

18

Activity
Report



IDIVAL the Healthcare Research Institute of Cantabria
Research is in our DNA

Since 1929



'18

Contents

○ Foreword	09
○ Valdecilla	13
○ IDIVAL	15
○ Organisational Structure	17
○ Support for researchers	25
○ Training	41
○ A few milestones in 2018	53
○ IDIVAL R&D&i Activity	61
○ Research Areas:	99
> Organ and Tissue Transplant and New Therapies Area	101
> Neurosciences Area	133
> Cancer Area	153
> Cross-disciplinary Area	193
> Infectious Diseases and Immune System Area	213
> Metabolism, Diseases of Ageing and Lifestyle Habits Area	239
> Associated Groups	249







○ Foreword





The still recent creation of Biohealth Research Institutes in major hospitals in Spain has proven to be a success by enabling basic and clinical scientists to interact. This is attested by the results of many of these institutes. To some extent, this year's IDIVAL Report is a reflection of our Institute's path during this term. Without being complacent, a quick review tells us that our Institute is making good progress. Firstly I would highlight the rise in Programmes to Drive Research. There are 13 in total and many of them (PostMir, Mentoring, Pre-doctoral, Next-Val and Pre-doctoral Mobility) aim to support and encourage young research talent, something that is essential to replace a successful generation at our hospital in just a few years.

Here, no effort can be too much. Two of the Programmes, appropriately, include Primary Healthcare and Nursing, a firm commitment by the current Regional Ministry. If generating young talent is to be a major goal for the future, we must not forget opening up to the outside, both in Spain and abroad. Milestones such IDIVAL's Management Director becoming the Director of ITEMAS, and IDIVAL leading a European project for the first time, indicate that we are working well in this endeavour and we must increasingly focus on that.

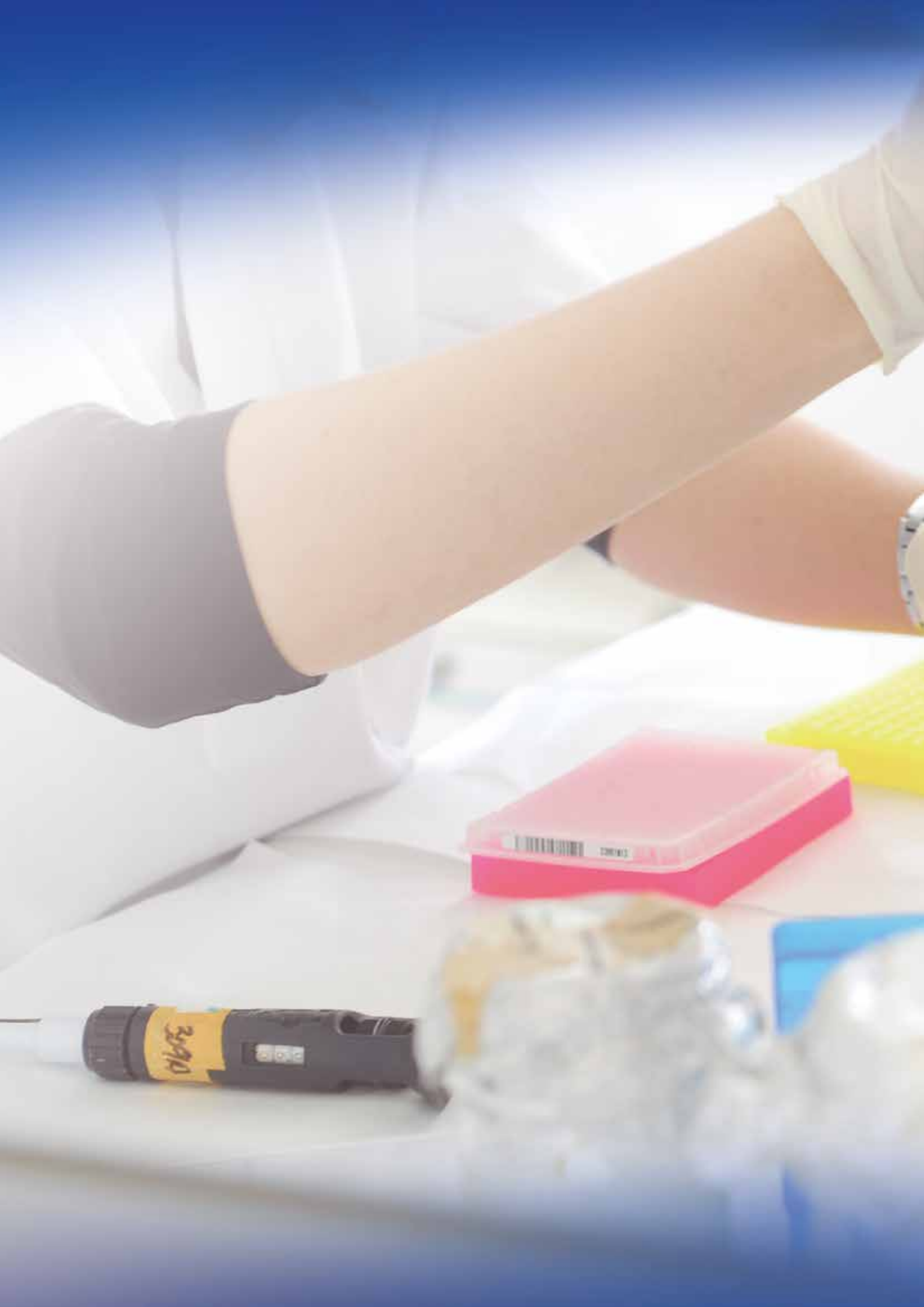
A Research Institute is essentially assessed by the number and quality of its scientific publications and research projects. Here our objective data for 2018 are also positive. IDIVAL researchers have published 458 articles over the past year. As proof of their quality, their average impact was 5.01 and over half of the

documents are in the first quartile. IDIVAL's global impact factor in 2018 was 2296, 11% more than 2017 and 22% more than four years ago. The same is true of the number of competitive research projects (90 in 2018) and clinical trials (300).

In short, the data show that IDIVAL has more than met its objectives in 2018, and Marqués de Valdecilla University Hospital management want to congratulate our researchers for their dedication, with special thanks to Benedicto Crespo, our Scientific Director, whom we wish all the best in his new job. Recent initiatives such as the Open Repository, the Colabora programme to attract donations, EVALTEC and the FUSIÓN intra-entrepreneurship proposal are testament to our desire for drive, innovation and transparency at IDIVAL, and they will ensure that the efforts of researchers and the Government of Cantabria at the Institute will benefit society as a whole.

Julio Pascual

Managing Director of the Marqués de Valdecilla University Hospital, member of the Board of Governors, and Chairman of the Executive Committee of the IDIVAL Board of Governors



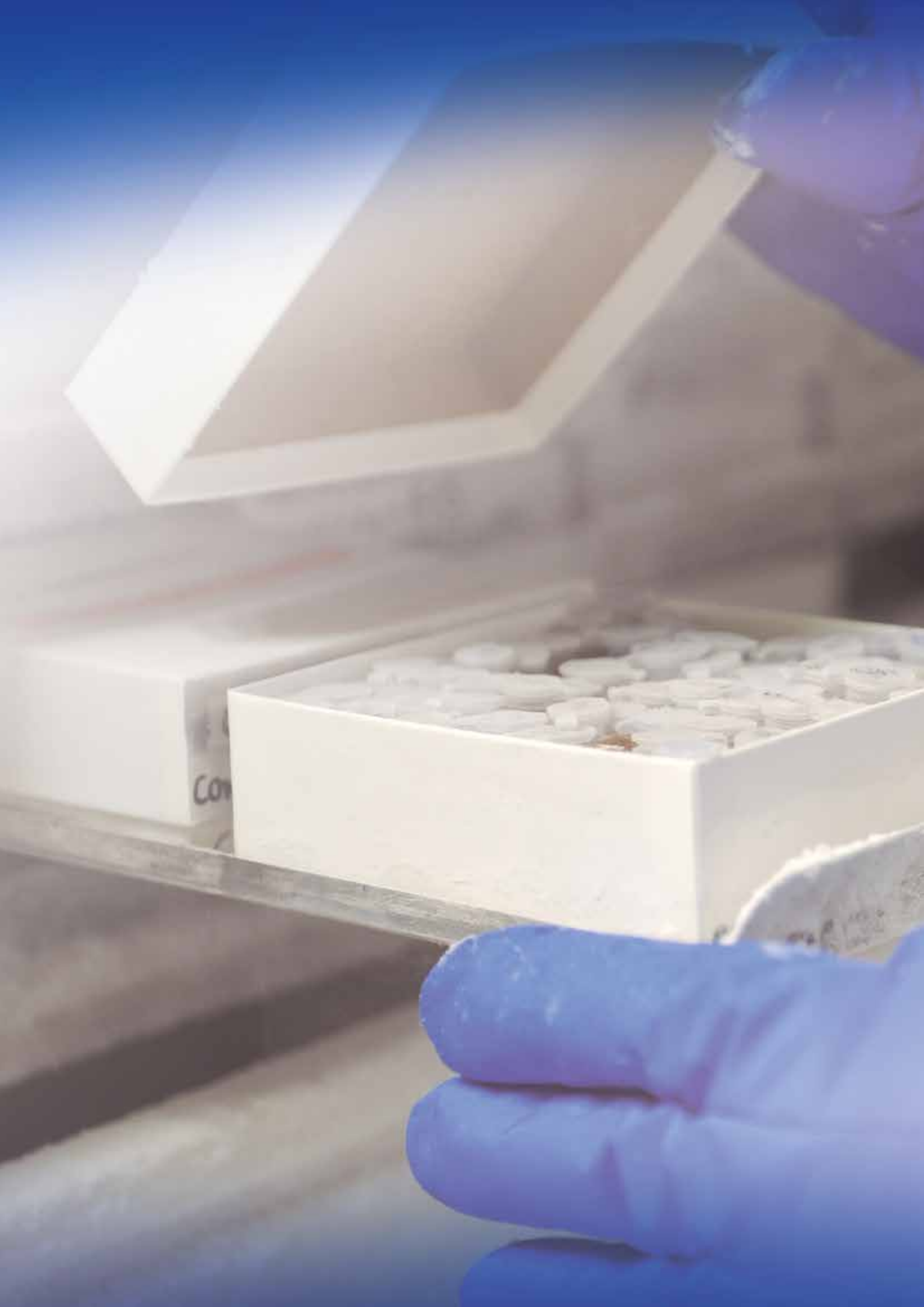


 Valdecilla

Valdecilla is the unifying brand which Ramón Pelayo de la Torriente, Marquis of Valdecilla, applied to the institutions which he created: the Marqués de Valdecilla University Hospital, the Marqués de Valdecilla Research Institute (IDIVAL), the Valdecilla Virtual Hospital, and the Marqués de Valdecilla Foundation, and which still maintains that original spirit of innovation, cross-border collaboration, and philanthropy. The innovative spirit of the Valdecilla brand is particularly evident in IDIVAL, which, as the Healthcare Research Institute of Cantabria, was conceived with the goal of promoting research

and innovation in the field of biomedical sciences at the Marqués de Valdecilla University Hospital with the contribution of the University of Cantabria, placing it at a level of national and international excellence. IDIVAL was conceived in late 2013 through an agreement between the Government of Cantabria and the University of Cantabria, as the successor to the Marqués de Valdecilla Training and Research Institute (IFIMAV). IFIMAV was established in 2002 as a research management unit within the Marqués de Valdecilla Foundation and evolved

following the model of health research institutes and in line with Royal Decree 339/2004 of 27 February. Therefore, the constitution of IDIVAL involves strong support by its founding institutions, the University of Cantabria and the Government of Cantabria, for health research in the Valdecilla environment. Taking over from IFIMAV, IDIVAL was launched in 2014 to harmoniously integrate basic, clinical and public health research, encouraging translational research and improving the application of its scientific progress to address the most prevalent health problems.





IDIVAL promotes, manages and develops the biomedical research of the Marqués de Valdecilla University Hospital and its environment. It is financed by the Government of Cantabria and the University of Cantabria.

IDIVAL encourages the development of knowledge.

IDIVAL drives activities for the development of excellent scientific output, and has established 19 high-impact research groups in six areas of research: Cancer, Neuroscience, Transplants, Infection and immunity, Metabolism, and Transversal. Another 13 groups are also contributing to its scientific output.

IDIVAL pursues excellence. In 2018, IDIVAL's researchers

published high-impact works in collaboration with some of the world's best research groups in various biomedical disciplines. Our impact factor was over 2,200 points in 2018. We have accumulated over 140,000 citations in international literature.

IDIVAL supports researchers.

In 2018, we developed different programmes to support innovation and research. IDIVAL issued grants for healthcare research worth over a million euros.

IDIVAL is committed to society. IDIVAL seeks to improve translational research and promote progress in Cantabria. Its goals include the development of knowledge, technological progress, and innovation in healthcare.

IDIVAL's current challenge is to maximise the application of research results to improve healthcare.

In partnership with prestigious institutions such as the Botín Foundation, IDIVAL has launched an ambitious innovation programme.

IDIVAL is a leading institution.

IDIVAL was recognised by the Carlos III Health Institute in 2015 as one of Spain's Healthcare Institutes and currently coordinates nationwide the Platform for Innovation in Medical and Healthcare Technologies -ITEMAS- promoted by the Carlos III Health Institute.



Organisational Structure

Governing and Advisory Bodies

IDIVAL is governed in accordance with its statutes, published in the Official Gazette of Cantabria (BOC No. 7 of 13 January 2014), by a Board, an Executive Committee, a Management Director, a Scientific Director and its own consulting bodies: Internal Scientific Council and External Scientific Council, appointed by the Board.

It is also advised by the Drug Research Ethics Committee of Cantabria and the Bioethics Committee at the University of Cantabria in compliance with the legal requirements for research.



□ Governance level □ Operational level □ Consultation level

The Board of IDIVAL

In accordance with IDIVAL's statutes, published in the Official Gazette of Cantabria of 13 January 2014, the board is the highest governing body of IDIVAL and has the highest level of representation. Its functions include approving the budget, the action plan and the annual report of the Institute as well as appointing the directors and members of advisory bodies. In 2018, the Board was made up of the following individuals:



President:

María Luisa Real González.

Minister of Health and Social Services of the Government of Cantabria.

Vice-president:

Ángel Pazos Carro.

Rector of the University of Cantabria.

Members:

María Antonia Mora González.

General Director of Planning and Healthcare, Regional Ministry of Health. Designated by the Regional Minister for Health.

María de la Cruz Reguera Andrés.

General Secretary. Regional Ministry of Health. Designated by the Regional Minister for Health.

Benigno Caviedes Altable.

Manager of the Cantabrian Health Service.

Javier León Serrano.

Vice Rector of Research and Knowledge Transfer. University of Cantabria.

Julio Pascual Gómez.

Managing Director of the Marqués de Valdecilla University Hospital.

Piero Crespo Baraja.

Professor at CSIC. Director of the Institute of Biomedicine and Biotechnology of Cantabria. Designated by the Rector of the University of Cantabria.

Manuel Gómez Fleitas.

Innovation Coordinator. General Surgery Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Surgery. University of Cantabria. Designated by the Managing Director of HUMV.

Pedro José Prada Gómez.

Head of the Radiotherapy Oncology Department. Marqués de Valdecilla University Hospital. Designated by the Managing Director of HUMV.

José Antonio Riancho Moral.

Section Head. Internal Medicine Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Psychiatry. University of Cantabria. Designated by the Rector of the University of Cantabria.

Javier Crespo García.

Head of the Digestive System Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Surgery. University of Cantabria. Designated by the Managing Director of HUMV.

Jesús Castillo Obeso.

Specialist in Family and Community

Medicine. José Barros Health Centre (Camargo). Designated by agreement between the Regional Minister for Health and the Rector of the University of Cantabria.

María del Carmen Fariñas Álvarez.

Head of the Infectious Diseases Department. Professor in the Department of Medicine and Surgery. Designated by agreement between the Regional Minister for Health and the Rector of the University of Cantabria.

Secretary, non-board:

Joaquín Cayón de las Cuevas.

Head of the Legal Counsel Office of the Regional Ministry of Health.

The IDIVAL Board renewed one of its members in 2018 and met on three occasions.

At these meetings, new members of the External Scientific Council were appointed, and the audited accounts and annual report for 2018 and action plans and budget for 2019 were approved.

Executive Committee

President:

Julio Pascual Gómez.

President according to the statutes as Managing Director of the Marqués de Valdecilla University Hospital.

Members:

Javier León Serrano.

Vice Rector of Research and Knowledge Transfer. University of Cantabria. Representative of the University of Cantabria.

María de la Cruz Reguera Andrés.

General Secretary. Regional Ministry of Health. Representative of the Healthcare Administration.

María Antonia Mora González.

General Director of Planning and Healthcare, Regional Ministry of Health. Representative of the Healthcare Administration.

José Antonio Riancho Moral.

Section Head. Internal Medicine Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Psychiatry. University of Cantabria. Representative of the University of Cantabria.

María del Carmen Fariñas Álvarez.

Head of the Infectious Diseases Department. Professor in the Department of Medicine and Surgery. Representative of the University of Cantabria.

IDIVAL's Executive Committee met three times in 2018 in order to monitor the agreements signed by the Foundation and prepare IDIVAL Board meetings in compliance with IDIVAL's statutes.



Senior Management

IDIVAL's senior management body consists of a Scientific Director and a Management Director, both appointed by the Board of Governors.



Scientific Director: the Scientific Director is the senior representative and spokesperson for the Foundation on scientific matters. He directs, plans and leads the Foundation's scientific policy, draws up the scientific plan for the Institute, and coordinates its execution. In 2018, the Board appointed **Benedicto Crespo Facorro** as Scientific Director of IDIVAL. Psychiatry Department Head at the Marqués de Valdecilla University Hospital and Professor at the University of Cantabria. At the time of completing this report, Dr Crespo-Facorro has left IDIVAL, moving to Seville in April 2019 as Department Head and Professor.



Management Director: the Management Director acts as representative and spokesperson for the Foundation before institutions regarding management activities, managing the internal organisation of the Institute and its research infrastructure. In 2018, the Management Director of IDIVAL was **Galo Peralta Fernández**.



External Scientific Council

The External Scientific Council contributes as a scientific advisor in achieving the scientific excellence pursued by IDIVAL. The External Scientific Council offers opinions at the request of the Board or the senior management of IDIVAL and advises on the evaluation of the Institute's activity.

Its members were proposed by IDIVAL's senior management and appointed by the IDIVAL Board in its meeting on 25 February 2014. The members are:

President:

Ángel Carracedo Álvarez.
Professor of Legal Medicine.
University of Santiago de Compostela.

Members:

Ana María Zubiaga Elordieta.
Professor of Genetics, University of the Basque Country, Faculty of Science and Technology. Head of the Genomics Department of the UPV/EHU.

Francesc Graus Ribas*.
Head of the Neurology Department. Hospital Clinic of Barcelona. University of Barcelona. IDIBAPS.

Francisco Mora Teruel*.
Professor of Human Physiology in the Faculty of Medicine at the Complutense University of Madrid. Professor of Molecular Physiology and Biophysics in the Faculty of Medicine at the University of Iowa.

Jordi Vila Estapé.
Head of the Bacteriology Department. Hospital Clinic of Barcelona. Professor of Microbiology. Autonomous University of Barcelona. CRESIB.

Miguel López-Botet Arbona.
Professor of Immunology, Pompeu Fabra University, Barcelona.

Josep M. Grinyó.
Senior Clinic. University Hospital of Bellvitge. University of Barcelona.

* Outgoing in 2018

** Incoming in 2018

Juan Bernal Carrasco*.

Professor of Research at the Spanish National Research Council (CSIC), Director of the Department of Endocrine and Nervous System Pathophysiology. Alberto Sols Biomedical Research Institute.

Miguel Delgado Rodríguez.

Professor of Preventive Medicine and Public Health. University of Jaén.

Rafael Cantón Moreno.

Head of the Microbiology Department of the Ramón y Cajal Hospital. Associate Professor of the Department of Microbiology, Faculty of Pharmacy. Complutense University Madrid.

Xosé Ramón Bustelo.

Director of the Genomics and Proteomics Unit. Centre of Cancer Research.
CSIC-University of Salamanca.

Manuel Elkin Patarroyo Murillo.**

Immunologist, Founding Executive Director of the Immunology Institute Foundation of Colombia.

Malu Martínez-Chantar**

Leading researcher of the CIC bioGUNE group, Derio, Vizcaya.

Francisco Sánchez Madrid**

Scientific Director of IIS-Princesa, Department Head and Professor of Immunology at La Princesa University Hospital of the Autonomous University of Madrid.

Ana Pérez Castillo**

Leading group researcher. Alberto Sols Biomedical Research Institute CSIC-UAM (IIBM) in Madrid.

Four new members joined the IDIVAL External Scientific Council in 2018, and three left. The External Scientific Council met once to review IDIVAL's new Strategic Plan, the 2018 report, the 2018 action plan, and the IDIVAL 2018 budget, and to assess new groups for incorporation.



Internal Scientific Council

The Internal Scientific Council is presided over by the Scientific Director of IDIVAL and is made up of researchers appointed by the Board. The Internal Scientific Council of IDIVAL was appointed by the Board at a meeting on 25 February 2014, based on a proposal by the Scientific Director.

In 2018 its members were:

María del Carmen Fariñas Álvarez.

Coordinator of the Infectious Diseases and Immune System Area. Head of the Infectious Diseases Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

José Antonio Riancho Moral.

Coordinator of the Metabolism, Diseases of Ageing and Lifestyle Habits Area. Section Head. Internal Medicine Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

Miguel Ángel Lafarga Coscojuela.

Representative of the University of Cantabria. Professor of Anatomy and Cellular Biology. University of Cantabria.

María Amor Hurlé González.

Representative of the University of Cantabria. Professor of Pharmacology. University of Cantabria.

Javier Crespo García.

Head of the Digestive System Department. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

Carlos Pipaón González.

IDIVAL researcher in the Haematologic Neoplasms and Haematopoietic Progenitor Cell Transplantation Group.

In 2018, the IDIVAL Internal Scientific Council met eight times and, among other business, it reviewed IDIVAL's grants programme, its strategic plan, its annual report, and the projects presented to various competitive calls for entries.

President:

Benedicto Crespo Facorro.

Scientific Director of IDIVAL. Section Head. Psychiatry Department at the Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

Members:

Marcos López Hoyos.

Coordinator of the Organ and Tissue Transplant and New Therapies Area. Head of the Immunology Department. Marqués de Valdecilla University Hospital.

Fernando Rivera Herrero.

Coordinator of the Cancer Area. Head of the Oncology Department. Marqués de Valdecilla University Hospital.

Javier Llorca Díaz.

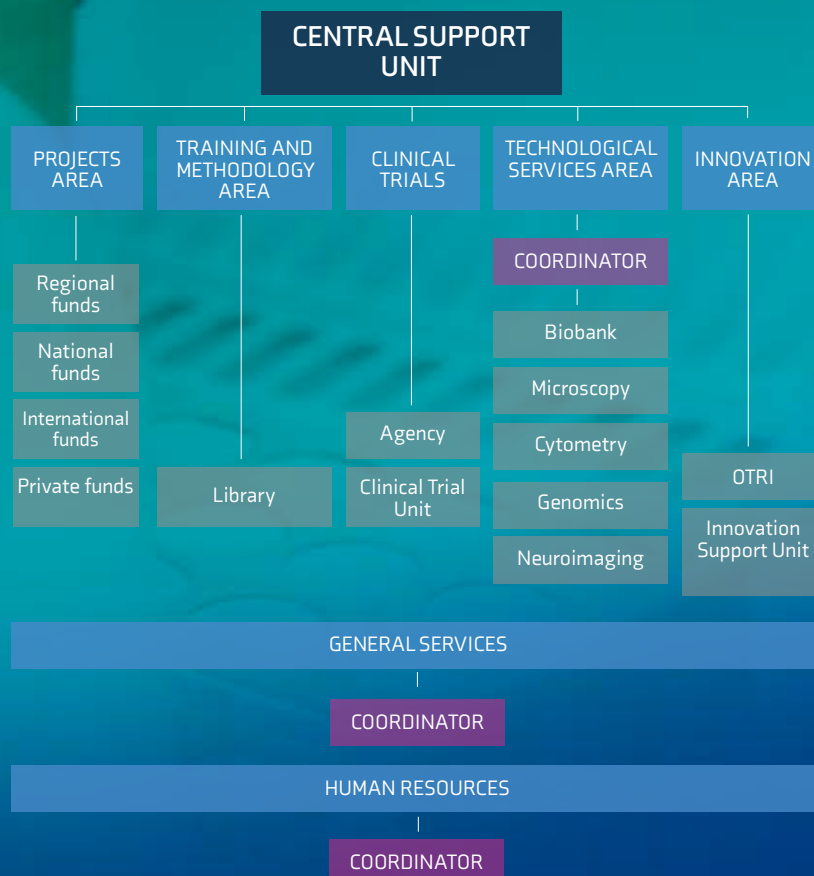
Coordinator of the Cross-disciplinary Area. Professor of Preventive Medicine and Public Health. University of Cantabria.





Support for Researchers

IDIVAL's Central Research Support Unit is divided into six areas: Projects Area, Training and Methodological Support Area, Clinical Trial Area, Technological Support Area, Innovation Area and General Services Area.



○ The IDIVAL building

IDIVAL has its own facilities, located within the Marqués de Valdecilla University Hospital complex. The IDIVAL building comprises 3,000 m². Located inside the building are most services of the Central Support Research Unit, as well as laboratory spaces for IDIVAL groups and meeting and work rooms for researchers.

○ General Services Area

○ Coordinator

Julio Muela Carriles (IDIVAL)

○ Technicians

Accounting: Javier Arce Sáiz (IDIVAL)

○ Administrative Personnel

Invoicing: Laura del Río Celis (IDIVAL)
Registry: Elena Calvo Llano (IDIVAL)

IDIVAL's General Services Area brings together the resources needed for administrative and legal management across all areas of IDIVAL.

○ Human Resources Area

○ Coordinator

Marta Abelleira Álvarez (IDIVAL)

○ Administrative personnel

María José San Emeterio (IDIVAL)

IDIVAL's Human Resources Area centralises aspects relating to the Institute's recruitment and labour relations.

○ Projects Area

○ Technicians

Beatriz García González (IDIVAL)
Charo González Cabria (IDIVAL)
Paloma González Álvarez (IDIVAL)
Natalia Puente Fernández (IDIVAL)

IDIVAL's Projects Area combines all the resources necessary to manage grants promoted by IDIVAL itself, as well as to request, implement and justify funds, both public and private, received by IDIVAL research groups.

○ Innovation Area

○ Research Results Transfer Office (OTRI):

Patricia Zorrilla de la Fuente (IDIVAL)

○ Innovation Unit

Carlos Fernández Martínez (IDIVAL)
María Wunsch Martínez (IDIVAL)

○ EValTec® Programme

Laura Herrero Urigüen (IDIVAL)
Marina Cano Iglesias (IDIVAL)

IDIVAL has an Innovation Area, which forms part of the ITEMAS Platform of the Carlos III Health Institute (ISCIII), a platform that has been coordinated nationwide by the IDIVAL Management Director, Galo Peralta, since July 2018.



The Innovation Area includes a Results Transfer Office (OTRI), which is part of the OTRI network.

This area aims to promote, enhance and disseminate research results amongst society, encouraging the interaction of researchers with the corporate and social environment, the management of its patents and business creation. It carries out actions for the promotion of innovative culture, research and evaluation of technological solutions, preparation and drafting of R&D projects and the search for financing, as well as all activities needed to ensure that the R&D results of IDIVAL research groups and researchers from the Cantabria Health Services reach society through public-private partnerships. The Innovation Area also supports strategies for innovation in patient care and organisation through the EValTec® programme, which uses human factor engineering techniques for assessing usability in medical technology selection and implementation processes and process redesign.

itemas **isciii**

○ Training and Methodology Support Area

IDIVAL, as part of its goal to strengthen and facilitate scientific training associated with research, provides library support to researchers and promotes, coordinates and performs training activities in this area throughout the year.



○ “Marquesa de Pelayo” Library

○ Head Librarian:

Mario Corral García. (IDIVAL)

The Marquesa de Pelayo Library is an active centre of biomedical information resources. Its mission is to contribute to raising the level of innovation and excellence in three fundamental areas of Cantabria’s public healthcare system: clinical care, teaching, and research, by an intensive use of information and communication technologies. The Library is governed by IDIVAL

and provides support for the public healthcare system throughout Cantabria. The library facilities, consisting of a Great Hall, classroom, copy services room, study room, periodicals library, video library, depositories of less used and antique holdings, two storerooms, and an administration and management area, are located in the Marqués de Valdecilla University Hospital. The electronic library, Biblioteca Virtual Marquesa de Pelayo, offers all its services (inter-library loans, reference, etc.) and online resources (organised according to the Haynes Pyramid) via the IDIVAL website, with direct access to its catalogue. The Library was first opened in 1929, the second oldest and the first fully modern library of its kind in Spain, designed to become a National Library of Medicine, on the initiative of Dr Wenceslao López Albo, the first Managing Director of Casa de

Salud Valdecilla, under the patronage of María Luisa Gómez de Pelayo, Marquesa de Pelayo, the niece of Ramón Pelayo de la Torriente, Marqués de Valdecilla. Since then, it has been considered one of Spain’s leading specialist libraries. In 2016 the library introduced a new platform providing access to its electronic resources, as part of the IDIVAL website, notably improving its accessibility.



Clinical Trial Area

The Clinical Trial Area includes a Clinical Trial Agency and a Clinical Trial Unit. The Agency provides support for

the management of clinical trials, and the Unit supports their performance. Both bodies are involved in advising, designing, evaluating, managing, implementing and executing clinical trials, including technical support for the Clinical Research Ethics Committee of Cantabria.

The Clinical Trial Area is part of the Platform for Clinical Research and Clinical Trial Units (SCREN, Spanish Clinical Research Network) promoted by the Carlos III Health Institute.

Clinical Trial Agency



The agency offers its organisation and resources to researchers to promote reliable clinical trials that can guarantee the quality of the study, patient safety and data reliability. It also provides support to the Clinical Research Ethics Committee of Cantabria.

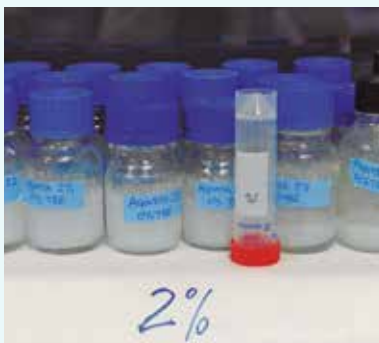
Technicians:

Blanca del Pozo Fernández.
(IDIVAL)

Lorena Martín Guerra.
(IDIVAL)

Lucía Lavín Alconero.
(IDIVAL)

Clinical Trial Unit



The IDIVAL Clinical Trial Unit, under the Clinical Pharmacology Department, located in the Marqués de Valdecilla University Hospital, has 250 m² of facilities equipped to care for nine patients simultaneously. It began operations in 2013, partially financed with funds from the Farmaindustria R&D programme.

Certified according to ISO 9001 standards. The Unit provides support for highly complex clinical trials in the Valdecilla environment.

In 2018, the Trials Unit started 29 new trials, four in phase I and 11 in phase II, with a total of 89 active trials at 16 different hospital services.



Team:

María Blanca Sánchez Santiago.
(Clinical Pharmacology Department, HUMV)

María Ángeles de Cos.
(Clinical Pharmacology Department, HUMV)

Javier Adín Ibarra.
(Clinical Pharmacology Department, HUMV)

Noelia Martín Vega
(Clinical Pharmacology Department, HUMV)

Nuria Sánchez Avelló.
(HUMV)

Technology Support Services Area

The Technology Support Services Area consists of four units: Biobank, Laser Microscopy Unit, Electron Microscopy Unit, Flow Cytometry and Cell Sorting Unit and Neuroimaging Unit.

Coordinator:

María José Marín Vidalled.
(IDIVAL).

Valdecilla Biobank



The Valdecilla Biobank is a hospital biobank that manages human biological samples in order to support biomedical research, through the collection, processing, storage and transfer of samples and associated clinical data for research projects, all in the strictest conditions of quality control and confidentiality.

The Valdecilla Biobank is authorised by the Ministry of Health of the Government of Cantabria, and is registered in the ISCIII biobank register. It is organised into three Nodes according to the types of samples handled: the DNA and Fluids Node, located on the ground floor of the IDIVAL building, and the Solid Samples Node and the Neurological Tissues Node in the Anatomical Pathology Department of the Marqués de Valdecilla Hospital. They all have sample collections of pathologies of high scientific interest while providing a variety of services through the use of their equipment, offering

comprehensive support to researchers whose projects involve the use of human biological samples. In the 2018-2020 call for financing of the ISCIII AES Platforms, the Valdecilla Biobank was re-accepted as part of the National Registry of Biobanks (Plataforma Red Nacional de Biobancos, PRNB), with €93,060 in financing for this period.

The Valdecilla Biobank has held the ISO9001:2015 certification for quality management since 2015.

Scientific Director:

Pascual Sánchez Juan.
(HUMV Neurology Department)

DNA AND FLUIDS NODE

Coordinator:

María José Marín Vidalled.
(IDIVAL)

DNA and Fluids Group Technicians:

Inés Santiuste Torcida. (IDIVAL)
Jana Arozamena García (IDIVAL)

SOLID SAMPLES NODE

Coordinator:

Santiago Montes Moreno.
(Anatomical Pathology Department, HUMV)

Solid Samples Group Technicians:

José Bernardo Revert Arce.
(IDIVAL)

NEUROLOGICAL TISSUES NODE

Coordinator:

Nuria Terán Villagrà.
(Anatomical Pathology Department, HUMV)

Technician:

Saray Pereda Marcos.
(IDIVAL)



Microscopy Unit



IDIVAL's Microscopy Unit is on the ground floor of the IDIVAL building. This unit offers confocal laser scanning microscopy, fluorescence microscopy, time-lapse, transmission electron microscopy (TEM), etc., for in-house and external research groups, and advice on their different applications. It also provides specific training in microscopy and preparation of samples for researchers and support staff through courses accredited by the Government of Cantabria's Commission on Continuing Education.

To offer the laser and live cell microscopy service, the Unit features state-of-the-art equipment consisting of two sets of image systems, a confocal laser scanning microscope (CLSM) and a fully-automated TIRF combined Nikon A1R, which captures high-quality confocal images of cells and molecular events at high speed and sensitivity, live-cell equipment with a motorised NIKON Ti microscope

and is equipped with an epifluorescence module, incubation and micro-injection systems and an optical system to monitor fast processes in live cells.

The electronic microscopy department has a JEOL JEM1011 transmission electron microscope, equipped with a high-resolution digital camera which provides excellent image quality. This microscope permits the analysis of ultra-thin sections of cells and tissues, and the observation of microorganism preparations and macromolecular complexes with negative stain contrasting.

In 2018, IDIVAL incorporated a new Raman NRS-4500 laser spectrometer by Jasco.

○ Scientific Coordinator, Laser Microscopy:

Mónica López Fanarraga. (UC)

○ Scientific Coordinator, Transmission Electron Microscopy:

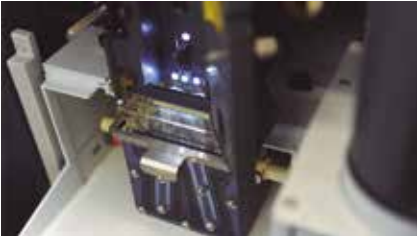
Miguel Lafarga Coscojuela. (UC)

○ Technical manager:

Fidel Madrazo Toca. (IDIVAL)



Cytometry and Cell Sorting Unit



The Flow Cytometry and Cell Sorting Unit (UCFSC) is in the IDIVAL building, located in the laboratory of the Transplantation and Autoimmunity Research group. This unit provides technical and methodological support in the use of flow cytometry and cell sorting, both for researchers at the centre and for any external group that needs it. It has an upgraded FACS Aria II cytometer/sorter

(BD Biosciences), a CytoFLEX cytometer (Beckman Coulter) and an AutoMACS Pro Separator magnetic separator (Miltenyi Biotec) for the sorting of cell populations in sterile conditions.

Each year the UCFSC organises a flow cytometry course for both researchers and healthcare personnel.

Accredited by the Government of Cantabria Commission on Continuing Training.

Scientific Coordinator:

Marcos López Hoyos.
(Immunology Department, HUMV)

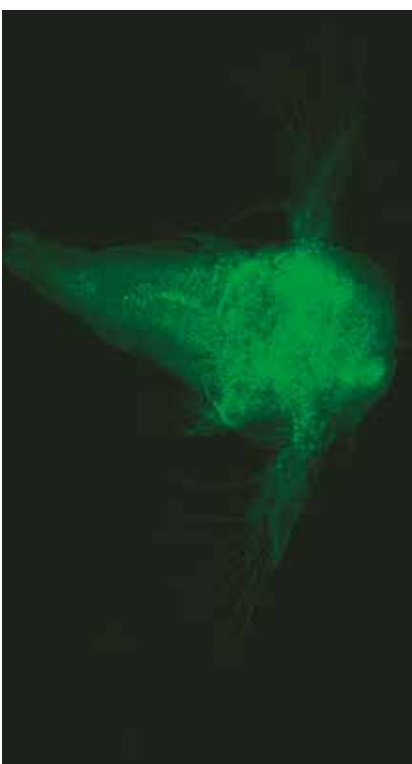
Technical Coordinator:

David San Segundo Arribas.
(Immunology Department, HUMV)

Technical manager:

David Merino Fernández.
(IDIVAL)

Neuroimaging Unit



The neuroimaging laboratory, on the 2nd floor of the IDIVAL building, has implemented and developed a wide range of techniques for analysing images of the human brain obtained by magnetic resonance imaging (MRI), which the Unit offers IDIVAL researchers and external groups in order to provide technical and methodological support in the design and execution of scientific studies.

The analysis techniques employed can obtain quantitative data on important cerebral variables (volume of cerebral structures or areas, cortical thickness, gyrification patterns, white matter structure, activity patterns, etc.) for the advancement of in vivo knowledge of the brain, and therefore, possible alterations in

severe mental illness, constituting a fundamental tool in brain research.

Scientific Coordinator:

Benedicto Crespo Facorro.
(Psychiatry Department, HUMV)

Technicians:

Diana Tordesillas Gutiérrez.
(CIBERSAM)

Víctor Ortiz de la Foz.
(IDIVAL)

Units supported by the University of Cantabria



IDIVAL has a number of facilities that the University of Cantabria offers its researchers, such as materials characterisation, chromatography, and animal housing and experimentation services.

Animal housing and experimentation services (SEEA)

Materials characterisation service (SERCAMAT)

Optical transmission microscopy service (SERMET)

Supercomputing service

Hydrobiology laboratory (Hydraulic research)

Chromatography service (SERCROM)

Advanced microscopy (IBBTEC)

Mass sequencing service (IBBTEC)

SAT UNITS

No. of requests

Service hours

* Scientific performance

FLOW CYTOMETRY	120	185	3
MICROSCOPY	299	817	16
NEUROIMAGING	5	1062,5	6

VALDECILLA BIOBANK

2018

Accumulated to 2018

Total samples included in the biobank	2547	33,539
No. sample transfer requests	11	166
Total samples transferred	10036	20,966
No. service requests	123	931
*Accumulated scientific performance	12	38

* No. of publications that used services provided by the units or samples transferred by the Valdecilla Biobank.

IDIVAL Research Grants

IDIVAL has a line of research grants focusing on fostering talent. One of these programmes has a clear educational focus so the description of its activity is featured in the training section of this report. In 2018, IDIVAL announced and awarded the following grants:

> **Inn-Val Grants.** Awarded to Innovation projects.

> **Next-Val Grants.** Awarded to projects for young researchers.

> **Ges-Val Grants.** A research management training scholarship.

> **Prim-Val Grants.** Grants for primary healthcare research projects.

> **Int-Val Grants.** For research intensification.

> **Ment-Val Grants.** Mentoring programme for resident doctors.

> **Support Grants.** Support programme for IDIVAL groups.

> **Summer internships.** Student grants.

> **Pre-doctoral contracts.** Combined IDIVAL-University of Cantabria contracts.

> **Innplant Programme.** Programme to embed clinical researchers as Heads of Department at the Marqués de Valdecilla University Hospital.

> **Wenceslao López Albo** Post-MIR contracts programme (described in the training section of the report).

> **National call for “Enfermería Valdecilla”** research projects.

> **Pre-doctoral mobility grants** for IDIVAL-UC pre-doctoral contract personnel.

The number and total amount of IDIVAL grants awarded in 2018 were as follows:

Programme	Priority	Budget (€)	Grants awarded
Post-MIR Programme	Post-Residency research training	109,667	1
Intensification	Prioritising research in healthcare personnel working in patient care	120,000	4
Mentoring	Specialists in training	32,000	4
Inplant Programme	Attracting new Heads of Department or Section	100,000	1
Research Managers	Research management training	93,365	2
Pre-doctoral programme	Pre-doctoral training	247,000	4
Next-Val Programme	New researcher projects	100,000	10
Inn-Val Programme	Innovation projects	100,000	11
Prim-Val Programme	Primary care projects	30,000	3
Support Programme	Support for the functioning of IDIVAL Groups	300,000	31
Summer Internships	Undergraduates in the biomedical field	3,200	4
Pre-doctoral mobility	Mobility grants for IDIVAL-UC pre-doctoral contract personnel	12,000	4
“Enfermería Valdecilla” research projects	Nursing research projects	4,000	1

Inn-Val Grants

In 2018, IDIVAL launched the fourth edition of the Inn-Val grants programme. This programme focuses on the development of innovative technological and healthcare projects in order to promote the transfer of

knowledge to society and the market, and to integrate external agents in the Valdecilla environment. The following projects were awarded grants in 2018:

Principal investigator	Project title	Amount granted (€)
Anchuelo Latorre, Javier Tomás	Impact of musical training on cognitive, functional and emotional variables in cancer patients with cognitive post-treatment effects	10,000
Maestre Alonso, José María	Implementation strategy for medical technology based on Human Factor engineering: the case of infusion pumps	9,480
Morales García, Dieter José	Determination of BRAF mutations by liquid biopsy in patients with suspected papillary thyroid carcinoma	8,000
Nistal Herrera, Juan Francisco	Design and assessment of small molecules similar to BMP-7 for the treatment of pathological cardiac remodelling	8,000
Ramos Vivas, José	Search and characterisation of lytic phages against clinically relevant hospital-acquired pathogens	10,000
Real Peña, Eusebio	Automated diagnosis of ophthalmological pathologies using OCT (DAPatOO)	12,500
Ruiz Arrebola, Samuel	Technique to optimise absorbed dose in intraoperative radiotherapy treatments	8,000
Suberviola Cañas, Borja	Gene transcription of human neutrophils as a tool to diagnose patients with sepsis	5,520
Valiente Barroso, Rafael	Multifunctional nanoparticles for treatment head/neck cancer with photo-induced hyperthermia	8,000
Vázquez Bourgon, Javier	Novel pharmacologic formulation of cannabidiol (CBD-loaded nanoparticles) and effect on antipsychotic-induced weight gain and related metabolic alterations	8,000
Viera Artiles, Jaime	System for improving spatial orientation in rigid optics endoscopy surgery	12,500

Next-Val Grants

In 2018 IDIVAL announced the fourth round of NEXT-VAL (NEXT generation VALdecilla) grants for the development of research projects led by new researchers from the

biohealthcare environment in Cantabria. The projects selected in 2018 were:

Principal investigator	Project title	Amount granted (€)
Casado Rojo, Alfonso	Retina and optic nerve analysis in patients with Alzheimer's	15,207
Cayón de las Cuevas, Joaquín	Gen-Ethics and Neuro-Ethics: Implementation of a bio-legal and bio-ethical framework for treatments to improve biology and bionics in humans	8,775
Cobo Sánchez, José Luis	Design and validation of an evaluation scale for the central venous catheter exit orifice for haemodialysis	7,200
González Legarreta, Lorena	Design of multifunctional nanoparticle for nanotheranostics (DiNMN)	8,775
Gozalo Margüello, Mónica	Burkholderia cepacia complex in cystic fibrosis: contribution of antibiotic resistance mechanisms and virulence factors.	16,250
Kislikova, María	Changes in mean arterial matrix in the context of uremia and cardiovascular disease	11,250
Mora Cuesta, Víctor Manuel	Interstitial lung disease biomarkers: Implication of IL-6. General and functional study	11,228
Palanca Cuñado, Ana Rosa	Blood test for early diagnosis of escleroderma	12,025
Sarabia Cobo, Carmen María	Multi-component therapy in addressing moderate/mild dementia in patients and their careers: intervention in the Community Centres of Santander	5,788
Suárez Pérez, Angela	Effectiveness of transcutaneous neuromuscular electrical stimulation in the treatment of critical patients: randomised clinical trial	2,783

GES-VAL grants

The Ges-Val programme aims to train research and innovation managers with an internship contract of up to two years in which they take on activities related to

monitoring, justifying and assessing research and innovation projects, including contract and human resources management. In 2018, two contracts were awarded to:

María Díez Sánchez.
Garazi Carbón Soto.

INT-VAL grants

The Int-Val programme (Intensification of research - Valdecilla) aims to release clinical practitioners with heavy research and/or innovation workloads from their other duties. IDIVAL funds the part-time or full-time substitution of doctors or nurses involved in research or innovation projects. Researchers benefiting from intensification grants in 2018 were:

Jon Infante Ceberio.
Head of the Neurology
Department of Marqués de Valdecilla University Hospital.
Duration: 6 months.

Benedicto Crespo Facorro.
Head of the Psychiatry
Department of Marqués de Valdecilla University Hospital.
Duration: 6 months.

Marcos López Hoyos.
Head of the Microbiology
Department of Marqués de Valdecilla University Hospital.
Duration: 6 months.

Marcos Gómez Ruiz.
Associate of the General Surgery
Department of Marqués de Valdecilla University Hospital.
Duration: 6 months.

MENT-VAL grants

Through the Ment-Val mentoring programme for resident doctors, IDIVAL helps to attract new clinical professionals in training. The grant is for young, investigation-oriented resident doctors who are seeking excellence and are interested in

following a custom specialised healthcare training period as an introduction to research. The selected candidates were:

Alba Fernández Rodríguez.
Resident in Intensive Medicine.

Alejandro Aguilera Fernández.
Resident in Nephrology.

Celia Garillete Cámara. Resident in Cardiology.

Ignacio Setién Santiago.
Resident in Cardiology.

Production Grants

In 2018, IDIVAL allocated funds for the operating costs of research groups, based on their activity in 2017. This grant was calculated considering the impact factor quartiles of each project in which a group member is the first or

last author, differentiating them from projects where authors from the group are neither the first nor last. The funds obtained by the group, the patents generated, RETIC or CIBER membership, participation in doctoral theses

and European projects, the existence of novice researchers, and the responsibility of any group members for any IDIVAL platform were also considered. The following production grants were allocated to IDIVAL groups in 2018:

Group	Amount in €
ANATOMICAL PATHOLOGY AND MOLECULAR PATHOLOGY	7,010
APOPTOSIS	3,133
CELL NUCLEUS BIOLOGY	4,209
CELL CYCLE, STEM CELLS AND CANCER	9,221
CYTOKINES AND GROWTH FACTORS IN THE PHENOMENA OF PATHOLOGICAL TISSUE PLASTICITY	6,180
CEPHALEA CLINIC AND GENETICS	6,943
HEALTHCARE LAW AND BIOETHICS	5,044
DIAGNOSIS AND TREATMENT USING IMAGING	2,765
NEURODEGENERATIVE DISEASES	16,711
GENETIC EPIDEMIOLOGY AND ATHEROSCLEROSIS IN SYSTEMIC INFLAMMATORY DISEASES	33,320
EPIDEMIOLOGY AND PATHOGENIC MECHANISMS OF INFECTIOUS DISEASES	10,694
TRANSLATIONAL HAEMATOPATHOLOGY	15,749
NANOVACCINES AND CELLULAR VACCINES BASED ON LISTERIA MONOCYTOGENES AND THEIR APPLICATIONS IN BIOMEDICINE	5,327
HEREDITARY HAEMORRHAGIC TELANGIECTASIA STUDY GROUP	2,934
CARDIOVASCULAR RESEARCH GROUP	10,266
PHOTONICS ENGINEERING	7,194
MOLECULAR IMAGING	6,536
INFECTION AND IMMUNITY AND DIGESTIVE PATHOLOGY	17,039
IMMUNOPATHOLOGY OF RHEUMATIC DISEASES	3,937
MELATONIN AND BREAST CANCER	2,828
MINERAL AND LIPID METABOLISM	11,332
CLINICAL AND MOLECULAR MICROBIOLOGY	9,417
NANOMEDICINE	18,955
HAEMATOLOGIC NEOPLASMS AND HAEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION	14,841
NEUROPHYSIOLOGY IN EPILEPSY AND NEUROINTENSIVES	6,211
NEW TECHNIQUES IN ABDOMINAL SURGERY	3,048
PSYCHIATRY	17,437
TRANSPLANTATION AND AUTOIMMUNITY	12,707
CLINICAL TRIALS, MEDICAL ONCOLOGY AND PALLIATIVE MEDICINE UNIT	22,208
NURSING RESEARCH	4,322
COMMUNITY HEALTHCARE	2,481



Pre-doctoral fellowships

In 2018, IDIVAL partnered with the University of Cantabria to launch a new pre-doctoral fellowship programme, in which seven candidates were selected (four funded by IDIVAL and three by the University of Cantabria) for a fellowship of up to four years with the goal of completing their doctoral theses.

The selected candidates and their thesis directors in 2018 were:

- **Pre-doctoral fellow: Verónica Pulito Cueto. Director: Miguel Ángel González-Gay Mantecón (HUMV)**

- **Pre-doctoral fellow: David Salcines Cuevas. Director: Carmen Álvarez Domínguez (IDIVAL)**

- **Pre-doctoral fellow: Ana Belén Salido Medina. Director: Juan Francisco Nistal Herrera (HUMV)**

- **Pre-doctoral fellow: José Ramón Sánchez De La Torre. Director: Jon Infante Ceberio (HUMV)**

Summer internships

IDIVAL, in partnership with the Institute of Biomedicine and Biotechnology of Cantabria (IBBTEC), funds summer internships for students in the biomedical and biotechnological fields at the IDIVAL research group laboratories. The grant funds an eight-week stay during the months of July, August

and September for students in their last year of undergraduate or master's degree studies in a biomedical subject (biology, biotechnology, nursing, pharmacy, medicine, dentistry, etc.) during the internship period. The students selected to work in the IDIVAL Group laboratories in 2018 were:

Alex Mur Espinosa
Carlos Wert Carvajal
Maite Garraza Obaldia
David Núñez Nepomuceno



95° E+OH

West Germany

80° E+O

West Germany

West Germany



o Training

Hospital sessions

This dissemination activity includes monthly scientific sessions which sees the participation of internationally renowned guests and IDIVAL researchers, who run sessions within the Marqués de Valdecilla University Hospital (HUMV) setting.

The 2018 weekly HUMV hospital sessions were the following:

January:

18: "Commitment to quality at HUMV: Best in Class Awards 2017". J. Pascual; C. Fariñas; J.M. Rabanal; M Drake; J. Crespo; J.C. Ruiz San Millán.

February:

1: "Auricular fibrillation, new approaches to classic arrhythmia. Dr Juan José Olalla Antolín-Head of the Cardiology Service Department".

8: "8: "Male with abdominal pain, metabolic acidosis and acute renal failure", Julia Beatriz G^a Reyero-R2 Pathological Anatomy / Zaida Salmón Glez-R5 Internal Medicine.

15: "Strategies to improve quality and safety in at-risk or critical patients: future perspectives". Dr M^a Cruz Martín Delgado-Head of the Intensive Care Medicine Department H. U. Torrejón. Madrid-President of the Spanish Intensive Care Medicine and Coronary Unit Society (SEMICYUC).

March:

1: "Current lines in healthcare and research in neuro-ophthalmology". Dr Alfonso Casado Rojo- Ophthalmology Department HUMV.

8: "ECMO. A system for gaining time or saving lives? Multidisciplinary approach". J.A Sarralde Aguayo-Cardiovascular Department HUMV and Camilo González Fernández-Intensive Care Medicine Department H. C. Asturias.

15: "The sick doctor care programme (PAIME): solidarity among doctors". José Ramón Pallas Álvarez - PAIME Coordinator at COMCantabria.

April:

12: "Optimising the results of surgery in elderly adults to remove this space through Geriatric Medicine". Dr Jesús Pérez del Molino Martín (Head of Geriatrics Department). Dr Manuel Gómez Fleitas (Technological Innovation Coordinator HUMV Professor of Surgery) Dr Begoña Busta Vallina (Head of the Traumatology and Orthopaedics Department) Dr Trinitario Pina Murcia (Medical management, HUMV).

19: "Applications of cell therapy in tumour pathology and regenerative treatments". Juan Irure Ventura -R4 Immunology Department.

May:

3: "3: "Endometriosis, the enigma of a benign disease". Elena Prieto Ruiz R4 Obstetrics and Gynaecology Department.

10: "Multiorgan failure in an immunosuppressed patient due to solid organ transplant". Lara Ruiz Martínez- R 3 Nephrology, Jorge Martínez-Echevarría Gil-Delgado. R 1 A P. Cristina Fernández Martínez. R3 Haematology.

24: "Let's avoid bad smoke together". Virginia Flor President of the Smoke-free hospital ethics committee, Carlos Amado Secretary, Cristina Renedo González.

June:

7: "Presentation of the results of the HUMV's Clinical Commissions". Mario Domínguez Esteban-Library committee; Ana Batle López-Medical record and information systems committee; Aitziber Illaro Uranga-Infections and Antibiotics Policy Committee. Moderator. Concepción Fariñas Álvarez.

8: "Laparoscopic abdominal wall surgery in major outpatient surgery. Current reality and options for the future". Juan Manuel Suarez Grau-Digestive Department- Hospital Quiron Sagrado Corazón.

14: "Rehabilitation in amputated patients. Step by step". Dr Casar Associate Rehabilitation Doctor.

21: "Tribute to Dr Ramón Agüero. - Pulmonary fibrosis". Dr Ferrán Morell (Emeritus professor U A Barcelona).

September:

27: "A Nobel medicine nominee in the hospital" (ORL). Dr Juan Manuel Espinosa Sánchez.

28: "University of Cantabria doctoral programme". Alberto Ruiz Jimeno - UC Vice Rector for Doctoral Studies.

October:

4: "Can we trust claims from clinical trial reports?". Dr Stuart J. Pocock, Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London.

11: "Current clinical contribution to nuclear medicine". Dr Remedios Quirce. Nuclear Medicine Associate HUMV.

25: "Minimally invasive monitoring. Clinical cases". Speaker Dr José Luis Rábago, HUMV.

November:

8: "HAH, DMH and WH: The triple A". Dr Manuel Fernández Miera Hospital at Home HUMV.

15: "Fever and weakness: an unexpected result". Dr Iria Sanles R5 MI - Dr. J. L. Lozano Polo Internal Medicine Specialist HUMV.

22: "Developments in paediatric cardiology" Dr Viadero Associate Paediatrics Doctor HUMV.

December:

13: "Use of systemic corticosteroids in community-acquired pneumonia". Karla Fabiola Escobar R3 - Sandra Tello R3 Pulmonology HUMV.

○ Training related to Support Unit Departments

Includes activities designed for researchers, organised and provided by Institute departments. In 2018,

the following activities were provided under this line:

○ Workshop: Patents, a key tool for research.

Patricia Zorrilla, Innovation Area (OTRI) IDIVAL.
30 January.

○ 5th Flow Cytometry Course.

Clinical and research techniques and applications.
David San Segundo (HUMV),
Maria José Marín (Technological Services Coordinator, IDIVAL).
4-7 June.

○ Dissemination activities

○ IV Long Live Science Workshops (March 2018).

The workshops were given by IDIVAL research personnel were:

DNA workshop. DNA workshop. This workshop allowed students to work with DNA samples to study their quality. Using spectrophotometry they determined the concentration and purity of nucleic acids and analysed the integrity of the DNA using electrophoresis in agarose gel. They also studied functionality by using PCR to amplify fragments of X and Y chromosomes that provide information on the sex of the sample individual.

Bacteria workshop. The workshop consisted of analysing two biological samples of the students using microscopy to examine the different bacterial morphologies and their movement.

Neuroimaging workshop. In this workshop students examined a anthropomorphic dummy and processed the images acquired.

Light and its Technologies helping Biomedical Engineering workshop. This workshop presented the opportunities offered by light and its photonic technologies for diagnosing and treating diseases. Experiments were

conducted in relation to optical radiation parameters (refraction, absorption, polarisation, etc.) and experimental demonstrations were given of the equipment currently used to diagnose and treat diseases in the hospital environment.

○ Scientific Coffee organised by IFCA (Institute of Physics of Cantabria).

José Ramos Vivas.

29 June 2018 "Healthcare scaremongering due to poor scientific practice".

Carmen Sarabia.

26 January 2018 "Brain and dark matter: the universe in the head".

○ First regional symposium of the Small World Initiative project (SWI@ SPAIN).

6 September 2018

○ 2018 Researchers' Night (28 September).

Organised by: the Scientific and Innovation Culture Unit of the University of Cantabria (UCC+i). IDIVAL took part in the 2018 Researchers' Night held on **28 September** with a series of workshops and visits to IDIVAL facilities:

1) Guided tour: "How do your cells talk to us?", by the **Pathological Anatomy Department of Marqués de Valdecilla Hospital.**

2) Workshop: "Your defences protect you from danger" by the IDIVAL Transplantation and Immunity group.

3) Workshop: "What do tests that assess intelligence and other cognitive domains consist of?" Workshop by the IDIVAL Psychiatry research group.

4) Workshop: "Would you like to see a research sample bank?" Workshop by Valdecilla Biobank personnel.

5) Conference: Nanovaccines: do vaccines serve a purpose? And nano what? What's that?, conference by the Nanovaccines and cellular vaccines based on *Listeria monocytogenes* and their applications in biomedicine research group.



IDIVAL also had a corporate stand in the Plaza Porticada where the "Genetic epidemiology and atherosclerosis in systemic inflammatory diseases" research group carried out different activities for visitors.

Science Week (5-16 November 2018).

Organised by: the Scientific and Innovation Culture Unit of the University of Cantabria (UCC+i) and the School of Science, in collaboration with the Spanish Foundation for Science and Technology (FECYT) and the Ministry of Science, Innovation and Universities.

Research Group and Technological Services activities organised by IDIVAL-UC-HUMV are briefly described below:

> Visit to the IDIVAL Microscopy Unit

> Visit to the Anatomical pathology and molecular pathology department of Marqués de Valdecilla University Hospital

> Visit to the IDIVAL Microbiology laboratory

> Visit to the Photonics Engineering department

Workshop 1: What is Internet? Where is Internet?

Workshop 2: What are the practical applications of light?

> Visit to the Transplantation and Autoimmunity Group



Collaborations with Universities

IDIVAL's research groups include 40 of the 132 associate professors working in the Marqués de Valdecilla University Hospital. Of the 26 professors from the University of Cantabria at the Marqués de Valdecilla University Hospital, 23 belong to IDIVAL groups.

In terms of training in the various fields related to research, IDIVAL researchers have collaborated on the organisation and implementation of training within different master's degree programmes:

Master's Degree in Molecular Biology and Biomedicine.

University of Cantabria and University of the Basque Country
Director: Dolores Delgado (Professor of Immunology. Department of Molecular Biology. University of Cantabria).

Master's Degree in Healthcare and Social Services

Management. Director: David Cantarero Prieto (University Professor in the Area of Applied Economics, Area of Public Tax Authority, Department of Economics of the University of Cantabria).

Master's Degree in the Study and Treatment of Pain. Rey Juan Carlos University and University of Cantabria.

Master's Degree: Introduction to Mental Health Research.

University of Cantabria; Complutense University of Madrid; Autonomous University of Barcelona; University of Barcelona and University of Cádiz in collaboration with CIBERSAM.

Innovation in Health.

An unavoidable opportunity.
Directors: Jesús Fernández Crespo (Director General of the Carlos III Health Institute), Alfonso Beltrán (Deputy Director General of International Research Programmes and Institutional Relations, Carlos III Health Institute), Galo Peralta Fernández (Management Director of IDIVAL). **2-4 July.** Annual landmark meeting in which IDIVAL collaborates with the Carlos III Health Institute.

Research Methodology

This section includes in-house training activities and programmes organised and financed directly by IDIVAL. In 2018, this section included the following activities:

3rd edition of the IDIVAL course on Good Clinical Practice.

18-22 June 2018
Course Director: Galo Peralta.
Duration: 10 hours.

2nd edition of the Research Methodology course.

12-16 November 2018. **Course Director:** Galo Peralta. **Duration:** 20 hours.

Specialist Training

The Marqués de Valdecilla University Hospital is accredited to train internal medical residents in various specialisations, internal psychology

residents, internal pharmaceutical residents, internal biology residents, internal chemistry residents and internal midwifery nursing residents. In 2018, the Marqués de Valdecilla University Hospital offered 82 places in 40 specialisations for 2019 (Official State Gazette 223, 2018). Furthermore, the Marqués de Valdecilla University Hospital participated in the training of the 20 places offered for a specialisation

in Family and Community Medicine for the Santander Area and for four specialists in Occupational Medicine.

The medical specialisations accredited in the Marqués de Valdecilla University Hospital and the number of places offered in the last call for specialised health training were:

Specialisation	No.	Specialisation	No.
Allergology	1	Internal Medicine	4
Clinical Analysis	1	Nuclear Medicine	2
Pathological Anatomy	3	Microbiology and Parasitology	1
Anaesthesiology and Reanimation	6	Nephrology	2
Digestive System	2	Pulmonology	2
Clinical Biochemistry	3	Neurosurgery	1
Cardiology	3	Clinical Neurophysiology	2
Cardiovascular Surgery	1	Neurology	2
General and Digestive Surgery	2	Obstetrics and Gynaecology	3
Oral and Maxillofacial Surgery	1	Ophthalmology:	1
Orthopaedic Surgery and Traumatology	2	Medical Oncology	2
Thoracic Surgery	1	Radiation Oncology	1
Medical-Surgical Dermatology	1	Otorhinolaryngology	1
Endocrinology and Nutrition	1	Paediatrics and Specific Areas	5
Hospital Pharmacy	2	Clinical Psychology	1
Clinical Pharmacology	2	Psychiatry	3
Haematology and Haemotherapy	3	Radiodiagnostics	4
Immunology	2	Hospital Radiophysics	1
Physical Medicine and Rehabilitation	1	Rheumatology	2
Intensive Care Medicine	3	Urology	1

Training new clinical researchers

IDIVAL's training programme in healthcare-related research and innovation is specifically for residents who have completed their specialisation and is known as the

Valdecilla López Albo post-residency programme. It has been active since 2003 as a way to promote training, attracting and consolidating talent in the Marqués de Valdecilla University Hospital environment.

This nationwide call invites recently-trained specialists from any centre in the country to develop a research programme supervised by the

Marqués de Valdecilla University Hospital over up to three years that should include a stay at one or more renowned international centres. In 2018, IDIVAL offered a grant for a two-year contract to one specialist; the Post-Residency Valdecilla contracts of a further five specialists were active at some point during 2018.

2018 Call

Ventura Irure, Juan. Immunology specialist, trained at HUMV.

Tutor: Marcos López Hoyos.

Project: Immunomonitoring cancer patients receiving immunotherapy treatments.

Residency abroad: Lowance Center, Atlanta, USA.

Duration: 24 months.

2017 Call

Velásquez Rodríguez, Carlos José.

Neurosurgery specialist, trained at HUMV.

Tutor: José Luis Fdez Luna.

Project: New prognosis markers in high-grade gliomas and feasibility study for developing an Outpatient Neuro-oncological Surgery programme at HUMV.

Residency abroad: Division of Neurosurgery, Toronto Western Hospital, Canada.

Duration: 24 months. (DURATION IN BOLD)

Ruiz Guerrero, Luis Javier.

Cardiology specialist.

Tutor: Javier Zueco

Project: Healthcare innovation project for the creation of an Inherited Cardiovascular Diseases Unit (UECF);

Cardiomyopathy, Aortopathy and Channelopathy, Preventing Sudden Death and Cardiopathy in Sport.

Residency abroad: Department of Hereditary Cardiovascular Diseases, St George's Hospital, London.

Duration: 24 months.

Sánchez Escamilla, Miriam.

Haematology specialist.

Tutor: Arancha Bermúdez

Project: Immunotherapy against Lymphoid Neoplasms using T lymphocytes with a Design Antigen Receptor.

Residency abroad: Haematopoietic Transplant Program, Memorial Sloan Kettering Cancer Center, New York.

Duration: 24 months.

2016 Call

Fabregat Borrás, Rosa.

Radiation Oncology specialist, trained at HUMV.

Tutor: Pedro Prada.

Project: Intraoperative radiotherapy as an innovation in healthcare treatment in the Public Health Service of Cantabria. Technical and clinical characteristics, methodology, dosage, and quality control.

Residency abroad: Gregorio Marañón University Hospital (Madrid)

European Institute of Oncology (Milan).

Duration: 18 months.

2015 Call

Kislíková, Mária.

Nephrology specialist, trained at HUMV.

Tutor: Ángel Martín de Francisco.

Project: Epigenetic Regulation of Arterial Smooth Muscle Phenotype in CKD-Associated Vascular Disease.

Stay abroad: Dr David Wheeler. The UCL Centre for Nephrology, University College of London.

Duration: 24 months.

Doctoral theses. Doctoral Programmes

IDIVAL researchers participate in the two active doctoral programmes in the Faculty of Medicine of the University of Cantabria:

> Doctorate in Molecular Biology and Biomedicine (coordinated by Dolores Delgado. The programme is quality accredited).

> Doctorate in Health Sciences (currently coordinated by institute researcher Benedicto Crespo-Facorro).

IDIVAL training activity is reflected in doctoral theses.

In 2018, IDIVAL groups participated in a total of 15 doctoral theses, either through their direction or authorship. The adjoining table lists theses read or directed by IDIVAL personnel.

Author and directors	Title	University
María Amada Pellico López, David Cantarero Prieto, María Paz Zulueta	Characteristics and Impact of Bed-Blocking. Case studies and controls in Cantabria.	Cantabria
María Del Pilar Mollinedo Sedano, José Luis Fernández Luna, Alberto Gandarillas Solinis	Primary skin cells as an in vitro model for ADNP syndrome: a new variant of the autism spectrum.	Cantabria
Javier Isaac Lera Torres, Marta Pascual Saez, David Cantarero Prieto	Tests in health economics: healthcare use.	Cantabria
Patricia Moreno Mencía, David Cantarero Prieto	Essays about econometric model subjects. Sample selection and endogeneity in the field of health. Economics and labour.	Cantabria
Paloma Lanza León, Marta Pascual Saez, David Cantarero Prieto	Essays about health economics: inequality, poverty and polarization.	Cantabria
María Esther Setién Suero, María Rosa Ayesa Arriola	Longitudinal study on the consumption of cannabis in the first episodes of psychosis.	Cantabria
Susana Hernández García, Enrique María Ocio San Miguel, Teresa Paino	Assessment of the synergic effect of the Kinesin Spindle Protein inhibitor filanesib (ARRY-520) in combination with immunomodulatory drugs in preclinical multiple myeloma models.	Cantabria
María Lázaro Díez, José Ramos Vivas, Marcos López Hoyos	Clinically relevant host-pathogen key interaction in acinetobacter species.	Cantabria
Jessica Alonso Molero, Antonio José Molina De La Hoz, Vicente Martín Sánchez	Peroxisome proliferator-activated receptor gamma coactivator 1 (pgc1) interactions and environmental factors in the development of colorectal cancer.	Cantabria
Rut Molinuevo Llarra, Alberto Gandarillas Solinis	Molecular control of the differentiation mitosis checkpoint of keratinocytes in response to DNA damage.	Cantabria
Eloísa González Lavado, Mónica López Fanárraga	Antitumour drug nanodispensers based on carbon nanotubes: design, assessment and biocompatibilisation.	Cantabria
Asier García Escarzaga, Igor Gutiérrez Zugasti, Adolfo Cobo García	Paleoclimate and the use of coastal resources during the Mesolithic in the region of Cantabria.	Cantabria
Marta Muñoz Ruiz, Ramón Merino Pérez, Jesús Merino Pérez	Role of BAMBI in the immune response of mucosa and in the development of inflammatory intestinal pathology and secondary neoplasms.	Cantabria
Isabel De Pedro González, Alberto Gandarillas Solinis	Role of Cdk1 mitosis kinase inhibitors in epidermoid differentiation.	Cantabria
María Juncal Ruiz, Benedicto Crespo Facorro, Marcos López Hoyos	Systemic immunoinflammatory response in subjects with a first psychotic episode	Cantabria

Progress Reports

This programme began as a joint initiative by the Biomedical Research Forum of Cantabria, consisting of researchers from IDIVAL, the University of Cantabria and the Institute of Biology and Biomedicine of Cantabria, as a continuation of the programme of research seminars presented by young researchers, in collaboration with clinical and basic researchers.

The 2018 programme included the following seminars, held at the Marqués de Valdecilla University Hospital.

Thursday 18/01/2018

Speaker:

Fulgencio Ruso Julve.

Pre-doc of the IDIVAL Psychiatry research group.

Title: Drug-Induced modulation of Clinical Response Genes to Antipsychotics (CRGAs) in Schizophrenia: integrating insights from human and cellular transcriptome.

Speaker:

Sara Remuzgo Martínez.

Member of the Genetic Epidemiology and Atherosclerosis in Systemic Inflammatory Diseases research group.

Title: Transcriptional study of genes associated with rheumatoid arthritis and cardiovascular disease.

Wednesday 14/02/2018

Speaker:

Nerea Iturrioz Rodríguez

Pre-doc of the IDIVAL Nanomedicine research group.

Title: Carbon nanotube coated particles as a possible delivery system.

Speaker:

Inmaculada Concepción Pérez del Molino Bernal.

Member of the HUMV Microbiology Department. **Title:** Mycobacterium

tuberculosis complex genotyping techniques.

Wednesday 14/03/2018

Speaker:

Javier Vázquez Bourgon

Associate Professor of Psychiatry at the University of Cantabria.

Title: Searching for early biomarkers of long-term hepatic alterations in non-affective psychosis.

Speaker:

Leticia de las Vecillas Sánchez

Specialist Doctor in the HUMV Allergology Area.

Title: Drug hypersensitivity and desensitization: mechanisms and new approaches.

Wednesday 11/04/2018

Speaker:

María Iglesias Escudero

Pre-doc of the IDIVAL Autoimmunity and Transplantation research group.

Title: Utility of myeloid-derived suppressor cells (MDSC) in monitoring renal transplant patients.

Speaker:

María Carcelen Labrador

Pre-doc of the IDIVAL Cytokines and Growth Factors in the Phenomena of Pathological Tissue Plasticity research group.

Title: MicroRNAs and neuropathic pain.

Wednesday 16/05/2018

Speaker:

Ángela Puente Sánchez

Specialist doctor in the Hepatology unit of the HUMV Digestive System Department.

Title: Liver fibrosis regression after hepatitis C eradication.

Speaker:

Catalina Díaz Ríos

Pre-doc of the IDIVAL Epidemiology and Pathogenic and Molecular Mechanisms of Infectious Diseases and Clinical Microbiology research group.

Title: Pseudomonas aeruginosa in cystic fibrosis: Evolution of the type VI secretion system (T6SS). Identification and functional characterisation of new T6SS components.

Wednesday 13/06/2018

Speaker:

Elena Navarro Palomares

Pre-doc of the IDIVAL Nanomedicine research group.

Title: Coating and functionalization of nanoparticles for biomedical applications.

Wednesday 24/10/2018

Speaker:

Carmen Lage Martínez

Pre-doc of the IDIVAL Neurodegenerative Diseases research group.

Title: Automated evaluation of eye movement and diagnostic utility in neurodegenerative diseases.

Speaker:

Nuria García Díaz

Pre-doc of the IDIVAL Translational Haematology research group.

Title: Deregulated mechanisms downstream of PLCG1 promoting cutaneous T cell lymphoma progression.

Wednesday 14/11/2018

Speaker:

Luis Ruiz Guerrero

Specialist doctor in the HUMV Cardiology Department.

Title: A family cardiovascular disease consultation.

Speaker:

Ana Freije León

Member of the IDIVAL Cell Cycle, Stem Cells and Cancer research group.

Title: New prognostic targets in oropharynx epidermoid carcinoma.

Wednesday 12/12/2018

Speaker:

Marta Drake Pérez

Specialist doctor in the HUMV Radiagnostics Department.

Title: Clinical applications of Synthetic MRI.

Speaker:

Eloísa González Lavado

Pre-doc of the IDIVAL Nanomedicine research group.

Title: Biodegradable carbon nanotubes maintain their antitumour effect.

Student training

The Public Health System of Cantabria has 171 Associate Professors in Health Sciences and 118 Full Professors and Professors at the University of Cantabria.

1. Undergraduate Studies in Medicine at the University of Cantabria. Courses at the Marqués de Valdecilla University Hospital cover students of the Faculty of Medicine in their third, fourth, fifth and sixth year of medical studies. The number of students enrolled in these courses in 2018 whose training involves the Marqués de Valdecilla University Hospital is as follows: 4th year of Medical Studies: 122, 5th year of Medical Studies: 168, 6th year of Medical Studies: 107

2. Summer internship programme. In 2013, IDIVAL, in collaboration with the Institute of Biomedicine and Biotechnology of Cantabria, launched a grant programme for students studying an undergraduate degree or diploma in any biomedical discipline (Biology, Biotechnology, Nursing, Pharmacy, Medicine, Dentistry, etc.) to spend a summer working in the laboratories of IDIVAL groups, a programme that has continued since then. The students awarded the grant and the research group in which they worked during the summer of 2018 appear in the IDIVAL grants section.

Santander Biomedical Lectures

The Biomedical Research Forum of Cantabria, consisting of Cantabria Healthcare Services, the Marqués de Valdecilla Research Institute (IDIVAL), the University of Cantabria and the Institute of Biomedicine and Biotechnology of Cantabria launched in 2016 the SANTANDER BIOMEDICAL LECTURES programme, a series of lectures intended to advance worldwide Biomedical knowledge.

Prestigious researchers at the top of the field worldwide are invited to lecture.

These lectures were an initiative of scientists at the different research centres of Cantabria to create a forum for discussing current advances in biomedicine, in which some of our region's research groups play a leading role.

They will also be a discussion forum for young researchers and healthcare personnel in our hospitals, and for the general public, and an opportunity to establish partnerships. The lectures in this programme in 2018 were:

Thursday 25/01/2018

Speaker:
Jose A. Bengoechea
Director, Wellcome-Wolfson Institute of Experimental Medicine - Queen's University Belfast - UK
Title: Superbugs: myth, reality or the new cell biologists.

Thursday 22/02/2018

Speaker:
Denis Duboule
École Polytechnique Fédérale de Lausanne - Switzerland
Title: The control of Hox Genes; From Mammalian Development to Human Genetic Syndromes.

Thursday 22/03/2018

Speaker:
Bente Langdahl
Department of Endocrinology and Internal Medicine - Aarhus University Hospital - Aarhus - Denmark
Title: New clinical, genetic and pharmacogenetic approaches to bone disorders.

Thursday 26/04/2018

Speaker:
Jorge Galán
Director, Department of Microbial Pathogenesis - Yale University - School of Medicine - New Haven, Connecticut - USA
Title: Pathogen restriction and host specificity: insights from the human pathogen Salmonella Typhi.

○ Thursday 31/05/2018

Speaker:

Fernando J. Corrales

Senior Scientist and head of the Proteomics Laboratory at the National Biotechnology Centre, CSIC

Title: Applications of proteomics in biomedicine.

Mechanisms and biomarkers in liver disease.

○ Thursday 28/06/2018

Speaker:

Juan Ignacio Aróstegui

Head of the unit of autoinflammatory diseases in the Immunology Service of the Hospital Clínic

Title: Diagnostic developments and rational bases of new treatments for inherited autoinflammatory diseases

○ Thursday 18/10/2018

Speaker:

Solomon Dadia

Deputy Director of Orthopaedic Oncology Dept & Head of Surgical 3D Printing Lab, Tel Aviv Medical Center.

Title: New trends in 3D printing.



○ Thursday 29/11/2018

Speaker:

José Alcami

Director of the Immunopathology Unit of AIDS. ISCIII.

Title: HIV cure, the next frontier.



○ Thursday 20/12/2018

Speaker:

Jordi Vila

Head of the Department of Clinical Microbiology - Clinic Hospital - University of Barcelona. Research Professor of the Institute of Global Health Barcelona.

Title: Acinetobacter baumannii paradigm of pan-resistance: future alternatives for treatment.



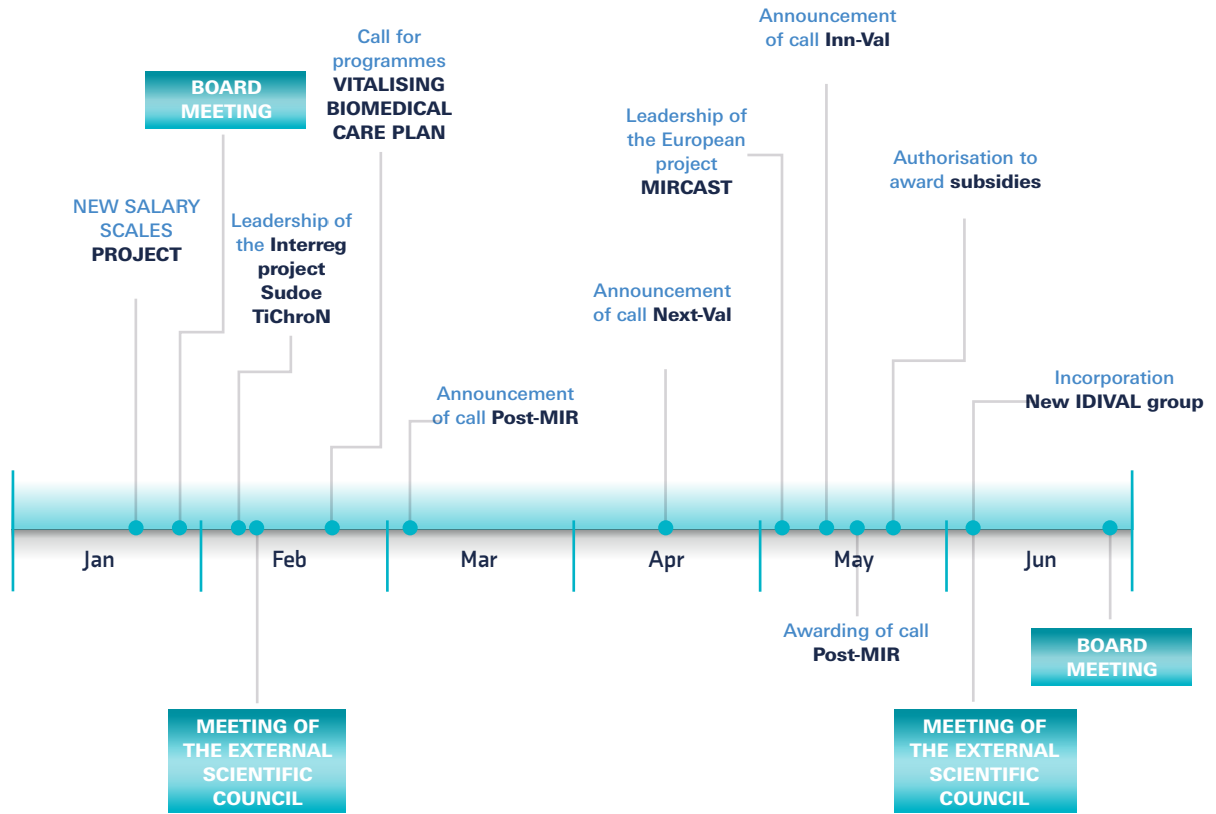
24/02/16

Admin
Info
Support
Feedback

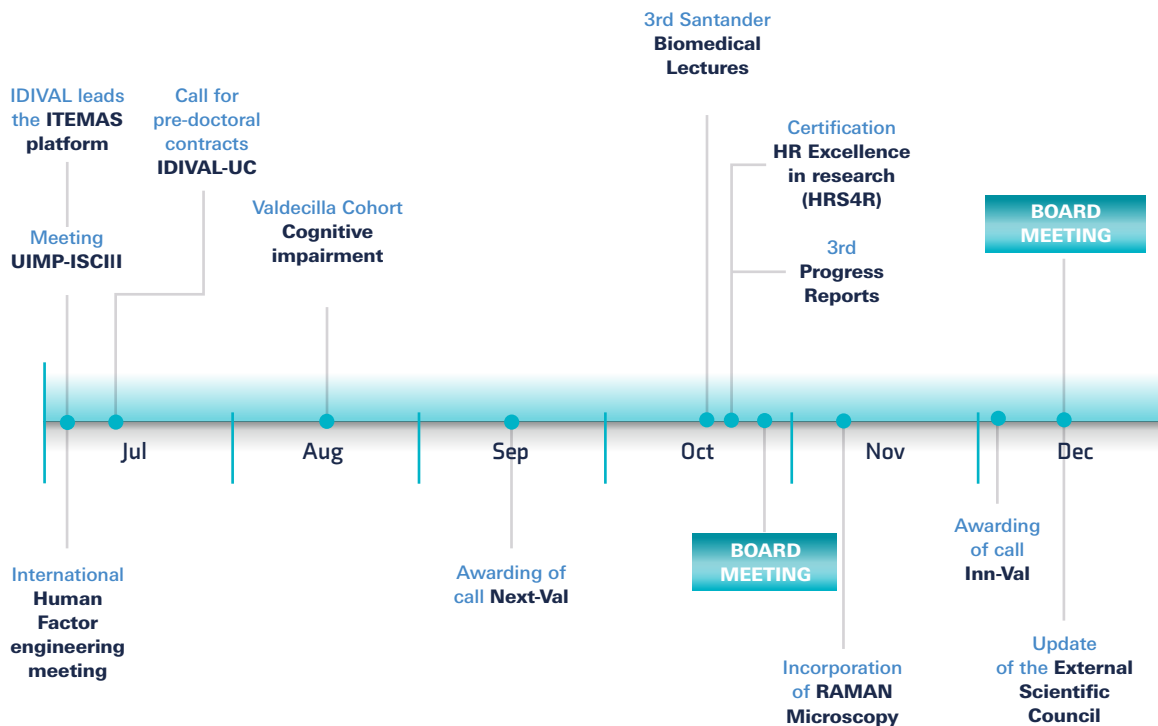


○ A few
milestones
in 2018

January / June



July / December



○ IDIVAL in the media

In 2018, the presence of IDIVAL in the media was relevant, as shown by numerous website visits, over 125,000 impacts for the IDIVAL brand and more than 2,800 accumulated news articles on the Google search engine at the time of publishing this report. IDIVAL has a shared audiovisual portal with the Marqués de Valdecilla University Hospital and the Valdecilla Virtual Hospital, the Somos Valdecilla Platform (www.somosvaldecilla.org) and Social Networks on this platform, in addition to having its own accounts and presence on Twitter (@IDIVALdireccion with more than 2,000 followers).

○ News stories from 2018

○ Cantabria leads a European healthcare project for the first time

The Office for Chronic Disease of the Cantabrian Health Service (CHS), in collaboration with the Valdecilla Healthcare Research Institute (IDIVAL), has led a European research project for the first time, focusing on healthcare innovation in chronic paediatric diseases.

Entitled the 'TiChroN Project', this project aims to bring new approaches associated with promoting health and improving care to children with chronic diseases, based on the use of new technologies, informed the Government in this press release. With a budget of 760,833 euros, financed from the European

Union 'Interreg SUDOE' programme, the project is one of 21 proposals approved of the 357 submitted between Spain, France and Portugal.

○ IDIVAL announces the annual call of the Vitalising Biomedical Care Plan

The plan includes 10 programmes which, as a whole, prioritise talent, internationalisation and innovation, with special emphasis in Primary Care and Nursing. It is structured into three project programmes (NextVal, for new researchers; InnVal, to develop research projects; and PrimVal, for Primary Care projects); two programmes for attracting talent (Mentoring, junior programme for new residents; and Innplant, senior programme for new department or section heads joining the Marqués de Valdecilla University Hospital from other centres); a programme to promote clinical researchers (intensification modality A and B), a pre-doctoral mobility programme and a research group support programme (Support).

○ IDIVAL leads the ITEMAS platform for innovation in medical and health technologies

Dr Galo Peralta, Management Director of IDIVAL, has been named National Coordinator for the Platform for Innovation in Medical and Health Technologies.

After eight years in operation, ITEMAS has consolidated Innovation Support Unit formed by experts who support innovation in Spain's main hospitals; it receives financing from the Carlos III Health Institute.

The overall objective of the ITEMAS platform is to promote a culture of innovation and facilitate the detection, management and enhancement of scientific and healthcare

knowledge in the field of medical and health technologies. For this purpose, ITEMAS tries to create value and improve the efficiency of the healthcare system, understanding that healthcare professionals and their environment have major capacities to generate knowledge and products from that knowledge.

○ IDIVAL and UC agree to openly disseminate their research publications

The Valdecilla Research Institute (IDIVAL) and the University of Cantabria (UC) have agreed to openly disseminate the results of their research publications in the university's institutional repository, UCrea. The Regional Minister for Health, María Luisa Real, and Rector of the University of Cantabria (UC), Ángel Pazos, have signed a collaboration agreement.

Signing this document establishes the mechanisms necessary for IDIVAL to use the 'UCrea Investigación' repository to conserve and disseminate with open access the publications of its researchers. The publications will always be scientific and a result of research work involving IDIVAL personnel.

○ New infection risk markers in lung transplant patients

Researchers from the Marqués de Valdecilla University Hospital and IDIVAL have taken part in a study recently published in The Journal of Heat and Lung Transplantation. This multi-centre paper involving IDIVAL and the Gregorio Marañón, 12 de Octubre, Puerta de Hierro, Val d'Hebron and La Fe hospitals. The work extends the spectrum of hypogammaglobulinemia, especially IgG, as a risk factor of infectious complications observed in other types of solid organ transplants, such as the heart. Its importance lies in that,

by measuring immunoglobulin levels in Immunology laboratories easily in clinical practice during the first days after the lung transplant, pulmonologists can adopt useful decisions to prevent infections and avoid subsequent complications.

○ IDIVAL is authorised to award subsidies by the Government of Cantabria

With an authorisation of the Government of Cantabria, IDIVAL acquires authority to award subsidies in compliance with current state regulations.

This generic authorisation must be followed by an authorisation based on each subsidy that IDIVAL will award before publication; they must be published in the national subsidy database.

○ Biodegradable carbon nanotubes trigger antitumour effects

The University of Cantabria-IDIVAL nanomedicine group has proven in a publication in the *Nanoscale* journal how certain chemical treatments improve the elimination of nanomaterials by in vitro and in vivo reticuloendothelial system cells in the peritumoral region once they have exerted their antitumour action. These results lead to new hopes in treating cancer where applying carbon nanotubes and other nanomaterials would significantly amplify the effects of traditional drugs to inhibit the microtubule dynamic by reducing cell resistance, the reappearance of tumours and, in short, improving survival in cancer patients.

