaca en España. Estudio EMAYIC"**. Sponsored by: Fundación Casa del Corazón. Sponsored's protocol code: EMAYIC / SEC-EDO-2020-01.

OCHOA MAZARRO, DOLORES. **"Ensayo clínico cruzado, aleatorizado de bioequivalencia de rasagilina 1 mg comprimidos bucodispersables vs rasagilina 1 mg comprimidos de liberación inmediata, tras su administración oral en dosis única a voluntarios sa-**

nos en ayunas". Sponsored by: Laboratorios Alter S.A. Sponsored's protocol code: UECHUP-RAS/21-1. Eudra CT: 2021-000315-23.

OCHOA MAZARRO, DOLORES. **"ENSAYO CLÍNICO CRUZADO, REPLICADO, ALEATORIZADO DE BIOEQUIVALENCIA DE MIRABEGRON 50 mg COMPRIMIDOS DE LIBERACIÓN PROLONGADA, TRAS SU ADMINISTRACIÓN ORAL EN DOSIS ÚNICA A VOLUNTARIOS SANOS EN PRESENCIA DE ALIMENTOS"**. Sponsored by: Laboratorios Normon S.A. Sponsored's protocol code: N-MIA-21-264. Eudra CT: 2021-000283-29.

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tirosina quinasa del FGFR, en sujetos con cáncer urotelial metastásico o no resecable. Sponsored by: JANSSEN-CILAG S.A. Sponsored's protocol code: 42756493BLC2001. Eudra CT: 2014-002408-26.

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e inmunología clínica. Sponsored's protocol code: SEA-OMA-2020-01.

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Ángela Gutiérrez. **Ensayo clínico piloto para evaluar la eficacia, seguridad y tolerabilidad del cambio a un tratamiento con Bictegravir/FTC/TAF(Bktarvy) más darunavir/cobicistat en pacientes infectados por VIH-1 altamente tratados.** Sponsored by: Asociación RIS (Red de Investigación en SIDA). Sponsored's protocol code: BIDA. Eudra CT: 2020-003103-34.

María Pilar López Martín. **Ensayo en Fase III, randomizado, multicéntrico con tratamiento abierto de tratuzumab deruxtecán (T-DXd;DS-8201a) frente a quimioterapia a elección del investigador en pacientes con cáncer de mama con expresión baja del receptor del factor de crecimiento e.** Spon-

sored by: AstraZenecaAB. Sponsored's protocol code: D9670C00001. Eudra CT: 2019-004493-26.

Guillermina Barril Cuadrado. **Estudio Adherence: adherencia a una dieta muy baja en proteínas suplementada con ceto/hidroxi-análogos (ernamin) en pacientes con enfermedad renal crónica no en diálisis**". Sponsored by: Laboratorios ERN. Sponsored's protocol code: ADHERENCE.

Fernando Suárez. **Ensayo clínico aleatorizado adaptativo, controlado, abierto y multicéntrico para investigar el rendimiento seguro y eficaz del sistema de tratamiento por electroestimulación diafragmática (Diaphragm Pacing Therapy system, DPTS) Lungpacer en pacientes en**. Sponsored by: Lungpacer Medical Inc. Sponsored's protocol code: P-300.

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Biomédica de Bellvitge (IDIBELL). Sponsored's protocol code: LORALAM. Eudra CT: 2020-000702-29.

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Dolores Ochoa Mazarro. **"ENSAYO CLÍNICO CRUZADO, ALEATORIZADO DE BIOEQUIVALENCIA DE MEMANTINA 20 MG COMPRIMIDOS BUCODISPERSABLES VS MEMANTINA 20 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-MEM-21-268. Eudra CT: 2021-003654-23.

Julio Ancochea Bermúdez. **Ensayo de fase III multicéntrico, aleatorizado y controlado para determinar la eficacia y la seguridad de dos niveles de dosis de Plitidepsin en comparación con el control en pacientes adultos que precisan de hospitalización para el tratamiento médico de**. Sponsored by: PHARMA MAR, S.A. Sponsored's protocol code: APL-D-003-20. Eudra CT: 2020-005951-19.

Dolores Ochoa Mazarro. **Estudio fase III, observador-ciego, aleatorizado, internacional para evaluar la consistencia de lotes de la vacuna candidata de GSK para inmunización materna frente al VRS, así como, la respuesta inmune, seguridad y reatogenicidad de esta vacuna candidat**. Sponsored by: GlaxoSmithKline. Sponsored's protocol code: 214709 (RSV MAT-010). Eudra CT: 2021-000357-26.

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Ana Isabel Ballesteros. **Análisis observacional del tratamiento con palbociclib en pacientes con cáncer de mama avanzado y/o metastásico RH+/HER2- en primera línea de tratamiento dentro de práctica clínica habitual.** Sponsored by: FIBHCSC. Sponsored's protocol code: PALBOSPAIN.

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CAROLINA CISNEROS. **Estudio de validación transversal de las versiones adaptadas localmente del cuestionario sobre el deterioro y el riesgo del asma (AIRQ) como herramienta que identifica a pacientes con asma en riesgo de resultados adversos por asma no controlada en Alemani.** Sponsored by: AstraZeneca. Sponsored's protocol code: D2287R00171 (España).

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Dolores Ochoa. **"Ensayo clínico cruzado, aleatorizado de bioequivalencia de dos formulaciones de ibuprofeno arginina 600 mg (comprimidos recubiertos con película versus granulado para solución oral) tras su administración oral en dosis única a voluntarios sanos en ayunas.** Sponsored by: ZAMBON SAU. Sponsored's protocol code: Z7100J01. Eudra CT: 2021-003442-21.

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Claudia Valenzuela. **Estudio fase III aleatorizado, doble ciego, controlado por placebo para evaluar la eficacia y seguridad del PRM-151 en pacientes con fibrosis pulmonar idiopática.** Sponsored by: HOFFMAN-LA ROCHE. Sponsored's protocol code: WA42293 (PRM-151-303). Eudra CT: 2020- 000791-38.

Dolores Ochoa Mazarro. **"Ensayo clínico cruzado, aleatorizado de bioequivalencia de sildenafil 100mg comprimidos recubiertos con película tras su administración oral en dosis única a voluntarios sanos en**

ayunas". Sponsored by: Laboratorios Alter S.A. Sponsored's protocol code: UECHUP-SIL/21-4. Eudra CT: 2021-003689-12.

Julio Ancochea. **"Estudio de extensión en una cohorte de pacientes adultos con infección por SARS-COV-2 que precisaban ingreso hospitalario y recibieron tratamiento con plitidepsina en el estudio APLICOV-PC".** Sponsored by: PHARMA MAR, S.A. Sponsored's protocol code: E- APLICOV-PC / AV-APL-A-003-21. Eudra CT: 2021-004966-37.

Mario Fernando Muñoz Guerra. **"Ensayo clínico aleatorizado, doble ciego, controlado con placebo y con tratamiento activo, para evaluar la eficacia analgésica y la seguridad de una combinación oral de ibuprofeno (arginina)-tramadol HCl administrada a pacientes con dolor moderado a severo.** Sponsored by: Farmalider S.A. Sponsored's protocol code: FMLD-IOTRA2- 47_FIII. Eudra CT: 2020-005530-15.

Jesús Sanz sanz. **"DGT/3TC frente a BIC/FCT/ TAF como terapia de mantenimiento en personas que viven con VIH: ensayo clínico abierto y aleatorizado".** Sponsored by: Fundación SEIMC-GESIDA. Sponsored's protocol code: PASO DOBLE GeSIDA 11720. Eudra CT: 2020-003686-18.

María Lourdes Iglesias de Ussel y Pérez. **"Ensayo clínico simple ciego para estudiar la tolerabilidad, eficacia, calidad de vida y adherencia de latanoprost/timolol sin conservantes (Fixaprost) comparados con bimatoprost/timolol con conservantes (Ganfort P) en pacientes con glaucoma de ángulo abierto.** Sponsored by: LABORATOIRES THÉA S.A.S. Sponsored's protocol code: LT2347-PIV-02/20. Eudra CT: 2020-000438-16.

Dolores Ochoa. **"Estudio abierto, aleatorizado, de dosis única, cruzado de dos secuencias y dos tratamientos, para evaluar la biodisponibilidad relativa de amilmetacresol, alcohol diclorobencílico y lidocaína hidrocloreto en voluntarios sanos, en ayunas".** Sponsored by: GEISER PHARMA S.L. Sponsored's protocol code: G08-04-01. Eudra CT: 2021-003423-15.

Cecilio Santander Vaquero. **"Ensayo de fase III, doble ciego en pacientes adultos y adolescentes con esofagitis eosinofílica para demostrar superioridad en comparación con placebo de un tratamiento ocasional y/o continuo de 48 semanas con comprimidos bucodispersables de budesonida p.** Sponsored by: Dr. Falk Pharma GmbH. Sponsored's protocol code: BUL-3/EER. Eudra CT: 2017-003516-39.

Almudena Zapatero Laborda. **"DAROL: Estudio observacional de darolutamida en pacientes con cáncer de próstata resistente a la castración no metastásico".** Sponsored by: BAYER HISPANIA S.L.U. Sponsored's protocol code: BAY-DAR-2021-01.

Lydia López Manzanares. **"Registro en España del uso de los inhibidores de la COMT en el manejo de pacientes con enfermedad de Parkinson que presentan fluctuaciones motoras tempranas (REONPARK)".** Sponsored by: LABORATORIOS BIAL S.A. Sponsored's protocol code: ES-BIAL-PD-001.

Ramón Colomer Bosch. **"Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo, en el que se evalúa abemaciclib con la hormonoterapia adyuvante de referencia en participantes con cáncer de mama HR+, HER-2+, de riesgo alto y con afectación ganglionar, que hayan co.** Sponsored by: Lilly S.A.U. Sponsored's protocol code: I3Y-MC-JPCW. Eudra CT: 2020-004035-24.

Fernando Alfonso Manterola. **"Primera investigación clínica en humanos del catéter para angioplastia coronaria transluminal percutánea recubierto de everolimus de Chansu Vascular Technologies: Evaluación clínica en el tratamiento de sujetos con reestenosis intrastent de lesiones de a.** Sponsored by: Chansu Vascular Technologies LLC. Sponsored's protocol code: TP1125.

Fernando Alfonso Manterola. **"Seguimiento clínico post-marketing del dispositivo Sequent SCB "all comes".** Sponsored by: B. Braun Melsungen AG. Sponsored's protocol code: SCORE.

Maria Teresa Carreras. **"Estudio en fase III multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar la eficacia, la seguridad y la tolerabilidad de AVP-786 (bromhidrato de deudextrometorfano [d6-DM]/sulfato de quinidina [Q]) para el tratamiento de la agit.** Sponsored by: Avanir Pharmaceuticals, Inc. Sponsored's protocol code: 20-AVP-786-307. Eudra CT: 2020-000798-26.

Ignacio de los Santos. **"Ensayo clínico doble-cego, controlado con placebo, aleatorizado, Fase Ib, de ApTOLL para el tratamiento de COVID-19".** Sponsored by: APTATARGETS S.L. Sponsored's protocol code: APTACOVID. Eudra CT: 2021-000026-99.

Javier Pérez Gisbert. **VACUNAS CONTRA LA COVID-19 EN LA ENFERMEDAD INFLAMATORIA INTESTINAL: EFICACIA, SEGURIDAD Y FACTORES IMPLICADOS.** Sponsored by: GETECCU. Sponsored's protocol code: VaCoVei.

Concepcion Pérez. **"Ensayo clínico de intervención en fase III, multicéntrico, aleatorizado, con doble enmascaramiento, controlado y con grupos paralelos para confirmar la eficacia y la seguridad de Qutenza en pacientes con dolor neuropático postquirúrgico.** Sponsored by: Avanir Pharmaceuticals, Inc. Sponsored's protocol code: AV001. Eudra CT: 2021-001409-64.

Fernando Alfonso Manterola. **"ESTUDIO ALEATORIZADO PARALELO PARA EVALUAR LA UTILIDAD DE LA REVISION ANGIOGRAFICA RUTINARIA 6 MESES DESPUES DEL INTERVENCIONISMO PERCUTANEO EN EL TRONCO CORONARIO IZQUIERDO (ESTUDIO ANGELINE".** Sponsored by: Fundación Epic. Sponsored's protocol code: EPIC23.