○ Ramales Council sponsors IDIVAL research

Ramales de la Victoria Town Council has donated 8,000 euros to the Marqués de Valdecilla Research Institute - IDIVAL. The funds come from the charity registration of participants in the

2nd Charity Walk against Cancer, a charitable sporting event that gathered 1,500 participants on 9 June and which was possible thanks to the collaboration of the Council and the Regional Ministry of Education, Culture and Sport of the Government of Cantabria. This donation will contribute to the research projects of Dr Prada Gómez, Head of the Radiotherapy Oncology Department at the Marqués de Valdecilla University Hospital.

○ IDIVAL researchers discover a novel mechanism that is key for the development of chronic pain

The IDIVAL research group in which includes María A. Hurlé, Professor of Pharmacology at the University of Cantabria, has described the critical role of microRNA-30c in the development of a variety of chronic and extremely incapacitating pain called neuropathic pain.

The paper published in a high-impact journal, *Science Translational Medicine*, reveals a novel mechanism mediated by microRNA-30c, which is key for the development of chronic neuropathic pain.

Treating animals with a molecule that neutralises microRNA-30c effectively combats neuropathic pain through a mechanism, mediated by TGF-beta, which improves the function of the natural system mammals have to protect against pain, exerted by endogenous opiodes. This grants microRNA-30c potential value as a biomarker for this pathology which is often difficult to diagnose clinically.

○ Presentation of Results of the First Symposium of the Small World Initiative Project

The first Small World Initiative Project held in our region took place on 6 September and was

organised by IDIVAL and the University of Cantabria.

This project aims to involve Secondary and Baccalaureate students in a real research project with a society service-learning strategy to solve the problem of increased infectious diseases caused by bacteria resistant to antibiotics. In Spain, in addition to IDIVAL, this international programme is run in 17 SWI@Spain National Network research centres and universities.

○ Presentation 3rd Santander Biomedical Lectures

Following the success of the previous editions of Santander Biomedical Lectures, the speakers at the third round of lectures are presented, including researchers renowned worldwide for their international contributions. In the line of previous years, this new edition, to be held from October 2018 to June 2019, will focus on a series of lectures dedicated to the progress of world knowledge in Biomedicine.

○ UIMP meeting: Innovation in Health, a vital opportunity

Once again, the Carlos III Health Institute and IDIVAL are organising a summer meeting at the Menéndez Pelayo International University in Santander, which this time will focus on aspects related to innovation in health, closely related to the actions carried out by the Platform for Innovation in Health Technologies, which belongs to the Carlos III Health Institute (ITEMAS).

The meeting, which has become an essential date in the annual events calendar for health research and innovation and involves some of the main names in innovation in health in our country, will present healthcare innovation organisation models

from other countries, such as the Irish or German model, or the Medstar model in Washington. Round tables will also tackle issues such as sustainability, entrepreneurship, new technologies, value contributed by innovation and success stories.

○ Valdecilla Cohort for the study of memory and Cognitive Impairment

The Cognitive Impairment Unit of the Marqués de Valdecilla University Hospital Neurology department, led by Dr Pascual Sanchez-Juan, launched the Valdecilla cohort in August for the study of memory and brain ageing. This project aims to study the evolution of a group of volunteers comprising patients with cognitive deterioration and healthy individuals, all aged over 55, in order to understand which factors help predict each person's risk of developing dementia, especially Alzheimer's.

The study was launched thanks to a collaboration with SIEMENS HEALTHINEERS with the participation of other Hospital services, such as Ophthalmology, Nuclear Medicine or Radiology, in addition to IDIVAL and the movement analysis laboratory of the Gimbernat Cantabria University School. Detailed analyses will be conducted with molecular imaging, magnetic resonance imaging and neurocognitive tests; genetic and environmental factors will also be studied.

○ Genetics helps to figure out the key components of fracture risk

A major international collaboration with the participation of José Antonio Riancho, IDIVAL Researcher, Head of the Internal Medicine Department of the Marqués de Valdecilla University Hospital and Professor at the University of Cantabria, has identified 15 genetic variants related to the

risk of suffering osteoporotic fractures, a significant health problem affecting over 9 million people in the world each year. The collaboration took another step forward and used genomic information on other risk factors to examine their role in causing fractures. Researchers found that only bone mineral density and muscle strength are directly involved in susceptibility to fracture.

The findings propose that interventions aimed at increasing bone mass and muscle function are more likely to prevent fractures than the general administering of calcium and vitamin D supplements.

○ The genetic profile of each patient can predict the effectiveness of antipsychotic treatment in schizophrenia

The collaborative research project recently published in the American Journal of Psychiatry by the Marqués de Valdecilla University Hospital-IDIVAL-CIBERSAM schizophrenic research group together with the Zucker Hillside Hospital (New York) and the international EUFEST consortium, used the global genetic fingerprint of patients and highlighted that the efficacy of antipsychotic treatment will have in patients can be partially predicted.

"Patients with low genetic risk are twice as likely to respond than those with high genetic risk". The findings may be of great interest in making clinical decisions and have been replicated in three independent patient cohorts.

○ Assessment of the therapeutic impact of PET/CT with 11C-Choline in the reappearance of prostate cancer

In a study published in Nuclear Medicine Communications, the official publication of the British Nuclear Medicine Society, a journal with a high impact

and international prestige, the Marqués de Valdecilla University Hospital Nuclear Medicine Department has communicated the results of patients with recurring biochemistry of prostate cancer following initial curative treatment. All patients had a positive PET/CT with 11C-Choline. The production and synthesis of the 11C-Choline radio therapy drug was conducted at the Nuclear Medicine Department Radiopharmacy Unit. The primary objective of the study was to determine the effect that result had on the clinical management of patients. Results showed a change in the clinical attitude expected in two thirds of patients (66.1%). As an added value, PET/CT with 11C-Choline identified a second unexpected neoplasm in 4.5% of patients (4 lung cancer and 1 colon cancer).

○ Epigenetic therapy in hepatocellular carcinoma

Researchers from CIMA (Applied Medical Research Centre of the University of Navarra), led by doctors Ávila and Fernández-Barena, publish an interesting paper in Hepatology, the official publication of the American Association for the Study of Liver Diseases (AASLD), one of the main international journals in the field. In this paper on experimental models such as over-expression of G9a and DNMT1 histone methyltransferase correlates with a poorer prognosis of hepatocellular carcinoma. By selectively inhibiting these two enzymes with the CM-272 drug we observe a powerful effect in terms of cell proliferation and tumour growth. This drug is especially effective in hypoxia, which is extremely relevant as CM272 interferes with the adaptation process of tumour angiogenesis. This treatment also appears to have antifibrotic properties on the liver.

○ **IDIVAL is at the forefront of national medical research in microscopy**

The Valdecilla Healthcare Research Institute (IDIVAL) has consolidated its position at the forefront as a national benchmark in microscopy by incorporating a RAMAN confocal image microscope, an addition to existing high-end electronic and confocal microscopy equipment. This new microscope lends speed in detecting the structure and biochemical composition of any organic or inorganic element, ease of use as the sample need

not be set, and the possibility of working with very small volumes.

○ **MIRCAST project, a European study led by IDIVAL**

The ultimate goal of MIRCAST is the prospective assessment of post-operative recovery, hospital stay, wound complications, serious complications and medium-term results (hernia, recurrence, etc.) of minimally invasive right colectomy, comparing intracorporeal anastomosis with extracorporeal, and comparing

conventional laparoscopic instruments with robotics. A network of more than 55 professionals and hospitals from eight European countries (Spain, France, Italy, Germany, United Kingdom, Finland, Denmark and Holland) will take part in MIRCAST, led by Dr Marcos Gómez from the Marqués de Valdecilla University Hospital.

○ **New tools for diagnosing and treating hepatocellular carcinoma**

A multidisciplinary team comprised of researchers from the Marqués de Valdecilla University Hospital, the



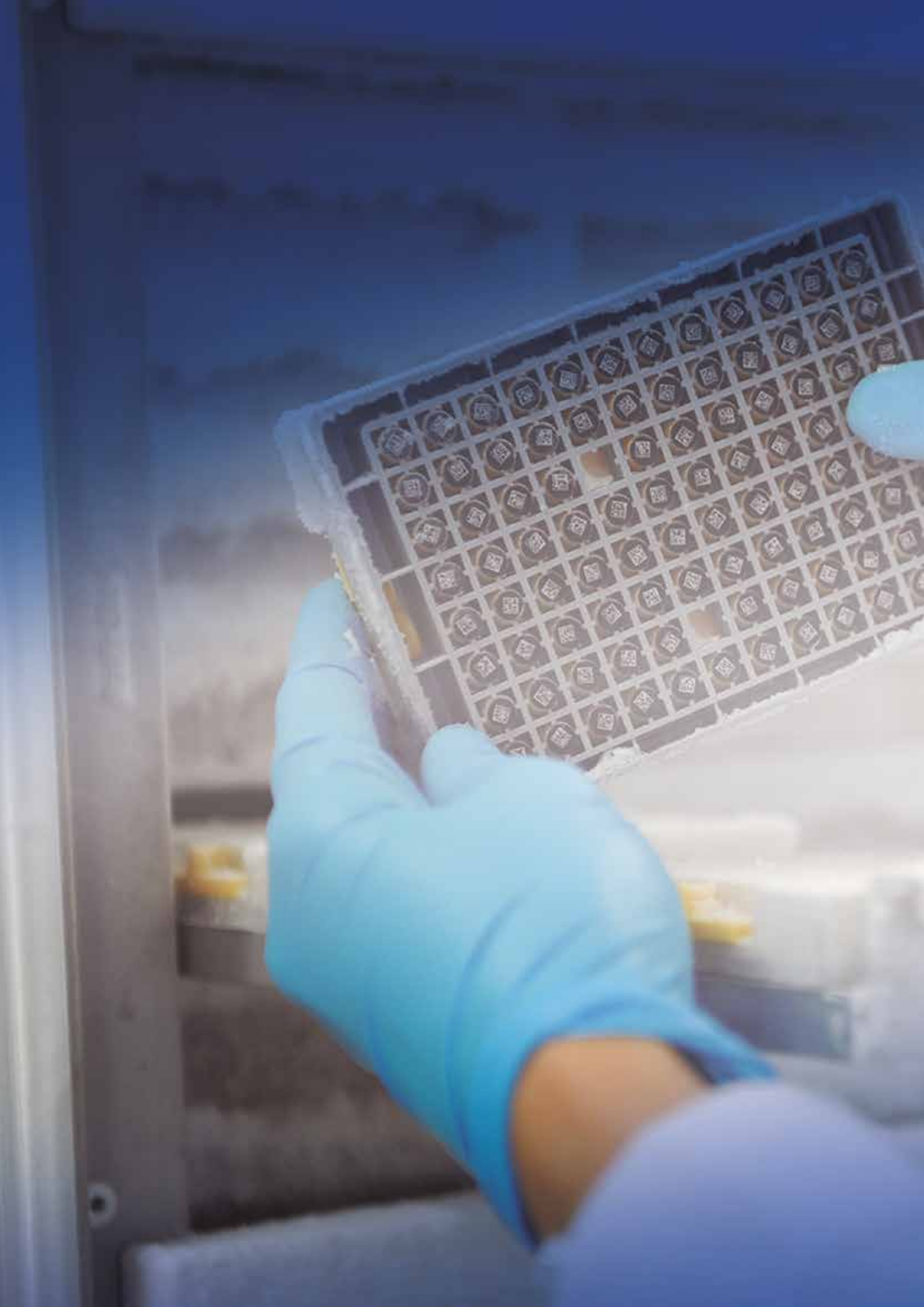
University of Cantabria and IDIVAL and IBBTEC research institutes, took the initiative to research HC. Thanks to obtaining public financing resources from the Carlos III Health Institute and private contributions (Fight for Life Foundation), the team has published its first contribution to liver cancer, proposing a route that includes liver cancer biopsies and their characterisation using genomic techniques for a detailed analysis of the characteristics of the tumour, a technique known as ultrasequencing. This detects genetic mutations in the tumour

lesions of each patient with liver cancer.

○ IDIVAL receives the European HRS4R human resources certificate

IDIVAL has recently received the excellence in human resources seal known as HRS4R. The seal a recognition by the pan-European Euraxess Initiative that IDIVAL complies with European standards in human resource management in research. To achieve this, the team comprising researchers and management personnel, has analysed the institute's situation in this field, identifying aspects

that require improvement and an action plan for implementing it according to the 40 principles of the European research human resources code. The certification process began in October 2016 by adhering to the code of conduct. During this process, the certifying agency, euraxess (<https://euraxess.ec.europa.eu/jobs/hrs4r>), verified compliance with its requirements via an action plan prepared by IDIVAL, which is already in use in around 60 actions that ultimately aim to promote and attract talent in research and that are available on the IDIVAL website.





○ IDIVAL R&D&i
Activity

IDIVAL financing in 2018

Revenue

IDIVAL recorded total revenue of €7.6 million in 2018. Revenue from the Government of Cantabria was €2.29 million, representing 30% of total revenue. The

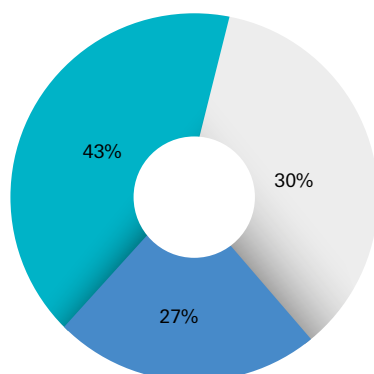
remaining revenue (70%) came from public and private competitive programmes at national and international level (€2.07 million) and the private agreements and

contracts signed during the year (€3.26 million).

IDIVAL REVENUE

Amount

Government of Cantabria	2,229,000.00
Competitive calls	2,069,683.40
Regional programmes	40,000.00
R&D National Plan	1,669,659.86
European Commission Programmes	104,907.34
Private competitive grants	255,116.20
Private contracts and agreements	3,263,272.47
Clinical testing	2,030,111.14
Service contracts	413,769.40
Collaboration agreements	57,563.19
Donations	761,828.74
Provision of services	25,963.51
TOTAL REVENUE	7,587,919.38



ORIGIN OF REVENUE, 2018
Percentage Distribution



Expenditure

IDIVAL's expenditure is essentially allocated to developing self-funded research projects, to the IDIVAL research grant programme and to structural costs (support personnel, in-house research personnel and operational costs)

In 2018, total expenditure for developing projects with specific financing was €3.1 million, €3.1 million in structural costs and €0.3 million in investments. The IDIVAL grant programme involved expenditure of €1.06 million

(Valdecilla López Albo Post-MIR contracts, productivity, research projects for new researchers, innovation projects, nursing projects, primary care, cofinancing projects and contracts, etc.).

Personnel

In 2018, IDIVAL had 32 Research Groups, consisting of researchers, collaborators and technical personnel, all belonging to the Marqués de Valdecilla University Hospital and the University of Cantabria. One of these research groups joined in 2018 after the assessment of the External Scientific Council. Of the 32 research groups, 19 are consolidated, 6 emerging, 6 associated clinical, and 1 newly created.

Of the 32 Research Groups, 21 are directed by head researchers involved with clinical activity, 9 by researchers of the University of Cantabria, 2 by Institute researchers, and 1 by Ministry of Health personnel.

In 2018, these groups had a total of 610 members, of which 46 were Primary Investigators on projects developed through competitive funding in active national or international calls over the last five years (2014-2018).

Personnel contracted by IDIVAL during 2018 belong to the following programmes:

Researcher Programmes	Number
Miguel Servet Programme (ISCIII):	3
IDIVAL Researchers:	6
Research Training Programme	
Rio Hortega Programme (ISCIII):	2
Sara Borell Programme (ISCIII):	1
Wenceslao López Albo Programme (IDIVAL):	6
Contracts for Research Projects	
IDIVAL-funded contracts	29
Public-funded contracts:	26
Privately-funded contracts:	34
Support Services	
Scren Programme (ISCIII):	2
Biobank network (ISCIII):	1
ITEMAS Platform (ISCIII):	4
Infrastructure technicians (MICINN):	1
IDIVAL support personnel:	22
Four individuals contracted through CIBER must be added to this list.	

Publications

In terms of production activity, IDIVAL researchers have published 458 indexed papers in 2018 (excluding conference papers published in journals). In 197 papers (43%), the first or last

author pertains to IDIVAL, and two or more IDIVAL groups participated in 177 (39%). 292 publications (64%) were in collaboration with authors from other countries.

The list of countries and the number of authors from each country is shown in the attached table.

Country	No. authors	Country	No. authors
Germany	315	Ireland	47
Argentina	17	Iceland	3
Australia	188	Israel	17
Austria	35	Italy	259
Belgium	56	Japan	15
Bolivia	2	Latvia	2
Brazil	22	Lithuania	2
Bulgaria	8	Malaysia	6
Cameroon	1	Malta	1
Canada	108	Mexico	17
Chile	5	Norway	85
China	51	Netherlands	19
Colombia	18	Panama	1
South Korea	3	Paraguay	1
Croatia	5	Poland	32
Cuba	1	Portugal	54
Denmark	75	Qatar	1
Ecuador	8	United Kingdom	423
Slovenia	7	Czech Republic	17
Spain	4433	Republic of South Africa	18
United States	762	Romania	2
Estonia	3	Russia	10
Finland	39	Singapore	11
France	190	Sweden	80
Georgia	3	Switzerland	63
Granada	2	Thailand	1
Greece	29	Taiwan	3
Hong Kong	6	Tunisia	24
Hungary	6	Turkey	7
India	5	Uruguay	2

Impact factor

In 2018, the cumulative impact factor of IDIVAL group publications was 2,296 (JCR 2017), with a percentage of

publications with an impact factor in the first quartile of 52%, and 100 (21.8%) of the papers published in 2018 had an impact

factor in the first decile of the specialisation.

Citations

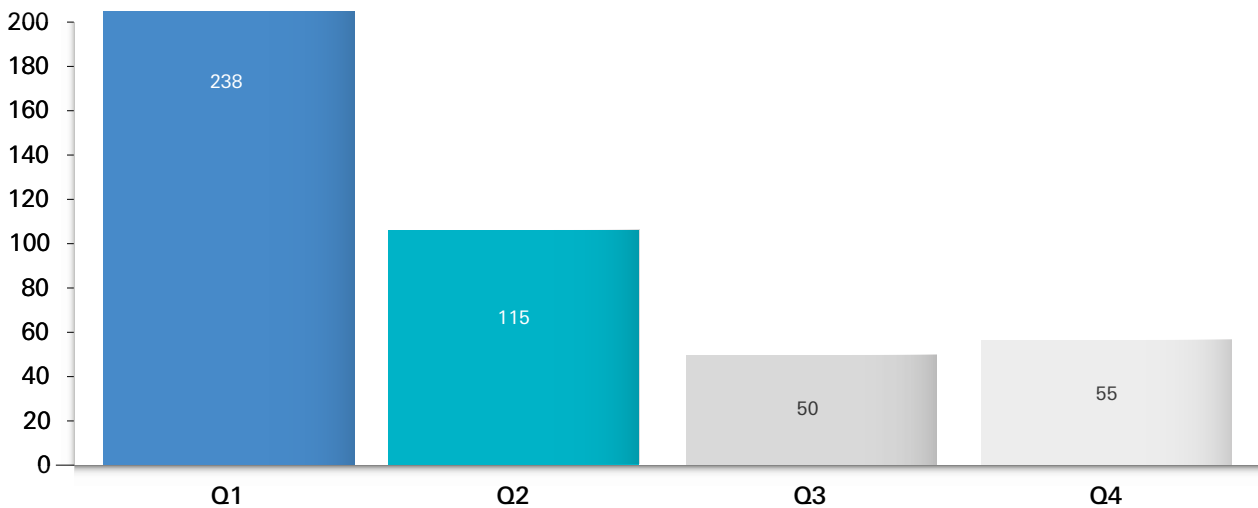
The first article by Valdecilla researchers was cited in 1930 and 1941. This was the paper published by Dr González Aguilar: González-Aguilar J. Contribution to the pathogeny of tendon tumours of giant cells. Journal of Bone and Joint Surgery, 1930; 12: 280-288.

Throughout 2018, the Valdecilla mark obtained 15,798 featured quotations according to data from the ISI web of knowledge platform (using the descriptor "valdecilla" in the corresponding affiliation field). Thus, by 2018 the Valdecilla brand had reached 140,000 accumulated

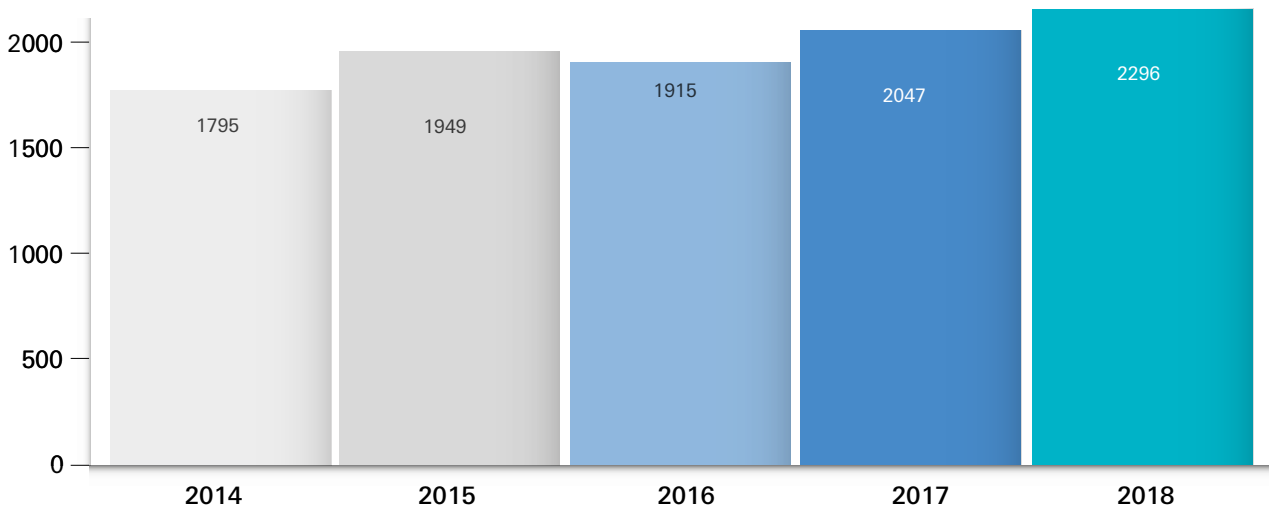
citations, and more than 210 works exceeded 100 citations.

In 2018, the IDIVAL brand had an impact in 101 written press new articles, 56 regional, 43 national and 2 international.

IDIVAL publications in 2018, distributed by quartile

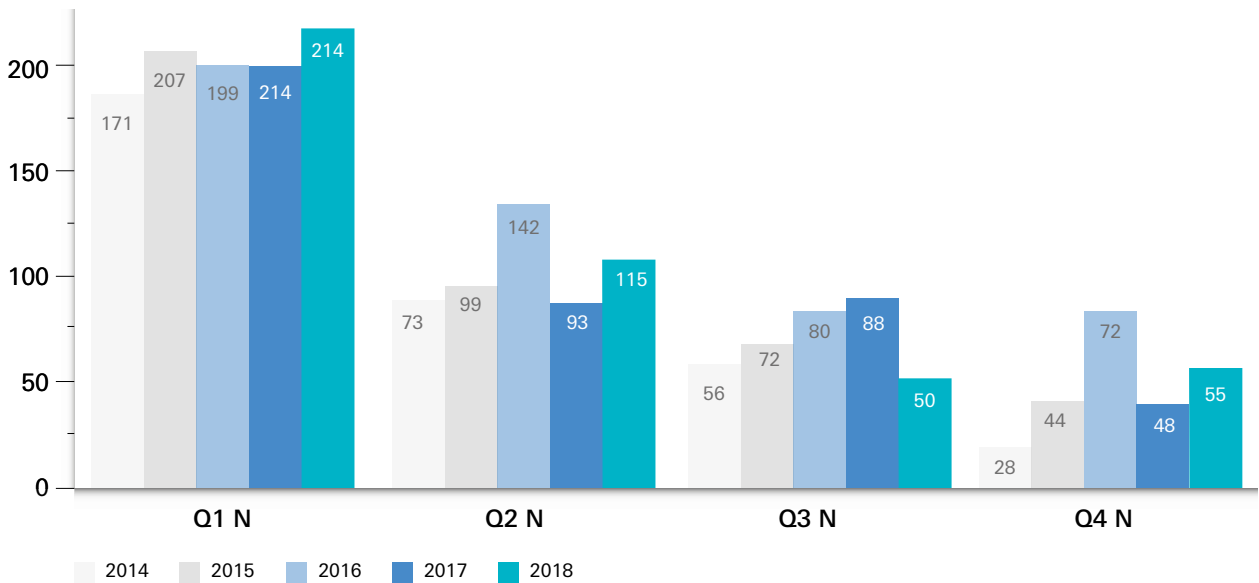


Evolution of the total impact factor



Evolution of impact factor distribution by quartile

Year	Q1		Q2		Q3		Q4		Total
	N	%	N	%	N	%	N	%	
2014	171	52.1%	73	22.3%	56	17.1%	28	8.5%	328
2015	207	49.1%	99	23.5%	72	17.1%	44	10.4%	422
2016	199	40.4%	142	28.8%	80	16.2%	72	14.6%	493
2017	214	48.3%	93	21%	88	19.9%	48	11%	443
2018	238	52.0%	115	25.1%	50	10.9%	55	12%	458





IDIVAL publications in 2018 by impact factor

(Excluding those derived from multi-centre collaborations)

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
ACTA NEUROPATHOLOGICA COMMUNICATIONS	5.414	1	5.414	1	2
ACTAS UROL ESP	1.26	1	1.26	4	9
ALCOHOL CLIN EXP RES	3.183	1	3.183	2	3
ALIMENTARY PHARMACOLOGY & THERAPEUTICS	7.357	2	14.714	1	1
ALZHEIMERS DEMENT	12.74	2	25.48	1	1
AM J TRANSPLANT	6.493	1	6.493	1	1
AMERICAN JOURNAL OF CARDIOLOGY	3.171	1	3.171	2	4
AMERICAN JOURNAL OF CLINICAL PATHOLOGY	2.413	1	2.413	2	4
AMERICAN JOURNAL OF GASTROENTEROLOGY	10.231	1	10.231	1	1
AMERICAN JOURNAL OF HEMATOLOGY	5.303	1	5.303	1	2
AMERICAN JOURNAL OF MEDICAL GENETICS PART B-NEUROPSYCHIATRIC GENETICS	3.016	1	3.016	2	4
AMERICAN JOURNAL OF NEURORADIOLOGY	3.653	2	7.306	1	2
ANAEROBE	2.742	1	2.742	2	5
ANALES DE PEDIATRÍA	1.318	2	2.636	3	7
ANN HEPATOL	1.576	1	1.576	4	9
ANN RHEUM DIS	12.35	4	49.4	1	1
ANNALS OF HEMATOLOGY	2.845	1	2.845	2	4
ANNALS OF NEUROLOGY	10.244	1	10.244	1	1
ANNALS OF ONCOLOGY	13.926	1	13.926	1	1
ANTIVIR RES	4.307	1	4.307	1	2
APPLIED CLAY SCIENCE	3.641	1	3.641	1	2
APPLIED ECONOMICS	0.75	1	0.75	3	8
APPLIED IMMUNOHISTOCHEMISTRY & MOLECULAR MORPHOLOGY: AIMM	2.042	1	2.042	2	3
ARCH BRONCONEUMOL	2.633	3	7.899	2	5
ARCHIVOS ESPANOLAS DE UROLOGÍA	0.465	2	0.93	4	10
ARTHRITIS & RHEUMATOLOGY	7.871	1	7.871	1	1
ARTHRITIS RESEARCH & THERAPY	4.269	4	17.076	2	3
ATEN PRIM	1.148	1	1.148	3	7
AUTOIMMUNITY REVIEWS	8.745	1	8.745	1	1
BBA-MOL BASIS DIS	5.108	1	5.108	1	2
BIOCHEMICAL PHARMACOLOGY	4.235	1	4.235	1	2
BIOL PSYCHIAT	11.982	1	11.982	1	1
BIOMACROMOLECULES	5.738	1	5.738	1	1
BIOMEDICAL OPTICS EXPRESS	3.482	1	3.482	1	2
BMC BIOINFORMATICS	2.213	1	2.213	1	3

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
BMC CANCER	3.288	4	13.152	2	5
BMC COMPLEM ALTERN M	2.109	1	2.109	2	3
BMC INFECTIOUS DISEASES	2.62	1	2.62	2	5
BMC PUBLIC HEALTH	2.42	1	2.42	2	4
BMJ OPEN	2.413	1	2.413	2	3
BONE MARROW TRANSPLANTATION	4.497	2	8.994	1	2
BRACHYTHERAPY	2.227	1	2.227	2	5
BRAIN BEHAVIOR AND IMMUNITY	6.306	1	6.306	1	1
BRAIN RES BULL	3.44	1	3.44	2	4
BREAST JOURNAL	2.424	1	2.424	2	4
BRIT J PSYCHIAT	5.867	1	5.867	1	1
BRITISH JOURNAL OF CANCER	5.922	2	11.844	1	2
BRITISH JOURNAL OF HAEMATOLOGY	5.128	2	10.256	1	2
BRITISH JOURNAL OF PHARMACOLOGY	6.81	1	6.81	1	1
CANCER EPIDEMIOL	2.888	1	2.888	1	3
CANCER LETTERS	6.491	1	6.491	1	2
CANCERS	5.326	1	5.326	1	2
CARDIOVASC ULTRASOUN	1.652	1	1.652	3	7
CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS	2.602	2	5.204	2	5
CELL DEATH AND DIFFERENTIATION	8	1	8	1	1
CELL DEATH DIS	5.638	2	11.276	1	3
CELL METAB	20.565	1	20.565	1	1
CELLULAR AND MOLECULAR LIFE SCIENCES	6.721	1	6.721	1	2
CEPHALALGIA	3.882	1	3.882	1	3
CHEST	7.652	1	7.652	1	2
CIR ESPAN	0.841	2	1.682	4	9
CIRC-CARDIOVASC INTE	6.504	1	6.504	1	2
CLIN COLORECTAL CANC	3.861	2	7.722	2	4
CLIN EXP RHEUMATOL	3.201	6	19.206	2	5
CLIN RES CARDIOL	4.455	1	4.455	2	3
CLINICAL & TRANSLATIONAL ONCOLOGY	2.392	3	7.176	3	7
CLINICAL EEG AND NEUROSCIENCE	1.807	1	1.807	3	7
CLINICAL INFECTIOUS DISEASES	9.117	2	18.234	1	1
CLINICAL MICROBIOLOGY AND INFECTION	5.394	2	10.788	1	1
CLINICAL NEUROPHYSIOLOGY	3.614	1	3.614	2	3

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
CULT MED PSYCHIAT	0.983	1	0.983	2	5
CURR OPIN CELL BIOL	10.015	1	10.015	1	1
CURR OPIN ORGAN TRAN	2.869	1	2.869	2	5
CURRENT OSTEOPOROSIS REPORTS	3.726	1	3.726	2	4
CURRENT PHARMACEUTICAL DESIGN	2.757	1	2.757	2	5
CURRENT RHEUMATOLOGY REPORTS	3.079	1	3.079	3	6
EJSO-EUR J SURG ONC	3.688	2	7.376	1	2
EMERGENCIAS	3.608	3	10.824	1	2
ENFERMEDADES INFECCIOSAS Y MICROBIOLOGÍA CLÍNICA	1.707	2	3.414	3	8
ENVIRON INT	7.297	3	21.891	1	1
ENVIRON POLLUT	4.358	1	4.358	1	2
ENVIRONMENTAL HEALTH PERSPECTIVES	8.309	1	8.309	1	1
EPILEPTIC DISORDERS	1.5	1	1.5	4	9
EUR CHILD ADOLES PSY	3.553	1	3.553	1	1
EUR J HEALTH ECON	2.601	1	2.601	1	2
EUR J MED GENET	2.004	1	2.004	3	7
EUR J NUTR	4.423	1	4.423	1	2
EUR PSYCHIAT	4.129	2	8.258	1	2
EUR RESPIR J	12.242	1	12.242	1	1
EUROINTERVENTION	4.417	1	4.417	2	3
EUROPACE	5.231	1	5.231	1	2
EUROPEAN HEART JOURNAL	23.425	1	23.425	1	1
EUROPEAN JOURNAL OF CANCER	7.191	1	7.191	1	2
EUROPEAN JOURNAL OF CLINICAL MICROBIOLOGY & INFECTIOUS DISEASES	2.537	1	2.537	2	5
EUROPEAN JOURNAL OF HAEMATOLOGY	2.595	2	5.19	3	6
EUROPEAN JOURNAL OF HEART FAILURE	10.683	2	21.366	1	1
EUROPEAN JOURNAL OF INTERNAL MEDICINE	3.282	2	6.564	1	2
EUROPEAN JOURNAL OF TRAUMA AND EMERGENCY SURGERY: OFFICIAL PUBLICATION OF THE EUROPEAN TRAUMA SOCIETY	1.704	1	1.704	2	5
EUROPEAN NEUROPSYCHOPHARMACOLOGY	4.129	1	4.129	1	2
EUROPEAN RADIOLOGY	4.027	1	4.027	1	2
EXPERT OPINION ON PHARMACOTHERAPY	3.475	1	3.475	2	3
EXPERT REVIEW OF CLINICAL IMMUNOLOGY	3.436	2	6.872	2	5
FASEB JOURNAL	5.595	1	5.595	1	1
FORENSIC SCI INT-GEN	5.637	1	5.637	1	1
FRONTIERS IN IMMUNOLOGY	5.511	1	5.511	1	2
FRONTIERS IN MOLECULAR NEUROSCIENCE	3.902	1	3.902	2	3

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
FRONTIERS IN PHYSIOLOGY	3.394	1	3.394	1	3
FUTURE MICROBIOL	3.19	1	3.19	2	4
FUTURE ONCOL	2.369	1	2.369	3	8
GACETA SANITARIA	1.581	4	6.324	3	6
GASTRIC CANCER	5.045	2	10.09	1	2
GASTROENT HEPAT-BARC	1.078	4	4.312	4	10
GASTROENTEROLOGY	20.773	1	20.773	1	1
GENET MED	9.937	1	9.937	1	1
GENOME MED	8.898	1	8.898	1	1
GLOBAL ECONOMIC REVIEW	0.273	1	0.273	4	10
HAEMATOLOGICA	9.09	4	36.36	1	1
HEAD NECK-J SCI SPEC	2.471	1	2.471	1	3
HEMATOLOGICAL ONCOLOGY	3.193	1	3.193	2	4
HEPATOL INT	4.117	1	4.117	2	3
HUMAN IMMUNOLOGY	1.994	1	1.994	4	9
HYPERTENSION	6.823	1	6.823	1	1
IEEE SENSORS JOURNAL	2.617	1	2.617	1	3
INFECT CONT HOSP EP	3.084	1	3.084	1	2
INT J BIOMETEOROL	2.577	3	7.731	2	4
INT J CLIN HLTH PSYC	3.9	1	3.9	1	2
INT J ENV RES PUB HE	2.145	3	6.435	2	3
INT J HYG ENVIR HEAL	4.848	1	4.848	1	1
INT J INFECT DIS	3.202	1	3.202	2	4
INT J MOL SCI	3.687	2	7.374	2	4
INT J OCCUP SAF ERGO	0.648	1	0.648	4	10
INT J ONCOL	3.333	1	3.333	2	5
INT J RADIAT ONCOL	5.554	1	5.554	1	1
INTENSIVE CARE MEDICINE	15.008	1	15.008	1	1
INTERACT CARDIOV TH	1.756	1	1.756	3	6
INTERNATIONAL IMMUNOPHARMACOLOGY	3.118	1	3.118	2	4
INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS	4.253	2	8.506	1	2
INTERNATIONAL JOURNAL OF CANCER	7.36	2	14.72	1	2
INTERNATIONAL JOURNAL OF CARDIOLOGY	4.034	4	16.136	2	4
INTERNATIONAL JOURNAL OF DERMATOLOGY	1.541	1	1.541	3	7
INTERNATIONAL JOURNAL OF NEUROPSYCHOPHARMACOLOGY	3.981	1	3.981	1	2
INTERNATIONAL JOURNAL OF OBESITY	5.151	1	5.151	1	2
INVESTIGATIONAL NEW DRUGS	3.502	1	3.502	1	3

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
J AM COLL CARDIOL	16.834	4	67.336	1	1
J CANCER RES CLIN	3.282	3	9.846	2	5
J CLIN NEUROSCI	1.64	1	1.64	4	8
J CRIT CARE	2.872	1	2.872	2	5
J CROHNS COLITIS	6.637	1	6.637	1	2
J DERMATOL TREAT	2.144	1	2.144	2	4
J GERIATR ONCOL	3.359	1	3.359	2	4
J HEMATOL ONCOL	7.333	1	7.333	1	1
J ORTHOP RES	3.414	1	3.414	1	2
J PAIN SYMPTOM MANAG	3.249	1	3.249	1	2
J PERIANESTH NURS	0.748	1	0.748	4	8
J PHYS-CONDENS MAT	2.617	1	2.617	2	5
J PSYCHOSOM RES	2.947	1	2.947	2	3
J SURG RES	2.051	1	2.051	2	5
J TISSUE ENG REGEN M	4.089	1	4.089	1	2
J UROLOGY	5.381	1	5.381	1	2
JACC-CARDIOVASC INTE	9.881	3	29.643	1	1
JAMA NEUROLOGY	11.46	2	22.92	1	1
JAMA PSYCHIATRY (TITLE CHANGES)	16.642	1	16.642	1	1
JOURNAL OF AFFECTIVE DISORDERS	3.786	1	3.786	1	2
JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY	13.258	1	13.258	1	1
JOURNAL OF ALZHEIMERS DISEASE	3.476	1	3.476	2	4
JOURNAL OF BIOMEDICAL OPTICS	2.367	1	2.367	2	4
JOURNAL OF BONE AND MINERAL METABOLISM	2.472	1	2.472	3	6
JOURNAL OF BONE AND MINERAL RESEARCH	6.314	1	6.314	1	1
JOURNAL OF CONTEMPORARY BRACHYTHERAPY	2.146	1	2.146	2	5
JOURNAL OF HAND THERAPY: OFFICIAL JOURNAL OF THE AMERICAN SOCIETY OF HAND THERAPISTS	1.04	1	1.04	4	8
JOURNAL OF HEART AND LUNG TRANSPLANTATION	7.955	1	7.955	1	1
JOURNAL OF HEPATOLOGY	14.911	2	29.822	1	1
JOURNAL OF HOSPITAL INFECTION	3.354	1	3.354	1	2
JOURNAL OF INFECTION	4.603	1	4.603	1	2
JOURNAL OF INFECTION AND CHEMOTHERAPY	1.777	1	1.777	4	8
JOURNAL OF INVESTIGATIONAL ALLERGOLOGY AND CLINICAL IMMUNOLOGY	3.457	1	3.457	2	5
JOURNAL OF LIGHTWAVE TECHNOLOGY	3.652	2	7.304	1	2
JOURNAL OF MEDICAL GENETICS	5.751	1	5.751	1	2
JOURNAL OF MOLECULAR AND CELLULAR CARDIOLOGY	5.296	1	5.296	1	2
JOURNAL OF NANOMATERIALS	2.207	1	2.207	2	5

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
JOURNAL OF NEUROINFLAMMATION	5.193	1	5.193	1	2
JOURNAL OF NEUROLOGY	3.783	4	15.132	1	3
JOURNAL OF PATHOLOGY	6.253	2	12.506	1	1
JOURNAL OF PHYSICAL CHEMISTRY C	4.484	1	4.484	1	2
JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY	4.095	1	4.095	1	3
JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY	4.287	1	4.287	1	2
JOURNAL OF THE NEUROLOGICAL SCIENCES	2.448	2	4.896	3	6
KIDNEY INT	8.429	1	8.429	1	1
LANCET	53.254	2	106.508	1	1
LANCET NEUROLOGY	27.138	1	27.138	1	1
LANCET ONCOLOGY	36.418	1	36.418	1	1
LASER PHYSICS	1.158	1	1.158	3	8
LEUKEMIA	10.023	3	30.069	1	1
LEUKEMIA & LYMPHOMA	2.644	1	2.644	2	5
LEUKEMIA RESEARCH	2.319	1	2.319	3	6
LIVER INTERNATIONAL	4.5	1	4.5	1	2
LIVER TRANSPLANTATION	3.752	1	3.752	1	2
MATURITAS	3.315	1	3.315	1	2
MEDICINA CLÍNICA	1.168	7	8.176	3	7
MEDICINA INTENSIVA	1.755	8	14.04	4	9
MEDICINE	2.028	3	6.084	2	4
MELANOMA RESEARCH	3.135	1	3.135	1	2
MICROB DRUG RESIST	2.344	3	7.032	3	6
MICROPOROUS AND MESOPOROUS MATERIALS	3.649	1	3.649	1	2
MOL MED REP	1.922	1	1.922	3	7
MOLECULAR NEUROBIOLOGY	5.076	1	5.076	1	2
MOLECULAR PSYCHIATRY	11.64	1	11.64	1	1
MOLECULES	3.098	2	6.196	2	4
MOVEMENT DISORDERS	8.324	3	24.972	1	1
NANO LETTERS	12.08	1	12.08	1	1
NANOSCALE	7.233	1	7.233	1	2
NAT REV RHEUMATOL	15.661	1	15.661	1	1
NATURE COMMUNICATIONS	12.353	3	37.059	1	1
NATURE GENETICS	27.125	1	27.125	1	1
NEFROLOGÍA	1.167	3	3.501	4	9
NEOPLASIA	4.994	1	4.994	1	3
NEUROBIOLOGY OF AGING	4.454	1	4.454	1	2
NEUROBIOLOGY OF DISEASE	5.227	1	5.227	1	2

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
NEUROCIURUGÍA	0.31	1	0.31	4	10
NEUROLOGÍA (BARCELONA, SPAIN)	1.938	3	5.814	3	7
NEUROLOGICAL SCIENCES	2.285	3	6.855	3	6
NEUROSCIENCE	3.382	1	3.382	2	5
NEUROSURG FOCUS	2.647	2	5.294	2	3
NEUROSURGERY	4.475	1	4.475	1	1
NEW ENGLAND JOURNAL OF MEDICINE	79.258	1	79.258	1	1
NEW JOURNAL OF CHEMISTRY	3.201	1	3.201	2	4
NICOTINE TOB RES	4.291	1	4.291	1	1
NURS EDUC TODAY	2.067	1	2.067	1	1
NURS OUTLOOK	2.425	1	2.425	1	1
NUTRIENTS	4.196	2	8.392	1	3
OBES SURG	3.895	1	3.895	1	1
ONCOIMMUNOLOGY	6.266	1	6.266	1	2
ONCOLOGIST	5.306	3	15.918	1	3
ONCOLOGY REPORTS	2.976	1	2.976	3	6
ONCOTARGET	5.168	2	10.336	1	3
OPEN FORUM INFECTIOUS DISEASES	3.24	1	3.24	2	4
OPHTHALMOLOGY	7.479	1	7.479	1	1
OPTICAL MATERIALS	2.32	1	2.32	2	4
OPTICS AND LASER TECHNOLOGY	2.503	1	2.503	2	4
OPTICS EXPRESS	3.356	1	3.356	1	3
OSTEOPOROSIS INTERNATIONAL	3.856	1	3.856	2	3
PAIN PHYSICIAN	2.556	1	2.556	3	6
PANCREAS	2.958	1	2.958	3	6
PATHOLOGY RESEARCH AND PRACTICE	1.466	1	1.466	3	7
PATIENT PREFER ADHER	1.733	1	1.733	2	5
PEDIATRIC INFECTIOUS DISEASE JOURNAL	2.305	1	2.305	2	4
PLOS ONE	2.766	16	44.256	1	3
POL ARCH MED WEWN	2.658	1	2.658	1	3
POL J PATHOL	0.865	1	0.865	4	9
POLYMER TESTING	2.247	1	2.247	2	4
PROG TRANSPLANT	1	1	1	4	8
PSYCHIATRY RESEARCH-NEUROIMAGING	2.223	2	4.446	2	5
PSYCHOL MED	5.475	2	10.95	1	1
PSYCHOPHARMACOLOGY	3.222	1	3.222	2	4
QJM-AN INTERNATIONAL JOURNAL OF MEDICINE	3.204	1	3.204	1	2
RADIOLOGY	7.469	1	7.469	1	1
RESUSCITATION	5.863	1	5.863	1	1

Journal	IF (JCR 2017)	No.	Total IF	Quartile	Decile
REVISTA CLÍNICA ESPAÑOLA	1.184	1	1.184	3	6
REVISTA DE ECONOMÍA MUNDIAL	0.415	1	0.415	4	9
REVISTA DE NEUROLOGÍA	0.601	4	2.404	4	10
REVISTA DE PSIQUIATRÍA Y SALUD MENTAL	2.233	1	2.233	2	5
REVISTA ESPAÑOLA DE ENFERMEDADES DIGESTIVAS	1.632	4	6.528	4	9
REVISTA ESPAÑOLA DE MEDICINA NUCLEAR E IMAGEN MOLECULAR	1.202	6	7.212	4	8
REVISTA ESPAÑOLA DE QUIMIOTERAPIA	0.605	1	0.605	4	10
REVISTA IBEROAMERICANA DE MICOLOGÍA	0.989	1	0.989	4	10
REVISTA PANAMERICANA DE SALUD PÚBLICA-PAN AMERICAN JOURNAL OF PUBLIC HEALTH	0.784	1	0.784	4	10
RHEUMATOL INT	1.952	2	3.904	4	9
RHEUMATOLOGY	5.245	1	5.245	1	2
ROM J MORPHOL EMBRYO	0.912	2	1.824	4	10
SCHIZOPHR RES	3.958	5	19.79	1	2
SCI TRANSL MED	16.71	1	16.71	1	1
SCIENCE	41.058	1	41.058	1	1
SCIENTIFIC REPORTS	4.122	12	49.464	1	2
SEIZURE-EUROPEAN JOURNAL OF EPILEPSY	2.839	1	2.839	2	5
SEMIN ARTHRITIS RHEU	4.356	4	17.424	1	2
SEMINARS IN DIAGNOSTIC PATHOLOGY	2.655	2	5.31	2	4
SENSORS-BASEL	2.475	1	2.475	2	3
SOC PSYCH PSYCH EPID	2.918	1	2.918	2	4
SOCIAL INDICATORS RESEARCH	1.648	1	1.648	2	3
SPECTROCHIMICA ACTA PART B-ATOMIC SPECTROSCOPY	2.854	1	2.854	1	3
STRAHLENTHER ONKOL	2.459	1	2.459	2	4
T ROY SOC TROP MED H	2.82	1	2.82	1	3
TARGET ONCOL	3.877	2	7.754	2	4
THIN SOLID FILMS	1.939	1	1.939	2	5
THORAX	9.655	1	9.655	1	1
THROMBOSIS AND HAEMOSTASIS	4.952	1	4.952	1	1
THROMBOSIS RESEARCH	2.779	1	2.779	2	5
TRANSFUSION	3.423	1	3.423	2	4
TRANSPL P	0.806	1	0.806	4	9
TRANSPLANT REV-ORLAN	2.364	1	2.364	3	6
TRANSPLANTATION	3.96	1	3.96	1	1
WORLD J EMERG SURG	3.198	1	3.198	1	2
WORLD JOURNAL OF CLINICAL CASES	1.931	1	1.931	2	4
WORLD NEUROSURG	1.924	1	1.924	2	5
GENERAL TOTAL		458	2296.105		

IDIVAL Research Group scientific production. Works with first or last author are differentiated from the others, separating those classified in the first quartile and first decile.

AREA	CODE	GROUP	Group*	No. of works	Total IF	N PU	N Q1	NQ1 PU	N D1	ND1 PU
Cancer	C1	ANATOMICAL AND MOLECULAR PATHOLOGY	C	6	10.65	0	1	1	0	0
Cancer	C2	APOPTOSIS	C	2	4.089	1	1	1	0	0
Cancer	C3	CELL CYCLE, STEM CELLS AND CANCER	C	6	33.35	3	6	3	3	1
Cancer	C4	TRANSLATIONAL HAEMATOPATHOLOGY	C	19	75.298	2	12	1	3	0
Cancer	C5	MOLECULAR IMAGING	C	20	38.506	10	5	1	1	0
Cancer	C6	MELATONIN AND BREAST CANCER	C	7	29.398	4	3	1	1	1
Cancer	C7	NEW TECHNIQUES IN ABDOMINAL SURGERY	CA	8	23.566	6	3	1	1	0
Cancer	C8	CELL SIGNALLING AND THERAPEUTIC TARGETS IN CANCER	C	12	78.448	7	8	4	5	1
Cancer	C9	CLINICAL TRIALS, MEDICAL ONCOLOGY AND PALLIATIVE MEDICINE UNIT	CA	39	285.685	1	23	0	5	0
Cancer	C10	NANOMEDICINE	NC	14	46.091	5	7	4	0	0
Infection and immunity	I1	GENETIC EPIDEMIOLOGY AND ARTERIOSCLEROSIS IN SYSTEMIC INFLAMMATORY DISEASES	C	48	238.737	24	25	11	12	4
Infection and immunity	I2	EPIDEMIOLOGY AND PATHOGENIC MECHANISMS OF INFECTIOUS DISEASES	C	38	146.89	8	19	2	6	0
Infection and immunity	I3	NANOVACCINES AND CELLULAR VACCINES BASED ON LISTERIA MONOCYTOGENES AND THEIR APPLICATIONS IN BIOMEDICINE	C	0	0	0	0	0	0	0
Infection and immunity	I4	IMMUNOPATHOLOGY OF RHEUMATIC DISEASES	C	5	21.159	0	3	0	0	0
Metabolism	M1	DIAGNOSIS AND TREATMENT USING IMAGING	CA	11	39.03	3	4	2	2	2
Metabolism	M2	MINERAL AND LIPID METABOLISM	C	32	125.299	14	14	4	7	2
Neurosciences	N1	CELL NUCLEUS BIOLOGY	C	6	37.805	5	6	5	2	1
Neurosciences	N2	CEPHALEA CLINIC AND GENETICS	CA	6	17.167	1	2	1	1	0
Neurosciences	N3	NEUROPHYSIOLOGY IN EPILEPSY AND NEUROINTENSIVES	CA	7	21.046	6	2	2	1	1
Neurosciences	N4	NEURODEGENERATIVE DISEASES	C	33	247.125	16	18	5	12	3
Neurosciences	N5	PSYCHIATRY	C	38	209.56	20	29	14	11	2
Cross-disciplinary	T1	COMMUNITY HEALTHCARE	CA	6	17.945	2	2	1	0	0
Cross-disciplinary	T2	HEALTHCARE LAW AND BIOETHICS	E	4	6.545	4	0	0	0	0
Cross-disciplinary	T3	NURSING RESEARCH	E	16	38.911	8	6	2	2	1
Cross-disciplinary	T4	HEALTH ECONOMICS AND HEALTH SERVICES MANAGEMENT	E	10	13.196	6	2	2	0	0
Cross-disciplinary	T5	EPIDEMIOLOGY AND PUBLIC HEALTH	C	36	185.376	6	24	3	9	0
Cross-disciplinary	T6	PHOTONICS ENGINEERING	C	8	22.393	8	5	5	0	0
Transplantation	Tp1	INFECTION AND IMMUNITY AND DIGESTIVE PATHOLOGY	C	31	172.52	8	15	5	7	2
Transplantation	Tp2	CYTOKINES AND GROWTH FACTORS IN THE PHENOMENA OF PATHOLOGICAL TISSUE PLASTICITY	C	11	69.163	5	8	5	3	2
Transplantation	Tp3	CARDIOVASCULAR RESEARCH GROUP	CA	20	144.188	3	12	1	9	1
Transplantation	Tp4	HAEMATOLOGIC NEOPLASMS AND HAEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION	C	18	74.266	1	9	1	5	0
Transplantation	Tp5	TRANSPLANTATION AND AUTOIMMUNITY	C	26	99.042	7	12	2	4	0

*Type of Group: C: consolidated; E: new; CA: associated clinical. **PU: articles with first or last group author

IDIVAL group scientific production

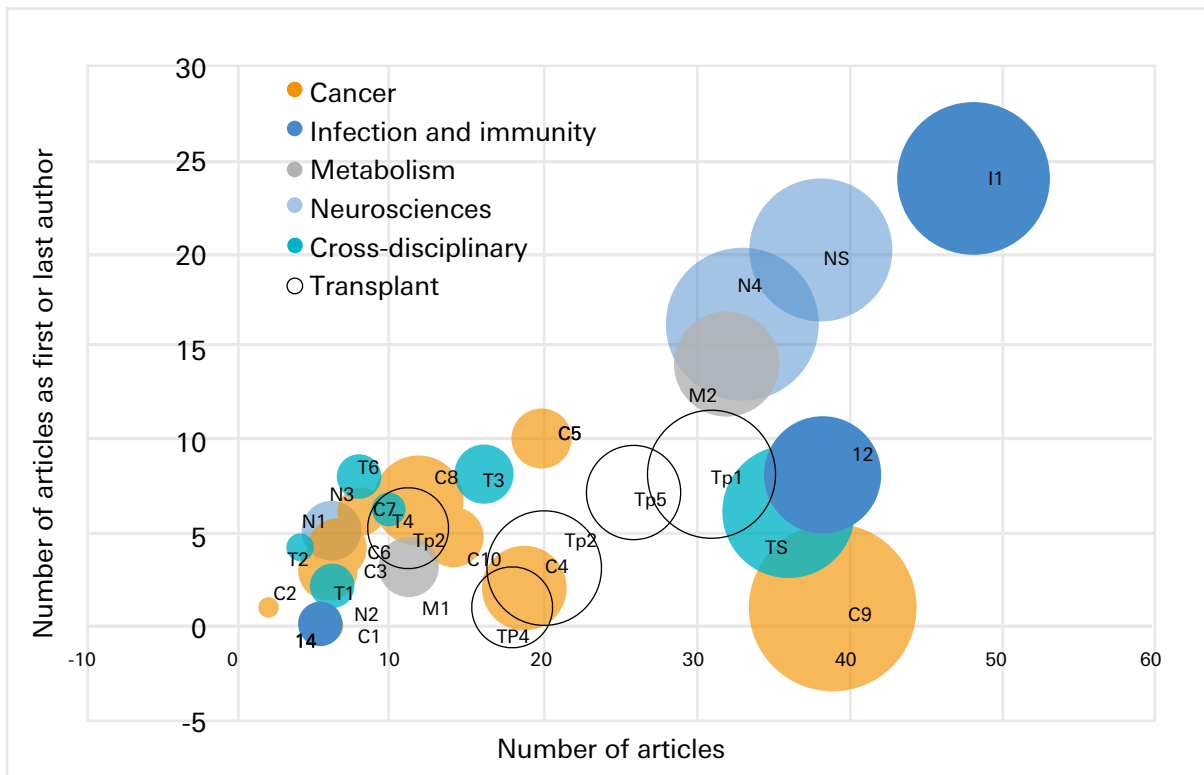


Figure 1. Graph representing scientific production of different IDIVAL groups in 2018. The area of each circle represents the impact factor of their work. The code for each group can be found in the table above.

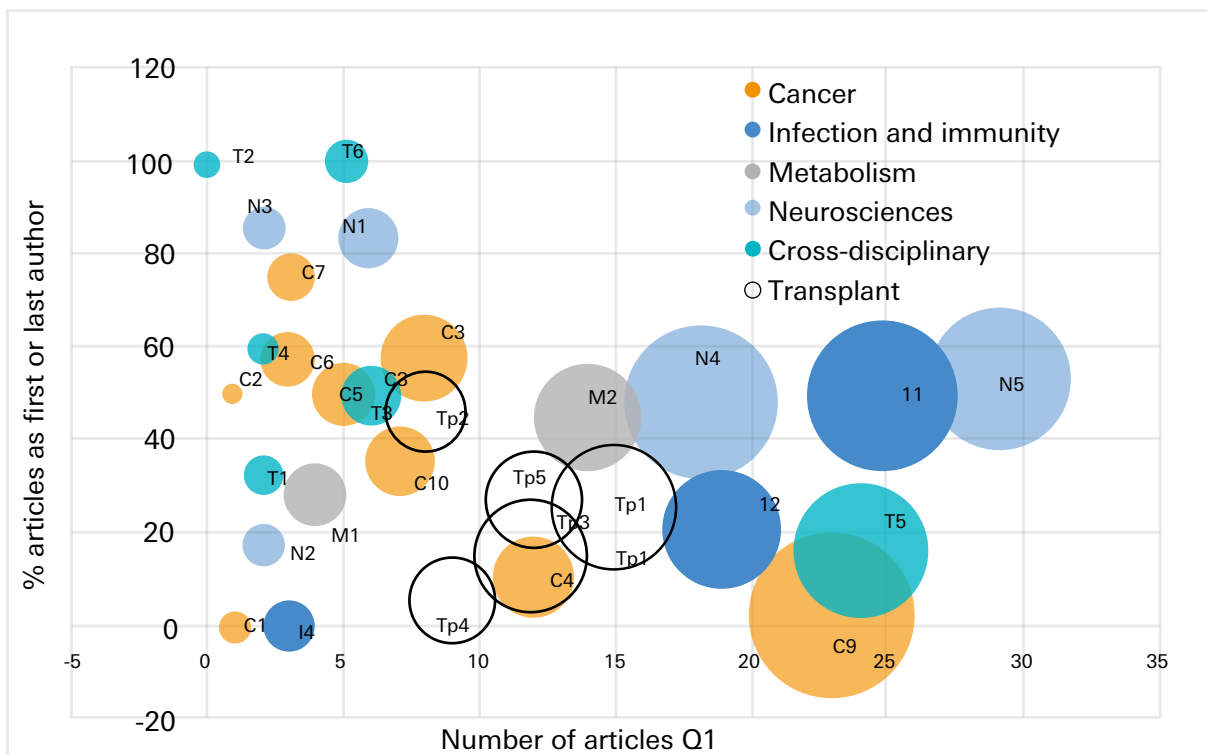


Figure 2. Graph representing scientific production of different IDIVAL groups in 2018. The area of each circle represents the impact factor of their work. The code for each group can be found in the table above.

Some representative articles

1. Alonso N, Estrada K, Albagha OME, Herrera L, Reppe S, Olstad OK, Gautvik KM, Ryan NM, Evans KL, Nielson CM, Hsu YH, Kiel DP, Markozannes G, Ntzani EE, Evangelou E, Feenstra B, Liu X, Melbye M, Masi L, Brandi ML, Riches P, Daroszewska A, Olmos JM, Valero C, Castillo J, Riancho JA, Husted LB, Langdahl BL, Brown MA, ..., **Ralston SH. Identification of a novel locus on chromosome 2q13, which predisposes to clinical vertebral fractures independently of bone density.** *Ann Rheum Dis* 2018. 77(3): 378 - 385. IF: 12.350 (Q1).
2. Annie C Isabwe G, Neuer MG, Sanchez LLV, Lynch DM, Marquis K, Castells M. **Hypersensitivity reactions to therapeutic monoclonal antibodies: Phenotypes and endotypes.** *J Allergy Clin Immunol* 2018. 142(1): 159-170.e2. IF: 13.258 (Q1).
3. Brainstorm Consortium, Anttila V, Bulik-Sullivan B, Finucane HK, Walters RK, Bras J, Duncan L, Escott-Price V, Falcone GJ, Gormley P, Malik R, Patsopoulos NA, Ripke S, Wei Z, Yu D, Lee PH, Turley P, Grenier-Boley B, Chouraki V, Kamatani Y, Berr C, Letenneur L, Hannequin D, Amouyel P, Boland A, Deleuze JF, Duron E, Vardarajan BN, Reitz C, ..., Neale BM. **Analysis of shared heritability in common disorders of the brain.** *SCIENCE* 2018. 360(6395). IF: 41.058 (Q1).
4. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Alvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setién E, Lopez-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. Microenvironment **Eradication of Hepatitis C: A Novel Treatment Paradigm.** *Am J Gastroenterol* 2018. 113(11): 1639 - 1648. IF: 10.231 (Q1).
5. de la Torre Hernández JM. **Mechanical Complications in Elderly Patients With Myocardial Infarction: Becoming Fewer But Just as Fatal.** *J Am Coll Cardiol* 2018. 72(9): 967 - 969. IF: 16.834 (Q1).
6. Delgado-Alvarado M, Dacosta-Aguayo R, Navalpotro-Gómez I, Gago B, Gorostidi A, Jiménez-Urbietta H, Quiroga-Varela A, Ruiz-Martínez J, Bergareche A, Rodríguez-Oroz MC. **Ratios of proteins in cerebrospinal fluid in Parkinson's disease cognitive decline: prospective study.** *Mov Disord* 2018. 33(11): 1809 - 1813. IF: 8.324 (Q1).
7. Diallo A, Jacobi H, Cook A, Labrum R, Durr A, Brice A, Charles P, Marelli C, Mariotti C, Nanetti L, Panzeri M, Rakowicz M, Sobanska A, Sulek A, Schmitz-Hübsch T, Schöls L, Hengel H, Melegh B, Filla A, Antenora A, Infante J, Berciano J, van de Warrenburg BP, Timmann D, Boesch S, Pandolfo M, Schulz JB, Bauer P, Giunti P, ..., **Tezenas du Montcel S. Survival in patients with spinocerebellar ataxia types 1, 2, 3, and 6 (EUROSCA): a longitudinal cohort study.** *Lancet Neurol* 2018. 17(4): 327 - 334. IF: 27.138 (Q1).
8. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, Colombo M, Craxi A, Crespo J, Day CP, Geier A, Kondili LA, Lazarus JV, Loomba R, Manns MP, Marchesini G, Negro F, Petta S, Ratziu V, Romero-Gomez M, Sanyal A, Schattenberg JM, Tacke F, Trautwein C, Wei L, Zeuzem S, Razavi H. **Modelling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030.** *J Hepatol* 2018. 69(4): 896 - 904. IF: 14.911 (Q1).
9. Fernández-Santiago R, Garrido A, Infante J, González-Aramburu I, Sierra M, Fernández M, Valldeoriola F, Muñoz E, Compta Y, Martí MJ, Ríos J, Tolosa E, Ezquerro M, **Barcelona LRRK2 Study Group. a-synuclein (SNCA) but not dynamin 3 (DNM3) influences age at onset of leucine-rich repeat kinase 2 (LRRK2) Parkinson's disease in Spain.** *Mov Disord* 2018. 33(4): 637 - 641. IF: 8.324 (Q1).
10. Gerace L, Tapia O. **Messages from the voices within: regulation of signaling by proteins of the nuclear lamina.** *CURR OPIN CELL BIOL* 2018. 52: 14 - 21. IF: 10.015 (Q1).
11. Jansen WJ, Ossenkoppele R, Tijms BM, Fagan AM, Hansson O, Klunk WE, van der Flier WM, Villemagne VL, Frisoni GB, Fleisher AS, Lleó A, Mintun MA, Wallin A, Engelborghs S, Na DL, Chételat G, Molinuevo JL, Landau SM, Mattsson N, Kornhuber J, Sabri O, Rowe CC, Parnetti L, Popp J, Fladby T, Jagust WJ, Aalten P, Lee DY, Vandenberghe R, ..., Zetterberg H. **Association of Cerebral Amyloid- β Aggregation With Cognitive Functioning in Persons Without Dementia.** *JAMA Psychiatry* 2018. 75(1): 84 - 95. IF: 16.642 (Q1).
12. Lafarga V, Tapia O, Sharma S, Bengoechea R, Stoecklin G, Lafarga M, Berciano MT. **CBP-mediated SMN acetylation modulates Cajal body biogenesis and the cytoplasmic targeting of SMN.** *Cell Mol Life Sci* 2018. 75(3): 527 - 546. IF: 6.721 (Q1).
13. Lipps C, Klein F, Wahlicht T, Seiffert V, Butueva M, Zauers J, Truschel T, Luckner M, Köster M, MacLeod R, Pezoldt J, Hühn J, Yuan Q, Müller PP, Kempf H, Zweigerdt R, Dittrich-Breiholz O, Pufe T, Beckmann R, Drescher W, Riancho J, Sañudo C, Korff T, Opalka B, Rebmann V, Göthert JR, Alves PM, Ott M, Schucht R, ..., **May T. Expansion of functional personalized cells with specific transgene combinations.** *Nat. Commun.* 2018. 9(1): 994 - 994. IF: 12.353 (Q1).
14. Montal V, Vilaplana E, Alcolea D, Pegueroles J, Pasternak O, González-Ortiz S, Clarimón J, Carmona-Iragui M, Illán-Gala I, Morenas-Rodríguez E, Ribosa-Nogué R, Sala I, Sánchez-Saudinos MB, García-Sebastian M, Villanúa J, Izagirre A, Estanga A, Ecay-Torres M, Iriondo A, Clerigue M, Tainta M, Pozueta A, González A, Martínez-Heras E, Llufríu S, Blesa R, Sanchez-Juan P, Martínez-Lage P, Lleó A, Fortea J. **Cortical microstructural changes along the Alzheimer's disease continuum.** *ALZHEIMERS DEMENT* 2018. 14(3): 340 - 351. IF: 12.740 (Q1).
15. Ochoa JP, Sabater-Molina M, García-Pinilla JM, Mogensen J, Restrepo-Córdoba A, Palomino-Doza J, Villacorta E, Martínez-Moreno M, Ramos-Maqueda J, Zorio E, Peña-Peña ML, García-Granja PE, Rodríguez-

Palomares JF, Cárdenas-Reyes IJ, de la Torre-Carpente MM, Bautista-Pavés A, Akhtar MM, Cicerchia MN, Bilbao-Quesada R, Mogollón-Jimenez MV, Salazar-Mendiguchía J, Mesa Latorre JM, Arnaez B, Olavarri-Miguel I, Fuentes-Cañamero ME, Lamounier A, Pérez Ruiz JM, Climent-Payá V, Pérez-Sánchez I, ..., Monserrat L. **Formin Homology 2 Domain Containing 3 (FHOD3) Is a Genetic Basis for Hypertrophic Cardiomyopathy..** J Am Coll Cardiol 2018. 72(20): 2457 - 2467. IF: 16.834 (Q1).

16. Ouyang X, Han SN, Zhang JY, Dioletis E, Nemeth BT, Pacher P, Feng D, Bataller R, Cabezas J, Stärkel P, Caballeria J, LePine Pongratz R, Cai SY, Schnabl B, Hoque R, Chen Y, Yang WH, Garcia-Martinez I, Wang FS, Gao B, Torok NJ, Kibbey RG, Mehal WZ. **Digoxin Suppresses Pyruvate Kinase M2-Promoted HIF-1a Transactivation in Steatohepatitis.** Cell Metab 2018. 27(5): 1156 - 1156. IF: 20.565 (Q1).

17. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, Radu MD, Joner M, Yu B, Jia H, Meneveau N, de la Torre Hernandez JM, Escaned J, Hill J, Prati F, Colombo A, di Mario C, Regar E, Capodanno D, Wijns W, Byrne RA, Guagliumi G, **ESC Scientific Document Group. Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions.** Eur Heart J 2018. 39(35): 3281 - 3300. IF: 23.425 (Q1).

18. Tramullas M, Francés R, de la Fuente R, Velategui S, Carcelén M, García R, Llorca J, Hurlé MA. **MicroRNA-30c-5p modulates neuropathic pain in rodents.** SCI TRANSL MED 2018. 10(453). IF: 16.710 (Q1).

19. Villahoz S, Yunes-Leites PS, Méndez-Barbero N, Urso K, Bonzon-Kulichenko E, Ortega S, Nistal JF, Vazquez J, Offermanns S, Redondo JM, Campanero MR. **Conditional deletion of Rcan1 predisposes to hypertension-mediated intramural hematoma and subsequent aneurysm and aortic rupture.** Nat. Commun. 2018. 9(1): 4795 - 4795. IF: 12.353 (Q1).

20. Abad A, Martínez-Balibrea E, Viéitez JM, Orduña VA, García Alfonso P, Manzano JL, Massutí B, Benavides M, Carrato A, Zanui M, Gallego J, Grávalos C, Conde V, Provencio M, Valladares M, Salazar R, Sastre J, Montagut C, Rivera F, Aranda E. **Genotype-based selection of treatment of patients with advanced colorectal cancer (SETICC): a pharmacogenetic-based randomized phase II trial.** Ann Oncol 2018. 29(2): 439 - 444. IF: 13.926 (Q1).



Research Projects

Grants active or awarded in 2018

Active Grants

Throughout 2018, IDIVAL groups maintained the following active projects in the R&D&i National Plan, research contracts and European projects.

Projects

1. PI 15/00009.

OCAMPO SOSA, ALAIN ANTONIO.

Functional identification and characterisation of new components of type VI secretion systems and the molecular basis of their regulation in clinical strains of *Pseudomonas aeruginosa*. CARLOS III HEALTH INSTITUTE. 2016-2018.

2. PI 15/00521.

OLMOS MARTÍNEZ, JOSÉ MANUEL.

Study of bone and mineral metabolism of the post-menopausal female and male population aged 50 and over receiving care from a health centre in Cantabria. CARLOS III HEALTH INSTITUTE. 2016-2018.

3. PI 15/00525.

GONZALEZ-GAY MANTECON, MIGUEL ANGEL

Genetic markers of atherosclerotic disease in Rheumatoid Arthritis. CARLOS III HEALTH INSTITUTE. 2016-2018.

4. PI 15/01224.

NISTAL HERRERA, JUAN FRANCISCO.

Bone morphogenetic protein 7 (BMP7): Potential therapeutic target in the pathological remodelling of the cardiovascular system. CARLOS III HEALTH INSTITUTE. 2016-2018.

5. PI 15/02138.

CRESPO GARCIA, JAVIER.

Endothelial dysfunction, subclinical atherosclerotic disease and cardiomyopathy in patients with HCV infection. Characterisation and potential reversibility with direct antiviral agents. CARLOS III HEALTH INSTITUTE. 2016-2018.

6. PI 15/01285.

OTERINO DURAN, AGUSTIN

Epigenetic modifications induced by adverse childhood experiences and endothelial damage in chronic migraines: case-control study. Murine experimental model creation. CARLOS III HEALTH INSTITUTE. 2016-2018.

7. PI 15/00069.

LLORCA DÍAZ, JAVIER.

Integration of genetic big data and clinical data: survival with breast cancer in the MCC-Spain study. CARLOS III HEALTH INSTITUTE. 2016-2018.

8. PI E15/00079.

CRESPO GARCIA, JAVIER.

Personalized Medicine in HCV infection: understanding and predicting hepatic and systemic responses in the era of the new antiviral drugs. CARLOS III HEALTH INSTITUTE. 2016-2018.

9. RTC-2015-3786-1.

GOMEZ ROMÁN, JAVIER.

Development of anti-CCR9 therapeutic antibodies for the personalised treatment of tumours- TERPERAN. CARLOS III HEALTH INSTITUTE. 2016-2018.

10. PI16/00156

VAQUE DIEZ, JOSE PEDRO.

New mechanisms in aggressive skin cancers: Applications to the diagnosis, prognosis and treatment of therapy-resistant melanoma and Merkel-cell carcinoma. CARLOS III HEALTH INSTITUTE. 2017-2019.

11. PI16/00915

RIANCHO MORAL, JOSE ANTONIO.

Study of mesenchymal stem cells in osteoporosis: Role of long non-coding RNAs (lncRNAs) and regenerative potential. CARLOS III HEALTH INSTITUTE. 2017-2019.

12. PI16/01103

RAMOS VIVAS, JOSE.

Integrated biology of infection and antimicrobial resistance of *Acinetobacter baumannii* and *A. pittii*. CARLOS III HEALTH INSTITUTE. 2017-2019.

13. PI16/01294

PIRIS PINILLA, MIGUEL ANGEL.

Aggressive lymphomas:

Interaction between the tumour genome and the microenvironment as a determinant of progression and response to therapy. CARLOS III HEALTH INSTITUTE. 2017-2019.

14. PI16/01397

MONTES MORENO, SANTIAGO.

Targeted exonic next generation sequencing for the molecular diagnosis and cell free tumour DNA analysis as a screening method for patients with DLBCL. CARLOS III HEALTH INSTITUTE. 2017-2019.

15. PI16/01415

FARIÑAS ALVAREZ, MARIA DEL CARMEN.

Impact of intestinal colonisation by multiresistant enterobacteriaceae in systemic infections, graft-versus-host disease (GVHD), and mortality in patients receiving transplants of allogeneic hematopoietic progenitor cells (Alo-HCT). CARLOS III HEALTH INSTITUTE. 2017-2019.

16. PI16/01535

FRANCIA GIL, MARIA VICTORIA.

Induction of conjugative pheromone-induced plasmid transfer. CARLOS III HEALTH INSTITUTE. 2017-2019.

17. PI16/01585

LOPEZ HOYOS, MARCOS.

Utility of the study of Myeloid-Derived Suppressor Cells (MDSC) when monitoring kidney transplants. CARLOS III HEALTH INSTITUTE. 2017-2019.

18. PI16/01652

SANCHEZ JUAN, PASCUAL. Study of rare variant genes associated with Alzheimer's disease in the Spanish population. CARLOS III HEALTH INSTITUTE. 2017-2019.

19. PI16/01656

JIMENEZ BONILLA, JULIO FRANCISCO.

5-Year study of a population with Mild Cognitive Impairment (MCI) previously evaluated with 11C-PIB and 18F-FDG PET/TAC. CARLOS

III HEALTH INSTITUTE. 2017-2019.

20. PI16/01717

MARTINEZ TABOADA, VICTOR MANUEL.

Study of the role of BAMBI, a regulator of TGF beta signalling, as a pathogenic factor and prognostic marker in rheumatoid arthritis. CARLOS III HEALTH INSTITUTE. 2017-2019.

21. CP16/00033

LOPEZ MEJÍAS, RAQUEL.

Cardiovascular risk assessment in patients with rheumatoid arthritis: the relevance of genetic markers. CARLOS III HEALTH INSTITUTE 2017-2019.

22. PI16-00496

LÓPEZ FANARRAGA, MÓNICA

Design and evaluation of multi-therapeutic nano-dispensers based on carbon nanotubes to treat tumours. CARLOS III HEALTH INSTITUTE. 2017-2019.

23. SAF2016-76046-R

CRESPO FACORRO, BENEDICTO.

Stratified treatment in schizophrenia: integrating results of the human and cellular transcriptome in antipsychotic treatment strategies. MINECO. 2017-2019.

24.SAF2016-75195-R

MERINO PÉREZ, JESÚS.

BAMBI, a regulator of TGF beta signalling, in cutaneous inflammation and differentiation of Human CD4 T Lymphocytes. MINECO. 2017-2019.

25. PI17/00156.

FERNÁNDEZ TORRE,

JOSE LUIS. Intracortical electroencephalography in coma patients with acute brain damage. CARLOS III HEALTH INSTITUTE. 2018-2020.

26. PI17/00936.

INFANTE CEBERIO, JON.

Study of motor, genetic and imaging biomarkers in prodromal Parkinson's disease associated with the G2019S mutation in LRRK2.

CARLOS III HEALTH INSTITUTE. 2018-2020.

27. PI17/01307

GANDARILLAS SOLINÍS, ALBERTO.

Therapeutic targets: common causes of genomic instability and malignancy in squamous cancer, for application in personalised medicine. CARLOS III HEALTH INSTITUTE. 2018-2020.

28. PI17/01399.

FERNÁNDEZ LUNA, JOSE LUIS.

Contribution of the hypoxia-od21 axis to the invasive capacity of glioblastoma. CARLOS III HEALTH INSTITUTE. 2018-2020.

29. PI17/01688.

PIPAON GONZÁLEZ, CARLOS.

The role of neddylation in chronic lymphocytic leukaemia, its value for prognosis and therapeutic applications. CARLOS III HEALTH INSTITUTE. 2018-2020.

30. DTS17/00055

CONDE PORTILLA, OLGA MARIA.

Design and development of a multimodal device for intraoperative cardiovascular diagnosis (IntraCardio). CARLOS III HEALTH INSTITUTE. 2018-2019.

○ Research and Mobility Contracts

CP117/00011

OCAMPO SOSA, ALAIN ANTONIO.

Miguel Servet Type II contract. CARLOS III HEALTH INSTITUTE 2018-2020.

CD17/00105

GONZÁLEZ LAGARRETA, LORENA.

Sara Borrell contract. CARLOS III HEALTH INSTITUTE 2018-2020.

PTA2015-11501-I.

PEREDA MARCOS, SARAY

Research Technical Support Contract MINECO 2017-2019.

MS16/00033

RAQUEL LÓPEZ MEJIAS.

Miguel Servet Type I contract. CARLOS III HEALTH INSTITUTE 2017-2021.

Active European Projects in 2018

EU12/01- PSYSCAN.

CRESPO FACORRO, BENEDICTO.

Translating neuroimaging findings from research into clinical practice. 7PM. European Commission.

EU13/01- PRECISESADS.

GONZÁLEZ-GAY, MIGUEL ÁNGEL.

Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases. FP7, Innovative Medicines Initiative. European Commission.

EU16/1. CHRODIS PLUS.

FERNANDEZ VIADERO, CARLOS.

Action on chronic diseases. European Commission.

ECT-2017-0371. VALER H2020.

CRESPO FACORRO, BENEDICTO.

Valdecilla initiative to promote European research. European Commission.

SOE2/P1/E0674. TiChroN.

LAPUENTE HEPPE, IGNACIO.

Use of ICTs as a tool to improve comprehensive care of children with chronic diseases. Interreg, Sudoe.

EU17/15

CRESPO FACORRO, BENEDICTO.

COST Action CA15211 Atmospheric Electricity Network: coupling with the Earth System, climate and biological systems

EU17/24.

LOPEZ FANARRAGA, MÓNICA.

COST Action BM1401 European Network on RAMAN-BASED Applications for clinical diagnosis (Raman4clinics)

EU17/26.

INFANTE CEBEIRO, JON. ICTUSnet

- Network of excellence for the development and implementation of innovative models in the integrated care of ictus.

EU17/27.

CAYÓN DE LAS CUEVAS,

JOAQUIN. HLPN Health Law and Policy Network. Erasmus+ Programme - Jean Monnet Activities.

EU18/08. PSYCH UP.

CRESPO FACORRO, BENEDICTO.

Improving support for people affected by psychological disorders during their training path.

EU18/12

RIANCHO MORAL, JOSE ANTONIO.

COST Action: GEMSTONE "Genomics cooSkeletal traits Translational Network".

Grants awarded

In 2018, IDIVAL researchers received a positive response on the following projects in the National Plan

PI18/00042.

LÓPEZ MEJIAS, RAQUEL.

Characterisation of molecular bases of IgA-mediated vasculitis. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/00043.

GONZÁLEZ-GAY MANTECÓN, MIGUEL ÁNGEL.

Genetic markers associated with metabolic syndrome and cardiovascular disease in rheumatoid arthritis. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/00380.

OCAMPO SOSA, ALAIN ANTONIO.

Type VI secretion system and ExIA exolysin as virulence markers in Pseudomonas aeruginosa in pneumonia association with mechanical ventilation. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/00543.

NISTAL HERRERA, JUAN FRANCISCO.

MicroRNAs: biomarkers with prognostic value and potential therapy targets for regression of cardiac hypertrophy. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/00762.

OLMOS MARTÍNEZ, JOSÉ MANUEL.

Study of bone and mineral metabolism of the post-menopausal female and male population aged 50 and over receiving care from a health centre in Cantabria. Camargo cohort. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/00827

DIERSSEN SOTOS, TRINIDAD.

Lifestyles and breast cancer - LifeBreast Test. CARLOS III HEALTH INSTITUTE 2019-2021.

PI18/01304

CRESPO GARCÍA, JAVIER.

Non-alcoholic steatohepatitis as an immunomediated inflammatory disease. Prevalence and characterisation. INSTInCT Study. CARLOS III HEALTH INSTITUTE 2019-2021.

CP18/00003

AYESA ARRIOLA, ROSA.

The study of intelligence and general neurocognitive function, that strongly overlap genetically, may be a promising approach for genetic research in schizophrenia spectrum disorders (from now SSD). CARLOS III HEALTH INSTITUTE 2019-2022.

DTS18/00022.

ÁLVAREZ DOMÍNGUEZ, CARMEN.

Validation of nanovaccines based on Listeria as combination immunotherapy in solid tumours. CARLOS III HEALTH INSTITUTE 2019-2020.

DTS18/00141.

FERNÁNDEZ LUNA, JOSÉ LUIS.

Nanoplasmonic sensor for the detection of tumour cells circulating in the blood.
CARLOS III HEALTH INSTITUTE
2019-2020.

MS18/00003.

AYESA ARRIOLA, ROSA.

Miguel Servet type I contract.
2019-2023

IF118-00027.

SANTAMARIA AGUIRRE, JAVIER.

IIS-business Doctorates in Health Sciences and Technologies. 2019-2022

Clinical trials

During 2018, IDIVAL authorised a total of 77 clinical trial contracts and 48 post-authorisation studies to be performed in the Marqués de

Valdecilla University Hospital and its area of influence. The list of major clinical trials approved in 2018 is shown in the attached table.

List of trials with contracts signed in 2018

Researcher	Clinical trial
CRESPO GARCÍA, JAVIER	AURORA: Phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the effectiveness and safety of cenicriviroc for treating hepatic fibrosis in adult patients with non-alcoholic steatohepatitis.
RIVERA HERRERO, FERNANDO	Phase 3, Multicenter, Randomized, Double-Blind, Placebo-controlled Study of AG-120 in Previously-treated Subjects with Nonresectable or Metastatic Cholangiocarcinoma with an IDH1 Mutation.
OTERINO DURÁN, AGUSTÍN	Multicentre, randomised, double-blind, parallel group, placebo-controlled, open period study to assess the effectiveness and safety of fremanezumab in prophylactic treatment of migraines in patients with an inadequate response to previous preventive treatments
RÚIZ SAN MILLÁN, JUAN CARLOS	Single-group ALXN1210 study in adult and teenage patients with atypical haemolytic-uremic syndrome (SHUa) with no prior treatment with complement inhibitors
GARCÍA RIVERO, JUAN LUIS	Multicentre, randomised, double-blind, placebo-controlled 12 week study to assess the effectiveness and safety of QAW039 added to standard base treatment of asthma in patients with uncontrolled asthma
BLANCO ALONSO, RICARDO	Multicentre, randomised, partial-blind, active control study to demonstrate reduction in radiographic progression with secukinumab compared to GP2017 (biosimilar to adalimumab) in week 104, and to assess safety, tolerability and long-term effectiveness in a 2-year period in patients with active ankylosing spondylitis
SÁNCHEZ JUAN, PASCUAL JESÚS	Multicentre, double-blind, randomised and parallel group-controlled study to research the effectiveness and safety of BI 425809, administered orally during a 12-week treatment period, compared to placebo in patients with cognitive deterioration due to Alzheimer's disease
YÁÑEZ SAN SEGUNDO, LUCRECIA	Phase 2, open, prospective and randomised study on the effectiveness of adding defibrotide to regular treatment of immunoprophylaxis for the prevention of acute graft-versus-host disease in adult and paediatric patients following allotransplantation of haematopoietic stem cells
CRESPO GARCÍA, JAVIER	Phase 2a, randomised, partially-blind and placebo-controlled study to assess the effectiveness, safety and pharmacokinetics of 24-week treatment with multiple doses of JNJ-56136379 in monotherapy and in combination with nucleotide analogue in patients with chronic hepatitis B virus infection
RIVERA HERRERO, FERNANDO	PANOVA-3: Fundamental, randomised and open study of simultaneous treatment with TFields (electrical fields for treating tumours, 150 kHz) and gemcitabine and nab-paclitaxel (paclitaxel bound to albumin in nanoparticle formation) as a first-line treatment of pancreatic adenocarcinoma in locally advanced stage.

Researcher	Clinical trial
LÓPEZ-BREA PIQUERAS, MARTA FRANCISCA	Phase 2/3, randomised, open and two-part study of dinutuximab and irinotecan versus irinotecan as second-line treatment in subjects with recurring or resistant small cell lung cancer
RIVERO TIRADO, MONTSERRAT	Suspension of TNF inhibitor treatment in patients with inflammatory bowel disease: multicentre, prospective and randomised clinical trial
FERNANDEZ FORCELLEDO, J. LUIS	Suspension of TNF inhibitor treatment in patients with inflammatory bowel disease: multicentre, prospective and randomised clinical trial
BLANCO ALONSO, RICARDO	Multicentre, randomised, double-blind and placebo-controlled study to assess the safety and effectiveness of upadacitinib in patients with active ankylosing spondylitis
CRESPO FACORRO, BENEDICTO	Phase 3 study to assess the safety, tolerability and long-term durability of the effect of treatment with ALKs3831 in subjects with schizophrenia or type 1 bipolar disorder
GARCÍA RIVERO, JUAN LUIS	Phase 3b, multicentre, randomised, double-blind, parallel group and placebo-controlled study to assess the safety and effectiveness of Benralizumab 30 mg SC in patients with severe asthma not controlled with common clinical practice
GARCÍA RIVERO, JUAN LUIS	Multicentre, randomised, placebo-controlled, parallel group study in two treatment periods to assess the safety of QAW039 added to existing treatment in patients with asthma not controlled with GINA steps 3, 4 and 5
DE LA TORRE HERNÁNDEZ, MARÍA	Edoxaban versus standard treatment and its effects on clinical results in patients JOSÉ subjected to transcatheter aortic valve implantation (in auricular fibrillation).
RODRÍGUEZ FDEZ, FERNANDO	Phase 3 trial to assess the effectiveness and safety on sublingual components in immunotherapy against domestic dust mites in children and teenagers (5 to 17 years) with allergic asthma induced by domestic dust mites
VÁZQUEZ SALVI, LUÍS	Randomised, double-blind and parallel group study to assess the effectiveness and safety of dulaglutide doses in research when added to metformin treatment in patients with type 2 diabetes mellitus
ZUECO GIL, JOSE JAVIER	Register with healthcare product: Optical coherence tomography study 9 months after pharmacoactive biostable albuminal polymer and sirolimus.
CRESPO GARCÍA, JAVIER	Randomised, double-blind, placebo-controlled, exploratory, phase 2a study to assess the safety and effectiveness of DS102 administered orally in patients with NAFLD
PIÑERA HACES, VICENTE C.	Phase 3, randomised, double-blind, active control, parallel group and multicentre study in haemodialysis participants with anaemia caused by chronic liver disease to assess the effectiveness, safety and pharmacokinetics of daprodustat administered three times a week, versus recombinant human erythropoietin, after having received recombinant human erythropoietin or similar
RIVERO TIRADO, MONTSERRAT	Phase 2a, randomised, double-blind, placebo-controlled, parallel group study to assess the effectiveness and safety of oral pf-06651600 and pf-06700841 as an induction and open extension treatment in patients with moderate or severe Crohn's disease
RIVERO TIRADO, MONTSERRAT	Phase 3b, multicentre, randomised, blind, active drug-controlled study to compare the effectiveness and safety of ustekinumab versus adalimumab in the treatment of patients with moderate or severe activity Crohn's disease not previously treated with biological drugs
NÚÑEZ CÉSPEDES, JAVIER	Phase 1b/2 Trial of Combined SGN-35 (BrentuximabVedotin) Therapy with cyclophosphamide, procarbazine, prednisone, etoposide and mitoxantrone (BrEPEM) for Older Patients with Untreated Hodgkin Lymphoma (HL)
SAINZ LASO, FERMÍN	Master DAPT
RIVERA HERRERO, FERNANDO	Open phase 1b/2 study of binimetinib administered in combination with nivolumab or nivolumab plus ipilimumab in patients with metastatic colorectal cancer with stable microsatellite (MSE) previously treated with RAS mutation
CRESPO GARCÍA, JAVIER	Multicentre, randomised, controlled and double-blind study of the effectiveness and safety of gastric endoscopic tubulation in patients with non-alcoholic steatohepatitis
GARCÍA RIVERO, JUAN LUIS	Multicentre, randomised, double-blind trial in parallel groups to assess the effectiveness and safety of PT010 compared to PT003 and PT009 in exacerbation of COPD during a 52-week treatment period, in subjects with COPD ranging from moderate to very severe.
GUTÉRREZ BAÑOS, JOSÉ LUÍS	Phase 3, randomised, double-blind, active drug (tolterodine) and placebo-controlled, international and multicentre study to assess the safety and effectiveness of vibegron in patients with symptoms of hyperactive bladder

Researcher	Clinical trial
DE JUAN FERRÉ, ANA	Phase 2 Olaparib maintenance trial following response to trabectedin and pegylated liposomal doxorubicin in recurring ovarian cancer
RODRÍGUEZ RODRÍGUEZ, ELOY M.	Multicentre, randomised, double-blind, placebo-controlled, parallel-group phase III study to assess the effectiveness and safety of gantenerumab in patients with early (prodromal to mild) Alzheimer's disease and sub-studies: "Longitudinal PET sub-study for amyloid associated with: phase 3, multicentre, randomised, double-blind, placebo-controlled and parallel group study to assess the effectiveness and safety of gantenerumab in patients with early (prodromal to mild) Alzheimer's disease and "exploratory PET sub-study for tau associated with: phase 3, multicentre, randomised, double-blind, placebo-controlled and parallel group study to assess the effectiveness and safety of gantenerumab in patients with early (prodromal to mild) Alzheimer's disease
CRESPO GARCÍA, JAVIER	Phase 2, randomised, double-blind, placebo-controlled and dose interval study to assess the safety, tolerability, pharmacokinetics and effectiveness of EDP-305 in patients with primary biliary cholangitis (PBC) with or without insufficient response to ursodeoxycholic acid (UDCA)
DURAN MARTINEZ, IGNACIO	Phase 3, randomised, double-blind, multicentre study of nivolumab as adjuvant treatment versus placebo in subjects with high risk invasive urothelial carcinoma
DURAN MARTINEZ, IGNACIO	The DUTRENEO Trial: A Prospective Study to Individualize the Approach with DUrvalumab (MED14736) and TREmelimumab in NEOadjuvant Bladder Cancer patients
DURAN MARTINEZ, IGNACIO	Phase 3, randomised, open and multicentre clinical trial to compare the effectiveness and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib monotherapy in first line treatment of subjects with advanced renal cell carcinoma (CLEAR)
LÓPEZ LÓPEZ, CARLOS	Phase 3, randomised, open, multicentre trial of durvalumab and tremelimumab as first line treatment in patients with Unresectable Hepatocellular Carcinoma (HIMALAYA)
DURAN MARTINEZ, IGNACIO	Phase 3, randomised, open study of nivolumab combined with cabozantinib or nivolumab and ipilimumab combined with cabozantinib versus sunitinib in participants with previously untreated advanced or metastatic renal cell carcinoma
RIVERA HERRERO, FERNANDO	Phase 3, randomised, blind, active controlled clinical trial of BMS-986213 (combination with fixed doses of relatlimab [anti-LAG-3] plus nivolumab) in combination with chemotherapy versus placebo plus chemotherapy as first line treatment in patients with locally advanced or metastatic unresectable gastric adenocarcinoma, LAG-3 positive
OTERINO DURÁN, AGUSTÍN	Randomised, double-blind study of galcanezumab versus placebo in adult patients with treatment-resistance migraine - CONQUER Study.
BERMÚDEZ RODRÍGUEZ, MARÍA A.	Phase 1, open trial searching for the dose of CC-93269, a BCMA X CD3 T cell antibody, in subjects with relapsed or resistant multiple myeloma
COLORADO ARAUJO, MARÍA DE LAS MERCEDES	Phase 1/2, Multicentre, Open-label Study of FT-2102 as a Single Agent and in Combination with Azacitidine in Patients with Acute Myeloid Leukaemia or Myelodysplastic Syndrome with an IDH1 R132 Mutation.
CRESPO GARCÍA, JAVIER	Phase 3, multicentre, randomised, double-blind, parallel group, placebo-controlled maintenance study on mirikizumab in patients with active moderate to severe ulcerative colitis
RIVERA HERRERO, FERNANDO	Phase 3, randomised and double-blind trial to compare trastuzumab plus chemotherapy and pembrolizumab with trastuzumab plus chemotherapy and placebo as first line treatment in participants with gastric adenocarcinoma or advanced gastroesophageal junction with HER2 positive (KEYNOTE 811)
LÓPEZ-BREA PIQUERAS, MARTA F.	Phase 1 study searching for the dose to assess the safety, tolerability, pharmacokinetics and preliminary effectiveness of CC-90011 in subjects with non-Hodgkin's lymphoma and relapsed and/or resistant solid tumours
LÓPEZ LÓPEZ, CARLOS	Open phase 1b trial with Lenvatinib plus Pembrolizumab in subjects with hepatocellular carcinoma
OTERINO DURÁN, AGUSTÍN	Single-group, 4-year open study to assess the effectiveness and safety of treatment with ocrelizumab in patients with progressive multiple sclerosis
DE LA TORRE HERNÁNDEZ, JOSÉ M.	Xience 28 Estudio Global
CRESPO GARCÍA, JAVIER	Phase 3, multicentre, randomised, double-blind, parallel group, placebo-controlled induction study on mirikizumab in patients with conventional and biological failure with active moderate to severe ulcerative colitis

Researcher	Clinical trial
LÓPEZ LÓPEZ, CARLOS	Phase 3, open and randomised study of atezolizumab in combination with bevacizumab versus sorafenib in patients with untreated locally advanced or metastatic hepatocellular carcinoma
RIVERO TIRADO, MONTSERRAT	Phase 2, randomised, double-blind and placebo-controlled study to assess the safety and effectiveness of BMS-986165 in patients with moderate to severe Crohn's disease
CIFRIÁN MARTÍNEZ, JOSÉ MANUEL	Phase 2, double-blind, placebo-controlled and randomised study to compare the effectiveness and safety of sotatercept (ACE-011) versus placebo when added to standard pulmonary arterial hypertension (PAH) treatment
DURAN MARTINEZ, IGNACIO	Phase 3, multicentre, randomised, double-blind, placebo-controlled study to research ipatasertib in combination with abiraterone plus prednisone/prednisolone, versus placebo in combination with abiraterone plus prednisone/prednisolone, in adult patients with metastatic castration-resistant prostate cancer, asymptomatic or slightly symptomatic, who have not been previously treated
CRESPO GARCÍA, JAVIER	Multicentre, randomised, double-blind study to assess the safety, tolerability and effectiveness of treatment combining tropifexor (LJN452) and cenicriviroc (CVC) in adult patients with non-alcoholic steatohepatitis (NASH) and hepatic fibrosis (TANDEM).
DURAN MARTINEZ, IGNACIO	Multicentre, single-group and open study of enfortumab vedotin (ASG-22CE) in the treatment of patients with locally advanced or metastatic urothelial cancer who have previously immune checkpoint inhibitors (CPI)
RODRÍGUEZ RODRÍGUEZ, ELOY M.	Multicentre long-term open phase 3 study (BN29552/ BN29553) of Crenezumab in patients with Alzheimer's disease
PORTILLO MARTÍN, JOSE ANTONIO	Treatment of high grade non-invasive urothelial bladder carcinoma by standard number and dose of intravesical BCG instillations versus a reduced number of intravesical instillations with a standard BCG dose
RODRÍGUEZ ENTEM, FELIPE	Cryoablation of pulmonary veins vs antiarrhythmic drugs in persistent auricular fibrillation (CRAFT)
GARCÍA RIVERO, JUAN LUIS	Clinical effectiveness of Fluticasone furoate/Umeclidinium bromide/Vilanterol in a single inhaler (TRELEGY® ELLIPTA®) versus triple therapy in various non-ELLIPTA devices in patients with COPD in standard clinical practice.
RIVERA HERRERO, FERNANDO	Phase 3, randomised and double-blind trial of pembrolizumab (MK-3475) plus chemotherapy versus placebo plus chemotherapy as first line treatment in participants with gastric adenocarcinoma or unresectable or metastatic gastroesophageal junction, without prior treatment and with HER2 negative (KEYNOTE-859)
SÁNCHEZ JUAN, PASCUAL JESÚS	Phase 3 multicentre, randomised, double-blind, placebo-controlled, parallel group study to assess the effectiveness, safety and tolerability of AVP-786 (deudextromethorphan hydrobromide [d6-DM]/quinidine sulphate [Q]) in treating anxiety in patients with Alzheimer's type dementia.
LÓPEZ-BREA PIQUERAS, MARTA F.	Phase 3, multicentre, randomised, double-blind, placebo-controlled study assessing the effectiveness and safety of canakinumab versus placebo as adjuvant therapy in adult patients with non-small cell lung cancer (NSCLC), completely resected (R0), in stage II-IIIa and IIIB (T>5 cm N2) according to AJCC/UICC v.8
BLANCO ALONSO, RICARDO	Phase 2, multicentre, randomised, double-blind, placebo-controlled study of to assess the effectiveness and safety of CC-220 in subjects with active systemic lupus erythematosus.
DURAN MARTINEZ, IGNACIO	Phase 2 study on the effectiveness and safety of Niraparib in men with castration-resistant metastatic prostate cancer and anomalies in DNA repair.
DURAN MARTINEZ, IGNACIO	Phase 3, randomised, open, multicentre and international trial to determine the effectiveness and safety of durvalumab combined with gemcitabine + cisplatin as neoadjuvant treatment followed by durvalumab monotherapy as adjuvant treatment in patients with muscle invasive bladder cancer (NIAGARA).
RIVERO TIRADO, MONTSERRAT	Multicentre, randomised, double-blind and placebo-controlled induction study to assess the effectiveness and safety of upadacitinib (ABT-494) in subjects with moderate to severe Crohn's disease who have had an insufficient response or intolerance to biological treatment.
RIVERO TIRADO, MONTSERRAT	Effectiveness of intravenous corticosteroid bolus plus treatment with oral corticosteroids versus oral corticosteroid monotherapy to treat moderate ulcerative colitis: multicentre and randomised clinical trial (CECUM)

Researcher	Clinical trial
DE LA TORRE HERNÁNDEZ, JOSÉ M.	Second-generation drU g-elutinG stents in diabetes: a Randomized trial (the SUGAR trial)
GARCÍA CASTAÑO, ALMUDENA	Phase 3, randomised and placebo-controlled trial to assess the safety and effectiveness of pembrolizumab (MK-3475) and lenvatinib (E7080/MK-7902) versus pembrolizumab monotherapy as first line intervention in participants with advanced melanoma (LEAP-003).
SUBERVIOLA CAÑAS, BORJA	Phase 3, randomised and placebo-controlled trial to assess the safety and effectiveness of pembrolizumab (MK-3475) and lenvatinib (E7080/MK-7902) versus pembrolizumab monotherapy as first line intervention in participants with advanced melanoma (LEAP-003).
DURAN MARTINEZ, IGNACIO	TRITON2: Multicentre, open phase 2 study of Rucaparib in patients with metastatic castration-resistant prostate cancer associated with homologous recombination deficiency, with Protocol CO-338-052 code (TRITON2)
DURAN MARTINEZ, IGNACIO	Open, multicentre, phase 1b study of JNJ-63723283, a PD-1 inhibitor, administered with Apalutamide in men with castration-resistant prostate cancer
GARCÍA CASTAÑO, ALMUDENA	Phase 2, randomised, double-blind and placebo-controlled study of cemiplimab versus the combination of cemiplimab plus ISA101b in treating subjects with HPV16-positive platinum-resistant oropharyngeal cancer (OPC)
RIVERO TIRADO, MONTSERRAT	Phase 3b, randomised, double-blind, multicentre study to assess the safety and effectiveness of intravenous reinduction therapy with Ustekinumab in patients with active moderate to severe Crohn's disease

Collaboration Agreements

In 2018, IDIVAL received contributions from various entities to support different initiatives.

Collaboration agreements are shown in the following table.

Collaborating entity	Purpose	Contribution
B. BRAUN MEDICAL, S.A.	Collaboration agreement to attend the 1st Course on Ultrasound Applied to Regional Anaesthesia	3000
FIGHT FOR LIFE ASSOCIATION	Collaboration agreement to develop the Nanovaccines based on Listeria and their application of anti-tumour therapy research project	12000
FIGHT FOR LIFE ASSOCIATION	Collaboration agreement to develop the New clinical markers for the diagnosis and treatment of hepatocellular carcinoma research project by the IDIVAL Infection and immunity and digestive pathology group	18000
ALERE HEALTHCARE, S.L.U.	Collaboration agreement to register for the ECCMID Congress	1188
ABBOTT LABORATORIES, S.A.	Collaboration agreement for two healthcare professionals to attend the 22nd SEIMC Congress	700
ABBOTT LABORATORIES, S.A.	Collaboration agreement for two healthcare professionals to attend the 28th ECCMID Congress	1000
BECTON DICKINSON, S. A. U. SEIMC and 28th ECCMID Congress	Collaboration agreement to attend the 22nd National	2000
BIOMERIEUX ESPAÑA, S.A.	Collaboration agreement to attend the 28th ECCMID Congress	1700
SMITH & NEPHEW, S.A.U	Collaboration agreement to attend the 14th SEHAD Congress	1045
ABBOTT LABORATORIES, S.A.	Collaboration agreement for two professionals to attend the 22nd SEIMC Congress	700
SANOFI AVENTIS, S.A.	Collaboration agreement to develop the Statistical Analysis of the Database of patients with Multiple Sclerosis in northern Spain research project	10000
BECTON DICKINSON, S. A. U.	Collaboration agreement to attend the 30th European Congress of Pathology	1782
Boehringer Ingelheim España, S.A.	Collaboration Agreement to regulate pulmonary fibrosis training placements at HUMV.	
CASA DEL CORAZÓN FOUNDATION	Short-term circulatory support with the use of near-infrared spectroscopy	22500
ABBOTT LABORATORIES, S.A.	Collaboration agreement to develop the Nutritional intervention in patients with Cystic Fibrosis research project	9000
BECTON DICKINSON, S. A. U.	Collaboration Agreement to attend the 47th Annual Meeting of the Spanish Cytology Society	1210
ROCHE FARMA, S.A.U.	Collaboration Agreement to finance the Marqués de Valdecilla UH Rheumatology Department Publications Plan 2018	24965
RESPIRA. SPANISH LUNG FOUNDATION - SEPAR; ITURBE	Assessment of the use of Osteopontin to diagnose idiopathic pulmonary fibrosis	5000
RESPIRA. SPANISH LUNG FOUNDATION - SEPAR	Interstitial lung disease biomarkers: Implication of IL-6. General and functional study	12000

Collaborating entity	Purpose	Contribution
Merck Sharp & Dhome España	Collaboration agreement to develop Dr Ricardo Blanco's research project at the Marqués de Valdecilla University Hospital Rheumatology Department	20000
GILEAD SCIENCES, S.L.U.	GILEAD17/30 11th edition of the Multidisciplinary Open Classroom in Hepatology	69100
BOSTON SCIENTIFIC IBERICA S.A.	Educational Grant Agreement for the 17th World Congress on Pain	6600
MERCK, S.L.	Collaboration agreement to develop medical training activities	13310
OXIMESA, S.L.	Collaboration agreement to develop the Improving adherence to treatment in SAHS patients research project	60000
MEDTRONIC IBERICA, S.A.	Subsidy contract for medical training and teaching of healthcare professionals in thoracic surgery	6400
Merck Sharp & Dhome España; Blanco Alonso, Ricardo	Agreement to support research and the publication of studies	6600
CAJA DE AHORROS DE SANTANDER Y CANTABRIA BANKING FOUNDATION	Collaboration Agreement to finance the 20th edition of the Valdecilla National Awards for Nursing Research Projects	6000
ASOCIACION ESPAÑOLA AND ADOLESCENT PSYCHIATRY	Development and assessment of the effectiveness of an intervention programme based on mindfulness in adolescents with anxiety-depressive symptomatology receiving care at a Child-Youth Mental Health Unit	10000
ROCHE FARMA, S.A.U.	Collaboration agreement to finance the Training programme for Neurology personnel in Cantabria	4000
Merck Sharp & Dhome España	Collaboration agreement to develop the Training programme in pulmonary hypertension	2479
Janssen-Cilag, S.A.	Agreement for cooperation in the IDIVAL scientific research grant programme	75000
ABBOTT LABORATORIES, S.A.	Collaboration agreement to develop the Nutritional intervention in patients with cystic fibrosis research project	6000
Merck Sharp & Dhome España	Collaboration agreement to develop research projects at the Sierrallana Regional Hospital Rheumatology Department	10000

Clinical practice guidelines

In 2018, IDIVAL researchers participated in the following clinical practice guidelines and consensus documents. The relevance of these guidelines as recommendations developed systematically to help professionals and patients make decisions about the most suitable healthcare and to select the most appropriate diagnostic or therapeutic options when addressing a health problem is unquestionable.

1. Albéniz E, Pellisé M, Gimeno García AZ, Lucendo AJ, Alonso Aguirre PA, Herreros de Tejada A, Álvarez MA, Fraile M, Herráiz Bayod M, López Rosés L, Martínez Ares D, Ono A, Parra Blanco A, Redondo E, Sánchez Yagüe A, Soto S, Díaz Tasende J, Montes Díaz M, Téllez MR, García O, Zuñiga Ripa A, Hernández Conde M, Alberca de Las Parras F, Gargallo C, Saperas E, Navas MM, Gordillo J, Ramos Zabala F, Echevarría JM, Bustamante M, González Haba M, González Huix F, González Suárez B, Vila Costas JJ, Guarner Argente C, Múgica F, Cobián J, Rodríguez Sánchez J, López Viedma B, Pin N, Marín Gabriel JC, Nogales Ó, de la Peña J, Navajas León FJ, León Brito H, Remedios D, Esteban JM, Barquero D, Martínez Cara JG, Martínez Alcalá F, Fernández Urién I, Valdivielso E; on behalf of the Spanish Endoscopic Resection Group of the Spanish Digestive Endoscopy Society. **Clinical guidelines for endoscopic mucosal resection of non-pedunculated colorectal lesions.** *Gastroenterol Hepatol.* 2018 Mar;41(3):175-190.

2. Albéniz E, Pellisé M, Gimeno-García AZ, Lucendo AJ, Alonso-Aguirre PA, Herreros de Tejada A, Álvarez MA, Fraile M, Herráiz Bayod M, López Rosés L, Martínez Ares D, Ono A, Parra Blanco A, Redondo E, Sánchez-Yagüe A, Soto S, Díaz-Tasende J, Montes Díaz M, Rodríguez-Téllez M, García O, Zuñiga Ripa A, Hernández Conde M, Alberca de Las Parras F, Gargallo CJ, Saperas E, Muñoz Navas M, Gordillo J, Ramos Zabala F, Echevarría JM, ..., Valdivielso E. **Clinical guidelines for endoscopic mucosal resection of non-pedunculated colorectal lesions..** *Rev Esp Enferm Dig* 2018. 110(3): 179 - 194.

3. Aller R, Fernández-Rodríguez C, Lo Iacono O, Bañares R, Abad J, Carrión JA, García-Monzón C, Caballería J, Berenguer M, Rodríguez-Perálvarez M, Miranda JL, Vilar-Gómez E, Crespo J, García-Cortés M, Reig M, Navarro JM, Gallego R, Genescà J, Arias-Loste MT, Pareja MJ, Albillos A, Muntané J, Jorquera F, Solà E, Hernández-Guerra M, Rojo MÁ, Salmerón J, Caballería L, Diago M, Molina E, Bataller R, Romero-Gómez M. **Consensus document. Management of non-alcoholic fatty liver disease (NAFLD). Clinical practice guideline.** *Gastroenterol Hepatol.* 2018 May; 41(5): 328-349.

4. Barreiro-de Acosta M, Marín-Jiménez I, Panadero A, Guardiola J, Cañas M, Gobbo Montoya M, Modino Y, Alcaín G, Bosca-Watts MM, Calvet X, Casellas F, Chaparro M, Fernández Salazar L, Ferreiro-Iglesias R, Ginard D, Iborra M, Manceñido N, Mañosa M, Merino O, Rivero M, Roncero O, Sempere L, Vega P, Zabana Y, Mínguez M, Nos P, Gisbert JP. **Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) and the Association of Crohn's Disease and Ulcerative Colitis Patients (ACCU) in the management of psychological problems in Inflammatory Bowel Disease patients.** *Gastroenterol Hepatol.* 2018 Feb;41(2):118-127.

5. Chaves F, Garnacho-Montero J, Del Pozo JL, Bouza E, Capdevila JA, de Cueto M, Domínguez MÁ, Esteban J, Fernández-Hidalgo N, Fernández Sampedro M, Fortún J, Guembe M, Lorente L, Paño JR, Ramírez P, Salavert M, Sánchez M, Vallés J. **Executive summary: Diagnosis and Treatment of Catheter-Related Bloodstream Infection: Clinical Guidelines of the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC) and the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC).** *Enferm Infecc Microbiol Clin.* 2018 Feb;36(2):112-119.

6. Chaves F, Garnacho-Montero J, Del Pozo JL, Bouza E, Capdevila JA, de Cueto M, Domínguez MÁ, Esteban J, Fernández-Hidalgo N, Fernández Sampedro M, Fortún J, Guembe M, Lorente L, Paño JR, Ramírez P, Salavert M, Sánchez M, Vallés J. **Diagnosis and treatment of catheter-related bloodstream infection: Clinical**

guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC). *Med Intensiva.* 2018 Jan - Feb;42(1):5-36.

7. de la Oliva P, Cambra-Lasaosa FJ, Quintana-Díaz M, Rey-Galán C, Sánchez-Díaz JI, Martín-Delgado MC, de Carlos-Vicente JC, Hernández-Rastrullo R, Holanda-Peña MS, Pilar-Orive FJ, Ocete-Hita E, Rodríguez-Núñez A, Serrano-González A, Blanch L; representing the Spanish Pediatrics Association (AEP), Spanish Pediatric Intensive Care Society (SECIP) and Spanish Intensive, Critical and Coronary Unit Care Society (SEMICYUC). **Admission, discharge and triage guidelines for paediatric intensive care units in Spain.** *Med Intensiva.* 2018 May; 42(4): 235-246.

8. de la Oliva P, Cambra-Lasaosa FJ, Quintana-Díaz M, Rey-Galán C, Sánchez-Díaz JI, Martín-Delgado MC, de Carlos-Vicente JC, Hernández-Rastrullo R, Holanda-Peña MS, Pilar-Orive FJ, Ocete-Hita E, Rodríguez-Núñez A, Serrano-González A, Blanch L; representing the Spanish Pediatrics Association (AEP), Spanish Pediatric Intensive Care Society (SECIP) and Spanish Intensive, Critical and Coronary Unit Care Society (SEMICYUC). **[Admission, discharge and triage guidelines for paediatric intensive care units in Spain].** *An Pediatr (Barc).* 2018 May;88(5):287.e1-287.e11.

9. de'Angelis N, Di Saverio S, Chiara O, Sartelli M, Martínez-Pérez A, Patrizi F, Weber DG, Ansaloni L, Biffi W, Ben-Ishay O, Bala M, Brunetti F, Gaiani F, Abdalla S, Amiot A, Bahouth H, Bianchi G, Casanova D, Coccolini F, Coimbra R, de'Angelis GL, De Simone B, Fraga GP, Genova P, Ivatury R, Kashuk JL, Kirkpatrick AW, Le Baleur Y, Machado F, Machain GM, Maier RV, Chichom-Mefire A, Memeo R, Mesquita C, Salamea Molina JC, Mutignani M, Manzano-Núñez R, Ordoñez C, Peitzman AB, Pereira BM, Picetti E, Pisano M, Puyana JC, Rizoli S, Siddiqui M, Sobhani I, Ten Broek RP, Zorcolo L, Carra MC, Kluger Y, Catena F. **2017 WSES guidelines for the management of iatrogenic colonoscopy perforation.** *World J Emerg Surg.* 2018 Jan 24;13:5.

10. López Cortés LE, Mujal Martínez A, Fernández Martínez de Mandojana M, Martín N, Gil Bermejo M, Solà Aznar J, Villegas Bruguera E, Peláez Cantero MJ, Retamar Gentil P, Delgado Vicente M, González-Ramallo VJ, Ponce González MÁ, Mirón Rubio M, Gómez Rodríguez de Mendarozqueta MM, Goenaga Sánchez MÁ, Sanroma Mendizábal P, Delgado Mejía E, Pajarón Guerrero M; **Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), the Spanish Domiciliary Hospitalisation Society (SEHAD) Group. Executive summary of outpatient parenteral antimicrobial therapy: Guidelines of the Spanish Society of Clinical Microbiology and Infectious Diseases and the Spanish Domiciliary Hospitalisation Society.**

Enferm Infecc Microbiol Clin. 2018 May 18. pii: S0213-005X(18)30168-X
 11. Santaballa A, García Y, Herrero A, Laínez N, Fuentes J, De Juan A, Rodríguez Freixinós V, Aparicio J, Casado A, García-Martínez E. **SEOM clinical guidelines in gestational Trophoblastic disease (2017).** *Clin Transl Oncol.* 2018 Jan;20(1):38-46.

12. Sconfienza LM, Albano D, Allen G, Bazzocchi A, Bignotti B, Chianca V, Facal de Castro F, Drakonaki EE, Gallardo E, Gielen J, Klauser AS, Martinoli C, Mauri G, McNally E, Messina C, Mirón Mombiela R, Orlandi D, Plagou A, Posadzy M, de la Puente R, Reijnierse M, Rossi F, Rutkauskas S, Snoj Z, Vucetic J, Wilson D, Tagliafico AS. **Clinical indications for musculoskeletal ultrasound**

updated in 2017 by European Society of Musculoskeletal Radiology (ESSR) consensus. *Eur Radiol.* 2018 Dec;28(12):5338-5351.

13. Sconfienza LM, Albano D, Allen G, Bazzocchi A, Bignotti B, Chianca V, Facal de Castro F, Drakonaki EE, Gallardo E, Gielen J, Klauser AS, Martinoli C, Mauri G, McNally E, Messina C, Mirón Mombiela R, Orlandi D, Plagou A, Posadzy M, de la Puente R, Reijnierse M, Rossi F, Rutkauskas S, Snoj Z, Vucetic J, Wilson D, Tagliafico AS. **Clinical indications for musculoskeletal ultrasound updated in 2017 by European Society of Musculoskeletal Radiology (ESSR) consensus.** *Eur Radiol.* 2018 Dec;28(12):5338-5351.

RETICS and CIBER with the participation of IDIVAL

The Carlos III Health Institute has promoted several Thematic Networks for Cooperative Research

(RETIC), and Platforms and Biomedical Research Centre Networks (CIBER) with the participation of IDIVAL groups. These organisational structures formed by a variable set of multidisciplinary centres and research groups in biomedicine aim to conduct cooperative research projects of general interest, centred on

a common specific area for the achievement of scientific objectives that would be difficult to achieve in a context of more restricted execution. IDIVAL participates in four CIBERs, five RETICS and three platforms. In 2018, IDIVAL coordinated the Platform for Innovation in Medical and Health Technologies (ITEMAS).

CIBER / RETIC / Platform	IDIVAL Group or Unit	PI
Mental Health CIBER (CIBERSAM)	Psychiatry	Benedicto Crespo Facorro
Neurodegenerative Diseases CIBER (CIBERNED)	Neurodegenerative Diseases	Jon Infante Ceberio
Epidemiology and Public Health CIBER (CIBERESP)	Epidemiology and Public Health	Javier Llorca Díaz
Bioengineering, Biomaterials and Nanomedicine Photonics Engineering (CIBER-BBN)	Photonics Engineering	José Miguel López Higuera
Spanish Network for Research in Infectious Diseases (REIPI)	Epidemiology and Pathogenic and Molecular Mechanisms of Infectious Diseases and Clinical Microbiology	Carmen Fariñas Álvarez
Network of Maternal and Children's Health and Development (RED SAMID)	Marqués de Valdecilla University Hospital	María Jesús Cabero
Thematic Network of Multiple Sclerosis	Cephalea Clinic and Genetics	Agustín Oterino Durán
Renal Research Network (REDinREN)	Transplantation and autoimmunity	Marcos López Hoyos
Research Network in Inflammation and Diseases Rheumatics (RIER)	Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	Miguel Ángel González-Gay Mantecón
Biobank Platform	IDIVAL	Pascual Sánchez Juan
Platform for Innovation in Healthcare Technologies (ITEMAS)	IDIVAL	Galo Peralta Fernández
Platform for Clinical Research and Clinical Trial Units (Scren)	IDIVAL	Benedicto Crespo Facorro

Innovation

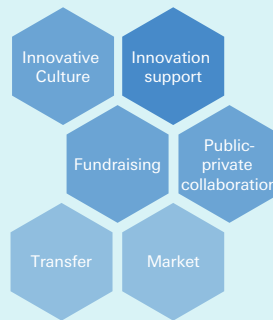
Introduction

Innovation is a key element of regional economic development. From the point of view of society, innovation in the healthcare sector means continuous improvement of the efficiency and productivity of national health systems, significantly improving patients' quality of life.

In Cantabria we are lucky enough to have the Marqués de Valdecilla University Hospital, which as well as attracting healthcare expertise can be regarded as one of the region's economic driving forces, as it transforms this knowledge into value.

IDIVAL's Innovation area consists of 5 people, structured as the Research Results Transfer Office (OTRI) and the Innovation Unit, and EValTec®.

Some of its milestones in 2018 were:



- An ambitious intra-entrepreneurship programme has been designed at the Cantabrian Health Service in collaboration with the Botín Foundation and Santander International Entrepreneurship Centre (CISE).

- The EValTec (Valdecilla Evaluation of Healthcare Technologies) has been consolidated with the development of premarket and postmarket for healthcare sector companies.

ITEMAS platform



The Platform for Innovation in Medical and Health Technologies (ITEMAS), promoted and financed by the Carlos III Health Institute (ISCIII), is a structure to support innovation in healthcare. It exists to help the innovation ideas of healthcare professionals generate value for the system, by favouring technology transfer, the culture of

innovation, and communication with the rest of society. The main tool of ITEMAS is the creation of Innovation Support Units (UAI) in hospitals.

These provide the resources and help needed so that healthcare professionals can turn their ideas and discoveries into reality for patients, creating a more sustainable National Health System.

Through its Innovation Unit, IDIVAL has been a node of this Platform since it began in 2010, and

currently finances the contracts of 3 of the professionals in the Area.

In 2018 Galo Peralta, Management Director of IDIVAL, began coordinating the Platform at the national level.

Transfer

For innovation and the transfer of research results to the market to be effective and have an impact on society, it is necessary to create an economic and legal environment conducive to innovation and economic development. IDIVAL adheres to Industrial Property Regulations, which govern the management and use of intellectual and industrial property rights and transfers to the market within the area of responsibility of the Healthcare Administration of Cantabria.

Since the establishment of the OTRI, the following have been presented:

- 23 Spanish patent applications to the Spanish Office of Patents and Brands (OEPM).
- 18 international patent applications through the Patent Cooperation Treaty (PCT).
- 4 European patent applications to the European Patent Office (EPO).
- 4 utility model applications to the Spanish Office of Patents and Brands (OEPM).
- 1 community design to the Spanish Office of Patents and Brands (OEPM).
- 3 Spanish brand applications to the Spanish Office of Patents and Brands (OEPM).

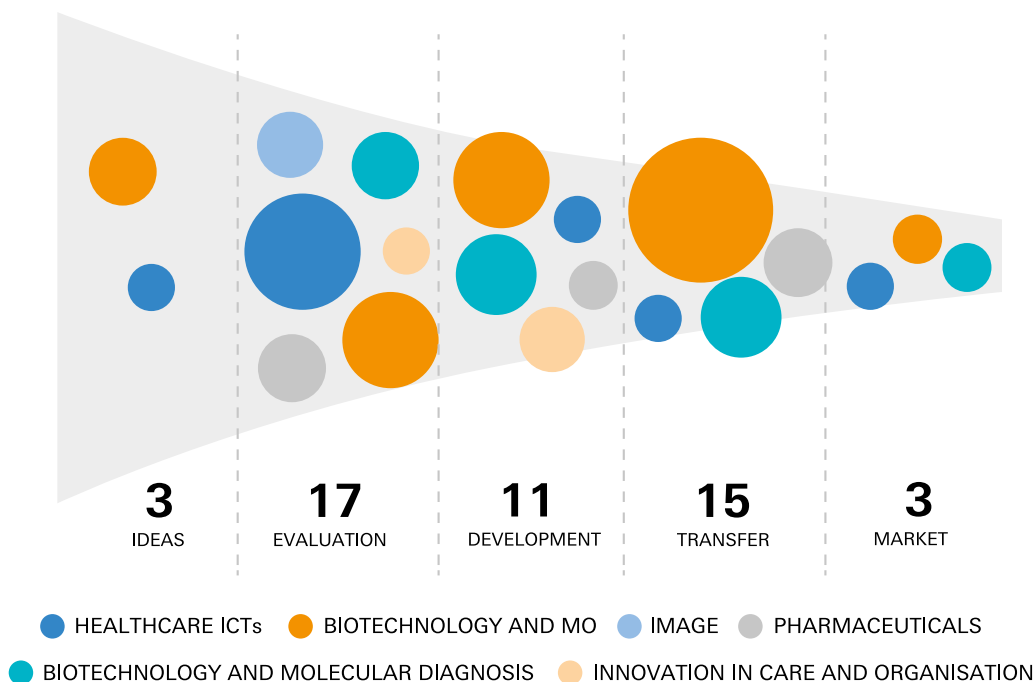
Of these, the following were processed in 2018:

Application no.	Title	Applicants	Inventor
PCT/EP2018/057681	System and device for positioning medical needles	CHS/UC	Pedro Prada Gómez Juan Ignacio Raba Díez Luis Rodríguez Cobo Adolfo Cobo García Olga Conde Portilla Jose Miguel López Higuera Jose Julián Valdiande Gutiérrez
PCT/EP2018/057761	Method for predicting therapeutic response to antipsychotic drugs	CHS/UC/CSIC/CIBER	Benedicto Crespo Facorro Jesús Vicente Sainz Maza
U201830853	Protective dressing for abdominal viscera in negative pressure therapy	CHS	Federico Castillo Suescun
U201830919	Reference navigation equipment in robot-assisted surgery with stereostatic navigation of organs and soft tissue in the pelvic area of a patient	CHS	Marcos Gómez Ruiz Alberto Calleja Iglesias Felipe Alonso Horga
P201830628	Multivalent vaccination for the treatment and prevention of tuberculosis, listeriosis and pneumonia	IDIVAL	Carmen Álvarez Domínguez Héctor Terán Navarro David Salcines Cuevas Ricardo Calderón González Isabel García Marco Marradi Soledad Penadés Ullate Elisabet Frande Cabanes

Application no.	Title	Applicants	Inventor
PCT/EP2018/070724	Cartridge, device and procedure for the detection, capture, identification and counting of circulating tumour cells	IDIVAL/CHS/UC/TEKNIKER/CELLBIOCAN	José Luis Fernández Luna Fernando Moreno García Ángela Barreda Góme Francisco González Fernández Deitze Otaduy del Paso
US16/079,477	Use a GNP-LLO91-99 complex for the treatment and prevention of cancer	IDIVAL/CHS	Carmen Álvarez Domínguez Ricardo Calderón González Elisabet Frande Cabanes Sonsoles Yáñez Díaz Eva Ferrández Fernández Soledad Penadés Ullate Marco Marradi Isabel García Martín Fernando Rivera Herrero
EP17715958.9	Use a GNP-LLO91-99 complex for the treatment and prevention of cancer	IDIVAL/CHS	Carmen Álvarez Domínguez Ricardo Calderón González Elisabet Frande Cabanes Sonsoles Yáñez Díaz Eva Ferrández Fernández Soledad Penadés Ullate Marco Marradi Isabel García Martín Fernando Rivera Herrero
P201800217	System and method for a blood sample cell count	IDIVAL/UC/FMV	Manuel Pérez Cagigal Jose Luis Arroyo Rodríguez Antonio Fuentes Ruiz Pedro José Valle Herrero

Innovation support

• According to the innovation funnel, ideas are distributed as follows:



Innovation support

IDIVAL's innovation management complies with UNE standard 166.002:2014, and its management system has been certified by DNV.

Its main activities are:

Promotion of the Culture of Innovation

To promote the culture of innovation in the Valdecilla environment, IDIVAL organises a series of courses and workshops that encourage creativity and teamwork, issues reports, and provides training on specific aspects of the innovation process, etc. The Innovation Unit has participated in various activities presented in the training section.

Technological Surveillance Newsletter

IDIVAL publishes a regular newsletter on technological surveillance which covers the bases of competitive financing for public and

private research and innovation projects, internal and external symposia relating to relevant research and innovation, and the latest publications produced in the Valdecilla environment. This newsletter will be available on the IDIVAL website and emailed to subscribers.

Innovation Funnel

The innovation projects managed by IDIVAL are classified into FIVE phases, defined below:

1. Capture. In this phase, the ideas that the unit captured in 2018 are considered, as well as those captured in previous years that did not advance to a later stage.

2. Analysis: This phase considers proposals for which market research, patentability reports, or product value or technical feasibility reports are being carried out.

3. Development: This phase includes ideas being developed

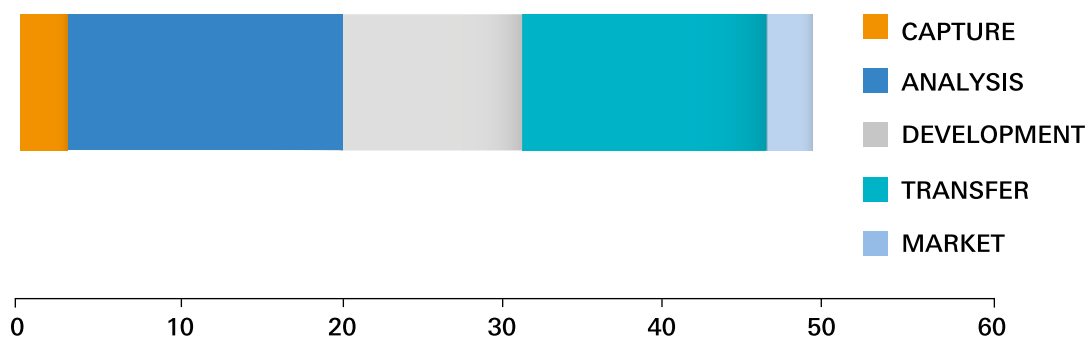
in the form of prototypes, approvals and/or trials.

4. Transfer: This phase includes ideas that have generated some type of commercial activity, e.g., contact with companies or potential licensees.

5. Market: This phase includes ideas in any of the following situations:

- a) Licensed to industry.
- b) Generated a spin-off.
- c) Forms part of an exclusive agreement with a company.
- d) Implemented in a healthcare centre (in the case of healthcare and organisational innovations).

• In 2018, the Innovation Area managed 44 ideas, distributed among the five stages as follows:

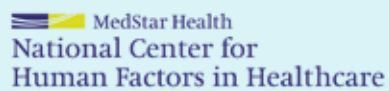


EValTec®



EValTec® is a project which aims to apply Human Factor Engineering as a tool for assessment and implementation of medical technology. It is the result of the collaboration of HUMV, the Valdecilla Virtual Hospital and IDIVAL, and its team is made up of professionals from the different institutions.

It has an alliance with Medstar Health Research Institute- National Center for Human Factors in Healthcare, Washington, a centre of recognised international prestige.



EValTec® considers the human factor to be a tool for making changes in organisations and improving patient safety. In 2018 it worked with the Cantabrian Health Service (CHS) in the technical assessment of volumetric and syringe infusion pumps in the context of a public tender to acquire these systems for a price of over 1 million euros, in the first action by Spain in this field. Human Factor methods were applied to assess them, such as heuristics and usability tests.

25 professionals participated in the usability test from units like the Day Hospital, ICU, neonatal ICU, and anaesthesia, the three hospitals in the region.

This assessment provided the opportunity for a deeper examination of the technology and how it can adapt to the needs of the different units where it will be used, so EValTec also collaborated in its implementation, developing a strategy based on training facilitators, leading professionals in the use of technology in the different units and hospitals.

At present EValTec® is ready to face new challenges, such as competing for funding, working with medical technology development companies to favour the development of more usable and safer devices, and the possibility of evaluating new technologies in the Cantabrian Health System.

Organisation Chart Groups and Areas

Cancer

- Translational Haematopathology. RR: **S. Montes Moreno**
- Clinical and Molecular Pathology. RR: **Javier Gómez-Román**
- Apoptosis. RR: **J. Hurlé González**
- Melatonin and Breast Cancer. RR: **S. Cos Corral**
- Cellular Signaling and Therapeutic Targets. RR: **J. L. Fernández-Luna**
- Cellular Cycle, Stem Cells and Cancer. RR: **A. Gandarillas Solinis**
- Molecular Imaging. RR: **J. I. Banzo Marraco**
- New Techniques in Abdominal Surgery. RR: **M. Gómez-Fleitas**
- Oncologic Clinical Trials Unit. RR: **F. Rivera Herrero**
- Nanomedicine. RR: **M. López Fanarraga**

Neurosciences

- Neurodegenerative Diseases. RR: **J. Infante Ceberiro**
- Psychiatry. RR: **B. Crespo Facorro**
- Nuclear Cell Biology. RR: **M. A. Lafarga Coscojuela**
- Epilepsy Neurophysiology and Brain Intensive Care. RR: **J. L. Fernández-Torre**
- Clinical and Genomics Research in Headache. RR: **A. Oterino Durán**

Transplantation

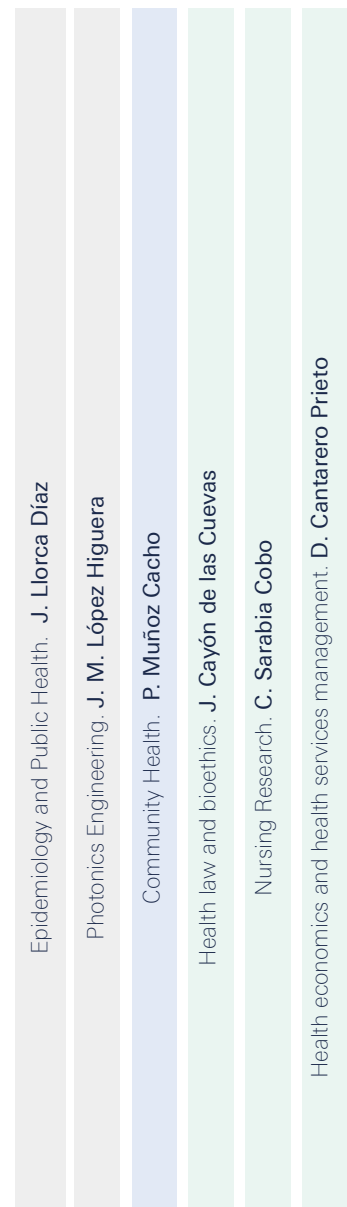
- Autoimmunity and Transplantation. RR: **M. López Hoyos**
- Haematological Neoplasms and Bone Marrow Transplantation. RR: **E. Ocio San Miguel**
- Cytokines, Growth Factors and Pathological Tissue Plasticity. RR: **J. F. Nistal Herrera**
- Infection Immunity and Digestive Diseases. RR: **J. Crespo García**
- Cardiovascular Research Group. RR: **J. A. Vázquez de Prada**

Infection and Immunity

- Rheumatic Diseases Immunopathology. RR: **J. Merino Pérez**
- Genetic Epidemiology and Atherosclerosis in Rheumatic Diseases. RR: **M. A. González-Gay**
- Epidemiology and Pathogenic Mechanisms of Infectious Diseases. RR: **C. Fariñas Álvarez**
- Listeria monocytogenes based nanovaccines and cellular vaccines and their application to biomedicine. RR: **C. Álvarez-Domínguez**

Metabolism, Ageing and Life Style

- Mineral and Lipid Metabolism. RR: **J. González-Macías**
- Imaging Diagnosis and Therapeutics. RR: **J. A. Parra Blanco**



▪ **Cross-disciplinary Area Epidemiology and Public Health***

RR. Responsible Researcher Consolidated Groups Associated Groups
Emerging Groups New Groups





○ Research
areas





**Organ Transplants
and Tissue and New
Therapies Area**

Marcos López Hoyos.

Coordinator of the Transplant Area
of Organs and Tissues and New
Therapies.

Head of Immunology Service.

Hospital Universitario Marqués de
Valdecilla

Cytokines and Growth Factors in Pathological Tissue Plasticity Phenomena



Consolidated group

Researchers

María Amor Hurlé González
Carmen Martínez-Cue Pesini

Group Responsible

Juan Francisco Nistal Herrera

Cardiovascular Surgery Service

Hospital Universitario Marqués de Valdecilla
Universidad de Cantabria



juanfrancisco.nistal@scsalud.es

Contributors

Manuel Cobo Belaustegui
Marta Crespo Hidalgo
Víctor Expósito García
Susana García Cerro
Raquel García López
Aritz Gil Ongay
Carlos Juárez Crespo
Miguel Fernando Llano Cardenal
Alba Puente Bedia
Luis Javier Ruiz Guerrero
Valentín Tascón Quevedo
Mónica Tramullas Fernández
Verónica Vidal Sánchez

Nurses

Elena Martín Delgado
Roberto Moreta Sánchez

Predoctoral

María Carcelen Labrador
Raquel Frances Romero
Ana Belén Salido Medina

Technicians

Ana María Cayón Gómez
María de las Nieves García Iglesias
María Eva García Iglesias

Research line

Pathological plasticity of myocardium. We are analysing the involvement of transforming growth factors beta (TGF- β s,

activin and BMPs) in the molecular pathophysiology of myocardial remodelling secondary to haemodynamic stress and in altered development.

1. 1. **Pathological plasticity of myocardium subjected to pressure overload.** Aortic stenosis is the most frequent valvular cause for surgery in our area and is associated with a left ventricular

hypertrophy which is a response of pathological significance in these patients. We are studying the molecular mechanisms of myocardial remodelling in this context using samples of myocardium of patients with aortic stenosis, a murine experimental model of this pathology and cell cultures.

1.2. Developmental variations and pathological plasticity of myocardium in Down syndrome.

El ratón Ts65Dn (trisomía de una región del cromosoma 16 homóloga a la del 21 humano) es un modelo experimental de síndrome de Down que reproduce sus características fenotípicas. Estudiamos la participación de la familia TGF- β en las alteraciones del desarrollo cardiaco encontradas en este modelo.

2. Pathological plasticity of the aortic wall. We are analysing the involvement of transforming growth factors beta in the molecular pathophysiology of the remodelling of the aortic wall in relation to aneurysm formation. Progressive dilation of the aorta carries high rates of morbidity and mortality. We are studying the role of TGF- β s in the molecular pathophysiology of the pathological remodelling of the aortic wall in aneurysm formation. We intend to: 1) Establish signalling pathways involved in the vascular chronic inflammatory process responsible for progressive aortic dilatation; 2) Identify biomarkers to assess the risk of rupture and assist in surgery indication; and 3) Establish new therapeutic targets

3. Pathological plasticity in the central nervous system.

3.1 Pathological neuronal plasticity of the nociceptive system.

The mechanisms linking TGF- β s and modulation of pain transmission, basally and in pathological plasticity models of the nociceptive system, are being analysed.

Chronic neuropathic pain is highly resistant to conventional drug treatment. We have demonstrated the involvement of the TGF- β family in processing the physiological nociceptive signal. We intend to study: a) Molecular mechanisms involving TGF- β in neuropathic pain, and experimental inflammatory pain; b) The interaction between TGF- β s and the endogenous opioid system; c) The involvement of TGF- β s in adaptive processes in chronic opioid therapy; d) The involvement

of TGF- β s in the hypoesthesia of experimental Down syndrome.

3.2. Pathological neuronal plasticity in learning and memory circuits.

We are analysing the mechanisms that connect the TGF- β family with cognitive variations and neurodegenerative disease in Down syndrome.

Down syndrome causes more cases of mental retardation and all patients develop an Alzheimer-type neuropathology early on. Deficits in the synthesis and transport of trophic factors could mediate these variations. Furthermore, the TGF- β family is involved in the pathophysiology of experimental Alzheimer's disease. We intend to evaluate the role of TGF- β in the cognitive variations found in the Ts65Dn mouse and evaluate different therapeutic strategies.

PUBLICATIONS

IMPACT FACTOR | 69.163

Original articles

1. Tramullas, M, Frances, R, de la Fuente, R, Velategui, S, Carcelen, M, García, R, Llorca, J, Hurle, MA. **MicroRNA-30c-5p modulates neuropathic pain in rodents.** *Sci. Transl. Med.* 2018;10:F.I.:16.710. [doi:10.1126/scitranslmed.aao6299]
2. Villahoz, S, Yunes-Leites, PS, Mendez-Barbero, N, Urso, K, Bonzon-Kulichenko, E, Ortega, S, Nistal, JF, Vazquez, J, Offermanns, S, Redondo, JM, Campanero, MR. **Conditional deletion of Rcan1 predisposes to hypertension-mediated intramural**

hematoma and subsequent aneurysm and aortic rupture.

Nat. Commun. 2018;9:4795-4795.F.I.:12.353. [doi:10.1038/s41467-018-07071-7]

3. Rueda, N, Vidal, V, García-Cerro, S, Narcis, JO, Llorens-Martin, M, Corrales, A, Lantigua, S, Iglesias, M, Merino, J, Merino, R, Martinez-Cue, C. **Anti-IL17 treatment ameliorates Down syndrome phenotypes in mice.** *Brain Behav. Immun.* 2018;73:235-251.F.I.:6.306. [doi:10.1016/j.bbi.2018.05.008]
4. Rodríguez-Manero, M, Oloriz, T, le Polain de Waroux JB, Burri, H, Kreidieh, B, de Asmundis, C, Arias, MA, Arbelo, E, Díaz Fernández B, Fernandez-Armenta, J, Basterra, N, Izquierdo, MT, Díaz-Infante, E, Ballesteros, G, Carrillo López A, García-Bolao, I, Benezet-Mazuecos, J, Expósito-García, V, Larraitz-Gaztanaga, Martínez-Sande, JL, García-Seara, J, Gonzalez-Juanatey, JR, Peinado, R. **Long-term prognosis of patients with life-threatening ventricular arrhythmias induced by coronary artery spasm.** *EUROPACE.* 2018;20:851-858.F.I.:5.231. [doi:10.1093/europace/eux052]
5. García-Cerro, S, Vidal, V, Lantigua, S, Berciano, MT, Lafarga, M, Ramos-Cabrer, P, Padro, D, Rueda, N, Martinez-Cue, C. **Cerebellar alterations in a model of Down syndrome: The role of the Dyrk1A gene.** *Neurobiol. Dis.* 2018;110:206-217.F.I.:5.227. [doi:10.1016/j.nbd.2017.12.002]
6. Vidal, V, García-Cerro, S, Martinez, P, Corrales, A, Lantigua, S, Vidal, R, Rueda, N, Ozmen, L, Hernandez, MC, Martinez-Cue, C. **Decreasing the Expression of GABA(A) alpha 5 Subunit-Containing Receptors Partially Improves Cognitive, Electrophysiological, and Morphological Hippocampal Defects in the Ts65Dn Model of Down Syndrome.** *Mol. Neurobiol.* 2018;55:4745-4762.F.I.:5.076. [doi:10.1007/s12035-017-0675-3]
7. Merino, D, Gil, A, Gómez, J, Ruiz, L, Llano, M, García, R, Hurle, MA, Nistal, JF. **Experimental modelling of cardiac pressure overload hypertrophy: Modified technique for precise, reproducible, safe and**

easy aortic arch banding-debanding in mice. *Sci Rep.* 2018;8:3167-3167.F.I.:4.122. [doi:10.1038/s41598-018-21548-x]

8. Regueiro, A, Falces, C, Pericas, JM, Muñoz P, Martínez-Selles, M, Valerio, M, Sousa Regueiro D, Castelo, L, de Alarcon, A, Cobo Belauastegui M, Goenaga, MA, Hidalgo-Tenorio, C, Martínez-Marcos, FJ, Gainzarain Arana JC, Miro, JM, y los investigadores del Grupo de Apoyo al Manejo de la Endocarditis Infecciosa. **Risk factors of pericardial effusion in native valve infective endocarditis and its influence on outcome: A multicenter prospective cohort study.** *Int. J. Cardiol.* 2018;273:193-198.F.I.:4.034. [doi:10.1016/j.ijcard.2018.08.010]

9. Giacomini, A, Stagni, F, Emili, M, Guidi, S, Salvalai, ME, Grilli, M, Vidal-Sánchez, V, Martínez-Cue, C, Bartesaghi, R. **Treatment with corn oil improves neurogenesis and cognitive performance in the Ts65Dn mouse model of Down syndrome.** *Brain Res.* Bull.2018;140:378-391.F.I.:3.440. [doi:10.1016/j.brainresbull.2018.06.009]

10. Block, A, Ahmed, MM, Rueda, N, Hernández, MC, Martínez-Cue, C, Gardiner, KJ. **The GABA(A) alpha 5-selective Modulator, RO4938581, Rescues Protein Anomalies in the Ts65Dn Mouse Model of Down Syndrome.** *Neuroscience.* 2018;372:192-212.F.I.:3.382. [doi:10.1016/j.neuroscience.2017.12.038]

11. Vicent, L, Saldivar, HG, Bouza, E, Muñoz P, Cuerpo, G, de Alarcón, A, Vidal, B, Cobo, M, Goenaga, MA, Carrasco-Chinchilla, F, Montejó, M, Galvez-Acebal, J, Hidalgo-Tenorio, C, Vinuesa-García, D, Martínez-Selles, M, GAMES investigators (Appendix 1). **Prognostic implications of a negative echocardiography in patients with infective endocarditis.** *Eur. J. Intern. Med.* 2018;52:40-48.F.I.:3.282. [doi:10.1016/j.ejim.2018.01.033]

Projects

1. Juan Francisco Nistal Herrera. **Ayuda por Producción al grupo de Citocinas y Factores de Crecimiento en los Fenómenos de Plasticidad Tisular Patológica.** APG/25.

2. Juan Francisco Nistal Herrera. Proteína morfogenética del hueso 7 (BMP7): **Posible diana terapéutica en el remodelado patológico del sistema cardiovascular.** PI15/01224. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. Juan Francisco Nistal Herrera. **Diabetic cardiomyopathy: searching for a therapeutic target.** FLM16/20. FUNDACIÓN LA MARATÓ DE TV3.

4. María Amor Hurlé González. **PREVAL17/05 María Carcelen Labrador.** PREVAL17/05.

5. Raquel García López. **BMP-7: a potential target in cardiac remodelling under pressure overload.** BAYER17/17. BAYER AG.

6. Mónica Tramullas Fernández. **El dolor crónico es un grave problema socio-económico-sanitario y el diseño de terapias dirigidas a su prevención y curación constituye un reto científico.** NVAL17/23.

7. Juan Francisco Nistal Herrera. **Estudio traslacional para la definición de dianas terapéuticas dirigidas contra el remodelado miocárdico patológico por sobrecarga de presión.** PREVAL18/03.

8. Juan Francisco Nistal Herrera. **MicroRNAs: biomarcadores con valor pronóstico y potenciales dianas terapéuticas para la regresión de la hipertrofia cardíaca.** PI18/00543. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

9. Juan Francisco Nistal Herrera. **Proyecto de investigación: Diseño y evaluación de pequeñas moléculas**

análogas de BMP-7 para el tratamiento del remodelado cardíaco patológico. INNVAL18/20.

10. Carmen Martínez-Cué. **Estrategias terapéuticas para paliar el deterioro cognitivo antes y después de la aparición de patología tipo Alzheimer en un modelo animal de síndrome de Down.** PSI2016-76194-R. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

11. María A. Hurlé. **MicroRNAs en dolor neuropático: biomarcadores moleculares y terapias dirigidas.** SAF2016-77732-R. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Clinical trials

1. Francisco Jesús González Vílchez. **Estudio multicéntrico, aleatorizado, doble ciego, de grupos paralelos, con control activo, para evaluar la eficacia y seguridad de LCZ696 comparado con valsartan, sobre la morbilidad y mortalidad en pacientes con insuficiencia cardíaca (Clase II-IV NYHA) con fracción de eyección preservada.** CLCZ696D2301. NOVARTIS FARMACEUTICA, S.A.

Authorship Thesis 2017

1. Sara Lantigua Romero. **Efecto de distintas estrategias terapéuticas sobre los déficits cognitivos y las alteraciones neuromorfológicas de un modelo de Síndrome de Down.** Director/s: Noemí Rueda Revilla, Carmen Martínez-Cue Pesini. UNIVERSIDAD DE CANTABRIA.

2. Víctor Expósito García. **Consecuencias eléctricas de la fibrosis miocárdica mediada por TGF- β , remodelado estructural y desarrollo de fibrilación auricular.** Director/s: Juan Francisco Nistal Herrera, María Amor Hurlé González. UNIVERSIDAD DE CANTABRIA.

3. Verónica Vidal Sánchez. **Efecto de la reducción de la inhibición mediada por los receptores GABAA α 5 y GABAB sobre las alteraciones funcionales y neuromorfológicas en un modelo de Síndrome de Down.** Director/s: Carmen Martínez-Cue Pesini. UNIVERSIDAD DE CANTABRIA.

Thesis Addressed 2017

1. María Ángeles Diego Mantecón. **Efecto de la administración de modulares alostéricos negativos**

selectivos para la subunidad GABAA α 5 sobre los procesos cognitivos implicados en las alteraciones de aprendizaje y memoria de un modelo de Síndrome de Down. Director/s: José Antonio Del Barrio Del Campo, Carmen Martínez-Cue Pesini. UNIVERSIDAD DE CANTABRIA.

2. Rosmari De La Puerta Huertas. **Participación de BMP7 (Bone Morphogenetic Protein 7) en la percepción del dolor y las conductas ansiosas.** Director/s: María Amor Hurlé González, Mónica Tramullas

Fernández. UNIVERSIDAD DE CANTABRIA.

3. Roberto De La Fuente Royano. **Valor clínico potencial de Microma-30C como biomarcador y diana terapéutica para el dolor neuropático.** Director/s: María Amor Hurlé González, Mónica Tramullas Fernández. UNIVERSIDAD DE CANTABRIA.



Cardiovascular research Group



Clinic group

Group Responsible

José Antonio Vázquez de Prada Tiffe

Cardiology Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



joseantonio.vazquezdeprada@scsalud.es

Contributors

José María Cuesta Cosgaya
Mónica Fernández-Valls Gómez
Víctor Fradejas Sastre
Tamara García Camarero
María Teresa García Unzueta
Francisco Jesús González Vílchez
Bernardo Alio Lavín Gómez
Dae Hyun Lee Hwang
Piedad Lerena Sáenz
Joffrey Eduardo Lujan Valencia
Iván Olavarri de Miguel
Javier Ruano Calvo
Cristina Ruisánchez Villar
Fermín Sainz Laso
Gabriela Veiga Fernández
Manuel Jesús Zarauza Navarro
José Javier Zueco Gil

Technicians

María Cristina Obregón Rodríguez

Jointly Responsible

José María de la Torre Hernández

Research lines

The Cardiovascular Research Group is actively working in the fields of Heart Failure and Heart Transplantation, Interventional Cardiology and the different modalities of Cardiac Imaging (2D and 3D echocardiography,

coronary angiography -including IVUS and optical coherence-, coronary CT angiography and Magnetic resonance Imaging). Our main areas of research are:

Cardiovascular Therapy.

a. Immunosuppression in Heart Transplantation, specifically the clinical implementation of new immunosuppressive approaches with proliferation signal inhibitors (mTOR inhibitors).

b. Drug eluting stents, especially in the setting of left main disease.

c. Percutaneous Structural Heart Disease Interventions

- Atrial septal defects closure

- Transcatheter aortic valve implantations (TAVI)

- Prosthetic leaks closure -Left atrial appendage closure

d. Preconditioning in acute coronary syndromes..

Cardiovascular Diagnosis:

a. Genetics in mitral valve prolapse

b. Prevalence and clinical significance of Coronary aneurysms.

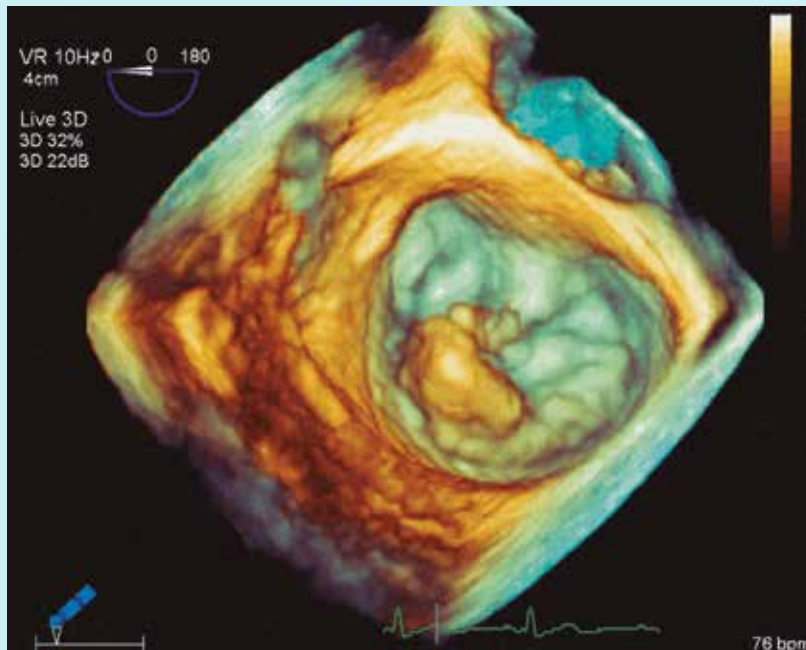


Figura. Three-dimensional echocardiogram demonstrating a mitral valve prolapse

Multimodality Cardiac Imaging.

1. Diagnosis and characterization of Cardiac Allograft Vasculopathy with intravascular ultrasonography (IVUS), optical coherence and virtual histology.
2. Transesophageal three-dimensional echocardiography in atrial septal defects and mitral valve prolapse.
3. Three-dimensional echocardiography evaluation of the mitral annulus.
4. Strain and strain-rate in diabetic and oncologic cardiomyopathy

PUBLICATIONS

IMPACT FACTOR | 170.018

Original articles

1. Räber L, Mintz GS, Koskinas KC, Johnson TW, Holm NR, Onuma Y, Radu MD, Joner M, Yu B, Jia H, Menevau N, de la Torre Hernández JM, Escaned J, Hill J, Prati F, Colombo A, di Mario C, Regar E, Capodanno D, Wijns W, Byrne RA, Guagliumi G,

ESC Scientific Document Group. **Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions.** Eur. Heart J.2018;39:3281-3300.F1.:23.425. [doi:10.1093/eurheartj/ehy285]

2. Barge-Caballero, E, Almenar-Bonet, L, González-Vilchez, F, Lambert-Rodriguez, JL, González-Costello, J, Segovia-Cubero, J, Castel-Lavilla, MA, Delgado-Jimenez, J, Garrido-Bravo, IP, Rangel-Sousa, D, Martinez-Selles, M, De la Fuente-Galán, L, Rabago-Juan-Aracil, G, Sanz-Julve, M, Hervas-Sotomayor, D, Mirabet-Perez, S, Muñoz J, Crespo-Leiro, MG. **Clinical outcomes of temporary mechanical circulatory support as a direct bridge to heart transplantation: a nationwide Spanish registry.** Eur. J. Heart Fail.2018;20:178-186.F1.:10.683. [doi:10.1002/ehjhf.956]

3. Comin-Colet, J, Manito, N, Segovia-Cubero, J, Delgado, J, García Pinilla JM, Almenar, L, Crespo-Leiro, MG, Sionis, A, Blasco, T, Pascual-Figal, D, González-Vilchez, F, Lambert-Rodriguez, JL, Grau, M, Bruguera, J, LION-HEART Study Investigators. **Efficacy and safety of intermittent intravenous outpatient administration of levosimendan in patients with advanced heart failure: the LION-**

HEART multicentre randomised trial. Eur. J. Heart Fail.2018;20:1128-1136.F1.:10.683. [doi:10.1002/ehjhf.1145]

4. Alfonso F, Pérez-Vizcayno MJ, Cuesta J, García Del Blanco B, García-Touchard A, López-Mínguez JR, Masotti M, Zueco J, Cequier A, Velázquez M, Moreno R, Mainar V, Domínguez A, Moris C, Molina E, Rivero F, Jiménez-Quevedo P, Gonzalo N, Fernández-Pérez C, **RIBS IV Study Investigators (Under the Auspices of the Interventional Cardiology. 3-Year Clinical Follow-Up of the RIBS IV Clinical Trial: A Prospective Randomized Study of Drug-Eluting Balloons Versus Everolimus-Eluting Stents in Patients With In-Stent Restenosis in Coronary Arteries Previously Treated With Drug-Eluting Stents.** JACC-Cardiovasc. Interv.2018;11:981-991.F1.:9.881. [doi:10.1016/j.jcin.2018.02.037]

5. Rodes-Cabau, J, Urena, M, Nombela-Franco, L, Amat-Santos, I, Kleiman, N, Munoz-Garcia, A, Atenza, F, Serra, V, Deyell, MW, Veiga-Fernandez, G, Masson, JB, Canadas-Godoy, V, Himbert, D, Castrodeza, J, Elizaga, J, Francisco Pascual J, Webb, JG, de la Torre, JM, Asmarats, L, Pelletier-Beaumont, E, Philippon, F. **Arrhythmic Burden as Determined by Ambulatory Continuous Cardiac Monitoring**

in Patients With New-Onset Persistent Left Bundle Branch Block Following Transcatheter Aortic Valve Replacement The MARE Study. *JACC-Cardiovasc. Interv.*2018;11:1495-1505.F.I.:9.881. [doi:10.1016/j.jcin.2018.04.016]

6. Chamandi, C, Barbanti, M, Munoz-García, A, Latib, A, Nombela-Franco, L, Gutiérrez-Ibáñez, E, Veiga-Fernandez, G, Cheema, AN, Cruz-Gonzalez, I, Serra, V, Tamburino, C, Mangieri, A, Colombo, A, Jiménez-Quevedo, P, Elizaga, J, Laughlin, G, Lee, DH, García Del Blanco B, Rodríguez-Gabella, T, Marsal, JR, Côté M, Philippon, F, Rodes-Cabau, J. Long-Term **Outcomes in Patients With New Permanent Pacemaker Implantation Following Transcatheter Aortic Valve Replacement.** *JACC-Cardiovasc. Interv.*2018;11:301-310.F.I.:9.881. [doi:10.1016/j.jcin.2017.10.032]

7. Tirado-Conte G, Rodés-Cabau J, Rodríguez-Olivares R, Barbanti M, Lhermusier T, Amat-Santos I, Toggweiler S, Cheema AN, Muñoz-García AJ, Serra V, Giordana F, Veiga G, Jiménez-Quevedo P, Campelo-Parada F, Loretz L, Todaro D, Del Trigo M, Hernández-García JM, García Del Blanco B, Bruno F, de la Torre Hernández JM, Stella P, Tamburino C, Macaya C, Nombela-Franco L. **Clinical Outcomes and Prognosis Markers of Patients With Liver Disease Undergoing Transcatheter Aortic Valve Replacement: A Propensity Score-Matched Analysis.** *Circ Cardiovasc Interv.* 2018;11:F.I.:6.504. [doi:10.1161/CIRCINTERVENTIONS.117.005727]

8. López-Moya, M, Melgar-Lesmes, P, Kolandaivelu, K, de la Torre Hernández JM, Edelman, ER, Balcells, M. **Optimizing Glutaraldehyde-Fixed Tissue Heart Valves with Chondroitin Sulfate Hydrogel for Endothelialization and Shielding against Deterioration.** *BIOMACROMOLECULES.* 2018;19:1234-1244.F.I.:5.738. [doi:10.1021/acs.biomac.8b00077]

9. De la Torre Hernández JM, Rumoroso, JR, Ojeda, S, Brugaletta, S, Cascon, JD, Ruisanchez, C, Sánchez Gilá J, Roa, J, Tizon, H, Gutiérrez, H, Larman, M, García Camarero T, Pinar, E, Diaz, JF, Pan, M, Morillas Bueno M, Oyonarte, JM, Ruiz Guerrero L, Ble, M, Rubio

Patón R, Arnold, R, Echegaray, K, de la Morena, G, Sabate, M. **Angina and Ischemia at 2 Years With Bioresorbable Vascular Scaffolds and Metallic Drug-eluting Stents. ESTROFA Ischemia BVS-mDES Study.** *Rev. Esp. Cardiol.*2018;71:327-334.F.I.:5.166. [doi:10.1016/j.recesp.2017.03.021]

10. González-Vilchez, F, Lamber, JL, Rangel, D, Almenar, L, de la Fuente, JL, Palomo, J, Díaz Molina B, Lage, E, Sánchez Lázaro I, Vázquez de Prada JA. **Efficacy and Safety of de Novo and Early Use of Extended-release Tacrolimus in Heart Transplantation.** *Rev. Esp. Cardiol.*2018;71:18-25.F.I.:5.166. [doi:10.1016/j.recesp.2017.03.015]

11. García-Pinilla, JM, Ferrero Torres M, González-Vilchez, F, Barge Caballero E, Masip, J, Segovia Cubero J. **Selection of the Best of 2017 in Acute and Chronic Heart Failure.** *Rev. Esp. Cardiol.*2018;71:298-299.F.I.:5.166. [doi:10.1016/j.recesp.2017.11.001]

12. Barge-Caballero, E, Gonzalez-Vilchez, F, Ferrero-Torres, M, Segovia-Cubero, J. **Selection of the Best of 2017 in Cardiac Transplant and Ventricular Assist Devices.** *Rev. Esp. Cardiol.*2018;71:300-301.F.I.:5.166. [doi:10.1016/j.recesp.2017.10.011]

13. Amat-Santos, IJ, Castrodeza, J, Nombela-Franco, L, Muñoz-García AJ, Gutierrez-Ibanes, E, de la Torre Hernández JM, Córdoba-Soriano, JG, Jiménez-Quevedo, P, Hernández-García, JM, González-Mansilla, A, Ruano, J, Tobar, J, Del Trigo, M, Vera, S, Puri, R, Hernández-Luis, C, Carrasco-Moraleja, M, Gómez, I, Rodes-Cabau, J, San Román, JA. **Tricuspid but not Mitral Regurgitation Determines Mortality After TAVI in Patients With Nonsevere Mitral Regurgitation.** *Rev. Esp. Cardiol.*2018;71:357-364.F.I.:5.166. [doi:10.1016/j.recesp.2017.08.013]

14. Melgar-Lesmes, P, Sanchez-Herrero, A, Lozano-Juan, F, Hernández JMT, Montell, E, Jiménez, W, Edelman, ER, Balcells, M. **Chondroitin Sulphate Attenuates Atherosclerosis in ApoE Knockout Mice Involving Cellular Regulation of the Inflammatory Response.** *Thromb. Haemost.*2018;118:1329-1339.F.I.:4.952 [doi:10.1055/s-0038-1657753]

15. De la Torre Hernández JM, Gonzalo, N, Otaegui, I, Rumoroso, JR, Gutiérrez, H, Alfonso, F, Marti, G, Serrador Frutos A, Brugaletta, S, Gómez Menchero A, García Camarero T, Biagioni, C, Escaned, J. **Device specificity of vascular healing following implantation of bioresorbable vascular scaffolds and bioabsorbable polymer metallic drug-eluting stents in human coronary arteries: the ESTROFA OCT BVS vs. BP-DES study.** *EuroIntervention.* 2018;14:1295-1303.F.I.:4.417. [doi:10.4244/EIJ-D-17-00952]

16. Vilanova, I, Hernández, JL, Mata, C, Duran, C, García-Unzueta, MT, Portilla, V, Fuentevilla, P, Corrales, A, Gonzalez-Vela, MC, González-Gay, MA, Blanco, R, González-López, MA. **Insulin resistance in hidradenitis suppurativa: a case-control study.** *J. Eur. Acad. Dermatol. Venereol.*2018;32:820-824.F.I.:4.287. [doi:10.1111/jdv.14894]

17. Barge-Caballero, E, Almenar-Bonet, L, Crespo-Leiro, MG, Brossa-Loidi, V, Rangel-Sousa, D, Gómez-Bueno, M, Ferrero-Torres, M, Díaz-Molina, B, Delgado-Jiménez, J, Martínez-Selles, M, López-Granados, A, De-la-Fuente-Galán, L, González-Costello, J, Garrido-Bravo, IP, Blasco-Peiro, T, Rábago-Juan-Aracil, G, González-Vilchez, F. **Preoperative Toxoplasma gondii serostatus does not affect long-term survival of cardiac transplant recipients. Analysis of the Spanish Heart Transplantation Registry.** *Int. J. Cardiol.*2018;250:183-187.F.I.:4.034. [doi:10.1016/j.ijcard.2017.09.215]

18. Cerrato, E, Echavarría-Pinto, M, D'Ascenzo, F, Gonzalo, N, Quadri, G, Quiros, A, de la Torre Hernández JM, Tomassini, F, Barbero, U, Nombela-Franco, L, Núñez-Gil I, Biondi-Zoccai, G, Macaya, C, Varbella, F, Escaned, J. **Safety of intermediate left main stenosis revascularization deferral based on fractional flow reserve and intravascular ultrasound: A systematic review and meta-regression including 908 deferred left main stenosis from 12 studies.** *Int. J. Cardiol.*2018;271:42-48.F.I.:4.034. [doi:10.1016/j.ijcard.2018.04.032]

19. López-Delgado, L, Riancho-Zarrabeitia, L, García-Unzueta, MT, Tenorio, JA, García-Hoyos, M, Lapunzina, P, Valero, C, Riancho,

JA. **Abnormal bone turnover in individuals with low serum alkaline phosphatase. Osteoporosis** Int.2018;29:2147-2150.F.I.:3.856. [doi:10.1007/s00198-018-4571-0]

20. Lozano, I, Sánchez Perez A, Sánchez-Insa, E, Mehan JCR, Gopar, S, Ruiz-Quevedo, V, Fernández, JF, Gómez-Jaume, A, Bayon, J, Lasa, G, Fernández-Portales, J, Hernández JMT, Mañas P, Pinar, E, Lopez-Palop, R, Albarran, A, de Leiras, SR. **Implementation of Institutional Protocols for Patients With Acute Coronary Syndrome: Nonclinical Factors Also Matter.** Am. J. Cardiol.2018;122:1804-1805.F.I.:3.171. [doi:10.1016/j.amjcard.2018.08.014]

21. Díaz Fernández JF, Camacho Freire SJ, Fernández Guerrero JC, Delarche, N, Bretelle, C, Zueco Gil J, Palop, RL, García Del Blanco B, Mainar Tello V, Albert, F. **Everolimus drug-eluting stent performance in patients with long coronary lesions: The multicenter Longprime registry.** Catheter. Cardiovasc. Interv.2018;92:493-501.F.I.:2.602. [doi:10.1002/ccd.27657]

22. Puri, R, Otaegui, I, Sabate, M, Serra-Penaranda, A, Puigfel, M, Perez de Prado A, Nombela-Franco, L, de la Torre Hernández JM, Ortas Nadal R, Iniguez-Romo, A, Jiménez, G, Fernández-Vazquez, F, Cuellas-Ramón, C, Gonzalo, N, Alfonso Jiménez Díaz V, Duocastella, L, Molina, M, Amoros, M, Perez, I, Barria Pérez A, Pelletier Beaumont E, Nicholls, SJ, García Del Blanco B, Rodes-Cabau, J. **Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite (R) drug-eluting stent: The ANCHOR study.** Catheter. Cardiovasc. Interv.2018;91:435-443.F.I.:2.602. [doi:10.1002/ccd.27189]

23. Amrute, JM, Athanasiou, LS, Rikhtegar, F, de la Torre Hernández JM, Camarero, TG, Edelman, ER. **Polymeric endovascular strut and lumen detection algorithm for intracoronary optical coherence tomography images.** J. Biomed. Opt.2018;23:1-14.F.I.:2.367. [doi:10.1117/1.JBO.23.3.036010]

Reviews

1. Riancho-Zarrabeitia, L, Cuberia, M, Muñoz P, López-Hoyos, M,

García-Canale, S, García-Unzueta, M, Hernández, JL, Martínez-Taboada, VM. **Vitamin D and antiphospholipid syndrome: A retrospective cohort study and meta-analysis.** Semin. Arthritis Rheum.2018;47:877-882.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.10.007]

Editorials

1. De la Torre Hernández JM. **Mechanical Complications in Elderly Patients With Myocardial Infarction Becoming Fewer But Just as Fatal.** J. Am. Coll. Cardiol.2018;72:967-969.F.I.:16.834. [doi:10.1016/j.jacc.2018.06.032]

Clinical Trials

1. José Javier Zueco Gil. **Estudio de resultados en pacientes tras la implantación de stends Endeavor frente a Cypher.** Estudio prospectivo, multicéntrico, aleatorizado, de 2 brazos y abierto, versión final 1.0 de 12 de abril 2007. Hoja de Información al Paciente y Consentimiento Informado, versión 1.5 de 16 de nov. de 2007., PROTECT. MEDTRONIC IBERICA, S.A..

2. José Javier Zueco Gil. **Estudio prospectivo, multicéntrico y aleatorizado (balón de paclitaxel vs stent farmacológico) del tratamiento percutáneo de los pacientes con reestenosis de un stent metálico convencional.** ESTUDIO RIBS V. Versión A05 de 1 de marzo de 2010. RIBS V (AAG-I-H-0920). FUNDACIÓN MÉDICA PARA LA INVESTIGACIÓN Y DESARROLLO EN EL ÁREA CARDIOVASCULAR.

3. José Javier Zueco Gil. **Eficacia y seguridad de la doble antiagregación comparada con la combinación de anticoagulación + doble antiagregación en pacientes con fibrilación auricular de bajo-moderado riesgo sometidos a implementación de un stent coronario.** MUSICA-2. GARCÍA DORADO, DAVID.

4. Francisco Jesús González Vilchez. **Estudio multicéntrico, doble ciego, aleatorizado y controlado con placebo para evaluar la eficacia y seguridad de la administración por vía intravenosa de dosis intermitentes de levosimendán en pacientes ambulatorios con**

insuficiencia cardíaca crónica avanzada. IMIM-LEV-0901. CONSORCI MAR PARC DE SALUT DE BARCELONA.

5. José Antonio Vázquez de Prada Tiffe. **Ensayo aleatorizado, doble ciego, controlado con placebo y con grupos paralelos para evaluar el efecto de SAR236553/ REGN727 sobre la aparición de acontecimientos cardiovasculares en pacientes que han experimentado recientemente un síndrome coronario agudo.** EFC11570. SANOFI AVENTIS, S.A..

6. José Antonio Vázquez de Prada Tiffe. **Estudio multicéntrico, aleatorizado, doble ciego, basado en eventos, que compara la eficacia y seguridad de Rivaroxaban oral con placebo en la reducción del riesgo de muerte, infarto de miocardio o ictus, en pacientes con insuficiencia cardíaca crónica y enfermedad arterial coronaria significativa tras una hospitalización por exacerbación de la insuficiencia cardíaca.** RIVAROXHFA3001/ BAY59-7939/16302. JANSSEN R&D IRELAND.

7. Francisco Jesús González Vilchez. **Estudio multicéntrico, aleatorizado, doble ciego, de grupos paralelos, con control activo, para evaluar la eficacia y seguridad de LCZ696 comparado con valsartan, sobre la morbilidad y mortalidad en pacientes con insuficiencia cardíaca** (Clase II-IV NYHA) con fracción de eyección preservada. CLCZ696D2301. NOVARTIS FARMACEUTICA, S.A..

8. José Javier Zueco Gil. **Registro de pacientes con Dispositivo Biorreabsorbible en la práctica clínica habitual.** Estudio Repara. COR-BVS-2013-01. SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA SEC.

9. Francisco Jesús González Vilchez. **Ensayo clínico fase II, multicéntrico, aleatorizado en grupos paralelos, doble ciego, controlado con placebo, de búsqueda de dosis para explorar los efectos farmacodinámicos, la seguridad, la tolerabilidad y la farmacocinética de cuatro regímenes de dosis distintos del estimulador oral sGC BAY1021189, durante 12 semanas, en pacientes con descompensación de la insuficiencia cardíaca y la fracción de eyección preservada.** BAY1021189/15829. BAYER HEALTHCARE AG.

10. José Javier Zueco Gil. **Ensayo clínico de un brazo para evaluar la eficacia de las intervenciones coronarias percutáneas (ICP) en la enfermedad coronaria de 3 vasos (E3V) de nueva aparición mediante la aplicación del Score SYNTAX II, el uso de guía de presión para la evaluación funcional y el uso de IVUS como guía del procedimiento, e implantación de un stent liberador de everolimus con recubrimiento abluminal biodegradable.** ECRI-002. EUROPEAN CARDIOVASCULAR RESEARCH INSTITUTE-2 (ECRI-2).

11. José Javier Zueco Gil. **Estudio prospectivo, aleatorizado, multicéntrico para evaluar la seguridad y eficacia del sistema del stent liberador de sirolimus en el tratamiento de pacientes con hasta dos lesiones arteriales coronarias de novo.** BIOFLOW IV. BIOTRONIK SE & CO. KG.

12. José María de la Torre Hernández. **Ensayo clínico, randomizado, doble ciego y controlado con placebo, de la melatonina intravenosa como terapia adyuvante a la reperfusión primaria con angioplastia transluminal percutánea en pacientes con infarto agudo de miocardio.** Melatonina/05. DOMINGUEZ RODRIGUEZ, ALBERTO.

13. José María de la Torre Hernández. **Acceso radial frente a acceso femoral y bivalirudina frente a heparina no fraccionada con o sin inhibidores de la glucoproteína IIb/IIIa como estrategia global para minimizar las complicaciones hemorrágicas en pacientes con síndrome coronario agudo sometidos a tratamiento invasivo.** RFBU11-I. SOCIETA ITALIANA DI CARDIOLOGIA INVASIVA GISE.

14. José María de la Torre Hernández. **Ensayo multinacional, aleatorizado, doble ciego, controlado con placebo, para evaluar el efecto de ticagrelor 90 mg dos veces al día sobre la incidencia de muerte cardiovascular, infarto de miocardio o ictus en pacientes con diabetes mellitus tipo 2.** D513BC00001. ASTRAZENECA AB.

15. José María de la Torre Hernández. **Efecto de la infusión intracoronaria de células madre mononucleares derivadas de la médula ósea (CMN-MO) sobre la mortalidad por**

cualquier causa en el infarto agudo de miocardio. BAMI-01. QUEEN MARY AND WESTFIELD COLLEGE.

16. José María de la Torre Hernández. **"Estudio TWILIGHT- Ticagrelor con Aspirina o sola en pacientes de alto riesgo después de una intervención coronaria".** ISSBRIL0345. ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI.

17. Francisco Jesús González Vilchez. **Estudio multicéntrico, aleatorizado, doble ciego, prospectivo para evaluar el efecto de sacubitril/valsartán vs. enalapril en la actividad física diaria utilizando un actígrafo de muñeca en pacientes adultos con insuficiencia cardíaca crónica".** CLCZ696B3301. NOVARTIS FARMACEUTICA, S.A..

18. Francisco Jesús González Vilchez. **Estudio doble ciego, aleatorizado, controlado con placebo y multicéntrico para evaluar la eficacia y la seguridad de omecantiv mecarbil en la mortalidad y morbilidad de sujetos con insuficiencia cardíaca crónica con fracción de eyección reducida.** 20110203. AMGEN, S.A..

19. José María de la Torre Hernández. **Xience 28 Estudio Global.** 17-311. ABBOT CARDIOVASCULAR SYSTEMS INC C/C ABBOTT VASCULAR INTERNATIONAL BVBA.

Postmarketing Studies and Other

1. Francisco Jesús González Vilchez. **Estudio epidemiológico para evaluar el manejo del tratamiento con esteroides en pacientes con trasplante cardíaco realizado en la era actual de la inmunosupresión en España.** AST-EST-2010-01. ASTELLAS PHARMA, S.A..

2. Manuel Jesús Zarauza Navarro. **Estudio Observacional Registro Europeo Multinacional sobre la Previención de Episodios Tromboembólicos en Fibrilación Auricular.** DSE-ANT-2011-01. DAIICHI SANKYO, INC.

3. Francisco Jesús González Vilchez. **Estudio multicéntrico, observacional, retrospectivo para evaluar la conversión de la formulación estándar de tacrolimus (Prograf(c)) a tacrolimus de liberación prolongada**

(Advagraf(c)) en pacientes con trasplante cardíaco. AST-TAC-2013-01. ASTELLAS PHARMA, S.A..

4. José Antonio Vázquez de Prada Tiffe. **Registro internacional prospectivo y multicéntrico de pacientes hombres y mujeres que han sido diagnosticados recientemente con fibrilación auricular y reciben tratamiento con Rivaroxabán.** TRI08890. THE TROMBOSIS RESEARCH INSTITUTE.

5. Fermín Sainz Laso. **Estudio observacional postautorización PRESSUREwire: Evaluación práctica de la reserva de fracción de flujo (FFR) y los índices alternativos asociados durante las intervenciones clínicas habituales.** CRD-795 / SJM-CIP-10136. SJM COORDINATION CENTER BVBA.

6. Fermín Sainz Laso. **Estudio observacional postautorización Registro prospectivo, de brazo único, multicéntrico, observacional, de utilización de stent liberador de zotarolimus RESOLUTE-ONYX™ en el intervencionismo coronario percutáneo en vasos pequeños.** DISCO 9. FUNDACIÓN DE INVESTIGACIÓN SANITARIA EN LEÓN FIS LEÓN.

7. José María de la Torre Hernández. **Estudio Onyx ONE; un estudio aleatorizado y controlado con el stent Resolute Onyx y tratamiento de doble antiagregación plaquetaria [DAPT] de un mes para pacientes con alto riesgo de sangrado.** ONYX ONE. MEDTRONIC BAKKEN RESEARCH CENTER, B.V.

8. José María de la Torre Hernández. **Registro de ihtDESTiny BD, Sistema de Stent Coronario Liberador de sirolimus abluminal. SOC-DES-2017-01.** SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA SEC.

Other Publications

1. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecochea, E, Faripas-elvarez, C, Fontalba, A, Zarauza, J, Ojeda, L, Parra, JA. **Nailfold capillaroscopy in hereditary hemorrhagic telangiectasia.** ANGIOGENESIS. 2018;21:144-144.