Alejandra Gullón Ojesto. **Estudio de fase 111, doble ciego, controlado con placebo y abierto, de la eficacia y la seguridad a largo plazo de Firibastat (QGC001) administrado por vía oral una vez al día durante un máximo de 48 semanas, en pacientes con hipertensión resistente/difíc.** Sponsored by: Quantum Genomics. Sponsored's protocol code: QGC001-3QG2. Eudra CT: 2021- 001404-14.

Virginia Meca. **"Estudio De Fase 111, Multicéntrico, Aleatorizado, Ooble Ciego Y Con Doble Simulación Para Evaluar La Seguridad Y La Eficacia De Ocrelizumab En Comparación Cc;>n_ Fingolimod En Niños Y Adolescentes Con Esclerosis M.últiple Remitente-Recurrente".** Sponsored by: HOFFMAN-LA ROCHE. Sponsored's protocol code: WN42086. Eudra CT: 2020-004128-41.

Diego Real de Alsua. **Evaluación de las oscilaciones neurales en personas adultas con o sin síndrome de Down mientras ejecutan tareas cognitivas".** Sponsored by: FUNDACIÓ INSTITUT HOSPITAL DEL MAR D'INVESTIGACIONS MÈDIQUES. Sponsored's protocol code: IMIMFT-CL_EEGDS.

Javier Garcia Septiem. **"Implantación de células derivadas del músculo esquelético para el tratamiento de la incontinencia fecal: un estudio clínico de fase III, aleatorizado, controlado, doble ciego y dos brazos de tratamiento".** Sponsored by: Innovacell AG. Sponsored's protocol code: IG-01-02-5-009.

Dolores Ochoa. **"Ensayo clínico aleatorizado de biodisponibilidad relativa de bencidamina hidrocloreto - 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. Eudra CT: 2022-000900-37.

Cecilio Santander Vaquero. **"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 induc.** Sponsored by: Dr. Falk Pharma GmbH.

BOOKS

Ibáñez Sandín, María Dolores. **El libro de las enfermedades alérgicas. La alergia a la leche.** pp. 231-243. 2021. ISBN 9788492937837.



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Abad Santos, Francisco. **Guía clínica para la atención al paciente long covid/ covid persistente**. 2021. ISBN 9788418576440.

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Communication and

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

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

The IIS Princesa uses two main tools to carry out this task: the web (www.iis-princesa.org) and the newsletter "Impact Factor". The Institute website www.iis-princesa.org, renewed in 2016 to adapt to the new trends of users, presents the most important news about its members, as well as information about courses, congresses, job offers or

detailed information of research groups. In addition, the website offers other services, such as the research calls alert service, which provides up to date information to subscribers about public and private, national or international calls.

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

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

Courses

Fecha/s	Título	Ponente/Director
23-feb	Curso de Soporte Vital para R1	Mariano Aguilar Mulet
24-feb	Curso de Soporte Vital para R1	Mariano Aguilar Mulet
25-feb	Curso de Soporte Vital para R1	Mariano Aguilar Mulet
8-abr	Curso de proveedor de Soporte Vital Básico	Mariano Aguilar Mulet
9-abr	Curso de proveedor de Soporte Vital Básico	Mariano Aguilar Mulet
13-abr	Curso de proveedor de Soporte Vital Básico	Mariano Aguilar Mulet
15-abr	Curso de proveedor de Soporte Vital Básico	Mariano Aguilar Mulet
15-abr	Novedades Terapéuticas	Borja Quiroga Gili
8 jun – 8 jul	Análisis de estadística aplicada a biomedicina en el entorno R. Nivel básico	Isidoro González Álvaro / Nuria Montes Casado
11-jun	Curso de Formación en Diabetes	Servicio de Endocrinología
22-jun	Curso First Touch	Servicio Urología
21 – 22 sept	Curso Vascular Residentes	Santiago Trillo Senin
27-sept – 1 dic	Curso de estadística aplicada a biomedicina en el entorno R	Isidoro González Álvaro / Nuria Montes Casado
28-30 sep	Curso de Soporte Vital para R1	Mariano Aguilar Mulet
30-sept	Novedades terapéuticas	Borja Quiroga Gili
7-nov	Curso de Formación Inicial Ecografía	Andrés von Wernitz Teleki
19-oct	Curso Excelencia Código Sepsis	Fernando Ramasco Rueda

Dissemination

Fecha/s	Título	Ponente/Director
22-oct	Formación Desfibrilador semiautomático	Angel Soria Coiradas
12 nov / 17 Dic / 20-ene 2022 / 21 ene-22	Curso Big Data	Daniel Álvarez Covos
dic-13 nov	Curso Internacional Soporte Vital Avanzado	Fernando Ramasco Rueda
16-nov	Curso Retos en infección Perioperatoria	Fernando Ramasco Rueda
17-18 nov	Competencias en Ecografía Clínica para Atención Primaria	Andrés von Wernitz Teleki
23 nov – 25-nov	Curso de Soporte Vital Avanzado del European Resuscitation Council (ERC)	Mariano Aguilar Mulet
30 nov – 2-dic	Curso de Soporte Vital Avanzado del European Resuscitation Council (ERC)	Mariano Aguilar Mulet

Workshops

Fecha/s	Título	Ponente/Director
2-nov	Design Thinking	Jorge Gómez Zamora / Lara Pérez Martínez
3-nov	¿Qué significa Respirar? Se explica para que usamos los pulmones y como se alteran con el uso del tabaco	Javier Aspa Marco
3-nov	Cirugía mínimamente invasiva. Cirugía del Siglo XXI	Guillermo Reyes Copa / Elena Martín Pérez / Ramón Moreno Balsalobre
4-nov	Simulación clínica Hospital de La Princesa. Abróchense los cinturones	Rosa Méndez Hernández / Jesús M. Nieves Alonso
5-nov	¿Cómo es la vida de un medicamento? Etapas del desarrollo clínico	Dolores Ochoa Mazarro / Manuel Román / Samuel Martín
5-nov	Inmunología del tubo digestivo: del laboratorio a los pacientes	María Chaparro / Alicia C. Marín / Montserrat Baldán / Laila Aldars / Lorena Ortega Moreno / Irene Soletto Fernández / Irene Mora / Cristina Ramírez
8-nov	Biobancos: la ciencia al alcance de todos	Mara Ortega Gómez / Laura Gómez Cabañas / Ángel Llancho Sánchez
10-nov	Dale un giro a tu dolor, aprende a manejarlo	Almudena Mateos González
10-nov	Tatuajes, piercings y enfermedades de transmisión sexual. Mitos y realidades	Pedro Rodríguez / Alejandra Reolid
11-nov	Investigación biomédica translacional. De la investigación básica a la aplicación clínica	Francisca Molina Jiménez / Jennifer Fernández Pacheco / Cecilio Santander Vaquero / Sergio Casabona Francés / Pedro Lorenzo Majano Rodríguez
12-nov	Investigación traslacional: línea directa entre el laboratorio y el paciente	Águeda González Rodríguez / Javier Egea Maíquez / Esther Rey Fernández / Yaiza García García

Sessions

Fecha/s	Título	Ponente/Director
28-29 oct	III Jornada de Neurogastroenterología y Motilidad	Cecilio Santander Vaquero
26 nov	XVI e-Simposium Nutrición en Enfermedad Renal Crónica: Abordaje Multidisciplinar	Guillermina Barril Cuadrado / Ángel Nogueira Pérez
30 nov	7ª Jornada Comité de Calidad Percibida (online)	Alberto Pardo Hernández
9 dic	Jornadas Centros de Salud Mental de Madrid (online)	José Luis Ayuso Mateos

Seminars

Fecha/s	Título	Ponente/Director
28-ene	Estudio de la función de PD-L1 y su interacción con PD-1 en la biología endotelial	Giulia Setti
4-feb	Transfer of extracellular vesicle-microRNA controls germinal center reaction and antibody production	Lola Fernández Messina
11-feb	Terapia dirigida con everolimus como nuevo tratamiento de la neumonía intersticial asociada a esclerodermia (SSc-ILD) en ratones PSGL-1 KO	Elena González Sánchez
18-feb	Polarización de macrófagos: posible relevancia en Covid-19	Ángel Corbí
25-feb	Mitochondria drive a bacteria-induced metabolic reprogramming in CD4+ T cells that orchestrates CD8+ T cell responses	Jesús Osuna
4-mar	Post-synaptic Dendritic Dells: Functional Reprogramming Upon Antigen Presentation	Diego Calzada Fraile
11-mar	Impacto de la hipoxia en la progresión de la enfermedad hepática metabólica	Águeda González Rodríguez
16-jun	ISG20L2, una exoribonucleasa en activación T	Ana Rodríguez Galán
15-abr	Modulación de la muerte celular en neutrófilos y monocitos por la interacción PSGL-1/Pselectina. Posible implicación en la patogénesis del SLE	Antonio Muñoz Callejas
22-abr	The role of ISG15 in dendritic cells and contact hypersensitivity	Irene Fernández Delgado
29-abr	Galectin-1 Expression in CD8+ T Lymphocytes Controls Inflammation in Contact Hypersensitivity	Raquel Castillo
6-may	Non-redundant roles of CD1c+ dendritic cells in perpetuation of rheumatoid arthritis pathology	Enrique Martín- Gayo
12-may	Procesos inflamatorios y moleculares subyacentes en patología pulmonar	María Josefa Calzada García

Fecha/s	Título	Ponente/Director
13-may	Efectos del inhibidor de tirosín quinasas dasatinib en el tráfico linfocitario	Ana Marcos Jiménez
19-may	Papel de la reprogramación metabólica e inducida por los factores de respuesta hipoxia (HIF) en fisiopatología	Julián Aragonés López
20-may	Treatment duration and immune exhaustion determines personalized dendritic-cell vaccine efficacy for chronic HIV patients	Marta Calvet Mirabent
26-may	¿Podemos reducir el daño por reperfusión en ictus, infarto de miocardio o cirugías? O cómo el manejo de Na ⁺ y Ca ²⁺ por las mitocondrias es importante para las señales redox y el daño oxidativo en hipoxia e isquemia	Antonio Martínez Ruiz
27-may	Infección por VIH-2 y respuesta al tratamiento con inhibidores de la integrasa	Silvia Requena
1-jun	RPTOR y ARL6IP como genes diana de microRNAs en psoriasis	Hortensia de la Fuente
2-jun	Open Science en investigación pública. Gestión de datos de investigación	Noa B. Martín Cofreces
10-jun	Evaluación de la reconstitución inmunitaria postrasplante autólogo de progenitores hematopoyéticos en pacientes con mieloma múltiple	Pilar Sanz Martín
17-jun	Extracellular vesicles from Listeria monocytogenes-infected dendritic cells alert the innate immune system	Raúl Izquierdo
24-jun	T cell immune specificity changes after vaccination in healthy and COVID-19 convalescents subjects	Laura Esparcia Pinedo
1-jul	Aberrant antiviral state of CD1c+ dendritic cells associates with NK cell activation and Sjogren's syndrome pathology	Ildefonso Sánchez Cerrillo
8-jul	Gal-1 and LAT1 as regulatory molecules in skin inflammatory diseases	Raquel Castillo
29-sept	Horizonte Europa	Esther Rodríguez Blanco / Carmen Bello / Juan Riese
30-sept	La Galectina 1 como posible biomarcador diagnóstico en enfermedades inflamatorias mediadas por mecanismos inmunes (EIMMI)	Ana Triguero
6-oct	Iniciativas de Programación Conjunta Internacional	Ignacio Baanante / Marina Moreno Llanos / Cándida Sánchez-Barco
7-oct	Impacto de la co-exposición a VIH y Schistosoma en la fisiopatología vascular pulmonar	Sandra Medrano García
14-oct	Papel del transportador de aminoácidos LAT1 en eritropoyesis y su regulación por el factor de respuesta a hipoxia HIF2a	Antonio Bouthelier
14-oct	Sesión formativa sobre el manejo de la herramienta del Editor CVN de la Fundación Española para la Ciencia y la Tecnología (FECYT) dirigida a personal investigador	Estefanía Gutiérrez