Infection, Immunity and Digestive Diseases



Consolidated group

Researchers

José Pedro Vaqué Díez

Contributors

Ana Álvarez Cancelo
María Teresa Arias Loste
Joaquín Cabezas González
Fernando Casafont Morencos

Beatriz Castro Senosiain

Marta Cobo Martín

Antonio Cuadrado Lavín

Soraya Curiel del Olmo

Ainhoa Díaz Pérez

Emilio Fábrega García

Tatiana Fernández Lanas

José Ignacio Ortea Ormaechea

Agustín García Blanco

Group Responsible

Javier Crespo García

Digestive Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



javier.crespo@scsalud.es

Pedro Luis Fernández Gil

María José García García

Patricia Huelín Álvarez

Paula Iruzubieta Coz

Francisco Javier Jiménez Pérez

Susana Llerena Santiago

Lorena López Montejo

Luis Martín Ramos

Susana Menéndez Secades

María Moris Folgueroso

Helena Pisonero Fraga

Ángela María Puente Sánchez

Laura Rasines Pérez

Montserrat Rivero Tirado

Carlos Rodríguez de Lope López

Álvaro Terán Lantarón

Nurses

Lidia Amigo Cabria

Laura García Laso

María Rita Millor Rojo

Predoctoral

Nuria García Díaz

Technicians

Lorena Cayón Estrada

Ángel Estebanez Gallo

Research lines

1. Hepatitis C.

To know the real epidemiology of hepatitis C virus infection in our country. To evaluate the role of

the innate immune system in the spontaneous clearance of C virus infection, as well as the evolution towards chronicity and its implication in response / failure to treatment with new direct acting antiviral agents (ADIs). Regarding the therapeutic failure, the viral variants associated with resistance will also be studied. In addition, we will study whether the hepatitis C virus is capable of

producing endothelial dysfunction, subclinical atheromatosis, disorder of mineral and bone metabolism or neurocognitive manifestations and its potential reversibility after curing the infection with the new ADD agents. Finally, we intend to study whether regression occurs in liver fibrosis after the response to DDA and the pathogenic role of the enzyme Lisil-oxidase like 2 (LOXL2) in this process.

2. Molecular characterization of specific cases of human cancer.

Potential implications in diagnosis and therapy. Oncogenic signaling mechanisms that control initiation, progression and response to therapy. Study from a personalized point of view, advanced cases of human cancer that at present lack effective therapies. Currently we have research projects in liver cancer as well as some types of aggressive skin cancers such as advanced melanoma, Merkel cell carcinoma and cutaneous T-cell lymphoma.

3. Fatty Liver Disease (EHDG).

Obesity and insulin resistance are associated with a chronic inflammatory state. Current evidence indicates that the activation of the signal transduced at the level of the innate immune system by receptors such as TLRs and NLRs plays a decisive role in the genesis of this inflammatory state. Both receptor families, together with RLRs, make up what we know as pattern recognition receptors (PRRs). However, the role played by PRRs in the pathogenesis of HDD is largely unknown. It is possible that differences in the gene and protein expression of these peripheral, hepatic and fatty receptors between obese and non-obese subjects translate into a different susceptibility to the development of fatty liver disease.

On the other hand, the severity of the histological lesion of GHTD has been associated with the concomitant presence of hypopnea sleep apnea syndrome. The role that intermittent hypoxia plays in the development of liver injury has been studied previously. However, there are no studies aimed at evaluating the effect of hypercapnia maintained at the hepatic level. For this reason, we intend to analyze the effect of chronic hypercapnia, with or without added hypoxemia, at the liver level with ex vivo models of primary culture of immortalized hepatocytes, by analysis of gene expression associated with glucose and lipid metabolism and regulatory genes of the immune response, as well as assessing the inflammatory response induced in these cells by the infusion of lipopolysaccharide.

The partial deficiency of the lysosomal acid lipase (LAL) enzyme is an inherited, autosomal recessive pathology of lipid metabolism characterized by accumulation in lysosomes, especially in the liver of cholesterol and triglyceride esters, which may erroneously be diagnosed in the adult as HDSH. This pathology is due to mutations of the LAL gene (LIPA), of which more than 40 mutations have been described. We intend to evaluate whether the active screening by mass sequencing of the LIPA gene in adults with a diagnosis of GDHD could be relevant from a clinical point of view.

4. Alcoholic liver disease. To study the pathophysiological mechanisms of acute alcoholic hepatitis and the search for molecular targets. Analysis of the hepatic transcriptome in patients with alcoholic liver disease for the development of molecular signatures of gene expression.

5. Liver cirrhosis and portal hypertension.

To characterize the natural history of hepatic cirrhosis and factors that may influence the portal pressure gradient. To evaluate the long-term role of new oral anticoagulants in the survival and development of complications of portal hypertension in patients with liver cirrhosis.

6. Liver transplantation.

To study non-invasive blood biomarkers of clinical events related to liver transplantation (rejection, infection, vascular pathology, biliary disease, and short- and long-term survival of the graft).

7. Cholestatic and autoimmune liver disease.

Characterize the natural history and physiopathological mechanisms of cholestatic and autoimmune liver diseases.

PUBLICATIONS

IMPACT FACTOR | 170.944

Original articles

1. Ezcurra, I, Fortea, JI, Crespo, J. **Low Phospholipid-Associated Cholelithiasis Syndrome Diagnosis.** *Gastroenterology*. 2018;155:17-19.F.I.:20.773. [doi:10.1053/j.gastro.2018.04.023]
2. Ouyang, XS, Han, SN, Zhang, JY, Dioletis, E, Nemeth, BT, Pacher, P, Feng, DC, Bataller, R, Cabezas, J, Stärkel P, Caballeria, J, LePine Pongratz R, Cai, SY, Schnabl, B, Hoque, R, Chen, YL, Yang, WH, Garcia-Martinez, I, Wang, FS, Gao, B, Torok, NJ, Kibbey, RG, Mehal, WZ. **Digoxin Suppresses Pyruvate Kinase M2-Promoted HIF-1 alpha Transactivation in Steatohepatitis (vol 27, pg 339, 2018).** *Cell Metab*.2018;27:1156-1156.F.I.:20.565. [doi:10.1016/j.cmet.2018.04.007]
3. Ampuero, J, Jimeno, C, Quiles, R, Rosales, JM, Llerena, S, Palomo, N, Cordero, P, Serrano, FJ, Urquijo, JJ, Moreno-Planas, JM, Ontanilla, G, Hernandez, M, Ortega-Alonso, A, Maraver, M, Bonacci, M, Rojas, A, Figueruela, B, Forn, X, Andrade, RJ, Luis Calleja J, Diago, M, Carmona, I, de la Mata, M, Buti, M, Crespo, J, Pascasio, JM, Navarro, JM, Salmeron, J, Romero-Gomez, M. **Impact of comorbidities on patient outcomes after interferon-free therapy-induced viral eradication in hepatitis C. J.** *Hepatol*.2018;68:940-948.F.I.:14.911. [doi:10.1016/j.jhep.2017.12.019]
4. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, Colombo M, Craxi A, Crespo J, Day CP, Geier A, Kondili LA, Lazarus JV, Loomba R, Manns MP, Marchesini G, Negro F, Petta S, Ratziu V, Romero-Gomez M, Sanyal A, Schattenberg JM, Tacke F, Trautwein C, Wei L, Zeuzem S, Razavi H. **Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. J.** *Hepatol*.2018;69:896-904.F.I.:14.911. [doi:10.1016/j.jhep.2018.05.036]

5. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Alvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setián E, Lopez-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. **Microenvironment Eradication of Hepatitis C: A Novel Treatment Paradigm.** *Am. J. Gastroenterol.* 2018;113:1639-1648.F.I.:10.231. [doi:10.1038/s41395-018-0157-x]

6. Chaparro, M, Garre, A, Ricart, E, Iborra, M, Mesonero, F, Vera, I, Riestra, S, García-Sánchez, V, Luisa De Castro M, Martín-Cardona, A, Aldeguez, X, Minguez, M, de-Acosta, MB, Rivero, M, Muñoz F, Andreu, M, Bargallo, A, González-Munoz, C, Pérez Calle JL, García-Sepulcre, MF, Bermejo, F, Huguet, JM, Cabriada, JL, Gutierrez, A, Mañosa M, Villoria, A, Carbajo, AY, Lorente, R, García-López, S, ..., GETECCU study group. **Short and long-term effectiveness and safety of vedolizumab in inflammatory bowel disease: results from the ENEIDA registry.** *Aliment. Pharmacol. Ther.* 2018;48:839-851.F.I.:7.357. [doi:10.1111/apt.14930]

7. Ampuero, J, Aller, R, Gallego-Duran, R, Banales, JM, Crespo, J, García-Monzón, C, Pareja, MJ, Vilar-Gomez, E, Caballeria, J, Escudero-García, D, Gómez-Camarero, J, Calleja, JL, Latorre, M, Albillas, A, Salmeron, J, Aspichueta, P, Lo Iacono, O, Frances, R, Benlloch, S, Fernández-Rodríguez, C, García-Samaniego, J, Estevez, P, Andrade, RJ, Turnes, J, Romero-Gómez, M, HEPAmet Registry. **The effects of metabolic status on non-alcoholic fatty liver disease-related outcomes, beyond the presence of obesity.** *Aliment. Pharmacol. Ther.* 2018;48:1260-1270.F.I.:7.357. [doi:10.1111/apt.15015]

8. Taxonera C, Ponferrada Á, Riestra S, Bermejo F, Saro C, Martín-Arranz MD, Cabriada JL, Barreiro-de Acosta M, de Castro ML, López-Serrano P, Barrio J, Suarez C, Iglesias E, Argüelles-Arias F, Ferrer I, Marín-Jiménez I, Hernández-Camba A, Bastida G, Van Domselaar M, Martínez-Montiel P, Olivares D, Rivero M, Fernández-Salazar L, Nantes Ó, Merino O, Alba C, Gisbert JP, CONVERT study group from GETECCU. **Serial Tuberculin Skin Tests Improve the Detection of Latent Tuberculosis Infection in Patients With Inflammatory Bowel Disease.** *J. Crohns Colitis.*

2018;12:1270-1279.F.I.:6.637. [doi:10.1093/ecco-jcc/jjy104]

9. Fernández-Ramos, D, Fernández-Tussy, P, Lopitz-Otsoa, F, Gutiérrez-de-Juan, V, Navasa, N, Barbier-Torres, L, Zubiete-Franco, I, Simon, J, Fernández, AF, Arbelaz, A, Aransay, AM, Lavin, JL, Beraza, N, Perugorria, MJ, Banales, JM, Villa, E, Fraga, MF, Anguita, J, Avila, MA, Berasain, C, Iruzubieta, P, Crespo, J, Lu, SC, Varela-Rey, M, Mato, JM, Delgado, TC, Martínez-Chantar, ML. **MiR-873-5p acts as an epigenetic regulator in early stages of liver fibrosis and cirrhosis.** *Cell Death Dis.* 2018;9:958-958.F.I.:5.638. [doi:10.1038/s41419-018-1014-y]

10. Mata-Garrido, J, Tapia, O, Casafont, I, Berciano, MT, Cuadrado, A, Lafarga, M. **Persistent accumulation of unrepaired DNA damage in rat cortical neurons: nuclear organization and ChIP-seq analysis of damaged DNA.** *Acta Neuropathol. Commun.* 2018;6:68-68.F.I.:5.414. [doi:10.1186/s40478-018-0573-6]

11. Llerena Santiago, S.; García-Díaz N; Curiel del Olmo, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, H, Varela, M, Santibáñez Margüello, M, Almaraz Pro, M^oC, Cereceda Company, L, Martínez Magunacelaya, N, Arias Loste, M.T; Puente Á, Martín-Ramos, L, Rodríguez de Lope López, C, Castillo Suescún, F, Cagigas-Fernandez C; I, P; Lopez-López C; López Hoyos, M, Llorca Díaz, J, Agüero Balbín, J, Crespo Facorro, B, Varela I; Piris Pinilla, M.A, Crespo García, J, Vaqué Díez, J.P. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR.** *Oncotarget.* 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

12. Cruces-Sande, M, Vila-Bedmar, R, Arcones, AC, Gonzalez-Rodriguez, A, Rada, P, Gutierrez-De-Juan, V, Vargas-Castrillon, J, Iruzubieta, P, Sanchez-Gonzalez, C, Formentini, L, Crespo, J, Garcia-Monzon, C, Martinez-Chantar, ML, Valverde, AM, Mayor, F, Murga, C. **Involvement of G protein-coupled receptor kinase 2 (GRK2) in the development of non-alcoholic steatosis and steatohepatitis in mice and humans.** *Biochim. Biophys. Acta-Mol. Basis Dis.* 2018;1864:3655-3667.F.I.:5.108. [doi:10.1016/j.bbdis.2018.09.027]

13. Fortea, JI, Zipprich, A, Fernandez-Mena, C, Puerto, M, Bosoi, CR, Almagro, J, Hollenbach, M, Bañares J, Rodriguez-Sanchez, B, Cercenado, E, Clement, MA, Rose, CF, Bañares R, Vaquero, J, Ripoll, C. **Enoxaparin does not ameliorate liver fibrosis or portal hypertension in rats with advanced cirrhosis.** *Liver Int.* 2018;38:102-112.F.I.:4.500. [doi:10.1111/liv.13510]

14. Fortea, JI, Fernandez-Mena, C, Puerto, M, Ripoll, C, Almagro, J, Bañares J, Bellon, JM, Bañares R, Vaquero, J. **Comparison of Two Protocols of Carbon Tetrachloride-Induced Cirrhosis in Rats - Improving Yield and Reproducibility.** *Sci Rep.* 2018;8:9163-9163.F.I.:4.122. [doi:10.1038/s41598-018-27427-9]

15. Rufinatscha, K, Ress, C, Folie, S, Haas, S, Salzmann, K, Moser, P, Dobner, J, Weiss, G, Iruzubieta, P, Arias-Loste, MT, Crespo, J, Tilg, H, Kaser, S. **Metabolic effects of reduced growth hormone action in fatty liver disease.** *Hepatology.* 2018;12:474-481.F.I.:4.117. [doi:10.1007/s12072-018-9893-7]

16. Suján, R, Cruz-Lemini, M, Altamirano, J, Simonetto, DA, Maiwall, R, Axley, P, Richardson, T, Desai, V, Cabezas, J, Vargas, V, Kamath, PS, Shah, VH, Sarin, SK, Bataller, R, Singal, AK. **A Validated Score Predicts Acute Kidney Injury and Survival in Patients With Alcoholic Hepatitis.** *Liver Transplant.* 2018;24:1655-1664.F.I.:3.752. [doi:10.1002/lt.25328]

17. Miravittles, M, Sliwinski, P, Rhee, CK, Costello, RW, Carter, V, Tan, J, Lapperre, TS, Alcazar, B, Gouder, C, Esquinas, C, Garcia-Rivero, JL, Kempainen, A, Tee, A, Roman-Rodriguez, M, Soler-Cataluna, JJ, Price, DB. **Evaluation of criteria for clinical control in a prospective, international, multicenter study of patients with COPD.** *Respir. Med.* 2018;136:8-14.F.I.:3.230. [doi:10.1016/j.rmed.2018.01.019]

18. Martínez-Rivera, C, Crespo, A, Pinedo-Sierra, C, Garcia-Rivero, JL, Pallares-Sanmartin, A, Marina-Malanda, N, Pascual-Erquicia, S, Padilla, A, Mayorlas-Alises, S, Plaza, V, Lopez-Vina, A, Picado, C. **Mucus hypersecretion in asthma is associated with rhinosinusitis, polyps and exacerbations.** *Respir.*

Med.2018;135:22-28.FI.:3.230.
[doi:10.1016/j.rmed.2017.12.013]

19. Massey, VL, Qin, LY, Cabezas, J, Caballeria, J, Sancho-Bru, P, Bataller, R, Crews, FT. TLR7-let-7 Signaling Contributes to Ethanol-Induced Hepatic Inflammatory Response in Mice and in Alcoholic Hepatitis.

Alcoholism (NY). 2018;42:2107-2122.FI.:3.183. [doi:10.1111/acer.13871]

20. Giampieri, F, Afrin, S, Stewart, D, McDougall, GJ, Brennan, R, Blyth, L, Gasparrini, M, Mazzoni, L, Capocasa, F, Alvarez-Suarez, JM, Bompadre, S, Nogueira Brás de Oliveira P, N Santos C, Masias, M, Agudo, P, Crespo, J, Mezzetti, B, Forbes-Hernandez, TY, Battino, M. Phytochemical Composition and Cytotoxic Effects on Liver Hepatocellular Carcinoma Cells of Different Berries Following a Simulated In Vitro Gastrointestinal Digestion. MOLECULES.

2018;23:FI.:3.098. [doi:10.3390/molecules23081918]

21. Gausman, V, Kandel, P, Van Riet, PA, Moris, M, Kayal, M, Do, C, Poneris, JM, Sethi, A, Gress, FG, Schrope, BA, Luk, L, Hecht, E, Jovani, M, Bruno, MJ, Cahen, DL, Wallace, MB, Gonda, TA. Predictors of Progression Among Low-Risk Intraductal Papillary Mucinous Neoplasms in a Multicenter Surveillance Cohort. PANCREAS. 2018;47:471-476.FI.:2.958. [doi:10.1097/MPA.0000000000001027]

22. Monsalve-Hernando, C, Crespo, L, Ferreiro, B, Martin, V, Aldeguer, X, Opio, V, Fernandez-Gil, PL, Gaspar, MJ, Romero, E, Lara, C, Santander, C, Torrealba, L, Savescu, T, Hermida, C. Phase IV noninferiority controlled randomized trial to evaluate the impact on diagnostic thinking and patient management and the test-retest reproducibility of the Gaxilose test for hypolactasia diagnosis. Medicine (Baltimore). 2018;97:FI.:2.028. [doi:10.1097/MD.00000000000013136]

23. Fortea, JI, Puente, A, Ruiz, P, Ezcurra, I, Vaquero, J, Cuadrado, A, Arias-Loste, MT, Cabezas, J, Llerena, S, Iruzubieta, P, Rodriguez-Lope, C, Huelin, P, Casafont, F, Fabrega, E, Crespo, J. Impact of an acute hemodynamic response-guided protocol for primary prophylaxis of variceal bleeding. World J. Clin.

Cases. 2018;6:611-623.FI.:1.931.
[doi:10.12998/wjcc.v6.i13.611]

Crespo, J, Teran, A. Endoscopy and sedation: an inseparable binomial for the gastroenterologist. Rev. Esp. Enferm. Dig.2018;110:250-252.FI.:1.632. [doi:10.17235/reed.2018.5585/2018]

24. Parés A, Albillos A, Andrade RJ, Berenguer M, Crespo J, Romero-Gómez M, Vergara M, Vendrell B, Gil A. Primary biliary cholangitis in Spain. Results of a Delphi study of epidemiology, diagnosis, follow-up and treatment. Rev. Esp. Enferm. Dig.2018;110:641-649.FI.:1.632. [doi:10.17235/reed.2018.5665/2018]

25. Albeniz, E, Pellise, M, Gimeno García AZ, Lucendo, AJ, Alonso Aguirre PA, Herreros de Tejada A, Alvarez, MA, Fraile, M, Herráiz Bayod M, López Rosés L, Martínez Ares D, Ono, A, Parra Blanco A, Redondo, E, Sánchez Yagüe A, Soto, S, Díaz Tasende J, Montes Díaz M, Tellez, MR, Garcia, O, Zuñiga Ripa A, Hernández Conde M, Alberca de Las Parras F, Gargallo, C, Saperas, E, Navas, MM, Gordillo, J, Ramos Zabala F, Echevarria, JM, ..., en nombre del Grupo Español de Resección Endoscópica de la Sociedad Española de. Clinical guidelines for endoscopic mucosal resection of non-pedunculated colorectal lesions. Gastroenterol. Hepatol.2018;41:175-190.FI.:1.078. [doi:10.1016/j.gastrohep.2017.08.013]

26. Aller, R, Fernandez-Rodríguez, C, Lo Iacono, O, Bañares R, Abad, J, Carrion, JA, Garcia-Monzon, C, Caballeria, J, Berenguer, M, Rodriguez-Peralvarez, M, López Miranda J, Vilar-Gomez, E, Crespo, J, Garcia-Cortes, M, Reig, M, Navarro, JM, Gallego-Duran, R, Genesca, J, Arias-Loste, MT, Pareja, MJ, Albillos, A, Muntane, J, Jorquera, F, Sola, E, Hernandez-Guerra, M, Rojo, MA, Salmeron, J, Caballeria, L, Diago, M, ..., Romero-Gomez, M. Consensus document. Management of non-alcoholic fatty liver disease (NAFLD). Clinical practice guideline. Gastroenterol. Hepatol.2018;41:475-476.FI.:1.078. [doi:10.1016/j.gastrohep.2018.05.011]

27. Aller, R, Fernandez-Rodríguez, C, lo Iacono, O, Bañares R, Abad, J, Carrion, JA, Garcia-Monzon, C, Caballeria, J, Berenguer, M, Rodriguez-Peralvarez, M, Miranda, JL, Vilar-Gomez, E, Crespo, J, Garcia-Cortes, M, Reig, M, Navarro, JM, Gallego, R,

Genesca, J, Arias-Loste, MT, Pareja, MJ, Albillos, A, Muntane, J, Jorquera, F, Sola, E, Hernandez-Guerra, M, Rojo, MA, Salmeron, J, Caballeria, L, Diago, M, ..., Romero-Gomez, M. Consensus document. Management of non-alcoholic fatty liver disease (NAFLD). Clinical practice guideline. Gastroenterol. Hepatol.2018;41:328-349.FI.:1.078. [doi:10.1016/j.gastrohep.2017.12.003]

28. Barreiro-de Acosta, M, Marin-Jimenez, I, Panadero, A, Guardiola, J, Cañas M, Gobbo Montoya M, Modino, Y, Alcain, G, Bosca-Watts, MM, Calvet, X, Casellas, F, Chaparro, M, Fernández Salazar L, Ferreiro-Iglesias, R, Ginard, D, Iborra, M, Manceñido N, Mañosa M, Merino, O, Rivero, M, Roncero, O, Sempere, L, Vega, P, Zabana, Y, Minguez, M, Nos, P, Gisbert, JP. Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) and the Association of Crohn's Disease and Ulcerative Colitis Patients (ACCU) in the management of psychological problems in Inflammatory Bowel Disease patients. Gastroenterol. Hepatol.2018;41:118-127.FI.:1.078. [doi:10.1016/j.gastrohep.2017.10.003]

29. Val-Bernal, JF, Martino, M, Yllera-Contreras, E, Castro-Senosian, B, Bueno-Ortiz, P. Intrapancreatic accessory spleen. Report of four cases diagnosed by ultrasound-guided fine-needle aspiration biopsy. Rom. J. Morphol. Embryol.2018;59:619-624.FI.:0.912.

30. Fernández Torres M, Angulo López I, Ruiz Bueno P, González Martínez M, Ruiz de Alegría Puig C, Rodríguez Lozano J, Agüero Balbín J, Crespo García J, Calvo Montes J. Spontaneous bacterial peritonitis caused by Listeria monocytogenes: eight case reports (1992-2017) and literature review. Rev. Esp. Quim.2018;31:532-536.FI.:0.605.

Reviews

1. Albéniz E, Pellisé M, Gimeno-García AZ, Lucendo AJ, Alonso-Aguirre PA, Herreros de Tejada A, Álvarez MA, Fraile M, Herráiz Bayod M, López Rosés L, Martínez Ares D, Ono A, Parra Blanco A, Redondo E, Sánchez-Yagüe A, Soto S, Díaz-Tasende J, Montes Díaz

M, Rodríguez-Téllez M, García O, Zuñiga Ripa A, Hernández Conde M, Alberca de Las Parras F, Gargallo CJ, Saperas E, Muñoz Navas M, Gordillo J, Ramos Zabala F, Echevarría JM, ..., Valdivielso E. **Clinical guidelines for endoscopic mucosal resection of non-pedunculated colorectal lesions.** Rev. Esp. Enferm. Dig. 2018;110:179-194.F.I.:1.632. [doi:10.17235/reed.2018.5086/2017]

Projects

1. Emilio Fábrega García. **CI06/16 FABREGA GARCIA, EMILIO.** CI06/16.

2. Montserrat Rivero Tirado. **CI 08/11 RIVERO TIRADO MONTSERRAT (REMICADE).** CI0811.

3. Montserrat Rivero Tirado. **Estudio observacional postautorización "Estudio de 5 años, no intervencionista, de registro de datos de Humira® (ADALIMUMAB) en pacientes con enfermedad de Crohn (EC) activa moderada a grave".** CI0927.

4. María Teresa Arias Loste. **Implicación de diferentes factores de la inmunidad innata y adaptativa en la etiopatogenia de la enfermedad hepática por depósito de grasa en pacientes con obesidad mórbida.** FEAD12/08. FUNDACION ESPAÑOLA DEL APARATO DIGESTIVO "FEAD".

5. Javier Crespo García. **Ayuda por Producción al Grupo de Infección en Inmunidad y Patología Digestiva.** APG/19.

6. Javier Crespo García. **Disfunción endotelial, ateromatosis subclínica y miocardiopatía en pacientes con infección por VHC. Caracterización y potencial reversibilidad con agentes antivirales directos.** PI15/02138. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

7. Javier Crespo García. **Personalized Medicine in HCV infection: understanding and predicting hepatic and systemic responses in the era of the new antiviral drugs.** PIE15/00079. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

8. Javier Crespo García. **Donaciones para el desarrollo de proyectos de investigación. BDP01.** ALLERGAN, S.A., ABBVIE SPAIN, S.L.U..

9. Javier Crespo García. **Contrato de servicios de investigación para el Estudio de la prevalencia de la Hepatitis C en la población española en 2015.** CSI15/10. MERCK SHARP & DHOME ESPAÑA.

10. Ángela María Puente Sánchez. **Regresión de la fibrosis hepática tras erradicación del virus de la hepatitis C.** Papel de la LOXL2. NVAL15/12.

11. Ángela María Puente Sánchez. **Contrato de servicios de investigación para el Estudio controlado y aleatorizado sobre la seguridad y eficacia del uso de heparinas de bajo peso molecular en la prevención de episodios trombóticos en pacientes cirróticos hospitalizados.** CSI16/05. LABORATORIOS FARMACEUTICOS ROVI, S.A..

12. Montserrat Rivero Tirado. **Convenio para la gestión del ensayo con código ABB-ADA-2013-01. Estudio observacional postautorización. Registro no intervencionista de larga duración para evaluar la seguridad y la efectividad de HUMIRA (ADALIMUMAB) en pacientes con colitis ulcerosa (CU) de actividad moderada a grave (LEGACY).** CCI16/10.

13. Javier Crespo García. **Contrato de servicios de investigación para el proyecto Program of screening, prevention and elimination of hepatitis C in Penitentiary Institutions in Cantabria, JAILFREE-C.** CSI16/02. GILEAD SCIENCES, INC.

14. Javier Crespo García. **Convenio para la gestión del ensayo con código H-030-014. Ensayo de eficacia, inmunogenicidad y seguridad de la vacuna de toxoides de CLOSTRIDIUM DIFFICILE en sujetos en riesgo de desarrollar infección por C. DIFFICILE (H-030-14).** CCI16/11. SANOFI PASTEUR INC.

15. José Pedro Vaqué Díez. **Nuevos mecanismos en cánceres agresivos de la piel: Aplicaciones**

al diagnóstico, pronóstico y terapia de melanoma resistente a terapia y carcinoma de células de Merkel. PI16/00156. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

16. María Teresa Arias Loste. **Repercusión de la hipercapnia crónica, con o sin hipoxia, a nivel hepático. Estudio en cultivo de hepatocitos y validación en una cohorte de pacientes con enfermedad hepática por depósito de grasa procedentes de práctica clínica habitual.** NVAL16/02.

17. Fernando Casafont Morencos. **Contrato de servicios de investigación para el proyecto Preceptorship en Trasplante Hepático y Hepato-Renal en el Hospital Universitario Marqués de Valdecilla.** CSI17/10. NOVARTIS ARGENTINA, S.A..

18. Javier Crespo García. **Curso de Capacitación en la creación de programas de evaluación integral y eliminación de la hepatitis C en prisiones y otros centros de internamiento.** GILEAD17/10. GILEAD SCIENCES, S.L.U., GILEAD SCIENCES, S.L.U..

19. José Ignacio Fortea Ormaechea. **Determinación no invasiva a través de biomarcadores del descenso de la presión portal al tratamiento con fármacos betabloqueantes en pacientes con cirrosis.** NVAL17/07.

20. José Pedro Vaqué Díez. **Caracterización de la ruta CREB1 y su papel en el desarrollo y progresión de MCC en la era de la inmunoterapia. Implicaciones en diagnóstico y terapia.** INVAL17/21.

21. Ángela María Puente Sánchez. **Beca para asistir a 3 Congresos.** GORE17/26. W.L.GORE Y ASOCIADOS, S.L..

22. Javier Crespo García. **XI edición del Aula Abierta Multidisciplinar en Hepatología.** GILEAD17/30. GILEAD SCIENCES, S.L.U..

23. Javier Crespo García. **Acuerdo de cooperación en el programa de becas de investigación científica de IDIVAL.** CI17/53/02. JANSSEN-CILAG, S.A., JANSSEN-CILAG, S.A..

24. Javier Crespo García. **Educación y seguimiento estrecho de pacientes con cirrosis hepática descompensada. Mejoría en calidad de vida, reingresos y mortalidad.** INCVAL17/04.

25. Montserrat Rivero Tirado. **Proyecto de Telemedicina para la asistencia de pacientes con Enfermedad Inflamatoria Intestinal: Creación y evaluación de una plataforma web para personal sanitario y pacientes.** INCVAL17/07.

26. Javier Crespo García. **Convenio de colaboración para el desarrollo del proyecto de investigación Nuevos marcadores clínicos para el diagnóstico y tratamiento de carcinoma hepatocelular del Grupo de infección e inmunidad y patología digestiva de IDIVAL.** CI18/10. ASOCIACION LUCHAMOS POR LA VIDA.

27. Javier Crespo García. **Esteatohepatitis no alcohólica como enfermedad inflamatoria inmunomediada. Prevalencia y caracterización.** Estudio INSTInCT. PI18/01304. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

28. Javier Crespo García. **Contrato de servicios de investigación para el estudio Prevalence of Antimitochondrial M2 Antibody in Spanish Population.** CS118/27. INTERCEPT PHARMA SPAIN, S.L.U. INTERCEPT.

29. Javier Crespo García. **Contrato de prestación de servicios para el desarrollo del proyecto Colorectal cancer omics collection.** CS118/18. UNIVERSAL DIAGNOSTICS, S.L..

30. Javier Crespo García. **Acuerdo de cooperación en el programa de becas de investigación científica de IDIVAL.** CI18/67/02. JANSSEN-CILAG, S.A..

31. Javier Crespo García. **Diagnosis and Characterization of Non-Alcoholic Fatty Liver Disease based on Artificial Intelligence.** GILEAD18/33. GILEAD SCIENCES, S.L.U..

32. José Pedro Vaqué Díez. **Convenio de colaboración para el desarrollo**

del poryecto "Nuevos mecanismos para el diagnóstico y tratamiento de cánceres agresivos de la piel: linfoma cutáneo de células T(CTCL) y carcinoma de células de Merkel (MCC)". CI19/18. ASOCIACIÓN LUCHAMOS POR LA VIDA.

33. Francisco Javier Jiménez Pérez. **Acuerdo de beca educativa para el apoyo de la participación de profesionales sanitarios en eventos educativos.** CI19/04. BOSTON SCIENTIFIC IBERICA S.A., BOSTON SCIENTIFIC IBERICA S.A..

34. Javier Crespo Garcia. **Convenio de donación en especie Modelo Mylab TM Six, objeto del presente documento y el donante dado el interés científico y de asistencia sanitaria que se derivan de las actividades desarrolladas por IDIVAL.** CI19/11. ABBVIE SPAIN, S.L.U..

Clinical Trials

1. Montserrat Rivero Tirado. **Estudio de Fase III, de grupos paralelos, controlado con placebo, doble ciego, aleatorizado, multicéntrico, internacional, para investigar la seguridad y eficacia de los comprimidos de liberación modificada de propionil-L-carnitina clorhidrato (ST 261) en pacientes afectados por colitis ulcerosa leve bajo tratamiento oral estable.** ST261 DM 11 006. SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A..

2. Javier Crespo García. **Estudio fase 3 de daclatasvir en combinación con peginterferón lambda 1a y ribavirina (RBV) o telaprevir en combinación con peginterferón alfa-2a y RBV en pacientes con hepatitis C crónica con genotipo 1b que no han recibido tratamiento previo o recidivantes previos al tratamiento con alfa/RBV.** AI452-021. BRISTOL-MYERS SQUIBB INTERNATIONAL CORPORATION (BMSIC).

3. Javier Crespo García. **Ensayo clínico aleatorizado de fase III para evaluar la eficacia y la seguridad del régimen en combinación de MK 5172/MK 8742 en sujetos que han presentado fracaso con un tratamiento previo con interferón pegilado y ribavirina (P/R) con infección crónica por el VHC GT1, GT4, GT5 y GT6.** 5172-068.

MERCK, SHARP&DOHME CORP. (MERCK).

4. Javier Crespo García. **Estudio abierto y multicéntrico para evaluar los resultados a largo plazo con ABT 450/ritonavir/ABT 267 (ABT 450/r/ABT 267) y ABT 333 con o sin ribavirina (RBV) en adultos con infección crónica por el virus de la hepatitis C (VHC) de genotipo 1 (TOPAZ I).** M14-423. ABBVIE DEUTSCHLAND GMBH&CO K.G.

5. Javier Crespo García. **Ensayo clínico de fase II, aleatorizado y abierto para estudiar la eficacia y la seguridad de la combinación de MK-5172 y MK-3682 con MK-8742 o MK-8408 en sujetos con infección crónica por el VHC de GT1, GT2 y GT4.** MK3682-011. MERCK, SHARP&DOHME CORP. (MERCK).

6. Carlos Rodríguez de Lope López. **Estudio de fase III, aleatorizado, doble ciego, controlado con simulación de ThermoDox® (doxorubicina liposomal liso-termosensible-LTLD) en carcinoma hepatocelular (HCC) utilizando un tiempo de tratamiento de ablación con radiofrecuencia estandarizado (RFA) ≥ 45 minutos para lesiones solitarias de ≥ 3 cm a ≤ 7 cm.** 104-13-302. CELSION CORPORATION, INC.

7. Javier Crespo García. **Estudio de Seguimiento a Largo Plazo para Evaluar la Durabilidad de la Respuesta Viroológica y/o los Patrones de Resistencia Viral de Sujetos con Hepatitis C Crónica que Han sido Tratados Previamente con MK-5172 en un Ensayo Clínico Previo.** 5172-017. MERCK, SHARP&DOHME CORP. (MERCK).

8. Javier Crespo García. **Estudio Fase 3, multicéntrico, abierto, con una sola rama de tratamiento para investigar la eficacia y seguridad de un régimen de tratamiento de 12 semanas de Simeprevir en combinación con Sofosbuvir en pacientes con infección crónica por el virus de la hepatitis C de genotipo 4, que no han recibido tratamiento previo o previamente tratados.** TMC435HPC3021. JANSSEN R&D IRELAND.

9. Javier Crespo García. **Ensayo de eficacia, inmunogenicidad y**

seguridad de la vacuna de toxoides de *Clostridium difficile* en sujetos en riesgo de desarrollar infección por *C. difficile*. H-030-014.

10. Javier Crespo García. **Estudio de fase 3, multicéntrico, aleatorizado, con doble enmascaramiento, a largo plazo y controlado con placebo para evaluar la seguridad y la eficacia del ácido obeticoólico en sujetos con esteatohepatitis no alcohólica.** 747-303. INTERCEPT PHARMACEUTICALS INC..

11. Javier Crespo García. **Estudio fase I, doble ciego, aleatorizado, controlado con placebo, de primera administración en humanos de JNJ-56136379 administrado vía oral para examinar la seguridad, tolerabilidad y farmacocinética tras dosis únicas ascendentes y un régimen de dosis múltiple en voluntarios sanos (Parte I), y tras varios regímenes de dosis múltiple en sujetos con hepatitis B crónica (Parte II).** 56136379HPB1001. JANSSEN SCIENCES IRELAND UC..

12. Javier Crespo García. **Estudio de fase II, abierto, multicéntrico, aleatorizado para evaluar la eficacia y seguridad de la combinación a dosis fija (CDF) de sofosbuvir/velpatasvir y la CDF de sofosbuvir/velpatasvir más ribavirina en pacientes con infección crónica por el VHC de genotipo 3 y cirrosis.** GS-US-342-2097. GILEAD SCIENCES, INC.

13. Javier Crespo García. **Ensayo Multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar emricasán (IDN 6556), un inhibidor de la caspasa de administración oral, en sujetos con Fibrosis por Esteatohepatitis no alcohólica (EHNA).** IDN-6556-12. PPD GLOBAL LTD.

14. Javier Crespo García. **Ensayo multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar emricasán, un inhibidor de la caspasa de administración oral, en sujetos con cirrosis por esteatohepatitis no alcohólica (EHNA) e hipertensión portal grave.** IDN-6556-14. PPD GLOBAL LTD.

15. Javier Crespo García. **Estudio aleatorizado, doble ciego, controlado con placebo, multicéntrico, de rango de dosis de prueba de concepto**

y de 24 semanas de tratamiento con IVA337 en pacientes adultos con esteatohepatitis no alcohólica (EHNA). **A randomized, double-blind, placebo-controlled, multicenter, dose-range, proof-of-concept, 24-week treatment study of IVA337 in adult subjects with nonalcoholic steatohepatitis (NASH).** IVA_01_337_HNAS_16_002. INVENTIVA SAS.

16. Javier Crespo García. **Estudio de fase III, multicéntrico, aleatorizado, doble ciego, controlado con placebo para evaluar la eficacia y seguridad de Elafibranor en pacientes con esteatohepatitis no alcohólica (EHNA) y fibrosis.** GFT505-315-1.

17. Javier Crespo García. **Investigación sobre la eficacia y la seguridad de tres niveles de dosis de semaglutida subcutánea administrada una vez al día frente a placebo en sujetos con esteatohepatitis no alcohólica.** Ensayo clínico de 72 semanas de duración, aleatorizado, doble-cego, controlado con placebo, con tres grupos paralelos, multicéntrico, multinacional. NN9931-4296. NOVO NORDISK PHARMA, S.A..

18. Montserrat Rivero Tirado. **Estudio en fase IIb, doble ciego, aleatorizado, controlado con placebo, con grupos paralelos y de búsqueda de dosis de PF-06651600 y PF-06700841 por vía oral como tratamiento de inducción y tratamiento crónico en pacientes con colitis ulcerosa moderada o grave.** B7981005. ICON CLINICAL RESEARCH LIMITED.

19. Javier Crespo García. **Estudio en fase III, aleatorizado, doble ciego y controlado con placebo para evaluar la seguridad y la eficacia de selonsertib en pacientes con cirrosis compensada debida a esteatohepatitis no alcohólica (EHNA).** GS-US-384-1944. GILEAD SCIENCES, INC.

20. Montserrat Rivero Tirado. **Estudio de prueba de concepto de BI 655130 como tratamiento complementario en pacientes con colitis ulcerosa activa de leve a moderada durante tratamiento con un inhibidor de TNF.** 1368.10. BOEHRINGER INGELHEIM ESPAÑA, S.A..

21. Javier Crespo García. **Estudio de fase III, aleatorizado, doble ciego,**

controlado con placebo para evaluar la seguridad y eficacia de selonsertib en pacientes con esteatohepatitis no alcohólica (EHNA) y fibrosis en puentes (F3). GS-US-384-1943. GILEAD SCIENCES, INC.

22. Javier Crespo García. **Ensayo fase II, multicéntrico, doble ciego, aleatorizado, de grupos paralelos y controlados con placebo para investigar la seguridad, tolerabilidad, farmacodinámica y farmacocinética de distintas dosis orales de BI 1467335 durante 12 semanas de tratamiento, en comparación con placebo en pacientes con evidencia clínica de EHNA.** 1386.4. BOEHRINGER INGELHEIM ESPAÑA, S.A..

23. Javier Crespo García. **AURORA: Estudio de fase III, multicéntrico, aleatorizado, con doble enmascaramiento, controlado con placebo, para evaluar la eficacia y seguridad de cenicriviroc para el tratamiento de la fibrosis hepática en pacientes adultos con esteatohepatitis no alcohólica.** 3152-301-002. ALLERGAN PHARMACEUTICAL INTERNATIONAL, LTD.,.

24. Javier Crespo García. **Estudio de fase 2a, aleatorizado, parcialmente ciego y controlado con placebo para evaluar la eficacia, la seguridad y la farmacocinética del tratamiento durante 24 semanas con dosis múltiples de JNJ-56136379 en monoterapia y en combinación con un análogo de nucleós(t)idos en pacientes con infección crónica por el virus de la hepatitis B.** 56136379HPB2001 (JADE). JANSSEN-CILAG, S.A..

25. Montserrat Rivero Tirado. **Estudio de fase IIIb, multicéntrico, aleatorizado, enmascarado ciego y controlado con fármaco activo para comparar la eficacia y seguridad de ustekinumab frente a adalimumab en el tratamiento de pacientes con enfermedad de Crohn con actividad moderada o grave previamente no tratados con fármacos biológicos.** CNT01275CRD3007 (SEAVUE). JANSSEN-CILAG, S.A..

26. Javier Crespo García. **Estudio en fase II, aleatorizado, doble ciego, controlado con placebo**

y de intervalo de dosis para evaluar la seguridad, tolerabilidad, farmacocinética y eficacia de EDP-305 en pacientes con colangitis biliar primaria (CBP) con o sin respuesta insuficiente al ácido ursodesoxicólico (AUDC). EDP 305-201.

27. Javier Crespo García. **Estudio de inducción en fase III, multicéntrico, aleatorizado, doble ciego, de grupos paralelos y controlados con placebo sobre mirikizumab en pacientes con fracaso convencional y biológico con colitis ulcerosa activa de moderada a grave.** I6T-MC-AMAN. ELI LILLY & COMPANY.

28. Javier Crespo García. **Estudio de mantenimiento en fase III, multicéntrico, aleatorizado, doble ciego, de grupos paralelos, controlado con placebo sobre mirikizumab en pacientes con colitis ulcerosa activa de moderada a grave.** I6T-MC-AMBG.

29. Javier Crespo García. **Estudio multicéntrico, aleatorizado, doble ciego para evaluar la seguridad, tolerabilidad y eficacia de un tratamiento que combina tropifexor (LJN452) y cenicriviroc (CVC) en pacientes adultos con esteatohepatitis no alcohólica (EHNA) y fibrosis hepática (TANDEM).** CLJC242A2201J. NOVARTIS FARMACEUTICA, S.A..

30. Montserrat Rivero Tirado. **Estudio de inducción multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar la eficacia y la seguridad de upadacitinib (ABT-494) en sujetos con enfermedad de Crohn de moderada a grave que han tenido una respuesta insuficiente o intolerancia a un tratamiento biológico.** M14-431. ABBVIE DEUTSCHLAND GMBH&CO K.G.

31. Javier Crespo García. **Estudio de fase 3, doble ciego, aleatorizado, controlado con placebo, multicéntrico para evaluar la eficacia y la seguridad del ácido obeticólico en pacientes con cirrosis compensada debida a esteatohepatitis no alcohólica.** 747-304. INTERCEPT PHARMACEUTICALS INC..

Postmarketing Studies and Other

1. Montserrat Rivero Tirado. **Registro no intervencionista de larga duración para evaluar la seguridad y la efectividad de HUMIRA® (adalimumab) en pacientes con colitis ulcerosa (CU) moderada activa o muy activa (LEGACY).** ABB-ADA-2013-01. ABBVIE SPAIN, S.L.U..

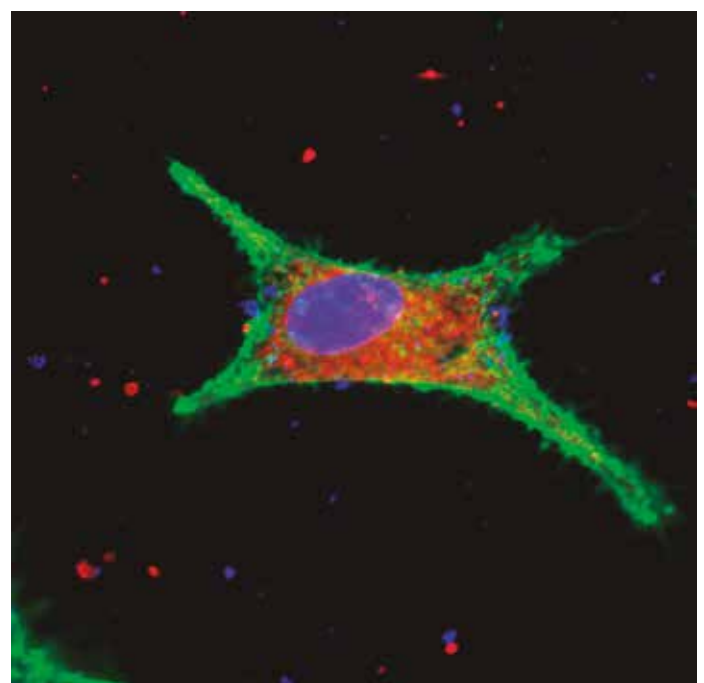
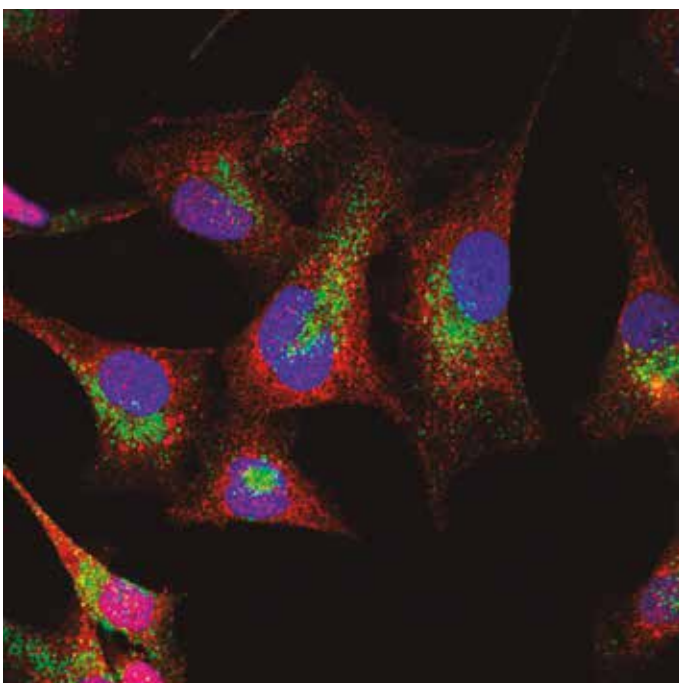
2. Montserrat Rivero Tirado. **Estudio observacional postautorización de**

seguridad ... of Golimumab in UC Using the Spanish ENEIDA Registry. MK8259-042-00.

Collaborations

Total Impact factor: 7.683

1. Medina-Caliz, I, García-Cortes, M, González-Jiménez, A, Cabello, MR, Robles-Díaz, M, Sanabria-Cabrera, J, Sanjuan-Jiménez, R, Ortega-Alonso, A, García-Munoz, B, Moreno, I, Jiménez-Pérez, M, Fernandez, MC, Gines, P, Prieto, M, Conde, I, Hallal, H, Soriano, G, Roman, E, Castiella, A, Blanco-Reina, E, Montes, MR, Quiros-Cano, M, Martín-Reyes, F, Lucena, MI, Andrade, RJ. **Herbal and Dietary Supplement-Induced Liver Injuries in the Spanish DILI Registry.** *Clin Gastroenterol Hepatol.* 2018;16:1495-1502.FI.:7.683. [doi:10.1016/j.cgh.2017.12.051]



○ Haematologic Neoplasms and Haematopoietic Stem Cells Transplantation



Consolidated group

Researchers

Carlos Pipaón González

Contributors

Lorena Álvarez Rodríguez

Cristina Amunárriz Águeda

José Luis Arroyo Rodríguez

María Ana Batlle López

María Aránzazu Bermúdez

Rodríguez

Sara Bravo Navas

Group Responsible

Enrique M^a Ocio San Miguel

Hematology Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



enriquem.ocio@scsalud.es

Montserrat Briz del Blanco
M^a de Las Mercedes Colorado Araujo
Miguel Ángel Cortes Vázquez
Sonia González De Villambrosía Pellón
Belén González-Mesones Galán
Andrés Insunza Gaminde
Mónica López Duarte
Guillermo Martín Sánchez
Carmen Montes Gaisán
María Josefa Muruzabal Sitges
Javier Núñez Céspedes
Rocío Pérez Montes
Carlos Richard Espiga
Iñigo Romón Alonso
Miriam Sánchez Escamilla
Lucrecia Yáñez San Segundo

Nurses

María del Carmen
García Casquero

Technicians

Aitana Altí Rodríguez
María Pilar González Echezarreta
Óscar Muñoz Pello
Alberto Vázquez de Castro Nogales

○ Research lines

Line 1. Cellular biology of hemopathies

1. Molecular characterization of hematological neoplasms (with special focus on the epigenetic modulation of the BCL6 and MYC genes), as well as the application of new molecular techniques for the search of new markers with early diagnostic potential and of application for monitoring and the search for therapeutic targets

2. Analysis of post-translational modifications in chronic lymphatic leukemia: study of the prognostic value and therapeutic applications. Study of purine analogue resistance mediated by kinases.

3. Biology and molecular genetics of MDS: prospective tracking of alterations in the FA-BRACA route.

Line 2. Therapeutic innovation

1. Preclinical evaluation of new therapeutic strategies in hematological neoplasms directed against specific targets of the tumor cell and their translation to the clinic.

2. Start-up and conduct of clinical trials in early stages (I and II) for different hematological diseases, both promoted by the industry and by cooperative groups.

3. Participation in clinical trials in advanced stages (III) in hematological diseases.

4. Clinical research of new strategies to improve the efficiency, results and quality of life of patients. Among others: optimization of the management of anticoagulant therapies; improvement of blood products and transfusion activity; collaboration with the Home Hospitalization unit.

Line 3. Transplant of hematopoietic progenitors, cellular therapy and immunotherapy

1. Improvement of the clinical results of allo-TPH in patients with different neoplastic pathologies
2. Study of different immunosuppression modalities, including post-transplant cyclophosphamide in high-risk allogeneic transplant.
3. Search for new therapeutic strategies in acute or chronic EHC, such as infusion of patient CMN treated with metopso-psoralen and subjected to extracorporeal phototherapy.
4. Research on the application of specific anti-CMV vaccine in patients with hematopoietic allogeneic transplantation to reduce associated complications.
5. Research (from the preclinical to the clinic) of new cell therapy strategies in patients with hematological diseases subjected or not to transplantation of hematopoietic progenitors: Clinical application of lymphocyte immunotherapy with modified T-receptor (CAR-T) in lymphoid neoplasms, mesenchymal cells for the treatment of GVHD of allogeneic transplantation and cell populations against CMV and EBV viruses

PUBLICATIONS

IMPACT FACTOR | 79.432

Original articles

1. Rodríguez-Otero, P, Mateos, MV, Martínez-López, J, Martín-Calvo, N, Hernández, MT, Ocio, EM, Rosiñol L, Martínez, R, Teruel, AI, Gutierrez, NC, Bargay, J, Bengoechea, E, Gonzalez, Y, de Oteyza, JP, Gironella, M, Encinas, C, Martín, J, Cabrera, C, Palomera, L, de Arriba, F, Cedena, MT, Paiva, B, Puig, N, Oriol, A, Blade, J, Lahuerta, JJ, San Miguel, JF. **Early myeloma-related death in elderly patients: development of a clinical prognostic score and evaluation of response sustainability**. *role. Leukemia*. 2018;32:2427-2434.F.I.:10.023. [doi:10.1038/s41375-018-0072-6]
2. Ruiz-Heredia, Y, Sánchez-Vega, B, Onecha, E, Barrio, S, Alonso, R, Martínez-Avila, JC, Cuenca, I, Agirre, X, Braggio, E, Hernandez, MT, Martínez, R, Rosiñol L, Gutierrez, N, Martín-Ramos, M, Ocio, EM, Echeveste, MA, de Oteyza, JP, Oriol, A, Bargay, J, Gironella, M, Ayala, R, Blade, J, Mateos, MV, Kortum, KM, Stewart, K, García-Sanz, R, Miguel JS, Lahuerta, JJ, Martínez-López, J. **Mutational screening of newly diagnosed multiple myeloma patients by deep targeted sequencing. Haematologica**. 2018;103:544-548.F.I.:9.090. [doi:10.3324/haematol.2018.188839]
3. van Straaten, S, Bierings, M, Bianchi, P, Akiyoshi, K, Kanno, H, Badell Serra I, Chen, J, Huang, XH, van Beers, E, Ekwattanakit, S, Güngör T, Kors, WA, Smiers, F, Raymakers, R, Yanez, L, Sevilla, J, van Solinge, W, Segovia, JC, van Wijk, R. **Worldwide study of hematopoietic allogeneic stem cell transplantation in pyruvate kinase deficiency. Haematologica**. 2018;103:82-86.F.I.:9.090. [doi:10.3324/haematol.2017.177857]
4. Catoya Villa S, Martínez-Losas, P, Sánchez Ceña J, de Tapia Majado B, Colorado, M, Canteli Álvarez Á. **Malignant Pericardial Effusion as a Presentation of AIDS: The Role of Flow Cytometry in Early Diagnosis**. *Rev. Esp. Cardiol*.2018;71:764-765.F.I.:5.166. [doi:10.1016/j.recesp.2017.05.016]
5. Montalban, C, Díaz-López, A, Martín, A, Baile, M, Sánchez, JM, Sancho, JM, García, O, Novelli, S, Monter-Rovira, A, Salar, A, Bastos, M, Gutierrez, A, Bento, L, Córdoba R, Arquero, T, González de Villambrosia S, Barranco, G, De Oña R, López Guillermo A, Rodríguez Salazar MJ, Dominguez, JF, Fernández, R, Queizan, JA, Rodríguez, J, Abraira, V, Garcia, JF, GELTAMO-IPI Project Investigators. **Differential prognostic impact of GELTAMO-IPI in cell of origin subtypes of Diffuse Large B Cell Lymphoma as defined by the Hans algorithm. Br J Haematol**. 2018;182:534-541.F.I.:5.128. [doi:10.1111/bjh.15446]
6. Avivi, I, Boumendil, A, Finel, H, Nagler, A, de Sousa, AB, Santasusana JMR, Vandenberghe, E, Afanasyev, B, Bordessoule, D, Moraleda, JM, Garcia, EC, Pohleisch, D, Garcia, GG, Thomson, K, Or, R, Beelen, D, Zuffa, E, Giebel, S, Berthou, C, Salles, G, Melpignano, A, Montoto, S, Dreger, P. **Autologous stem cell transplantation for primary mediastinal B-cell lymphoma: long-term outcome and role of post-transplant radiotherapy. A report of the European Society for Blood and Marrow Transplantation. Bone Marrow Transplant**.2018;53:1001-1009.F.I.:4.497. [doi:10.1038/s41409-017-0063-7]
7. Jiménez-Ubieto, A, Grande, C, Caballero, D, Yáñez L, Hernández-García, MT, Novelli, S, Arranz, R, Ferreira, JJ, Bobillo, S, Mercadal, S, Galeo, A, Jimenez, JL, Moraleda, JM, Vallejo, C, Albo, C, Perez, E, Marrero, C, Magnano, L, Palomera, L, Jarque, I, Martínez-Sánchez, P, Martín, A, Coria, E, Lopez-Guillermo, A, Salar, A, Lahuerta, JJ, GELTAMO (Grupo Español de Linfomas y Trasplantes de Médula Ósea) Cooperative Stu. **Secondary malignancies and survival outcomes after autologous stem cell transplantation for follicular lymphoma in the pre-rituximab and rituximab eras: a long-term follow-up analysis from the Spanish GELTAMO registry**. *Bone Marrow Transplant*.2018;53:780-783.F.I.:4.497. [doi:10.1038/s41409-018-0096-6]
8. García, D, Aguilera, A, Antolin, F, Arroyo, JL, Lozano, M, Sanroma, P, Romon, I. **Home transfusion: three decades of practice at a tertiary care hospital. Transfusion**. 2018;58:2309-2319.F.I.:3.423. [doi:10.1111/trf.14816]
9. Steegmann, JL, Colomer, D, Gomez-Casares, MT, Garcia-Gutierrez, V, Orti, G, Ramirez-Payer, A, Olavarria, E, Vall-Llovera, F, Giraldo, P, Conde, E, Vallansot, R, Lopez-Lorenzo, JL, Palomera, L, Alvarez-Larran, A, Conesa, V, Bautista, G, Casas, L, Giles, F, Hochhaus, A, Casado-Montero, LF. **An analysis of the kinetics of molecular response during the first trimester of treatment with nilotinib in newly diagnosed chronic myeloid leukemia patients in chronic phase (vol 143, pg 2059, 2017). J. Cancer Res. Clin. Oncol**.2018;144:187-188.F.I.:3.282. [doi:10.1007/s00432-017-2532-1]

10. Jiménez-Ubieto, A, Grande, C, Caballero, D, Yáñez L, Novelli, S, Hernández-García, MT, Manzanares, M, Arranz, R, Ferreiro, JJ, Bobillo, S, Mercadal, S, Galeo, A, Jiménez, JL, Moraleda, JM, Vallejo, C, Albo, C, Perez, E, Marrero, C, Magnano, L, Palomera, L, Jarque, I, Martínez-Sánchez, P, Martín, A, Coria, E, Lopez-Guillermo, A, Salar, A, Lahuerta, JJ, GELTAMO (Grupo Español de Linfomas y Trasplantes de Médula Ósea) Cooperative Stu. **Autologous stem cell transplantation may be curative for patients with follicular lymphoma with early therapy failure who reach complete response after rescue treatment.** *Hematol. Oncol.* 2018;36:765-772.FI.:3.193. [doi:10.1002/hon.2553]

11. Bobillo, S, Abrisqueta, P, Sánchez-Gonzalez, B, Gine, E, Romero, S, Alcoceba, M, González-Barca, E, González de Villambrosía Pellón, Sonia, Sancho, JM, Gomez, P, Bento, L, Montoro, J, Montes, S, López, A, Bosch, F, Grupo Español de Linfomas/ Trasplante Autólogo de Médula Ósea (GEL/TAMO cooperati. **Posttransplant monomorphic Burkitt's lymphoma: clinical characteristics and outcome of a multicenter series.** *Ann. Hematol.* 2018;97:2417-2424.FI.:2.845. [doi:10.1007/s00277-018-3473-8]

12. Pérez-Rodríguez, A, Batlle, J, Corrales, I, Borràs N, Rodríguez-Trillo, A, Loures, E, Cid, AR, Bonanad, S, Cabrera, N, Moret, A, Parra, R, Mingot-Castellano, ME, Navarro, N, Altisent, C, Perez-Montes, R, Marcellini, S, Moreto, A, Herrero, S, Soto, I, Fernández Mosteirín N, Jimenez-Yuste, V, Alonso, N, de Andrés Jacob A, Fontanes, E, Campos, R, Paloma, MJ, Bermejo, N, Berruoco, R, Mateo, J, ..., López-Fernández, MF. **Role of multimeric analysis of von Willebrand factor (VWF) in von Willebrand disease (VWD) diagnosis: Lessons from the PCM-EVV-ES Spanish project.** *PLoS One.* 2018;13:FI.:2.766. [doi:10.1371/journal.pone.0197876]

13. Ribera, JM, Morgades, M, Montesinos, P, Martino, R, Barba, P, Soria, B, Bermúdez, A, Moreno, MJ, Gonzalez-Campos, J, Vives, S, Gil, C, Abella, E, Guàrdia R, Martínez-Carballeira, D, Martínez-Sánchez, P, Amigo, ML, Mercadal, S, Serrano, A, Lopez-Martinez, A, Vall-Llovera, F, Sanchez-Sanchez, MJ, Peñarrubia MJ, Calbacho, M, Mendez, JA, Bergua, J, Cladera, A,

Tormo, M, García-Belmonte, D, Feliu, E, ..., PETHEMA Group, Spanish Society of Hematology. **Efficacy and safety of native versus pegylated Escherichia coli asparaginase for treatment of adults with high-risk, Philadelphia chromosome-negative acute lymphoblastic leukemia.** *Leuk. Lymphoma.* 2018;59:1634-1643.FI.:2.644. [doi:10.1080/10428194.2017.1397661]

14. Gayoso, J, Balsalobre, P, Kwon, M, Herrera, P, Bermudez, A, Sampol, A, Jimenez, S, Lopez-Corral, L, Serrano, D, Piñana JL, Pascual, MJ, Heras, I, Bento, L, Varela, R, Humala, K, Zabalza, A, Laiglesia, A, Bastos-Oreiro, M, Perez-Corral, A, Martinez-Laperche, C, Buño I, Diez-Martin, JL, GETH (Grupo Español de Trasplante Hematopoyético) Spain. **Busulfan-based myeloablative conditioning regimens for haploidentical transplantation in high-risk acute leukemias and myelodysplastic syndromes.** *Eur J Haematol.* 2018;101:332-339.FI.:2.595. [doi:10.1111/ejh.13103]

15. Ribera, JM, Garcia, O, Gil, C, Mercadal, S, García-Cadenas, I, Montesinos, P, Barba, P, Vives, S, Gonzalez-Campos, J, Tormo, M, Esteve, J, Lopez, A, Moreno, MJ, Ribera, J, Alonso, N, Bermúdez, A, Amigo, ML, Genesca, E, Garcia, D, Vall-Llovera, F, Bergua, JM, Guàrdia R, Monteserin, MC, Bernal, T, Calbacho, M, Martinez, MP, Feliu, E, PETHEMA Group. **Comparison of intensive, pediatric-inspired therapy with non-intensive therapy in older adults aged 55-65 years with Philadelphia chromosome-negative acute lymphoblastic leukemia.** *Leuk. Res.* 2018;68:79-84.FI.:2.319. [doi:10.1016/j.leukres.2018.03.010]

16. Cañueto J, Ocio, EM, Roman-Curto, C. **Aggressive primary cutaneous CD30+lymphoproliferative disorder in an organ transplant recipient in sustained complete remission with brentuximab vedotin.** *Int. J. Dermatol.* 2018;57:153-155.FI.:1.541. [doi:10.1111/ijd.14214]

Reviews

1. Caers, J, Paiva, B, Zamagni, E, Leleu, X, Blade, J, Kristinsson, SY, Touzeau, C, Abildgaard, N, Terpos, E, Heusschen, R, Ocio, E, Delforge, M, Sezer, O, Beksac, M, Ludwig, H, Merlini, G, Moreau, P, Zweegman, S,

Engelhardt, M, Rosiñol L. **Diagnosis, treatment, and response assessment in solitary plasmacytoma: updated recommendations from a European Expert Panel.** *J. Hematol. Oncol.* 2018;11:10-10.FI.:7.333. [doi:10.1186/s13045-017-0549-1]

Projects

1. Carlos Pipaón González. **02/200700153 FANCOGENE. FANCOGENE.**
2. Carlos Richard Espiga. **Ayuda por producción al grupo de Neoplasias Hematológicas y Trasplante de Progenitores Hematopoyéticos.** APG/15.
3. Sonia González de Villambrosía Pellón. **Convenio para la gestión del ensayo con código CAMN107A2303. Estudio fase III, multicéntrico, abierto, aleatorizado de imatinib frente a nilotinib, en pacientes adultos con leucemia mieloide crónica cromosoma Filadelfia positivo (Ph+) en fase crónica (LMC-FC) de nuevo diagnóstico.** CCI14/15. NOVARTIS FARMACEUTICA, S.A..
4. Sonia González de Villambrosía Pellón. **Convenio para la gestión del ensayo con código CAMN107A2408. Estudio fase II abierto de único brazo de remisión libre de tratamiento después de conseguir una rm4.5 sostenida con nilotib.** CCI14/19. NOVARTIS FARMACEUTICA, S.A..
5. Carlos Richard Espiga. **Donación para el desarrollo de proyectos de investigación.** CI15/31. CELGENE S.L.
6. Lucrecia Yáñez San Segundo. **Convenio para la gestión del ensayo con código ACE-CL-006. Estudio de fase 3, aleatorizado, multicéntrico y abierto para evaluar la no inferioridad de acp-196 frente a ibrutinib en sujetos con leucemia linfocítica crónica de alto riesgo tratados previamente.** CCI16/09.
7. Carlos Pipaón González. **Papel de la neddilación en Leucemia Linfática Crónica, su valor pronóstico y aplicaciones terapéuticas.** PI17/01688. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
8. Carlos Pipaón González. **Estudio prospectivo del valor del gen PRKACA como marcador**

de respuesta a fludarabina.
INNVAL17/13.

9. María Aránzazu Bermúdez Rodríguez. **Convenio de colaboración para el desarrollo del proyecto de investigación MM Monitor: Base de datos de gestión hospitalaria de pacientes con mieloma múltiple.** C117/52/01. CELGENE S.L.

Clinical Trials

1. Sonia González de Villambrosía Pellón. **Estudio fase III, multicéntrico, abierto, aleatorizado de imatinib frente a nilotinib, en pacientes adultos con leucemia mieloide crónica cromosoma Filadelfia positivo (Ph+) en fase crónica (LMC-FC) de nuevo diagnóstico, versión 19 de junio de 2007.** Modificación internacional nº 2 de 19 de junio de 2007, CAMN107A2303. NOVARTIS FARMACEUTICA, S.A..

2. María Aránzazu Bermúdez Rodríguez. **Estudio de fase III, multicéntrico, aleatorizado, abierto, para comparar la eficacia y seguridad de la Pomalidomida en combinación con dosis bajas de Dexametasona frente a dosis altas de Dexametasona en pacientes con Mieloma múltiple Refractorio o Recidivante y Refractario, Vs. de 15 de octubre de 2010, incluyendo los cambios implementados con la enmienda 1, HIP y CI para España, Vs de 14 de diciembre de 2010, basaso en la Vs maestra inglesa de 15 de octubre de 2010.** CC-4047-MM-003. CELGENE CORPORATION.

3. María Aránzazu Bermúdez Rodríguez. **Estudio Abierto, multicéntrico, de grupo único, para estudiar la seguridad y eficacia de Pomalidomida (cc-4047) en monoterapia en pacientes con mieloma múltiple refractario o recidivante y refractario, Vs. de 15 de octubre de 2010, incluyendo los cambios implementados con la enmienda 1, HIP y CI para España, Vs de 14 de diciembre de 2010, basaso en la Vs maestra inglesa de 15 de octubre de 2010.** CC-4047-MM-003/C. CELGENE CORPORATION.

4. Sonia González de Villambrosía Pellón. **Estudio Fase II, abierto, de un único brazo, de remisión libre de tratamiento en pacientes con Leucemia Mieloide Crónica (LMC)**

en fase crónica (FC) después de conseguir una RM4.5 sostenida con nilotinib. CAMN107A2408. NOVARTIS FARMACEUTICA, S.A..

5. María Aránzazu Bermúdez Rodríguez. **Estudio de fase 3 aleatorizado, doble ciego y controlado con placebo para evaluar la eficacia protectora y la seguridad de una vacuna terapéutica, ASP0113, en receptores seropositivos para el citomegalovirus (CMV) sometidos a alotrasplante de células hematopoyéticas (ATCH).** 0113-CL-1004. ASTELLAS PHARMA GLOBAL DEVELOPMENT, INC.

6. María Ana Batlle López. **Estudio fase II aleatorizado y multicéntrico de dos brazos de tratamiento (R-COMP versus R-CHOP) en pacientes de edad avanzada (>60años) con / infama difuso de células B grandes (LDCBG)/Linfoma folicular grado IIIb no localizado de nuevo diagnóstico.** GEL-R-COMP-2013. DYNAMIC SCIENCE, S.L..

7. Mª de las Mercedes Colorado Araujo. **Estudio Fase III, multicéntrico, aleatorizado, abierto de Azacitidina (Vidaza®) frente a Fludarabina y Citarabina (Esquema Fluga) en pacientes ancianos con leucemia mieloide aguda de nuevo diagnóstico.** FLUGAZA. FUNDACIÓN PETHEMA HOSPITAL CLÍNICO SAN CARLOS, SERV. HEMATOLOGÍA.

8. Lucrecia Yáñez San Segundo. **Estudio de fase 3, aleatorizado, multicéntrico y abierto para evaluar la no inferioridad de ACP 196 frente a Ibrutinib en sujetos con leucemia linfocítica crónica de alto riesgo tratados previamente.** ACE-CL-006. ACERTA PHARMA, BV..

9. Lucrecia Yáñez San Segundo. **Estudio de fase 3, aleatorizado, multicéntrico, abierto, con tres grupos, de Obinutuzumab en combinación con Clorambucilo, ACP 196 en combinación con Obinutuzumab y ACP 196 en monoterapia, en sujetos con leucemia linfocítica crónica sin tratamiento previo.** ACE-CL-007. ACERTA PHARMA, BV..

10. Lucrecia Yáñez San Segundo. **A Randomized, Multicenter, Open-Label, Phase 3 Study of Acalabrutinib (ACP-196) Versus Investigator's Choice of Either**

Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia. ACE-CL-309. ACERTA PHARMA, BV..

11. Lucrecia Yáñez San Segundo. **A Phase 3 Randomized Study of the Efficacy and Safety of Posaconazole versus Voriconazole for the Treatment of Invasive Aspergillosis in Adults and Adolescents (Phase 3; Protocol No. MK-5592-069).** 5592-069. MERCK, SHARP&DOHME CORP. (MERCK).

12. Mª de las Mercedes Colorado Araujo. **Estudio de fase III, doble ciego, controlado con placebo de quizartinib (AC220) administrado en combinación con quimioterapia de inducción y consolidación, y administrado como terapia de mantenimiento a sujetos de 18 a 75 años con leucemia mielógena aguda FLT3-ITD (+) de nuevo diagnóstico (QuANTUM First).** AC220-A-U302. DAIICHI SANKYO, INC.

13. María Aránzazu Bermúdez Rodríguez. **Estudio de fase 2, aleatorizado, con doble enmascaramiento y controlado con placebo para evaluar la eficacia y la tolerabilidad del Entospletinib, un inhibidor selectivo de SYK, en combinación con corticosteroides sistémicos como tratamiento de primera línea en pacientes con enfermedad crónica de injerto contra huésped (EICHc).** GS-US-406-1840. GILEAD SCIENCES, INC.

14. Carmen Montes Gaisán. **Ensayo clínico en fase III, aleatorizado, abierto y multicéntrico para comparar isatuximab (SAR650984) en combinación con pomalidomida y dosis bajas de dexametasona frente a pomalidomida y dosis bajas de dexametasona en pacientes con mieloma múltiple refractario o recidivante y refractario.** EFC14335.

15. Lucrecia Yáñez San Segundo. **Estudio de fase III aleatorizado, doble ciego y controlado con placebo, de itacitinib o placebo en combinación con corticosteroides para el tratamiento de primera línea de la enfermedad de injerto contra huésped en fase aguda.** INCB 39110-301. INCYTE CORPORATION.

16. Sonia González de Villambrosía Pellón. **Estudio en fase II de TAK-659**

en pacientes con linfoma difuso de células B grandes recidivante o resistente después de dos o más líneas previas de quimioterapia.

C34004. MILLENNIUM PHARMACEUTICALS, INC.

17. María Aránzazu Bermúdez Rodríguez. **Estudio de fase 3, multicéntrico, aleatorizado, doble ciego, con doble simulación, con control activo para evaluar la eficacia y la seguridad de maribavir en comparación con valganciclovir para el tratamiento de la infección por citomegalovirus (CMV) en receptores de un trasplante de células madre hematopoyéticas.** SHP620-302. SHIRE HUMAN GENETIC THERAPIES, INC..

18. María Aránzazu Bermúdez Rodríguez. **Ensayo Fase I, abierto, de búsqueda de dosis de CC-93269, un anticuerpo BCMA X CD3 de células T, en sujetos con mieloma múltiple en recaída y refractario.** CC-93269-MM-001. CELGENE INTERNATIONAL II S.À.R.L..

Postmarketing Studies and Other

1. Sonia González de Villambrosía Pellón. **El Gen MYC en los síndromes mielodisplásicos: papel en la patogenia de la enfermedad.** 2009.119. FUNDACIÓN MARQUÉS DE VALDECILLA.

2. Andrés Insunza Gaminde. **Estudio observacional post-autorización para evaluar la evolución en**

la práctica clínica habitual de pacientes recién diagnosticados de síndrome mielodisplásico (SMD) o leucemia mielomonocítica crónica (LMC), en función del momento de inicio de tratamiento activo. CEL-SMD-2012-01. CELGENE S.L..

3. Carmen Montes Gaisán. **Registro observacional post-autorización para evaluar el impacto clínico del inicio de la terapia antitumoral de rescate en pacientes con mieloma múltiple (MM) en recaída biológica asintomática frente al inicio del tratamiento en el momento de la recaída sintomática.** CEL-MIE-2012-02. CELGENE S.L..

4. Sonia González de Villambrosía Pellón. **Estudio observacional prospectivo para identificar los aspectos clínicos que conducen a la toma de decisiones terapéuticas en pacientes con mielofibrosis.".** Estudio TRATABILIDAD. GEM-MIE-2014-01. GRUPO ESPAÑOL DE ENFERMEDADES MIELOPROLIFERATIVAS CRÓNICAS PH NEGATIVAS GEMFIN.

5. Andrés Insunza Gaminde. **EPAS Estudio Post-autorización de seguridad (EPAS) prospectivo, no intervencionista, diseñado como Registro de Enfermedad de pacientes con síndromes mielodisplásicos (SMD) de bajo riesgo (IPSS bajo e intermedio-1) con delección 5q aislada y dependencia transfusional.** CC-5013-MDS-010. CELGENE INTERNATIONAL SARL.

6. Rocío Pérez Montes. **Estudio para la verificación del funcionamiento del Sistema microINR por parte del usuario no profesional.** QA-01-2016-01-P. ILINE MICROSYSTEMS, S.L..

7. Carmen Montes Gaisán. **Caracterización Clínico-Sociodemográfica de los pacientes con mieloma múltiple en recaída sintomática y/o refractarios en España.** TAK-MMR-2017-01. TAKEDA FARMACEUTICA ESPAÑA, S.A..

Other publications

Thesis Addressed 2018

1. Susana Hernández García. **Evaluación del efecto sinérgico del inhibidor de la "Kinesin Spindle Protein" Filanesib (arry-520) en combinación con fármacos inmunomoduladores en modelos preclínicos de Mieloma Múltiple.** Director/s: Enrique María Ocio San Miguel, Teresa Paino. UNIVERSIDAD DE SALAMANCA.



○ Transplantation and Autoimmunity



Consolidated group

Researchers

Manuel Antonio Arias Rodríguez
Victor Manuel Martínez Taboada
Eduardo Miñambres García
Emilio Rodrigo Calabia

Contributors

María De Los Ángeles Ballesteros Sanz
Paloma Barreda Monteoliva
Lara Belmar Vega

Adalberto Benito Hernández
Gema Fernández Fresnedo
José Óscar García Ruiz
María Milagros Heras Vicario
María Kislikova
Luis Martín Penagos
María José Ortiz González
Ana Rosa Palanca Cuñado
Rosa Palomar Fontanet
Vicente Celestino Piñera Haces
M^a Ángeles Ramos Barrón

Group Responsible

Marcos López Hoyos

Immunogy Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



marcos.lopez@scsalud.es



Juan Carlos Ruiz San Millán
David San Segundo Arribas
Cristina Serrano
Mara Serrano Soto
Jorge Alberto Suárez Rodríguez
Silvia Torices del Val
Rosalia Valero San Cecilio
Ana Victoria Villar Ramos

Nurses

M^a Consuelo Agüeros Blanco
Montserrat González García
Raquel Pelayo Alonso
María del Camino
Villa Llamazares

Predoctoral

María Iglesias Escudero
David Maestro Lavín
Jorge Ruiz del Río

Technicians

Sandra Raso Torres

○ Research lines

Line 1: Transplantation of solid organs

1. Non-invasive biomarkers in blood and urine of clinical

events transplant related of **solid organs** (rejection, infection, immunosuppression conversion, short-term and long-term graft survival). This line focuses on soluble and cellular markers related to the immune response in allotransplantation and more recently. In addition, we included the study of molecular profiles predictive of failure of renal function and

increase of fibrosis in initial stages. Together with our own studies, we participated in REDINREN (Research Network on Renal Diseases: RD16 / 0009/027). At the same time, we have transferred the study of biomarkers to lung transplantation since it is a very potent clinical activity in our center, which has already allowed us to obtain results quickly, which have demonstrated specific

differences between kidney and lung transplantation. Soluble markers of humoral rejection. This line of research has made it possible to transfer to the clinic the monitoring of anti-HLA antibodies in desensitization treatments in renal transplants of patients hypersensitized with live donors. Thanks to this line, our center attracts patients from other regions and has allowed us to be part of the national cross-renal donation program. This line of work is also included in the REDINREN program and we lead within the network. We consider this line one of the greatest potential of clinical transference.

2. Immunoregulation in kidney and lung transplantation. To evaluate the effect that changes in blood and tissues of cellular populations with immunoregulatory capacity may have on the long-term evolution of the transplant in general and of the renal in particular. In the case of renal transplantation we have found a clear influence of the level of pharmacological immunosuppression on the number and function of regulatory T cells. In addition, in lung transplantation we have verified how a certain number of regulatory T cells in blood prior to transplantation play a prognostic role in the incidence of rejection. This line together with the previous one receives regular competitive financing from the ISCIII.

3. Intensive treatment of donors to increase the number of grafts suitable for transplantation. Intensive treatment of multiorgan donors based on specific ventilatory therapy, extrapulmonary water-guided hemodynamic goals, and hormone therapy increases the number of transplantable pulmonary grafts. This increase in the number of available pulmonary grafts is due to the improvement in oxygenation of the lungs in the period between death and organ harvesting. This specific treatment is associated with an increase in the rest of organs to improve the perfusion and oxygenation of all of them.

The use of regional normothermic perfusion to deceased donors by circulatory criteria has allowed to reduce the ischemic damage of the grafts due to the deleterious effect of the cardiac arrest, and to simultaneously extract and successfully transplant all types of grafts (lungs, liver, Pancreas and kidneys). Both lines of research have

developed multicentric studies with funding from the Mutua Madrileña Foundation.

Line 2: Inflammation and autoimmune diseases

1. Inflammatory diseases associated with aging (giant cell arteritis, polymyalgia rheumatica and rheumatoid arthritis of onset in the elderly). These syndromes, which are very prevalent in the elderly population, are mainly treated with corticosteroids, which are accompanied by a high toxicity. Studies investigate the role of cytokines, regulatory cells and alterations of innate immunity, with the ultimate goal of developing less toxic and more effective therapies. We used cellular markers (phenotypic and functional), serological and genetic (expression and genetic polymorphisms). More recently we have started a line of work on arthritis in connection with FIS-funded FG-beta signaling.

2. Antiphospholipid syndrome. The role that the innate immune response (specifically the TLR) and the different immunoregulatory populations may play in the pathogenesis of this disease is studied. We also analyzed the clinical results of the Unit of Autoimmune Gravidarum Pathology and performed a beta study to evaluate new methods of measurement of diagnostic antibodies in this pathology. In particular, we are validating the usefulness of new immunoglobulin isotypes (IgA) against phospholipids as well as the value of other antibodies against other phospholipids not included in the diagnostic criteria so far.

3. Biomarkers. The group has a large library associated with clinical data collected since 1997. This library allows the study and validation of new markers involved in the diagnosis, prognosis and response to the treatment of autoimmune pathology. In addition, we have all the type of tests necessary for the development and serological studies of autoimmunity. As a result of the exploitation of this library we have defined new diagnostic uses of antibodies not explored until now (anti-PR3) in pathologies such as inflammatory bowel disease with IDIVAL's group of digestive pathology.

Also using this library, we began to take the first steps in an ambitious

project that proposes the use of nanosensors as a tool in the diagnosis of patients with systemic diseases of unknown etiology such as scleroderma. We intend to perform the concept test, implementation and tuning of the prototype diagnostic test plate for its application in the clinical environment.

PUBLICATIONS

IMPACT FACTOR | 99.042

Original articles

1. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Alvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setién E, Lopez-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. **Microenvironment Eradication of Hepatitis C: A Novel Treatment Paradigm.** *Am. J. Gastroenterol.* 2018;113:1639-1648.FI.:10.231. [doi:10.1038/s41395-018-0157-x]
2. Sarmiento, E, Cifrian, J, Calahorra, L, Bravo, C, Lopez, S, Laporta, R, Ussetti, P, Sole, A, Morales, C, de Pablos, A, Jaramillo, M, Ezzahouri, I, Garcia, S, Navarro, J, Lopez-Hoyos, M, Carbone, J. **Monitoring of early humoral immunity to identify lung recipients at risk for development of serious infections: A multicenter prospective study.** *J. Heart Lung Transplant.* 2018;37:1001-1012.FI.:7.955. [doi:10.1016/j.healun.2018.04.001]
3. Moreso, F, Crespo, M, Ruiz, JC, Torres, A, Gutierrez-Dalmau, A, Osuna, A, Perello, M, Pascual, J, Torres, IB, Redondo-Pachon, D, Rodrigo, E, Lopez-Hoyos, M, Seron, D. **Treatment of chronic antibody mediated rejection with intravenous immunoglobulins and**

rituximab: A multicenter, prospective, randomized, double-blind clinical trial. *Am. J. Transplant.*2018;18:927-935.FI.:6.493. [doi:10.1111/ajt.14520]

4. Gonzalez-Guerrero, C, Morgado-Pascual, JL, Cannata-Ortiz, P, Ramos-Barron, MA, Gomez-Alamillo, C, Arias, M, Mezzano, S, Egido, J, Ruiz-Ortega, M, Ortiz, A, Ramos, AM. **CCL20 blockade increases the severity of nephrotoxic folic acid-induced acute kidney injury.** *J. Pathol.*2018;246:191-204.FI.:6.253. [doi:10.1002/path.5132]

5. Morales, JM, Serrano, M, Martinez-Flores, JA, Gainza, FJ, Marcen, R, Arias, M, Escuin, F, Pérez, D, Andrés, A, Martínez, MA, Maruri, N, Alvarez, E, Castañer JL, Lopez-Hoyos, M, Serrano, A. **Pretransplant IgA-Anti-Beta 2 Glycoprotein I Antibodies As a Predictor of Early Graft Thrombosis after Renal Transplantation in the Clinical Practice: A Multicenter and Prospective Study.** *Front. Immunol.*2018;9:468-468.FI.:5.511. [doi:10.3389/fimmu.2018.00468]

6. Cáceres, RA, Chavez, T, Maestro, D, Palanca, AR, Bolado, P, Madrazo, F, Aires, A, Cortajarena, AL, Villar, AV. **Reduction of cardiac TGF beta-mediated profibrotic events by inhibition of Hsp90 with engineered protein.** *J. Mol. Cell. Cardiol.*2018;123:75-87.FI.:5.296. [doi:10.1016/j.yjmcc.2018.08.016]

7. Juncal-Ruiz, M, Riesco-Davila, L, de la Foz, VOG, Ramirez-Bonilla, M, Martinez-Garcia, O, Irure-Ventura, J, Leza, JC, Lopez-Hoyos, M, Crespo-Facorro, B. **The effect of excess weight on circulating inflammatory cytokines in drug-naive first-episode psychosis individuals.** *J. Neuroinflamm.*2018;15:63-63.FI.:5.193. [doi:10.1186/s12974-018-1096-6]

8. Llerena Santiago, Susana, García-Díaz N, Curiel del Olmo, Soraya, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, Helena, Varela M, Santibáñez Margüello, Miguel, Almaraz Pro, María del Carmen, Cereceda Company, Laura, Martínez Magunacelaya, Nerea, Arias Loste, María Teresa, Puente Á, Martín-Ramos L, Rodríguez de Lope López, Carlos, Castillo Suescun, Federico, Cagigas-Fernández C, Isidro P, López-López C, López Hoyos, 9. Marcos, Llorca Díaz, Javier, Agüero Balbín, Jesús, Crespo Facorro,

Benedicto, Varela I, Piris Pinilla, Miguel Ángel, Crespo García, Javier, Vaqué Díez, José Pedro. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR.** *Oncotarget.* 2018;9:30869-30882.FI.:5.168. [doi:10.18632/oncotarget.25766]

10. Narvaez, J, Borrell, H, Sánchez-Alonso, F, Rúa-Figueroa, I, Lopez-Longo, FJ, Galindo-Izquierdo, M, Calvo-Alen, J, Fernández-Nebro, A, Olive, A, Andreu, JL, Martínez-Taboada, V, Nolla, JM, Pego-Reigosa, JM, RELESSER Study Group. **Primary respiratory disease in patients with systemic lupus erythematosus: data from the Spanish rheumatology society lupus registry (RELESSER) cohort.** *Arthritis Res. Ther.*2018;20:280-280.FI.:4.269. [doi:10.1186/s13075-018-1776-8]

11. Ferrández, E, Gutiérrez, O, Segundo DS, Fernández-Luna, JL. **NF kappa B activation in differentiating glioblastoma stem-like cells is promoted by hyaluronic acid signaling through TLR4.** *Sci Rep.* 2018;8:6341-6341.FI.:4.122. [doi:10.1038/s41598-018-24444-6]

12. Juncal-Ruiz, M, Riesco-Davila, L, Ortiz García de la Foz, Víctor, Martínez-García, O, Ramírez-Bonilla, M, Ocejón-Vinals, JG, Leza, JC, López-Hoyos, M, Crespo-Facorro, B. **Comparison of the anti-inflammatory effect of aripiprazole and risperidone in 75 drug-naive first episode psychosis individuals: A3 months randomized study.** *Schizophr. Res.* 2018;202:226-233.FI.:3.958. [doi:10.1016/j.schres.2018.06.039]

13. Álvarez-Rodríguez, L, Riancho-Zarrabeitia, L, Calvo-Alen, J, López-Hoyos, M, Martínez-Taboada, V. **Peripheral B-Cell Subset Distribution in Primary Antiphospholipid Syndrome.** *Int. J. Mol. Sci.*2018;19:FI.:3.687. [doi:10.3390/ijms19020589]

14. de Las Vecillas, L, Bartolome-Zavala, B, Asensio, E, San Segundo, D, Rodriguez, F, Montecchiani, V, Anton, E. **Hypersensitivity to Chironomid Larvae in a Nonatopic Patient: Safe Diagnosis Tools to Identify a Potent Allergen.** *J. Invest. Allergol. Clin. Immunol.*2018;28:259-260.FI.:3.457. [doi:10.18176/jiaci.0250]

15. Herrera-Gomez, F, del Aguila, W, Tejero-Pedregosa, A, Adler, M, Padilla-Berdugo, R, Maurtua-Briseno-Meiggs, A, Pascual, J, Pascual, M, San Segundo D, Heidt, S, Alvarez, FJ, Ochoa-Sangrador, C, Lambert, C. **The number of FoxP3 regulatory T cells in the circulation may be a predictive biomarker for kidney transplant recipients: A multistage systematic review.** *Int. Immunopharmacol.*2018;65:483-492.FI.:3.118. [doi:10.1016/j.intimp.2018.10.028]

16. Coll, M, Ferrer-Costa, C, Pich, S, Allegue, C, Rodrigo, E, Fernandez-Fresnedo, G, Barreda, P, Mates, J, Martinez de Francisco AL, Ortega, I, Iglesias, A, Campuzano, O, Salas, E, Arias, M, Brugada, R. **Role of genetic and electrolyte abnormalities in prolonged QTc interval and sudden cardiac death in end-stage renal disease patients.** *PLoS One.* 2018;13:FI.:2.766. [doi:10.1371/journal.pone.0200756]

17. Villar, A, Zarrabeitia, MT, Fdez-Arroyabe, P, Santurtun, A. **Integrating and analyzing medical and environmental data using ETL and Business Intelligence tools.** *Int. J. Biometeorol.*2018;62:1085-1095.FI.:2.577. [doi:10.1007/s00484-018-1511-9]

18. Santurtun, A, Villar, A, Zarrabeitia, MT. **Who is legally responsible for deaths caused by air pollution?.** *Int. J. Biometeorol.*2018;62:2063-2064.FI.:2.577. [doi:10.1007/s00484-018-1616-1]

19. Ballesteros, MA, Rubio-Lopez, MI, San Martin, M, Padilla, A, Lopez-Hoyos, M, Llorca, J, Miñambres E. **Serum levels of S100B from jugular bulb as a biomarker of poor prognosis in patients with severe acute brain injury.** *J. Neurol. Sci.*2018;385:109-114.FI.:2.448. [doi:10.1016/j.jns.2017.12.017]

20. Fernández Castro M, Sánchez-Piedra, C, Andreu, JL, Martínez-Taboada V, Olive, A, Rosas, J, SJOGRENSER Group, part of the Spanish Society of Rheumatology Systemic Autoimmun. **Factors associated with severe dry eye in primary Sjogren's syndrome diagnosed patients.** *Rheumatol. Int.*2018;38:1075-1082.FI.:1.952. [doi:10.1007/s00296-018-4013-5]

21. González de Molina Ortiz FJ, Gordó Vidal F, Estella García A, Morondo Valdeolmillos P, Fernández Ortega JF, Caballero López J, Pérez Villares PV, Ballesteros Sanz MA, de Haro López C, Sanchez-Izquierdo Riera JA, Serrano Lázaro A, Fuset Cabanes MP, Terceros Almanza LJ, Nuvials Casals X, Baldirà Martínez de Irujo J, grupos de trabajo de la Sociedad Española de Medicina Intensiva, Crítica y Unida. **"Do not do" recommendations of the working groups of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) for the management of critically ill patients.** *Med. Intensiv.* 2018;42:425-443.F.I.:1.755. [doi:10.1016/j.medin.2018.04.001]

22. Monge Rafael P, Martin de Francisco AL, Fernandez-Fresnedo, G. **Denosumab an chronic kidney disease: Severe life-threatening hypocalcemia.** *Nefrologia.* 2018;38:97-98.F.I.:1.167. [doi:10.1016/j.nefro.2017.01.004]

23. Gonzalez-Castro, A, Ortiz-Lasa, M, Rodriguez-Borregan, JC, Rodrigo Calabia E, Ruiz San Millan JC, Dierssen Soto T. **Influence of Proportion of Normal Saline Administered in the Perioperative Period of Renal Transplantation on Kalemia Levels.** *Transplant Proc.* 2018;50:569-571.F.I.:0.806. [doi:10.1016/j.transproceed.2017.06.040]

24. Sáenz-Jalón, M, Ballesteros-Sanz, MA, Sarabia-Cobo, CM, Roscales-Bartolome, E, Fernández, MS, Canal-Cobo, G, Higuero-Piris, C, Velez-Carrera, B, Sanjuan, GV, García-Cobo, S, Torres-Manrique, B, Miguel Martín ME. **Assessment of the Pneumatic Ischemia Technique Using the Limb Occlusion Pressure During Upper Limb Surgery.** *J. PeriAnesthesia Nurs.* 2018;33:699-707.F.I.:0.748. [doi:10.1016/j.jopan.2016.08.017]

25. Chico-Fernández, M, Sánchez-Casado, M, Ballesteros-Sanz, MA, Llupart-Pou, JA. **Severe head injury in Spain.** *Neurocirugia.* 2018;29:107-108.F.I.:0.310. [doi:10.1016/j.neucir.2017.01.001]

Reviews

1. Riancho-Zarrabeitia, L, Cuberia, M, Muñoz P, Lopez-Hoyos, M, García-Canale, S, García-Unzueta, M, Hernández, JL, Martínez-Taboada,

VM. **Vitamin D and antiphospholipid syndrome: A retrospective cohort study and meta-analysis.** *Semin. Arthritis Rheum.* 2018;47:877-882.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.10.007]

2. Miñambres E, Rubio, JJ, Coll, E, Dominguez-Gil, B. **Donation after circulatory death and its expansion in Spain.** *Curr. Opin. Organ Transpl.* 2018;23:120-129.F.I.:2.869. [doi:10.1097/MOT.0000000000000480]

Projects

1. Juan Carlos Ruiz San Millán. CI 08/12 - ABBOT LABORATORIES, S.A (ESTUDIO VITAL). CI081201. Marcos López Hoyos. **Ayuda por Producción al Grupo de Investigación de Trasplante y Autoinmunidad.** APG/04. FUNDACIÓN INSTITUTO DE INVESTIGACIÓN MARQUÉS DE VALDECILLA IDIVAL.

2. Víctor Manuel Martínez Taboada. **Identificación de variantes génicas relevantes de la vía de NFkB y sus consecuencias funcionales en pacientes con artritis reumatoide.** *Influencia en el desarrollo y pronóstico de la enfermedad.* FER13/13. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R., FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

3. Gema Fernández Fresnedo. **Convenio para la gestión del ensayo con código M11-352.** *Ensayo multicéntrico, internacional, aleatorizado, doble ciego, con grupos paralelos y controlado con placebo del efecto del Atrasentan sobre los resultados renales de sujetos con diabetes tipo 2 y nefropatía.* **SONAR: Ensayo de nefropatía diabética con Atrasentan.** CCI15/04.

4. Manuel Antonio Arias Rodríguez. **Donaciones para el desarrollo de proyectos de investigación.** BDP06. **Eduardo Miñambres García.** *Efecto de la perfusión regional normotérmica sobre la modulación de la isquemia en la donación en asistolia controlada (Maastricht III). Correlación de biomarcadores séricos y anatomopatológico con la evolución posterior de los injertos hepáticos y renales.* FMM16/05.

FUNDACIÓN MUTUA MADRILEÑA. INVESTIGACIÓN MÉDICA.

5. Marcos López Hoyos. **Utilidad del estudio de las Células Mieloides Supresoras (MDSC) en la monitorización del trasplante renal.** PI16/01585. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

6. Víctor Manuel Martínez Taboada. **Estudio del papel BAMBÍ, un regulador de la señalización por TGFbeta, como factor patogénico y marcador pronóstico en la artritis reumatoide.** PI16/01717. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

7. Marcos López Hoyos. **Red de Investigación de Enfermedades Renales.** RD16/0009/0027. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

8. David San Segundo Arribas. **Células mieloides supresoras (MDSC) e inmunoregulación en trasplante renal: efecto diferencial entre inhibidores de calcineurina y de mTOR y evaluación como biomarcadores post-trasplante.** NVAL16/22.

9. Marcos López Hoyos. **PREVAL17/02 María Iglesias Escudero.** **PREVAL17/02.** UNIVERSIDAD DE CANTABRIA, FUNDACIÓN INSTITUTO DE INVESTIGACIÓN MARQUÉS DE VALDECILLA IDIVAL.

10. Marcos López Hoyos. **Contrato de servicios de investigación para el Estudio centralizado anticuerpos anti-HLA.** **CSI17/14.** FUNDACION INSTITUT DE RECERCA DEL HOSPITAL VALL D'HEBRON.

11. Ana Victoria Villar Ramos. **Proyecto: Nanosensor test for fibrosis diagnosis in scleroderma patients.** INVAL17/22.

12. Marcos López Hoyos. **Sistema analítico automatizado basado en biomarcadores fecales para el diagnóstico de enfermedades inflamatorias intestinales (CAL100).** **RTC-2017-6564-1.** MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES MINECO.

13. María Kislikova. **Cambios en la matriz de la media arterial en el contexto de uremia y enfermedad cardiovascular.** NVAL18/09.

14. Ana Rosa Palanca Cuñado. **Blood test for early diagnosis of escleroderma.** NVAL18/11.

15. Ana Victoria Villar Ramos. **Sistema de alerta genético para la protección contra la fibrosis cardiaca in vivo.** PREVAL19/05.

16. Emilio Rodrigo Calabia. **TRANSVAL18/01 EMILIO RODRIGO CALABIA.** TRANSVAL18/01.

17. Marcos López Hoyos. **Convenio de colaboración para la financiación de la asistencia al Congreso SEI de la Sociedad Española de Inmunología que se celebrará en Sevilla los días 30 de Mayo a 1 de Junio de 2019.** CI19/19. THE BINDING SITE LTD GROUP SUCURSAL EN ESPAÑA.

18. Marcos López Hoyos. **Convenio de colaboración para el desarrollo de proyectos de investigación en el Servicio de Inmunología del Hospital Universitario Marqués de Valdecilla.** CI19/21. DIAGNOSTICA LONGWOOD, S. L..

Clinical Trials

1. Juan Carlos Ruiz San Millán. **Estudio clínico abierto, multicéntrico, con dos ramas de tratamiento para investigar la función renal en un régimen inmunosupresor basado en advagraf® con o sin sirolimus en pacientes receptores de un trasplante renal.** PMR-EC-1212. ASTELLAS PHARMA, S.A..

2. Juan Carlos Ruiz San Millán. **Tratamiento con inmunoglobulinas y rituximab en el rechazo crónico humoral en el trasplante: Estudio multicéntrico, prospectivo, randomizado y controlado con placebo.** TRITON. SERÓN MICAS, DANIEL.

3. Gema Fernández Fresnedo. **Ensayo multicéntrico internacional, aleatorizado, doble ciego, con grupos paralelos y controlado con placebo del efecto de atrasentan sobre los resultados renales de sujetos con diabetes tipo 2 y nefropatía" SONAR: ensayo de nefropatía diabética con atrasentan.** M11-352. ABBVIE INC.

4. Gema Fernández Fresnedo. **Estudio aleatorizado, doble ciego, motivado por los acontecimientos, controlado con placebo y multicéntrico, de los efectos de la canagliflozina en los resultados renales y cardiovasculares en sujetos con diabetes mellitus tipo 2 y nefropatía diabética.** 28431754DNE3001. JANSSEN-CILAG INTERNATIONAL, NV.

Postmarketing Studies and Other

1. Vicente Celestino Piñera Haces. **Estudio no intervencionista para investigar la seguridad, la efectividad y la adherencia de Velphoro® a corto y a largo plazo en la vida real en pacientes con hiperfosfatemia sometidos a hemodiálisis o a diálisis peritoneal.** FRE-VEL-2016-01. KANTAR HEALTH S.A.U..

2. Juan Carlos Ruiz San Millán JUAN CARLOS RUÍZ SAN MILLÁN. **Estudio**

observacional y multicéntrico de farmacovigilancia (NI-PASS) sobre el uso de Binocrit. HX505-507.

Thesis Addressed 2018

1. María Lázaro Díez. **Interacciones clave Hospedador-Patógeno en especies de Acinetobacter de relevancia clínica.** Director/s: José Ramos Vivas, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.

2. María Juncal Ruiz. **Respuesta Inmunoinflamatoria sistémica en sujetos con un primer episodio psicótico.** Director/s: Benedicto Crespo Facorro, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.

Books and Book Chapters

1. Miñambres García, Eduardo. **Management of the potential donor after brain death. Guide to the Quality and Safety of Organs for Transplantation.** 2018.95-108.







o **Neurosciences
Area**

Benedicto Crespo Facorro

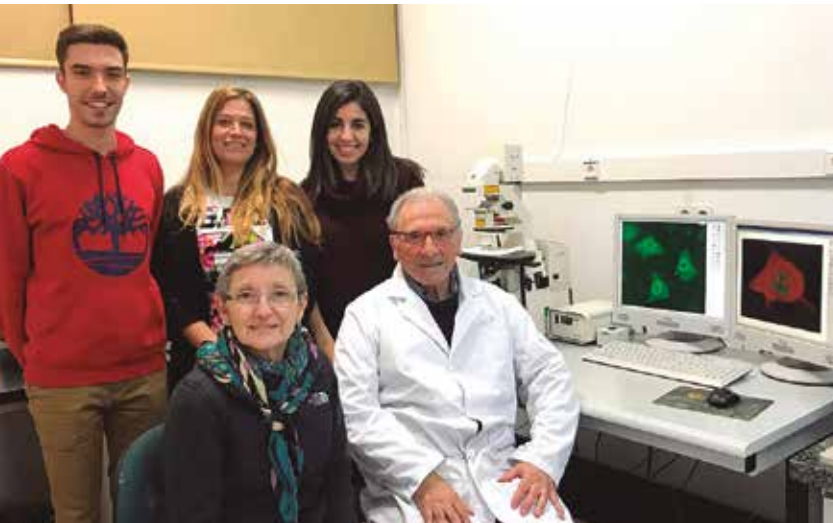
Coordinator of the
Neuroscience Area.

Section Chief, Psychiatry.

Hospital Universitario Marqués de
Valdecilla.

Professor of the Department
of Medicine and Psychiatry.
Universidad de Cantabria.

Nuclear Cell Biology



Consolidated group

Group Responsible

Miguel Ángel Lafarga Coscojuela

Department of Anatomy and Cell Biology

School of Medicine
Universidad de Cantabria



lafargam@unican.es

Researchers

Álvaro Rada Iglesias

Contributors

María Soledad Castillo Iglesias

Nazel Diban Gómez

Olga Tapia Martínez

Ane Urriaga Mendía

Predocctoral

Jorge Mata Garrido

Josep Oriol Narcis Majos

Jointly Responsible

María Teresa Berciano Blanco

Research lines

Line 1. Role of motor neuron survival factor (SMN) acetylation in the Cajal nuclear body assembly (Cajal body, CB): importance in spinal muscular atrophy (SMA).

The core of Cajal (CB, Fig. 1) is the nuclear power plant that directs the final assembly and quality control of the snRNPs and snoRNPs (small nuclear nucleolar ribonucleoproteins) involved in the splicing of pre-mRNAs and in the maturation of pre-rRNAs. The

mutation in the gene encoding one of its essential proteins, SMN (Survival Motor Neuron), is responsible for spinal muscular atrophy (SMA), which causes motor neuron degeneration and is the main cause of genetic-based mortality in the childhood. In addition to SMNs and snRNPs and snoRNPs, another essential component of CB is the coilin nucleating protein. The fundamental objective of this line is to analyze the mechanisms that regulate the molecular assembly of the CB and its importance in the SMA. We have recently shown that the SMN protein is a substrate of SUMO1 and that its conjugation with SUMO is another factor regulating the formation of CBs. We are currently studying the impact of another post-translational modification of SMN, acetylation, on the assembly of snRNPs and snoRNPs and the formation of CBs. Our preliminary experiments indicate that SMN is acetylated by acetyltransferase and CBP analysis with mass spectrometry demonstrates that acetylation modifies the interactions of the SMN with its target proteins, affecting the cellular

localization of the protein and its ability to nuclear CBs.

Line 2. Importance of dysfunction of nuclear compartments of spinal motor neurons in the cellular and molecular pathophysiology of spinal muscular atrophy (SMA) in murine model SMNd7.

As discussed above, mutation or deletion of the SMN1 gene in SMA produces a severe deficiency of the functional SMN protein, leading to degeneration and death of spinal neurons. In the pathophysiology of SMA, three essential mechanisms exist at the level of spinal motoneurons: splicing dysfunction of pre-mRNAs, axonal transport alterations and dysfunction of the neuromuscular synapse. All of them contribute to neurodegeneration and, consequently, to atrophy and muscular paralysis. Our research focuses on deepening the nuclear mechanisms affected by the disease, which results in an alteration of the nuclear metabolism of the RNAs in

the motoneurons (Fig. 2). SMA has reported a deficit in the assembly of snRNPs for the spliceosome, the molecular machinery that governs the splicing of pre-mRNAs. The Cajal nuclear body (CB) is a nuclear power plant that governs the assembly and nuclear trafficking of snRNPs and snoRNPs to the spliceosome and nucleolus, respectively. In this context, we consider that the loss of CBs and their interactions with the nucleolus, required for the transport of snoRNPs involved in nucleolar processing of rRNAs, are responsible for the severe disruption of splicing and biogenesis of ribosomes in the motoneurons of The SMA. To investigate these nuclear mechanisms we used the transgenic mouse SMNd7 as a model of SMA type I, the most severe that causes the degeneration of motor neurons and death of animals between postnatal days 13 and 16.

Line 3. Neuronal response to DNA damage: importance in neurodegeneration. There is growing evidence in the literature that defects in DNA repair and the consequent accumulation of DNA lesions play an important role in the molecular pathophysiology of multiple neurodegenerative processes. Our goal is to analyze the nuclear processing of DNA damage in normal, ganglionic and cerebral cortex neurons irradiated with X-rays (4 Gy) to induce DNA double-strand breaks. In this model we have observed that most of the neuronal DNA breaks are repaired in the first 24 hours, but there are persistent foci of unrepaired DNA that remain for months in a specific nuclear compartment. We have characterized the structural, molecular and spatial organization of this nuclear compartment as well as its transcriptional repression (Fig. 3). In addition we are characterizing with ChIP-seq techniques DNA sequences enriched in the "persistent foci" of cortical neurons. We have identified 17 sequences associated with genes essential for neuronal homeostasis whose dysfunction is related to pictures of human neuropathology. This line opens a new horizon that should allow to identify neural genes very vulnerable to DNA damage or difficult to repair, whose accumulation of lesions may be involved in neurodegenerative diseases

PUBLICATIONS

IMPACT FACTOR | 37.805

Original articles

1. Lafarga, V, Tapia, O, Sharma, S, Bengoechea, R, Stoecklin, G, Lafarga, M, Berciano, MT. **CBP-mediated SMN acetylation modulates Cajal body biogenesis and the cytoplasmic targeting of SMN.** *Cell. Mol. Life Sci.* 2018;75:527-546.F.I.:6.721. [doi:10.1007/s00018-017-2638-2]
2. Rueda, N, Vidal, V, García-Cerro, S, Narcis, JO, Llorens-Martin, M, Corrales, A, Lantigua, S, Iglesias, M, Merino, J, Merino, R, Martínez-Cue, C. **Anti-IL17 treatment ameliorates Down syndrome phenotypes in mice.** *Brain Behav. Immun.* 2018;73:235-251.F.I.:6.306. [doi:10.1016/j.bbi.2018.05.008]
3. Mata-Garrido, J, Tapia, O, Casafont, I, Berciano, MT, Cuadrado, A, Lafarga, M. **Persistent accumulation of unrepaired DNA damage in rat cortical neurons: nuclear organization and ChIP-seq analysis of damaged DNA.** *Acta Neuropathol. Commun.* 2018;6:68-68.F.I.:5.414. [doi:10.1186/s40478-018-0573-6]
4. García-Cerro, S, Vidal, V, Lantigua, S, Berciano, MT, Lafarga, M, Ramos-Cabrer, P, Padro, D, Rueda, N, Martínez-Cue, C. **Cerebellar alterations in a model of Down syndrome: The role of the Dyrk1A gene.** *Neurobiol. Dis.* 2018;110:206-217.F.I.:5.227. [doi:10.1016/j.nbd.2017.12.002]
5. Narcis, JO, Tapia, O, Tarabal, O, Piedrafita, L, Caldero, J, Berciano, MT, Lafarga, M. **Accumulation of poly(A) RNA in nuclear granules enriched in Sam68 in motor neurons from the SMN Delta 7 mouse model of SMA.** *Sci Rep.* 2018;8:9646-9646.F.I.:4.122. [doi:10.1038/s41598-018-27821-3]

Reviews

1. Gerace, L, Tapia, O. **Messages from the voices within: regulation of signaling by proteins of the nuclear lamina.** *Curr. Opin. Cell Biol.* 2018;52:14-21.F.I.:10.015. [doi:10.1016/j.ceb.2017.12.009]

Proyectos

1. Miguel Ángel Lafarga Coscojuela. **Ayuda por Producción al Grupo de Biología Celular del Núcleo.** APG/09.
2. Olga Tapia Martínez. **La atrofia muscular espinal (SMA).** NVAL17/22.
3. Olga Tapia Martínez. **Diseño de estructuras biopoliméricas funcionalizadas con grafeno para el desarrollo de cultivos neuronales en modelos celulares de patología de la motoneurona.** INVAL17/20.

Other publications

Authorship Thesis 2017

1. Jorge Mata Garrido, María Teresa Berciano Blanco, Miguel Ángel Lafarga Coscojuela. **Organización y dinámica de los focos nucleares permanentes de reparación del daño del DNA en Neuromas.** UNIVERSIDAD DE CANTABRIA.

Books and Book Chapters

1. Riancho Zarrabeitia, Javier, Ruiz Soto, María, Terán Villagra, Nuria, Berciano Blanco, José Ángel, Berciano Blanco, María Teresa, Lafarga Coscojuela, Miguel Ángel. **Compensatory motor neuron response to chromatolysis in the murine hSOD1-G93-A model of amyotrophic lateral sclerosis.** *Compensatory Mechanisms in Neurodegenerative Disorders.* 2017.

Headache Clinic and Genetics



Associated group

Researchers

Agustín Oterino Durán

Neurology Service

Hospital Universitario Marqués de Valdecilla



agustin.oterino@gmail.com

Researchers

Julio Pascual Gómez

Colaboradores

Jesús Castillo Obeso
 Vicente González Quintanilla
 Rosa María Martínez Nieto
 Silvia Montes Gómez
 Enrique Jesús Palacio Portilla
 Sata Pérez Pereda
 Estrella Quintela Obregón
 Álvaro Rada Iglesias
 María Toriello Suárez

Nurses

Silvia Gutiérrez González

Research lines

1. Genetics of migraines.

The group has maintained its epidemiological-clinical and basic research activity (mainly in genetic association studies) in the field of cephalalgias. Within this first aspect, we should highlight the demonstration of the dose-dependent association between migraines and tobacco, and studies focusing on proving the usefulness of new neuromodulators (topiramate and zonisamide) in the treatment of refractory chronic migraines. In the field of genetics, the epistatic interaction of genes related to oestrogen metabolism in migraines (oestrogen receptor ESR2) has been described in 594 subjects grouped in 132 families, confirming

the existence of a genetic factor in the pathogenesis of migraines as related to sex hormones; we further researched the association of genes of the folate metabolic pathway and migraines, confirming the association of migraines with aura and high homocysteine levels. We have recently demonstrated that there is significant endothelial activation in migraine sufferers and that this activation is more pronounced in chronic migraines. Furthermore, we demonstrated that there are variants of certain subunits of GABA associated with migraines in general.

2. Clinical and Genetic Research in Multiple Sclerosis.

- HLA haplotype study regarding the origin within the region. Influence of HLA on multiple sclerosis.
- Study of vascular damage associated with Multiple Sclerosis by analysing circulating endothelial cells: the

correlation of endothelial activation with the severity and stage of the disease.

PUBLICATIONS

IMPACT FACTOR | 17.167

Original articles

1. Moreso, F, Crespo, M, Ruiz, JC, Torres, A, Gutierrez-Dalmau, A, Osuna, A, Perello, M, Pascual, J, Torres, IB, Redondo-Pachon, D, Rodrigo, E, Lopez-Hoyos, M, Seron, D. **Treatment of chronic antibody mediated rejection with intravenous immunoglobulins and rituximab: A multicenter, prospective, randomized, double-blind clinical trial. Am. J. Transplant.** 2018;18:927-935.F.I.:6.493. [doi:10.1111/ajt.14520]

2. Ramos, ML, Garcia-Cabo, C, Leira, R, Dominguez, C, Pozo-Rosich, P, Vila, C, Lainez, MJ, Pascual, J. **Comorbidity between idiopathic overactive bladder and chronic migraine. Cephalalgia.** 2018;38:581-584.FI.:3.882. [doi:10.1177/0333102417690127]

3. Herrera-Gomez, F, del Aguila, W, Tejero-Pedregosa, A, Adler, M, Padilla-Berdugo, R, Murtua-Briseno-Meiggs, A, Pascual, J, Pascual, M, San Segundo D, Heidt, S, Alvarez, FJ, Ochoa-Sangrador, C, Lambert, C. **The number of FoxP3 regulatory T cells in the circulation may be a predictive biomarker for kidney transplant recipients: A multistage systematic review. Int. Immunopharmacol.**2018;65:483-492.FI.:3.118. [doi:10.1016/j.intimp.2018.10.028]

4. Olmos, JM, Hernandez, JL, Martinez, J, Pariente, E, Castillo, J, Prieto-Alhambra, D, Gonzalez-Macias, J. **Prevalence of vertebral fracture and densitometric osteoporosis in Spanish adult men: The Camargo Cohort Study. J. Bone Miner. Metab.**2018;36:103-110.FI.:2.472. [doi:10.1007/s00774-017-0812-0]

Reviews

1. Fernandez, O, Tintore, M, Saiz, A, Calles-Hernandez, MC, Comabella, M, Ramio-Torrenta, L, Oterino, A, Izquierdo, G, Tellez, N, Garcia-Merino, JA, Brieua, L, Arnal-Garcia, C, Aladro, Y, Mendibe-Bilbao, MD, Meca-Lallana, JE, Romero-Pinel, L, Ginestal, R, Martinez-Gines, ML, Arroyo, R, Rodriguez-Antiguedad, A. **Review of the novelties from the 2017 ECTRIMS Congress, presented at the 10th Post-ECTRIMS Meeting (II). Rev. Neurologia.** 2018;67:50-62.FI.:0.601. [doi:10.33588/m.6702.2018193]

2. Fernandez, O, Tintore, M, Saiz, A, Calles-Hernandez, MC, Comabella, M, Ramio-Torrenta, L, Oterino, A, Izquierdo, G, Tellez, N, Garcia-Merino, JA, Brieua, L, Arnal-Garcia, C, Aladro, Y, Mendibe-Bilbao, MD, Meca-Lallana, JE, Romero-Pinel, L, Ginestal, R, Martinez-Gines, ML, Arroyo, R, Rodriguez-Antiguedad, A. **Review of the novelties from the 2017 ECTRIMS Congress, presented at the 10th Post-ECTRIMS Meeting (I). Rev. Neurologia.** 2018;67:15-27.FI.:0.601. [doi:10.33588/m.6701.2018192]

Projects

1. Agustín Oterino Durán. **Modificaciones epigenéticas inducidas por experiencias adversas infantiles y daño endotelial en la migraña crónica: estudio de casos y controles. Creación de modelo experimental murino.** PI15/01285. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. Agustín Oterino Durán. **Red Temática de Esclerosis Múltiple.** RD16/0015/0023. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Clinical Trials

1. Agustín Oterino Durán. **Estudio de fase II, multicéntrico, aleatorizado, de grupos paralelos, con enmascaramiento de los evaluadores para evaluar la eficacia, la seguridad y la tolerabilidad de las dosis de 0,5, 3, 10 y 20 mg del acetato de plovámero en comparación con Copaxone en pacientes con esclerosis múltiple remitente recidivante.** EMR200575-001. MERCK KGAA.

2. Agustín Oterino Durán. **Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo, en el que se evalúa LY2951742 en pacientes con migraña episódica - Estudio EVOLVE-2.** IQ-MC-CGAH. LILLY, S.A..

3. Agustín Oterino Durán. **Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo, en el que se evalúa LY2951742 en pacientes con migraña crónica - Estudio REGAIN.** IQ-MC-CGAI. LILLY, S.A..

4. Agustín Oterino Durán. **Ensayo de fase 3 de grupos paralelos, doble ciego, aleatorizado y controlado con placebo, para evaluar la eficacia y la seguridad de ALD403 administrado por vía intravenosa en pacientes con migraña crónica. ALD403-CLIN-011.** ALDER BIOPHARMACEUTICALS, INC.

5. Agustín Oterino Durán. **Estudio multicéntrico, doble ciego, aleatorizado, de 12 semanas de tratamiento para comparar la eficacia y seguridad de AMG 334 70 mg subcutáneo una vez al mes frente a placebo en pacientes adultos con migraña episódica**

que han fracasado entre 2-4 tratamientos profilácticos (LIBERTY). CAMG334A2301. NOVARTIS FARMACEUTICA, S.A..

6. Agustín Oterino Durán. **Estudio multicéntrico, aleatorizado, doble ciego, de grupos paralelos, controlado con placebo con un período abierto, para evaluar la eficacia y la seguridad de fremanezumab en el tratamiento profiláctico de la migraña en pacientes con una respuesta inadecuada a los tratamientos preventivos anteriores.** TV48125-CNS-30068.

7. Agustín Oterino Durán. **Estudio aleatorizado, doble ciego de galcanezumab frente a placebo, en pacientes adultos con migraña resistente al tratamiento - Estudio CONQUER.** IQ-MC-CGAW. LILLY, S.A.

Postmarketing Studies and Other

1. Agustín Oterino Durán. **Estudio observacional, no intervencionista, para evaluar los cambios en la calidad de vida en pacientes tratados con teriflunomida en práctica. Clínica habitual.** SAN-TER-2015-02. SANOFI AVENTIS, S.A.

2. Agustín Oterino Durán. **Estudio observacional, global y multicéntrico para recoger información sobre seguridad y documentar la utilización del fármaco Tecfidera® (fumarato de dimetilo) en su uso en la práctica médica rutinaria del tratamiento de la esclerosis múltiple (ESTEEM).** 109MS401.

3. Agustín Oterino Durán. **La carga de la migraña en centros de cefalea especializados que tratan pacientes que han fallado a tratamientos preventivos (BECOME).** CAMG334A3301. NOVARTIS FARMACEUTICA, S.A.

Other Publications 2018

1. Duran, AO, Gómez, D, Cantarero, D, Blázquez, C, Toriello, M, Perez-Pereda, S, Quintanilla, VG. **New oral treatments decrease the switch to second-line therapies in multiple sclerosis. A 9-years retrospective, clinical and budget impact study.** *Mult. Scler.* J.2018;24:815-815.

Neurodegenerative diseases



Consolidated group

Researchers

José Ángel Berciano Blanco
Eloy Manuel Rodríguez Rodríguez
Pascual Jesús Sánchez Juan

Contributors

Santos Bringas Tejero
Elena Carmen Gallardo Agromayor
Antonio García García
María García Martínez
María Isabel González Aramburu

Group Responsible

Jon Infante Ceberio

Neurology Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



jon.infante@scsalud.es



Andrés González Mandly
Andrea González Suárez
Carmen Lage Martínez
Sara López García
José Ignacio Mateo Fernández
Ana Lara Pelayo Negro
Ana Pozueta Cantudo
Javier Riancho Zarrabeitia
Antonio Sánchez Rodríguez
María José Sedano Tous
María Sierra Peña
José Luis Vázquez Higuera

Nurses

Martha Kazimierczak

Predoctoral

José Ramón Sánchez de la Torre

Technicians

M^o del Coro
Sánchez Quintana

Research lines

1. Research in peripheral neuropathies:

- Clinical-molecular correlations in hereditary neuropathies
- Pathophysiology of Guilláin-Barré syndrome

2. Dementia research: the dementia line focuses on clinical research linked to the activity of the Cognitive Impairment Unit and the "Valdecilla Study for Memory and Brain Aging" project. It presents three fundamental areas:

- **Neuropsychology:** description of cognitive and behavioral alteration profiles with clinical utility in the main dementias.
- **Genetics:** as a founding group of the DEGESCO group, we are

coordinators of national dementia genetics projects and collaborate in the main international consortia of Alzheimer's genetics.

- **Biomarkers:** in the line dedicated to biomarkers of Alzheimer's disease, we highlight our studies with CSF markers and PIB PET in collaboration with the Nuclear Medicine group of HUMV.

3. Research in Parkinson's disease:

- Clinical-molecular biomarkers in Parkinson's disease associated with the G2019S mutation of LRRK2

- Genetic Epidemiology of Parkinson's disease

4. Research on hereditary ataxias:

- Clinical-molecular correlations of hereditary ataxias.
- Multimodal biomarkers in hereditary ataxias

5. Research in ELA:

Epidemiology and new therapies in ELA

PUBLICATIONS

IMPACT FACTOR | 247.125

Original articles

1. Riancho J, Sánchez-Juan P. **Circulating Extracellular Vesicles in Human Disease. N. Engl. J. Med.**2018;379:2180-2180.F.I.:79.258. [doi:10.1056/NEJMc1813170]

2. Diallo, A, Jacobi, H, Cook, A, Labrum, R, Durr, A, Brice, A, Charles, P, Marelli, C, Mariotti, C, Nanetti, L, Panzeri, M, Rakowicz, M, Sobanska, A, Sulek, A, Schmitz-Hubsch, T,

Schöls L, Hengel, H, Melegh, B, Filla, A, Antenora, A, Infante, J, Berciano, J, van de Warrenburg, BP, Timmann, D, Boesch, S, Pandolfo, M, Schulz, JB, Bauer, P, Giunti, P, ..., Tezenas du Montcel S. **Survival in patients with spinocerebellar ataxia types 1, 2, 3, and 6 (EUROSCA): a longitudinal cohort study. Lancet Neurol.**2018;17:327-334.F.I.:27.138.

3. Jansen WJ, Ossenkoppele R, Tijms BM, Fagan AM, Hansson O, Klunk WE, van der Flier WM, Villemagne VL, Frisoni GB, Fleisher AS, Lleó A, Mintun MA, Wallin A, Engelborghs S, Na DL, Chételat G, Molinuevo JL, Landau SM, Mattsson N, Kornhuber J, Sabri O, Rowe CC, Parnetti L, Popp J, Fladby T, Jagust WJ, Aalten P, Lee DY, Vandenberghe R, ..., Zetterberg H. **Association of**

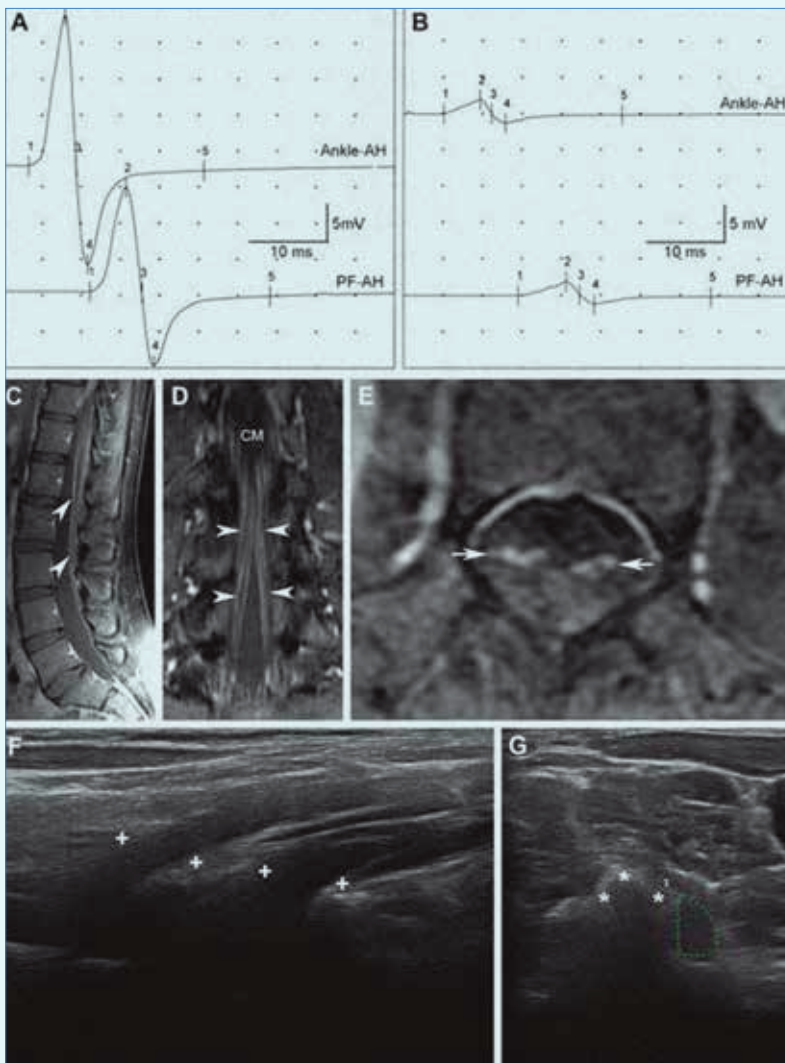


Figure 1. Picture taken from the paper by Berciano et al (JNNP 2016; 87: 563-5. Epub 2015 May 13) showing electrophysiological and imaging findings in a patient with the paraparetic and axonal form of GBS. (A) Tibial nerve motor conduction velocity (MCV) study on day 4 after onset showing normal compound muscle action potential (CMAP) morphology, both on distal (ankle to abductor hallucis [AH] muscle) and proximal stimulation (popliteal fossa [PF] to AH); proximal CMAP amplitude is 14.4 mV, and distal CMAP amplitude is 18.9 mV (normal, = 3); MCV is 47 m/s (normal, = 41). (B) On day 12, note severe CMAP amplitude reduction to 1.7 mV, both on distal and proximal stimulation. Comparatively with the previous study, at this stage there was a mild slowing of MCV (passing from 47 m/s to 39.4 m/s) and prolongation of F-wave latency (55.5 ms; normal, = 55), which seems to be proportional to the observed CMAP reduction. Post contrast sagittal (C) and coronal (D) T1-weighted, fat-saturation MR images of the lower thoracic and lumbosacral spine, performed on day 4, showing diffusely thickened cauda equine (arrowheads), which in the axial image (L1 level) selectively involves the anterior roots (E, arrows); CM indicates conus medullaris. (F) Sagittal sonogram of the right ventral rami of C6-C7 cervical nerves (callipers) performed on day 3; note their characteristic homogeneous hypoechoic texture with partial loss of the surrounding perineural hyperechoic rims. (G) Short-axis sonogram the right ventral ramus of the C7 spinal nerve showing the cross sectional area (dotted green tracing) measuring 27.47 mm² (control, 12.29 ± 5.3 mm²). Note blurred margins and the absence of the physiologic hyperechoic rim. Asterisks indicate the posterior tubercle of the seventh transverse vertebral process

Cerebral Amyloid- β Aggregation With Cognitive Functioning in Persons Without Dementia.

JAMA Psychiatry. 2018;75:84-95.F.I.:16.642. [doi:10.1001/jamapsychiatry.2017.3391]

4. Montal, V, Vilaplana, E, Alcolea, D, Pegueroles, J, Pasternak, O, Gonzalez-Ortiz, S, Clarimon, J, Carmona-Iragui, M, Illan-Gala, I, Morenas-Rodriguez, E, Ribosa-Nogue, R, Sala, I, Sanchez-Saudinos, MB, Garcia-Sebastian, M, Villanua, J, Izagirre, A, Estanga, A, Ecay-Torres, M, Iriondo, A, Clerigue, M, Tainta, M, Pozueta, A, Gonzalez, A, Martinez-Heras, E, Llufrui, S, Blesa, R, Sanchez-Juan, P, Martinez-Lage, P, Lleo, A, Fortea, J. **Cortical microstructural changes along the Alzheimer's disease continuum.** *Alzheimers. Dement.* 2018;14:340-351.F.I.:12.740. [doi:10.1016/j.jalz.2017.09.013]

5. Mattsson, N, Groot, C, Jansen, WJ, Landau, SM, Villemagne, VL, Engelborghs, S, Mintun, MM, Lleo, A, Molinuevo, JL, Jagust, WJ, Frisoni, GB, Ivanoiu, A, Chetelat, G, Resende de Oliveira C, Rodrigue, KM, Kornhuber, J, Wallin, A, Klimkiewicz-Mrowiec, A, Kandimella R, Popp, J, Aalten, PP, Aarsland, D, Alcolea, D, Almdahl, IS, Baldeiras, I, van Buchem MA, Cavedo, E, Chen, K, Cohen, AD, ..., Ossenkoppele, R. **Prevalence of the apolipoprotein E epsilon 4 allele in amyloid beta positive subjects across the spectrum of Alzheimer's disease.** *Alzheimers. Dement.* 2018;14:913-924.F.I.:12.740. [doi:10.1016/j.jalz.2018.02.009]

6. Riancho, J, Gil-Bea, FJ, López de Munain A. **Retinoids and Amyotrophic Lateral Sclerosis.** *JAMA Neurol.* 2018;75:1153-1153.F.I.:11.460. [doi:10.1001/jamaneurol.2018.2242]

7. Bergeron, D, Gorno-Tempini, ML, Rabinovici, GD, Santos-Santos, MA, Seeley, W, Miller, BL, Pijnenburg, Y, Keulen, MA, Groot, C, van Berckel BNM, van der Flier WM, Scheltens, P, Rohrer, JD, Warren, JD, Schott, JM, Fox, NC, Sanchez-Valle, R, Grau-Rivera, O, Gelpi, E, Seelaar, H, Papma, JM, van Swieten JC, Hodges, JR, Leyton, CE, Piguot, O, Rogalsky EJ, Mesulam, MM, Koric, L, Nora, K, ..., Ossenkoppele, R. **Prevalence of amyloid-beta pathology in distinct variants of primary progressive**

aphasia. *Ann. Neurol.* 2018;84:729-740.F.I.:10.244. [doi:10.1002/ana.25333]

8. Fernandez-Santiago, R, Garrido, A, Infante, J, Gonzalez-Aramburu, I, Sierra, M, Fernandez, M, Valdeoriola, F, Muñoz E, Compta, Y, Marti, MJ, Rios, J, Tolosa, E, Ezquerro, M, Barcelona LRRK2 Study Group. **Alpha-Synuclein (SNCA) but not dynamin 3 (DNM3) influences age at onset of leucine-rich repeat kinase 2 (LRRK2) Parkinson's disease in Spain.** *Mov. Disord.* 2018;33:637-641.F.I.:8.324. [doi:10.1002/mds.27295]

9. Peran, P, Barbagallo, G, Nemmi, F, Sierra, M, Galitzky, M, Traon, APL, Payoux, P, Meissner, WG, Rascol, O. **MRI supervised and unsupervised classification of Parkinson's disease and multiple system atrophy.** *Mov. Disord.* 2018;33:600-608.F.I.:8.324. [doi:10.1002/mds.27307]

10. Lupo, V, Frasquet, M, Sanchez-Monteagudo, A, Pelayo-Negro, AL, Garcia-Sobrinho, T, Sedano, MJ, Pardo, J, Misiego, M, Garcia-Garcia, J, Sobrido, MJ, Martinez-Rubio, MD, Chumillas, MJ, Vilchez, JJ, Vazquez-Costa, JF, Espinos, C, Sevilla, T. **Characterising the phenotype and mode of inheritance of patients with inherited peripheral neuropathies carrying MME mutations.** *J. Med. Genet.* 2018;55:814-823.F.I.:5.751. [doi:10.1136/jmedgenet-2018-105650]

11. Cantero, JL, Atienza, M, Sanchez-Juan, P, Rodriguez-Rodriguez, E, Vazquez-Higuera, JL, Pozueta, A, Gonzalez-Suarez, A, Vilaplana, E, Pegueroles, J, Montal, V, Blesa, R, Alcolea, D, Lleo, A, Fortea, J. **Cerebral changes and disrupted gray matter cortical networks in asymptomatic older adults at risk for Alzheimer's disease.** *Neurobiol. Aging.* 2018;64:58-67.F.I.:4.454. [doi:10.1016/j.neurobiolaging.2017.12.010]

12. Suñer-Soler R, Grau-Martin, A, Terceno, M, Silva, Y, Davalos, A, Sanchez, JM, Font-Mayolas, S, Gras, E, Rodrigo, J, Kazimierzczak, M, Malagon, C, Serena, J. **Biological and Psychological Factors Associated With Smoking Abstinence Six Years Post-Stroke.**

Nicotine Tob. Res. 2018;20:1182-1188.F.I.:4.291. [doi:10.1093/ntr/ntx151]

13. Infante, J, Garcia, A, Serrano-Cardenas, K, Gonzalez-Aguado, R, Gazulla, J, de Lucas, EM, Berciano, J. **Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) with chronic cough and preserved muscle stretch reflexes: evidence for selective sparing of afferent Ia fibres.** *J. Neurol.* 2018;265:1454-1462.F.I.:3.783. [doi:10.1007/s00415-018-8872-1]

14. Jacobi, H, du Montcel, ST, Bauer, P, Giunti, P, Cook, A, Labrum, R, Parkinson, MH, Durr, A, Brice, A, Charles, P, Marelli, C, Mariotti, C, Nanetti, L, Sarro, L, Rakowicz, M, Sulek, A, Sobanska, A, Schmitz-Hubsch, T, Schöls L, Hengel, H, Baliko, L, Melegh, B, Filla, A, Antenora, A, Infante, J, Berciano, J, Van De Warrenburg, BP, Timmann, D, Szymanski, S, ..., Klockgether, T. **Long-term evolution of patient-reported outcome measures in spinocerebellar ataxias.** *J. Neurol.* 2018;265:2040-2051.F.I.:3.783. [doi:10.1007/s00415-018-8954-0]

15. Berciano, J, Teran-Villagra, N. **Sneddon syndrome and non-bacterial thrombotic endocarditis: a clinicopathological study.** *J. Neurol.* 2018;265:2143-2145.F.I.:3.783. [doi:10.1007/s00415-018-8962-0]

16. Lage, C, Suarez, AG, Pozueta, A, Riancho, J, Kazimierzczak, M, Bravo, M, Jimenez Bonilla J, de Arcocha Torres M, Quirce, R, Banzo, I, Vazquez-Higuera, JL, Rabinovici, GD, Rodriguez-Rodriguez, E, Sanchez-Juan, P. **Utility of Amyloid and FDG-PET in Clinical Practice: Differences Between Secondary and Tertiary Care Memory Units.** *J. Alzheimers Dis.* 2018;63:1025-1033.F.I.:3.476. [doi:10.3233/JAD-170985]

17. Fernandez, A, Salgado, M, Garcia, A, Buxo, E, Vera, R, Adeva, J, Jimenez-Fonseca, P, Quintero, G, Llorca, C, Cañabate M, Lopez, LJ, Muñoz A, Ramirez, P, Gonzalez, P, Lopez, C, Reboredo, M, Gallardo, E, Sanchez-Canovas, M, Gallego, J, Guillen, C, Ruiz-Miravet, N, Navarro-Perez, V, De la Camara, J, Ales-Diaz, I, Pazo-Cid, RA, Carmona-Bayonas, A.

Prognostic factors for survival with nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer in real-life practice: the ANICE-PaC study. *BMC Cancer*. 2018;18:1185-1185.F.I.:3.288. [doi:10.1186/s12885-018-5101-3]

18. Berciano, J. Neuropathic Pain in Early Guillain-Barre Syndrome. *Pain Physician*. 2018;21:279-280.F.I.:2.556.

19. Riancho, J, Gil-Bea, FJ, Castanedo-Vazquez, D, Sedano, MJ, Zufiria, M, de Eulate GFG, Poza, JJ, de Munain, AL. Clinical evidences supporting the Src/c-Ab1 pathway as potential therapeutic target in amyotrophic lateral sclerosis. *J. Neurol. Sci*.2018;393:80-82.F.I.:2.448. [doi:10.1016/j.jns.2018.08.013]

20. Gazulla, J, Almarcegui, C, Berciano, J. Reversible inflammatory neuropathy superimposed on Charcot-Marie-Tooth type 1A disease. *Neurol. Sci*.2018;39:793-794.F.I.:2.285. [doi:10.1007/s10072-017-3195-z]

21. Martinez-Dubarbie, F, Herrera-Calvo, G, Drake-Perez, M, Riancho, J. Unilateral isolated hypoglossal neuropathy associated to jugular paraganglioma. *Neurol. Sci*.2018;39:971-972.F.I.:2.285. [doi:10.1007/s10072-018-3256-y]

22. Berciano, J, Garcia, A. Letter regarding the article: "A novel missense variant (Gin220Arg) of GNB4 encoding guanine nucleotide-binding protein, subunit beta-4 in a Japanese family with autosomal dominant motor and sensory neuropathy". *Eur. J. Med. Genet*.2018;61:43-44.F.I.:2.004. [doi:10.1016/j.ejmg.2017.07.005]

23. Pérez-Pereda, S, Lage-Martinez, C, Paredes, MJ, Infante, J. Recurrent meningoencephalitis due to allopurinol. *Neurologia*. 2018;33:557-558.F.I.:1.938. [doi:10.1016/j.nrl.2017.03.0100213]

24. Fernández-Torre, JL, Paramio-Paz, A, Lopez-Delgado, A, Martín-García, M, Gonzalez-Aramburu, I, Hernández-Hernández, MA. De novo absence status epilepticus of late onset (DNASLO) precipitated by oral treatment with cefuroxime: description of an ambulatory

case. Epileptic Disord.2018;20:73-76.F.I.:1.500. [doi:10.1684/epd.2017.0938]

25. Jiménez-Bonilla, JF, Quirce, R, de Arcocha-Torres, M, Martínez-Rodríguez, I, Martínez-Amador, N, Sánchez-Juan, P, Pozueta, A, Martín-Laez, R, Banzo, I, Rodríguez-Rodríguez, E. C-11-PIB retention patterns in white and grey cerebral matter in idiopathic normal pressure hydrocephalus patients. A visual analysis. *Rev. Esp. Med. Nucl. Imagen Mol*.2018;37:87-93.F.I.:1.202. [doi:10.1016/j.remnm.2017.07.006]

26. Cortes-Donate, VE, Pérez-Lorensu, PJ, García-García, A, Asociación de Monitorización Intraquirúrgica Neurofisiológica Española Amine AMI, Sociedad Española de Neurofisiología Clínica Senfc SENCs, Grupo de Trabajo de Monitorización Neurofisiológica Intraoperatoria de la Senfc. Intraoperative neurophysiological monitoring in Spain: its beginnings, current situation and future prospects. *Rev. Neurología*. 2018;66:315-320.F.I.:0.601. [doi:10.33588/rm.6609.2018004]

Reviews

1. Sconfienza, LM, Albano, D, Allen, G, Bazzocchi, A, Bignotti, B, Chianca, V, Facal de Castro F, Drakonaki, EE, Gallardo, E, Gielen, J, Klauser, AS, Martinoli, C, Mauri, G, McNally, E, Messina, C, Mirón Mombiela R, Orlandi, D, Plagou, A, Posadzy, M, de la Puente, R, Reijnierse, M, Rossi, F, Rutkauskas, S, Snoj, Z, Vucetic, J, Wilson, D, Tagliafico, AS. Clinical indications for musculoskeletal ultrasound updated in 2017 by European Society of Musculoskeletal Radiology (ESSR) consensus. *Eur. Radiol*.2018;28:5338-5351.F.I.:4.027. [doi:10.1007/s00330-018-5474-3]

2. Riancho, J, Bosque-Varela, P, Pérez-Pereda, S, Povedano, M, de Munain, AL, Santurtun, A. The increasing importance of environmental conditions in amyotrophic lateral sclerosis. *Int. J. Biometeorol*.2018;62:1361-1374.F.I.:2.577. [doi:10.1007/s00484-018-1550-2]

3. Serrano-Cardenas, KM, Sanchez-Rodriguez, A, Pozueta, A, Pelayo, AL, Riancho, J. Mesial encephalitis: an uncommon presentation of neurosyphilis: a case report and review of the literature. *Neurol. Sci*.2018;39:173-176.F.I.:2.285. [doi:10.1007/s10072-017-3109-0]

4. Martín-Laez, R, Valle-San Román, N, Rodríguez-Rodríguez, EM, Marco-de Lucas, E, Berciano Blanco JA, Vázquez-Barquero, A. Current concepts on the pathophysiology of idiopathic chronic adult hydrocephalus: Are we facing another neurodegenerative disease?. *Neurología*. 2018;33:449-458.F.I.:1.938. [doi:10.1016/j.nrl.2016.03.010]

Projects

1. José Ángel Berciano Blanco. Validation of prognostic and disease biomarkers for Charcot-Marie-Tooth disease 1A (CMTA1). *AFM11/06*. MAX-PLANCK-INSTITUTE FOR EXPERIMENTAL MEDICINE.

2. Jon Infante Ceberio. AYUDA POR PRODUCCIÓN AL GRUPO DE ENFERMEDADES NEURODEGENERATIVAS. *APG/11*.

3. Pascual Jesús Sánchez Juan. Plataforma de Biobancos. PT13/0010/0024. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

4. Jon Infante Ceberio. CIBERNED Enfermedades Neurodegenerativas. *CB06/05/0037*.

5. José Ángel Berciano Blanco. Donaciones para el desarrollo de proyectos de investigación. *BDP24*.

6. Pascual Jesús Sánchez Juan. Convenio para la gestión del ensayo con código RH-VAL-2013-01. Estudio de validación de una prueba diagnóstica multiparamétrica en sangre para el diagnóstico de la enfermedad de Alzheimer. *CCI16/07*. RAMAN HEALTH TTECHNOLOGIES, S.L..

7. Pascual Jesús Sánchez Juan. **Donaciones para el desarrollo de proyectos de investigación.** BDP59. NEGRETE INCERA, OSCAR, CERRO SAEZ, FERNANDO, GONZALEZ GUTIERREZ, INES, VILLAR RABA, RUBEN.

8. Pascual Jesús Sánchez Juan. **Estudio de variantes raras en genes asociados a Enfermedad de Alzheimer en población española.** PI16/01652. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

9. Javier Riancho Zarrabeitia. **Enfermedad de Alzheimer y Síndrome de Down: una aproximación clínica y experimental.** NVAL16/21.

10. Javier Riancho Zarrabeitia. **Nuevos agonistas del RXR como tratamiento de la ELA.** INNVAL16/11.

11. Pascual Jesús Sánchez Juan. **PREVAL17/03 Carmen Lage Martínez.** PREVAL17/03. FUNDACION INSTITUTO DE INVESTIGACION MARQUES DE VALDECILLA IDIVAL.

12. Pascual Jesús Sánchez Juan. **Contrato de servicios de investigación para el Estudio descriptivo de los movimientos oculares mediante Oscanntm y su valor en la asistencia diagnóstica en enfermedades neurodegenerativas.** CSI17/02.

13. Jon Infante Ceberio. **Estudio de biomarcadores motores, genéticos y de imagen en la enfermedad de Parkinson prodrómica asociada a la mutación G2019S de LRRK2.** PI17/00936. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

14. Carmen Lage Martínez. **Apraxia en enfermedades neurodegenerativas: Desarrollo de una herramienta diagnóstica cuantitativa y aplicación en la valoración del impacto sobre actividades de la vida diaria.** NVAL17/14.

15. Jon Infante Ceberio. **ICTUSnet - Red de excelencia para el desarrollo y la implementación de modelos innovadores de atención integrada del ictus.** EU17/26.

16. Pascual Jesús Sánchez Juan. **Plataforma de Biobancos.** PT17/0015/0019. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

17. Eloy Manuel Rodríguez Rodríguez. **Proyecto piloto para el desarrollo de una plataforma web de teleasistencia al paciente con deterioro cognitivo.** INVAL17/08.

18. Pascual Jesús Sánchez Juan. **Contrato de servicios de investigación para el proyecto Valdecilla Study for Memory and Brain Aging.** CSI18/10. SIEMENS HEALTHCARE S.L.U..

Clinical Trials

1. Andrés González Mandly. **Registro internacional prospectivo, de observación, multicéntrico, de un solo grupo, con inscripción consecutiva y posterior a la comercialización del desviador de flujo Surpass en arterias intracraneales.** SURMOUNT. STRYKER NEUROVASCULAR.

2. Eloy Manuel Rodríguez Rodríguez. **Estudio en Fase III, multicéntrico, aleatorizado, doble ciego, controlado con Placebo y de grupos paralelos para evaluar la eficacia y seguridad de crenezumab en pacientes con enfermedad de Alzheimer de prodrómica a leve.** BN29552. ROCHE FARMA, S.A.U..

3. Eloy Manuel Rodríguez Rodríguez. **Estudio en fase III, multicéntrico, aleatorizado, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y seguridad de crenezumab en pacientes con enfermedad de alzheimer de prodrómica a leve.** BN29553. ROCHE FARMA, S.A.U..

4. Pascual Jesús Sánchez Juan. **Estudio multicéntrico, doble ciego, aleatorizado y controlado de grupos paralelos para investigar la eficacia y seguridad de BI 425809, administrado oralmente durante un periodo de tratamiento de 12 semanas, comparado con placebo en pacientes con deterioro cognitivo debido a enfermedad de Alzheimer.** 1346.23.

5. Eloy Manuel Rodríguez Rodríguez. **Estudio de Fase III, multicéntrico, aleatorio, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y seguridad de Gantenerumab en pacientes con enfermedad de Alzheimer precos (de PRODRÓMI-CA A Leve) y los Sub-estudios: "Subestudio longitudinal de PET para Amiloide asociado a: Estudio de Fase III, multicéntrico, aleatorio, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y seguridad de Gantenerumab en pacientes con enfermedad de Alzheimer precos (de Prodrómica a Leve)" y "Subestudio explotario de PET para TAU asociado a : Estudio de Fase III, multicéntrico aleatorio, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y seguridad de Gantenerumab en pacientes con enfermedad de Alzheimer precos (de Prodrómica a Leve).** WNNWN29922. F. HOFFMANN-LA ROCHE LTD.

Postmarketing Studies and Other

1. María José Sedano Tous. **Estudio observacional, no intervencionista para evaluar los cambios en la calidad de vida en pacientes con esclerosis múltiple remitente recurrente tratados con alemtuzumab (Lemtrada®) en condiciones de práctica clínica habitual.** SAN-ALE-2015-03. GENZYME EUROPE, B.V..

2. María Sierra Peña. **Estudio observacional postautorización Calidad de vida y lesiones accidentales en el paciente con epilepsia y crisis tónico-clónicas generalizadas (Estudio QUIN-GTC).** EST-EPI-2016-01. ESTEVE PHARMACEUTICALS, S.A..

Collaborations 2018

Total Impact Factor 58.997

1. Armangue, T, Spatola, M, Vlaga, A, Mattozzi, S, Carceles-Cordon, M, Martinez-Heras, E, Llufríu, S, Muchart, J, Erro, ME, Abraira, L, Moris, G, Monros-Gimenez, L, Corral-Corral, I, Montejo, C, Toledo, M, Bataller, L, Secondi, G,

Ariño H, Martínez-Hernández E, Juan M, Marcos MA, Alsina L, Saiz A, Rosenfeld MR, Graus F, Dalmau J. **Frequency, symptoms, risk factors, and outcomes of autoimmune encephalitis after herpes simplex encephalitis: a prospective observational study and retrospective analysis.** *Lancet Neurol.* 2018;17:760-772.F.I.:27.138. [doi:10.1016/S1474-4422(18)30244-8]

2. Kia DA, Sabir MS, Ahmed S, Trinh J, Bandres-Ciga S. **LRP10 in alpha-synucleinopathies.** *Lancet Neurol.* 2018;17:1032-1032.F.I.:27.138. [doi:10.1016/S1474-4422(18)30401-0]

3. Borm CDJM, Krismer F, Wenning GK, Seppi K, Poewe W, Pallecchia MT, Barone P, Johnsen EL, Østergaard K, Gurevich T, Djaldetti R,

Sambati L, Cortelli P, Petrovic I, Kostic VS, Brožová H, Ruzicka E, Marti MJ, Tolosa E, Canesi M, Post B, Nonnekes J, Bloem BR. **Axial motor clues to identify atypical parkinsonism: A multicentre European cohort study.** *Parkinsonism Relat. Disord.* 2018;56:33-40.F.I.:4.721. [doi:10.1016/j.parkreldis.2018.06.015]



○ Neurophysiology in Epilepsy and Neurointensive care



Associated group

Group Responsible

José Luis Fernández Torre

Neurophysiology Service

Hospital Universitario Marqués de Valdecilla



joseluis.fernandezt@scsalud.es

Contributors

Francisco Javier Adin Ibarra
Miguel Ángel Hernández Hernández
María Soledad Holanda Peña
David Mato Mañas

○ Research lines

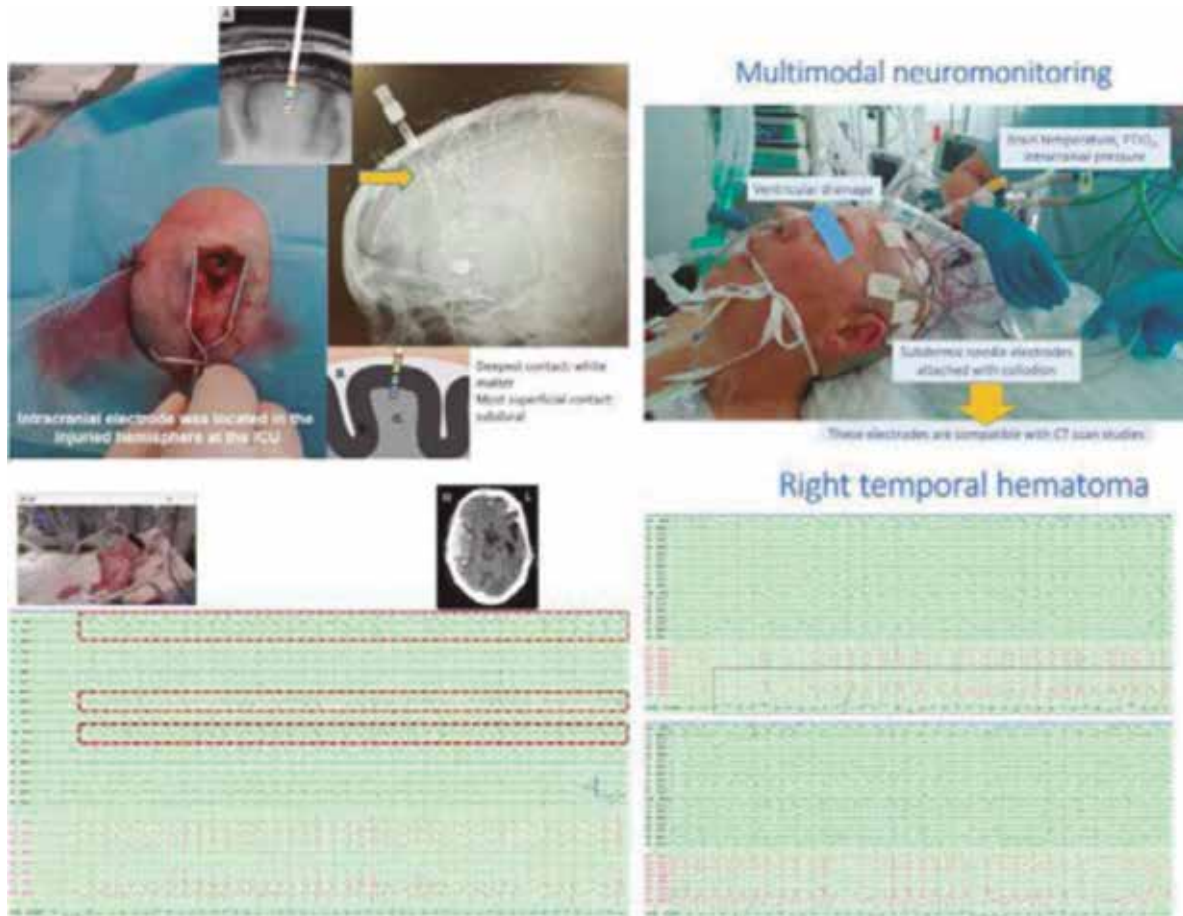
1. Convulsive status epilepticus.
2. Not convulsive status epilepticus.
3. Non-convulsive malignant or super-refractory status epilepticus.
4. Multimodal neuromonitoring including intracerebral electrodes in patients in coma with acute brain damage.
5. EEG patterns prognosis in cerebral anoxia.
6. Post-anoxic myoclonic epilepticus status.
7. Diagnostic situations of clinical brain death with electrical activity in the EEG.
8. Diagnosis of stem-brain death.
9. Coma. Brain structures involved in consciousness. Default Mode Network.
10. EEG-neuroimaging correlation in periodic electroencephalographic alterations.
11. EEG predictors of vasospasm in subarachnoid hemorrhage.
12. SESA syndrome (subacute encephalopathy with seizures in alcoholics).
13. Pharmacological neurotoxicity in critical patients. Border syndromes between non-convulsive status epilepticus / epileptiform encephalopathy.
14. Bispectral index (bispectral index, BIS) and its correlation with EEG records.
15. EEG-neuroimaging correlation in childhood epilepsy.
16. Experimental models of status epilepticus. Electroencephalographic phases of the status epilepticus.

PUBLICATIONS

FACTOR IMPACT | 21.046

Original articles

1. Fernández-Torre, JL, López-Delgado, A, Hernández-Hernández, MA, Paramio-Paz, A, Pia-Martínez, C, Orizaola, P, Martín-García, M. [Postanoxic alpha, theta or alpha-theta coma: Clinical setting and neurological outcome. RESUSCITATION.](#) 2018;124:118-125.F.I.:5.863. [doi:10.1016/j.resuscitation.2017.12.022]



2. Fernández-Torre, JL, Banzo, I, Ortega-Valin, F, Orozco-Sevilla, E, Martínez-Rodríguez, I, Marco de Lucas E. **Subacute encephalopathy with seizures in alcoholics (SESA) syndrome: further evidence supporting that may lie on the ictal-interictal continuum.** *J. Neurol.*2018;265:2448-2450.F.I.:3.783. [doi:10.1007/s00415-018-9010-9]

3. Fernández-Torre, JL, Paramio-Paz, A, Lorda-de Los Ríos I, Martín-García, M, Hernández-Hernández, MA. **Pupillary hippus as clinical manifestation of refractory autonomic nonconvulsive status epilepticus: Pathophysiological implications.** *Seizure.* 2018;63:102-104.F.I.:2.839. [doi:10.1016/j.seizure.2018.11.006]

4. Kaplan, PW, Billnitzer, A, Fernández-Torre, JL. **Subacute Encephalopathy With Seizures in Alcoholics (SESA) Presenting as Focal Nonconvulsive Status Epilepticus.** *Clin. EEG Neurosci.*2018;49:414-416.F.I.:1.807. [doi:10.1177/1550059417747435]

5. Fernández-Torre, JL, Paramio-Paz, A, Rodríguez-Borregan, JC, Orizaola, P, Bosque-Varela, P, Hernandez-Hernandez, MA. **Super-refractory nonconvulsive status epilepticus due to self-poisoning with metaldehyde.** *J. Clin. Neurosci.*2018;47:134-136.F.I.:1.640. [doi:10.1016/j.jocn.2017.10.017]

6. Fernández-Torre, JL, Paramio-Paz, A, López-Delgado, A, Martín-García, M, González-Aramburu, I, Hernández-Hernández, MA. **De novo absence status epilepticus of late onset (DNASLO) precipitated by oral treatment with cefuroxime: description of an ambulatory case.** *Epileptic Disord.*2018;20:73-76.F.I.:1.500. [doi:10.1684/epd.2017.0938]

Reviews

1. Walter, U, Fernandez-Torre, JL, Kirschstein, T, Laureys, S. **When is "brainstem death" brain death? The case for ancillary testing in primary infratentorial brain lesion.** *Clin. Neurophysiol.*2018;129:2451-2465.F.I.:3.614. [doi:10.1016/j.clinph.2018.08.009]

Projects

1. José Luis Fernández. **Electroencefalografía intracortical en pacientes en coma con daño cerebral agudo.** PI17/00156. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Other publications

Authorship Thesis 2017

1. Miguel Ángel Hernández Hernández. **Persistencia de actividad eléctrica cerebral tras el diagnóstico clínico de muerte encefálica: Incidencia, impacto y análisis comparativo del electroencefalograma frente a la angiografía por tomografía computarizada.** Director/s: José Luis Fernández Torre, José Luis Hernández Hernández. UNIVERSIDAD DE CANTABRIA.

○ Psychiatry



Group Responsible

Researchers

María Rosa Ayesa Arriola
Diana Tordesillas Gutiérrez

Contributors

Jesús Ángel Artal Simón
Laura Carral Fernández
Carlos Cobo Corrales
Javier Alejandro Cuartas Micieces
Manuel Delgado Alvarado
Luis Gaite Pindado
Andrés Gómez Del Barrio
Elsa Gómez Ruíz
Jana González Gómez

Group Responsible

Benedicto Crespo Facorro

Psychiatry Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



benedicto.crespo@sccsalud.es



César González-Blanch Bosch
José Andrés Herrán Gómez
María Juncal Ruiz
Sara Herrera Castanedo
Jacqueline María Mayoral Van Son
María Soraya Otero Cuesta
Beatriz Payá González
Rocío Pérez Iglesias
M^a Luz Ramírez Bonilla
Paula Suárez Pinilla
Javier Vázquez Bourgon

Nurses

María del Carmen Flor Gómez

Predoctoral

Fulgencio Ruso Julve
Luis Manuel Fernández Cacho

Technicians

Víctor Ortíz García De La Foz
María Esther Setién Suero
Margarita Miguel Corredera

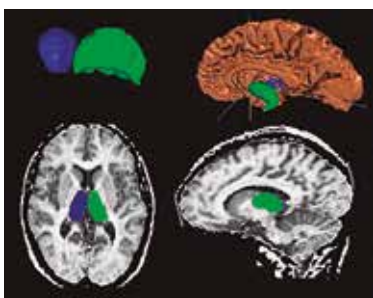
Research lines

1- Brain Neuroimaging in Non Affective Psychosis (NAP).

Responsibles: R. ROIZ SANTIÁÑEZ Y D. TORDESILLAS GUTIÉRREZ.

The techniques of brain imaging, such as magnetic resonance imaging (MRI), allow exploring the presence of structural alterations from the first clinical phases of the disease (neurodevelopmental abnormalities) and also study the onset of morphological changes during the course of the disease (neurodegeneration processes). Our work in this area aims to:

- To Compare the volume of gray and white matter in the cortex between patients and controls
- To Determine the existence of differences in volume of the basal ganglia between patients and controls
- A longitudinal study to detect structural changes over time in people with schizophrenia, and
- To study the relationship between variables related to brain structure and other clinical and / or genetic variables.



At present, we are developing research by DTI to explore alterations in the integrity of white matter tracts. Another line of recent research is the development of spectroscopy techniques to assess neuronal processes genesis.

2- Genomic of non-affective psychosis.

Responsible: Dr. B. CRESPO-FACORRO

In this field, our group has focused its work on two main lines of

activity. Firstly, in the field of Pharmacogenetics, we work on the study of single nucleotide polymorphisms (SNPs) of candidate genes, specifically the genes involved in dopaminergic neurotransmission, serotonergic and candidate genes in linking regions. The aim is to determine whether single nucleotide polymorphisms are associated with psychotic symptomatology, evolution and response to treatment. Also, we work in the field of “imaging genetics” genetic variations associated with brain alterations; In particular, gene expression studies are being carried out to identify genes whose expression is different in people with a first psychotic episode with respect to people not affected by the disease and also in possible differences in gene expression in people with a first Psychotic episode before starting treatment and after one year of pharmacological treatment.

3- Epidemiology and Clinical characteristics of non-affective psychosis.

Responsible: Dr. B. CRESPO FACORRO.

The main objectives of this research are:

- To investigate the incidence of psychosis in Cantabria and likely related factors.
- To identify the profile of symptoms during early phases of the illness.
- To describe predictors of outcome.
- To advance in the knowledge of biological markers (neuroimage, biochemical, genetic) of Schizophrenia.
- To study new short- and long-term therapeutic, pharmacological, psychotherapeutic interventions in the treatment of non-affective psychosis. Special interest in treating metabolic side effects associated with antipsychotic treatments.

4- Cognition in non affective psychosis.

Responsible: Dr. R. AYESA ARRIOLA.

The main objectives of this research are:

- To evaluate the course of early cognitive function in a sample of first episodes of psychosis individuals.
- To examine the relationship between cognitive functions and clinical variables.
- To evaluate the influence of cognitive function in the outcome and prognosis of the disease.

5. Research and Intervention program focused on the early phases of eating disorders.

Responsible: Dr. J.A. GÓMEZ DEL BARRIO.

It consists of a bio-psychosocial line of research and a therapeutic intervention and prevention focused on early phases of eating disorders

- Implement an early, multidisciplinary and multi-factorial evaluation and intervention protocol for all patients that develop an eating disorder in the area referenced by the Psychiatric Service of Hospital Universitario Marqués de Valdecilla.
- Research the early phases of the disease— the psychological, biological, and social components of eating disorders.
- Identify and define the risk factors of developing eating disorders, as well as the nature and characteristics of prodromal symptoms and earliest clinical manifestations.
- Evaluate the response to interventions, as well as the evolutionary course of the disease, researching bio-psycho-social factors that condition them.
- Evaluate the costs derived from treatment, as well as the level of patient and family satisfaction.

The line of investigation incorporates the following studies:

Intervention study focused on cognitive processes in eating disorders. Responsible: Laura Carral Fernandez y J.A. Gomez del Barrio. This study is framed under an investigation contract Rio Hortega (CM10/0017).

This program focuses on intervention and therapeutic strategies based on new technology for early phases

of eating disorders. Responsibles: Dra. Jana Gonzalez Gomez and Dr. J.A. Gomez del Barrio. This program integrates DETECTA (DEtecion TEmpрана en Cantabria de Trasornos Alimentarios) and is framed under a research scholarship, financed by IDIVAL (Lopez Albo WLA 02/11).

6.- Research and Pharmacological Interventions Program for Early Phases of Psychoses in children and adolescents population.

Responsibles: Dr. S. OTERO CUESTA AND Dr. B. PAYÁ GONZÁLEZ.

This is a research program focused on mental health problems of young people. The main areas of interest are:

a. Clinical trials on effectiveness and safety of new drugs for children and adolescents psychiatric disorders.

b. Research on Prevention Strategies and Bio-psycho-social Interventions for Early Phases of Psychosis in children and adolescents.

7.- Strategies of assessment in mental health.

Responsibles: Dr. L. GAITE PINDADO Y Dr. S. HERRERA CASTANEDO.

a. To develop and consolidate a network of health professionals interested in investigating mental health services and needs.

b. To promote the development and dissemination of investigations on instruments of assessment and indicators of outcome (including economic indicators).

8. Molecular basis of non-affective psychosis.

Responsibles: DR. P. SUÁREZ PINILLA Y DR. B. CRESPO FACORRO.

The range of clinical features shows that schizophrenia affects multiple brain circuits, and also peripheral pathways. Recently, we have been developing the research in this field through the study of serum and PBMCs (peripheral blood mononuclear cells). Our work in this area aims to:

a. Detect blood biomarkers

and altered cellular signaling pathways leading to diagnose patients with a first episode of psychosis from healthy controls, combined with clinical practice.

b. Determine peripheral differences between patients with an episode of non-affective psychosis and healthy controls, from the onset and over time.

c. Conduct a longitudinal study of the change in biomarkers over time in people with schizophrenia.

d. Study the relationship between changes in peripheral molecules and correlate with longitudinal severity scores.

e. Detect biomarkers to predict treatment response.

9- Classification and assessment of disability in mental health.

Responsibles: Dr. S. HERRERA CASTANEDO Y Dr. L. GAITE PINDADO.

Since 1993, our research group has been involved in the development, publication and dissemination of the International Classification of Functionality (ICF) and related instruments of assessment (i.e., World Health Organization Disability Assessment Schedule 11 (WHO-DAS 11)).

In addition, in 2011, the Project for the development of the Spanish version of the International Classification of Functioning, Disability and Health-Children and Youth Version of WHO, has been completed with its final publication and the beginning of the dissemination of the same.

PUBLICATIONS

IMPACT FACTOR | 141.533

Original articles

1. Van Erp TGM, Walton, E, Hibar, DP, Schmaal, L, Jiang, WH, Glahn, DC, Pearlson, GD, Yao, NL, Fukunaga, M, Hashimoto, R, Okada, N, Yamamori, H, Bustillo, JR, Clark, VP, Agartz, I, Mueller, BA, Cahn, W, de Zwarte SMC,

Hulshoff Pol HE, Kahn, RS, Ophoff, RA, van Haren NEM, Andreassen, OA, Dale, AM, Doan, NT, Gurholt, TP, Hartberg, CB, Haukvik, UK, Jørgensen KN, ..., Turner JA. [Cortical Brain Abnormalities in 4474 Individuals With Schizophrenia and 5098 Control Subjects via the Enhancing Neuro Imaging Genetics Through Meta Analysis \(ENIGMA\) Consortium. *Biol. Psychiatry.* 2018;84:644-654.F.I.:11.982. \[doi:10.1016/j.biopsych.2018.04.023\]](#)

2. Kelly, S, Jahanshad, N, Zalesky, A, Kochunov, P, Agartz, I, Alloza, C, Andreassen, O, Arango, C, Banaj, N, Bouix, S, Bousman, CA, Brouwer, RM, Bruggemann, J, Bustillo, J, Cahn, W, Calhoun, V, Cannon, D, Carr, V, Catts, S, Chen, J, Chen, JX, Chen, X, Chiapponi, C, Cho, KK, Ciullo, V, Corvin, AS, Crespo-Facorro, B, Cropley, V, De Rossi, P, ..., [Donohoe, G. Widespread white matter microstructural differences in schizophrenia across 4322 individuals: results from the ENIGMA Schizophrenia DTI Working Group. *Mol. Psychiatr.* 2018;23:1261-1269.F.I.:11.640. \[doi:10.1038/mp.2017.170\]](#)

3. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Álvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setién E, López-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. [Microenvironment Eradication of Hepatitis C: A Novel Treatment Paradigm. *Am. J. Gastroenterol.* 2018;113:1639-1648.F.I.:10.231. \[doi:10.1038/s41395-018-0157-x\]](#)

4. Delgado-Alvarado, M, Dacosta-Aguayo, R, Navalpotro-Gomez, I, Gago, B, Gorostidi, A, Jiménez-Urbietta, H, Quiroga-Varela, A, Ruiz-Martínez, J, Bergareche, A, Rodríguez-Oroz, MC. [Ratios of proteins in cerebrospinal fluid in Parkinson's disease cognitive decline: prospective study. *Mov. Disord.* 2018;33:1809-1814.F.I.:8.324. \[doi:10.1002/mds.27518\]](#)

5. Walton E, Hibar DP, van Erp TGM, Potkin SG, Roiz-Santiañez R, Crespo-Facorro B, Suárez-Pinilla P, van Haren NEM, de Zwarte SMC, Kahn RS, Cahn W, Doan NT, Jørgensen KN, Gurholt TP, Agartz I, Andreassen OA, Westlye LT, Melle I, Berg AO, Mørch-Johnsen L, Færden A, Flyckt L, Fatouros-Bergman H, Karolinska Schizophrenia Project Consortium

(KaSP), Jönsson EG, Hashimoto R, Yamamori H, Fukunaga M, Jahanshad N, ..., Karolinska Schizophrenia Project consortium (KaSP). **Prefrontal cortical thinning links to negative symptoms in schizophrenia via the ENIGMA consortium.** *Psychol. Med.* 2018;48:82-94.F.I.:5.475. [doi:10.1017/S0033291717001283]

6. Juncal-Ruiz, M, Riesco-Dávila, L, de la Foz, VOG, Ramirez-Bonilla, M, Martínez-García, O, Irure-Ventura, J, Leza, JC, Lopez-Hoyos, M, Crespo-Facorro, B. **The effect of excess weight on circulating inflammatory cytokines in drug-naive first-episode psychosis individuals.** *J. Neuroinflamm.* 2018;15:63-63.F.I.:5.193. [doi:10.1186/s12974-018-1096-6]

7. Martino, J, Gómez, E, de Lucas, EM, Mato, D, Vázquez-Bourgon, J. **Intraoperative Identification and Preservation of Verbal Memory in Diffuse Gliomas: A Matched-Pair Cohort Study.** *Neurosurgery.* 2018;83:1209-1218.F.I.:4.475. [doi:10.1093/neuros/hyx617]

8. Pelayo-Terán, JM, Gajardo-Galán, V, Gómez-Revuelta, M, Ortiz-García de la Foz V, Ayesa-Arriola, R, Tabares-Seisdedos, R, Crespo-Facorro, B. **Duration of active psychosis and functional outcomes in first-episode non-affective psychosis.** *Eur. Psychiat.* 2018;52:29-37.F.I.:4.129. [doi:10.1016/j.eurpsy.2018.03.003]

9. Canal-Rivero, M, López-Morinigo, JD, Setién-Suero, E, Ruiz-Veguilla, M, Ayuso-Mateos, JL, Ayesa-Arriola, R, Crespo-Facorro, B. **Predicting suicidal behaviour after first episode of non-affective psychosis: The role of neurocognitive functioning.** *Eur. Psychiat.* 2018;53:52-57.F.I.:4.129. [doi:10.1016/j.eurpsy.2018.06.001]

10. Ayesa-Arriola, R, Terán JMP, Morínigo JDL, Rivero, MC, Setien-Suero, E, Al-Halabi, S, Cuesta, MJ, David, AS, Crespo-Facorroa, B. **The dynamic relationship between insight and suicidal behavior in first episode psychosis patients over 3-year follow-up.** *Eur. Neuro psychopharmacol.* 2018;28:1161-1172.F.I.:4.129. [doi:10.1016/j.euroneuro.2018.05.005]

11. González-Blanch, C, Hernández-de-Hita, F, Muñoz-Navarro R,

Ruiz-Rodríguez, P, Medrano, LA, Cano-Vindel, A. **The association between different domains of quality of life and symptoms in primary care patients with emotional disorders.** *Sci Rep.* 2018;8:11180-11180.F.I.:4.122. [doi:10.1038/s41598-018-28995-6]

12. Gómez-Revuelta, M, Pelayo-Terán, JM, Juncal-Ruiz, M, Ortiz García de la Foz, Víctor, Vázquez-Bourgon, J, González-Pinto, A, Crespo-Facorro, B. **Long-Term Antipsychotic Effectiveness in First Episode of Psychosis: A 3-Year Follow-Up Randomized Clinical Trial Comparing Aripiprazole, Quetiapine, and Ziprasidone.** *Int. J. Neuropsychopharmacol.* 2018;21:1090-1101.F.I.:3.981. [doi:10.1093/ijnp/pyy082]

13. Setién-Suero, E, Martínez-García, O, de la Foz, VOG, Vázquez-Bourgon, J, Correa-Ghisays, P, Ferro, A, Crespo-Facorro, B, Ayesa-Arriola, R. **Age of onset of Cannabis use and cognitive function in first-episode non-affective psychosis patients: Outcome at three-year follow-up.** *Schizophr. Res.* 2018;201:159-166.F.I.:3.958. [doi:10.1016/j.schres.2018.05.036]

14. Juncal-Ruiz, M, Riesco-Dávila, L, Ortiz García de la Foz, Víctor, Martínez-García, O, Ramirez-Bonilla, M, Oejo-Vinals, JG, Leza, JC, López-Hoyos, M, Crespo-Facorro, B. **Comparison of the anti-inflammatory effect of aripiprazole and risperidone in 75 drug-naive first episode psychosis individuals: A3 months randomized study.** *Schizophr. Res.* 2018;202:226-233.F.I.:3.958. [doi:10.1016/j.schres.2018.06.039]

15. Álvarez-Jiménez, M, Gleeson, JF, Bendall, S, Penn, DL, Yung, AR, Ryan, RM, Eleftheriadis, D, D'Alfonso, S, Rice, S, Miles, C, Russon, P, Lederman, R, Chambers, R, González-Blanch, C, Lim, MH, Killackey, E, McGorry, PD, Nelson, B. **Enhancing social functioning in young people at Ultra High Risk (UHR) for psychosis: A pilot study of a novel strengths and mindfulness-based online social therapy.** *Schizophr. Res.* 2018;202:369-377.F.I.:3.958. [doi:10.1016/j.schres.2018.07.022]

16. Treen Calvo D, Gimenez-Donoso, S, Setién-Suero, E, Toll Privat A, Crespo-Facorro, B, AYESA ARRIOLA, MARÍA ROSA. **Targeting recovery in first**

episode psychosis: The importance of neurocognition and premorbid adjustment in a 3-year longitudinal study. *Schizophr. Res.* 2018;195:320-326.F.I.:3.958. [doi:10.1016/j.schres.2017.08.032]

17. Hickling, LM, Pérez-Iglesias, R, Ortiz-García de la Foz V, Balanza-Martinez, V, McGuire, P, Crespo-Facorro, B, Ayesa-Arriola, R. **Tobacco smoking and its association with cognition in first episode psychosis patients Lauren.** *Schizophr. Res.* 2018;192:269-273.F.I.:3.958. [doi:10.1016/j.schres.2017.04.018]

18. Sainz, J, Prieto, C, Ruso-Julve, F, Crespo-Facorro, B. **Blood Gene Expression Profile Predicts Response to Antipsychotics.** *Front. Molec. Neurosci.* 2018;11:73-73.F.I.:3.902. [doi:10.3389/fnmol.2018.00073]

19. Cano-Vindel, A, Muñoz-Navarro R, Medrano, LA, Ruiz-Rodríguez, P, González-Blanch, C, Gómez-Castillo, MD, Capafons, A, Chacon, F, Santolaya, F, PsicAP Research Group. **A computerized version of the Patient Health Questionnaire-4 as an ultra-brief screening tool to detect emotional disorders in primary care.** *J Affect Disord.* 2018;234:247-255.F.I.:3.786. [doi:10.1016/j.jad.2018.01.030]

20. Ayesa-Arriola, R, Canal Rivero M, Delgado-Alvarado, M, Setién-Suero, E, González-Gómez, J, Labad, J, David, AS, Crespo-Facorro, B. **Low-density lipoprotein cholesterol and suicidal behaviour in a large sample of first-episode psychosis patients.** *World J. Biol. Psychiatry.* 2018;19:158-161.F.I.:3.713. [doi:10.1080/15622975.2017.1414305]

21. Castro-Fornieles, J, Bargallo, N, Calvo, A, Arango, C, Baeza, I, González-Pinto, A, Parellada, M, Graell, M, Moreno, C, Otero, S, Janssen, J, Rapado-Castro, M, de la Serna, E. **Gray matter changes and cognitive predictors of 2-year follow-up abnormalities in early-onset first-episode psychosis.** *Eur. Child Adolesc. Psych.* 2018;27:113-126.F.I.:3.553. [doi:10.1007/s00787-017-1013-z]

22. Vázquez-Bourgon, J, Pérez-Iglesias, R, Ortiz-García de la Foz V, Suárez Pinilla P, Díaz Martínez Á, Crespo-Facorro, B. **Long-term metabolic**

effects of aripiprazole, ziprasidone and quetiapine: a pragmatic clinical trial in drug-naïve patients with a first-episode of non-affective psychosis. *Psychopharmacology*. 2018;235:245-255.F.I.:3.222. [doi:10.1007/s00213-017-4763-x]

23. Ranlund, S, Calafato, S, Thygesen, JH, Lin, K, Cahn, W, Crespo-Facorro, B, de Zwart SMC, Diez, A, Di Forti, M, GROUP, Iyegbe C, Jablensky A, Jones R, Hall MH, Kahn R, Kalaydjieva L, Kravariti E, McDonald C, McIntosh AM, McQuillin A, PEIC, Picchioni M, Prata DP, Rujescu D, Schulze K, Shaikh M, Touloupoulou T, van Haren N, van Os J, ..., Bramon E. **A polygenic risk score analysis of psychosis endophenotypes across brain functional, structural, and cognitive domains.** *Am. J. Med. Genet. B*. 2018;177:21-34.F.I.:3.016. [doi:10.1002/ajmg.b.32581]

24. Priede, A, Andreu, Y, Martínez, P, Conchado, A, Ruiz-Torres, M, González-Blanch, C. **The factor structure of the Medical Outcomes Study-Social Support Survey: A comparison of different models in a sample of recently diagnosed cancer patients.** *J. Psychosomat. Res.* 2018;108:32-38.F.I.:2.947. [doi:10.1016/j.jpsychores.2018.02.008]

25. Lopez-Morinigo, JD, Fernandes, AC, Shetty, H, Ayesa-Arriola, R, Bari, A, Stewart, R, Dutta, R. **Can risk assessment predict suicide in secondary mental healthcare? Findings from the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Case Register.** *Soc. Psychiatry Psychiatr. Epidemiol.* 2018;53:1161-1171.F.I.:2.918. [doi:10.1007/s00127-018-1536-8]

26. González-Blanch, C, Medrano, LA, Muñoz-Navarro R, Ruiz-Rodríguez, P, Moriana, JA, Limonero, JT, Schmitz, F, Cano-Vindel, A, PsicAP Research Group. **Factor structure and measurement invariance across various demographic groups and over time for the PHQ-9 in primary care patients in Spain.** *PLoS One*. 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0193356]

27. García, S, Alberich, S, Martínez-Cengotitabengoa, M, Arango, C,

Castro-Fornieles, J, Parellada, M, Baeza, I, Moreno, C, Mico, JA, Berrocoso, E, Graell, M, Otero, S, Simal, T, González-Pinto, A. **The complex association between the antioxidant defense system and clinical status in early psychosis.** *PLoS One*. 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0194685]

28. Tordesillas-Gutiérrez, D, Ayesa-Arriola, R, Delgado-Alvarado, M, Robinson, JL, López-Morinigo, J, Pujol, J, Domínguez-Ballesteros, ME, David, AS, Crespo-Facorro, B. **The right occipital lobe and poor insight in first-episode psychosis.** *PLoS One*. 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0197715]

29. González-Blanch, C, Hernández-de-Hita, F, Muñoz-Navarro R, Ruiz-Rodríguez, P, Medrano, LA, Moriana, JA, Cano-Vindel, A, PsicAP Research Group. **Domain-specific associations between disability and depression, anxiety, and somatization in primary care patients.** *Psychiatry Res.* 2018;269:596-601.F.I.:2.223. [doi:10.1016/j.psychres.2018.09.007]

30. Calvete, E, las Hayas, C, Gómez Del Barrio A. **Longitudinal associations between resilience and quality of life in eating disorders.** *Psychiatry Res.* 2018;259:470-475.F.I.:2.223. [doi:10.1016/j.psychres.2017.11.031]

31. Dranca, L, de Abetxuko Ruiz de Mendarozketa L, Goñi A, Illarramendi, A, Navalpotro Gomez I, Delgado Alvarado M, Cruz Rodríguez-Oroz M. **Using Kinect to classify Parkinson's disease stages related to severity of gait impairment.** *BMC BIOINFORMATICS*. 2018;19:471-471.F.I.:2.213. [doi:10.1186/s12859-018-2488-4]

32. Guerra Diez JL, Gaité Pindado L, Álvarez, CA, Leonardo Cabello MT, Álvarez Granda L, Cabero Pérez MJ. **Influence of demographic changes on the number of visits to hospital emergency departments: 13 years experience.** *An. Pediatr.* 2018;88:322-328.F.I.:1.318. [doi:10.1016/j.anpedi.2017.06.012]

33. Gimenez-Donoso, S, Treen-Calvo, D, Setién-Suero, E, Tirapu-Ustarroz, J, Crespo-Facorro, B, Ayesa-Arriola, R. **Evaluation of verbal inhibitory control with the Stroop Test**

in early episodes of psychosis with the experience of traumatic events in infancy. *Rev. Neurologia*. 2018;67:115-120.F.I.:0.601. [doi:10.33588/rn.6704.2017499]

Projects

1. Benedicto Crespo Facorro. **Investigación genómica en pacientes con un primer episodio de esquizofrenia: Identificación de marcadores genéticos y farmacogenéticos.** ACI07/03. FUNDACION RAMÓN ARECES.
2. Benedicto Crespo Facorro. **CIBERSAM Salud Mental. CB07/09/2001.** INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
3. Benedicto Crespo Facorro. **Ayuda por Producción al Grupo de Investigación de Psiquiatría. APG/02.** Benedicto Crespo Facorro. **Translating neuroimaging findings from research into clinical practice.** EU12/01- PSYSCAN. COMISIÓN EUROPEA.
4. Benedicto Crespo Facorro. **20101299. Estudio Fase II, aleatorio, doble ciego, controlado con placebo, para evaluar el efecto del AMG 747, como tratamiento adicional, sobre los síntomas negativos de la esquizofrenia.** (ESTUDIO 299)". cci1310.
5. Benedicto Crespo Facorro. **Ayudas para contratos predoctorales para la formación de doctores.** BES-2014-070615. MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO.
6. Benedicto Crespo Facorro. **Convenio para la gestión del ensayo con código ABR49490. Estudio europeo de antipsicóticos de acción prolongada en esquizofrenia (EULAST).** CCI16/21.
7. Benedicto Crespo Facorro. **Solución tecnológica para la prevención de recaídas y la rehabilitación en esquizofrenia.** INNVAL16/03.
8. Manuel Delgado Alvarado. **Dispositivo de realidad aumentada en combinación con feedback mecánico subsensorial en el**

tratamiento de los bloqueos de la marcha en la enfermedad de Parkinson. INNVAL16/04.