Fecha/s	Título	Ponente/Director
21-oct	Blocking SLC7A5-mediated amino acid uptake by T cells efficiently prevents graft vs host disease	Nieves Fernández-Gallego
20-oct	Biobancos: Ciencia Abierta para Todos	María del Mar
28-oct	SCAD vs AT-AMI: differential miRNA profile and pathophysiological insights	Marta Lozano Prieto
3-nov	Investigación multicéntrica traslacional en infección por <i>Helicobacter pylori</i> y Enfermedad Inflamatoria Intestinal	Francisco Javier Pérez Gisbert
4-nov	Analysis of Expression of Different Histone Deacetylases in Autoimmune Thyroid Disease	Pablo Sacristán
10-nov	La investigación clínica en el Servicio de Neurología	José Aurelio Vivancos Mora
11-nov	Papel de los linfocitos T de memoria residentes en la persistencia del VIH en tejido	Meritxell Genescà
17-nov	La investigación clínica en Enfermería	Sergio González Álvarez
25-nov	Esofagitis Eosinofílica: búsqueda de biomarcadores mínimamente invasivos	Pedro Majano
1-dic	Astrocytes in Metabolism	Julie Ann Chowen King
2-dic	Macrophage-Mediated Subversion of Anti-Tumour Immunity	Paloma Sánchez Mateos
15-dic	Nuevas aproximaciones en Química Médica para el tratamiento de enfermedades neurodegenerativas	Cristóbal de los Ríos Salgado
16-dic	Linfocitos Treg y Th17: de linajes, subpoblaciones y estadios de diferenciación	Roberto González Amaro

Training carried out on the Plataforma Conocimiento Princesa

Fecha/s	Título	Ponente/Director
19 abr - 9 may	Metodología en cuidados enfermeros	Antonio Cano Manchón
26 abr - 12 may	Soporte vital básico para personal sanitario	Diana Parrado López
10 may - 18 jul	El e-learning en sanidad	M. Elena Fernández Martínez
10 may - 13 jun	Código Sepsis Princesa	Grupo Código Sepsis
24 may - 20 jun	Píldoras formativas telemáticas: minivídeos docentes	M. Elena Fernández Martínez
4 oct - 2 nov	Simulación en el manejo de la vía aérea	Noemí Díaz Velasco
18 oct - 7 nov	Metodología en cuidados enfermeros	Antonio Cano Manchón
18 oct - 18 nov	Soporte vital avanzado para personal sanitario	Diana Parrado López
25 oct - 14 nov	Medidas preventivas en la atención a pacientes con enfermedades infecto-contagiosas	Dra. Manuela García Cebrián
1 nov - 5 dic	Código sepsis princesa	Grupo Código Sepsis

Continuing education La Princesa

Título	Ponente/Director
Competencias en Ecografía Clínica Urgencias Princesa	Andrés von Wernitz teleki / Ana María Martínez Molina / Emilia Roy Vallejo / Fernando Alfageme Roldan / Francisco Javier Val de Santos / Iñigo Guerra Molina / Jorge Sorando Ortín / Jose Ignacio Alonso González / Juan Mariano Aguilar Mulet / Sonia González Del Val
Competencias en Ecografía Clínica para Atención Primaria	Andrés von Wernitz teleki / Ana María Martínez Molina / Emilia Roy Vallejo / Fernando Alfageme Roldan / Francisco Javier Val de Santos / Iñigo Guerra Molina / Jorge Sorando Ortín / José Ignacio Alonso González / Juan Mariano Aguilar Mulet / Sonia González del Val
Metodología enfermera	Antonio Cano Manchón / María José Rubio Pérez
Código Sepsis Princesa	Azucena Bautista Hernández / David Jiménez Jiménez / Fernando Ramasco Rueda / Rosa Méndez Hernández
Medidas preventivas en la atención a pacientes con enfermedades infectocontagiosas	Álvaro Morales Caballero / Amparo López- Guerrero Almansa / Arantxa Ortega Sánchez / Ignacio Redondo Pascual / Jesús Merino Pérez / Juan Soler Ruiz / Manuela García Cebrián
Simulación en el manejo de la vía aérea	Diana Parrado / Elena Rojo Rodríguez / Jesús Nieves / Noemí Díaz Velasco / Sheila Santidrián
Curso sobre retos en antibioterapia en el paciente crítico	Fernando Ramasco Rueda / Carlos Figueroa / Carmen Vallejo / David Arribas Méndez / Diana Parrado / Julia Hernando Santos / Mar Orts Rodríguez / María Semiglia / Nelly Zurita Cruz / Rafael González de Castro / Rosa Méndez Hernández / Sheila Santidrián / Sonia Expósito Carazo
Competencias en Ecografía Clínica para Atención Primaria	Andrés von Wernitz teleki / Ana María Martínez Molina / Emilia Roy Vallejo / Fernando Alfageme Roldan / Francisco Javier Val de Santos / Iñigo Guerra Molina / Jorge Sorando Ortín / José Ignacio Alonso González / Juan Mariano Aguilar Mulet / Sonia González del Val
Urgencias quirúrgicas. Actualización diagnóstica y terapéutica	Andrés von Wernitz teleki / Francisco Javier Val de Santos / Iñigo Guerra Molina / Jorge Sorando Ortín / Juan Mariano Aguilar Mulet / María Cristina Santiago Poveda
Código Sepsis Princesa	Andrés von Wernitz teleki / Azucena Bautista Hernández / Carmen de las Cuevas / Carmen Saez Bejar / David Jiménez Jiménez / Fernando Ramasco Rueda / Iñigo García Sanz / María Semiglia / María José Rubio Pérez / Marta Chicot Llano / Natalia Pascual Gómez / Nelly Zurita Cruz / Rosa Méndez Hernández / Sara Navarro Ausere / Tamara Soler
Metodología enfermera	Antonio Cano Manchón / María José Rubio Pérez / Susana Cabrera Fernández
Soporte Vital Avanzado para personal sanitario	Diana Parrado / Elena Rojo Rodríguez / Francisco Javier Val de Santos / Juan Mariano Aguilar Mulet / María Cristina Santiago Poveda / Noemí Díaz Velasco

Título	Ponente/Director
Soporte Vital Básico para personal sanitario	Diana Parrado / Elena Rojo Rodríguez / Francisco Javier Val de Santos / Juan Mariano Aguilar Mulet / María Cristina Santiago Poveda / Noemí Díaz Velasco
Actualización en oftalmología	Eduardo López Palacios / Paula Marticorena Álvarez
Competencias digitales docentes en formación virtual: diseño instruccional y herramientas prácticas	M ^a Elena Fernández Martínez
Curso Avanzado en eLearning: Creación de Minivideos Docentes	M ^a Elena Fernández Martínez
Curso de Bienvenida a los nuevos Residentes	Jorge Sorando Ortín / Juan Mariano Aguilar Mulet
Curso de Historia Clínica Electrónica	Francisco Javier Val de Santos / Juan Mariano Aguilar Mulet
Electrocardiografía	Amparo Benedicto Buendia / Juan Mariano Aguilar Mulet
Soporte Vital Inmediato para Residentes	Ana del Rey Ubago / Ana María Martínez Molina / Andrés von Wernitz teleki / Bárbara Retana Fernández / Diana Parrado / Elena Rojo Rodríguez / Elvira Contreras Murillo / Francisco Javier Val de Santos / Javier Martín Ruiz / Jorge Sorando Ortín / Luis Picazo García / Lydia Chao Rico / María Cruzate Aparicio / Marta Caño Hortonedá / Noemí Díaz Velasco / Raquel Caminero García / Sonia González del Val / Teresa Coco / Beatriz González Chesa / Juan Mariano Aguilar Mulet / María Cristina Santiago Poveda
Curso de Traumatología para nuevos residentes	Juan Mariano Aguilar Mulet / Rafael Carbonell
Cirugía para nuevos Residentes	Juan Mariano Aguilar Mulet / Adrián Martín Segura / Álvaro Gancedo Quintana / Ana Escobar Delgado / Cynthia Lana Esteban / Iñigo García Sanz / Jose María Lopesino / Julia Revuelta Ramírez / Lara Blanco Terés / Livia Delgado Burdalo / Ramón Sanz Ongil / Rocío Maqueda / Rodrigo Tovar Pérez
Curso de interpretación básica de radiología simple	Itxaso Galán González / José Manuel Muñoz / Juan Mariano Aguilar Mulet
Actualización en medicamentos biológicos y biosimilares	Carolina Aguilar Guisado / Isabel Barcia Martín / Mercedes García Gimeno / Susana Sánchez Suárez
Manejo de la disfagia orofaríngea en el paciente geriátrico	Elisa Martín de Francisco Muga / Inés Alonso González / Luisanna Sambrano
Taller de suturas de heridas. Hospital El Escorial	Libertad Martín Prieto / Mar de Castro Marinas / Pablo Cereceda Barbero / Sonia Morales Artero

ANNUAL
REPORT OF
SCIENTIFIC
ACTIVITY

2021



AREA 1



CELLULAR AND MOLECULAR ETIOPATHOGENIC MECHANISMS IN INFLAMMATORY AND AUTOIMMUNE DISEASES



- **LINE 1.1** INTERCELLULAR COMMUNICATION IN THE INFLAMMATORY RESPONSE
- **LINE 1.2** CELLULAR AND MOLECULAR RESPONSES TO HYPOXIA
- **LINE 1.3** ANIMAL MODELS OF INFLAMMATORY DISEASES AND INTERCELLULAR SIGNALLING
- **LINE 1.5** CELLULAR MECHANISMS AND MOLECULAR DETERMINANTS OF 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

GROUP 1



Head of laboratory



Research interest



Sánchez Madrid, Francisco



Group members

- Alfranca González, Arantzazu
- Bustos Morán, Eugenio
- Cibrián Vera, Danay
- de la Fuente Flores, Hortensia
- Fernández Delgado, Irene
- Fernández Messina, Lola
- Martín Cofreces, Noa Beatriz
- Martín Gayo, Enrique
- Moreno Gonzalo, Olga
- Ramírez Huesca, Marta Esther
- Rojas Gómez, Amelia
- Saiz Álvarez, María Laura
- Sánchez Alonso, Santiago
- Ursa Pecharromán, María Ángeles
- Vallejo Rodríguez, María Ángeles
- Vara Vega, Alicia

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 ani-

mal 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.



Major grants

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- Sánchez Madrid, Francisco. La dinámica de la red molecular del centrosoma de los linfocitos T controla la actividad anti-patogénica de las células dendríticas: papel del interactoma FOSTER. Fundación Ramón Areces. 2018-2021.
- Sánchez Madrid, Francisco. Inmunometabolismo de la psoriasis (IPD). Ayudas a equipos de investigación científica Fundación BBVA. 2018-2021.
- Sánchez Madrid, Francisco. Readyng 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.
- Martín Gayo, Enrique. Impact of immunotherapy with trained dendritic cells boosting CD8+ T cell cytotoxic function in HIV-1 chronic patients at different times since art initiation GLD19/00168. GILEAD. 2020-2021.
- Sánchez Madrid, Francisco. Dinámica de la respuesta inmunitaria como predictor del curso evolutivo de la enfermedad COVID-19. Implicaciones para la toma de decisiones terapéuticas. PREDINMUN COVID. Fondo Supera Covid-19 CRUE-Banco Santander. 2020- 2021.
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- Sánchez Madrid, Francisco. Microscopio óptico de fluorescencia para la observación de muestras gruesas y tejidos: Mesoscopia. IFEQ21/00085. ISCIII 2022.



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GROUP 3



Head of laboratory



Yáñez Mó, María

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

- Benayas López, Beatriz
- López Martín, Soraya
- Palma Cobo, Miguel
- Toribio Serrano, Víctor



Major grants

- Yáñez Mó, María. Translational NeTwork for the CLinical application of Extracellular VesicleS (Tentacles). RED2018-102411-T. Agencia Estatal de Investigación. 2020-2021.



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

Granted 2021:

- 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.



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GROUP 56



Head of laboratory



Urzainqui Mayayo, Ana Carmen



Group members

- González Sánchez, María Elena
- Muñoz Callejas, Antonio
- Silván Montoya, Javier



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, 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 P-Selectin and PSGL-1 aged female KO mice develop pulmonary arterial hypertension (PAH), the most severe form of connective tissue-related autoimmune diseases, due to increased levels of Angiotensin II and endothelial dysfunction, with low production of NO (González-Tajuelo et al., Arthritis and Rheumatol. 2019). Remarkably, clinical studies with patients indicate that PSGL-1 and P-selectin expression 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.