9. César González-Blanch Bosch. **Coste-efectividad del tratamiento psicológico grupal transdiagnóstico para trastornos mentales comunes en un Centro de Salud (PsicAPCantabria): un ensayo clínico controlado aleatorizado.** INNVAL16/08.

10. Benedicto Crespo Facorro. **Tratamiento estratificado en esquizofrenia: integrando resultados de transcriptoma humano y celular en las estrategias de tratamiento antipsicótico.** SAF2016-76046-R. MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO.

11. Benedicto Crespo Facorro. **COST Action CA15211 Atmospheric Electricity Network: coupling with the Earth System, climate and biological systems.** EU17/15.

12. Javier Vázquez Bourgon. **Searching for early biomarkers of long-term hepatic, metabolic and endothelial dysfunction in non-affective psychosis.** A 10-year follow-up study. NVAL17/24.

13. Benedicto Crespo Facorro. **Plataforma de Unidades de Investigación Clínica y Ensayos Clínicos (Scren).** PT17/0017/0039. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

14. Francisco Galo Peralta Fernández. **Iniciativa de promoción a la investigación europea Valdecilla (VALER H2020).** ECT-2017-0371. MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES MINECO.

15. Benedicto Crespo Facorro. **PSYCH UP, Improving support for people affected by psychological disorders during their training path.** EU18/08. EUROPEAN COMMISSION.

16. María Rosa Ayesa Arriola. **The study of intelligence and general neurocognitive function, that strongly overlap genetically, may be a promising approach for genetic research in schizophrenia spectrum disorders (from now SSD).** MS18/00003_AYUDA. INSTITUTO DE

SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

17. Javier Vázquez Bourgon. **Novel pharmacologic formulation of cannabidiol (CBDloaded nanoparticles) and effect on antipsychotic-induced weight gain and related metabolic alterations.** INNVAL18/30.

Clinical Trials

1. Beatriz Payá González. **Estudio de fase III, abierto, multicéntrico, para proporcionar acceso al clorhidrato de guanfacina de liberación prolongada a sujetos europeos con trastorno por déficit de atención con hiperactividad (TDAH) que participaron en el estudio SPD503-315 o SPD503-316.** SPD503-318. SHIRE PHARMACEUTICAL DEVELOPMENT LIMITED.

2. Benedicto Crespo Facorro. **Estudio europeo de antipsicóticos de acción prolongada en esquizofrenia.** ABR49490. FOUNDATION EUROPEAN GROUP FOR RESEARCH IN SCHIZOPHRENIA EGRIS.

3. Javier Vázquez Bourgon. **Estudio de fase II, aleatorizado, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y la seguridad de 4 dosis orales de BI 425809 una vez al día durante un periodo de tratamiento de 12 semanas en pacientes con esquizofrenia.** 1346.9. BOEHRINGER INGELHEIM ESPAÑA, S.A..

4. Beatriz Payá González. **Estudio intervencional, aleatorizado, con doble enmascaramiento, controlado con placebo, con control activo (fluoxetina) y dosis fija de vortioxetina en pacientes pediátricos de 7 a 11 años con trastorno depresivo mayor (TDM).** 12709A. H. LUNDBECK A/S.

5. Benedicto Crespo Facorro. **Placebo-controlled trial in subjects at Ultra-high Risk for Psychosis with Omega-3 fatty acidS in Europe (PURPOSE).** ABR54654. UNIVERSITY MEDICAL CENTER UTRECHT.

6. Beatriz Payá González. **Estudio de extensión a largo plazo, abierto y con flexibilidad de dosis de vortioxetina en niños y adolescentes de 7 a 18 años de edad con trastorno**

depresivo mayor (TDM). 12712A. H. LUNDBECK A/S.

7. Beatriz Payá González. **Estudio de extensión a largo plazo sin interrumpir el tratamiento, abierto y con flexibilidad de dosis de vortioxetina en niños y adolescentes de 7 a 17 años de edad con trastorno depresivo mayor (TDM).** 12712B. H. LUNDBECK A/S.

8. Benedicto Crespo Facorro. **Estudio para evaluar el efecto de ALKS 3831, en comparación con olanzapina, sobre el peso corporal en adultos jóvenes con esquizofrenia, trastornos esquizofreniformes o trastorno bipolar I con la enfermedad en fase inicial.** ALK3831-A307. ALKERMES INC ALKERMES.

Postmarketing Studies and Other

1. Javier Vázquez Bourgon. **Estudio transversal y revisión retrospectiva de los pacientes con síntomas persistentes de esquizofrenia para estimar la utilización de recursos médicos y la carga de la enfermedad.** ROC-ESQ-2013-01. ROCHE FARMA, S.A.U..

2. Jesús Ángel Artal Simón. **Estudio epidemiológico observacional, transversal, multicéntrico e internacional para evaluar la prevalencia de las crisis de agitación en pacientes psiquiátricos.** FER-ANT-2013-01. FERRER INTERNACIONAL, S.A..

Other publications

Thesis Addressed

1. María Esther Setién Suero. **ESTUDIO LONGITUDINAL SOBRE EL CONSUMO DE CANNABIS EN PRIMEROS EPISODIOS DE PSICOSIS.** Director/s: María Rosa Ayesa Arriola. UNIVERSIDAD DE CANTABRIA.

2. María Juncal Ruiz. **RESPUESTA INMUNOINFLAMATORIA SISTÉMICA EN PRIMEROS EPISODIOS DE PSICOSIS.** Directors: Benedicto Crespo Facorro, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.



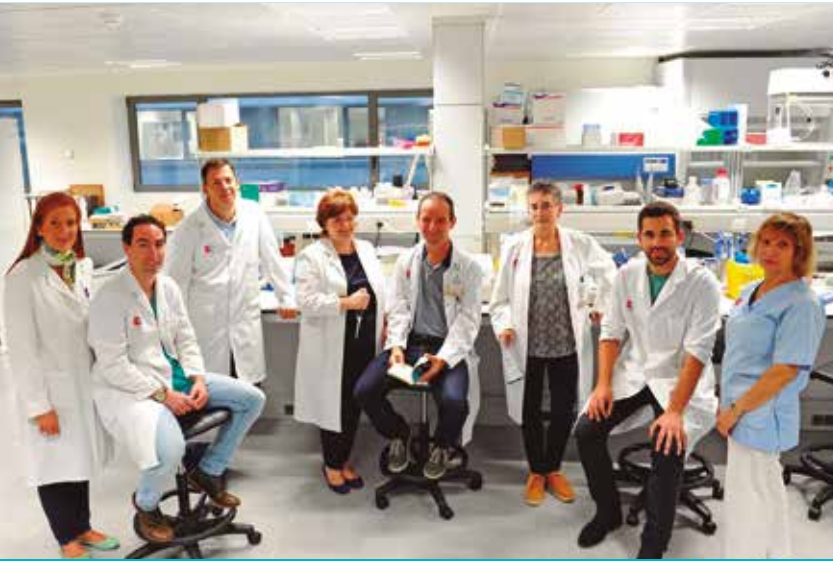


**Cancer
Area**

Fernando Rivera Herrero
Coordinator of the Cancer Area.

Head of the Oncology Service.
Hospital Universitario Marqués de
Valdecilla

○ Anatomical and Molecular Pathology



Consolidated group

Group Responsible

**José Javier
Gómez Román**

Pathology Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



josejavier.gomez@scsalud.es

Researchers

José Fernando Val Bernal

Contributors

Ainara Azueta Etxebarria
Pablo Miguel Bueno Ortíz
Clara Isabel Caballero Escudero
Clara Isabel Esparza del Valle
Francisco Javier Freire Salinas
María Pilar García-Berbel Molina
Servando Lazuen Fernández
Sara Marcos González
Javier Martín López
Marta Mayorga Fernández
Víctor Jacinto Ovejero Gómez
Steliana Florina Racean

Nurses

Montserrat Fernández Álvarez
María Montserrat Nicolás Martínez

Technicians

María Dolores Herrera Cisneros

Research lines

1. Predictive markers and diagnostics in solid tumors based on techniques advanced molecular:

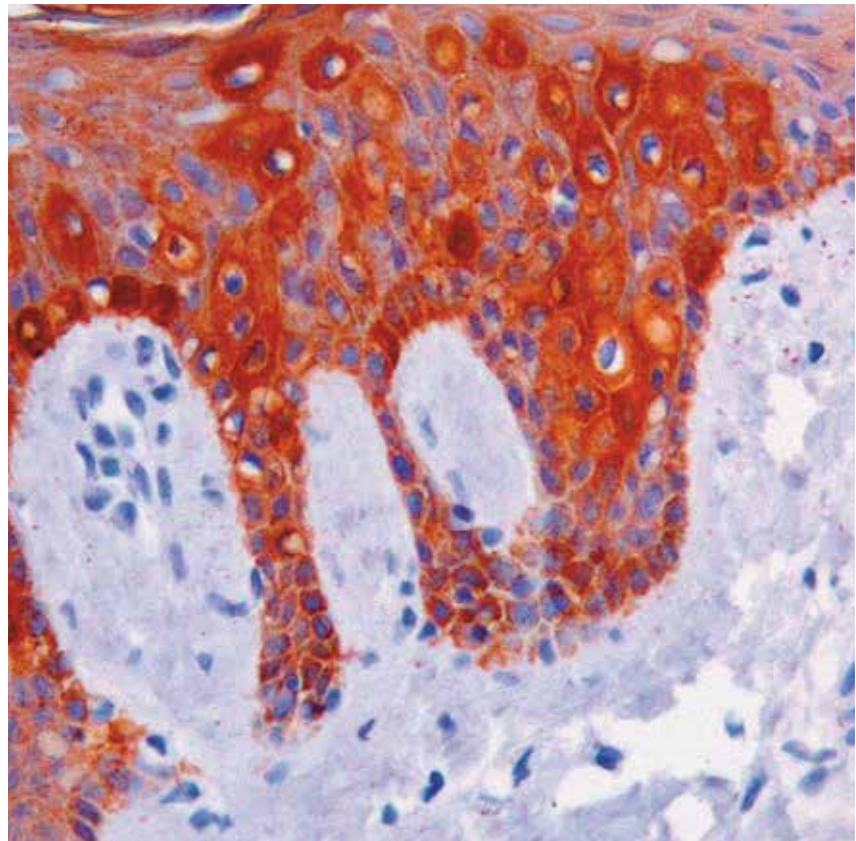
Our concern continues to be to establish the bridge between basic and clinical research by applying new technologies that help to make therapeutic decisions. Our work focuses on obtaining new markers that may be susceptible to their use in diagnosis and as predictive markers of response to drugs of different neoplasms (MAMACAN and TERPERAN projects based on epithelial-mesenchymal transition molecules such as Collagen Xlalfa1 or CCR9).

2. Incorporation of the technology of massive sequencing (Next Generation Sequencing):

The task of diagnosing neoplastic pathology goes from making determinations on a single molecule to panels of genes with repercussions on the therapy to be applied. We have incorporated to the armamentarium of the group the two most powerful technologies at present in this sense as it is that of Illumina and that of ThermoFisher with which besides giving service to the hospital routine we provide collaborations to other units in research projects.

3. We incorporated the diagnosis of hereditary cancer associated with mutations in BRCA1 and 2 with new technologies based on massive sequencing, decreasing the number of extrahospitalary referrals and the waiting time of the patients of the hereditary cancer unit of the Oncology Service.

4. Application of the results obtained and implementation in the clinical care routine. The results of basic research take a



long time until they can be used in practice. Our mission is to speed up the use of biomarkers that have already proven their usefulness in assistance. Thus, we have already incorporated several of the most prevalent tumors such as lung cancer (mutations in EGFR, ALK and ROS1), breast cancer (Her2neu overexpression), colon cancer (mutations in KRAS, NRAS and BRAF) and brain tumors (allelic losses of 1p and 19q regions and methylation of the MGMT promoter), malignant melanoma (mutations in the BRAF oncogene) and other tumor types where there are treatments that improve the quality of life and survival of patients.

5. Development of Liquid Biopsy: The monitoring of patients with cancer is essential due to the existence of new treatments and the development of resistance to them. It is necessary to detect these resistances in the earliest possible way. We have implemented BEAMING technology to diagnose mutations in colon cancer in free

DNA in plasma with a sensitivity of 0.01% allelic frequency. We also have other technologies for diagnosis in free DNA in plasma for lung cancer, especially aimed at detecting the resistance mutation T790M.

6. Development of Immunotherapy in cancer.

Immunotherapy is one of the most promising fields in new cancer therapies. The use of the so-called "companion tests" are mandatory according to the regulatory agencies for the prescription. We have developed all the markers associated with specific anti PD1 and anti PD-L1 therapies. For this, we are involved in the clinical establishment and in new models of anti PD-L1 antibodies SP142, SP263, 22C3 and 28-8. The availability of all antibodies allows the participation in new clinical trials in new tumor models.

7. We actively collaborate with groups from Cantabria, Spain and international in several lines

of work. With the University of Cantabria with active projects in relation to Legal Medicine (utility of DNA extraction methods in old samples) and the IBBTEC in Genómica (Dr Ignacio Varela with several projects in execution using massive sequencing procedures). With Dr. Carmen Álvarez from IDIVAL in the project for the development of nanoparticle-based vaccines against melanoma. The collaboration with national research groups is mainly with the CIMA of the University of Navarra in its line of oncology led by Professor Luis Montuenga in the field of lung cancer and with the University of Oviedo and various hospitals of the national network in the role of the epithelium-mesenchyme transition in breast cancer. We receive rotating professionals from different hospitals in the national network to deepen their teaching. The collaboration extends to European countries as well as to the group of Dr Julian Downward of the London Research Institute investigating factors of resistance to drugs that inhibit tyrosine kinase activity in lung cancer. We also collaborated with MD Anderson Hospital in a neuroendocrine tumor evaluation project and its new classification (Dr. Cesar Moran)

PUBLICATIONS

IMPACT FACTOR | 10.646

Original articles

1. Bleau, AM, Redrado, M, Nistal-Villan, E, Villalba, M, Expósito, F, Redin, E, de Aberasturi, AL, Larzabal, L, Freire, J, Gómez-Román, J, Calvo, A. **miR-146a targets c-met and abolishes colorectal cancer liver metastasis.** *Cancer Lett.* 2018;414:257-267.F.I.:6.491. [doi:10.1016/j.canlet.2017.11.008]
2. Val-Bernal, JF, Martino, M, Romay, F, Yllera, E. **Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal metastases of clear cell renal cell carcinoma.** *Pathol. Res. Pract.*2018;214:949-956.F.I.:1.466. [doi:10.1016/j.prp.2018.05.021]
3. Val-Bernal, JF, Martino, M, Yllera-Contreras, E, Castro-Senosiain, B, Bueno-Ortiz, P. **Intrapancreatic accessory spleen. Report of four cases diagnosed by ultrasound-guided fine-needle aspiration biopsy.** *Rom. J. Morphol. Embryol.*2018;59:619-624.F.I.:0.912.
4. Val-Bernal, JF, Cagigal, ML, Mazorra, R. **Low-fat, plexiform spindle cell lipoma of the lip expressing S100 protein: a neural tumor simulator.** *Rom. J. Morphol. Embryol.*2018;59:385-390.F.I.:0.912.
5. Val-Bernal, JF, Hermana, S, Gómez-Román, JJ. **Incidental, Low-fat variant of spindle cell lipoma: a novel tumour of the small intestine.** *Pol. J. Pathol.*2018;69:82-86.F.I.:0.865. [doi:10.5114/pjp.2018.75341]
6. José Javier Gómez Román. **Ayuda por Producción al grupo de Investigación de Anatomía Patológica y Patología Molecular.** APG/01.
7. José Javier Gómez Román. **Desarrollo de anticuerpos terapéuticos anti-CCR9 para el tratamiento personalizado de tumores- TERPERAN.** RTC-2015-3786-1. MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO.
8. José Javier Gómez Román. **Donación para el desarrollo de proyectos de investigación del Dr. José Javier Gómez Román del Servicio de Anatomía Patológica del Hospital Universitario Marqués de Valdecilla.** CI15/22. ROCHE DIAGNOSTICS, S. L. ROCHE, ROCHE FARMA, S.A.U..
9. José Javier Gómez Román. **Contrato de servicios de investigación para el proyecto Desarrollo y validación de un Kit de detección de genotipos de HPV sin extracción en un sistema lab-on-a-chip.** CSI16/11. GENOMICA S.A.U..
10. José Javier Gómez Román. **Contrato de servicios de investigación para el proyecto Determinación de muestras del biomarcador del gen NKRAS.** CSI16/06. AMGEN, S.A..
11. José Javier Gómez Román. **Contrato de servicios de investigación para el proyecto Elaboración del test para determinar la expresión de PD-L1.** CSI17/01. BRISTOL-MYERS SQUIBB, S.A.U..
12. José Javier Gómez Román. **Contrato de servicios de investigación para el proyecto Molecular DX para el diagnóstico de precisión e BRAF.** CSI17/11. NOVARTIS FARMACEUTICA, S.A..
13. José Javier Gómez Román. **Contrato de servicios de investigación para la determinación de biomarcadores RAS y BRAF en muestras de sangre o tejido de pacientes con cáncer colorrectal metastásico.** CSI17/22. MERCK, S.L..
14. José Javier Gómez Román. **Convenio de colaboración para el desarrollo del proyecto de**

Projects

1. José Javier Gómez Román. **Desarrollo y validación de métodos y productos de diagnóstico contra el carcinoma infiltrante de mama (MAMACAN).** IPT 2011-1817-900000. MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO.

investigación Determinación genómica en muestras de pacientes con cáncer de pulmón no microcítico. CI17/26. PFIZER, S.L.U..

11. José Javier Gómez Román. **Contrato para el desarrollo del Proyecto Use of Next Generation Sequencing (NGS) and Control Liquid Biopsy for Detection of Alk and ROS1 Resistance Mutations in a Spanish Population.** CI18/68. PFIZER, S.L.U..

12. José Javier Gómez Román. **Convenio de colaboración para llevar a cabo las actividades de investigación que, congruentes con sus fines estatutarios, se describen en el pacto 1.2: La Actividad es la siguiente:**

“Analytical Validation of the Next-Generation Sequencing Assays in lung cancer samples”. CI19/02.

ROCHE FARMA, S.A.U..
13. José Javier Gómez Román. Adhesión al programa de biomarcadores dentro de la mejora de la gestión de la patología del cáncer. CI19/14.

Authorship Thesis 2017

1. María Pilar García-Berbel Molina. **Utilidad del COL11A1 como marcador pronóstico de infiltración tumoral.** Director/s: Francisco Javier Freire Salinas, José Javier Gómez Román. UNIVERSIDAD DE CANTABRIA.

Thesis Addressed

1. Lucía García-Berbel Molina. **Determinación de biomarcadores pronósticos en papilomas intraductales mamarios.** Director/s: Francisco Javier Freire Salinas, José Javier Gómez Román. UNIVERSIDAD DE CANTABRIA.

Instituto de
Investigación
Valdecilla

IDIVAL

○ Apoptosis



Consolidated group

Group Responsible

**Juan M. Hurlé
Gonzalez**

Department of Molecular
Biology

School of Medicine
Universidad de Cantabria



hurlej@unican.es

Researchers

Juan Antonio Montero Simón

Contributors

Juan Antonio García-Porrero Pérez
Carlos Ignacio Lordá Díez

Predoctoral

Beatriz García-Riart Monzón
Cristina Sánchez Fernández

○ Research lines

We are interested in the development of the vertebrate limb using avian and mouse embryos as experimental models. The aim of our research

is to uncover molecular signals which regulate the differentiation of skeletal progenitors and also to provide information about limb morphogenesis. Genes identified by different molecular strategies are functionally analyzed through gain-of- and loss-of-function experiments. Gain-of-function experiments are performed through the overexpression of the selected genes employing viral infections or plasmid electroporation. Loss-of-function experiments are made with short hairpin RNAi or CRISPR-Cas9 approaches. Our major research field is the formation of the digits. During

this process mesodermal progenitors of the embryonic limb bud follow two alternative fates: in the future digit regions, mesodermal cells aggregate and differentiate into cartilage, joints and fibrous tissues such as tendons or ligaments; in the interdigital regions, cells do not condense and instead undergo massive cell death. The goal of these studies is to obtain information of relevance in regenerative medicine to direct the differentiation of stem cells into skeletal tissues and to provide basic information about the mechanisms accounting for programmed cell death.

PUBLICATIONS

IMPACT FACTOR | 4.089

Original articles

1. Lorda-Diez, CI, Montero, JA, Sánchez-Fernández, C, García-Porrero, JA, Chimal-Monroy, J, Hurlé, JM. **Four and a half domain 2 (FHL2) scaffolding protein is a marker of connective tissues of developing digits and regulates fibrogenic differentiation of limb mesodermal progenitors.** *J. Tissue Eng. Regen. Med.* 2018;12:2062-2072. F.I.:4.089. [doi:10.1002/term.2637]

2. Gayoso S, Pérez-Borreda P, Gutierrez A, García-Porrero JA, Marco de Lucas E, Martino J. **Ventral Precentral Fiber Intersection Area: A Central Hub in the Connectivity of Perisylvian Associative Tracts.** *Oper Neurosurg (Hagerstown).* 1;F.I.:0.000. [doi:10.1093/ons/opy331]

Projects

1. Juan M. Hurlé González. **Ayuda por Producción al Grupo de Apoptosis.** APG/08.

Authorship Thesis

1. Beatriz García-Riart Monzón. **Análisis del perfil de los microrna en la eliminación de los progenitores esqueléticos de los espacios interdigitales embrionarios.** Director/s: Juan M Hurlé Gonzalez, Juan Antonio Montero Simón. UNIVERSIDAD DE CANTABRIA.

Cell Cycle, Stem Cells and Cancer



Consolidated group

Group Responsible

Alberto Gandarillas Solinis

Fundación Instituto de Investigación

Marqués de Valdecilla
IDIVAL



agandarillas@idival.org

Contributors

Higinio Ayala Gutiérrez
José Manuel Bernal Marco
Ernesto de Diego García
Isabel de Pedro González
Verónica Fernández González
Inmaculada Fernández Jiménez
Ana Freije León
Jesús Galán Vidal
María Fe García Reija
Patricia López Santos
Carmelo Morales Angulo
Sergio Obeso Aguera
Ramón Sanz Giménez-Rico
Ana Tardaguila Calvo
María Soledad Trugeda Carrera
Sandra Patricia Vergara Pastrana

Predoctoral

Lizbeth Araceli Contreras Lara
Lucía San Juan Naharro
Natalia Sanz Gómez

Technicians

Darío Alves Polo
Laura Ceballos Castillo

Research lines

Epithelia are the tissues most frequently affected by cancer. Among them, squamous cell carcinoma (SCC) is the second most common cancer and one of the leading causes of cancer death (Ferlay et al., 2010; <http://www.wcrf.org>; <https://www.cancer.gov/>; <http://www.cancer.org/>; <https://www.cancerresearchuk.org/>). SCC typically appears in the

stratified epithelia of the skin, oral cavity, pharynx, larynx, esophagus, cervix, but is also common in some simple epithelia such as the lung. It constitutes 20% of epithelial cancer in the skin, 90% in the head and neck, 20-80% in the esophagus, or 25-30% in the lung. It is usually aggressive and has a poor prognosis and treatment, except in the case of the skin where it is usually detected early and eliminated by surgery. Even so, in the skin, SCC metastasizes in 4-5% of cases (Karia et al., 2013).

Only the head and neck SCC (HNSCC in English) causes around 200,000 deaths per year in the world (Ferlay et al., 2010). In Spain, about 12,000 cases are diagnosed each year (SEOM, 2014).

There is growing evidence that epidermoid epithelia could have a common regulation, and therefore common alterations would give rise to epidermoid carcinomas. These epithelia are continuously exposed to the action of mutagens such as ultraviolet light from the sun, alcohol or tobacco. For these reasons they need powerful cellular and molecular mechanisms. These mechanisms go through a correct control of Stem Cells and homeostasis. The main objective of our group is the investigation of these mechanisms and their alteration in hyperproliferative problems, fundamentally those that lead to cancer. We use and develop technologies in vitro, in situ and in vivo to study the different

tissues and squamous carcinomas. We are currently studying common regulatory mechanisms in melanocytes. We seek to apply the knowledge generated through the reciprocal transfer between the laboratory (molecular mechanisms of the cell cycle), the industry (exploitation of the results) and the clinic (obtaining biopsies, characterization, monitoring, new diagnoses or therapies).

The main lines currently active are:

- Mechanisms of homeostasis of the epidermis and other epidermoid epithelia against genetic damage.
- Mechanisms of control of mitosis and epidermoid and melanocytic differentiation.
- Alterations of the control mitosis-differentiation in squamous cancer.
- In vitro applications for personalized medicine in: Stem cells. Cancer. Rare, hereditary diseases or developmental syndromes. Through the culture of primary cells of skin and mucosa (keratinocytes, melanocytes, fibroblasts).

PUBLICATIONS

IMPACT FACTOR | 33.350

Original articles

1. Sarmiento, E, Cifrian, J, Calahorra, L, Bravo, C, Lopez, S, Laporta, R, Ussetti, P, Sole, A, Morales, C, de Pablos, A, Jaramillo, M, Ezzahouri, I, Garcia, S, Navarro, J, Lopez-Hoyos, M, Carbone, J. **Monitoring of early humoral immunity to identify lung recipients at risk for development of serious infections: A multicenter prospective study.** *J. Heart Lung Transplant.* 2018;37:1001-1012.F.I.:7.955. [doi:10.1016/j.healun.2018.04.001]
2. de Pedro, I, Alonso-Lecue, P, Sanz-Gomez, N, Freije, A, Gandarillas, A. **Sublethal UV irradiation induces squamous differentiation via a p53-independent, DNA damage-mitosis checkpoint.** *Cell Death Dis.* 2018;9:1094-1094.F.I.:5.638. [doi:10.1038/s41419-018-1130-8]
3. Alvarez-Teijeiro, S, Garcia-Inclan, C, Villaronga, MA, Casado, P, Hermida-Prado, F, Granda-Diaz, R, Rodrigo, JP, Calvo, F, del-Rio-Ibiseate, N, Gandarillas, A, Moris, F, Hermsen, M, Cutillas, P, Garcia-Pedrero, JM. **Factors Secreted by Cancer-Associated Fibroblasts that Sustain Cancer Stem Properties in Head and Neck Squamous Carcinoma Cells as Potential Therapeutic Targets.** *Cancers.* 2018;10:F.I.:5.326. [doi:10.3390/cancers10090334]

4. García-Cenador, B, Blanco-Gozalo, V, López-Montanes, D, Sanz Giménez-Rico JR, Lopez-Novoa, JM, López-Hernández, FJ. **Cardiotrophin-1 Improves Kidney Preservation, Graft Function, and Survival in Transplanted Rats.** *Transplantation.* 2018;102:404-412.F.I.:3.960. [doi:10.1097/TP.0000000000002313]

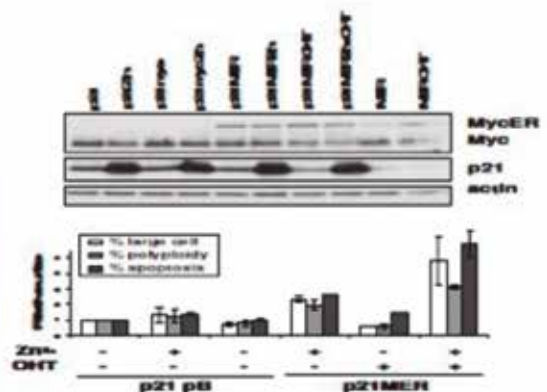
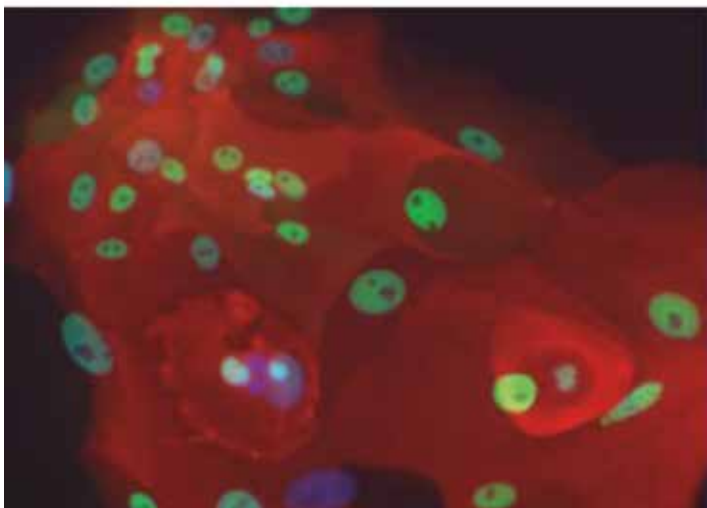
5. Sanz-Gómez, N, Freije, A, Ceballos, L, Obeso, S, Sanz, JR, García-Reija, F, Morales-Angulo, C, Gandarillas, A. **Response of head and neck epithelial cells to a DNA damage-differentiation checkpoint involving polyploidization.** *Head Neck-J. Sci. Spec. Head Neck.* 2018;40:2487-2497.F.I.:2.471. [doi:10.1002/hed.25376]

Reviews

1. Gandarillas, A, Molinuevo, R, Sanz-Gomez, N. **Mammalian endoreplication emerges to reveal a potential developmental timer.** *Cell Death Differ.* 2018;25:471-476.F.I.:8,000. [doi:10.1038/s41418-017-0040-0]

Projects

1. Alberto Gandarillas Solinis. **Ayuda por Producción al Grupo de Ciclo Celular, Determinación de Células Madre y Cáncer.** APG/24. FUNDACIÓN INSTITUTO DE INVESTIGACIÓN MARQUÉS DE VALDECILLA IDIVAL.



2. Alberto Gandarillas Solinis. **Nuevas Rutas y Estrategias Hacia el Cáncer de Células Escamosas.** PI14/00900. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. Alberto Gandarillas Solinis. **Convenio de colaboración para la cobertura de una beca para la realización y desarrollo del proyecto de investigación Rutas moleculares que bloquean la división celular de la piel en respuesta al daño del ADN inducido por el sol.** C115/36. INDUSTRIAL FARMACEUTICA CANTABRIA, S.A..

4. Alberto Gandarillas Solinis. **PREVAL16/04 Natalia Sanz Gómez.** PREVAL16/04. FUNDACIÓN INSTITUTO DE INVESTIGACIÓN MARQUÉS DE VALDECILLA IDIVAL.

5. Alberto Gandarillas Solinis. **Dianas terapéuticas causantes de inestabilidad genómica y malignidad comunes al cáncer escamoso, para su aplicación en medicina personalizada.** PI17/01307. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

6. Ana Freije León. **Nuevas dianas pronósticas en el carcinoma epidermoide de orofaringe y aplicaciones en la personalización del tratamiento.** NVAL17/08.

7. Natalia Sanz Gómez. **MPREVAL18/04 NATALIA SANZ GÓMEZ.** MPREVAL18/04.

8. Alberto Gandarillas Solinis. **Identificación de reguladores moleculares de la diferenciación escamosa como biomarcadores comunes al cáncer epidermoide.** PREVAL19/06.

Authorship Thesis 2018

1. Isabel De Pedro González. **Papel de inhibidores de la Quinasa de Mitosis CDK1 en la Diferenciación Epidermoide.** Director/s: Alberto Gandarillas Solinis. UNIVERSIDAD DE CANTABRIA.

2. Rut Molinuevo Llaría. **Molecular Control of the Differentiation-Mitosis Checkpoint of Keratinocytes in Response to DNA Damage.** Director/s: Alberto Gandarillas Solinis. UNIVERSIDAD DE CANTABRIA.

Thesis Addressed 2018

1. María Del Pilar Mollinedo Sedano. **Células primarias de piel como modelo in vitro del Síndrome ADNP: Una nueva variante del espectro autista.** Director/s: José Luis Fernández Luna, Alberto Gandarillas Solinis. UNIVERSIDAD DE CANTABRIA.



Translational Hematopathology



Emerging group

Group Responsible
Santiago Montes Moreno

Pathology Service
Hospital Universitario
Marqués de Valdecilla



santiago.montes@scsalud.es

Contributors

Julia García Reyero
María del Carmen González Vela
Irene Hernández Alcochel
Nerea Martínez Magunacelaya
María Martino González
Arantza Onaindia Pérez

Technicians

María Pilar Díaz García
Ainara González Pereña
Enriqueta Pumarejo Gómez

Research lines

The activity of the Translational Hematopathology group focuses on:

1. Development of translational research projects in clinical trials

with new drugs for patients with lymphoma.

2. Tune-up and clinical validation of new technologies for the molecular diagnosis of patients with hematolymphoid neoplasms. Liquid biopsy for the genotyping of cases of LBDCG included in prospective clinical trials.

Currently, a line of advancement of our group is the optimization of a genotyping protocol from free circulating tumor DNA in plasma (liquid biopsy) of patients with diffuse B-cell Large Lymphoma.

We have recently demonstrated the feasibility and usefulness of this technology in patients included in a multicentre clinical trial promoted by the GELTAMO group (Cell Free Tumor DNA for DLBCL Genotyping in a Phase II Randomized Trial Comparing Standard RCHOP Versus Brcap As First Line Treatment in Patients with Poor IPI DLBCL). Figure 1A.

Our group, complete with the HUMV pathology service, leads a centralized molecular and anatomopathological diagnostic platform for the clinical trial samples for patients with

diffuse large cell lymphoma B from the national cooperative group GELTAMO (Spanish Lymphomas Group and Transplant Bone marrow, GELBRCAP21 (No. EudraCT: 2012-005138-12), GEL-RCOMP 2013 (No. EudraCT: 2013-001065-17), LR-ESHAP (No. EudraCT: 2010-018463-41), IBDCL (No. EudraCT: 2015-005390-21) This project has funding from national funds (MINECO, PI16 / 1397)

Identification of genetic alterations involved in the pathogenesis of large cell B-cell lymphoma and its progression.

Diffuse large-cell lymphoma B (LBDCG) is the most common form of non-Hodgkin's lymphoma in our country and accounts for 80% of aggressive lymphomas, with an upward-trend incidence that represents about 93,000 new cases a year in Europe. (GLOBOCAN (IARC) The precise subclassification of the different entities of LBDCG has clinical relevance from the point of view of prognosis and selection of therapy since there are a series of phenotypes of aggressive clinical behavior (high grade B lymphoma with "double / triple hit", ABC subtype LBDCG, plasmablastic lymphoma) for which standard immunochemotherapy is ineffective. Recent studies using massive sequencing of the genome and the exome are identifying recurrent genetic alterations in the NFkB, BCR, JAK / STAT pathways, modifying genes of histones and genes related to the immune response, among others. Some of these alterations are associated with specific phenotypes and can be targeted therapy targets.

Recent data from our group (S Montes-Moreno, et al. Modern Pathology 2017) reinforce the relevance of the MYC oncogene in plasmablastic lymphoma and describe, for the first time, somatic mutations in PRDM1 / blimp1 in this type of neoplasm, revealing new molecular mechanisms of the disease (Figure 1B). The recent implementation of NGS-directed sequencing technologies in cases of LBDCG is revealing that mutational profiles are associated with specific clinicopathological variants and condition their phenotype. Recent observations from our group confirm

that the application of directed sequencing methods of the exome using NGS allows to trace the clonal evolution of the refractory LBDCG and may have an impact on the selection of the optimal therapy (García-Reyero et al., Clonal Evolution in primary diffuse large B cell lymphoma of the Central Nervous System, AIMM, 2018, epub) (Figure 1C).

PUBLICATIONS

IMPACT FACTOR | 75.298

Original articles

1. Suárez-González, J, Martínez-Laperche, C, Martínez, N, Rodríguez-Macías, G, Kwon, M, Balsalobre, P, Carbonell, D, Chicano, M, Serrano, D, Triviño JC, Piris, MA, Gayoso, J, Díez-Martín, JL, Buño I. **Whole-exome sequencing reveals acquisition of mutations leading to the onset of donor cell leukemia after hematopoietic transplantation: a model of leukemogenesis. *Leukemia.*** 2018;32:1822-1826.FI.:10.023. [doi:10.1038/s41375-018-0042-z]
2. Martín-Varillas, JL, Calvo-Río, V, Beltrán, E, Sánchez-Burson, J, Mesquida, M, Adán, A, Hernández, MV, Garfella, MH, Pascual, EV, Martínez-Costa, L, Sellas-Fernández, A, Cordero-Coma, M, Díaz-Llopis,

M, Gallego, R, Salom, D, Ortego, N, García-Serrano, JL, Callejas-Rubio, JL, Herreras, JM, García-Aparicio, A, Maiz, O, Blanco, A, Torre, I, Díaz-Valle, D, Pato, E, Aurrecochea, E, Caracul, MA, Gamero, F, Minguez, E, ..., Blanco, R. **Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behcet's Disease. *Ophthalmology.*** 2018;125:1444-1451.FI.:7.479. [doi:10.1016/j.ophtha.2018.02.020]

3. García-Barchino, MJ, Sarasquete, ME, Panizo, C, Morscio, J, Martínez, A, Alcoceba, M, Fresquet, V, Gonzalez-Farre, B, Paiva, B, Young, KH, Robles, EF, Roa, S, Celay, J, Larrayoz, M, Rossi, D, Gaidano, G, Montes-Moreno, S, Piris, MA, Balanzategui, A, Jiménez, C, Rodríguez, I, Calasanz, MJ, Larrayoz, MJ, Segura, V, García-Munoz, R, Rabasa, MP, Yi, SH, Li, JY, Zhang, MZ, ..., Martínez-Climent, JA. **Richter transformation driven by Epstein-Barr virus reactivation during therapy-related immunosuppression in chronic lymphocytic leukaemia. *J. Pathol.*** 2018;245:61-73.FI.:6.253. [doi:10.1002/path.5060]

4. Pardo, E, Díez Baeza E, Salas, Q, García, T, Sancho, JM, Monzón, E, Moraleta, JM, Córdoba, R, de la Cruz, F, Queizán, JA, Rodríguez, MJ, Navarro, B, Hernández, JA, Díez, R, Vahi, M, Viguria, MC, Canales, M, Peñarrubia MJ, Gonzalez-Lopez, TJ, Montes-Moreno, S, González-Barca, E, Caballero, D, Martín, A, from the GELTAMO Spanish Collaborative Group.. **A new prognostic model identifies patients aged 80 years and older with diffuse large B-cell lymphoma who may benefit from curative treatment: A multicenter, retrospective analysis by the Spanish GELTAMO group. *Am. J. Hematol.*** 2018;93:867-873.FI.:5.303. [doi:10.1002/ajh.25107]

5. Atienza-Mateo, B, Calvo-Río, V, Beltrán, E, Martínez-Costa, L, Valls-Pascual, E, Hernández-Garfella, M, Atanes, A, Cordero-Coma, M, Miquel Nolla J, Carrasco-Cubero, C, Loricera, J, Gonzalez-Vela, MC, Vegas-Revenga, N, Fernández-Díaz, C, Demetrio-Pablo, R, Dominguez-Casas, LC, Luis Martín-Varillas J, Palmou-Fontana, N, Hernandez, JL, Gonzalez-Gay, MA, Blanco, R. **Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behcet's disease: multicentre retrospective study.**

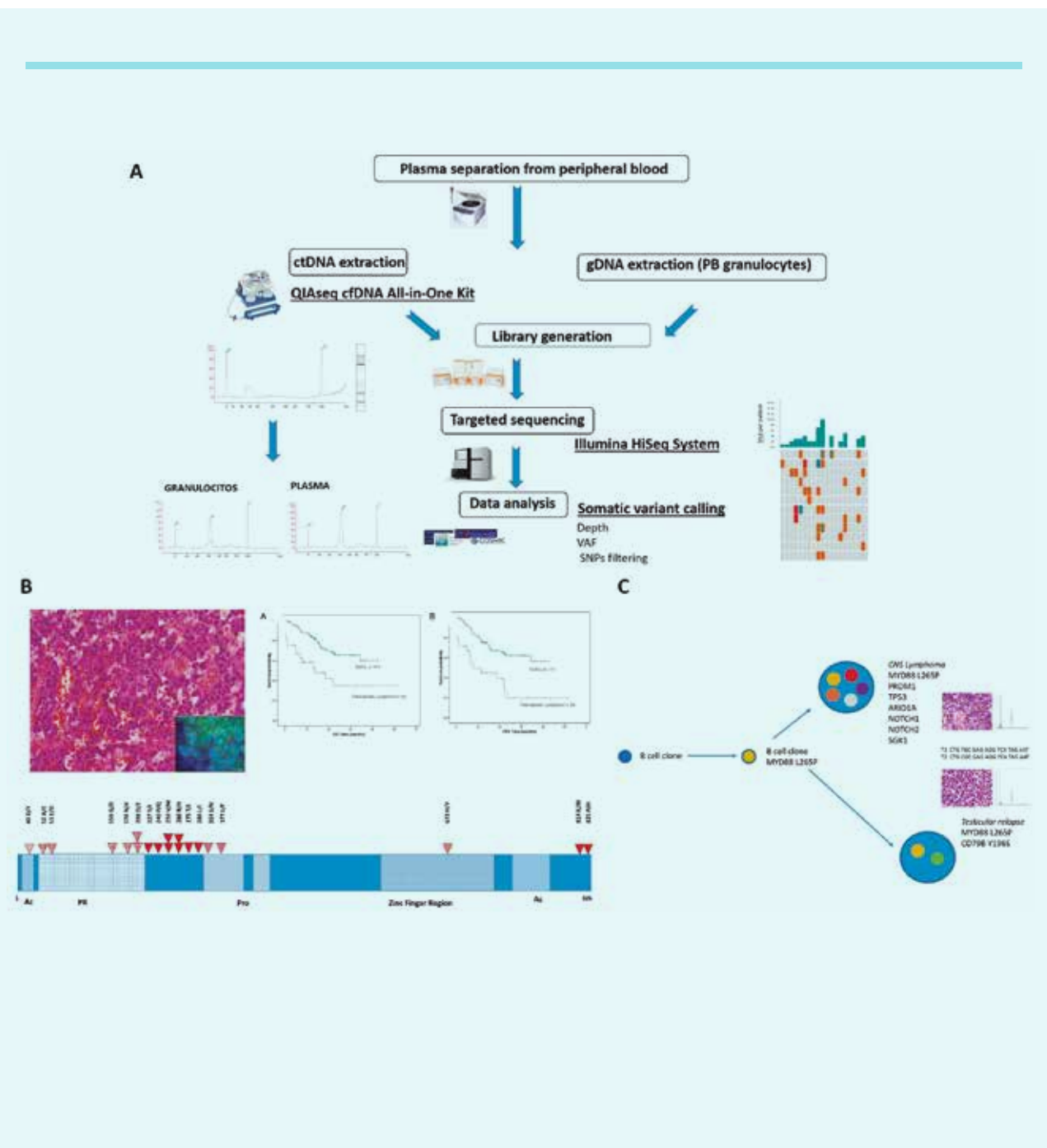


Figure 1. A. Diagram of the genotyping process using NGS from Liquid Biopsy. **B.** The molecular characterization of plasmablastic lymphoma allows to explain the interaction between neoplasm driver genes

(MYC) and other regulatory genes (PRDM1 / Blimp1) revealing new molecular mechanisms of the disease (Plasmablastic lymphoma phenotype is determined by genetic alterations in MYC and PRDM1 Modern Pathology 2017). **C.** The

new methods of directed sequencing of the exome using NGS allow to trace the clonal evolution of the refractory LBDCG (Clonal Evolution in primary diffuse large B cell lymphoma of the Central Nervous System, AIMM, 2018).

RHEUMATOLOGY. 2018;57:856-864.F.I.:5.245. [doi:10.1093/rheumatology/kex480]

6. Llerena Santiago, S, García-Díaz N, Curiel del Olmo, S, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, H, Varela M, Santibáñez Margüello, Mi, Almaraz Pro, M.C., Cereceda Company, L, Martínez Magunacelaya, N, Arias Loste, M.T, Puente Á, Martín-Ramos L, Rodríguez de Lope López, C, Castillo Suescun, F, Cagigas-Fernández C, I P, López-López C, López Hoyos, M, Llorca Díaz, J, Agüero Balbín, J, Crespo Facorro, B, Varela I, Piris Pinilla, M.A., Crespo García, J, Vaqué Díez, J.P. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR.** *Oncotarget.* 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

7. Manso, R, Martínez-Magunacelaya, N, Chamizo, C, Rojo, F, Piris, MA, Rodríguez-Pinilla, SM. **Mutual regulation between BCL6 and a specific set of miRNAs controls T-FH phenotype in peripheral T-cell lymphoma.** *Br J Haematol.* 2018;182:587-590.F.I.:5.128. [doi:10.1111/bjh.14824]

8. Vilanova, I, Hernández, JL, Mata, C, Durán, C, García-Unzueta, MT, Portilla, V, Fuentevilla, P, Corrales, A, González-Vela, MC, Gonzalez-Gay, MA, Blanco, R, Gonzalez-Lopez, MA. **Insulin resistance in hidradenitis suppurativa: a case-control study.** *J. Eur. Acad. Dermatol. Venereol.* 2018;32:820-824.F.I.:4.287. [doi:10.1111/jdv.14894]

9. Bobillo, S, Abrisqueta, P, Sánchez-González, B, Gine, E, Romero, S, Alcoceba, M, Gonzalez-Barca, E, González de Villambrosia Pellón, Sonia, Sancho, JM, Gomez, P, Bento, L, Montoro, J, Montes, S, Lopez, A, Bosch, F, Grupo Español de Linfomas/ Trasplante Autólogo de Médula Ósea (GEL/TAMO cooperati. **Posttransplant monomorphic Burkitt's lymphoma: clinical characteristics and outcome of a multicenter series.** *Ann. Hematol.* 2018;97:2417-2424.F.I.:2.845. [doi:10.1007/s00277-018-3473-8]

10. González-López, MA, Lacalle, M, Mata, C, López-Escobar, M, Corrales, A, López-Mejias, R, Rueda, J, González-Vela, MC, Gonzalez-Gay, MA, Blanco,

R, Hernandez, JL. **Carotid ultrasound is useful for the cardiovascular risk stratification in patients with hidradenitis suppurativa.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0190568]

11. Montes-Moreno, S, Routbort, MJ, Lohman, EJ, Barkoh, BA, Kanagal-Shamanna, R, Bueso-Ramos, CE, Singh, RR, Medeiros, LJ, Luthra, R, Patel, KP. **Clinical molecular testing for ASXL1 c.1934dupG p.Gly646fs mutation in hematologic neoplasms in the NGS era.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0204218]

12. Manso, R, Martínez-Magunacelaya, N, Eraña-Tomás I, Monsalvez, V, Rodríguez-Peralto, JL, Ortiz-Romero, PL, Santonja, C, Cristobal, I, Piris, MA, Rodríguez-Pinilla, SM. **Mycosis fungoides progression could be regulated by microRNAs.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0198477]

13. Siliezar, MM, Muñoz CC, Solano-Iturri, JD, Ortega-Comunian, L, Mollejo, M, Montes-Moreno, S, Piris, MA. **Spontaneously Ruptured Spleen Samples in Patients With Infectious Mononucleosis Analysis of Histology and Lymphoid Subpopulations.** *Am. J. Clin. Pathol.* 2018;150:310-317.F.I.:2.413. [doi:10.1093/AJCP/AQY056]

14. Val-Bernal, JF, Martino, M, Romay, F, Yllera, E. **Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal metastases of clear cell renal cell carcinoma.** *Pathol. Res. Pract.* 2018;214:949-956.F.I.:1.466. [doi:10.1016/j.prp.2018.05.021]

15. Val-Bernal, JF, Martino, M, Yllera-Contreras, E, Castro-Sensiain, B, Bueno-Ortiz, P. **Intrapancreatic accessory spleen. Report of four cases diagnosed by ultrasound-guided fine-needle aspiration biopsy.** *Rom. J. Morphol. Embryol.* 2018;59:619-624.F.I.:0.912.

Reviews

1. González-Barca E, Coronado M, Martín A, Montalbán C, Montes-Moreno S, Panizo C, Rodríguez G, Sancho JM, López-Hernández A, Spanish Lymphoma Group (GELTAMO). **Spanish Lymphoma**

Group (GELTAMO) guidelines for the diagnosis, staging, treatment, and follow-up of diffuse large B-cell lymphoma. *Oncotarget.* 2018;9:32383-32399.F.I.:5.168. [doi:10.18632/oncotarget.25892]

2. Piris, MA, Aguirregoicoa, E, Montes-Moreno, S, Celeiro-Munoz, C. **Castleman Disease and Rosai-Dorfman Disease.** *Semin. Diagn. Pathol.* 2018;35:44-53.F.I.:2.655. [doi:10.1053/j.semdp.2017.11.014]

3. Oishi, N, Montes-Moreno, S, Feldman, AL. **In situ neoplasia in lymph node pathology.** *Semin. Diagn. Pathol.* 2018;35:76-83.F.I.:2.655. [doi:10.1053/j.semdp.2017.11.001]

Projects

1. Santiago Montes Moreno. **Diagnóstico molecular en linfoma B de célula grande.** NVAL15/09.

2. Santiago Montes Moreno. **Targeted exonic next generation sequencing for the molecular diagnosis and cell free tumor DNA analysis as screening method for patients with DLBCL.** PI16/01397. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Thesis Addressed 2017

1. Glenda Mariuxi Bermudez Pinargote. **Neoplasia folicular in situ y neoplasia de células del manto in situ: Incidencia y significado clínico.** Director/s: Miguel Ángel Piris Pinilla, Santiago Montes Moreno. UNIVERSIDAD CANTABRIA.

Books and Book Chapters

1. Montes Moreno, Santiago; Villanueva Mollejo, Manuela; Fraga, Máximo; García, Juan Fernando, José Luis, Villar, Martínez, Antonio, Rodríguez Pinilla, Socorro María, Mayordomo Aranda, Empar, Batlle López, María Ana, Rozman, María, García Sanz, Ramón. **Recomendaciones para el estudio histopatológico, inmunohistoquímico, citogenético y molecular e informe diagnóstico de los procesos neoplásicos linfoides. Consenso SEAP_SEHH-GOTEL. Libro blanco de anatomía patológica de la SEAP.** 2017.65.

Molecular Imaging



Consolidated group

Group Responsible

José Ignacio Banzo Marraco

Nuclear Medicine Service

Hospital Universitario Marqués de Valdecilla



joseignacio.banzo@scsalud.es

Researchers

Julio Francisco Jiménez Bonilla
María Isabel Martínez Rodríguez

Contributors

María de Arcocha Torres
Iván García Martín
Néstor Anibal Martínez Amador
Pedro José Prada Gómez
Remedios Quirce Pisano
María Ángeles Revilla García
María Aida Sánchez Salmón

Research lines

1. Molecular Imaging of Glucose Metabolism in Oncology.

- Imaging Criteria for measuring the Metabolic Response to treatment in Oncology.
- Assessment of the role of 18F-FDG PET/CT on the effect of

biologic therapy in solid tumours.

- Tissue characterization of pulmonary lesions by 18F-FDG PET/CT.
- Assessment of the role of 18F-FDG PET/CT to the nodal staging of lung cancer.

2. Molecular Imaging in the study assessment of the mineralization and inflammation of the carotid atheroma plaque.

- To define an acquisition

protocol of 18F-FDG PET/CT to study the carotid plaque metabolism

- To assess the inflammation process of the carotid plaque by 18F-FDG PET/CT
- To assess the calcification process of the carotid plaque by 18FNa PET/CT
- To monitor the response to anti-inflammatory treatment by 18F-FDG PET/CT
- To study the carotid plaque

stability and to identify the vulnerable plaque by molecular imaging techniques

3. Assessment and evaluation of the clinical impact of 18F-FNa PET/CT and 18F-FDG PET/CT in the management of atherosclerosis in diabetic patients.

- To establish an acquisition protocol for 18F-FNa PET/CT and 18F-FDG PET/CT for the study of atherosclerosis in diabetic patients
- To identify uptake patterns in different vascular territories of the body in diabetic patients
- To evaluate the correlation between the arterial uptake of 18F-Fna and cardiovascular risk factor of diabetes.

4. Molecular Imaging of the protein b-amyloid in the study of the cognitive impairment and assessment of its clinical impact.

- Identification of patients with Alzheimer's disease
- To establish an acquisition protocol for b-amyloid imaging using 11C-PIB PET/CT
- To determine the 11C-PIB retention patterns in the brain
- To study the contribution of 11C-PIB PET/CT in the study of cognitive impairment
- To identify the patients with b amyloid deposit in the brain
- To assess the role of 11C-PIB in differential diagnose of dementias
- To evaluate quantitatively the contribution of 11C-PIB

5. Molecular Imaging in the early diagnosis and extension of vasculitis.

- To establish an acquisition protocol for 18F-FDG in patients with suspicion of large vessel vasculitis.
- To determine the biokinetics of FDG in the large vessels was, to establish the optimum time for image acquisition
- To identify the normal uptake patterns in different vascular territories

- To quantify the arterial wall activity in relation to the global vascular activity

- To calculate the standard uptake values (SUV) in normal subjects and in patients with arterial wall inflammation

6. Research and Development of new molecular imagen radiotracers.

- To study the application of radiotracers for prostate cancer recurrence
- To assess the role of 11C-methionine in primary hyperparathyroidism
- To evaluate the role of 11C-methionine in the suspicion of brain tumour recurrence
- To carry out the synthesis and clinical and to assess the clinical contribution of 18F-FLT
- To carry out the synthesis and develop.

FDG PET/CT in the follow-up of large-vessel vasculitis: A study of 37 consecutive patients. Semin. Arthritis Rheum.2018;47:530-537.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.08.009]

2. Fernández-Torre, JL, Banzo, I, Ortega-Valin, F, Orozco-Sevilla, E, Martínez-Rodríguez, I, Marco de Lucas E. **Subacute encephalopathy with seizures in alcoholics (SESA) syndrome: further evidence supporting that may lie on the ictal-interictal continuum. J. Neurol.**2018;265:2448-2450.F.I.:3.783. [doi:10.1007/s00415-018-9010-9]

3. Lage, C, Suárez, AG, Pozueta, A, Riancho, J, Kazimierczak, M, Bravo, M, Jiménez Bonilla J, de Arcocha Torres M, Quirce, R, Banzo, I, Vázquez-Higuera, JL, Rabinovici, GD, Rodríguez-Rodríguez, E, Sánchez-Juan, P. **Utility of Amyloid and FDG-PET in Clinical Practice: Differences Between Secondary and Tertiary Care Memory Units. J. Alzheimers Dis.**2018;63:1025-1033.F.I.:3.476. [doi:10.3233/JAD-170985]

4. Loricera J, Hernández JL, García-Castaño A, Martínez-Rodríguez I, González-Gay MÁ, Blanco R. **Subclinical aortitis after starting nivolumab in a patient with metastatic melanoma. A case of drug-associated aortitis?. Clin. Exp. Rheumatol.**2018;36 Suppl 111:171-171.F.I.:3.201.

5. Prada, PJ, Cardenal, J, García Blanco A, Anchuelo, J, Ferri, M, Díaz de Cerio I, Vázquez, A, Pacheco, M, Ruiz Arrebola S. **Long-term outcomes in patients younger than 60 years of age treated with brachytherapy for prostate cancer. Strahlenther. Onkol.**2018;194:311-317.F.I.:2.459. [doi:10.1007/s00066-017-1238-2]

6. Prada, PJ, Ferri, M, Cardenal, J, Blanco, AG, Anchuelo, J, Díaz de Cerio I, Vazquez, A, Pacheco, M, Raba, I, Ruiz, S. **High-dose-rate interstitial brachytherapy as monotherapy in one fraction of 20.5 Gy for the treatment of localized prostate cancer: Toxicity and 6-year biochemical results. BRACHYTHERAPY.** 2018;17:845-851.F.I.:2.227. [doi:10.1016/j.brachy.2018.06.002]

PUBLICATIONS

IMPACT FACTOR | 38.506

Original articles

1. Martínez-Rodríguez, I, Jiménez-Alonso, M, Quirce, R, Jiménez-Bonilla, J, Martínez-Amador, N, De Arcocha-Torres, M, Loricera, J, Blanco, R, González-Gay, MA, Banzo, I. **F-18-**

7. Latorre, JA, Galdos, P, Buznego, LA, Blanco, AG, Cardenal, J, Ferri, M, de Cerio, ID, Arrojo, E, Sierrasesumaga, N, Noriega, MG, Ferre, AD, Fabregat, R, Ruiz, S, Prada, PJ. **Accelerated partial breast irradiation in a single 18 Gy fraction with high-dose-rate brachytherapy: preliminary results.** *J. Contemp. Brachytherapy.* 2018;10:58-63.F.I.:2.146. [doi:10.5114/jcb.2018.73994]

8. Berastegui García E, Camara Rosell ML, Estevez Cid F, Sánchez Domínguez E, Ríos Barrera R, Sbraga, F, García Puente J, Rosello Díez E, Cuerpo Caballero GP, Bustamante Munguira J, Reyes Copa G, Tena Pajuelo M, Serrano Fiz S, Buendía Miñano JA, García Martín I, Cuenca Castillo J, Cánovas López S, González Pinto A, Ruyra Baliarda X. **Perceval Less Invasive Aortic Replacement Register: multicentric Spanish experience with the Perceval S bioprosthesis in moderate-high-risk aortic surgery.** *Interact Cardiovasc. Thorac. Surg.* 2018;26:596-601.F.I.:1.756. [doi:10.1093/icvts/ivx384]

9. Banzo, I, Martínez-Rodríguez, I, Martínez-Amador, N, Jiménez-Alonso, M, Quirce, R, Jiménez-Bonilla, J. **"Miner's cap-like" solitary frontal bone metastasis from rectal adenocarcinoma on F-18-FDG PET/CT.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:189-190.F.I.:1.202. [doi:10.1016/j.remnm.2017.06.002]

10. Jiménez-Bonilla, JF, Quirce, R, de Arcocha-Torres, M, Martínez-Rodríguez, I, Martínez-Amador, N, Sánchez-Juan, P, Pozueta, A, Martín-Laez, R, Banzo, I, Rodríguez-Rodríguez, E. **C-11-PIB retention patterns in white and grey cerebral matter in idiopathic normal pressure hydrocephalus patients. A visual analysis.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:87-93.F.I.:1.202. [doi:10.1016/j.remnm.2017.07.006]

11. Gómez-de la Fuente, FJ, Martínez-Rodríguez, I, de Arcocha-Torres, M, Quirce, R, Jiménez-Bonilla, J, Martínez-Amador, N, Banzo, I. **Contribution of C-11-Choline PET/CT in prostate carcinoma biochemical relapse with serum PSA level below 1 ng/ml.** *Rev. Esp. Med. Nucl. Imagen*

Mol. 2018;37:156-162.F.I.:1.202. [doi:10.1016/j.remnm.2017.10.001]

12. García Garzón JR, de Arcocha Torres M, Delgado-Bolton, R, Ceci, F, Álvarez Ruiz S, Orcajo Rincón J, Caresia Aróztegui AP, García Velloso MJ, García Vicente AM, Oncology Task Force of Spanish Society of Nuclear Medicine and Molecular Imaging. **Ga-68-PSMA PET/CT in prostate cancer.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:130-138.F.I.:1.202. [doi:10.1016/j.remnm.2017.07.004]

13. Orcajo-Rincón, J, Caresia-Arortegui, AP, Del Puig Cózar-Santiago M, García-Garzón, JR, de Arcocha-Torres, M, Delgado-Bolton, RC, García-Velloso, MJ, Álvarez-Ruiz, S, García-Vicente, AM. **Radium-223 in the treatment of bone metastasis in patients with castration-resistant prostate cancer. Review and procedure.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:330-337.F.I.:1.202. [doi:10.1016/j.remnm.2018.02.007]

14. Martínez-Amador, N, Martínez-Rodríguez, I, García-Castano, A, Jiménez-Bonilla, J, Quirce, R, Banzo, I. **Unexpected breast metastasis from cutaneous melanoma on F-18-FDG PET/CT.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:390-391.F.I.:1.202. [doi:10.1016/j.remnm.2018.03.001]

15. Jiménez-Bonilla, JF, Gonzalez-Gay, MA, Banzo, I. **Usefulness of 18F-FDG-PET/CT imaging in a patient with neurosarcooidosis.** *Med. Clin.* 2018;151:464-465.F.I.:1.168. [doi:10.1016/j.medcli.2018.02.024]

Editorials

1. Lara, PC, Rodríguez, A, Ferrer, C, Aristu, JJ, Prada, PJ, Muñoz J, Arenas, M, Pérez-Montero, H. **Rescuing Spanish Radiation Therapy: The Role of Leadership and Opportunity.** *Int. J. Radiat. Oncol. Biol. Phys.* 2018;100:292-296.F.I.:5.554. [doi:10.1016/j.ijrobp.2017.09.006]

2. Jiménez-Bonilla, JF, Banzo, I. **Non-oncological applications of PET/CT.** *Med. Clin.* 2018;150:387-389.F.I.:1.168. [doi:10.1016/j.medcli.2017.10.026]

Projects

1. José Ignacio Banzo Marraco. **Ayuda por Producción al Grupo de Imagen Molecular.** APG/30.

2. Pedro José Prada Gómez. **Radioterapia intraoperatoria como tratamiento de innovación asistencial en el Sistema Sanitario Público de Cantabria. Características técnicas y clínicas, metodología, dosimetría y control de calidad.** WLA16/04.

3. Julio Francisco Jiménez Bonilla. **Estudio evolutivo a los 5 años en una población con Deterioro Cognitivo Leve (DCL) evaluada previamente con 11C-PIB y 18F-FDG PET/TAC.** PI16/01656. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

4. Pedro José Prada Gómez. **Contrato de Patrocinio talleres de braquiterapia prostática LDR en tiempo real, oncología intervencionista de la mama, braquiterapia prostática HDR en tiempo real y braquiterapia ginecológica guiada por ultasonidos (IGABT) durante el XIX Congreso SEOR que se celebrará en Santander los días 8 al 10 de junio de 2017.** CS117/06. IPSEN PHARMA, S.A..

5. Pedro José Prada Gómez. **Donaciones para el desarrollo de proyectos de investigación. BDP65.** KYOWA KIRIN FARMACEUTICA S.L.U., LABORATORIOS Q PHARMA, S.L., FUNDACION ESPAÑOLA DE ONCOLOGIA RADIOTERAPICA FEOR, AYUNTAMIENTO DE RAMALES DE LA VICTORIA.

6. María de Arcocha Torres. **Síntesis de 11C- metionina. Un novedoso radiofármaco para la exploración PET/TC en el estudio del mieloma múltiple.** NVAL17/06.

7. Pedro José Prada Gómez. **Contrato de Patrocinio talleres prácticos con quirófanos durante el "XIX Congreso SEOR" que se celebrará en Santander los días 8 al 10 de junio de 2017.** CS117/25. BRAINLAB SALES GMBH.

8. José Ignacio Banzo Marraco. **Contrato de Servicios de**

Investigación para el desarrollo del Estudio en fase II/III multicéntrico, aleatorizado, doble ciego y controlado con placebo sobre dos terapias con potencial para influir sobre la enfermedad en individuos que padecen o presentar riesgo de padecer enfermedad de alzheimer hereditaria dominante (DIAN-TU-001). CSI18/14. IQVIA RDS SPAIN, S.L..

9. Pedro José Prada Gómez. **Evaluation of the Pathfinder 3D device for Brachytherapy.** CSI19/10/02. ECKERT&ZIEGLER BEBIG GMBH.

Clinical Trials

1. Pedro José Gómez Prada. **Ensayo clínico de prueba de concepto, multicéntrico, prospectivo, aleatorizado, abierto y paralelo, para valorar la eficacia de la braquiterapia con o sin tratamiento hormonal con triptorelina 22,5mg semestral en pacientes con cáncer de próstata recurrente previamente tratados con radioterapia.** IPS-TRI-2010-03. IPSEN PHARMA, S.A..

2. Iván García Martín. **RE-GENERATION: Estudio clínico sobre la seguridad y eficacia de RELAY-Pro y de RELAY NBS Pro para el tratamiento de patologías en aórtica torácica.** IP-0011-14. BOLTON MEDICAL ESPAÑA, S.L.U..

Postmarketing Studies and Other

1. María Ángeles Revilla García. **Validación del cuestionario ACTS en pacientes con Fibrilación Auricular (FA) tratados con anticoagulantes orales (ACOs) en consultas de medicina interna y neurología de España.** BAY-ACO-2014-01. BAYER HISPANIA, S.L..

Thesis Addressed 2018

1. Marcos Pajarón Guerrero. **Auto-administración de tratamiento antimicrobiano domiciliario.** Director/s: María Del Carmen Fariñas Álvarez, José Ramón De Berrazueta Fernández. UNIVERSIDAD DE CANTABRIA.

Other Publications

1. Jiménez-Bonilla, JF, Quirce, R, De Arcocha-Torres, M, Martínez-Rodríguez, I, Carril, JM, Jiménez-Alonso, M, Banzo, I, Pozueta, A, Martín-Laez, R, Rodríguez-Rodríguez, E. **Amyloid brain deposition in idiopathic normal pressure hydrocephalus assessed by 11C-PIB PET/CT.** Eur. J. Nucl. Med. Mol. Imaging. 2016;43:134-134.

2. López-Defillo, JL, Martínez-Rodríguez, I, De Arcocha-Torres, M, Jiménez-Bonilla, J, Quirce, R,

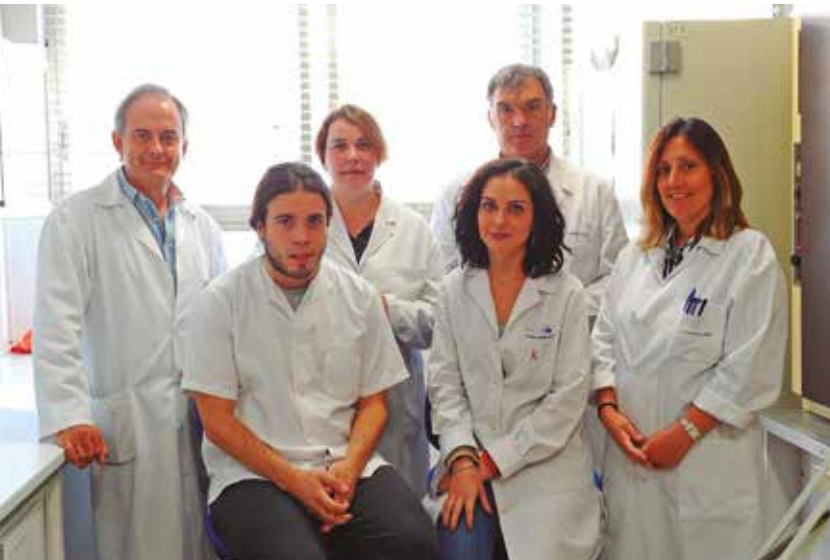
Jiménez-Alonso, M, Gómez-De La Fuente, F, Lavado-Pérez, C, Martínez-Amador, N, Banzo, I. **Contribution of 11C-Methionine PET/CT in the management of patients with brain tumors.** Eur. J. Nucl. Med. Mol. Imaging. 2016;43:261-261.

3. Domínguez Rodríguez, F., Ramos, A, Bouza, E, Muñoz, P, Valerio, MC, Farinas, C, De Berrazueta, JR, Zarauza, J, Pericas Pulido, J. M., Pare, JC, De Alarcon, A, Sousa, D, Rodríguez Bailon, I., Montejo-Baranda, M, García-Pavía, P.

Infective endocarditis in hypertrophic cardiomyopathy: should antibiotic prophylaxis be reconsidered?. Eur. Heart J.2016;37:1015-1015.

4. Jiménez-Alonso, M, Martínez-Rodríguez, I, Lavado-Pérez, C, Lñopez-Defillo, J, Quirce, R, Jiménez-Bonilla, J, De Arcocha-Torres, M, Meza-Escobar, D, Loricera, J, González-Gay, M, Banzo, I. **Semiquantitative analysis of 18F-FDG PET/CT in the follow-up of large vessel vasculitis.** Eur. J. Nucl. Med. Mol. Imaging. 2016;43:62-62.

Melatonin and Breast Cancer



Consolidated group

Group Responsible

Samuel Cos Corral

Department of Physiology and Pharmacology

School of Medicine
Universidad de Cantabria



coss@unican.es

Contributors

Carolina Alonso González
Alicia Verónica González Cabeza
Carlos Manuel Martínez Campa
Noemí Rueda Revilla

Predocctoral

Alicia González González
Javier Menéndez Menéndez

Technicians

José Antonio Cos Cossío
Gema Viar Ruiz

Research lines

Our group focuses its research on the actions of melatonin, the main hormone produced in the pineal gland, on the genesis and development of hormone-dependent mammary tumors. In vivo, either experimental manipulations that activate the pineal gland or the exogenous administration of melatonin, reduce the incidence and development of spontaneous mammary tumors or chemically-

induced mammary tumors in rodents, while pinealectomy or experimental conditions involving a reduction in melatonin synthesis stimulate mammary carcinogenesis. In vitro, melatonin inhibits proliferation and invasiveness of human breast cancer cells. The antitumoral properties of melatonin are based on its ability to interact with estrogen-signaling pathways. Two types of mechanisms have been proposed to explain these oncostatic actions of melatonin: a) downregulation of the circulating levels of gonadal estrogens, and b) direct actions at the tumoral level interfering with the activation of the estrogen receptor, therefore behaving as a SERM (selective estrogen receptor modulator). In last

years, research activity in our group focuses on the description of a third mechanism by which melatonin may reduce the development of estrogen-dependent tumors, based on the ability of melatonin to modulate estrogen synthesis in both tumoral and peritumoral surrounding tissues, behaving as a SEEM (selective estrogen enzyme modulator)

The research that we are currently developing centers on:

- a) To study, on the one hand, the ability of melatonin to modulate the activity of some enzymes (aromatase, sulfatase, 17 β -dehydrogenase, sulfotransferase) involved in the

synthesis of estrogens at tumor level, and, then, to analyze the possible intracellular mediators through which melatonin regulates the activity and expression of these enzymes.

b) To study the ability of melatonin to modulate the angiogenesis and to antagonize the effects of estrogens on new blood vessel formation in hormone-dependent breast cancer.

c) To study the ability of melatonin to increase the sensibility of human breast cancer cells to the action of radiotherapy in base to its actions modulating the enzymes that participate in the synthesis of estrogens and its antiestrogenic actions.

d) To study the protective effects of melatonin on the molecular changes induced by chemotherapy used in the treatment of breast cancer.

e) To study the protective effects of chronic treatment with melatonin on cognitive and neuromorphological deficits in Ts65Dn mouse, a model of Down syndrome.

PUBLICATIONS

IMPACT FACTOR | 29.398

Original articles

1. Rueda, N, Vidal, V, García-Cerro, S, Narcis, JO, Llorens-Martin, M, Corrales, A, Lantigua, S, Iglesias, M, Merino, J, Merino, R, Martínez-

Cue, C. **Anti-IL17 treatment ameliorates Down syndrome phenotypes in mice. Brain Behav. Immun.**2018;73:235-251.F.I.:6.306. [doi:10.1016/j.bbi.2018.05.008]

2. García-Cerro, S, Vidal, V, Lantigua, S, Berciano, MT, Lafarga, M, Ramos-Cabrer, P, Padro, D, Rueda, N, Martínez-Cue, C. **Cerebellar alterations in a model of Down syndrome: The role of the Dyrk1A gene. Neurobiol. Dis.**2018;110:206-217.F.I.:5.227. [doi:10.1016/j.nbd.2017.12.002]

3. Vidal, V, García-Cerro, S, Martínez, P, Corrales, A, Lantigua, S, Vidal, R, Rueda, N, Ozmen, L, Hernández, MC, Martínez-Cue, C. **Decreasing the Expression of GABA(A) alpha 5 Subunit-Containing Receptors Partially Improves Cognitive, Electrophysiological, and Morphological Hippocampal Defects in the Ts65Dn Model of Down Syndrome. Mol. Neurobiol.**2018;55:4745-4762.F.I.:5.076. [doi:10.1007/s12035-017-0675-3]

4. Block, A, Ahmed, MM, Rueda, N, Hernández, MC, Martínez-Cue, C, Gardiner, KJ. **The GABA(A) alpha 5-selective Modulator, RO4938581, Rescues Protein Anomalies in the Ts65Dn Mouse Model of Down Syndrome. Neuroscience.** 2018;372:192-212.F.I.:3.382. [doi:10.1016/j.neuroscience.2017.12.038]

5. Alonso-González, C, Menéndez-Menéndez, J, González-González, A, González, A, Cos, S, Martínez-Campa, C. **Melatonin enhances the apoptotic effects and modulates the changes in gene expression induced by docetaxel in MCF-7 human breast cancer cells. Int. J. Oncol.**2018;52:560-570.F.I.:3.333. [doi:10.3892/ijo.2017.4213]

6. González-González, A, González, A, Alonso-González, C, Menéndez-Menéndez, J, Martínez-Campa, C, Cos, S. **Complementary actions of melatonin on angiogenic factors, the angiopoietin/Tie2 axis and VEGF, in co-cultures of human endothelial and breast cancer cells. Oncol. Rep.**2018;39:433-441.F.I.:2.976. [doi:10.3892/or.2017.6070]

Reviews

1. González-González, A, Mediavilla, MD, Sánchez-Barcelo, EJ. **Melatonin: A Molecule for Reducing Breast Cancer Risk. MOLECULES.** 2018;23:F.I.:3.098. [doi:10.3390/molecules23020336]

Projects

1. Samuel Cos Corral. **Ayuda por Producción al Grupo de Melatonina y Cáncer Mamario.** APG/12.
2. Samuel Cos Corral. **Donaciones para el desarrollo de proyectos de investigación.** BDP56. Asociación Cultural El Desván Solidario.
3. Carolina Alonso González. **Estudio de los efectos sensibilizadores de la melatonina a la quimioterapia neoadyuvante en el tratamiento del cáncer de mama.** NVAL16/01.

Thesis Addressed 2017

1. Sara Lantigua Romero. **Efecto de Distintas Estrategias Terapéuticas sobre los Déficits Cognitivos y las Alteraciones Neuromorfológicas de un Modelo Síndrome de Down.** Director/s: Noemí Rueda Revilla, Carmen Martínez-Cue Pesini. UNIVERSIDAD DE CANTABRIA.

Nanomedicine



Group of new establishment

Group Responsible

Mónica López Fanárraga

Department of Molecular Biology

School of Medicine
Universidad de Cantabria



monica.lopez@unican.es

Researchers

Rafael Valiente Barroso

Contributors

Fernando Aguado Menéndez
Íñigo Casafont Parra
Fidel Ángel Fernández Fernández
Lorena García Hevia
Jesús Antonio González Gómez
Lorena González Legarreta
Fernando González Martínez
Rosa Martín Rodríguez
Débora Muñoz Guerra
Ana Carmen Perdigón Aller
Carlos Renero Lecuna
Carmen Pesquera González
Nuria Terán Villagra
Juan Carlos Villegas Sordo

Predoctoral

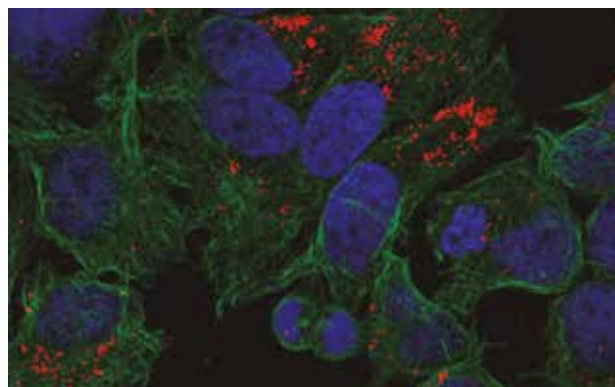
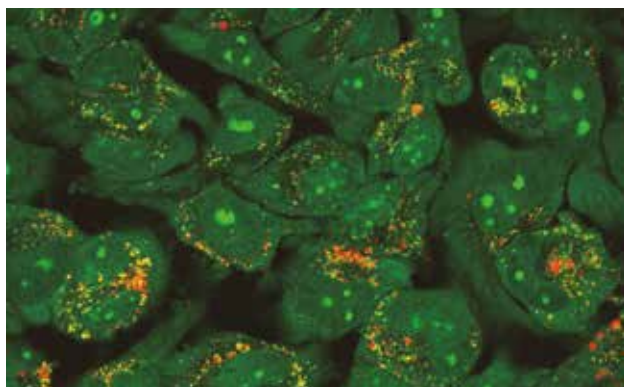
Nerea Iturrioz Rodríguez
Elena María Navarro Palomares
Esperanza Padín González
Ana Rodríguez Ramos
Mahsa Sarami Foroshani
Lourdes María Valdivia Fernández

Research lines

The Nanomedicine group was created in 2014 after being positively accredited by the External Scientific Committee of the ISCiii-IDIVAL Institute. The group is

composed by scientists specialised in the fields of medicine, molecular/cellular biology, biotechnology, pharmacy, physics and chemistry at the IDIVAL institute, but we have several close external collaborators, mostly clinicians. The group has two functional units, the physicochemical subgroup, that self-finances (Directed by Rafael Valiente) that is specialised in the fields of spectroscopy, nanomaterial synthesis and characterisation, and the biomedical group, located at the

Faculty of Medicine. Both groups belong to the IDIVAL-Nanomedicine group. The biomedical group directed by ML Fanarraga has so far participated in two consecutive AES projects dedicated to the use of carbon nanotubes in cancer P113/01074 and PI16/00496. The mission of our research is to understand the interactions between nanomaterials and proteins/cells/tissues -at the in vitro and in vivo levels to obtain products with a "high added value" for



biomedicine and biotechnology, and to develop therapeutic solutions for diseases where traditional therapies are inefficient.

Thus far, major contributions of the Fanarraga group have been achieved in the field of nanotechnology against cancer. In 2012, we first demonstrated the intrinsic anti-tumoral properties of CNT. We have demonstrated how CNTs interact with cell membrane receptors, are phagocytosed finally invading the cellular cytoplasm where they biomimetically interact with the microtubules, assembling biosynthetic tubulin polymers (ACS Nano 2012;6:6614). This interaction triggers important cellular biomechanical changes in highly proliferate cells interfering with microtubule dynamics resulting in "taxol-like" effects. We have pioneered the studies demonstrating how this "intrinsic" property of CNTs leads to anti-proliferative, anti-migratory and cytotoxic effects in different cancer cells in vitro, and significant anti-tumoral effects in vivo, even in solid melanoma models produced with taxol-resistant cells (Adv Healthc Mater. 2014;3:424; Nanomed 2014;9:1581-8; Curr Pharm Des. 2015;21:1920; Adv Healthc Mater. 2015;4:1640; Adv Healthc Mater. 2016;5:1080; Nanoscale. 2016; 8:10963; Biomaterials. 2017;114:62; Int J Nanomed 2017;12:6317; etc). Recently we have developed a method to bio-compatibilize CNTs, improving in vivo degradation by the local tumour associated macrophages (Nanoscale 2018; 10:11013). Our recent results support a role of CNTs as active-by-design nanocarriers significantly boosting the effect of classical chemotherapy, preventing resistance (Oncotarget, 2019 in press). Finally, in the context of our last project we

have designed interesting CNTs coated nanomaterials to control the subcellular destiny of the nanocarrier systems (Angew.Chem. Int. Ed.2017;56:13736).

PUBLICATIONS

IMPACT FACTOR | 46.091

Original articles

- González-Lavado, E, Iturrioz-Rodríguez, N, Padin-González, E, González, J, García-Hevia, L, Heuts, J, Pesquera, C, Gonzalez, F, Villegas, JC, Valiente, R, Fanarraga, ML. **Biodegradable multi-walled carbon nanotubes trigger anti-tumoral effects.** *NANOSCALE.* 2018;10:11013-11020.F.I.:7.233. [doi:10.1039/c8nr03036g]
- Mata-Garrido, J, Tapia, O, Casafont, I, Berciano, MT, Cuadrado, A, Lafarga, M. **Persistent accumulation of unrepaired DNA damage in rat cortical neurons: nuclear organization and ChIP-seq analysis of damaged DNA.** *Acta Neuropathol. Commun.* 2018;6:68-68.F.I.:5.414. [doi:10.1186/s40478-018-0573-6]
- Marcano, L, Munoz, D, Martín-Rodríguez, R, Orue, I, Alonso, J, García-Prieto, A, Serrano, A, Valencia, S, Abrudan, R, Barquín, LF, García-Arribas, A, Muela, A, Fdez-Gubieda, ML. **Magnetic Study of Co-Doped Magnetosome Chains.** *J. Phys. Chem. C.* 2018;122:7541-7550.F.I.:4.484. [doi:10.1021/acs.jpcc.8b01187]
- Berciano, J, Terán-Villagra, N. **Sneddon syndrome and non-bacterial thrombotic endocarditis: a clinicopathological study.** *J. Neurol.* 2018;265:2143-2145.F.I.:3.783. [doi:10.1007/s00415-018-8962-0]
- Pesquera, C, Aguado, F, González, F, Blanco, C, Rodríguez, L, Perdigón, AC. **Tunable interlayer hydrophobicity in a nanostructured high charge organomica.** *Microporous Mesoporous Mat.* 2018;263:77-85.F.I.:3.649. [doi:10.1016/j.micromeso.2017.12.006]
- Perdigón, AC, Pesquera, C, Cota, A, Osuna, FJ, Pavon, E, Alba, MD. **Heteroatom framework distribution and layer charge of sodium Taeniolite.** *Appl. Clay Sci.* 2018;158:246-251.F.I.:3.641. [doi:10.1016/j.clay.2018.03.036]
- Barreda, AI, Otaduy, D, Martín-Rodríguez, R, Merino, S, Fernández-Luna, JL, González, F, Moreno, F. **Electromagnetic behavior of dielectric objects on metallic periodically nanostructured substrates.** *Opt. Express.* 2018;26:11222-11237.F.I.:3.356. [doi:10.1364/OE.26.011222]
- Lago, EL, Seijas, JA, de Pedro, I, Fernández, JR, Vázquez-Tato, MP, González, JA, Rilo, E, Segade, L, Cabeza, O, Fernández, CDR, Arosa, Y, Algnamat, BS, Varela, LM, Troncoso, J, de la Fuente, R. **Structural and physical properties of a new reversible and continuous thermochromic ionic liquid in a wide temperature interval:** [BMIM](4)[Ni(NCS)(6)]. *New J. Chem.* 2018;42:15561-15571.F.I.:3.201. [doi:10.1039/c8nj03294g]

9. Blanco-García, S, Aguado, F, González, J, Rodríguez, F. **A Raman study of the pressure-induced densification of SiO₂-based glass-ceramics.** *J. Phys.-Condes. Matter.* 2018;30:304002-304002.F.I.:2.617. [doi:10.1088/1361-648X/aacb1a]

10. Fischer, S, Ivaturi, A, Jakob, P, Kramer, KW, Martin-Rodríguez, R, Meijerink, A, Richards, B, Goldschmidt, JC. **Upconversion solar cell measurements under real sunlight.** *Opt. Mater.* 2018;84:389-395.F.I.:2.320. [doi:10.1016/j.optmat.2018.05.072]

11. Ferreno, D, Mananes, A, Rabago, D, Casado, JA, González, JA, Gómez, S, Carrascal, IA, Ruiz, E, Diego, S, Gómez, F, Sarachaga, E. **Mechanical behavior and microstructural changes in polyurethane exposed to high doses of X rays, gamma rays or neutron irradiation.** *Polym. Test.* 2018;67:359-369.F.I.:2.247. [doi:10.1016/j.polymertesting.2018.03.033]

12. Santamaría-Aguirre, J, Alcocer-Vallejo, R, López-Fanarraga, M.

Drug Nanoparticle Stability Assessment Using Isothermal and Nonisothermal Approaches.

J. Nanomater. 2018;F.I.:2.207. [doi:10.1155/2018/3047178]

13. Gutiérrez-Cano, V, Rodríguez, F, González, JA, Díaz, V. **Thermal degradation of hydrophobic graphite-based thin film nano-coatings observed by Raman spectroscopy.** *THIN SOLID FILMS.* 2018;648:8-11.F.I.:1.939. [doi:10.1016/j.tsf.2017.12.023]

Projects

1. Mónica López Fanarraga. **Contratos Juan de la Cierva-Formación. FJCI-2015-25306.** MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO, MINISTERIO DE CIENCIA, INNOVACION Y UNIVERSIDADES MINECO.

2. Mónica López Fanarraga. **Diseño y evaluación antitumoral de nano-dispensadores multi-terapéuticos basados en nanotubos de carbono.** **PI16/00496.** INSTITUTO DE SALUD

CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Authorship Thesis 2018

1. Eloísa González Lavado. **Nanodispensadores de fármacos antitumorales basados en Nanotubos de Carbono: Diseño, Evaluación y Biocompatibilización.** Director/s: Mónica López Fanarraga. UNIVERSIDAD DE CANTABRIA.



○ New Techniques in Abdominal Surgery



Associated group

Group Responsible

**Manuel
Gómez Fleitas**

Surgery Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



manuel.gomezf@scsalud.es

Researchers

Luis Antonio Herrera Noreña

Contributors

Joaquín Alonso Martín
Federico Castillo Suescun
Julio José del Castillo Diego
Ramón Agustín Domínguez Díez
María José Fernández Díaz
Roberto Fernández Santiago
Elena García Somacarrera
Marcos Gómez Ruiz
Mónica González Noriega
Gonzalo Gutiérrez Fernández
Fernando Luis Hernanz de La Fuente
Gina Llado Jordan
Antonio López Useros
Cesar Baldomero Madrazo Leal
José Carlos Manuel Palazuelos
José Ignacio Martín Parra
Dieter José Morales García
Carlos Ortega Morales
Rodrigo Perea Muñoz
María Riaño Molleda
Juan Carlos Rodríguez Sanjuan
Isabel Seco Olmedo

○ Research lines

- **Liver tumour pathology.** Staging, new diagnosis and therapeutic techniques.
- **Pancreatic tumour pathology.** Staging, new diagnosis and therapeutic techniques.
- **Biliary tumour pathology and nonneoplastic pathology.** Implementing new clinical surgical procedures (Laparoscopic choledocholithotomy).
- **Results in tumour pathology.** Thermal ablation of hepatocellular carcinoma as a bridge to transplantation and Xenotransplantation.
- **Obesity surgery.** Effects of bariatric surgery on the morbidity factors of obesity in steatohepatitis and ghrelin levels. Evaluation of results.
- **Breast cancer.** Tumour excision using image-guided techniques. Oncoplastic surgical techniques for breast cancer surgery.
- **Research on new techniques for training surgeons.** Development of simulators for training in surgical and endoscopic techniques. Impact of training with simulation methods in the teaching of professionals. Development of simulation models for training in teamwork, communication skills and critical situations.

PUBLICATIONS

IMPACT FACTOR | 23.566

Original articles

1. Fernández-Santiago, R, Garrido, A, Infante, J, González-Aramburu, I, Sierra, M, Fernández, M, Valldeoriola, F, Muñoz E, Compta, Y, Martí, MJ, Rios, J, Tolosa, E, Ezquerro, M, Barcelona LRRK2 Study Group. **alpha-synuclein (SNCA) but not dynamin 3 (DNM3) influences age at onset of leucine-rich repeat kinase 2 (LRRK2) Parkinson's disease in Spain. *Mov. Disord.* 2018;33:637-641.F.I.:8.324. [doi:10.1002/mds.27295]**
2. Llerena Santiago, Susana, García-Díaz N, Curiel del Olmo, Soraya, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, Helena, Varela M, Santibáñez Margüello, Miguel, Almaraz Pro, María del Carmen, Cereceda Company, Laura, Martínez Magunacelaya, Nerea, Arias Loste, María Teresa, Puente Á, Martín-Ramos L, Rodríguez de Lope López, Carlos, Castillo Suescuen, Federico, Cagigas-Fernández C, Isidro P, López-López C, López Hoyos, Marcos, Llorca Díaz, Javier, Agüero Balbín, Jesús, Crespo Facorro, Benedicto, Varela I, Piris Pinilla, Miguel Ángel, Crespo García, Javier, Vaqué Díez, José Pedro. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR. *Oncotarget.* 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]**
3. Hernanz, F, González-Noriega, M, Arozamena, B, Solano, J, García, J. **Bilateral synchronous breast malignant phyllodes in a pregnant woman. *Breast J.* 2018;24:412-413.F.I.:2.424. [doi:10.1111/tbj.12961]**

4. Morales-García, D. **Towards the centralization of digestive oncologic surgery: changes in activity, techniques and outcome. *Rev. Esp. Enferm. Dig.* 2018;110:65-66.F.I.:1.632. [doi:10.17235/reed.2017.5252/2017]**

5. Morales-García, D, Alcázar-Montero, JA, Sanz-Sánchez, M, Miguelena-Bobadilla, JM. **Simulation as a surgical teaching model. *Cir. Espan.* 2018;96:313-314.F.I.:0.841. [doi:10.1016/j.ciresp.2018.02.013]**

6. Ruiz-Gómez, JL, Martín-Parra, JI, González-Noriega, M, Redondo-Figuero, CG, Manuel-Palazuelos, JPC. **Simulation as a Surgical Teaching Model. *Cir. Espan.* 2018;96:12-17.F.I.:0.841.**

7. Gutiérrez-Diez, MC, Benito-González, MA, Sancibrián, R, Gandarillas-González, MA, Redondo-Figuero, C, Manuel-Palazuelos, JC. **A study of the prevalence of musculoskeletal disorders in surgeons performing minimally invasive surgery. *Int. J. Occup. Saf. Ergon.* 2018;24:111-117.F.I.:0.648. [doi:10.1080/10803548.2017.1337682]**

Reviews

1. Lorenzon, L, Biondi, A, Carus, T, Dziki, A, Espin, E, Figueiredo, N, Ruiz, MG, Mersich, T, Montroni, I, Tanis, PJ, MISiCOL Task Force, Benz SR, Bianchi PP, Biehl M, Broeders I, De Luca R, Delrio P, D'Hondt M, Fürst A, Grosek J, Guimaraes Videira JF, Herbst F, Jayne D, Lázár G, Miskovic D, Muratore A, Helmer Sjo O, Scheinin T, Tomazic A, ..., D'Ugo D. **Achieving high quality standards in laparoscopic colon resection for cancer: A Delphi consensus-based position paper. *EJSO.* 2018;44:469-483.F.I.:3.688. [doi:10.1016/j.ejso.2018.01.091]**

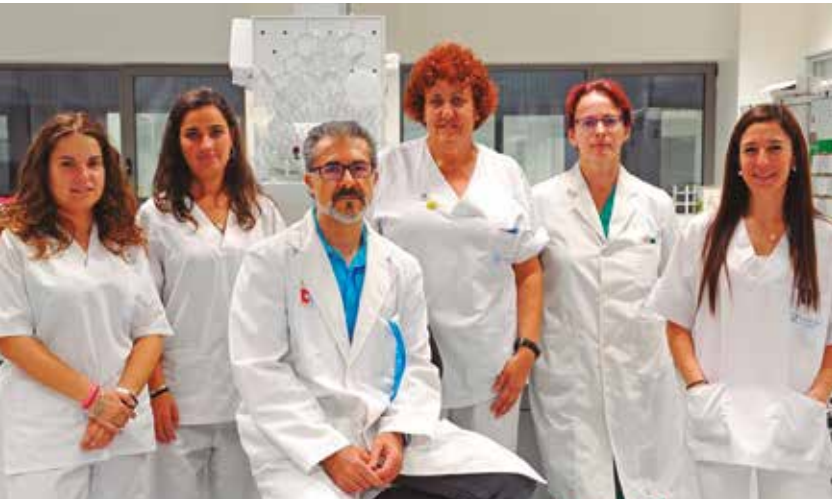
Clinical Trials

1. Julio José del Castillo Diego. **Ensayo clínico multicéntrico, prospectivo, controlado y aleatorizado de no inferioridad, del tratamiento del cáncer de recto T2-T3s (superficial) N0, M0 mediante quimioterapia preoperatoria y microcirugía endoscópica transanal (TEM) versus escisión total del mesorecto (ETM), versión 01 de 1 de julio de 2009. TAU-TEM-2009-01. SERRA, XAVIER.**
2. Julio José del Castillo Diego. **Estudio multicéntrico, aleatorizado, controlado con placebo y doble ciego para evaluar la eficacia y la tolerabilidad del hidrocloruro de diltiazem al 2 % en el tratamiento de la fisura anal crónica, y un periodo de seguimiento de 24 semanas. 150601.**

Thesis Addressed 2017

1. Nerea Ruiz. **Trasplante hepático a partir de donantes en asistolia controlada con uso de necmo. Director/s: Juan Carlos Rodríguez Sanjuan. UNIVERSIDAD DE CANTABRIA.**

Cell Signalling and Therapeutic Targets in Cancer



Consolidated group

Group Responsible

José Luis Fernández Luna

Molecular Genetics Unit
Hospital Universitario Marqués de Valdecilla



joseluis.fernandezl@scsalud.es

Researchers

Juan Martino González

Contributors

César Bellota Antón
Ana María Fontalba Romero
Francisco González Fernández
Fernando Moreno Gracia
Carlos José Velásquez Rodríguez

Technicians

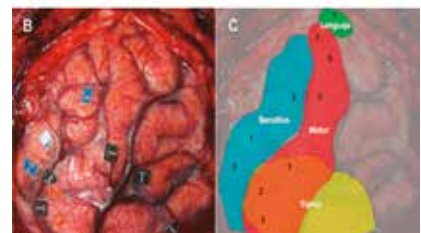
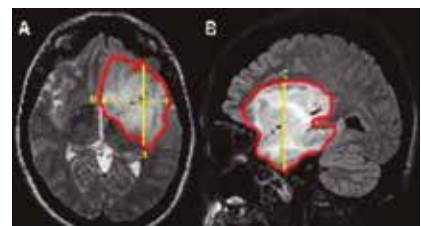
María Olga Gutiérrez Saiz

Research lines

1. Study of the invasive capacity of glioblastoma stem cells (GSCs). The capacity of glioblastoma (GBM) cells to invade the surrounding parenchyma is one of the main problems for an efficient therapeutic strategy because it makes complete

resection nearly impossible. Among the GBM cells there is a small population (<5%) with the capacity to regenerate the tumor and with features similar to those found in adult stem cells. They are the so-called cancer stem cells. If the current hypothesis is right, this cell population is the proper target for new therapeutic strategies. We aim to identify molecular mediators of migration and invasion of GSCs.

2. Development of in vitro models to study the response of GBM cells to chemotherapy in physiological environments.



Most in vitro studies to measure the cellular response to chemotherapy use cell cultures on 2D surfaces. There are many evidences about the role of the biophysic features of the microenvironment in cellular processes studied in vitro (diferentiation, migration, survival). In order to optimize more physiological in vitro models of chemotherapy response, closer to in vivo models, we are studying the behaviour of GBM cells (GSCs and tumor parenchymal

cells) following exposure to chemotherapeutic agents in different microenvironments.

3. Screening of novel compounds addressed to cancer stem cells by using computational and biologic platforms. Currently, there are different undergoing clinical trials addressed to kill cancer stem cells. However, a lack of proof of concept still persist, which means that there are no drugs approved for this indication. This novel therapeutic area is open to different experimental approaches including combinatorial chemistry, re - profiling and virtual screening, among others. In co - llaboration with a start-up from the Bioinformatics Unit at Centro de Biologia Molecular Severo Ochoa (CSIC), we have established a platform that joints computational screening of 5 million compounds with the validation of candidates in biological models in vitro and in vivo. Target cells are cancer stem cells from GBM and colon cancer.

4. Development of a biosensor device to detect, quantify and isolate circulating tumor cells from cancer patients: SENTIR Project. This device, based on optical principles and a microfluidic system, is being developed jointly by IDIVAL (group of cell signaling and therapeutic targets and group of Medical Oncology), University of Cantabria (optics group of the Faculty of Sciences), the center Technological group IK4-TEKNIKER (micro-manufacturing group) and the Cantabrian biotech company CELLBIOCAN. Currently, the assembly of an experimental prototype is being finalized, which will be optimized until it reaches a final product with which a clinical validation will be performed with samples from cancer patients. The objective is to quantify blood CTCs as a predictor, and to isolate them for further genetic analysis, which will allow a personalized selection of the treatment.

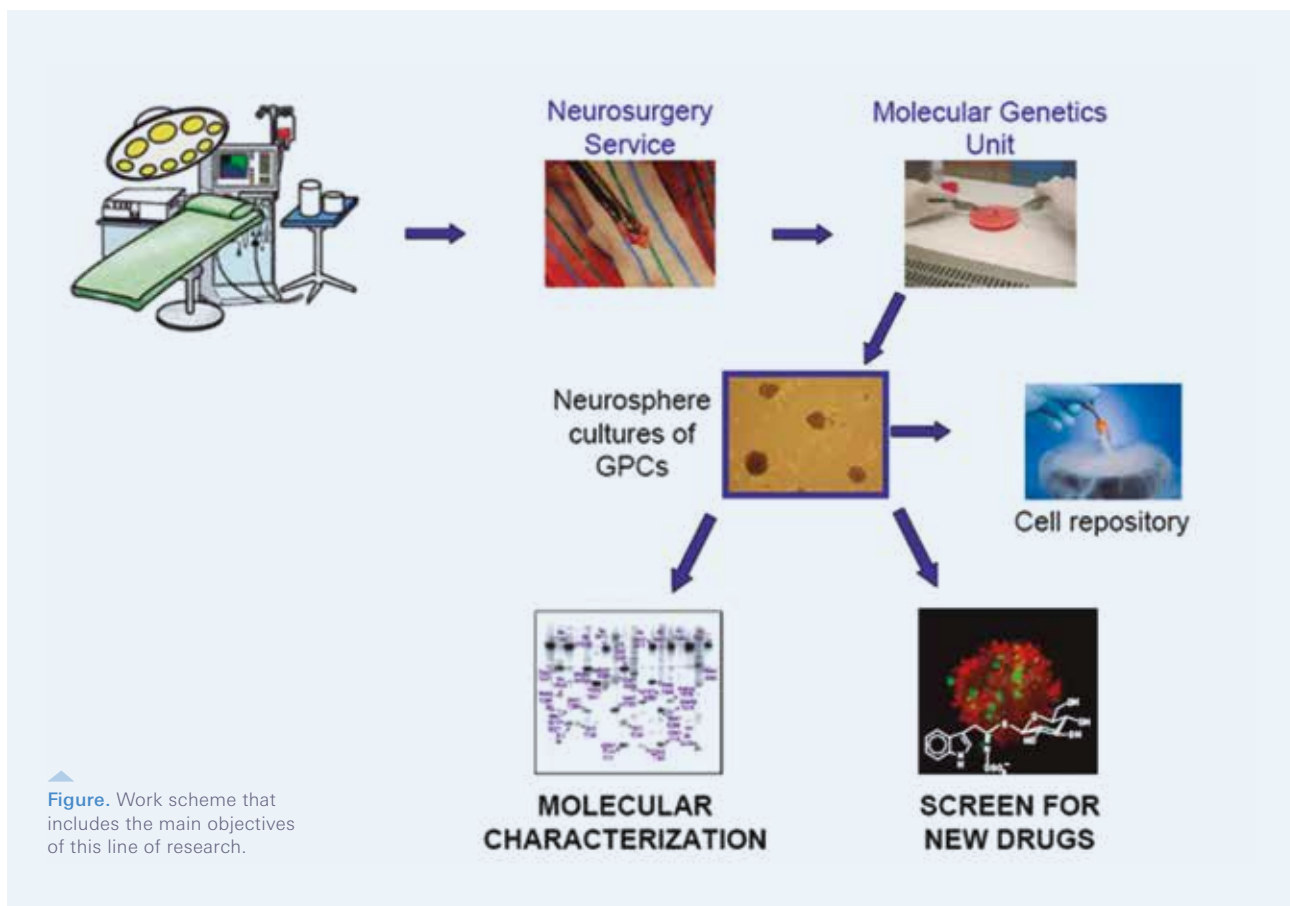
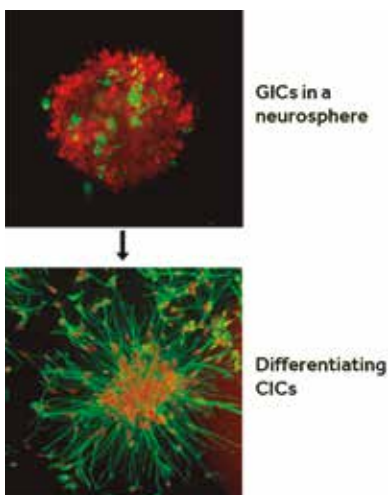


Figure. Work scheme that includes the main objectives of this line of research.

PUBLICATIONS

IMPACT FACTOR | 78.448

Original articles

1. Domínguez, F, Cuenca, S, Bilinska, Z, Toro, R, Villard, E, Barriales-Villa, R, Ochoa, JP, Asselbergs, F, Sammani, A, Franaszczyk, M, Akhtar, M, Coronado-Albi, MJ, Rangel-Sousa, D, Rodríguez-Palomares, JF, Jiménez-Jaimez, J, García-Pinilla, JM, Ripoll-Vera, T, Mogollon-Jimenez, MV, Fontalba-Romero, A, García-Medina, D, Palomino-Doza, J, de Gonzalo-Calvo, D, Cicerchia, M, Salazar-Mendiguchia, J, Salas, C, Pankuweit, S, Hey, TM, Mogensen, J, Barton, PJ, ..., **European Genetic Cardiomyopathies Initiative Investigators. Dilated Cardiomyopathy Due to BLC2-Associated Athanogene 3 (BAG3) Mutations. J. Am. Coll. Cardiol.** 2018;72:2471-2481.F.I.:16.834. [doi:10.1016/j.jacc.2018.08.2181]
2. Ochoa, JP, Sabater-Molina, M, García-Pinilla, JM, Mogensen, J, Restrepo-Cordoba, A, Palomino-Doza, J, Villacorta, E, Martínez-Moreno, M, Ramos-Maqueda, J, Zorio, E, Peña-Peña ML, García-Granja, PE, Rodríguez-Palomares, JF, Cardenas-Reyes, IJ, de la Torre-Carpente, MM, Bautista-Paves, A, Akhtar, MM, Cicerchia, MN, Bilbao-Quesada, R, Mogollon-Jimenez, MV, Salazar-Mendiguchia, J, Mesa Latorre JM, Arnaez, B, Olavarri-Miguel, I, Fuentes-Canamero, ME, Lamounier, A, Pérez Ruiz JM, Climent-Paya, V, Perez-Sanchez, I, ..., Monserrat, L. **Formin Homology 2 Domain Containing 3 (FHOD3) Is a Genetic Basis for Hypertrophic Cardiomyopathy. J. Am. Coll. Cardiol.** 2018;72:2457-2467.F.I.:16.834. [doi:10.1016/j.jacc.2018.10.001]
3. Zhang, X, Li, XQ, Reish, ME, Zhang, D, Su, NQ, Gutierrez, Y, Moreno, F, Yang, WT, Everitt, HO, Liu, J. **Plasmon-Enhanced Catalysis: Distinguishing Thermal and Nonthermal Effects. Nano Lett.** 2018;18:1714-1723.F.I.:12.080. [doi:10.1021/acs.nanolett.7b04776]
4. Perez-Beteta, J, Molina-Garcia, D, Ortiz-Alhambra, JA, Fernandez-

Romero, A, Luque, B, Arregui, E, Calvo, M, Borrás, JM, Melendez, B, Rodríguez de Lope Á, Moreno de la Presa R, Iglesias Bayo L, Barcia, JA, Martino, J, Velasquez, C, Asenjo, B, Benavides, M, Herruzo, I, Revert, A, Arana, E, Perez-Garcia, VM. **Tumor Surface Regularity at MR Imaging Predicts Survival and Response to Surgery in Patients with Glioblastoma. Radiology.** 2018;288:218-225.F.I.:7.469. [doi:10.1148/radiol.2018171051]

5. Martino, J, Gómez, E, de Lucas, EM, Mato, D, Vázquez-Bourgon, J. **Intraoperative Identification and Preservation of Verbal Memory in Diffuse Gliomas: A Matched-Pair Cohort Study. Neurosurgery.** 2018;83:1209-1218.F.I.:4.475. [doi:10.1093/neuros/nyx617]

6. Ferrandez, E, Gutiérrez, O, Segundo DS, Fernández-Luna, JL. **NF kappa B activation in differentiating glioblastoma stem-like cells is promoted by hyaluronic acid signaling through TLR4. Sci Rep.** 2018;8:6341-6341.F.I.:4.122. [doi:10.1038/s41598-018-24444-6]

7. Barreda, AI, Saleh, H, Litman, A, González, F, Geffrin, JM, Moreno, F. **On the scattering directionality of a dielectric particle dimer of High Refractive Index. Sci Rep.** 2018;8:7976-7976.F.I.:4.122. [doi:10.1038/s41598-018-26359-8]

8. Barreda, AI, Otaduy, D, Martín-Rodríguez, R, Merino, S, Fernández-Luna, JL, González, F, Moreno, F. **Electromagnetic behavior of dielectric objects on metallic periodically nanostructured substrates. Opt. Express.** 2018;26:11222-11237.F.I.:3.356. [doi:10.1364/OE.26.011222]

9. Almeida, JP, Velasquez, C, Karekezi, C, Marigil, M, Hodaie, M, Rutka, JT, Bernstein, M. **Global neurosurgery: models for international surgical education and collaboration at one university. Neurosurg. Focus.** 2018;45:F.I.:2.647. [doi:10.3171/2018.7.FOCUS18291]

10. Velásquez C, Gómez E, Martino J. **Mapping visuospatial and self-motion perception functions in the left parietal lobe. Neurosurg. Focus.** 2018;45:F.I.:2.647.

[doi:10.3171/2018.10.FocusVid.18286]

11. Velasquez, C, Tambirajoo, K, Franceschini, P, Eldridge, PR, Farah, JO. **Upper Cervical Spinal Cord Stimulation as an Alternative Treatment in Trigeminal Neuropathy. World Neurosurg.** 2018;114:641-646.F.I.:1.924. [doi:10.1016/j.wneu.2018.03.044]

Reviews

1. Martin-Laez, R, Valle-San Román, N, Rodríguez-Rodríguez, EM, Marco-de Lucas, E, Berciano Blanco JA, Vázquez-Barquero, A. **Current concepts on the pathophysiology of idiopathic chronic adult hydrocephalus: Are we facing another neurodegenerative disease?. Neurologia.** 2018;33:449-458.F.I.:1.938. [doi:10.1016/j.nrl.2016.03.010]

Projects

1. José Luis Fernández Luna. **Ayuda por Producción al Grupo de Investigación de Señalización Celular y Dianas Terapéuticas.** APG/03.
2. José Luis Fernández Luna. **Convenio de Colaboración para el desarrollo del proyecto de investigación Proyecto Marina: Utilización de IPCs como Modelo de Estudio de una Nueva Enfermedad Rara.** C114/09.
3. José Luis Fernández Luna. **Contrato de servicios de investigación para el proyecto Detección de Biomarcadores en Cáncer con nanotecnología plasmódica (Proyecto SENTIR).** CSI15/21.
4. José Luis Fernández Luna. **Donación para el desarrollo del proyecto de investigación Utilización de IPCs como modelo de estudio de una nueva enfermedad rara. Proyecto Marina.** C116/41. HIJAS DE LA CARIDAD SAN VICENTE DE PAUL "COLEGIO SAN JOSE DE ASTILLERO".
5. José Luis Fernández Luna. **Nuevos marcadores pronósticos**

en gliomas de alto grado y estudio de factibilidad para el desarrollo de un programa de cirugía neuro-oncológica ambulatorias en el HUMV. WLA17/04.

6. José Luis Fernández Luna. **Contribución del eje hipoxia-od21 a la capacidad invasiva del glioblastoma.** PI17/01399. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

7. José Luis Fernández Luna. **Desarrollo de un sensor nanoplasmónico para la detección de células tumorales circulantes en sangre de pacientes con cáncer.** FIPSE17/28. FUNDACION PARA LA INNOVACION Y LA PROSPECTIVA EN SALUD EN ESPAÑA "FIPSE".

8. José Luis Fernández Luna. **Sensor nanoplasmónico para la detección de células tumorales circulantes en sangre.** DTS18/00141. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Authorship Thesis 2018

1. María Del Pilar Mollinedo Sedano. **Células Primarias de piel como modelo in vitro del Síndrome ADNP: Una nueva variante del espectro autista.** Director/s: José Luis Fernández Luna, Alberto Gandarillas Solinis. UNIVERSIDAD DE CANTABRIA.

Other Publications

1. Zarrabeitia, R, Salcedo, M, Farithas-elvarez, C, SantibAthez, M, Pascual, C, Limia, C, Setharis, B, Fontalba, A, Recio-Poveda, L, Marua Botella, Luisa, Antonio Parra, Jose. **Euroqol 5D test to evaluate quality of life in patients with hereditary haemorrhagic telangiectasia (HHT) in Spain.** ANGIOGENESIS. 2018;21:167-167.

2. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecoechea, E, Faripas-elvarez, C, Fontalba,

A, Zarauza, J, Ojeda, L, Parra, JA. **Nailfold capillaroscopy in hereditary hemorrhagic telangiectasia.** ANGIOGENESIS. 2018;21:144-144.

Clinical Trials Unit, Medical Oncology and Palliative Medicine



Associated group

Group Responsible

Fernando Rivera Herrero

Oncology Service
Hospital Universitario Marqués de Valdecilla



fernando.rivera@scsalud.es

Contributors

Yolanda Blasco Mesonero
Ana de Juan Ferré
Ignacio Durán Martínez
Almudena García Castaño
Borja Gómez Mediavilla
Carmen Hinojo González
Carlos López López
José Manuel López Vega
Marta Francisca López-Brea Piqueras
Eva Martínez de Castro
Nerea Muñoz Unceta
Matilde Salledo Lambea
Noelia Vega Gil

Nurses

Fátima Antía Gesto Moral

Technicians

M^a Fátima González Cuenca
María Jano García
Helena Zarrabeitia Puente

Research lines

Clinical trials in solid tumors
Nowadays our Unit starts around thirty new clinical trials every year, many of them in Phases II and III, becoming a leading center in Spain

on development of some lines of new drugs, particularly anti-EGFR therapies, anti-VGF and anti-PD-L1.

This line of research is well established, it is the basis of the group's publications and has an intense activity.

PUBLICATIONS

IMPACT FACTOR | 285.685

Original articles

1. Powles, T, Duran, I, van der Heijden, MS, Loriot, Y, Vogelzang, NJ, De Giorgi, U, Oudard, S, Retz, MM, Castellano, D, Bamias, A, Flechon, A, Gravis, G, Hussain, S, Takano, T, Leng, N, Kadel, EE, Banchereau, R, Hegde, PS, Mariathasan, S, Cui, N, Shen, XD, Derleth, CL, Green, MC, Ravaud, A. **Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma**

(IMvigor211): a multicentre, open-label, phase 3 randomised controlled trial. *Lancet*.

2018;391:748-757.F.I.:53.254. [doi:10.1016/S0140-6736(17)33297-X]

2. Kudo, M, Finn, RS, Qin, S, Han, KH, Ikeda, K, Piscaglia, F, Baron, A, Park, JW, Han, G, Jassem, J, Blanc, JF, Vogel, A, Komov, D, Evans TRJ, Lopez, C, Dutcus, C, Guo, M, Saito, K, Kraljevic, S, Tamai, T, Ren, M, Cheng, AL. **Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet*.** 2018;391:1163-1173.F.I.:53.254. [doi:10.1016/S0140-6736(18)30207-1]

3. Rimassa, L, Assenat, E, Peck-Radosavljevic, M, Pracht, M, Zagonel, V, Mathurin, P, Rota Caremoli E, Porta, C, Daniele, B, Bolondi, L, Mazzaferro, V, Harris, W, Damjanov, N, Pastorelli, D, Reig, M, Knox, J, Negri, F, Trojan, J, Lopez, CL, Personeni, N, Decaens, T, Dupuy, M, Sieghart, W, Abbadessa, G, Schwartz, B, Lamar, M, Goldberg, T, Shuster, D, Santoro, A, Bruix, J. **Tivantinib for second-line treatment of MET-high, advanced hepatocellular carcinoma (METIV-HCC): a final analysis of a phase 3, randomised, placebo-controlled study. *Lancet Oncol*.**2018;19:682-693.F.I.:36.418. [doi:10.1016/S1470-2045(18)30146-3]

4. Abad, A, Martínez-Balibrea, E, Vieitez, JM, Orduña VA, García Alfonso P, Manzano, JL, Massuti, B, Benavides, M, Carrato, A, Zanui, M, Gallego, J, Gravalos, C, Conde, V, Provencio, M, Valladares-Ayerbes, M, Salazar, R, Sastre, J, Montagut, C, Rivera, F, Aranda, E. **Genotype-based selection of treatment of patients with advanced colorectal cancer (SETICC): a pharmacogenetic-based randomized phase II trial. *Ann. Oncol*.**2018;29:439-444.F.I.:13.926. [doi:10.1093/annonc/mdx737]

5. Zugazagoitia, J, Biosca, M, Olivera J, Eugenia Olmedo M, Domine, M, Nadal, E, Carlos Ruffinelli J, Muñoz N, María Luna A, Hernández, B, Martínez, M, Gallego, I, Martínez de Castro E, Font, C, Calvo, V, Martínez-Marín, V, Corral, J, Nogueron, E, Mondejar, R,

García Escobar I, Salvador-Coloma, C, Juan, O, Sánchez Cánovas M, Valdivia, J, Ochoa, MP, López Castro R, Obispo, B, Pangua, C, Sereno, M, ..., Manzano, A. **Incidence, predictors and prognostic significance of thromboembolic disease in patients with advanced ALK-rearranged non-small cell lung cancer. *Eur. Resp. J*.**2018;51:F.I.:12.242. [doi:10.1183/13993003.02431-2017]

6. Paumard-Hernandez, B, Calvete, O, Inglada Pérez L, Tejero, H, Al-Shahrour, F, Pita, G, Barroso, A, Carlos Triviño J, Urioste, M, Valverde, C, González Billalabeitia E, Quiroga, V, Francisco Rodríguez Moreno J, Fernández Aramburo A, Lopez, C, Maroto, P, Sastre, J, José Juan Fita M, Duran, I, Lorenzo-Lorenzo, I, Iranzo, P, García Del Muro X, Ros, S, Zambrana, F, María Autran A, Benitez, J. **Whole exome sequencing identifies PLEC, EXO5 and DNAH7 as novel susceptibility genes in testicular cancer. *Int J Cancer*.** 2018;143:1954-1962.F.I.:7.360. [doi:10.1002/ijc.31604]

7. Aranda, E, García-Alfonso, P, Benavides, M, Sánchez Ruiz A, Guillen-Ponce, C, Safont, MJ, Alcaide, J, Gomez, A, Lopez, R, Manzano, JL, Méndez Ureña M, Sastre, J, Rivera, F, Gravalos, C, Garcia, T, Martín-Valades, JI, Falco, E, Navalon, M, González Flores E, Ma García Tapiador A, Ma López Muñoz A, Barrajon, E, Reboredo, M, García Teijido P, Viudez, A, Cardenas, N, Díaz-Rubio, E, Spanish Cooperative Group for the Treatment of Digestive Tumours (TTD). **First-line mFOLFOX plus cetuximab followed by mFOLFOX plus cetuximab or single-agent cetuximab as maintenance therapy in patients with metastatic colorectal cancer: Phase II randomised MACRO2 TTD study. *Eur. J. Cancer*.** 2018;101:263-272.F.I.:7.191. [doi:10.1016/j.ejca.2018.06.024]

8. Muñoz Martín AJ, Ortega, I, Font, C, Pachon, V, Castellón, V, Martínez-Marín, V, Salgado, M, Martínez, E, Calzas, J, Ruperez, A, Souto, JC, Martín, M, Salas, E, Soria, JM. **Multivariable clinical-genetic risk model for predicting venous thromboembolic events in patients with cancer. *Br. J. Cancer*.**

2018;118:1056-1061.F.I.:5.922. [doi:10.1038/s41416-018-0027-8]

9. Peeters, M, Price, T, Taieb, J, Geissler, M, Rivera, F, Canon, JL, Pentheroudakis, G, Koukakis, R, Burdon, P, Siena, S. **Relationships between tumour response and primary tumour location, and predictors of long-term survival, in patients with RAS wild-type metastatic colorectal cancer receiving first-line panitumumab therapy: retrospective analyses of the PRIME and PEAK clinical trials. *Br. J. Cancer*.** 2018;119:303-312.F.I.:5.922. [doi:10.1038/s41416-018-0165-z]

10. Díaz-Serrano, A, Angulo, B, Domínguez, C, Pazo-Cid, R, Salud, A, Jiménez-Fonseca, P, León, A, Galan, MC, Alsina, M, Rivera, F, Plaza, JC, Paz-Ares, L, Lopez-Ríos, F, Gómez-Martin, C. **Genomic Profiling of HER2-Positive Gastric Cancer: PI3K/Akt/mTOR Pathway as Predictor of Outcomes in HER2-Positive Advanced Gastric Cancer Treated with Trastuzumab. *Oncologist*.** 2018;23:1092-1102.F.I.:5.306. [doi:10.1634/theoncologist.2017-0379]

11. Nuñez-Valdovinos B, Carmona-Bayonas, A, Jiménez-Fonseca, P, Capdevila, J, Castaño-Pascual Á, Benavent, M, Pi Barrio JJ, Teule, A, Alonso, V, Custodio, A, Marazuela, M, Segura, A, Beguiristain, A, Llanos, M, Martínez Del Prado MP, Díaz-Perez, JA, Castellano, D, Sevilla, I, Lopez, C, Alonso, T, García-Carbonero, R. **Neuroendocrine Tumor Heterogeneity Adds Uncertainty to the World Health Organization 2010 Classification: Real-World Data from the Spanish Tumor Registry (R-GETNE). *Oncologist*.** 2018;23:422-432.F.I.:5.306. [doi:10.1634/theoncologist.2017-0364]

12. García-Alfonso, P, Benavides, M, Falco, E, Muñoz A, Gómez, A, Sastre, J, Rivera, F, Montagut, C, Salgado, M, Lopez-Ladrón, A, López, R, Ruiz de Mena I, Duran, G, Aranda, E, Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD). **Single-Agent Regorafenib in Metastatic Colorectal Cancer Patients with Any RAS or BRAF Mutation Previously Treated with FOLFOXIRI plus Bevacizumab**

(PREVIUM Trial). Oncologist.

2018;23:1271.F.I.:5.306. [doi:10.1634/theoncologist.2018-0316]

13. Llerena Santiago, S, García-Díaz N, Curiel del Olmo, S, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, H, Varela M, Santibáñez Margüello, M, Almaraz Pro, M.C., Cereceda Company, L, Martínez Magunacelaya, N, Arias Loste, M. T., Puente Á, Martín-Ramos L, Rodríguez de Lope López, C, Castillo Suescun, F, Cagigas-Fernández C, Isidro P, López-López C, López Hoyos, M, Llorca Díaz, J, Agüero Balbín, J, Crespo Facorro, B, Varela I, Piris Pinilla, M.A., Crespo García, J, Vaqué Díez, J.P. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR. Oncotarget.** 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

14. Carmona-Bayonas, A, Jiménez-Fonseca, P, Custodio, A, Sánchez Cánovas M, Hernández, R, Pericay, C, Echavarría, I, Lacalle, A, Visa, L, Rodríguez Palomo A, Mangas, M, Cano, JM, Buxo, E, Álvarez-Manceño, F, García, T, Lorenzo, JE, Ferrer-Cardona, M, Viudez, A, Azkarate, A, Ramchandani, A, Arias, D, Longo, F, López, C, Sánchez Bayona R, Limón, ML, Díaz-Serrano, A, Fernández Montes A, Sala, P, Cerda, P, ..., AGAMENON study group. **Anthracycline-based triplets do not improve the efficacy of platinum-fluoropyrimidine doublets in first-line treatment of advanced gastric cancer: real-world data from the AGAMENON National Cancer Registry. GASTRIC CANCER.** 2018;21:96-105.F.I.:5.045. [doi:10.1007/s10120-017-0718-5]

15. Calderón, C, Jiménez-Fonseca, P, Ferrando, PJ, Jara, C, Lorenzo-Seva, U, Beato, C, García-García, T, Castelo, B, Ramchandani, A, Muñoz MM, Martínez de Castro E, Ghanem, I, Mangas, M, Carmona-Bayonas, A. **Psychometric properties of the Shared Decision-Making Questionnaire (SDM-Q-9) in oncology practice. Int. J. Clin. Health Psychol.** 2018;18:143-151.F.I.:3.900. [doi:10.1016/j.ijchp.2017.03.001]

16. Alsina M, Rivera F, Ramos FJ, Galán M, López R, García-Alfonso P,

Alés-Martínez JE, Queralt B, Antón A, Carrato A, Grávalos C, Méndez-Vidal MJ, López C, de Mena IR, Tabernero J, Giral J, Aranda E, **Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD) and Grupo. A phase II Study Evaluating Combined Neoadjuvant Cetuximab and Chemotherapy Followed by Chemoradiotherapy and Concomitant Cetuximab in Locoregional Oesophageal Cancer Patients. TARGET ONCOL.** 2018;13:69-78.F.I.:3.877. [doi:10.1007/s11523-017-0536-z]

17. Alsina M, Rivera F, Ramos FJ, Galán M, López R, García-Alfonso P, Alés-Martínez JE, Queralt B, Antón A, Carrato A, Grávalos C, Méndez-Vidal MJ, López C, de Mena IR, Tabernero J, Giral J, Aranda E, **Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD) and Grupo. Correction to: A Phase II Study Evaluating Combined Neoadjuvant Cetuximab and Chemotherapy Followed by Chemoradiotherapy and Concomitant Cetuximab in Locoregional Oesophageal Cancer Patients. TARGET ONCOL.** 2018;13:79-79.F.I.:3.877. [doi:10.1007/s11523-017-0544-z]

18. Grávalos, C, Carrato, A, Tobeña M, Rodríguez-Garrote, M, Soler, G, Vieitez, JM, Robles, L, Valladares-Ayerbes, M, Polo, E, Limón, ML, Safont, MJ, Martínez de Castro E, García-Alfonso, P, Aranda, E, Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD). **A Randomized Phase II Study of Axitinib as Maintenance Therapy After First-line Treatment for Metastatic Colorectal Cancer. Clin. Colorectal Canc.** 2018;17:323-329.F.I.:3.861. [doi:10.1016/j.clcc.2018.02.004]

19. Siena, S, Rivera, F, Taieb, J, Peeters, M, Prenen, H, Koukakis, R, Demonty, G, Köhne CH. **Survival Outcomes in Patients With RAS Wild Type Metastatic Colorectal Cancer Classified According to Kohne Prognostic Category and BRAF Mutation Status. Clin. Colorectal Canc.** 2018;17:50.F.I.:3.861. [doi:10.1016/j.clcc.2017.09.006]

20. Carmona-Bayonas, A, Jiménez-Fonseca, P, Echavarría, I, Sánchez Cánovas M, Aguado, G, Gallego, J,

Custodio, A, Hernández, R, Viudez, A, Cano, JM, Martínez de Castro E, Macías, I, Martín Carnicero, A, Garrido, M, Mangas, M, Álvarez Manceño F, Visa, L, Azkarate, A, Ramchandani, A, Fernández Montes A, Longo, F, Sánchez, A, Pimentel, P, Limon, ML, Arias, D, Cacho Lavín D, Sánchez Bayona R, Cerda, P, García Alfonso P, AGAMENON Study Group. **Surgery for metastases for esophageal-gastric cancer in the real world: Data from the AGAMENON national registry. EJSO.** 2018;44:1191-1198.F.I.:3.688. [doi:10.1016/j.ejso.2018.03.019]

21. García Del Muro X, Maurel, J, Martínez Trufero J, Lavernia, J, López Pousa A, de Las Peñas R, Cubedo, R, Berros, JP, Casado Herráez A, de Juan, A, Martín Broto J. **Phase II trial of ifosfamide in combination with the VEGFR inhibitor sorafenib in advanced soft tissue sarcoma: a Spanish group for research on sarcomas (GEIS) study. Invest. New Drugs.** 2018;36:468-475.F.I.:3.502. [doi:10.1007/s10637-018-0583-z]

22. Visa, L, Jimenez-Fonseca, P, Martinez, EA, Hernandez, R, Custodio, A, Garrido, M, Viudez, A, Buxo, E, Echavarría, I, Cano, JM, Macías, I, Mangas, M, de Castro, EM, García, T, Manceño FÁ, Montes, AF, Azkarate, A, Longo, F, Serrano, AD, Lopez, C, Hurtado, A, Cerda, P, Serrano, R, Gil-Negrete, A, Carnicero, AM, Pimentel, P, Ramchandani, A, Carmona-Bayonas, A, AGAMENON Study Group. **Efficacy and safety of chemotherapy in older versus non-older patients with advanced gastric cancer: A real-world data, non-inferiority analysis. J. Geriatr. Oncol.** 2018;9:254-264.F.I.:3.359. [doi:10.1016/j.jgo.2017.11.008]

23. Espinosa, M, Roldán-Romero, JM, Durán, I, de Álava, E, Apellániz-Ruiz, M, Cascon, A, Garrigos, C, Robledo, M, Rodríguez-Antona, C. **Advanced sporadic renal epithelioid angiomyolipoma: case report of an extraordinary response to sirolimus linked to TSC2 mutation. BMC Cancer.** 2018;18:561-561.F.I.:3.288. [doi:10.1186/s12885-018-4467-6]

24. Fernández, A, Salgado, M, García, A, Buxo, E, Vera, R, Adeva, J, Jiménez-Fonseca, P, Quintero, G,

Llorca, C, Cañabate M, López, LJ, Muñoz A, Ramírez, P, González, P, López, C, Reboredo, M, Gallardo, E, Sánchez-Canovas, M, Gallego, J, Guillen, C, Ruiz-Miravet, N, Navarro-Pérez, V, De la Cámara, J, Ales-Díaz, I, Pazo-Cid, RA, Carmona-Bayonas, A. **Prognostic factors for survival with nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer in real-life practice: the ANICE-PaC study.** *BMC Cancer.* 2018;18:1185-1185.F.I.:3.288. [doi:10.1186/s12885-018-5101-3]

25. Taieb, J, Rivera, F, Siena, S, Karthaus, M, Valladares-Ayerbes, M, Gallego, J, Geissler, M, Koukakis, R, Demonty, G, Peeters, M. **Exploratory analyses assessing the impact of early tumour shrinkage and depth of response on survival outcomes in patients with RAS wild-type metastatic colorectal cancer receiving treatment in three randomised panitumumab trials.** *J. Cancer Res. Clin. Oncol.* 2018;144:321-335.F.I.:3.282. [doi:10.1007/s00432-017-2534-z]

26. Taieb, J, Rivera, F, Siena, S, Karthaus, M, Valladares-Ayerbes, M, Gallego, J, Geissler, M, Koukakis, R, Demonty, G, Peeters, M. **Exploratory analyses assessing the impact of early tumour shrinkage and depth of response on survival outcomes in patients with RAS wild-type metastatic colorectal cancer receiving treatment in three randomised panitumumab trials (vol 144, pg 321, 2018).** *J. Cancer Res. Clin. Oncol.* 2018;144:795-797.F.I.:3.282. [doi:10.1007/s00432-018-2591-y]

27. Calderón, C, Jiménez-Fonseca, P, Jara, C, Hernández, R, Martínez de Castro E, Varma, S, Ghanem, I, Carmona-Bayonas, A. **Comparison of Coping, Psychological Distress, and Level of Functioning in Patients With Gastric and Colorectal Cancer Before Adjuvant Chemotherapy.** *J. Pain Symptom Manage.* 2018;56:399-405.F.I.:3.249. [doi:10.1016/j.jpainsymman.2018.05.010]

28. Loricera J, Hernández JL, García-Castaño A, Martínez-Rodríguez I, González-Gay MÁ, Blanco R. **Subclinical aortitis after starting nivolumab in a patient with metastatic melanoma. A case**

of drug-associated aortitis?. *Clin. Exp. Rheumatol.* 2018;36 Suppl 111:171-171.F.I.:3.201.

29. González-Cao, M, Mayo de Las Casas C, Jordana Ariza N, Manzano, JL, Molina-Vila, MA, Soriano, V, Puertolas, T, Balada, A, Soria, A, Majem, M, Montagut, C, Muñoz E, Rodríguez-Abreu, D, Pérez, E, García, A, Cortés, J, Drozdowskyj, A, Karachaliou, N, Rosell, R, Spanish **Melanoma Group. Early evolution of BRAFV600 status in the blood of melanoma patients correlates with clinical outcome and identifies patients refractory to therapy.** *Melanoma Res.* 2018;28:195-203.F.I.:3.135. [doi:10.1097/CMR.0000000000000432]

30. Ashcroft, J, Duran, I, Hoefeler, H, Lorusso, V, Lueftner, D, Campioni, M, Intorcía, M, Bahl, A. **Healthcare resource utilisation associated with skeletal-related events in European patients with multiple myeloma: Results from a prospective, multinational, observational study.** *Eur J Haematol.* 2018;100:479-487.F.I.:2.595. [doi:10.1111/ejh.13044]

31. Santaballa, A, García, Y, Herrero, A, Lainez, N, Fuentes, J, De Juan, A, Rodríguez Freixinós V, Aparicio, J, Casado, A, García-Martínez, E. **SEOM clinical guidelines in gestational trophoblastic disease (2017).** *Clin. Transl. Oncol.* 2018;20:38-46.F.I.:2.392. [doi:10.1007/s12094-017-1793-0]

32. Carles, J, Méndez, MJ, Pinto, A, Sáez, MI, Arranz, JA, Maroto, P, López-Criado, P, Mellado, B, Donas, JG, Hernando, S, León, L, del Alba, AG, Lainez, N, Esteban, E, Reyes, G, Pérez-Gracia, JL, Germa, JR, López-Brea, M, Perez-Valderrama, B, Moretones, C, Castellano, D. **Radium-223 international early access program: results from the Spanish subset.** *Future Oncol.* 2018;14:41-50.F.I.:2.369. [doi:10.2217/fon-2017-0297]

33. Martínez-Amador, N, Martínez-Rodríguez, I, García-Castano, A, Jiménez-Bonilla, J, Quirce, R, Banzo, I. **Unexpected breast metastasis from cutaneous melanoma on F-18-FDG PET/CT.** *Rev. Esp. Med. Nucl. Imagen Mol.* 2018;37:390-391.F.I.:1.202. [doi:10.1016/j.remnm.2018.03.001]

Reviews

1. Carmona-Bayonas, A, Sánchez-Canovas, M, Plasencia, JM, Custodio, A, Martínez de Castro E, Virizuela, JA, Ayala de la Peña F, Jiménez-Fonseca, P. **Key points to optimizing management and research on cancer-associated thrombosis.** *Clin. Transl. Oncol.* 2018;20:119-126.F.I.:2.392. [doi:10.1007/s12094-017-1692-4]

2. Medina-Lopez, RA, Taron, M, Osman-García, I, Duran, I. **Molecular biology of castration resistant prostate cancer.** *Arch. Esp. Urol.* 2018;71:639-650.F.I.:0.465.

Projects

Clinical Trials

1. Marta Francisca López-Brea Piqueras. **Estudio en fase 3, aleatorizado, con doble enmascaramiento, controlado, con placebo, para el acetato de abiraterona (CB7630) más prednisona en pacientes asintomáticos o con síntomas leves que padecen cáncer de próstata metastásico resistente a la castración, versión 1.0 del 11/02/2009.** HIP/CI v 1.1 del 20/07/2009. COU-AA-302. JANSSEN-CILAG, S.A..

2. José Manuel López Vega. **Estudio fase III aleatorizado, abierto de lapatinib, trastuzumab, la administración secuencial de ambos y la administración combinada de ambos como tratamiento adyuvante en pacientes con cáncer de mama HER2/ErbB2 positivo.** EGF106708/CLAP016B2301. GLAXOSMITHKLINE, S.A..

3. Marta Francisca López-Brea Piqueras. **Estudio en fase 3, aleatorizado y abierto, de la eficacia y seguridad de PF-02341066 frente a quimioterapia estándar (pemetrexed o docetaxel) en pacientes con cáncer de pulmón no microcítico (NSCLC) avanzado que presentan una translocación o inversión en el locus del gen de la quinasa de linfoma anaplásico, versión 3 de agosto de 2009.** A8081007. PFIZER LIMITED.

4. Marta Francisca López-Brea Piqueras. **Estudio en fase 2, abierto,**

con un solo grupo de tratamiento, de la eficacia y seguridad de PF02341066 en pacientes con cáncer de pulmón no microcítico (NSCLC) avanzado que presentan una translocación o inversión en el locus del gen de la quinasa de linfoma anaplásico, versión Enmienda 2 de 27 de agosto de 2009,. A8081005. PFIZER LIMITED.

5. Fernando Rivera Herrero. **Ensayo fase IIb randomizado para evaluar la eficacia de Gemcitabina-Erlotinib vs Gemcitabina-Erlotinib-Capecitabina en pacientes con cáncer de páncreas metastático, protocolo vs final de 2 de septiembre de 2010.** TTD-10-01. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

6. Fernando Rivera Herrero. **Estudio SCOT - Tratamiento oncológico de corta duración - Estudio de Quimioterapia Adyuvante en Cáncer Colorrectal.** SCOT. FUNDACIO INSTITUT DE RECERCA DEL HOSPITAL VALL D'HEBRON.

7. Carlos López López. **Estudio fase II aleatorizado de doble ciego de la combinación de Sandostatina LAR con Axitinib vs Sandostatina LAR con placebo en pacientes con carcinomas neuroendocrinos avanzados y bien diferenciados de origen no pancreático (Carcinoides), protocolo Vs. 1 de 3 de mayo de 2011, HIP y CI Vs 3 de mayo de 2011.** AXI-IIG-02. GRUPO ESPAÑOL DE TUMORES NEUROENDOCRINOS, S.A. GETNE.

8. Fernando Rivera Herrero. **Estudio fase II con axitinib como tratamiento de mantenimiento en pacientes con carcinoma colorrectal metastático.** TTD-11-01/AXI-IIG-01. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

9. Ana de Juan Ferré. **Ensayo fase I/II multicéntrico y prospectivo de nilotinib y adriamicina como tratamiento neoadyuvante en liposarcomas y leiomiomas retroperitoneo.** EC10-150 RETRONEO. MARTÍN BROTO, JAVIER.

10. José Manuel López Vega. **Estudio multicéntrico, doble ciego, randomizado, controlado con placebo, para comparar quimioterapia más trastuzumab**

y placebo con quimioterapia más trastuzumab y pertuzumab, como tratamiento adyuvante en pacientes con cáncer de mama primario Her2-positivo operable. BIG 4-11/BO25126/TOC4939G. F. HOFFMANN-LA ROCHE LTD.

11. Marta Francisca López-Brea Piqueras. **Ensayo clínico fase IIb, abierto, aleatorizado de afatinib versus gefitinib en primera línea de tratamiento en pacientes con adenocarcinoma de pulmón avanzado con mutación del EGFR.** 1200.123. BOEHRINGER INGELHEIM ESPAÑA, S.A..

12. José Manuel López Vega. **Ensayo fase II multicéntrico, abierto, de dos cohortes para determinar la eficacia y seguridad de pertuzumab en combinación con trastuzumab y vinorelbine en pacientes de primera línea de cáncer de mama avanzado (localmente avanzado o metastásico) HER-2 positivo.** MO27782. F. HOFFMANN-LA ROCHE LTD.

13. José Manuel López Vega. **Estudio fase III prospectivo, no randomizado y abierto de dos cohortes, multicéntrico y multinacional para asegurar la seguridad de administración asistida o autoadministración de trastuzumab subcutáneo como tratamiento adyuvante en pacientes con carcinoma de mama precoz operable HER-2+.** MO28048. ROCHE FARMA, S.A.U..

14. Fernando Rivera Herrero. **Ensayo clínico fase III aleatorizado, para evaluar la eficacia de FOLFOX + bevacizumab versus FOLFOXIRI + bevacizumab como tratamiento de primera línea de pacientes con cáncer colorrectal metastático no tratado previamente con tres o más células tumorales circulantes.** TTD-12-01. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

15. Fernando Rivera Herrero. **Ensayo clínico fase II aleatorizado para explorar la influencia del estado de BRAF y PI3K, en la eficacia de FOLFIRI + Bevacizumab ó Cetuximab, como tratamiento de primera línea de pacientes con cáncer colorrectal metastático con KRAS nativo y menos de tres**

células tumorales circulantes. TTD-12-02. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

16. Fernando Rivera Herrero. **Estudio en fase II, multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar la eficacia y la seguridad de onartuzumab (MetMab) en combinación con 5-fluorouracilo, ácido fólico y oxaliplatino (mFolfox6) en pacientes con cáncer gastroesofágico positivo para Met, negativo para Her2, metastático.** YO28322. F. HOFFMANN-LA ROCHE LTD.

17. Fernando Rivera Herrero. **Ensayo clínico abierto, multicéntrico, de un único brazo, para evaluar la seguridad y Calidad de Vida Relacionada con la Salud de aflibercept en pacientes con cáncer colorrectal metastático (CCRM) previamente tratados con un régimen conteniendo oxaliplatino.** AFLIBC06097. SANOFI AVENTIS, S.A..

18. Fernando Rivera Herrero. **Ensayo clínico abierto, aleatorizado, de fase III, de cisplatino y 5-fluorouracilo con o sin panitumumab, en pacientes con carcinoma esofágico de células escamosas (ESCC) avanzado o metastático, no resecable.** AIO-STO-0309. AIO-STUDIEN-GGMBH.

19. Ana de Juan Ferré. **Ensayo clínico fase II aleatorizado, abierto y multicéntrico, para determinar la toxicidad y eficacia de quimioterapia pre-quirúrgica con o sin Bevacizumab en pacientes con Cáncer de Ovario Avanzado.** GEICO-1205. GRUPO ESPAÑOL DE INVESTIGACION EN CANCER DE OVARIO GEICO.

20. Almudena García Castaño. **COMBI-AD: Estudio de fase III, aleatorizado y doble ciego de dabrafenib (GSK2118436) en COMBINACIÓN con trametinib (GSK1120212) frente a dos placebos en el tratamiento Adyuvante del melanoma de alto riesgo con la mutación BRAF V600 tras resección quirúrgica.** BRF115532. GLAXOSMITHKLINE, S.A.

21. Carlos López López. **Estudio abierto, controlado, aleatorizado y multicéntrico que compara la eficacia y la seguridad de infusiones intravenosas lentas repetidas de 2 dosis de doxorrubicina Transdrug (DT) (20 mg/m² o 30 mg/m²) con las del mejor tratamiento de referencia (MTR) en pacientes con carcinoma hepatocelular avanzado (CHC) tras fracaso o intolerancia a sorafenib. Estudio ReLive.** BA2011/03/04. ONXEO, S.A..

22. Fernando Rivera Herrero. **Estudio de fase 3, multicéntrico, abierto y aleatorizado de nab-paclitaxel más gemcitabina en comparación con gemcitabina en monoterapia como tratamiento adyuvante en sujetos con adenocarcinoma pancreático extirpado quirúrgicamente.** ABI-007-PANC-003. CELGENE CORPORATION.

23. Fernando Rivera Herrero. **Ensayo IMPALA: Evaluación de un tratamiento de mantenimiento inmunomodulador en pacientes con cáncer colorrectal metastásico con reducción del tumor durante el tratamiento de inducción. Un ensayo en fase III.** MGN1703-C06. MOLOGEN AG.

24. Marta Francisca López-Brea Piqueras. **Ensayo clínico de fase III aleatorizado de comparación de pembrolizumab (MK-3475) frente a paclitaxel, docetaxel o vinflunina en pacientes con cáncer urotelial metastásico recidivante o progresivo.** MK3475-045. MERCK, SHARP&DOHME CORP. (MERCK).

25. José Manuel López Vega. **Estudio multicéntrico, abierto, de un único brazo de extensión de Pertuzumab administrado en monoterapia o en combinación con otros tratamientos antitumorales en pacientes previamente incluidos en estudios de Pertuzumab esponsorizados por Hoffmann-La Roche.** MO29406. F. HOFFMANN-LA ROCHE LTD.

26. Carlos López López. **Estudio fase II para evaluar la actividad y seguridad de TH-302 en combinación con sunitinib para pacientes con tumores neuroendocrinos pancreáticos (pNET) bien o moderadamente diferenciados metastásicos no**

tratados previamente. GETNE-1408. GRUPO ESPAÑOL DE TUMORES NEUROENDOCRINOS, S.A. GETNE.

27. Almudena García Castaño. **Estudio de extensión (transferencia) abierto, de Vemurafenib en pacientes con neoplasia maligna con la mutación BRAFV600 incluidos previamente en un protocolo anterior de Vemurafenib.** GO28399. F. HOFFMANN-LA ROCHE LTD.

28. Marta Francisca López-Brea Piqueras. **Ensayo clínico abierto y multicéntrico de nivolumab (BMS-936558) en monoterapia en sujetos con cáncer de pulmón no microcítico (CPNM) epidermoide avanzado o metastásico que han recibido al menos una línea de tratamiento sistémico previa para el tratamiento del CPNM epidermoide en estadio IIIB/IV.** CA209-171. BRISTOL-MYERS SQUIBB INTERNATIONAL CORPORATION (BMSIC).

29. Fernando Rivera Herrero. **Ensayo clínico de fase III, aleatorizado y abierto de pembrolizumab (MK 3475) frente a paclitaxel en sujetos con adenocarcinoma gástrico o de la unión gastroesofágica avanzado que han presentado progresión después del tratamiento de primera línea con platino y fluoropirimidinas.** MK3475-061. MERCK, SHARP&DOHME CORP. (MERCK).

30. Marta Francisca López-Brea Piqueras. **Estudio Fase III, abierto, aleatorizado, de MPDL3280A (Anticuerpo ANTI-PD-L1) en combinación con Carboplatino + Paclitaxel con o sin Bevacizumab comparado con Carboplatino + Paclitaxel + Bevacizumab en pacientes con cáncer de Pulmón no epidermoide no microcítico en estadio IV que no han recibido quimioterapia previa.** GO29436. F. HOFFMANN-LA ROCHE LTD.

31. Marta Francisca López-Brea Piqueras. **Estudio fase III, Abierto, Multicéntrico, Aleatorizado que evalúa la eficacia y seguridad de MPDL3280A (Anticuerpo ANTI PD L1) en combinación con Carboplatino + Paclitaxel o MPDL3280A en combinación con Carboplatino + Nab Paclitaxel comparado con Carboplatino + Nab**

Paclitaxel en pacientes con cáncer de pulmón no microcítico escamoso estadio IV que no han recibido quimioterapia previa. GO29437. F. HOFFMANN-LA ROCHE LTD.

32. Carlos López López. **Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo, de ramucirumab y las mejores medidas complementarias frente a placebo y las mejores medidas complementarias como tratamiento de segunda línea en pacientes con carcinoma hepatocelular y con la alfafetoproteína (AFP) basal elevada, tras un tratamiento de primera línea con sorafenib.** I4T-MC-JVDE. LILLY, S.A..

33. Carlos López López. **Ensayo para evaluar la eficacia de lenvatinib en tumores neuroendocrinos metastásicos (Estudio Talent).** GETNE1509. GRUPO ESPAÑOL DE TUMORES NEUROENDOCRINOS, S.A. GETNE.

34. Fernando Rivera Herrero. **Ensayo clínico de fase III, aleatorizado, controlado con tratamiento activo, con enmascaramiento parcial y con detección de biomarcadores, de pembrolizumab en monoterapia y en combinación con cisplatino + 5-fluorouracilo frente a placebo + cisplatino + 5-fluorouracilo como tratamiento de primera línea en sujetos con adenocarcinoma gástrico o de la unión gastroesofágica (UGE) avanzado.** MK3475-062. MERCK, SHARP&DOHME CORP. (MERCK).

35. Fernando Rivera Herrero. **Estudio de fase II, aleatorizado, doble ciego controlado con placebo de MM- 141 más nab-paclitaxel y gemcitabina en comparación con nab-paclitaxel y gemcitabina en el tratamiento de primera línea para el cáncer de páncreas metastásico.** MM-141-07-02-02. MERRIMACK PHARMACEUTICALS, INC.

36. Fernando Rivera Herrero. **Ensayo aleatorizado de fase 2 en el que se evalúan dosis alternativas de ramucirumab en combinación con paclitaxel como tratamiento de segunda línea en pacientes con adenocarcinoma gástrico o de la unión gastroesofágica, localmente avanzado o metastásico e resecable.** I4T-MC-JVCZ. LILLY, S.A..

37. Marta Francisca López-Brea Piqueras. **Estudio en fase III, abierto y aleatorizado para investigar la eficacia y seguridad de atezolizumab (anticuerpo Anti-PD-L1) en comparación con el tratamiento de soporte óptimo después de quimioterapia adyuvante basada en cisplatino en pacientes seleccionados por PD-L1 con cáncer de pulmón no microcítico en estadio IB-IIIa totalmente resecado.** GO29527. F. HOFFMANN-LA ROCHE LTD.

38. Fernando Rivera Herrero. **Estudio en fase II de pembrolizumab (MK 3475) en monoterapia en sujetos tratados previamente por un carcinoma colorrectal con alta inestabilidad de microsatélites o con reparación de errores de apareamiento deficiente, localmente avanzado irreseccable o metastásico (estadio IV) (KEYNOTE 164).** MK-3475-164. MERCK, SHARP&DOHME CORP. (MERCK).

39. Fernando Rivera Herrero. **Estudio de fase III de pembrolizumab (MK-3475) frente a quimioterapia en el carcinoma colorrectal en estadio IV con inestabilidad de microsatélites alta (MSI-H) o con defectos en la reparación de los errores de emparejamiento (dMMR) (KEYNOTE-177).** MK3475-177. MERCK, SHARP&DOHME CORP. (MERCK).

40. Carlos López López. **Tratamiento de inducción con FOLFOX con o sin Aflibercept seguido de quimio-radioterapia (QT/RT) en adenocarcinoma de recto localmente avanzado de alto riesgo. Ensayo abierto, Fase II, aleatorizado.** GEMCAD-1402. GRUPO ESPAÑOL MULTIDISCIPLINAR EN CÁNCER DIGESTIVO GEMCAD.

41. Fernando Rivera Herrero. **Ensayo clínico multicéntrico randomizado, de tratamiento de mantenimiento basado en Biomarcadores para primera línea de cáncer colorrectal metastásico (Modul).** MO29112. ROCHE FARMA, S.A.U..

42. Fernando Rivera Herrero. **Estudio en fase 1b/2 del tratamiento combinado con Ibrutinib en tumores**

gastrointestinales y genitourinarios avanzados seleccionados. PCYC-1128-CA. SYNEOS HEALTH UK LTD..

43. Marta Francisca López-Brea Piqueras. **Estudio abierto y multicéntrico en fase III de brigatinib (AP26113) frente a crizotinib en pacientes con cáncer de pulmón avanzado con ALK positiva.** AP26113-13-301. ARIAD PHARMACEUTICALS, INC..

44. Fernando Rivera Herrero. **Estudio aleatorizado fase 2 de comparación de diferentes dosis-pautas de tratamiento de inducción (primer ciclo) de regorafenib en pacientes con cáncer colorrectal metastásico (mCRC).** TTD-16-01. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

45. Fernando Rivera Herrero. **Estudio fase II para evaluar la eficacia de FOLFIRI + aflibercept en pacientes con cáncer colorrectal metastásico tratado previamente con oxaliplatino con o sin polimorfismos de ACE.** TTD-16-02. GRUPO DE TRATAMIENTO DE LOS TUMORES DIGESTIVOS GRUPO TTD.

46. Carlos López López. **Estudio multicéntrico, fase 2 de nivolumab en combinación con ipilimumab para pacientes con tumores pediátricos sólidos avanzados del adulto.** GETHI021. DYNAMIC SCIENCE, S.L..

47. Marta Francisca López-Brea Piqueras. **Ensayo en fase III, aleatorizado, multicéntrico, abierto y comparativo para determinar la eficacia de durvalumab o durvalumab y tremelimumab en combinación con quimioterapia basada en platino como tratamiento de primera línea en pacientes con cáncer de pulmón microcítico (CPM) en enfermedad avanzada (estadio IV).** D419QC00001. ARAZENECA FARMACÉUTICA SPAIN, S.A..

48. Marta Francisca López-Brea Piqueras. **Estudio de Fase III Multicéntrico, randomizado, controlado con placebo de Atezolizumab (Anticuerpo Anti-PD-L1) en Monoterapia y en combinación con Quimioterapia basada en Platino**

en pacientes con carcinoma urotelial, localmente avanzado o metastásico no tratado previamente. WO30070. F. HOFFMANN-LA ROCHE LTD.

49. Eva Martínez de Castro. **Apixabán para el tratamiento del tromboembolismo venoso en pacientes con cáncer: Un estudio prospectivo aleatorizado abierto y ciego para el evaluador - El estudio CARAVAGGIO.** FADOI.03.2016. FONDAZIONE FADOI.

50. Fernando Rivera Herrero. **A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-controlled Study of AG-120 in Previously-treated Subjects with Nonresectable or Metastatic Cholangiocarcinoma with an IDH1 Mutation.** AG120-C-005. AGIOS PHARMACEUTICALS, INC..

51. Marta Francisca López-Brea Piqueras. **Estudio de Fase II/ III, aleatorizado, abierto y de dos partes, de dinutuximab e irinotecán versus irinotecán como tratamiento de segunda línea en sujetos con cáncer de pulmón microcítico en recidiva o resistente.** DIV-SCLC-301. UNITED THERAPEUTICS CORPORATION.

52. Ignacio Durán Martínez. **Estudio de fase 3 aleatorizado, doble ciego, multicéntrico, de nivolumab como tratamiento adyuvante frente a placebo en sujetos con Carcinoma urotelial invasivo de alto riesgo.** CA209-274.

53. Ignacio Durán Martínez. **CA209-901.** CA209-901.

54. Fernando Rivera Herrero. **Ensayo de fase III, aleatorizado y doble ciego para comparar trastuzumab más quimioterapia y pembrolizumab con trastuzumab más quimioterapia y placebo como tratamiento de primera línea en participantes con adenocarcinoma gástrico o de la unión gastroesofágica avanzado con HER2 positivo (KEYNOTE 811).** MK-3475-811. MERCK SHARP & DHOME ESPAÑA.

55. Fernando Rivera Herrero. **Estudio clínico de fase 3, aleatorizado y doble ciego de pembrolizumab (MK-3475) más quimioterapia en comparación**

con placebo más quimioterapia como tratamiento de primera línea en participantes con adenocarcinoma gástrico o de la unión gastroesofágica irresecable o metastásico, sin tratamiento previo y con HER2 negativo (KEYNOTE-859). MK-3475-859. MERCK, SHARP&DOHME CORP. (MERCK).

56. Ignacio Durán Martínez. **Estudio abierto, multicéntrico, fase 1b de JNJ-63723283, un inhibidor de la PD-1, administrado con Apalutamida en hombres con cáncer de próstata metastásico resistente a castración.** 5602192PCR2032. JANSSEN-CILAG, S.A.

Postmarketing Studies and Other

1. Almudena García Castaño. **Estudio de la prevalencia, la clasificación sindrómica y el control del dolor mixto en pacientes atendidos en los servicios de oncología médica en España.** SP-GRT-EPI-2014-02. GRÜNENTHAL PHARMA, S.A..

2. Marta Francisca López-Brea Piqueras. **REASSURE – Estudio no intervencionista para la evaluación a largo plazo de la seguridad del agente emisor de partículas alfa Radio-223 en pacientes con cáncer de próstata metastásico resistente**

a la castración (mCRPC). BAY-RAD-2015-01. BAYER HISPANIA, S.L..

3. Carlos López López. **Estudio epidemiológico, observacional, retrospectivo y multicéntrico para evaluar las características del tratamiento con gemcitabina y nab-paclitaxel en pacientes con adenocarcinoma de páncreas metastásico tratados en primera línea en la práctica clínica habitual.** Estudio ANICE-PaC. GIT-ADE-2015-02.

4. Eva Martínez de Castro. **Estudio observacional retrospectivo sobre el tratamiento del cáncer colorrectal metastásico (CCRm) en España.** BAY-ONC-2016-01. BAYER HISPANIA, S.L..

5. Fernando Rivera Herrero. **Estudio observacional postautorización con otros diseños diferentes al de seguimiento prospectivo.** C13-1. GERCOR.

6. Eva Martínez de Castro. **Estudio observacional postautorización Caracterización del Riesgo de Trombosis en Pacientes con Cáncer (Estudio CARTAGO).** AJT-ACO-2016-01. Trujillo Santos, Antonio Javier.

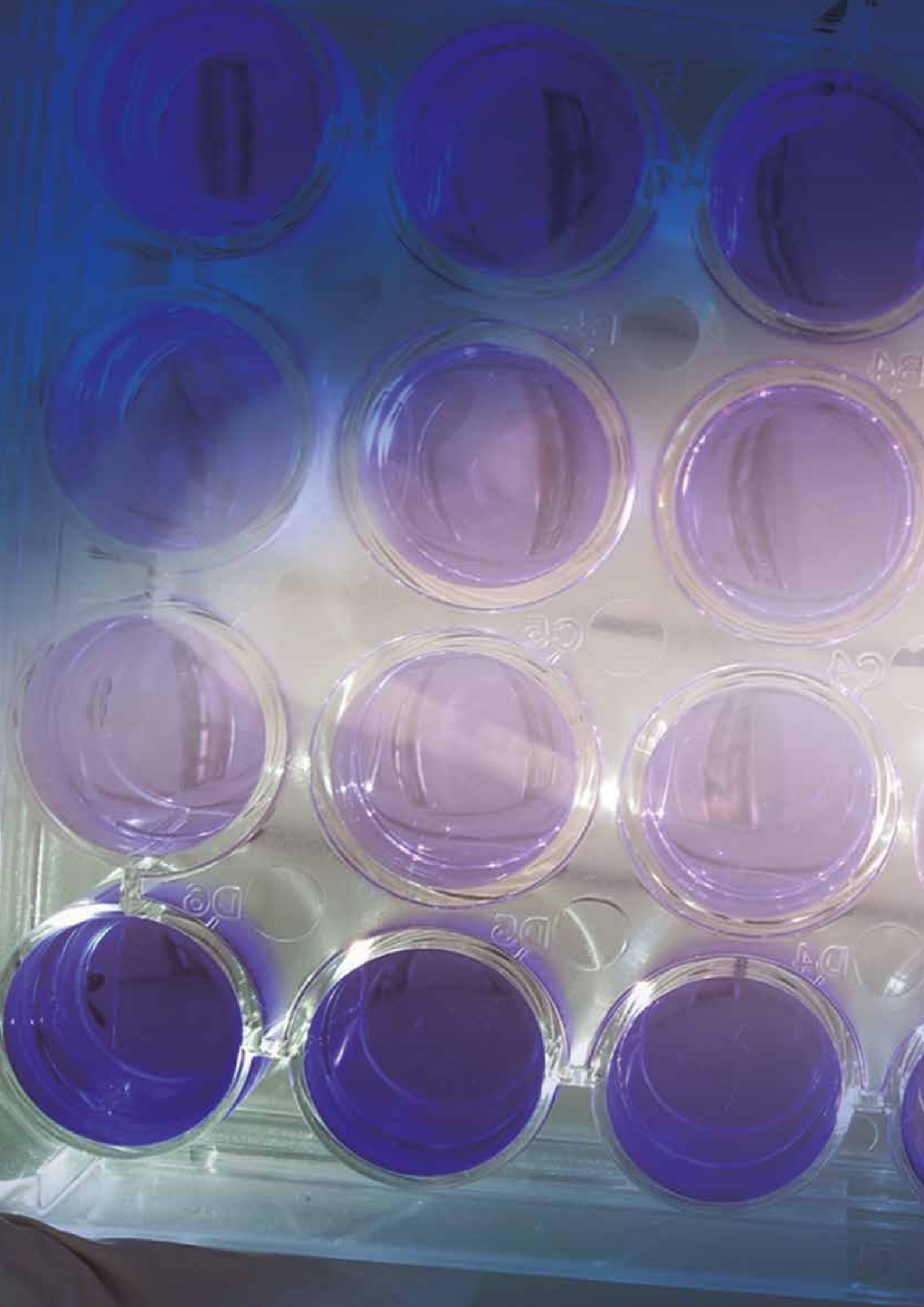
7. Marta Francisca López-Brea Piqueras. **Patrón de uso y seguridad/efectividad de nivolumab en la práctica oncológica rutinaria.** CA 209-234.

Other Publications 2018

1. Zarrabeitia, R, Salcedo, M, Bueno, J, MarquOs, S, Setharis, B, Coduras, A, GonzAlez-Pascual, A, Anta, M, Cuesta, M, Rodriguez Prado, Sara. **Epidemiology of hereditary haemorrhagic telangiectasia in Spain: experience of the HHT unit in hospital Sierrallana.** ANGIOGENESIS. 2018;21:166-167.

2. Zarrabeitia, R, Salcedo, M, Farithas-elvarez, C, SantibAthez, M, Pascual, C, Limia, C, Setharis, B, Fontalba, A, Recio-Poveda, L, Marua Botella, Luisa, Antonio Parra, Jose. **Euroqol 5D test to evaluate quality of life in patients with hereditary haemorrhagic telangiectasia (HHT) in Spain.** ANGIOGENESIS. 2018;21:167-167.

3. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecoechea, E, Faripas-elvarez, C, Fontalba, A, Zarauza, J, Ojeda, L, Parra, JA. **Naifold capillaroscopy in hereditary hemorrhagic telangiectasia.** ANGIOGENESIS. 2018;21:144-144.





**o Cross-
Disciplinary
Area**

Javier Llorca Díez
Coordinator of the Cross-
Disciplinary Area

**Professor of Preventive Medicine
and Public Health.**
Universidad de Cantabria.

Epidemiology and Public Health

Group Responsible

Javier Llorca Díaz

Department of Preventive Medicine and Public Health
School of Medicine
Universidad de Cantabria



javier.llorca@unican.es



Centro de Investigación Biomédica en red
Epidemiología y Salud Pública

Researchers

Trinidad Dierssen Sotos
Ines Gómez Acebo
María Paz Rodríguez Cundín

Contributors

Jessica Alonso Molero
María Fernández Ortiz

Predoctoral

Camilo Palazuelos Calderón



Research lines

1. Epidemiology of cancer:

Development of methods for estimating confidence intervals of the population attributable fraction (Stat Med) and its ascription when risk factors are not additive (J Clin Epidemiol). Analysis of competing risks of death using Gompertzian models (Mech Ageing Develop; J Epidemiol Commun Health; Rev Esp Cardiol), Markov chains with conditional independence (Int J Epidemiol) and in lack of independence (J Clin Epidemiol).

Line started in 2009 when entering the MCC-Spain project. There have been recruited 10000 participants between cases (breast, prostate, colorectal, stomach and Chronic lymphocytic leukemia) and controls in the different nodes of the project (Asturias,

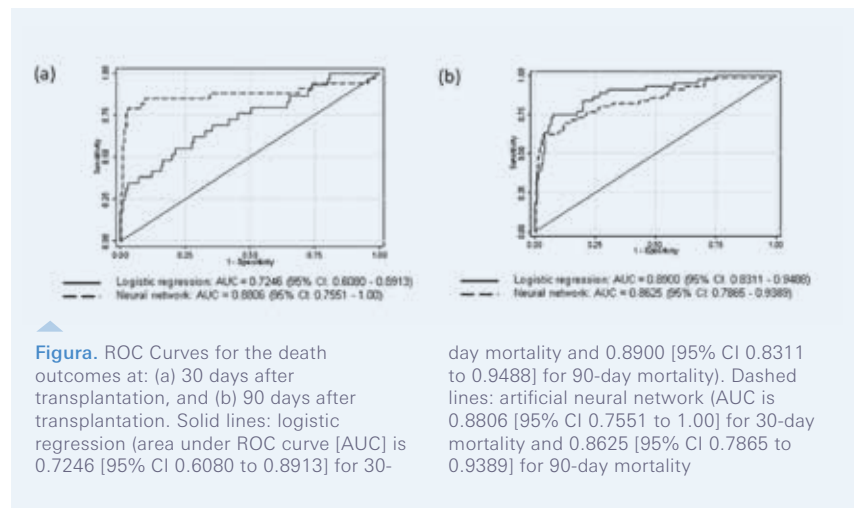


Figura. ROC Curves for the death outcomes at: (a) 30 days after transplantation, and (b) 90 days after transplantation. Solid lines: logistic regression (area under ROC curve [AUC] is 0.7246 [95% CI 0.6080 to 0.8913] for 30-

day mortality and 0.8900 [95% CI 0.8311 to 0.9488] for 90-day mortality). Dashed lines: artificial neural network (AUC is 0.8806 [95% CI 0.7551 to 1.00] for 30-day mortality and 0.8625 [95% CI 0.7865 to 0.9389] for 90-day mortality)

Cantabria, León, Guipúzcoa, Navarre, Gerona, Barcelona, Valencia, Murcia, Granada, Huelva and Madrid). The Cantabria node is the 4th in number of participants (after Of Madrid, Barcelona and Leon).

Our group has obtained three FIS projects as IP for this project in 2009 (5 Projects coordinated by the Cantabria node), 2012 (4 projects coordinated

by The Madrid node) and 2015 (3 projects coordinated by the Cantabria node). In addition to participating with collaborating researchers in projects of 2011 and 2014 Led by CREAL, the National Center for Epidemiology and the ICO-Belvitge.

MCC-Spain began publishing its results in mid-2015 and at the moment Has published 27 articles, of which the node

of Cantabria has led 3 on Consumption of drugs and breast cancer (BMC Cancer, PlosOne and Breast Cancer Research and Treatment).

With the 2015 project, a turn in the project is initiated to transform the cases into Cohorts for the study of prognostic factors. To this end, the Coordinating committee of MCC-Spain, including from November 2016 to Javier Llorca as a follow-up coordinator.

2. Epidemiology of rheumatic diseases:

Line initiated in 2000 in collaboration with the group of Dr. González-Gay (then, In the Hospital Xeral Calde de Lugo). We have worked on rheumatoid arthritis, arteritis Of giant cells, Schönlein-Henoch's disease, ankylosing spondylitis, Psoriatic arthropathy among others, giving rise to a large number of articles in first Decile / quartile and to the presentation of 7 doctoral theses. At this point, we continue Fundamentally in two sub-lines: cardiovascular risk in diseases Rheumatic and genetic factors that influence this risk.

3. Clinical Epidemiology:

In these years, the line of clinical epidemiology has focused The transplant, especially the lung, giving rise to 18 articles and 5 theses.

4. Epidemiological method:

Our former line of epidemiological method has been refocused towards the Research of new methods to study gene-gene and gene-environment interaction; This includes regression with lasso and ridge penalty, artificial neural networks, and Bayesian networks. This refocus should begin to produce End of 2017

PUBLICATIONS

IMPACT FACTOR | 181.180

Original articles

1. Schumacher FR, Al Olama AA, Berndt SI, Benlloch S, Ahmed M, Saunders EJ, Dadaev T, Leongamornlert D, Anokian E, Cieza-Borrella C, Goh C, Brook MN, Sheng X, Fachal L, Dennis J, Tyrer J, Muir K, Lophatananon A, Stevens VL, Gapstur SM, Carter BD, Tangen CM, Goodman PJ, Thompson IM, Batra J, Chambers S, Moya L, Clements J, Horvath L, ..., Eeles RA. **Association analyses of more than 140,000 men identify 63 new prostate cancer susceptibility loci.** *Nature Genet.*2018;50:928-936.F.I.:27.125. [doi:10.1038/s41588-018-0142-8]
2. Tramullas, M, Frances, R, de la Fuente, R, Velategui, S, Carcelen, M, Garcia, R, Llorca, J, Hurler, MA. **MicroRNA-30c-5p modulates neuropathic pain in rodents.** *Sci. Transl. Med.*2018;10.F.I.:16.710. [doi:10.1126/scitranslmed.aao6299]
3. Dadaev, T, Saunders, EJ, Newcombe, PJ, Anokian, E, Leongamornlert, DA, Brook, MN, Cieza-Borrella, C, Mijuskovic, M, Wakerell, S, Olama AAA, Schumacher, FR, Berndt, SI, Benlloch, S, Ahmed, M, Goh, C, Sheng, X, Zhang, Z, Muir, K, Govindasami, K, Lophatananon, A, Stevens, VL, Gapstur, SM, Carter, BD, Tangen, CM, Goodman, P, Thompson, IM, Batra, J, Chambers, S, Moya, L, ..., Kote-Jarai Z. **Fine-mapping of prostate cancer susceptibility loci in a large meta-analysis identifies candidate causal variants.** *Nat. Commun.*2018;9:2256-2256.F.I.:12.353. [doi:10.1038/s41467-018-04109-8]
4. Solans, M, Castello, A, Benavente, Y, Marcos-Gragera, R, Amiano, P, Gracia-Lavedan, E, Costas, L, Robles, C, González-Barca, E, de la Banda, E, Alonso, E, Aymerich, M, Campo, E, Dierssen-Sotos, T, Fernandez-Tardon, G, Olmedo-Requena, R, Gimeno, E, Castaño-Vinyals G, Aragonés, N, Kogevinas, M, de Sanjose, S, Pollan, M, Casabonne, D. **Adherence to the Western, Prudent, and Mediterranean dietary patterns and chronic lymphocytic leukemia in the**

MCC-Spain study. *Haematologica.* 2018;103:1881-1888.F.I.:9,090. [doi:10.3324/haematol.2018.192526]

5. García-Saenz, A, Sánchez de Miguel A, Espinosa, A, Valentín, A, Aragonés, N, Llorca, J, Amiano, P, Martín Sánchez V, Guevara, M, Capelo, R, Tardon, A, Peiro-Pérez, R, Jiménez-Moleon, JJ, Roca-Barcelo, A, Pérez-Gómez, B, Dierssen-Sotos, T, Fernández-Villa, T, Moreno-Iribas, C, Moreno, V, García-Pérez, J, Castaño-Vinyals G, Pollan, M, Aube, M, Kogevinas, M. **Evaluating the Association between Artificial Light-at-Night Exposure and Breast and Prostate Cancer Risk in Spain (MCC-Spain Study).** *Environ. Health Perspect.*2018;126:47011-47011.F.I.:8.309. [doi:10.1289/EHP1837]
6. Kogevinas, M, Espinosa, A, Castello, A, Gómez-Acebo, I, Guevara, M, Martin, V, Amiano, P, Alguacil, J, Peiro, R, Moreno, V, Costas, L, Fernández-Tardón, G, Jiménez, JJ, Marcos-Gragera, R, Pérez-Gómez, B, Llorca, J, Moreno-Iribas, C, Fernández-Villa, T, Oribe, M, Aragonés, N, Papantoniou, K, Pollan, M, Castano-Vinyals, G, Romaguera, D. **Effect of mistimed eating patterns on breast and prostate cancer risk (MCC-Spain Study).** *Int J Cancer.* 2018;143:2380-2389.F.I.:7.360. [doi:10.1002/ijc.31649]
7. Vallès X, Alonso, MH, López-Caleya, JF, Diez-Obrero, V, Dierssen-Sotos, T, Lope, V, Molina-Barcelo, A, Chirlaque, MD, Jiménez-Moleon, JJ, Fernández Tardón G, Castilla, J, Amiano, P, Capelo, R, Castaño-Vinyals G, Guino, E, Molina de la Torre AJ, Moreno-Iribas, C, Pérez Gómez B, Aragonés, N, Llorca, J, Martin, V, Kogevinas, M, Pollan, M, Moreno, V. **Colorectal cancer, sun exposure and dietary vitamin D and calcium intake in the MCC-Spain study.** *Environ. Int.*2018;121:428-434.F.I.:7.297. [doi:10.1016/j.envint.2018.09.030]
8. Font-Ribera, L, Gràcia-Lavedan E, Aragonés, N, Perez-Gomez, B, Pollan, M, Amiano, P, Jimenez-Zabala, A, Castaño-Vinyals G, Roca-Barcelo, A, Ardanaz, E, Burgui, R, Molina, AJ, Fernández-Villa, T, Gómez-Acebo, I, Dierssen-Sotos, T, Moreno, V, Fernández-Tardon, G, Peiro, R, Kogevinas, M, Villanueva, CM. **Long-term exposure to trihalomethanes in drinking water and breast cancer in the Spanish multicase-control study**

on cancer (MCC-SPAIN). *Environ. Int.* 2018;112:227-234.F.I.:7.297. [doi:10.1016/j.envint.2017.12.031]

9. Castello, A, Boldo, E, Amiano, P, Castaño-Vinyals G, Aragonés, N, Gómez-Acebo, I, Peiro, R, Jimenez-Moleon, JJ, Alguacil, J, Tardon, A, Cecchini, L, Lope, V, Dierssen-Sotos, T, Mengual, L, Kogevinas, M, Pollan, M, Pérez-Gómez, B, MCC-Spain Researchers. **Mediterranean Dietary Pattern is Associated with Low Risk of Aggressive Prostate Cancer: MCC-Spain Study. *J. Urol.*** 2018;199:430-437.F.I.:5.381. [doi:10.1016/j.juro.2017.08.087]

10. Llerena Santiago, Susana, García-Díaz N, Curiel del Olmo, Soraya, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, Helena, Varela M, Santibáñez Margüello, Miguel, Almaraz Pro, María del Carmen, Cereceda Company, Laura, Martínez Magunacelaya, Nerea, Arias Lose, María Teresa, Puente Á, Martín-Ramos L, Rodríguez de Lope López, Carlos, Castillo Suescun, Federico, Cagigas-Fernández C, Isidro P, López-López C, López Hoyos, Marcos, Llorca Díaz, Javier, Agüero Balbín, Jesús, Crespo Facorro, Benedicto, Varela I, Piris Pinilla, Miguel Ángel, Crespo García, Javier, Vaqué Díez, José Pedro. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR. *Oncotarget.*** 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

11. Castello, A, Fernández de Larrea N, Martin, V, Dávila-Batista, V, Boldo, E, Guevara, M, Moreno, V, Castaño-Vinyals G, Gómez-Acebo, I, Fernández-Tardon, G, Peiro, R, Olmedo-Requena, R, Capelo, R, Navarro, C, Pacho-Valbuena, S, Pérez-Gómez, B, Kogevinas, M, Pollan, M, Aragonés, N, Mcc-Spain Researchers. **High adherence to the Western, Prudent, and Mediterranean dietary patterns and risk of gastric adenocarcinoma: MCC-Spain study. *GASTRIC CANCER.*** 2018;21:372-382.F.I.:5.045. [doi:10.1007/s10120-017-0774-x]

12. O'Callaghan-Gordo, C, Kogevinas, M, Cirach, M, Castaño-Vinyals G, Aragonés, N, Delfrade, J, Fernández-Villa, T, Amiano, P, Dierssen-Sotos, T, Tardon, A, Capelo, R, Peiro-Perez, R, Moreno, V, Roca-Barcelo, A, Pérez-Gómez, B, Vidan, J, Molina, AJ, Oribe, M, Gràcia-Lavedan E, Espinosa, A, Valentín, A, Pollan, M, Nieuwenhuijsen,

MJ. **Residential proximity to green spaces and breast cancer risk: The multicase-control study in Spain (MCC-Spain). *Int. J. Hyg. Environ. Health.*** 2018;221:1097-1106.F.I.:4.848. [doi:10.1016/j.ijheh.2018.07.014]

13. de Batlle, J, Gracia-Lavedan, E, Romaguera, D, Mendez, M, Castaño-Vinyals G, Martin, V, Aragonés, N, Gómez-Acebo, I, Olmedo-Requena, R, Jimenez-Moleon, JJ, Guevara, M, Azpiri, M, Llorens-Ivorra, C, Fernández-Tardon, G, Lorca, JA, Huerta, JM, Moreno, V, Boldo, E, Pérez-Gómez, B, Castilla, J, Fernández-Villa, T, Barrio, JP, Andreu, M, Castells, A, Dierssen, T, Altzibar, JM, Kogevinas, M, Pollan, M, Amiano, P. **Meat intake, cooking methods and doneness and risk of colorectal tumours in the Spanish multicase-control study (MCC-Spain). *Eur. J. Nutr.*** 2018;57:643-653.F.I.:4.423. [doi:10.1007/s00394-016-1350-6]

14. García-Pérez, J, Lope, V, Pérez-Gómez, B, Molina, AJ, Tardon, A, Díaz Santos MA, Ardanaz, E, O'Callaghan-Gordo, C, Altzibar, JM, Gomez-Acebo, I, Moreno, V, Peiro, R, Marcos-Gragera, R, Kogevinas, M, Aragonés, N, Lopez-Abente, G, Pollán M. **Risk of breast cancer and residential proximity to industrial installations: New findings from a multicase-control study (MCC-Spain). *Environ. Pollut.*** 2018;237:559-568.F.I.:4.358. [doi:10.1016/j.envpol.2018.02.065]

15. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Mijares, V, Exposito, R, Mata, C, Portilla, V, Blanco, R, Hernandez, JL, Llorca, J, Gualillo, O, Lope-Mejias, R, Gonzalez-Gay, MA. **Association of circulating calprotectin with lipid profile in axial spondyloarthritis. *Sci Rep.*** 2018;8:13728-13728.F.I.:4.122. [doi:10.1038/s41598-018-32199-3]

16. Ibáñez-Sanz G, Diez-Villanueva, A, Vilorio-Marqués, L, Gracia, E, Aragonés, N, Olmedo-Requena, R, Llorca, J, Vidan, J, Amiano, P, Nos, P, Fernández-Tardon, G, Rada, R, Chirlaque, MD, Guino, E, Dávila-Batista, V, Castaño-Vinyals G, Pérez-Gómez, B, Miron-Pozo, B, Dierssen-Sotos, T, Etxeberria, J, Molinuevo, A, Álvarez-Cuenllas, B, Kogevinas, M, Pollan, M, Moreno, V. **Possible role of chondroitin sulphate and glucosamine for primary prevention of colorectal cancer. Results from the MCC-Spain study. *Sci Rep.*** 2018;8:2040-2040.F.I.:4.122.