Main research lines:

- Study of the interstitial pneumonia associated to scleroderma (SSc-ILD) and lupus (SLE-ILD), which is one of the main causes of death in these diseases.
- Analysis of the cells and molecular components implicated in the development of this pathology 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.



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.
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GROUP 9



Head of laboratory



Aragonés López, Julián



Group members

- Bouthelier de Pedro, Antonio
- Elorza Peregrina, Ainara Estíbaliz
- Fuertes Yebra, Esther
- Guajardo Grence, Andrea
- Meléndez Rodríguez, Florinda del Coral
- Mesa Ciller, Claudia
- Ordóñez Navadijo, Ángel
- Soro Arnaiz, Inés
- Torres Capelli, María del Mar
- Urrutia Elorduy, Andrés Amalio
- Yang Li, Qilong Oscar



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 of the central biological functions executed by the HIF factors. 1) HIF factors and renal cell carcinoma: the HIF factors are induced in hypoxic areas in the inner core of the solid tumors but in clear cell renal cell carcinoma (ccRCC) - which loss Vhl (the main repressor of HIFs in normoxia) - show constitutive HIF expression irrespectively of the oxygen levels of the tumor. In these tumors HIF1 shows its cell autonomous anti-proliferative capability, whereas HIF2 acts as an oncoprotein. 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 impact remarkably in ccRCC progression. Independently of these projects in 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 chronic obstructive pulmonary disease (COPD) and sleep-apnea hypoapnea syndrome (SAHS) are the most common respiratory diseases causing illness and death, and are being projected to be the third leading cause of death worldwide by 2020. They are characterized by

an insufficient level of oxygen in the blood (hypoxemia), continuous in the COPD and intermittent in the SAHS, and they are associated to pulmonary oxidative damage, an exaggerated inflammatory response in the lung and systemically. Surprisingly, despite the fact that lung tissue – bronchial epithelium – 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 together 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 (i) lung protection and repair (ii) ventilation and (iii) their potential to identify novel biomarkers for diagnosis and prognosis of fatal respiratory diseases. 3) Role of HIF oxygen sensing pathways in cellular adaptation to hypoxia through the mitochondrial reprogramming. Along this line, NDUFA4L2 is a target gene of hypoxia-inducible factors (HIF) that has the ability to decrease overall mitochondrial oxygen consumption through the inhibition of mitochondrial complex I. These properties of NDUFA4L2 also diminish the production of reactive oxygen species (ROS) in mitochondria, which is essential for cell protection against oxidative damage associated to hypoxic scenarios. Thus, although the protective role of NDUFA4L2 in in vitro scenarios where ROS are important for cell viability is well known, it is also crucial to know the pathophysiological role of NDUFA4L2 in vivo. We have recently generated NDUFA4L2-deficient mice to understand its in vivo role in disease models associated to hypoxia.



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Major grants

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GROUP 7



Head of laboratory



Martínez Ruiz, Antonio

We are now investigating the involvement of NCLX in reperfusion after stroke. Our work proposes NCLX as a pharmacological target in the treatment of diseases in which hypoxia and reactive oxygen species production are present, including recovery and reperfusion after ischemic stroke.

2. Oxidative post-translational modifications and redox proteomics

We have previously studied the functional role of S-nitrosylation and we have developed methods for detecting oxidative cysteine post-translational modifications (thiol redox proteomics), which we have applied to the study of neurogenesis, ebselen- induced oxidative stress and drug-induced erythrocyte death. We are currently studying the role of protein sulfhydrylation, an oxidative modification of cysteines with sulfhydryl acid, H₂S. In a collaborative international project, we are currently studying the role of protein sulfhydrylation in neurogenesis in Down syndrome.



Group members

- Choya Foces, Carmen
- Delgado Martín, Susana
- Hugo Pereira, Martín



Research interest

1. Redox signalling in the response to hypoxia

We previously showed that different cell types produce a superoxide burst in acute hypoxia, which can be a signal for cell adaptation through acute responses as well as through activation of the HIF pathway. We have investigated the mechanisms that lead to this acute production of superoxide. We have discovered that hypoxia triggers a conformational shift in mitochondrial complex I that increases its D form, which acidifies the mitochondrial matrix, and that this functional shift of complex I is a key step in the superoxide burst. We have also discovered that mitochondrial Na⁺/Ca²⁺ exchanger (NCLX) is involved in this superoxide burst, showing that mitochondrial Na⁺ import by NCLX alters oxidative phosphorylation and induces superoxide production.



Major grants

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Publications (1)

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GROUP 8



Head of laboratory



Calzada García, María Josefa



Group members

– Sevilla Montero, Javier



Research interest

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

of the matricellular protein thrombospondin-1 (TSP-1) in the context of chronic pulmonary diseases characterized by a decrease in oxygen tension and pulmonary hypertension, these including Pulmonary Arterial Hypertension (PAH) and Chronic obstructive pulmonary disease (COPD).

These pathologies are rapidly progressive pulmonary vascular diseases with a multifactorial etiopathogenesis that result in loss of pulmonary function and emphysema, right-sided heart failure and ultimately death. However, the underlying cellular and molecular mechanisms are largely unknown. Our recently published results shed light on some of the processes in which TSP-1 actively participates in the development of PAH and point to this protein as a causal molecule in experimental and clinical PAH and therefore represents a candidate therapeutic target (Rogers NM. et al. Cardiovascular Res. 2017; Labrousse-Arias D. et al Cardiovascular Res. 2016). In addition TSP1 has been observed in epithelial, bronchial and alveolar macrophage cells of patients with COPD, increase that is magnified as the disease progresses. We are currently investigating the role of hypoxia/TSP-1 and smoke exposure/TSP-1 in vascular remodeling in chronic lung diseases such as PAH and COPD. In particular, the role of TSP-1 in arterial muscularization, and whether it promotes the differentiation of pulmonary artery adventitial fibroblasts (PAAF) into more contractile myofibroblasts.

To these aims we have optimized techniques such as Traction Force Microscopy (TFM) to evaluate the functional relevance of contractility molecular markers on these cells and CLARITY, a technique that allows high-resolution information from a complex system, while maintaining the global perspective needed to understand system function.



Major grants

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GROUP 10



Head of laboratory



Cadenas Álvarez, Susana



Group members

– Mata Villanueva, Ana



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.



Major grants

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Publications (1)

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GROUP 11



Head of laboratory



Mayor Menéndez, Federico



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



Group members

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- Martins Neves, María Margarida
- Navarro Lérda, Inmaculada
- Ortega Giménez, Alba
- Ramos Barbeito, Paula
- Ribas Núñez, Catalina
- Sanz Flores, María

frequent clinical co-morbidities, pointing to this protein as a potentially relevant “synergic” therapeutic target. The group pursues the following lines of investigation:

1. Integrative role of GRK2 in the crosstalk of signalling cascades acting within the breast tumour microenvironment
2. GRK2 in epidermal homeostasis and in keratinocyte-immune cells crosstalk and potential pathological implications in skin inflammatory diseases and in squamous cell carcinomas.
3. GRK2 in obesity and insulin resistance-related contexts: participation of GRK2 in determining the pro-inflammatory profile of macrophages and impact of myeloid GRK2 in inter-organ crosstalk in cardiometabolic disease.
4. Explore the functional implications of the Gal-pHq interactome on autophagy and nutrient sensing and on oxidative stress processes and its impact on endothelial cell function and cardiovascular disease.

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Major grants

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- Mayor Menéndez, Federico. INFLAMUNE-CM: Nuevos mecanismos moleculares y celulares implicados en la fisiopatología inmune y enfermedades inflamatorias. B2017/BMD-3671. Comunidad de Madrid. 2018-2021.
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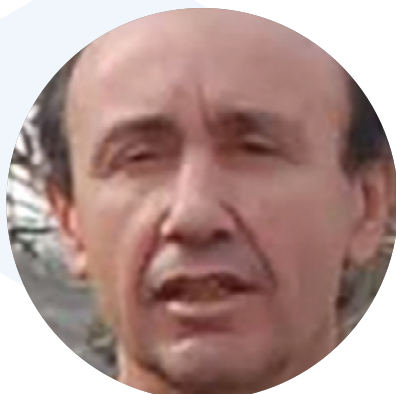
GROUP 12



Head of laboratory



Group members



Fresno Escudero, Manuel

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- Callejas Hernández, Francisco
- Cuesta Rubio, Natalia
- de Chorro y de Villa-Ceballos, María de los Ángeles
- Galán Martínez, Javier
- García Prieto, Teresa
- Gironès Pujol, Nuria
- Jiménez Martínez, Marta
- Maza Moreno, María del Carmen
- Merino Valverde, Javier
- Stamatakis Andriani, Konstantinos
- Torres Gérica, Patrici
- Úbeda Cantera, María

**Research interest**

We are analyzing the involvement of Pathogen recognition receptors (as TLRs or galectin) and Cyclooxygenase (Cox)-2/prostaglandins (PGs) in the immune system and inflammatory pathologies as obesity, cancer and sepsis. 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 also found that galectin-1 (Gal-1) deficiency abolished diet induced obesity and insulin resistance in mice. Gal-1 is needed for the differentiation of preadipocytes by regulation of the key proadipogenic transcription factor PPAR- γ and in the differentiation of brown adipocytes

Cox2 inhibitors reduce cancer but their therapeutic use has been hampered by their side effects. As an alternative, we have analyzed genes regulated by Cox2 or PGs that may provide a protooncogenic advantage. Among those, mPGES-1, DUSP10, Trop2 and many from the TGF β pathway, as PMEPA1, which, interestingly, were induced by PGF2a. DUSP10 controls stress response to serum deprivation and confluence arrest and binds and dephosphorylates Yes-associated protein 1 (YAP) in colorectal cancer. PGF2a TGF β -PMEPA1 pathway is a critical mediator of epithelial plasticity and ovarian carcinoma progression. Those molecules are amenable to drug discovery, lacking the unwanted side effects of COX-2 pharmacological inhibitors.

Interestingly, PGF2a induces Cox-2 and DUSP10, having a very important pathogenic role in animal models of inflammatory bowel disease (IBD), a leading cause of colorectal cancer, since the use of pharmacological PGF2a antagonists prevents IBD

On the other hand, TCFL5 is a member of the bHLH transcription factor family with multiple isoforms in both humans and mice. Complete deletion of the isoforms drastically reduces tumor properties

of colon cancer cells. Interestingly, the two major isoforms (TCFL5 and CHA) showed a reciprocal regulation and different functions in the cell, with CHA exercising a protumoral effect. TCFL5 / CHA expression is essential for NF κ B2 activity regulating the expression of anti-apoptotic genes such as BCL2 and also controlling the expression of the pluripotency markers SOX2, NANOG and KLF4.

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

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

Finally, in the infection by the protozoan parasite *T. cruzi* we are working on the impact of *T. cruzi* genetic variability on the clinical outcome and immunopathology of Chagas' disease as well as 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- γ 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.

- Fresno Escudero, Manuel. TDFL5/CHA en la diferenciación y activación de linfocitos B y T en la generación de leucemias. PID2019-104760RB-100. AEI. 2020-2023.
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Major grants

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- Fresno Escudero, Manuel. INFLAMUNE-CM. Nuevos mecanismos moleculares y celulares implicados en la fisiopatología inmune y enfermedades inflamatorias. B2017/BMD-3671. Comunidad de Madrid. 2018-2021.
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GROUP 13



Head of laboratory



Penela Márquez, Petronila



Group members

- **Albitre Sanz, Ángela**
- **Ortiz del Castillo, Belén**
- **Rivas Guerrero, Verónica**



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.



Major grants

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Publications (2)

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GROUP 17



Head of laboratory



Murga Montesinos, Cristina

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:

1. 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.



Group members

– **Concepción Arcones, Alba**



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.

2. 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.
3. 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.



Major grants

Granted 2021:

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Publications (2)

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GROUP 18



Head of laboratory



Iñiguez Peña, Miguel Ángel



Group members

- **Bago Plaza, Ángel**
- **Renshaw Calderón, Ana**



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.



Major grants

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Head of laboratory



Blanco Guerra, Carlos Alberto



Group members

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



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

GROUP 20

allergy, including bronchial asthma and rhinoconjunctivitis, is a research priority target for most health organizations. Nowadays, allergen specific immunotherapy is the only way to modify the natural course of allergic respiratory diseases. Meanwhile, food & drug allergies are also rising problems, due to both the potential severity of reactions and to their great impact on patient quality of life. In this context, our group has the following main research lines, in collaboration with the allergy research network ARADyAL (ISCIII RD16/0006):

- Searching for biomarkers of allergy severity: multicentric BIOGRAL study led by Dr. Barber from San Pablo CEU University and funded by ISCIII, including patients with respiratory- food- and drug-allergies, is now ongoing.
- Immunotherapy for respiratory allergy: a 2-yr placebo controlled clinical trial has been finished, checking immunological changes induced by grass-pollen immunotherapy on respiratory allergy, a doctoral thesis is in the writing phase.
- A study on severe bronchial asthma treated with biological drugs, cooperating with San Pablo CEU university, is ongoing.
- Cross-reactivity between Cupressus arizonica and Cryptomeria japonica has been checked in collaboration with ALK-Abello.
- A study on adverse reactions to iodinated- and gadolinium-contrasts led by Dr. Vega is ongoing, in which tolerance to alternative contrasts is assessed by means of a protocol of fast challenge tests at full dose. First results have been already published and a doctoral thesis will soon be presented.
- We have participated in a research project (Retos Investigación: Proyectos I+D+i 2017,

MINECO) with Dra. Cuadrado from INIA (National Food Research Institute), focused on nut allergy. Both DNA- and immunological- biosensors will be developed.

- Possible cross-reactivity between peanut and the new food called miracle berry has been checked in collaboration with the biotechnology Dept. of Madrid Polytechnic University.
- Flaxseed allergy has been characterized in collaboration with Madrid Complutense University.
- Dra. Múgica and Dra. Ramos are collaborating with the Spanish Allergy Society in the Allergodata study, recording patients treated with biological drugs.
- Dr. Daschner continues with its productive research lines on Anisakis allergy, which made it possible, in a collaborative study with the ISCIII, to perform an epidemiological analysis of Hospitalizations due to Anisakiasis and establish a new estimate of nationwide allergy cases. He continues to work in the field of Evolutionary Medicine with a multidisciplinary approach and in collaboration with the National Museum of Natural Sciences.

- 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 its modulation by the microbiota, the mast cell-neuron axis during allergen immunotherapy and the impact of allergic disease on the development of atherosclerosis. (<https://www.jimenezsaizlab.com/>).



Major grants

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

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GROUP 15



Head of laboratory



Ibáñez Sandín, María Dolores



Group members

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



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 Pru p3 (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.



Major grants

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Publications (7)

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Meseguer Arce J, Miralles JC, Montoro de Francisco AM, Poza Guedes P, Rodríguez Del Río P, OmaBASE task force (Pediatric Allergy Committee, Spanish Society of Allergy and. **Oral immunotherapy in severe cow's milk allergic patients treated with omalizumab: Real life survey from a Spanish registry.** Pediatr Allergy Immunol 32 (6): 1287- 1295. 2021. PMID: 33835593. IF: 6,377. DOI: 10.1111/pai.13517.

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GROUP 21

LINE 1.6 INFLAMMATORY PROCESSES IN NEPHROLOGICAL DISEASES



Head of laboratory



Barril Cuadrado, Guillermina



Group members

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



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.



Publications (12)

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GROUP 22



Head of laboratory



Research interest



Ancochea Bermúdez, Julio



Group members

- Alonso Pérez, Tamara
- Barrio Mayo, María del Mar
- Boukichou Abdelkader, Nisa
- Capote Moreno, Ana Laura
- Chicot Llano, Marta
- Cisneros Serrano, Carolina Victoria
- García Castillo, Elena
- García Pérez, Francisco Javier
- Girón Moreno, Rosa María
- Gómez Punter, Rosa Mar
- Landete Rodríguez, Pedro
- Marcos, María Celeste
- McFarland, Jonathan James Reid
- Peláez Laderas, Adrián
- Pérez González, María Patricia
- Rubio Bueno, Pilar
- Ruiz Álvarez, Inés
- Soriano Ortiz, Joan Bautista
- Valenzuela, Claudia
- Vázquez Espinosa, Emma
- Zamora García, Enrique Domingo
- Melero Moreno, Carlos

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

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

General objectives:

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

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

Additionally, persistent COVID is currently a new disease with a major impact on public health in

Spanish society. In Spain, it is estimated that between 400,000 and 800,000 people suffer or will suffer from persistent COVID, as 10-16% of patients still have symptoms one year after overcoming acute COVID. For this reason, our team has also been interested in studying the long-term sequelae of persistent COVID.

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

Plan of actions for 2020-2022

Further develop, maintain and strengthen the research group on chronic respiratory conditions at the Health Research Institute Princesa (IP).

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

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GROUP 24



Head of laboratory



Research interest



Majano Rodríguez, Pedro Lorenzo



Group members

- Casabona Francés, Sergio
- de la Morena López, Felipe
- Fernández-Pacheco Esteban, Jennifer
- Herranz Pérez, Raquel
- Laserna Mendieta, Emilio José
- Martín Domínguez, Verónica
- Martínez Pérez, Jorge
- Miranda García, Pablo
- Molina Jiménez, Francisca
- Moreno Monteagudo, José Andrés
- Muñoz Codoceo, Rosa Ana
- Pérez Fernández, María Teresa
- Santander Vaquero, Cecilio

**Associated Clinical Group Hospital
General de Tomelloso**

- Lucendo Villarín, Alfredo José
- Arias Arias, Ángel Jesús
- Arias González, Laura
- González Cervera, Jesús

MAIN:

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 in-

dustrialized 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.



Major grants

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Fernández LA, [Lucendo AJ](#). **Comparison of a new rapid method for determination of serum anti-adalimumab and anti-infliximab antibodies with two established ELISA kits.** J Pharm Biomed Anal 198: 114003-114003. 2021. PMID: 33714800. IF: 3,935. DOI: 10.1016/j.jpba.2021.114003.

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GROUP 23



Head of laboratory



García Buey, Luisa Consuelo



Group members

- Caldas Álvarez, María
- González Moreno, Leticia
- Mendoza Jiménez-Ridruejo, Jorge
- Real Martínez, Yolanda



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 ef-

fective. 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.



Publications (5)

Nyssen OP, Perez-Aisa A, Tepes B, et al. **Adverse Event Profile During the Treatment of Helicobacter pylori: A Real-World Experience of 22,000 Patients From the European Registry on H. pylori Management (Hp-EuReg).** Am J Gastroenterol 116 (6): 1220-1229. 2021. PMID: 33840725. IF: 10,864. DOI: 10.14309/ajg.0000000000001246.

Caldas, Maria, Perez-Aisa, Angeles, Tepes, Bojan, et al. **The Role of Statins on Helicobacter pylori Eradication: Results from the European**

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GROUP 25



Head of laboratory



Research interest



Marazuela Azpíroz, Mónica



Group members

- Aguirre Moreno, Nerea
- Araujo Castro, Marta
- Caldas Álvarez, María
- Carrillo Lozano, Elena
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- Justel Enriquez, Alicia
- Knott Torcal, Carolina
- Martínez Hernández, Rebeca
- Muñoz de Nova, José Luis
- Pérez Casas, Andrés
- Ramos Levi, Ana María
- Ruiz Roso Guerra, María de Belén
- Sacristán Gómez, Pablo
- Sampedro Núñez, Miguel Antonio
- Sánchez de la Blanca Carrero, Nuria
- Serrano Somavilla, Ana

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 (EBio-Medicine. 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 Transcriptomics.

Another area of investigation of the group is the study of mechanisms resulting in evasion of im-

mune 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.



Major grants

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GROUP 26



Head of laboratory



Research interest



Argente Oliver, Jesús



Group members

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- Campillo Calatayud, Ana
- Canelles Ortiz, Sandra
- Chowen King, Julie Ann
- Collado Pérez, Roberto
- Frago Fernández, Laura María
- García Piqueras, Jorge
- Güemes Hidalgo, María
- Guerra Cantera, Santiago
- Jiménez Hernaiz, María
- Martín Rivada, Álvaro
- Martos Moreno, Gabriel Ángel
- Pozo Román, Jesús

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 affection 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, hypo-

thalamal 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.



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.
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GROUP 5



Head of laboratory



García Monzón, Carmelo



Group members

- Carraro Casieri, Raffaele
- del Pozo Maroto, Elvira
- García García, Yaiza
- Rodríguez de Cía, Javier
- Sáez Sáez, Alicia



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 re-

main incompletely defined, most investigations indicate that insulin resistance plays a pivotal role in NAFLD set-up. 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. 1) To unravel the molecular mechanisms involved in the pathogenesis of NASH searching for potential therapeutic targets. We are exploring the role of autophagy in the development of NASH. We recently reported that autophagic flux is impaired in hepatocytes from NASH patients and murine models of NASH and we are, therefore, proposing to investigate in the next future whether therapies aimed to restore the autophagic flux might prevent or attenuate the progression of NAFLD. We are also addressing the role of intermittent hypoxia in the pathogenesis of NAFLD by analyzing the expression levels of hypoxia-inducible factors 1 and 2 in liver biopsies and serum of NASH patients and murine models of NASH as well as the impact of hypoxia on the mitochondrial function in human hepatocytes under experimental conditions of lipid overload. 2) Identification of biomarkers able to be used for noninvasive diagnosis of NASH. We have shown that genetic variants of SLC2A1 are associated with NAFLD and that circulating levels of soluble CD36 is an independent factor associated with advanced steatosis in NAFLD but not in patients with chronic hepatitis C virus (HCV) infection. More recently, we have reported that the combination of ultrasound and HOMA score is useful for noninvasive diagnosis of patients with NASH. We are now pursuing diagnostic tools based on ELISA multiplex using proteins of pathogenic relevance in chronic liver diseases. 3) Impact of the new direct-acting antivirals on carbohydrate and lipid metabolism in patients with chronic hepatitis C treated with these highly effective antiviral drugs: Implications for the cardiovascular morbidity and mortality. It is well known that chronic HCV infection is

associated with insulin resistance and type 2 diabetes mellitus together with alterations in hepatic lipid metabolism. The discovery of new direct-acting antiviral agents has become a huge advance in the treatment of HCV infection. Among them, sofosbuvir and other new antivirals in combination with ribavirin has improved considerably the sustained virological response of HCV infection. However, little is known about their effects on carbohydrate and lipid metabolic profiles in patients treated with these new direct-acting agents and their potential mechanistic actions. On that basis, we propose to determine the effects of sofosbuvir and other direct-acting antivirals on HCV-induced metabolic complications such as insulin resistance, hyperglycemia and dyslipidemia. Moreover, the impact of therapy with sofosbuvir and other related agents on metabolic disturbances induced by the impairment of autophagic flux in HCV infection will be analyzed. In summary, we believe that our lines of investigation could shed light, in the next future, on key aspects for the pathogenesis and therapy of NAFLD and other chronic liver diseases as well as for the noninvasive diagnosis of NASH.



Major grants

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GROUP 42



Head of laboratory



González Rodríguez, Águeda



Group members

- Chavez Isaza, Stephanía
- Domínguez Alcón, Lucía Soledad
- El Bouayadi Mohamed, Liliam
- Landete Rodríguez, Pedro
- Marañón Barnusell, Patricia
- Muñoz Olmedo, José Manuel
- Peñaloza González, Ángela Lucía
- Rey Fernández, Esther



Research interest

Today's lifestyle is characterised by an abundance of calories, reduced physical activity and increased life expectancy, which has triggered the incidence of obesity in epidemic proportions in recent decades, and is particularly alarming in the child population. This increase in obesity incidence is associated with a series of metabolic pathologies, including type 2 diabetes mellitus, non-alcoholic fatty liver disease and atherosclerosis, which have led to

research projects dedicated to clarifying the molecular mechanisms that trigger them. This grouping of metabolic and cardiovascular risk factors is known as Metabolic Syndrome.

Our research group is made up of basic and clinical researchers, who actively collaborate to develop high level translational research focused on the study of the molecular bases of Metabolic Syndrome and hepatic pathologies. The group therefore pursues three fundamental lines of research.

1. Study of metabolic complications associated with chronic diseases. On the one hand, we are evaluating the effects of sofosbuvir, one of the new direct-acting antiviral agents that has become a breakthrough in the treatment of chronic hepatitis C, metabolic complications and cell death associated with that disease. On the other hand, we are exploring possible factors (degree of systemic inflammation and hypoxia, among others) responsible for the association between the most prevalent chronic respiratory diseases and the appearance of cardiovascular and metabolic disorders.
2. Identification and characterisation of new molecular targets involved in peripheral insulin resistance associated with metabolic damage. We are looking for new therapeutic targets associated with inflammatory processes, studying their implication in inflammation induced by a high-fat diet and consequences on insulin response in peripheral tissues, including the liver.
3. Impact of Bone Morphogenetic Proteins on hepatic pathophysiology. Bone morphogenetic proteins are growth factors that are booming due to their pleiotropic role in different cellular processes, but their involvement in the pathogenesis of the liver is a topic that has hardly been

investigated. Liver pathophysiology includes non-alcoholic fatty liver disease (NAFLD), acute liver failure, liver fibrosis or cirrhosis, viral hepatitis, hepatocellular carcinoma and alcoholic fatty liver. This line of research therefore seeks to identify the role of these proteins in liver damage progression, leading to the generation of new direct biomarkers for non-invasive diagnosis/prognosis of the different evolutionary phases of these pathologies, thus contributing to the design of new, more effective and less invasive diagnostic tools.



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AREA 2



TRANSLATIONAL NEUROSCIENCE



- **LINE 2.1** NEUROPHARMACOLOGY AND NEUROPROTECTION
- **LINE 2.3** CLINICAL PHARMACOLOGY AND PHARMACOGENETICS
- **LINE 2.4** DIAGNOSTIC AND THERAPEUTIC ADVANCES IN AFFECTIVE DISORDERS
- **LINE 2.5** NEUROSURGERY OF EPILEPSY
- **LINE 2.6** CEREBROVASCULAR DISEASES



Head of laboratory



García López, Manuela



Group members

- Baena Ropero, Irene
- del Sastre López, Eric
- Fernández Mendivil, Cristina
- Luengo Martín, Enrique
- Mayo Mariscal de Gante, Paloma Pilar
- Peñasco Iglesias, Sara
- Rodríguez Ortega, Elisa
- Trigo Alonso, Paula
- Varela Jeraldo, Teresa Isabel



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

GROUP 16

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 and 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 pre-clinical 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 multi-target 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.



Major grants

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GROUP 28



Head of laboratory



de los Ríos Salgado, Cristóbal



Group members

- Calzaferri, Francesco
- Cano Abad, María Francisca
- de Pascual y del Castillo, Ricardo
- Fernández Martín, Ana
- García de Diego, Antonio Miguel
- García García, Antonio
- Martín Alcalá, Gabriel
- Ruiz Ruiz, Cristina
- Viejo de Navas, Lucía



Research interest

My current work focuses on the validation of new therapeutic targets for the treatment 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.



Major grants

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GROUP 41



Head of laboratory



Egea Máiquez, Francisco Javier



Group members

- Farré Alins, Victor
- López Rodríguez, Ana Belén
- Narros Fernández, Paloma
- Palomino Antolín, Alejandra



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 brain injury and neurodegenerative diseases.

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

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

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

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

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

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



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.

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GROUP 32



Head of laboratory



Abad Santos, Francisco

- Ochoa Mazarro, María Dolores
- Ovejero Benito, María del Carmen
- Pérez Hernández, Concepción
- Pintos Sánchez, Elena
- Queipo García, María José
- Román Martínez, Irene
- Román Martínez, Manuel
- Saiz Rodríguez, Miriam
- Sánchez Jiménez, Patricia
- Santos Molina, Elena
- Soria Chacartegui, Paula
- Villapalos García, Gonzalo
- Zubiaur Precioso, Pablo



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 1 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



Group members

- Campodónico, Diana María
- Casajus Rey, Ana
- Elizalde Horcada, Marcos
- Flores Ruiz, María Eugenia
- Gómez Fernández, Antía
- Koller, Dora
- Martín Vílchez, Samuel
- Mejía Abril, Gina Paola
- Navares Gómez, Marcos
- Novalbos Reina, Jesús Miguel

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. Last year, several clinical trials on the COVID-19 vaccine were conducted in our unit.

The group's research focuses mainly on the pharmacogenetics of several drugs prescribed for the treatment of various diseases, so that eventually this knowledge could help physicians to prescribe the best treatment for each patient in a personalised way. In 2020, 311 patients benefited from pharmacogenetic testing. We have also implemented pharmacogenetic testing through OpenArray, using a customised chip that can simultaneously analyse 120 SNPs located in 43 different genes. This technology has enabled us to significantly increase our portfolio of pharmacogenetic tests available to support physicians in prescribing medicines. Seven funded projects were active in 2020. In addition to projects funded in previous years, Francisco Abad Santos received new funding in 2020 (ICI20/00131) to evaluate a pharmacogenetics-guided tramadol prescribing strategy. Another important line of research focuses on therapeutic drug monitoring, mainly for antipsychotics and tyrosine kinase inhibitors.



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.
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GROUP 33



Head of laboratory



Ayuso Mateos, José Luis



Group members

- **Alcañiz Rodríguez, Montserrat**
- **Cabello Salmerón, María**
- **Castelletti, Chiara**
- **de la Fuente Carrillo, Javier**
- **de la Torre Luque, Alejandro F.**
- **Delgado Parada, Eduardo**
- **Dolz del Castellar Blanco, Blanca**
- **Eugui Anta, Estefanía Irene**
- **Ezquiaga Terrazas, María Elena**
- **Fernandez Natal, Cora**
- **Izquierdo Zarzo, Ana**
- **Lara Pérez, Elvira**
- **Leal Leturia, Itziar**
- **López García, María Pilar**
- **Martín María, Natalia**
- **Martínez Cano, Herminio**
- **Miret García, Marta**
- **Moreno Agostino, Darío**
- **Morillo Cuadrado, Daniel Vicente**

- **Ortiz-Tallo Moya, Ana**
- **Rico Uribe, Laura Alejandra**
- **Rodríguez McGreevy, Kerry**
- **Sánchez Carro, Yolanda**
- **Torio Palmero, Iosune**
- **Unzeta Conde, Belén**
- **Vieira Campos, Alba**



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 well-being. 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 (AG-ES-CM project).

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

1. "Trajectories on mental health, physical health and functioning: Third wave survey of a Spanish cohort of the adult population", which is aimed to carry out a third time point assessment to know trajectories of health in ageing people as well as recruiting new people to make generational comparisons.
2. "CIBERSAM cohorts about FEP cases and controls", which is aimed to create a common cohort from different existing cohorts with first episode patients and controls, and follow-up the common cohort at 5, 10 and 15 years.
3. "Emotional fluctuation in daily life. Ecological analysis of depressive symptomatology in the general population" which is aimed to analyse the mood fluctuations throughout the day in a general population sample using mobile Apps.
4. "European Welfare Models and Mental Wellbeing in Final Years of Life", which is addressed to gather information on the components of wellbeing and welfare in people older than 80 years.
5. "Peripheral oxidative stress and inflammatory markers in Major Depressive Disorder", focuses on finding biological markers in Major Depressive Disorder.
6. "Metabolic Dysfunctions associated with Pharmacological Treatment of Schizophrenia

(TREATMENT)" in which we evaluate how short-term antipsychotic drug responses impact long-term metabolic control to identify and validate biomarkers with clinically predictive value for targeting drug induced metabolic dysfunctions.

7. "Psychiatric Ratings using Intermediate Stratified Markers (PRISM)", whose overall objective is to develop a quantitative biological approach to the understanding and classification of the endophenotypes that contribute to neuropsychiatric diseases, to accelerate the discovery and development of better treatments for patients with Alzheimer and Schizophrenia.



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. SYNCHROS: Synergies for Cohorts in health: integrating the role of all Stakeholders. SYNCHROS: 825884. 2019-2021.
- Ayuso Mateos, José Luis. AGES-CM2: Ambiente y genes en esquizofrenia. B2017/BMD- 3740. Comunidad de Madrid. 2018-2021.

Granted 2021:

- 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.



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GROUP 34



Head of laboratory



Pastor Gómez, Jesús



Group members

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- de Dios Tomás, Eva
- Domínguez Gadea, Luis
- García Navarrete, Eduardo
- Luque Cárdenas, Cecilia
- Martín Plasencia, Pilar
- Meilan Paz, María Luisa
- Navas García, Marta
- Pintor Zamora, Miguel
- Pulido Rivas, Paloma
- Rocío Martín, Esmeralda
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- Vega Zelaya, Lorena Carolina
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Research interest

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

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

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

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

The topics we are working on include the following:

- a. Identification of basal ganglia subnuclei by extracellular recording.
- b. Physiopathology of somatosensory thalamus, by means of somatosensory evoked potentials, electrically elicited.
- c. Connectivity in epilepsy. To do that, we are studying diffusion tensor imaging and fractional anisotropy, as well as electrophysiological recordings acquired by means of scalp or intracranial recordings.

- d. Genetics and epi-genetics in epilepsy.
- e. Quantified EEG (qEEG) to use as biomarker for different pathologies. Among those fields specially targeted by this technique are patients in Intensive Care Units and neurological and psychiatric illness.
- f. Cortico-cortical connectivity, especially for language function.



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GROUP 35



Head of laboratory



Research interest



Vivancos Mora, José Aurelio



Group members

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

Associated Group

- Ayala Rodrigo, José Luis
- Pagán Ortiz, Josué
- Risco Martín, José Luis

THE MAIN RESEARCH LINES OF THIS GROUP ARE:***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 neuro-radiology 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



Major grants

- Vivancos Mora, José Aurelio. MULTI-TARGET&VIEW-CM: imagen multimodal de la respuesta terapéutica a estrategias multidiana en enfermedades neurológicas. B2017/BMD-3688. Comunidad de Madrid. 2018-2021.
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ANNUAL
REPORT OF
SCIENTIFIC
ACTIVITY

2021



AREA 3



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

GROUP 36



Head of laboratory



Research interest



González Álvaro, Isidoro



Group members

- Ahijón Lana, María
- Castañeda Sanz, Santos
- Clemente Garulo, Daniel
- García de Vicuña Pinedo, Rosario
- García Vadillo, Jesús Alberto
- Gómez León, María de las Nieves
- Llorente Cubas, Irene María
- López Robledillo, Juan Carlos
- Montes Casado, Nuria
- Ortiz García, Ana María
- Rodríguez García, Sebastián de la Cruz
- Tomero Muriel, Eva Gloria
- Triguero Martínez, Ana
- Uriarte Ecenarro, Miren
- Vicente Rabaneda, Esther Francisca

The main goal for our group is personalized medicine in the field of autoimmune/inflammatory rheumatic disorders (mainly rheumatoid arthritis, spondyloarthritis, systemic lupus erythematosus, giant cell arteritis and scleroderma). Our efforts are focused on providing new knowledge about two unmet needs for rheumatologists: severity biomarkers and predictors of response to disease modifying. anti-rheumatic drugs, either synthetic or biological. For the last five years, to achieve these objectives, we have consolidated our collaborations both at a local level in our Institute 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 will end in 2018, our group will continue including patients in the IIS-IP Bio-bank, and we will expand the sample collection to JAK-inhibitors.

On the other hand, we maintain an intense collaborative effort with groups of the Network of Inflammation and Rheumatic Diseases (RIER), which belongs to the RETICS 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 last two years, and especially during 2020, we have collaborated with Dr Amaya Puig Kröger 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.



Major grants

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GROUP 37



Head of laboratory



Research interest



Daudén Tello, Esteban



Group members

- Aragüés Montañes, Maximiliano
- Chicharro Manso, Pablo
- Collado Rodríguez, María Teresa
- Crespo Martín, Olga
- de Argila Fernández-Durán, Diego
- de la Fuente Flores, Hortensia
- Delgado Jiménez, Yolanda
- Duarte Flórez, Pablo
- Fraga Fernández, Javier
- Freih Fraih, Alwalid
- García García, María Carmen
- Gómez Gago, María Jesús
- Llamas Velasco, María del Mar
- Muñoz Aceituno, Ester
- Muñoz Hernández, Patricia
- Reolid Pérez, Alejandra
- Rodríguez Jiménez, Pedro Antonio
- Sánchez Pérez, Abilio Javier
- Santamaría Domínguez, Cristina

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

1. Immune-mediated inflammatory diseases (IMID), particularly including psoriasis, atopic dermatitis and hidradenitis. The main lines of investigation are: a) Immunoregulatory molecules as biomarkers predicting response to biological therapies and disease severity in IMIDs. These are a group of diseases that display inflammation as a major pathogenic mechanism. Their long-term impact has been alleviated by the implementation of biological therapy. Despite the growing knowledge on the etiopathogenesis of these diseases and the marked improvement in their management represented by biologic therapy, markers of the severity of the disease or to predict whether patients will be refractory to treatment are lacking. We are searching for new predictive biomarkers of IMID severity and responsiveness to biologics; b) Gene Expression Profile in patients with IMIDs c) Epigenetic biomarkers as predictors of therapeutic response to biologic drugs in psoriasis; d) Immunoregulatory molecules and their therapeutic potential. We investigate the possible role of GADD45, ICOSL, TSP-1, and galectins in the immunopathogenesis of psoriasis, and the possibility of finding new therapeutic targets for the treatment of this disease; e) Survival analysis of conventional systemic therapies and biologics in psoriasis; f) Identification of Copy- Number Variants associated with the risk of developing psoriasis and psoriatic arthritis, using a genome-wide analysis approach; g) Study of optimization strategies (dose reduction, increase of the administration interval) in the treatment of moderate-to- severe psoriasis with systemic agents; h) Regulation of CXCL12 and RAPTOR by novel miR-

NAs and their role during the inflammatory process in Psoriasis: i) Integrative study of systemic inflammation in chronic inflammatory skin diseases and its association with cardiovascular disease.

2. Eczematous dermatitis. Study on the prevalence of allergens as responsible for allergic contact dermatitis in the Spanish population

3. Connective Tissue Diseases. Determination of the association of myositis-specific autoantibodies and myositis-associated autoantibodies with clinically amyopathic dermatomyositis.

4. Photobiology. Studies on epidemiology, clinical phenotypes, and photobiology of solar urticaria.



Major grants

Granted 2021:

- 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.



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GROUP 38



Head of laboratory



Research interest



Pérez Gisbert, Francisco Javier



Group members

- Acosta Rubio, Diana
- Aldars García, Laila
- Baldán Martín, Montserrat
- Beceiro Pedreño, María José
- Casanova González, María José
- Chaparro Sánchez, María
- Durán Vegue, Almudena
- Fernández Tomé, Samuel
- García Donday, María
- Garre Vázquez, Ana Isabel
- Jaén Calvo, Cristina
- Marín Gómez, Alicia Carmen
- Mora Gutiérrez, Irene
- Ortega Moreno, Lorena
- Palomino Pérez, Laura María
- Parra Pineda, Pablo
- Ramírez Belinchón, Cristina Mercedes
- Román San Martín, Alicia
- Soleto Fernández, Irene
- Velasco Rodríguez-Belvís, Marta

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 com-

munity, 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 (SEGHN), 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.



Major grants

- Pérez Gisbert, Javier. Identificación de biomarcadores de respuesta al tratamiento con fármacos biológicos en la enfermedad inflamatoria intestinal mediante abordaje proteómico y de citometría de masas PI18/00622. ISCIII. 2019-2021.
- 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.

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- Pérez Gisbert, Javier / Baldan Martín, Montserrat. Effect of tofacitinib on coagulation and platelet function, and its role in thromboembolic events. Pfizer. Investigator Initiated Sponsored Research. 2021.
- Chaparro Sánchez, María / Pérez Gisbert, Javier. Tofacitinib in ulcerative colitis: real world evidence. (To-ReWard Study). Pfizer. Investigator Initiated Sponsored Research. 2021.
- Pérez Gisbert, Javier. Analysis Of The Effectiveness And Safety Of Switching From Originator To Biosimilar Adalimumab In Patients With Inflammatory Bowel Disease. Biogen. Investigator Initiated Sponsored Research. 2021.
- 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.
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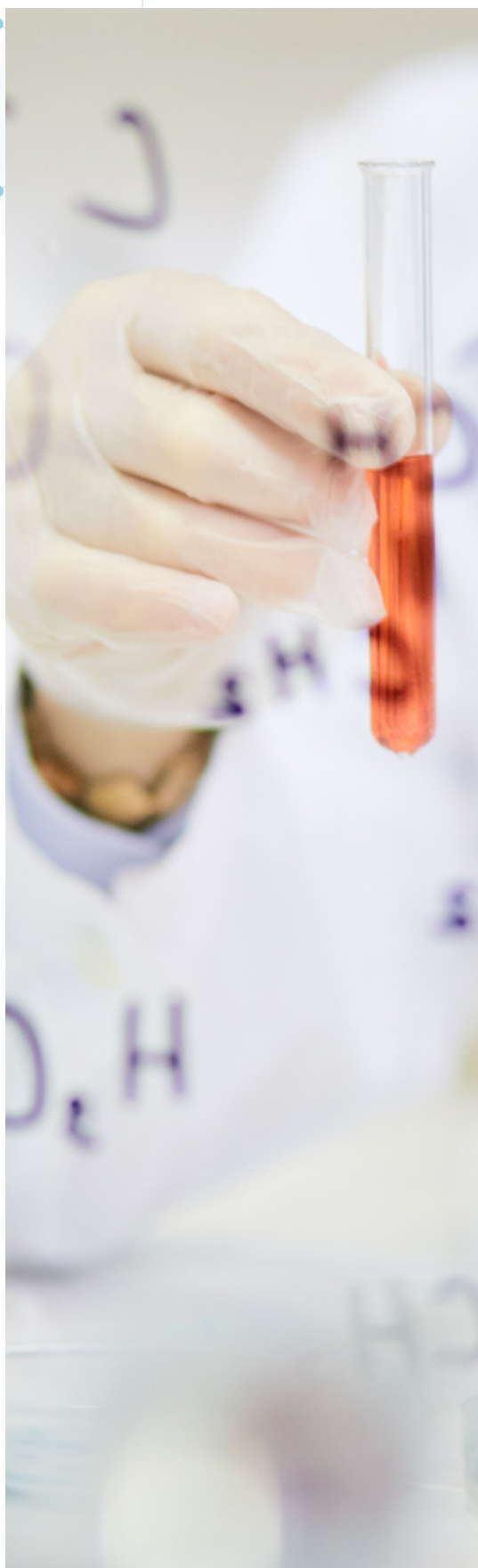
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GROUP 39



Head of laboratory



Research interest



Madero López, Luis



Group members

- Aguado Bueno, Beatriz
- Andion Catalán, Maitane
- Bautista Sirvent, Francisco José
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- Castillo Sanz, Andrés Gaspar
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- Molina Angulo, Blanca
- Ramírez Orellana, Manuel
- Ruano Domínguez, David
- Rubio San Simón, Alba
- Sebastián Pérez, Elena
- Sevilla Navarro, Julián
- Vicuña Andrés, Isabel

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 pre-clinical 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 immuno-

therapy 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 Cellular Immunotherapy. Tumor-infiltrating lymphocytes (TILs).

Childhood leukemias.

Haematopoietic progenitor cell transplantation.



Major grants

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GROUP 44



Head of laboratory



Steegmann Olmedillas, Juan Luis



Group members

- Alegre Amor, Adrián
- Arranz Muñoz, Eva María
- Arranz Sáez, María Reyes
- Benzo Callejo, Gonzalo
- Cannata Ortiz, María Jimena
- Figuera Álvarez, Ángela
- García-Noblejas Moya, Ana María
- Gómez García de Soria, Valle
- Jiménez Braña, Jimena
- Loscertales Pueyo, Javier
- Sanz de Benito, María Ángeles



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, epide-

miological 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.



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GROUP 4.5



Head of laboratory



Fernández Ruiz, Elena



Group members

- Carracedo Rodríguez, María Rosa
- Delgado Wicke, Pablito
- Santos Roncero, Santa Matilde



Research interest

Chromosomal translocations and gene mutations are frequently associated with the etiology of hematologic neoplasms. The JAK family of non-receptor tyrosine kinases (which comprises four members: JAK1, JAK2, JAK3 and TYK2) are involved in cytokine signaling on immune and hematopoietic cells and are crucial to normal hematopoiesis through the recruitment of downstream effectors of cell proliferation and survival. Recently, it has been reported that 10% of high risk pediatric acute lymphoblastic leukemia (ALL) cases bear activated JAK2 mutations, and could be potential candidates for JAK2 inhibitor therapeutic intervention. Acute lymphoblastic leukemia (ALL) is the most

common neoplasm in childhood and although most cases respond to treatment, 20% relapse, shortening survival. Therefore, we analyzed high risk ALL samples with next generation sequencing (NGS) to determine the percentage of JAK-family receptor mutations in the Spanish population. ALL samples were obtained from hospitals throughout the country. We found that mutations in TP53 and JAK2 are independent prognostic biomarkers in B-cell ALL. Furthermore, for TYK2, we provide evidence of naturally occurring catalytic loss-of-function TYK2 variants and reduced expression of TYK2 in B-ALL patients.

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



Major grants

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GROUP 46



Head of laboratory



Muñoz Calleja, Cecilia



Group members

- Cuesta Mateos, Carlos
- Díaz Fernández, Paula
- Marcos Jiménez, Ana María
- Pérez García, Yaiza



Research interest

Lymphocyte migration is involved in the pathogenesis of many diseases. Its control constitutes a target for different forms of immunotherapy. Conversely, other forms of immunotherapy can affect lymphocyte migration, leading to secondary effects, either desirable or not. Chemokines mediate recirculation of lymphocytes. The chemokine receptor CCR7 is involved in the homing of lymphocytes through secondary lymphoid organs (SLO) since access to lymph node (LN) of naïve T cells (TN), B-cells, dendritic cells (DC), and central memory T-cells (TCM) is mediated by CCR7, which recognizes the homeostatic

chemokines CCL19 and CCL21, two cognate ligands known to be expressed in SLOs.

CCR7 also mediates the lymph node dissemination of lymphoid malignancies and inflammatory cells. CCR7 is highly expressed on different lymphoid malignancies and several proofs of concept have demonstrated the therapeutic benefit of targeting either the molecule or the downstream signaling.

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is potentially curative for many blood disorders. However, it is often associated to post-transplant complications, being some of the most common the occurrence of graft-versus-host disease (GvHD) and CMV reactivation. GvHD occurs after the recipient antigens are recognized as foreign by donor naïve T cells. These antigens are presented in the context of the major histocompatibility complex (MHC) of mature DCs of the host or the donor, present in the SLOs. Consequently, it is necessary for both donor T lymphocytes and DCs to reach the SLOs through a homing migratory process, which is largely mediated by CCR7 and its ligands CCL19 and CCL21, as mentioned before. Alloantigens include minor histocompatibility antigens (mHAgs), which arise from nonsynonymous single nucleotide polymorphism differences between donor and recipient. However, to date only about 50 mHAgs have been reported.

Immune recovery after allo-HSCT is one of the most important factors conditioning the outcome of this therapeutic procedure since it affects the incidence of infections, GvHD and relapse. However, little is known about the association between the pattern of reconstitution of different immune cells and overall survival.

Dasatinib is a tyrosine kinase inhibitor used for the treatment of chronic myeloid leukemia that has immunomodulatory effects, including a lymphocytosis occurring in most patients that has been associated to a better outcome.

Our group aims at three objectives:

Assessment of the efficacy of CCR7 immunotherapy.

1. We are testing humanized versions of anti-CCR7 antibodies to treat ex vivo different lymphoid cancers, including B and T cell leukemias. We are analyzing their complement dependent or cell dependent cytolytic activity. Animal models of primary human T cell leukemias or GVHD are being used to evaluate the in vivo efficacy of targeting CCR7.

2. Identification of biomarkers of immune reconstitution that may be associated to CMV reactivation, GvHD and overall survival after HSCT.

In a cohort of 300 patients who were treated at our hospital with an allogeneic stem cell transplantation, we have measured:

- Different T cell subsets including naïve, stem cell-like memory, central memory and effector memory, at different time points (30, 60, 90, 180 and 360 days post- transplant).
- The activation state of lymphocyte populations weekly after HSCT and up to one year, based on the expression of the activation markers HLA-DR, CD25 and NKG2C.
- CMV-specific response of the donor's T-cells, based on their expression of Interferon- gamma when co-cultured with CMV peptides.

We are analyzing the association between the proportions and absolute numbers of the different T subsets and different clinical variables such as GVHD, CMV reactivation and overall survival.

Additionally, in collaboration with Dr. Catherine Wu from Dana Farber Cancer Institute (Boston, MA), we are studying the presence of tissue-specific mHAGs,

which could act as predictive biomarkers of GVHD development and severity.

3. Characterization of the immunomodulatory effects of dasatinib.

Here, we follow the hypothesis that adhesion and/or transmigration of lymphocytes across the HEV barrier may be impaired after dasatinib treatment.

We have performed several in vitro and in vivo experiments, including homing and egress assays, as well as intravital microscopy on popliteal lymph nodes, in order to address whether dasatinib has direct effects on the adhesive and migratory abilities of T and B lymphocytes. We are currently verifying our findings on human chronic myeloid leukemia patients.



Major grants

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GROUP 58



Head of laboratory



Alfonso Manterola, Fernando



Group members

- Bastante Valiente, Teresa
- Benedicto Buendía, Amparo
- Cuesta Cuesta, Francisco Javier
- del Val Martín, David
- Díez Villanueva, Pablo
- García Guimaraes, Marcos Manuel
- Moreno Carriles, Rosa María
- Reyes Copa, Guillermo
- Rivero Crespo, Fernando
- Seidelberger, Bernhard
- Suárez Sipmann, Fernando



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.



Major grants

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GROUP 48



Head of laboratory



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Group members

- Cecconi Duca, Alberto
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- Ortega Rabbione, Guillermo José
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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.



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- 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.

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- 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.



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GROUP 57



Head of laboratory



Research interest



Suárez Fernández, Carmen



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- Ibáñez Sanz, Patricia
- Moldenhauer Díaz, Fernando
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- Vinuesa Sebastián, María Mercedes
- Von Wernitz Teleki, Andrés Carlos

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

Age is an important determinant of arterial and venous outcomes. However, usual clinical practice in a general setting reveals a disproportionately low use of cardiovascular medications and intensive treatment in elderly patients that could otherwise benefit from their use. On the other hand, there probably is an excessive use of these medications in patients with cognitive impairment and short life expectancy. There is not enough information about cardiovascular therapies in very elderly patients with multiple comorbidities/diseases.

The purpose of this group is:

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





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.

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- 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.



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GROUP 49



Head of laboratory



Research interest



Novella Arribas, Blanca



Group members

- Cubillo Serna, Ana
- Fernández Luque, María Jesús
- Gallego Arenas, Ángela
- González Gamarra, Amelia
- Loeches Belinchón, María del Pilar
- López González, Javier
- Mayayo Vicente, María Soledad
- Rodríguez Salvanês, Francisco José
- Ruiz Díaz, María Lourdes
- Ruiz López, Marta
- Sánchez Alcalde, Rosa María
- Sánchez Gómez, Luis María
- Sierra García, María Belén

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.



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GROUP 50



Head of laboratory



de los Santos Gil, Ignacio



Group members

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- Bautista Hernández, Azucena
- de la Cámara de Llanza, Rafael
- García-Fraile Fraile, Lucio Jesús
- Gutiérrez Liarte, Ángela
- Sáez Béjar, Carmen María
- Sanz Sanz, Jesús



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 HE-PAVIR 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.



Major grants

- Santos Gil, Ignacio de los. Red Española de Investigación en Sida (RIS). RD16/0025/0012. IS-CIII. 2017-2021.



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Galván-Román JM, Rodríguez-García SC, Roy-Vallejo E, et al. **IL-6 serum levels predict severity and response to tocilizumab in COVID-19: An observational study.** J Allergy Clin Immunol 147 (1): 72-. 2021. PMID: 33010257. IF: 10,793. DOI: 10.1016/j.jaci.2020.09.018.

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GROUP 51



Head of laboratory



Aspa Marco, Francisco Javier



Group members

- Fernández Jiménez, Guillermo
- Galván Román, José María
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- Gómez Gutiérrez, Manuel
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- Lancho Sánchez, Ángel
- Luquero Bueno, Sergio
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- Ortega Gómez, María del Mar
- Rajas Naranjo, Olga
- Rodríguez Serrano, Diego Aníbal
- Vega Piris, Lorena



Research interest

MicroRNAs (miRNAs) are a family of endogenous, small, noncoding RNA molecules that modulate physiological and pathological pro-

cesses 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.



Major grants

- Aspa Marco, Francisco Javier. Análisis molecular del condensado de aire exhalado en el manejo del nódulo pulmonar solitario. Asociación Española contra el Cancer. 2019-2021.



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GROUP 52



Head of laboratory

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- Zurita Cruz, Nelly Daniela



Research interest



Alarcón Cavero, Teresa

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



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- Llorca Otero, Laura
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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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GROUP 40

LINE 3.8 INDIVIDUALIZED MEDICINE IN SOLID TUMORS



Head of laboratory



Colomer Bosch, Ramón



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- Pita Carranza, Antonio José
- Quintela Fandiño, Miguel Ángel
- Ramírez Herráiz, Esther
- Rogado Revuelta, Jacobo
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- Sánchez Torres, José Miguel
- Serra López-Matencio, José María
- Serrano Pardo, Rosario
- Toquero Díez, Patricia
- Torres Waldhaus, Natalia
- Vargas Díez, Erich Alberto
- Viamontes Ugalde, Francisco Eduardo



Research interest

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

Our line of translational research is focused on the discovery of biomarkers for assessing the effects

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



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GROUP ASSOCIATED 3



Head of laboratory

Cordero Ampuero, José

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Group members

- Alday Muñoz, Enrique
- Casa de Pantoja, Vicente Jesús
- Fernández Bermejo, Esther
- González Guijarro, Juan Jacobo
- Marín Aráez, Emilio
- Orts Rodríguez, Mar
- Planas Roca, Antonio
- Ramasco Rueda, Fernando
- Teba del Pino, Fernando

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Research interest

1. Prosthetic joint infection
2. Long-term results in total hip arthroplasty
3. Hip fracture

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GROUP 53



Head of laboratory



Zapatero Laborda, Almudena



Group members

- Adrados de Llano, María Magdalena
- Arellano Gañan, Ramón Cristóbal
- Castro Tejero, Pablo
- Cruz Conde, José Alfonso
- Martín de Vídals Cervantes, María del Carmen
- Murillo González, María Teresa
- Pérez González, Leopoldo
- Roch González, María



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 collaboration with CNIO (co-sponsor).

d. Collection of biological markers within the EORTC research project platform 1822 E2-RADlatE- OligoCare: A pragmatic observational cohort study to evaluate radical radiotherapy for oligo-metastatic cancer patients.

2. Advances in Prostate Cancer Treatment:

a. A phase III clinical trial to determine the optimum duration of androgen deprivation alongside high-dose radiotherapy in localized intermediate and high-risk PCa patients ("Phase III Trial comparing Long-Term Versus Short-Term Androgen Deprivation Combined With High-Dose Radiotherapy For Localized Prostate Cancer: GICOR Protocol DART01/05". EudraCT 2005-000417-36 ClinicalTrials.gov, number NCT02175212). 5-year data reported in Lancet Oncol 2015 and In J Radiat Oncol Biol Phys 2016. Substudy analysis of prognostic and predictive value of Testosterone nadir is ongoing.

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-IG-RT) versus three-dimensional conformal radiotherapy (3DCRT): comparative results on patients treated in a single institution, which demonstrate the significant reduction in acute and late genitourinary and rectal toxicity in patients with prostate cancer treated with IM-RT-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 Radio-

therapy in Patients With Localized Prostate Cancer, Protocol ID: CaP-VMAT-DIL. ClinicalTrials.gov Identifier: NCT03030625. Active recruitment.

- Participation in a Phase II clinical trial: Tratamiento de las Oligo-metástasis de Cancer de Prostata Mediante SBRT- Código SBRT-SG 05. NCT02192788.

STAGE: Recruitment completed.

- Participation in a Phase II clinical trial EC/2018/0130PEACE V/STORM: A randomized phase II trial for the Salvage Treatment of OligoRecurrent nodal prostate cancer Metastases (STORM).PROMOTOR: Ghent University. GICOR

4. Multi-Institutional Data Base Register in PCa:

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

5. BLADDER CANCER - BLADDER SPARING PROGRAM

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



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Gonzalez de Villambrosia, Sonia, Bastos, Mariana, Menarguez Palanca, Javier, Gayoso Cruz, Jorge,



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GROUP 54



Head of laboratory



Cerezo Padellano, Laura



Group members

- López Elzaurdía, Consuelo
- López Rodríguez, Mario
- Marín Palomo, Alicia
- Muñoz Guerra, Mario Fernando
- Naval Gías, Luis
- Raboso García-Baquero, Eduardo
- Rodríguez Campo, Francisco José
- Rodríguez Carnero, Pablo



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 distinct 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: 1) 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. 2) Advance in organ preservation treatment in locally advanced head and neck within a multidisciplinary approach of chemotherapy, radiotherapy and immunotherapy. 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. 3) 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. 4) 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.



Publications (5)

Muñoz-Guerra MF, Rodríguez-Campo FJ, Escorial-Hernández V, Brabyn PJ, Fernández- Domínguez M, Naval-Gías L. **The minimally invasive arthroscopic anterior myotomy in the treatment of internal derangement of the temporomandibular joint. A detailed description of the surgical technique.** J Stomatol Oral Maxillofac Surg 122 (1): 50-55. 2021. PMID: 32376499. IF: 1,569. DOI: 10.1016/j.jormas.2020.04.006.

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M, Naval-Gías L. **Is There a Relationship Between Age, Personal Factors or Surgical Findings, and Outcome After Temporomandibular Joint Arthroscopy?** J Oral Maxillofac Surg 79 (5): 1000-1008. 2021. PMID: 33434521. IF: 1,895. DOI: 10.1016/j.joms.2020.12.016.

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GROUP 59



Head of laboratory



Olivier Gómez, Carlos Manuel



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- López-Fando Lavalle, Luis
- Otta Oshiro, Renan Javier
- San José Manso, Luis Alberto

**Research interest**

Our group focused on different research areas.

Erectile dysfunction: Endothelial dysfunction is one of the first symptoms of erectile dysfunction (ED) and is closely related to atherosclerosis and risk factors such as diabetes mellitus (DM), both of them characterized by inflammatory and oxidative advanced state. Vardenafil is one of the more effective

5-phosphodiesterase inhibitors in patients with ED and DM. We have determined plasma proteome of patients with DM and the effect of vardenafil administration in the expression of proteins related to inflammatory oxidative stress and cellular homeostasis. We have observed a significant negative correlation between plasma levels of beta-tropomyosin and IIEF-EF score. Elevated levels of beta-tropomyo-



sin in plasma indicate cell damage and loss of cellular regenerative capacity.

Urothelial cancer: Exosomes extracellular vesicles are potent intercellular mediators containing membrane and cytosolic proteins, mRNA and specific miRNA, which in turn can be obtained from fluids such as urine. We have analyzed urinary exosomes,

miRNA and protein content in order to find diagnostic markers for bladder urothelial cancer. Some of the miRNAs that are involved in tumor cell proliferation, inhibition of tumor suppressor genes, activation of EMT and metastatic state, are significantly reduced in urinary exosomes from patients with bladder urothelial carcinoma and may be useful as non-invasive diagnostic biomarkers in bladder cancer.

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



Publications (2)

de la Cruz, Julia E., Fernandez, Inmaculada, Sanz-Miguelanez, Juan Luis, Fernandez- Aparicio, Tomas, Sanchez-Margallo, Francisco Miguel, Soria, Federico. **Assessment of the Grades of Vesicoureteral Reflux in Stented Ureters: An Experimental Study.** Urol Int 105 (7-8): 554-559. 2021. PMID: 33951641. IF: 2,089. DOI: 10.1159/000515613.

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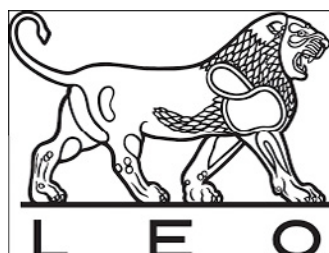
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