[doi:10.1038/s41598-018-20349-6]
17. Dierssen-Sotos, T, Gomez-Acebo, I, Palazuelos, C, Fernandez-Navarro, P, Altzibar, JM, González-Donquiles, C, Ardanaz, E, Bustamante, M, Alonso-Molero, J, Vidal, C, Bayo-Calero, J, Tardon, A, Salas, D, Marcos-Gragera, R, Moreno, V, Rodríguez-Cundin, P, Vinyals, GC, Ederra, M, Vilorio-Marques, L, Amiano, P, Pérez-Gómez, B, Aragonés, N, Kogevinas, M, Pollan, M, Llorca, J. **Validating a breast cancer score in Spanish women. *The MCC-Spain study. Sci Rep.*** 2018;8:3036-3036.F.I.:4.122. [doi:10.1038/s41598-018-20832-0]

18. Estebanez, N, Gomez-Acebo, I, Palazuelos, C, Llorca, J, Dierssen-Sotos, T. **Vitamin D exposure and Risk of Breast Cancer: a meta-analysis. *Sci Rep.*** 2018;8:9039-9039.F.I.:4.122. [doi:10.1038/s41598-018-27297-1]

19. Lope, V, Castello, A, Mena-Bravo, A, Amiano, P, Aragonés, N, Fernández-Villa, T, Guevara, M, Dierssen-Sotos, T, Fernández-Tardon, G, Castaño-Vinyals G, Marcos-Gragera, R, Moreno, V, Salas-Trejo, D, Diaz-Santos, M, Oribe, M, Romieu, I, Kogevinas, M, Priego-Capote, F, Perez-Gómez, B, Pollan, M. **Serum 25-hydroxyvitamin D and breast cancer risk by pathological subtype (MCC-Spain). *J. Steroid Biochem. Mol. Biol.*** 2018;182:4-13.F.I.:4.095. [doi:10.1016/j.jsbmb.2018.04.005]

20. Boldo, E, Castello, A, Aragonés, N, Amiano, P, Pérez-Gomez, B, Castaño-Vinyals G, Martin, V, Guevara, M, Urtiaga, C, Dierssen-Sotos, T, Fernández-Tardon, G, Moreno, V, Solans, M, Peiro, R, Capelo, R, Gómez-Acebo, I, Castilla, J, Molina, AJ, Castells, X, Altzibar, JM, Lope, V, Kogevinas, M, Romieu, I, Pollan, M, MCC-Spain Researchers. **Meat intake, methods and degrees of cooking and breast cancer risk in the MCC-Spain study. *Maturitas.*** 2018;110:62-70.F.I.:3.315. [doi:10.1016/j.maturitas.2018.01.020]

21. Dierssen-Sotos, T, Palazuelos-Calderón, C, Jiménez-Moleon, JJ, Aragonés, N, Altzibar, JM, Castaño-Vinyals G, Martin-Sánchez, V, Gómez-Acebo, I, Guevara, M, Tardon, A, Pérez-Gómez, B, Amiano, P, Moreno, V, Molina, AJ, Alonso-Molero, J, Moreno-Iribas, C, Kogevinas, M, Pollan, M, Llorca, J. **Reproductive risk factors in breast cancer and genetic hormonal pathways: a gene-environment**

interaction in the MCC-Spain project. *BMC Cancer*. 2018;18:280-280.F.I.:3.288. [doi:10.1186/s12885-018-4182-3]

22. Rueda-Gotor, J, Llorca, J, Corrales, A, Parra, JA, Portilla, V, Genre, F, Blanco, R, Agudo, M, Fuentevilla, P, Expósito, R, Mata, C, Pina, T, González-Juanatey, C, González-Gay, MA.

Cardiovascular risk stratification in axial spondyloarthritis: carotid ultrasound is more sensitive than coronary artery calcification score to detect high-cardiovascular risk axial spondyloarthritis patients. *Clin. Exp. Rheumatol*.2018;36:73-80.F.I.:3.201.

23. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Ubilla, B, Mijares, V, Fernandez-Diaz, C, Portilla, V, Blanco, R, Hernández, JL, Llorca, J, López-Mejías, R, González-Gay, MA. **Implication of osteoprotegerin and sclerostin in axial spondyloarthritis cardiovascular disease: a study of 163 Spanish patients.** *Clin. Exp. Rheumatol*.2018;36:302-309.F.I.:3.201.

24. Benavente, Y, Casabonne, D, Costas, L, Robles, C, Alonso, E, de la Banda, E, González-Barca, E, Marcos-Gragera, R, Llorca, J, Tardon, A, Monleon, JJ, Aymerich, M, Campo, E, Gimeno-Vázquez, E, Castaño-Vinyals G, Aragonés, N, Pollan, M, Kogevinas, M, de Sanjose, S. **Established and suggested exposures on CLL/SLL etiology: Results from the CLL-MCC-Spain study.** *Cancer Epidemiol*.2018;52:106-111.F.I.:2.888. [doi:10.1016/j.canep.2017.12.012]

25. Gómez-Acebo, I, Dierssen-Sotos, T, Palazuelos, C, Fernández-Navarro, P, Castaño-Vinyals G, Alonso-Molero, J, Urtiaga, C, Fernández-Villa, T, Ardanaz, E, Rivas-del-Fresno, M, Molina-Barcel, A, Jiménez-Moleon, JJ, García-Martínez, L, Amiano, P, Rodríguez-Cundin, P, Moreno, V, Pérez-Gómez, B, Aragonés, N, Kogevinas, M, Pollan, M, Llorca, J. **Pigmentation phenotype and prostate and breast cancer in a select Spanish population-A Mendelian randomization analysis in the MCC-Spain study.** *PLoS One*. 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0201750]

26. Ballesteros, MA, Rubio-López, MI, San Martín, M, Padilla, A, López-Hoyos, M, Llorca, J, Miñambres E. **Serum levels of S100B from**

jugular bulb as a biomarker of poor prognosis in patients with severe acute brain injury. *J. Neurol. Sci*.2018;385:109-114.F.I.:2.448. [doi:10.1016/j.jns.2017.12.017]

27. Gómez-Acebo, I, Dierssen-Sotos, T, de Pedro, M, Pérez-Gómez, B, Castaño-Vinyals G, Fernández-Villa, T, Palazuelos-Calderón, C, Amiano, P, Etxeberria, J, Benavente, Y, Fernández-Tardon, G, Salcedo-Bellido, I, Capelo, R, Peiro, R, Marcos-Gragera, R, Huerta, JM, Tardon, A, Barricarte, A, Altzibar, JM, Alonso-Molero, J, Davila-Batista, V, Aragonés, N, Pollan, M, Kogevinas, M, Llorca, J. **Epidemiology of non-steroidal anti-inflammatory drugs consumption in Spain. The MCC-Spain study.** *BMC Public Health*. 2018;18:1134-1134.F.I.:2.420. [doi:10.1186/s12889-018-6019-z]

28. Jiménez Alfonso A, Escudero Acha P, Ortiz-Lasa, M, Chicote, E, Dierssen-Soto, T, González-Castro, A. **Life-support treatments at end of life: Costs and ethical aspects. Point of view in an intensive care unit based on Q methodology.** *Med. Intensiv*.2018;42:558-561.F.I.:1.755. [doi:10.1016/j.medin.2018.03.007]

29. Rios, A, López-Navas, A, López-López, A, Gómez, FJ, Iriarte, J, Herruzo, R, Blanco, G, Llorca, FJ, Asunsolo, A, Sánchez, P, Gutiérrez, PR, Fernández, A, de Jesús, MT, Alarcón, LM, del Olivo, M, Fuentes, L, Hernández, JR, Virseda, J, Yelamos, J, Bondia, JA, Hernandez, AM, Ayala, MA, Ramirez, P, Parrilla, P. **Do Spanish Medical Students Understand the Concept of Brain Death?.** *Prog. Transplant*.2018;28:77-82.F.I.:1.000. [doi:10.1177/1526924817746687]

30. González-Castro, A, Ortiz-Lasa, M, Rodríguez-Borregan, JC, Rodrigo Calabia E, Ruiz San Millán JC, Dierssen Soto T. **Influence of Proportion of Normal Saline Administered in the Perioperative Period of Renal Transplantation on Kalemia Levels.** *Transplant Proc*. 2018;50:569-571.F.I.:0.806. [doi:10.1016/j.transproceed.2017.06.040]

Reviews

1. López-Mejías, R, Castañeda S, Genre, F, Remuzgo-Martínez, S, David Carmona F, Llorca, J, Blanco, R, Martín, J, González-Gay, MA. **Genetics**

of immunoglobulin-A vasculitis (Henoch-Schonlein purpura): An updated review. *Autoimmun. Rev*.2018;17:301-315.F.I.:8.745. [doi:10.1016/j.autrev.2017.11.024]

Projects

1. Javier Llorca Díaz. **Ayuda por producción al Grupo de Epidemiología y Salud Pública.** APG/29.

2. Trinidad Dierssen Sotos. **Estilos de vida y cáncer de mama - Ensayo LifeBreast.** PI18/00827. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Authorship Thesis

1. Jessica Alonso Molero. **Interacciones de Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1 (PGC1) y Factores Medioambientales en el desarrollo del cáncer colorrectal.** Director/s: Antonio José Molina De La Hoz, Vicente Martin Sanchez. UNIVERSIDAD DE CANTABRIA.

Collaborations

1. Matejčić, M, Saunders, EJ, Dadaev, T, Brook, MN, Wang, K, Sheng, X, Olama AAA, Schumacher, FR, Ingles, SA, Govindasami, K, Benlloch, S, Berndt, SI, Albanes, D, Koutros, S, Muir, K, Stevens, VL, Gapstur, SM, Tangen, CM, Batra, J, Clements, J, Gronberg, H, Pashayan, N, Schleutker, J, Wolk, A, West, C, Mucci, L, Kraft, P, Cancel-Tassin, G, Sorensen, KD, ..., Haiman CA. **Germline variation at 8q24 and prostate cancer risk in men of European ancestry.** *Nat. Commun*.2018;9:4616-4616.F.I.:12.353. [doi:10.1038/s41467-018-06863-1]

2. Ortiz-Fernández L, David Carmona F, López-Mejías R, González-Escribano MF, Lyons PA, Morgan AW, Sawalha AH, Smith KGC, González-Gay MA, Martín J. **Cross-phenotype analysis of ImmunoChip data identifies KDM4C as a relevant locus for the development of systemic vasculitis.** *Ann. Rheum. Dis*.2018;77:589-595.F.I.:12.350. [doi:10.1136/annrheumdis-2017-212372]

Community health



Associated group

Group Responsible

**Pedro
Muñoz Cacho**

Teaching Unit of Family
and Community Medicine
Cantabrian Health Service



pedro.munoz@scsalud.es

Contributors

Héctor Alonso Valle
María Andrés Gómez
Francisco Javier Ayesta Ayesta
Yolanda Borrego Izquierdo
Joaquín Cañal Villanueva
José María Castillo Oti
Rafael Julián Colás Chacartegui
Lorena de Carlos Negro
Ángel de la Mora Parra
Mónica del Amo Santiago
María Teresa Gil Urquiza
Luis Gutiérrez Bardeci
Mónica Hernández Herrero
Fernando Martín Fuente
Luis Otero García
Álvaro Peña Irún
Sandra Piris García
Patricia Rodríguez Fernández
Manuel Antonio Tazón Varela
Carlos Teja Santamaría

Research lines

The group currently has three main lines of research: diabetes, smoking and emergencies.

In the line of diabetes we are participating in the study PREDAPS, which is a multicenter national follow-up study of two cohorts of patients (subjects with prediabetes criteria and healthy controls) started in 2012, consists of 1184 prediabetics and 838 controls. Four articles have been

published and are being drafted and are about to be submitted for evaluation. It has also collaborated in a genetic study related to the risk of developing diabetes in which three Autonomous Communities participate at the national level (Madrid, Catalonia and Cantabria) within CIBERDEM (CIBER of Diabetes and Associated Metabolic Diseases). In addition one of the areas of interest of the group is diabetic retinopathy, in this sense has been finalized in 2016, an epidemiological study in Cantabria to update the prevalence of this complication. The possible contribution of vitamin D deficiency as a risk factor for diabetic retinopathy and the possible use of certain micrnas as predictors of

diabetic retinopathy are also being investigated.

Smoking. At present there is an active follow-up project, which includes patients who participated in the groups of tobacco cessation in primary care from 2006 to the present, in the health center of Puertochico; In these have participated something more than 520 people. The aim is to establish long-term effectiveness, ie beyond the 12-month period commonly used as an international benchmark for evaluating the effectiveness of interventions. This would be a novel contribution, and may serve to establish the need to mark an assessment at three or five years as a standard.

In the **urgency and emergency area**, a cohort study is used to establish the prognostic capacity of ultrasensitive troponin T for early and late mortality in community acquired pneumonias, in which the emergency professionals of the hospitals of Laredo And Valdecilla. The aim is to evaluate the predictive capacity of the aminoterminal fragment of the Cerebral Natriuretic Pro-peptide in order to predict mortality in pneumonias. The objective of this study was to use the same protocol for the collection of variables and follow-up of patients. Acquired in the community, and which provided positive results. In this study we explored the utility of troponin T results, not significant because of the small sample number available for this marker, but with a better diagnostic yield curve than that of the main objective (NT Pro-BNP).

In addition we propose with the incorporation of two nurses, one of them matron, to initiate a new line in the area of breastfeeding materna, one of the priority lines of the Health Plan of Cantabria. We have experience in this research topic, in particular we obtained funding in a competitive call in 2008, which served to verify the proper functioning of the methodology of collection and monitoring of the cohort. At the moment we are finishing the analysis of the final survey of 2009 after the seguimiento that ended in 2016.

PUBLICATIONS

IMPACT FACTOR | 23.111

Original articles

1. Sangros, FJ, Torrecilla, J, Giraldez-García, C, Carrillo, L, Mancera, J, Mur, T, Franch, J, Diez, J, Goday, A, Serrano, R, García-Soidan, FJ, Cuatrecasas, G, Igual, D, Moreno, A, Millaruelo, JM, Carramiñana F, Ruiz, MA, Perez, FC, Iriarte, Y, Lorenzo, A, González, M, Álvarez, B, Barutell, L, Mayayo, MS, del Castillo, M, Navarro, E, Malo, F, Cambra, A, Lopez, R, ..., Regidor, E. **Association of General and Abdominal Obesity With Hypertension, Dyslipidemia and Prediabetes in the PREDAPS Study.** *Rev. Esp. Cardiol.* 2018;71:170-177.F.I.:5.166. [doi:10.1016/j.recesp.2017.04.010]
2. Llorens, P, Javaloyes, P, Martín-Sánchez, FJ, Jacob, J, Herrero-Puente, P, Gil, V, Garrido, JM, Salvo, E, Fuentes, M, Alonso, H, Richard, F, Lucas, FJ, Bueno, H, Parissis, J, Muller, CE, Miró Ò, ICA-SEMES Research Group. **Time trends in characteristics, clinical course, and outcomes of 13,791 patients with acute heart failure.** *Clin. Res. Cardiol.* 2018;107:897-913.F.I.:4.455. [doi:10.1007/s00392-018-1261-z]
3. Tazon-Varela, MA, Ortíz de Salido-Menchaca J, Leibar-Loiti, A, Muñoz-Cacho P. **The health care system as a means of contagion during the 2016-2017 flu season.** *Emergencias.* 2018;30:209-210.F.I.:3.608.
4. Sanroma, P, Muñoz P, Miron-Rubio, M, Aguilera, A, Estrada, O, García, D, González-Ramallo, VJ, Pajarón, M, Sgaramella, GA, González, CR, Mujal, A, Abad, A, Sole, A, González, S, Escalada, C, Vitoria, I, Gómez, MJ, Parra, JJ, Sampedro, I, Pereda, I. **Effectiveness and safety of ertapenem used in**

hospital-at-home units: data from Spanish Outpatient Parenteral Antimicrobial Therapy Registry. *Future Microbiol.* 2018;13:1363-1373.F.I.:3.190. [doi:10.2217/fmb-2018-0065]

5. Miró Ò, Javaloyes, P, Gil, V, Jacob, J, Herrero-Puente, P, Martín-Sánchez, FJ, Salvo, E, Alonso, H, Juan Gómez MÁ, Parissis, J, Llorens, P, en nombre del grupo de investigación ICA-SEMES. **Mortality after an episode of acute heart failure in a cohort of patients with intermediate ventricular function: Global analysis and relationship with admission department.** *Med. Clin.* 2018;151:223-230.F.I.:1.168. [doi:10.1016/j.medcli.2017.11.025]
6. Tazón-Varela, MA, Alonso-Valle, H, Muñoz-Cacho P. **The N-terminal pro brain natriuretic peptide as a predictor of mortality in patients with community acquired pneumonia.** *Med. Clin.* 2018;150:366-367.F.I.:1.168. [doi:10.1016/j.medcli.2017.09.018]

Reviews

1. Riancho-Zarrabeitia, L, Cuberia, M, Muñoz P, López-Hoyos, M, García-Canale, S, García-Unzueta, M, Hernández, JL, Martínez-Taboada, VM. **Vitamin D and antiphospholipid syndrome: A retrospective cohort study and meta-analysis.** *Semin. Arthritis Rheum.* 2018;47:877-882.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.10.007]

Authorship Thesis

1. María Teresa Gil Urquiza. **Factores que intervienen en el inicio y mantenimiento de la lactancia materna en Cantabria.** Director/s: Pedro Muñoz Cacho. UNIVERSIDAD DE CANTABRIA.

Health Law and Bioethics



Emerging group

Group Responsible

Joaquín Cayón de las Cuevas

Head of Legal Counsel Office
Ministry of Health



cayon_j@cantabria.es

Contributors

Silvia de Diego Lagüera
Milagros Estrada Martínez
Gustavo Merino Gómez
Guillermina Navarro Caballero
María Paz Zulueta
Daniel Pérez González
Ángela Ruiz Sáenz
María Díez Sánchez

Research lines

1: Biolaw and Bioethics

1.1.- Legal protection of health data.

This line of research is part of the implementation of autonomous projects of a legal nature, or in the cross-sectional contribution to biomedical projects that require the corresponding analysis of the impact of the right to privacy by the proposed actions. This line includes the bio-legal analysis of the uses and applications of big data in health and the studies on access and preservation of the clinical history.

1.2.- Informed consent in the assistance and in the investigation.

It addresses informed consent, a legal figure from the double dimension of healthcare practice and research activity. Within this line, the abandonment of the conception of informed consent as a defensive

medicine tool and its redesign as a tool for empowerment and doctor-patient communication.

1.3.- Reproductive rights and assisted reproduction techniques.

It confronts reproductive rights from a double perspective: negative and positive. From the first one, the scope of the "right to non-procreation" is examined with the links that this has with the problem of sterilization, both voluntary and forced in case of incapacitated persons. From the positive side ("right to procreate"), the determination of the bio-legal scope of assisted human reproduction techniques forms part of this line of research.

1.4.- Legal and ethical dimension of the transplanting activity.

In addition to examining the regulation of transplants, both living donor and deceased donor, and the analysis that raises the complex dynamic transplant, this line specifically addresses the so-called principle of self-sufficiency, the problem of the shortage of organs and tissues and the progressive integration of public policies regarding organ donation and transplantation.

1.5.- Legal aspects of vaccines.

This line includes the dialectic voluntary vaccination - compulsory vaccination, the problem of off-label vaccines, the transparency and homogeneity of the vaccination calendar and, finally, consent in minors and responsibility derived from vaccination (or, where appropriate, non-vaccination).

1.6.- Medical responsibility.

In this line, we address civil, criminal and administrative litigation liability for damages caused by defective health services and products.

2.- Sanitary rights as a tool for optimizing the assistance management

2.1.- Extrajudicial resolution of conflicts in the sanitary field (health mediation).

The articulation of hetero-compositive tools for extrajudicial resolution of health conflicts-internal and external-is studied, presided over by the principles of voluntariness, impartiality and agility.

2.2.- Normative articulation of waiting lists.

The normative approach of the phenomenon of waiting lists is studied:

- Reimbursement of healthcare expenses in cases of assistance provided by means other than the NHS
- Compensation for patrimonial liability of the Public Administrations, when the delay has caused damage.
- Maximum time guarantee systems.

2.3.- Normative Impact Analysis of health programs.

Within the framework of these policies to improve regulation, the Normative Impact Analysis is configured as a method to assess the different existing regulatory options to achieve a specific health objective, as well as the positive and negative effects of each one. of them.

2.4.- Health organization, hiring and human resources.

It addresses the study of flexible organizational and legal models in the field of human resources management models and health contracts, through the analysis of innovative public procurement and HTA

2.5.-Globalization and Health Law: Global Health Law.

The category of Global Health Law is studied, the globalization of the health phenomenon and its incidence in health care, especially through the international treaties on cross-border assistance, pharmaceutical patents and foreign trade of drugs.

PUBLICATIONS

IMPACT FACTOR | 6.545

Original articles

1. Paz-Zulueta, M, Álvarez-Paredes, L, Rodríguez Díaz JC, Paras-Bravo,

P, Andrada Becerra ME, Rodríguez Ingelmo JM, Ruiz García MM, Portilla, J, Santibáñez Margüello, Miguel. **Prevalence of high-risk HPV genotypes, categorised by their quadrivalent and nine-valent HPV vaccination coverage, and the genotype association with high-grade lesions. BMC Cancer.** 2018;18:112-112.F.I.:3.288. [doi:10.1186/s12885-018-4033-2]

2. Paras-Bravo, P, Alonso-Blanco, C, Paz-Zulueta, M, Palacios-Cena, D, Sarabia-Cobo, CM, Herrero-Montes, M, Boixadera-Planas, E, Fernández-de-las-Penas, C. **Does Jacobson's relaxation technique reduce consumption of psychotropic and analgesic drugs in cancer patients? A multicenter pre-post intervention study. BMC Complement. Altern. Med.**2018;18:139-139.F.I.:2.109. [doi:10.1186/s12906-018-2200-2]

3. Fernández-Feito, A, Antón-Fernández, R, Paz-Zulueta, M. **Sexual risk behaviours and PAP testing in university women vaccinated against human papillomavirus. Aten. Prim.**2018;50:291-298.F.I.:1.148. [doi:10.1016/j.aprim.2017.05.007]

Thesis Addressed

1. María Amada Pellico López. Características e impacto del Bed-Blocking. **Estudios de casos y controles en Cantabria.** Director/s: David Cantarero Prieto, María Paz Zulueta. UNIVERSIDAD DE CANTABRIA.

Books and chapters of books

1. Cayón de las Cuevas, J.: **"Europeizzazione o nazionalizzazione del Diritto Sanitario? Il paradigma della riproduzione assistita"** en COLAPIETRO, C., ATRIPALDI, M., FARES, G., IANNUZZI, A. (ed.) I Modello di welfare sanitario tra qualità e sostenibilità. Esperienze a confronto. ISBN 978-88-9391-414-7, Editoriale Scientifica, Napoli, 2018, pp. 53-74. Impacto SPI 2018: 42ª editorial internacional de Derecho http://ilia.cchs.csic.es/SPI/prestigio_sector_2018_2.php?materia=Derecho&tabla_esp=spi_editoriales_derecho&tabla_extr=spi_editoriales_derecho_extr

2. Cayón de las Cuevas, J.: **"Lucha contra el dopaje y protección de la salud en el deporte: una revisión**

crítica de su tratamiento en el ordenamiento internacional y en el Derecho interno" en TORRUBIA CHAMALTA, B. (Coord.), Herramientas transformadoras del conflicto: el deporte y la cultura de paz, ISBN: 978-84-9177-856-1, Thomson Reuters Aranzadi, 2018, Cizur Menor, pp.131-138. Impacto SPI 2018: 1ª editorial nacional de Derecho http://ilia.cchs.csic.es/SPI/prestigio_sector_2018_2.php?materia=Derecho&tabla_esp=spi_editoriales_derecho&tabla_extr=spi_editoriales_derecho_extr

3. Cayón de las Cuevas, J.: **"E-pharmacies and falsified medicines: challenges and concerns from a patient safety approach"** in SYMEONIDOU-KASTANIDOU, E., KIPOURIDOU, K., MILAPIDOU M., VASILEIOU, M. (ed.), *Medicine, Law and the Internet*, ISBN 978-960-622-451-5, Nomiki Bibliothiki, Atenas, 2018, pp. 265-274.

4. Cayón de las Cuevas, J./ Ruiz Sáenz, A.: **"Simulación clínica: su necesaria implantación como exigencia legal e imperativo ético"** en AITH, F., FALCÃO, M., BALBINOT, R., DALLARI, S. (org.), *Anais do VII Congresso Ibero-Americano de Direito Sanitário- Direito à saúde em Estados Democráticos: experiências contemporâneas*, ISBN 978-85-68314-02-9, Centro de Estudos e Pesquisas de Direito Sanitário (CEPEDISA), Sao Paulo, 2018, pp. 709-710.

5. Merino Gómez, G.: **"Compulsory vaccination vs. patient's rights"** en COLAPIETRO C., ATRIPALDI M., FARES G. E IANNUZZI A., I Modeli di welfare sanitario tra qualità e sostenibilità. Esperienze a confronto. ISBN 978-88-9391-414-7, Ed. Editoriale Scientifica s.r.l., Napoli, 2018, pp. 353-367. Impacto SPI 2018: 42ª editorial internacional de Derecho http://ilia.cchs.csic.es/SPI/prestigio_sector_2018_2.php?materia=Derecho&tabla_esp=spi_editoriales_derecho&tabla_extr=spi_editoriales_derecho_extr

6. Merino Gómez, G.: **"Los nuevos reglamentos europeos sobre productos sanitarios"** en AITH, F., FALCÃO, M., BALBINOT, R., DALLARI, S. (org.), *Anais do VII Congresso Ibero-Americano de Direito Sanitário- Direito à saúde em Estados Democráticos: experiências contemporâneas*, ISBN 978-85-68314-02-9, Centro de Estudos e Pesquisas de Direito Sanitário (CEPEDISA), Sao Paulo, 2018, 697-699.

○ Photonic engineering group



Consolidated group

Group Responsible

**José Miguel
López Higuera**

Electronic Technology and
Systems and Automatic
EngiNeering Department

School of Industrial Engineering and
Telecommunications
Universidad de Cantabria



miguel.lopezhiguera@unican.es

Researchers

Olga María Conde Portilla

Contributors

Adolfo Cobo García
José Alberto Gutiérrez Gutiérrez
Mauro Matías Lomer Barboza
Francisco Javier Madruga Saavedra
Marina Martínez Minchero
Jesús María Mirapeix Serrano
Arturo Pardo Franco
Antonio Quintela Incera
María Ángeles Quintela Incera
Eusebio Real Peña
Luis Rodríguez Cobo

○ Research lines

The Photonic Engineering Group (GIF) is an R + D + I group that focuses its activities on Light Sciences and Technologies (Photonics), horizontal (transversal) field, considered one of the six key technologies (KET's) for the development of Europe. Being horizontal, the GIF applies its platform of knowledge, technique and resources (obtained or generated in any sector of application) to solve real problems in any sector of application among which is the health and medicine. Due to the structure of the GIF, to

which it works in a horizontal field and its philosophy of action the GIF must be judged and valued for its global production in the period of time considered.

In addition to the above and indicated in the different sections of this report, the activity of the group in the strategic lines defined in its program "Photonics for Life and Health" is increasing over time both in terms of collaborations with researchers and clinicians from different specialties from regional, national and European institutions and companies. The most relevant are described very succinctly:

Within the strategic line of Medical Diagnostic Tools based on photonic imaging techniques, activities have

been developed in two INNVAL projects (DICUTEN and DAPatOO) and one Art. 83 project (DiFoMO) associated with another INNVAL (INNVAL17 / 10) in a DTS project (INTRACARDIO) and in an intramural project with another group of the CIBER-BBN of the Polytechnic University of Madrid (MultiCardio3D-OCT) and in the project funded by the Parliament of Cantabria (POS-UC-2018-16) which deals with transfer the optical biopsy by optical coherence tomography to clinical practice.

a) Within the strategic line of devices and systems (including the smart ones) for better diagnosis and monitoring of diseases with special emphasis on the elderly population, activities are developed within the INNyCRON project (INCVAl 17/05

directed by Carlos Viadero trying to assess the chronicity, sarcopenia and frailty of the elderly through a structured light tool, as well as the activities included in the project Challenges- Collaboration TeDFES (RTC-2017-6321-1) recently presented at a press conference given its scope.

b) Within the line of light-matter interaction as a basis for new light-based therapies, the European project ENM JTC 2018 (PANIPAC) of the hypercompetitive EURONANOMED III program has been achieved to develop a nanomedicine based on functionalized nanoparticles activated by light to activate the immune system against pancreatic cancer. On the other hand, at the national level, the CIBER-BBN and CIBER-ONC (NaTBiL) seed project has been obtained in a competitive public call (including oral defense before a jury of 24 members in ISC III), in which, in collaboration with an ONCOMET research project in Santiago de Compostela, is to demonstrate the feasibility of performing PDT internal therapies activated by light generated by bioluminescence. Likewise, work is being done on the CIBER-BBN intramural project (ACTI-BUBBLE) with nine other CIBER-BBN groups focused on the development of a nanomedicine to fight tumors in the brain.

c) Also within the framework of projects financed with funds from the national plan, companies and their own, work is being carried out on the development of detection and measurement systems of interest for health, being explicitly mentioning what concerns optical devices to guarantee quality. food

About PEG-JM-Review CHUs-JM (16-03-2017)

Photonics (Light Sciences and Technologies) has been declared by the European Union one of its six Key Enabling Technologies and by USA one of its essential technologies for its development. It is a horizontal (or transversal) field of knowledge with impact in all the application sectors.

The Photonics Engineering Group (PEG) of the University of Cantabria generates knowledge and technique in the Photonic field with a special focus on solving real problems (not yet resolved or insufficiently determined) and, in the search for their solution, generate knowledge and technique that gives rise to publications, thesis and patents. During this process Information and Communication Technologies (ICT) can be used as an appropriate supplement.

PEG is formed by 26 research, scientific and technical staff following a dynamic model, where a part of the members are dedicated more intensively to the generation of knowledge and training, during a period of time, and the others, to the application of knowledge and technique performing development and innovation for the optimization of their interaction and the transference of results to the productive sector. This, in turn, feedback the group with real problems to be solved and resources to best carry out their mission. PEG has a R&D&I Photonics Laboratory (457 m²) equipped with facilities of Optical Fiber, Optical, Opto-Electronic, Electronic, Climatic, Thermal imaging characterization, Additive Manufacturing, Lasers, etc.

More than 50 R&D&I projects have been carried out with companies to improve their production processes or the quality of their products; or even, to innovate or to develop new products. The developed (and transferred) knowledge and technique have been able to improve their productivity and/or ensure their qualities. In addition, four spin-offs have emerged from PEG: TELNOS, Optical and Telecommunications systems (2005); Empiric Technologies, SL (2010), Sadiq Engineering (2011) and Edronica (2016).

Main Research Lines

Since its foundation (1992) PEG has been focused on Photonic/Optical/Fiber optic sensors; fiber light sources; Optoelectronics Instrumentation; Techniques of detection, Measurement and

Monitoring of events and processes using image for any sector of application. Without neglecting collaborations proposed from other sectors, PEG has very recently decided to focus its work on R&D&I, mainly, in life sciences and health. This decision is backed by a great progress in the Photonics knowledge, methods and techniques able to be used in biological sciences and health that are significantly contributing to the solution of several of the "societal challenges" of our time [as defined in the Lund Declaration www.vr.se/lunddeclaration2015].

PEG has joined the Centro de Investigación Biomédica en Red (CIBER-BBN) of IS Carlos III (2016), and also joined at the Instituto de Investigación Sanitaria de Valdecilla (IDIVAL) and set the "Photonics for the Life and Health" program which includes four strategic R&D lines:

- 1.** Medical diagnostic tools based on Photonic Imaging (Multi, Hyperspectral, OCT, Thermography, etc);
- 2.** Devices and Systems (including those referred to as smart) for a better diagnosis and monitoring of diseases with special emphasis in the elderly population;
- 3.** Interaction of light-matter as a basis for new therapies based on light and/or the manufacture of micro/nano structures by interaction of laser-matter for diagnosis and therapy;
- 4.** Optical devices without contact and Optoelectronic Efficient Systems (low cost or cost-effective) for quality and safety and security of food.



PUBLICATIONS

IMPACT FACTOR | 22.393

Original articles

1. Cuevas, AR, Fontana, M, Rodríguez-Cobo, L, Lomer, M, López-Higuera, JM. **Machine Learning for Turning Optical Fiber Specklegram Sensor into a Spatially-Resolved Sensing System. Proof of Concept. J. Lightwave Technol.** 2018;36:3733-3738.F.I.:3.652. [doi:10.1109/JLT.2018.2850801]
2. Ruiz-Lombera, R, Fuentes, A, Rodríguez-Cobo, L, López-Higuera, JM, Mirapeix, J. **Simultaneous Temperature and Strain Discrimination in a Conventional BOTDA via Artificial Neural Networks. J. Lightwave Technol.** 2018;36:2114-2121.F.I.:3.652. [doi:10.1109/JLT.2018.2805362]
3. Pardo, A, Gutiérrez-Gutiérrez, JA, Lihacova, I, López-Higuera, JM, Conde, OM. **On the spectral signature of melanoma: a non-parametric classification framework for cancer detection in hyperspectral imaging of melanocytic lesions. Biomed Opt Express.** 2018;9:6283-6301.F.I.:3.482. [doi:10.1364/BOE.9.006283]
4. García-Escarzaga, A, Clarke, LJ, Gutiérrez-Zugasti, I, González-Morales, MR, Martínez, M, López-Higuera, JM, Cobo, A. **Mg/Ca profiles within archaeological mollusc (Patella vulgata) shells: Laser-Induced Breakdown Spectroscopy compared to Inductively Coupled Plasma-Optical Emission Spectrometry. Spectrosc. Acta Pt. B-Atom. Spectrosc.** 2018;148:8-15.F.I.:2.854. [doi:10.1016/j.sab.2018.05.026]
5. Ruiz-Lombera, R, Rodríguez-Cobo, L, López-Higuera, JM, Mirapeix, J. **Feasibility Study of a Fiber Ring Laser Working on the SLM Regime in a BOTDA Sensor. IEEE Sens. J.** 2018;18:4947-4953.F.I.:2.617. [doi:10.1109/JSEN.2018.2834563]

6. Rodríguez-Cobo, L, Ruiz-Lombera, R, Quintela, MA, Mirapeix, J, López-Higuera, JM. **Single longitudinal mode fiber ring laser. Opt. Laser Technol.** 2018;107:361-365.F.I.:2.503. [doi:10.1016/j.optlastec.2018.05.038]

7. Rodríguez-Cobo, L, Pérez-Herrera, RA, Quintela, MA, Ruiz-Lombera, R, López-Amo, M, López-Higuera, JM. **Virtual FBGs Using Saturable Absorbers for Sensing with Fiber Lasers. Sensors.** 2018;18:F.I.:2.475. [doi:10.3390/s18113593]

8. Pérez-Herrera, RA, López-Amo, M, Rodríguez, L, Ventura, D, López-Higuera, JM. **Wavelength converter using a highly Er-doped optical fiber ring laser. Laser Phys.** 2018;28:F.I.:1.158. [doi:10.1088/1555-6611/aa9eb0]

Projects

1. Olga María Conde Portilla. **Fusioderm, Fusión de tecnologías fotónicas para el diagnóstico dermatológico.** DTS15/00238. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
2. Olga María Conde Portilla. **Diagnóstico de cuerdas tendinosas de la válvula mitral humana mediante análisis multi-enfoque: óptico, mecánico, micro-estructural y anatómico (DICUTEN).** INNVAL16/02.
3. Olga María Conde Portilla. **Diseño y desarrollo de un dispositivo multimodal para diagnóstico cardiovascular intraoperatorio (IntraCardio).** DTS17/00055. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
4. José Miguel López Higuera. **Ayuda por producción al Grupo de Ingeniería Fotónica.** APG/35.
5. Eusebio Real Peña. **Diagnóstico Automatizado de Patologías Oftalmológicas mediante OCT" (DAPatOO).** INNVAL18/23.

6. José Miguel López Higuera. **Advanced Fibre Lasers and Coherent Source as Tools For Society; Acción Cost MP1401; Manufacturing and Life Science;** 2010-2018.

7. José Miguel López Higuera. **Proyecto semilla CIBER-BBN y CIBER-ONC, "PDT Based on Nanoconjugates Triggered by BioLigh" (NaTBiL), IP: José M. López-Higuera,** 2018-2020, en colaboración con el grupo de investigación ONCOMET). 3

8. José Miguel López Higuera. **Proyecto intramural del CIBER-BBN del Instituto de Salud Carlos III, "Theragnostic Ultrasound Active Nanocarriers for The Non-Invasive Drug Delevary to Brin Tumors" (ACTI-BUBBLE, Coordinador: Carlos Rodríguez Abreu)**

9. José Miguel López Higuera. **Proyecto intramural del CIBER-BBN del Instituto de Salud Carlos III, Multimodal cardiovascular diagnosis based on 3D features segmentation of OCT and PS-OCT images.**

Postmarketing Studies and Other

1. Olga María Conde Portilla. **Diagnóstico de aneurismas de aorta mediante nuevas técnicas ópticas de imagen (DA2TOI).** 2010.013.

Thesis Addressed

1. Asier García Escarzaga. **Paleoclima y aprovechamiento de recursos costeros durante el Mesolítico en la región cantábrica.** Director/s: Igor Gutierrez Zugasti, Adolfo Cobo García. UNIVERSIDAD DE CANTABRIA.

Nursing research group



Emerging group

Group Responsible

Carmen María Sarabia Cobo

Nursing Department

Faculty of Nursing
Universidad de Cantabria.



carmen.sarabia@unican.es

Researchers

Miguel Santibáñez Margüello

Contributors

Rebeca Abajas Bustillo
Ana Rosa Alconero Camarero
Francisco José Amo Setién
Aroa Delgado Uría
María Jesús Dura Ros
Rosario Fernández Peña
Silvia González Gómez,
María Carmen Ortego Maté
Paula Parás Bravo
Isabel Pérez Loza
María Sáenz Jalón
Raquel Sarabia Lavín
Tamara Sillió García
Eduardo Vázquez de Castro

Research lines

L1. Nursing care in cardiovascular area. IP: Ana Rosa Alzonero. Contributors: Víctor Fradejas. Silvia González.

Research on the impact of gender on coronary disease stands out. The contributions in this sense make it possible to specify the treatment more effectively and to establish preventive measures aimed at the female group. It is a pioneering research in our country, also led by a nurse.

L2. Care in aging and dementias. IP Carmen Sarabia Cobo.

This line is especially productive with several contributions such as:

The validation in Spanish of the ICECAP-O questionnaire assessing quality of life, adapted to the population with institutionalized dementia. This instrument has special relevance because it is simple but provides valuable information about the quality of life of the people and can be answered by caregivers, something decisive in the advanced stages of dementia.

Also noteworthy is the research in the elderly population and with slight Cognitive Impairment

regarding the emotional processing of Emotional Facial Expressions. The most important contribution is that this is one of the first studies carried out that values that the most prodromal phases of dementia affect the recognition of facial expressions, something little studied until now. This fact opens an important door to research on communication with these patients as well as the role that cognitive processing plays in emotional processing during dementias.

Another important contribution is the use of new mechanisms in the improvement of stress and burnout in professionals and caregivers of people with dementia, a group with high stress rates. First-time use of the Heart Coherence technique in professionals and caregivers for

managing and managing stress has contributed to improving their quality of life and indirectly improving the care they provide. On the other hand the use of this technique has shown to have longitudinal effects maintained in the time being easy and simple to apply.

L3. Social networks and health. IP Rosario Fernández.

Particularly important are the work related to the study of personal networks in health, a very little explored area at the national level. The contributions of the group allow a better understanding of the networks of social support of family caregivers contributing to improve the support that should be provided at the professional level. This line especially highlights the study of personal networks and health-related quality of life.

L4. Chronicity, dependency, caregivers. IP Carmen Ortego. Contributors: Carmen Sarabia, Rosario Fernández, M Jesus Durá, Rebeca Abajas, Francisco Amo.

This line has just been opened thanks to funding from the University of Cantabria in a competitive national call for emerging research groups. The funded project will work with chronicity and caregivers in Primary Care through interventions based on advanced practice nursing.

L5. Care in relation to nutrition. IP M Jesus Durá Ros. Contributors: Carmen Sarabia Cobo, Rebeca Abajas, Francisco Amo.

The main contribution of this line has been a joint project with the University of Bradford (work pending publication) relating the impact of stress on eating habits. Collaboration will also be initiated in a nationally funded competitive project of the Department of Chemistry of the UC on the wastage of nutrients in human food consumption.

L6. Teaching, educational innovation and scientific dissemination. IP Carmen Sarabia. Contributors: Ana Rosa

Alconero, Silvia González, María Sáenz.

We have led for the first time in Spain the study of the application of clinical simulation in training in palliative care, carrying out the creation and validation of the first battery of tests aimed at assessing satisfaction with own learning in nursing students in our country. Research in teaching methodologies is becoming relevant in nursing faculties worldwide, especially in the application of new technologies such as clinical simulation. We have also carried out the Spanish validation of the test. On the other hand, regarding the use of new educational methodologies, our group stands out as the most productive in Online Massive and Open Online Courses (MOOCS) related to Clinical Safety and psychosocial skills at the Spanish speaking level, with more than 200,000 students enrolled in their courses in The MiriadaX Platform, having received a prize for the best MOOC course in 2014 (Potencia tu mente course).

The MOOC courses contribute in a remarkable way to the scientific dissemination in the area of health, having been cataloged by Universia, our courses as the ones with the greatest media impact on health in 2015 and 2016.

L7. Medical-surgical nursing and patient safety. IP María Sáenz Jalón. Contributor Carmen Sarabia

Our group has developed the first global study led by nurses to assess the impact of the LOOP ischemia technique versus the traditional method in upper limb surgery, obtaining the second National Nursing Research Award from HUMV in 2012. The LOOP technique is Safer and more effective for patients and our study has been presented at various Traumatology congresses, leading to its implementation by different hospitals nationwide.

Another outstanding line of our team is to have carried out the second largest study in patients on the characteristics and morbidity factors in hip fracture in elderly

people in our country. This study, in the process of publication, will benefit patients by highlighting the major risk factors associated with surgery (as demonstrated by the use of anticoagulants, which has been scarcely investigated to date). Also noteworthy is another pioneering research in our country, within the clinical safety in the surgical field, as is the unnecessary study of surgical doors during the interventions. This study, carried out in collaboration with engineers, will determine the causes, times and reasons for opening doors with the consequent commitment of clinical safety of the patient during the intervention. The study will allow posteriori to carry out educational interventions with the professionals of the operating room to sensitize to a problem not very visible, according to the literature.

L8. Application of Artificial Intelligence to the field of Nursing. IP Raquel Sarabia Lavín. Contributor: Paula Parás, Eduardo Vázquez.

Nursing as a profession, is not exempt from the changes and transformations originated by the use of emerging technologies, or the influence they have and will have about its development. Specifically, the technologies based on Artificial Intelligence are having a great impact in the world of health. The conjunction of these technologies in Nursing will allow us to build intelligent, autonomous systems with the capacity to prediction that help in their day to day, both professionals and patients. The objective is not to replace the human character of nursing, since we consider that the Technology and humanism are complementary elements in health care general and specifically in nursing care.

This group has recently collaborated in the definition and development of an application mobile and web, which provides an intelligent system for the prevention of ulcers by pressure (UPP). The project, aimed at helping and guiding non-professional caregivers in the basic care, provides a tool to prevent, patients at risk of suffer from UPP,

suffer this important ailment. The project called "Smart UPP" has been one of the projects supported through the SODERCAN program I + C = + C 2016 of support for R & D projects in the field of ICT (Ref. TI16-IN-026). In addition, since the application of these technologies brings legal obligations with In relation to the protection, treatment and exploitation of personal data, there is a researchers specialized in the legal framework that regulates these legal aspects.

PUBLICATIONS

IMPACT FACTOR | 34.621

Originals articles

1. Llerena Santiago, Susana, García-Díaz N, Curiel del Olmo, Soraya, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, Helena A, Varela M, Santibáñez Margüello, Miguel, Almaraz Pro, María del Carmen, Cereceda Company, Laura; Martínez Magunacelaya, Nerea; Arias Loste, María Teresa; Puente Á; Martín-Ramos L; Rodríguez de Lope López, Carlos; Castillo Suescun, Federico; Cagigas-Fernández C; Isidro P; Lopez-López C; López Hoyos, Marcos; Llorca Díaz, Javier; Agüero

Balbín, Jesús; Crespo Facorro, Benedicto; Varela I; Piris Pinilla, Miguel Ángel; Crespo García, Javier; Vaqué Díez, José Pedro.

Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR. *Oncotarget*. 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

2. Arias-Guillén, M, Sánchez Menéndez MM, Alperi, M, Riestra-Menendez, S, González Budiño MT, García-Clemente, MM, Martínez-González, S, Enriquez, Al, Alonso-Arias, R, Palacios Gutiérrez JJ, Santibáñez M, Coto-Segura, P, Cambor, PM, Garcia-Alfonso, L, Morante, I, Escalante, P. **High rates of tuberculin skin test positivity due to methotrexate therapy: False positive results?.** *Semin. Arthritis Rheum*.2018;48:538-546.F.I.:4.356. [doi:10.1016/j.semarthrit.2018.03.018]

3. Abajas Bustillo R, Leal Costa C, Ortego Mate MDC, Zonfrillo, MR, Seguí Gómez M, Durá Ros MJ. **Classification of the severe trauma patient with the Abbreviated Injury Scale: degree of correlation between versions 98 and 2005 (2008 update).** *Emergencias*. 2018;30:41-44.F.I.:3.608.

4. Paz-Zulueta, M, Álvarez-Paredes, L, Rodríguez Díaz JC, Paras-Bravo, P, Andrada Becerra ME, Rodríguez

Ingelmo JM, Ruiz García MM, Portilla, J, Santibáñez Margüello, Miguel. **Prevalence of high-risk HPV genotypes, categorised by their quadrivalent and nine-valent HPV vaccination coverage, and the genotype association with high-grade lesions.** *BMC Cancer*. 2018;18:112-112.F.I.:3.288. [doi:10.1186/s12885-018-4033-2]

5. Fernández-de-las-Penas, C, Ambite-Quesada, S, Fahandezh-Saddi Díaz H, Paras-Bravo, P, Palacios-Cena, D, Cuadrado, ML. **The Val158Met polymorphism of the catechol-O-methyltransferase gene is not associated with long-term treatment outcomes in carpal tunnel syndrome: A randomized clinical trial.** *PLoS One*. 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0205516]

6. Fernández-Munoz, JJ, Cigaran-Méndez, M, Navarro-Pardo, E, Pérez-de-Heredia-Torres, M, Paras-Bravo, P, Fernández-de-las-Penas, C. **Is the association between health-related quality of life and fatigue mediated by depression in patients with multiple sclerosis? A Spanish cross-sectional study.** *BMJ Open*. 2018;8:F.I.:2.413. [doi:10.1136/bmjopen-2017-016297]

7. Fernández-Pena, R, Molina, JL, Valero, O. **Personal Network**

Analysis in the Study of Social Support: The Case of Chronic Pain. *Int. J. Environ. Res. Public Health.* 2018;15:F.I.:2.145. [doi:10.3390/ijerph15122695]

8. Paras-Bravo, P, Alonso-Blanco, C, Paz-Zulueta, M, Palacios-Cena, D, Sarabia-Cobo, CM, Herrero-Montes, M, Boixadera-Planas, E, Fernández-de-las-Penas, C. **Does Jacobson's relaxation technique reduce consumption of psychotropic and analgesic drugs in cancer patients? A multicenter pre-post intervention study.** *BMC Complement. Altern. Med.* 2018;18:139-139.F.I.:2.109. [doi:10.1186/s12906-018-2200-2]

9. Alconero-Camarero, AR, Sarabia-Cobo, CM, González-Gómez, S, Ibáñez-Rementería I, Lavín-Alconero, L, Sarabia-Cobo, AB. **Nursing students' emotional intelligence, coping styles and learning satisfaction in clinically simulated palliative care scenarios: An observational study.** *Nurse Educ Today.* 2018;61:94-100.F.I.:2.067. [doi:10.1016/j.nedt.2017.11.013]

10. Abajas Bustillo R, Amo Setién FJ, Ortego Mate MDC, Seguí Gómez M, Durá Ros MJ, Leal Costa C. **Predictive capability of the injury severity score versus the new injury severity score in the categorization of the**

severity of trauma patients: a cross-sectional observational study. *Eur J Trauma Emerg Surg.* 2018;F.I.:1.704. [doi:10.1007/s00068-018-1057-x]

11. Amo-Setién FJ, Leal-Costa C, Abajas-Bustillo R, González-Lamuño D, Redondo-Figuero C, EXERNET Research Group. **Factors associated with grip strength among adolescents: An observational study.** *J HAND THER.* 2018;F.I.:1.040. [doi:10.1016/j.jht.2018.10.005]

12. Gea-Caballero, V, Castro-Sánchez, E, Juárez-Vela, R, Sarabia-Cobo, C, Díaz-Herrera, MA, Martínez-Riera, JR. **Professional practice environment in Nursing.** *Rev. Panam. Salud Publica.* 2018;42:F.I.:0.784. [doi:10.26633/RPSP.2018.48]

13. Sáenz-Jalon, M, Ballesteros-Sanz, MA, Sarabia-Cobo, CM, Roscales-Bartolome, E, Fernández, MS, Canal-Cobo, G, Higuero-Piris, C, Velez-Carrera, B, Sanjuan, GV, Garcia-Cobo, S, Torres-Manrique, B, Miguel Martín ME. **Assessment of the Pneumatic Ischemia Technique Using the Limb Occlusion Pressure During Upper Limb Surgery.** *J. PeriAnesthesia Nurs.* 2018;33:699-707.F.I.:0.748. [doi:10.1016/j.jopan.2016.08.017]

Reviews

1. Albuquerque-Sendin, F, Ferrari, AV, Rodrigues-de-Souza, DP, Paras-Bravo, P, Velarde-García, JF, Palacios-Cena, D. **The experience of being a psychiatric nurse in South Africa: A qualitative systematic review.** *Nurs. Outlook.* 2018;66:293-310.F.I.:2.425. [doi:10.1016/j.outlook.2018.01.002]

Other Publications

1. Zarrabeitia, R, Salcedo, M, Farithas-elvarez, C, SantibAthez, M, Pascual, C, Limia, C, Setharis, B, Fontalba, A, Recio-Poveda, L, Marua Botella, Luisa, Antonio Parra, Jose. **Euroqol 5D test to evaluate quality of life in patients with hereditary haemorrhagic telangiectasia (HHT) in Spain.** *ANGIOGENESIS.* 2018;21:167-167.

Health economics and health services management

Group Responsible

David Cantarero Prieto

Professor of in the Area of Applied Economics.

Department of Economy from the Universidad de Cantabria



david.cantarero@unican.es

Contributors

Carla Blázquez Fernández
 María González Diego
 Paloma Lanza León
 Javier Isaac Lera Torres
 Marta Pascual Saez
 Flora Pérez Hernández



Emerging group

Research lines

1. Socioeconomic determinants of health and use of health resources. Demand and immigration. Health expenditure and health and socio-health financing: projects, articles and presentations to national and international congresses. Economic analysis of health decisions and their spending as well as implications in, among other fields, public health. Some aspects are carried out in collaboration (articles and papers to national and international congresses) since 2014 with the IDIVAL group of epidemiology and public health whose head is Dr. Javier Llorca.

2. Economy of the drug (analysis of the pharmaceutical sector). Economic evaluation of programs and technologies. Health information systems: projects, articles and papers at national and international conferences: research in economics and medicine management, efficiency-equity of health and pharmaceutical services (as well as technologies) of administrations and health organizations.

3. Economy of mental health: given the greater need to approximate within the category of mental disorders the cost per patient and in particular, the cost of psychotic disorders in this line of R & D analyzes the cost generated by patients who debutan with an episode of psychosis, so that if they are treated within a specific assistance protocol, which includes hospitalization and consultations, it can be based on the socioeconomic determinants of these patients to show that part of the

expense is associated with direct costs in health services, non-health costs (informal care) and indirect costs (loss of work productivity, chronic disability, etc.). This line is in collaboration (projects, articles and presentations to national and international conferences in progress) since 2016 with the IDIVAL group of psychiatry whose responsible is Dr. Benedicto Crespo).

4. Econometrics of health and habits and quality of life. Theoretical and applied models of decision making in health and social services. Economics of disability, dementia and dependence in one of these lines of R & D determine the resources used and the costs associated with the management of multiple sclerosis (MS) depending on its severity based on clinical practice. The clinical and sociodemographic characteristics of patients with MS, the morbidity of patients in the observation period and the treatment administered, as

well as approximate the indirect costs associated with the loss of productivity of these patients are also described. This line is in collaboration (projects, articles and papers to national and international conferences in progress) since 2016 with the group IDIVAL clinic and genetics of headaches which is responsible for Dr. Agustín Oterino in another of these lines of R & D given that in many patients their cases are in states of total cognitive and / or functional dependence, this implies a high impact on the quality of life of patients and their families. The high health and social costs are analyzed, considering also the main reasons for the institutionalization of patients, etc. This line is in collaboration (projects, articles and papers to national and international congresses in progress) since 2017 with the IDIVAL group of neurodegenerative diseases and with the IDIVAL group of nurses responsible for the teacher Carmen Sarabia.

5. Economic analysis and evaluation of public policies.

Economy of health expenditure. Efficiency. Methods and tools for evaluating public policies (projects, articles and presentations to national and international congresses): from this R & D group the master and expert (postgraduate) in the direction and management of health services of the University of Cantabria in collaboration with the Health Department of the Government of Cantabria and research into improving the efficient management and equitable management of health services as well as their economic impact

PUBLICATIONS

IMPACT FACTOR | 13.196

Original articles

1. Cantarero-Prieto, D, Pascual-Sáez, M, Blázquez-Fernández, C. **Social isolation and multiple chronic diseases after age 50: A European macro-regional analysis.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0205062]

2. Pascual, M, Cantarero, D, Lanza, P. **Health polarization and inequalities across Europe: an empirical approach.** *Eur. J. Health Econ.* 2018;19:1039-1051.F.I.:2.601. [doi:10.1007/s10198-018-0997-8]

3. Cantarero-Prieto, D, Pascual-Sáez, M, Blázquez-Fernández, C. **What is Happening with Quality of Life Among the Oldest People in Southern European Countries? An Empirical Approach Based on the SHARE Data.** *Soc. Indic. Res.* 2018;140:1195-1209.F.I.:1.648. [doi:10.1007/s11205-017-1828-5]

4. Blázquez-Fernández C, Cantarero-Prieto D, Pascual-Sáez M. **On the nexus of air pollution and health expenditures: new empirical evidence.** *Gac. Sanit.* 2018;F.I.:1.581. [doi:10.1016/j.gaceta.2018.01.006]

5. Moreno, P, Rodríguez-Poo, J, Cantarero, D. **A new approach to understanding labour supply of disabled people.** *Appl. Econ.* 2018;50:2147-2155.F.I.:0.750. [doi:10.1080/00036846.2017.1392000]

6. Sáez, MP, Cantarero-Prieto, D, Manso, JRP. **Gross inland energy consumption inequality in Europe: an empirical approach.** *Rev. Econ. Mund.* 2018;149-163.F.I.:0.415.

7. Blázquez-Fernández, C, Cantarero-Prieto, D, Pascual-Sáez, M. **Does Rising Income Inequality Reduce Life Expectancy? New Evidence for 26 European Countries (1995-2014).** *Global Econ. Rev.* 2018;47:464-479.F.I.:0.273. [doi:10.1080/1226508X.2018.1526098]

Editorials

1. Bermúdez-Tamayo, C, Hernandez, MN, Alguacil, J, Vozmediano, EB, Cantarero, D, Portiño MC, Casino, G, Sanchez, EC, Calvente, MG, Zapata LIG, Epstein, D, Hernan, M, Linares, C, Garcia, LP, Cantero MTR, Segura, A, Zunzunegui, MV, Sarria, A, Peiro, R, Alvarez-Dardet, C. **GACETA SANITARIA in 2017. Improving the quality of our journal.** *Gac. Sanit.* 2018;32:117-120.F.I.:1.581. [doi:10.1016/j.gaceta.2018.02.002]

2. Epstein, D, Bermúdez-Tamayo, C, Cantarero, D, Negrín Hernández MÁ, Álvarez-Dardet, C. **Special edition of GACETA SANITARIA on evidence-based decision making in public health.** *Gac. Sanit.* 2018;32:403-404.F.I.:1.581. [doi:10.1016/j.gaceta.2018.05.001]

Authorship Thesis

1. Javier Isaac Lera Torres. **Ensayos en Economía de Salud: Utilización Sanitaria.** Director/s: Marta Pascual Saez, David Cantarero Prieto. UNIVERSIDAD DE CANTABRIA.

2. Paloma Lanza León. **Essays about health economics: inequality, poverty and polarization.** Director/s: Marta Pascual Saez, David Cantarero Prieto. UNIVERSIDAD DE CANTABRIA.

Thesis Addressed

1. María Amada Pellico López. **Características e impacto del bed-blocking. estudios de casos y controles en Cantabria.** Director/s: David Cantarero Prieto, María Paz Zulueta. UNIVERSIDAD DE CANTABRIA.

2. Patricia Moreno Mencía. **Essays about econometric models subject to sample selection and endogeneity in the field of health economics and labour.** Director/s: David Cantarero Prieto. UNIVERSIDAD DE CANTABRIA.

Other Publications

1. Durán, AO, Gómez, D, Cantarero, D, Blázquez, C, Toriello, M, Pérez-Pereda, S, Quintanilla, VG. **New oral treatments decrease the switch to second-line therapies in multiple sclerosis. A 9-years retrospective, clinical and budget impact study.** *Mult. Scler. J.* 2018;24:815-815. mTOR. Oncotarget. 2018;9:30869-30882.F.I.:5





**○ Infectious
Diseases and
Immune System
Area**

**María Carmen Fariñas
Álvarez**

Coordinator of the Area of
Infectious Diseases and Immune
System.

**Head of the Infectious Service.
Hospital Universitario Marqués
de Valdecilla**

Professor of the Department of
Medicine and Psychiatry.
Universidad de Cantabria.

Genetic epidemiology and atherosclerosis in systemic inflammatory diseases

Group Responsible

**Miguel Ángel
González-Gay
Mantecón**

Reumatology Service

Hospital Universitario
Marqués de Valdecilla



miguelangel.gonzalezgay@scsalud.es



María Cristina Mata Arnaiz
Víctor Manuel Mora Cuesta
Natalia Palmou Fontana
M^a Enriqueta Peiró Callizo
Genma Pérez Paredes
Trinitario Pina Murcia
Diana Prieto Peña
Federico Rehbergeer Bescos
Sara Remuzgo Martínez
Leyre Riancho Zarrabeitia
Javier Rueda Gotor
Nuria Vegas Revenga
Losune Vilanova Vadaniz

Nurses

Virginia Portilla González
Patricia Vicente Gómez

Predoctoral

Verónica Pulito Cueto

Technicians

Javier García Fernández
Leticia Lera Gómez
Verónica Mijares Díaz
Enar Pons Sierra



Consolidated group

Researchers

Ricardo Blanco Alonso
Raquel López Mejías

Contributors

Pilar Alonso Lecue
Susana Armesto Alonso
Belén Atienza Mateo
Inés Margarita Ayerbe Cintra
Luis Miguel Blasco Mata
Mónica Patricia Calderón Goercke
Vanesa Calvo del Río
Benigno Casanueva Fernandez
Beatriz Castro Gutiérrez

José Manuel Cifrián Martínez
Germana Consuegra Romero
Alfonso Fernando Corrales Martínez
Lucía Cristina Domínguez Casas
Marta Drake Monfort
Sonia María Fernández Rozas
José Héctor Fernández Llaca
Virginia Franco Gutiérrez
Fernanda Genre
Marcos Antonio González López
David Iturbe Fernández
Marina Lacalle Calderon
Javier Loricera García
María Marcellán Fernández,
Cristina Martínez Dubois

Research lines

1.-Epidemiology of autoimmune diseases (mainly rheumatoid arthritis (RA), giant cell arteritis, scleroderma, spondyloarthropathies (EspA), systemic lupus erythematosus (SLE), psoriasis, antisynthetic syndrome, interstitial lung disease, Shöenlein-Henoch purpura (PSH), aortitis, fibromyalgia and hidradenitis suppurativa). We analyze incidence, clinical spectrum and evolutionary course of these diseases. In many cases, these data are unknown in the Spanish population, which puts our center as a reference for the knowledge of these diseases in southern European population.

2.- Cardiovascular risk (CV) and vascular disease in autoimmune diseases (mainly RA, EspA, SLE, psoriasis and hidradenitis suppurativa). Role of inflammation and genetics in their development and clinical presentation. We analyzed the markers (analytical, clinical and imaging) associated with inflammation that may be involved in the development of CV events and early mortality in patients with chronic inflammatory rheumatologic diseases.

3.- Genetic, serum and gene expression profiles of autoimmune diseases and their associated comorbidities (mainly RA, giant cell arteritis, scleroderma, EspA, SLE, psoriasis, antisynthetic syndrome, interstitial lung disease, aortitis and PSH). Study of the genetic predisposition pattern of susceptibility as well as analysis of serum biomarkers and gene expression profiles in rheumatologic autoimmune inflammatory diseases and their associated comorbidities.

4.- Therapeutic strategy with biological agents in patients with autoimmune diseases (mainly RA, EspA and psoriasis). Effect on clinical parameters of the disease and the development of CV disease. Based strictly on clinical indication for lack of response to conventional standard therapy, in those patients that due to the severity of the disease require biological treatments, we

analyze the impact of these therapies on the progression of atherosclerotic disease, analyzing serum markers and clinical parameters Associated with an increased risk of CV mortality and the implication of these drugs in their pathogenesis as potentially “protective” therapies against the development of CV disease progression.

5- Role of endothelial progenitor cells in the pathophysiology of interstitial lung disease associated with rheumatoid arthritis

PUBLICATIONS

IMPACT FACTOR | 245.703

Original articles

1. Loricera, J, Blanco, R.

A closer look at skin involvement in vasculitis. *Nat. Rev. Rheumatol.*2018;14:187-188.F.I.:15.661. [doi:10.1038/nrrheum.2018.26]

2. Cavagna, L, Castañeda S, Scire, C, Gonzalez-Gay, MA, AENEAS Collaborative Grp Members.

Antisynthetase syndrome or what else? Different perspectives indicate the need for new classification criteria. *Ann. Rheum. Dis.*2018;77:F.I.:12.350. [doi:10.1136/annrheumdis-2017-212368]

3. Ortiz-Fernández L, David Carmona F, López-Mejías R, González-Escribano MF, Lyons PA, Morgan AW, Sawalha AH, Smith KGC, González-Gay MA, Martín J. **Cross-phenotype analysis of Immunochip data identifies KDM4C as a relevant locus for the development of systemic vasculitis.** *Ann. Rheum. Dis.*2018;77:589-595.F.I.:12.350. [doi:10.1136/annrheumdis-2017-212372]

4. Crowson, CS, Rollefstad, S, Ikdahl, E, Kitas, GD, van Riel PLCM,

Gabriel, SE, Matteson, EL, Kvien, TK, Douglas, K, Sandoo, A, Arts, E, Wållberg-Jonsson S, Innala, L, Karpouzas, G, Dessein, PH, Tsang, L, El-Gabalawy, H, Hitchon, C, Ramos, VP, Yáñez IC, Sfikakis, PP, Zampeli, E, Gonzalez-Gay, MA, Corrales, A, Laar MV, Vonkeman, HE, Meek, I, Semb AG, A Trans-Atlantic Cardiovascular Consortium for Rheumatoid Arthritis (ATACC-RA). **Impact of risk factors associated with cardiovascular outcomes in patients with rheumatoid arthritis.** *Ann. Rheum. Dis.*2018;77:48-54.F.I.:12.350. [doi:10.1136/annrheumdis-2017-211735]

5. Castañeda S, Cavagna, L, Gonzalez-Gay, MA. **New Criteria Needed for Antisynthetase Syndrome.** *JAMA Neurol.*2018;75:258-259.F.I.:11.460. [doi:10.1001/jamaneurol.2017.3872]

6. Márquez, A, Kerick, M, Zhernakova, A, Gutiérrez-Achury, J, Chen, WM, Onengut-Gumuscu, S, González-Álvaro, I, Rodríguez-Rodríguez, L, Ríos-Fernández, R, González-Gay, MA, Coeliac Disease Immunochip Consortium, Rheumatoid Arthritis Consortium International for Immunochip (RACI), International Scleroderma Group, Type 1 Diabetes Genetics Consortium, Mayes MD, Raychaudhuri S, Rich SS, Wijmenga C, Martín J. **Meta-analysis of Immunochip data of four autoimmune diseases reveals novel single-disease and cross-phenotype associations.** *Genome Med.*2018;10:97-97.F.I.:8.898. [doi:10.1186/s13073-018-0604-8]

7. Sarmiento, E, Cifrián, J, Calahorra, L, Bravo, C, López, S, Laporta, R, Ussetti, P, Sole, A, Morales, C, de Pablos, A, Jaramillo, M, Ezzahouri, I, García, S, Navarro, J, López-Hoyos, M, Carbone, J. **Monitoring of early humoral immunity to identify lung recipients at risk for development of serious infections: A multicenter prospective study.** *J. Heart Lung Transplant.*2018;37:1001-1012.F.I.:7.955. [doi:10.1016/j.healun.2018.04.001]

8. Castañeda S, Cavagna, L, Gonzalez-Gay, MA, AENEAS (American-European Network of Antisynthetase Syndrome) collaborative grou. **Consideration of antisynthetase syndrome**

features in classifying patients as having idiopathic inflammatory myopathy: comment on the article by Lundberg et al. *Arthritis Rheumatol.* 2018;70:975-976.F.I.:7.871. [doi:10.1002/art.40478]

9. Martín-Varillas, JL, Calvo-Río, V, Beltrán, E, Sánchez-Burson, J, Mesquida, M, Adan, A, Hernández, MV, Garfella, MH, Pascual, EV, Martínez-Costa, L, Sellas-Fernández, A, Cordero-Coma, M, Díaz-Llopis, M, Gallego, R, Salom, D, Ortego, N, García-Serrano, JL, Callejas-Rubio, JL, Herreras, JM, García-Aparicio, A, Maiz, O, Blanco, A, Torre, I, Díaz-Valle, D, Pato, E, Aurrecochea, E, Caracuel, MA, Gamero, F, Minguez, E, ..., Blanco, R. **Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behcet's Disease.** *Ophthalmology.* 2018;125:1444-1451.F.I.:7.479. [doi:10.1016/j.ophtha.2018.02.020]

10. Blasco, LM. **Refutation is a strong word for partial evidence in ASIA.** *J Allergy Clin Immunol Pract.* 2018;6:707-708.F.I.:6.966. [doi:10.1016/j.jaip.2017.11.017]

11. del Real, A, Riancho-Zarrabeitia, L, Riancho, JA. **Epigenetic Aging in Osteoporosis.** *J. Bone Miner. Res.* 2018;33:1902-1903.F.I.:6.314. [doi:10.1002/jbmr.3567]

12. de Pedro, I, Alonso-Lecue, P, Sanz-Gómez, N, Freije, A, Gandarillas, A. **Sublethal UV irradiation induces squamous differentiation via a p53-independent, DNA damage-mitosis checkpoint.** *Cell Death Dis.* 2018;9:1094-1094.F.I.:5.638. [doi:10.1038/s41419-018-1130-8]

13. Atienza-Mateo, B, Calvo-Río, V, Beltrán, E, Martínez-Costa, L, Valls-Pascual, E, Hernández-Garfella, M, Atanes, A, Cordero-Coma, M, Miquel Nolla J, Carrasco-Cubero, C, Loricera, J, González-Vela, MC, Vegas-Revenga, N, Fernández-Díaz, C, Demetrio-Pablo, R, Domínguez-Casas, LC, Luis Martín-Varillas J, Palmou-Fontana, N, Hernández, JL, Gonzalez-Gay, MA, Blanco, R. **Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behcet's disease: multicentre retrospective study.** *RHEUMATOLOGY.* 2018;57:856-864.F.I.:5.245. [doi:10.1093/rheumatology/kex480]

14. Fernández-Díaz, C, Loricera, J, Castañeda S, López-Mejias, R, Ojeda-García, C, Olive, A, Rodríguez-Muguruza, S, Carreira, PE, Pérez-Sandoval, T, Retuerto, M, Cervantes-Perez, EC, Flores-Robles, BJ, Hernandez-Cruz, B, Urruticoechea, A, Maiz-Alonso, O, Arboleya, L, Bonilla, G, Hernández-Rodríguez, I, Palma, D, Delgado, C, Expósito-Molinero, R, Ruibal-Escribano, A, Álvarez-Rodríguez, B, Blanco-Madrigal, J, Bernal, JA, Vela-Casasempere, P, Rodríguez-Gómez, M, Fito, C, Ortiz-Sanjuán, F, ..., Blanco, R. **Abatacept in patients with rheumatoid arthritis and interstitial lung disease: A national multicenter study of 63 patients.** *Semin. Arthritis Rheum.* 2018;48:22-27.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.12.012]

15. Martínez-Rodríguez, I, Jiménez-Alonso, M, Quirce, R, Jiménez-Bonilla, J, Martínez-Amador, N, De Arcocha-Torres, M, Loricera, J, Blanco, R, González-Gay, MA, Banzo, I. **F-18-FDG PET/CT in the follow-up of large-vessel vasculitis: A study of 37 consecutive patients.** *Semin. Arthritis Rheum.* 2018;47:530-537.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.08.009]

16. Vilanova, I, Hernández, JL, Mata, C, Durán, C, García-Unzueta, MT, Portilla, V, Fuentevilla, P, Corrales, A, González-Vela, MC, González-Gay, MA, Blanco, R, González-López, MA. **Insulin resistance in hidradenitis suppurativa: a case-control study.** *J. Eur. Acad. Dermatol. Venereol.* 2018;32:820-824.F.I.:4.287. [doi:10.1111/jdv.14894]

17. Rueda-Gotor, J, Genre, F, Corrales, A, Blanco, R, Fuentevilla, P, Portilla, V, Expósito, R, Mata, C, Pina, T, González-Juanatey, C, Rodríguez-Rodríguez, L, González-Gay, MA. **Detection of high cardiovascular risk patients with ankylosing spondylitis based on the assessment of abdominal aortic calcium as compared to carotid ultrasound.** *Arthritis Res. Ther.* 2018;20:195-195.F.I.:4.269. [doi:10.1186/s13075-018-1684-y]

18. Nash, P, Mease, PJ, McInnes, IB, Rahman, P, Ritchlin, CT, Blanco, R, Dokoupilova, E, Andersson, M, Kajekar, R, Mpofu, S, Pricop, L, FUTURE 3 study group. **Efficacy and safety of secukinumab administration by autoinjector in**

patients with psoriatic arthritis: results from a randomized, placebo-controlled trial (FUTURE 3). *Arthritis Res. Ther.* 2018;20:47-47.F.I.:4.269. [doi:10.1186/s13075-018-1551-x]

19. Julia, A, López-Longo, FJ, Pérez Venegas JJ, Bonàs-Guarch S, Olivé À, Andreu, JL, Aguirre-Zamorano, MA, Vela, P, Nolla, JM, de la Fuente JLM, Zea, A, Pego-Reigosa, JM, Freire, M, Diez, E, Rodríguez-Almaraz, E, Carreira, P, Blanco, R, Taboada, VM, Lopez-Lasanta, M, Corbeto, ML, Mercader, JM, Torrents, D, Absher, D, Marsal, S, Fernández-Nebro, A. **Genome-wide association study meta-analysis identifies five new loci for systemic lupus erythematosus.** *Arthritis Res. Ther.* 2018;20:100-100.F.I.:4.269. [doi:10.1186/s13075-018-1604-1]

20. González-Serna, D, Ortiz-Fernández, L, Vargas, S, García, A, Raya, E, Fernández-Gutiérrez, B, López-Longo, FJ, Balsa, A, González-Álvaro, I, Narvaez, J, Gómez-Vaquero, C, Sabio, JM, García-Portales, R, González-Escribano, MF, Tolosa, C, Carreira, P, Kiemenev, L, Coenen MJH, Witte, T, Schneider, M, González-Gay, MA, Martín, J. **Association of a rare variant of the TNFSF13B gene with susceptibility to Rheumatoid Arthritis and Systemic Lupus Erythematosus.** *Sci Rep.* 2018;8:8195-8195.F.I.:4.122. [doi:10.1038/s41598-018-26573-4]

21. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Mijares, V, Expósito, R, Mata, C, Portilla, V, Blanco, R, Hernández, JL, Llorca, J, Gualillo, O, López-Mejias, R, González-Gay, MA. **Association of circulating calprotectin with lipid profile in axial spondyloarthritis.** *Sci Rep.* 2018;8:13728-13728.F.I.:4.122. [doi:10.1038/s41598-018-32199-3]

22. López-Delgado, L, Riancho-Zarrabeitia, L, García-Unzueta, MT, Tenorio, JA, García-Hoyos, M, Lapunzina, P, Valero, C, Riancho, JA. **Abnormal bone turnover in individuals with low serum alkaline phosphatase.** *Osteoporosis Int.* 2018;29:2147-2150.F.I.:3.856. [doi:10.1007/s00198-018-4571-0]

23. Álvarez-Rodríguez, L, Riancho-Zarrabeitia, L, Calvo-Alen, J, López-Hoyos, M, Martínez-Taboada, V. **Peripheral B-Cell Subset Distribution in Primary**

Antiphospholipid Syndrome.

Int. J. Mol. Sci. 2018;19:F1.:3.687. [doi:10.3390/ijms19020589]

24. Castañeda S, Atienza-Mateo, B, Martín-Varillas, JL, Serra López-Matencio JM, González-Gay, MA.

Anakinra for the treatment of adult-onset Still's disease. *Expert Rev. Clin. Immunol.* 2018;14:979-992.F1.:3.436. [doi:10.1080/1744666X.2018.1536548]

25. Ferraz-Amaro, I, López-Mejias, R, Tejera-Segura, B, de Vera-González, AM, Ubilla, B, Olmos, JM, Hernandez, JL, Gonzalez-Gay, MA. **Amylin in the insulin resistance of patients with rheumatoid arthritis. *Clin. Exp. Rheumatol.* 2018;36:421-427.F1.:3.201.**

26. Rueda-Gotor, J, Llorca, J, Corrales, A, Parra, JA, Portilla, V, Genre, F, Blanco, R, Agudo, M, Fuentevilla, P, Expósito, R, Mata, C, Pina, T, González-Juanatey, C, González-Gay, MA. **Cardiovascular risk stratification in axial spondyloarthritis: carotid ultrasound is more sensitive than coronary artery calcification score to detect high-cardiovascular risk axial spondyloarthritis patients. *Clin. Exp. Rheumatol.* 2018;36:73-80.F1.:3.201.**

27. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Ubilla, B, Mijares, V, Fernández-Díaz, C, Portilla, V, Blanco, R, Hernández, JL, Llorca, J, López-Mejias, R, González-Gay, MA. **Implication of osteoprotegerin and sclerostin in axial spondyloarthritis cardiovascular disease: a study of 163 Spanish patients. *Clin. Exp. Rheumatol.* 2018;36:302-309.F1.:3.201.**

28. Loricera J, Hernández JL, García-Castaño A, Martínez-Rodríguez I, González-Gay MÁ, Blanco R. **Subclinical aortitis after starting nivolumab in a patient with metastatic melanoma. A case of drug-associated aortitis?. *Clin. Exp. Rheumatol.* 2018;36 Suppl 111:171-171.F1.:3.201.**

29. González-Gay, MA, Montecucco, C, Selva-O'Callaghan, A, Trallero-Araguas, E, Molberg, O, Andersson, H, Rojas-Serrano, J, Pérez-Román, DI, Bauhammer, J, Fiehn, C, Neri, R, Barsotti, S, Lorenz, HM, Doria, A,

Ghirardello, A, Iannone, F, Giannini, M, Franceschini, F, Cavazzana, I, Triantafyllis, K, Benucci, M, Infantino, M, Manfredi, M, Conti, F, Schwarting, A, Sebastiani, G, Iuliano, A, Emmi, G, Silvestri, E, ..., AENEAS (American and European Network of Antisynthetase Syndrome) collaborative. **Timing of onset affects arthritis presentation pattern in antisynthetase syndrome. *Clin. Exp. Rheumatol.* 2018;36:44-49.F1.:3.201.**

30. González-Serna, D, Carmona, EG, Ortego-Centeno, N, Simeon, CP, Solans, R, Hernández-Rodríguez, J, Tolosa, C, Castañeda S, Narvaez, J, Martínez-Valle, F, European GCA Consortium, European Scleroderma Group, Witte T, Neumann T, Holle J, Beretta L, Boiardi L, Emmi G, Cimmino MA, Vaglio A, Herrick AL, Denton CP, Salvarani C, Cid MC, Morgan AW, Fonseca C, González-Gay MA, Martín J, Márquez A. **A TNFSF13B functional variant is not involved in systemic sclerosis and giant cell arteritis susceptibility. *PLoS One.* 2018;13:F1.:2.766. [doi:10.1371/journal.pone.0209343]**

31. González-López, MA, Lacalle, M, Mata, C, López-Escobar, M, Corrales, A, López-Mejias, R, Rueda, J, González-Vela, MC, González-Gay, MA, Blanco, R, Hernández, JL. **Carotid ultrasound is useful for the cardiovascular risk stratification in patients with hidradenitis suppurativa. *PLoS One.* 2018;13:F1.:2.766. [doi:10.1371/journal.pone.0190568]**

32. Castaneda, S, González-Juanatey, C, González-Gay, MA. **Inflammatory Arthritis and Heart Disease. *Curr. Pharm. Design.* 2018;24:262-280.F1.:2.757. [doi:10.2174/1381612824666180123102632]**

33. González-Gay, MA, Rueda-Gotor, J. **Atherosclerosis in ankylosing spondylitis: clinical implications. *Pol. Intern. Med.* 2018;128:409-410.F1.:2.658. [doi:10.20452/pamw.4324]**

34. Quiros, S, de la Rosa, D, Uranga, A, Madero, R, Amaro, R, Bruguera, N, García, JA, Gómez, C, Iturbe, D, Lera, R, Luque, L, Martínez, AJ, Mínguez, P, Navarro, A, Sánchez, G, Suárez-Cuartin, G. **Screening for Latent Tuberculosis Infection in Patients who are Candidate for**

Biological Therapies in Spain? A Multidisciplinary Survey. *Arch. Bronconeumol.* 2018;54:510-517.F1.:2.633. [doi:10.1016/j.arbres.2018.04.004]

35. Carretero, G, Puig, L, Carrascosa, JM, Ferrandiz, L, Ruiz-Villaverde, R, de la Cueva, P, Belinchon, I, Vilarrasa, E, del Rio, R, Sanchez-Carazo, JL, Lopez-Ferrer, A, Peral, F, Armesto, S, Eiris, N, Mitxelena, J, Vilar-Alejo, J, Ara M, Soria, C, From the Spanish Group of Psoriasis.. **Redefining the therapeutic objective in psoriatic patients candidates for biological therapy. *J. Dermatol. Treat.* 2018;29:334-346.F1.:2.144. [doi:10.1080/09546634.2017.1395794]**

36. Riancho-Zarrabeitia, L, Rasilla, DF, Roye, D, Fdez-Arroyabe, P, Santurtun, A. **Kawasaki disease in Spanish paediatric population and synoptic weather types: an observational study. *Rheumatol. Int.* 2018;38:1259-1266.F1.:1.952. [doi:10.1007/s00296-018-4066-5]**

37. Franco-Gutiérrez, R, Pérez-Pérez, AJ, Franco-Gutiérrez, V, Testa-Fernández, AM, Vidal-Pérez, RC, López-Reboiro, ML, Puebla-Rojo, VM, Santos-Álvarez, M, Crespo-Leiro, MG, González-Juanatey, C. **Usefulness of carotid ultrasonography in the diagnosis of coronary artery disease in patients undergoing exercise echocardiography. *Cardiovasc. Ultrasound.* 2018;16:26-26.F1.:1.652. [doi:10.1186/s12947-018-0143-x]**

38. Jiménez-Bonilla, JF, González-Gay, MA, Banzo, I. **Usefulness of 18F-FDG-PET/CT imaging in a patient with neurosarcoidosis. *Med. Clin.* 2018;151:464-465.F1.:1.168. [doi:10.1016/j.medcli.2018.02.024]**

Reviews

1. López-Mejias, R, Castañeda S, Genre, F, Remuzgo-Martínez, S, David Carmona F, Llorca, J, Blanco, R, Martín, J, González-Gay, MA. **Genetics of immunoglobulin-A vasculitis (Henoch-Schonlein purpura): An updated review. *Autoimmun. Rev.* 2018;17:301-315.F1.:8.745. [doi:10.1016/j.autrev.2017.11.024]**

2. Francisco, V, Pino, J, González-Gay, MA, Mera, A, Lago, F, Gómez, R, Mobasher, A, Gualillo, O.

Adipokines and inflammation: is it a question of weight?. Br. J. Pharmacol.2018;175:1569-1579.F.I.:6.810. [doi:10.1111/bph.14181]

3. Riancho-Zarrabeitia, L, Cuberia, M, Muñoz P, López-Hoyos, M, García-Canale, S, García-Unzueta, M, Hernández, JL, Martínez-Taboada, VM. **Vitamin D and antiphospholipid syndrome: A retrospective cohort study and meta-analysis. Semin. Arthritis Rheum.** 2018;47:877-882.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.10.007]

4. del Real, A, Riancho-Zarrabeitia, L, Lopez-Delgado, L, Riancho, JA. **Epigenetics of Skeletal Diseases. Curr. Osteoporos. Rep.**2018;16:246-255.F.I.:3.726. [doi:10.1007/s11914-018-0435-y]

5. González-Gay, MA, Pina, T, Prieto-Pena, D, Calderón-Goercke, M, Blanco, R, Castañeda S. **Drug therapies for polymyalgia rheumatica: a pharmacotherapeutic update. Expert Opin. Pharmacother.**2018;19:1235-1244.F.I.:3.475. [doi:10.1080/14656566.2018.1501360]

6. González-Gay, MA, Pina, T, Prieto-Pena, D, Calderón-Goercke, M, Blanco, R, Castañeda S. **Current and emerging diagnosis tools and therapeutics for giant cell arteritis. Expert Rev. Clin. Immunol.**2018;14:593-605.F.I.:3.436. [doi:10.1080/1744666X.2018.1485491]

7. Francisco, V, Perez, T, Pino, J, Lopez, V, Franco, E, Alonso, A, Gonzalez-Gay, MA, Mera, A, Lago, F, Gomez, R, Gualillo, O. **Biomechanics, obesity, and osteoarthritis. The role of adipokines: When the levee breaks. J. Orthop. Res.**2018;36:594-604.F.I.:3.414. [doi:10.1002/jor.23788]

8. Francisco, V, Pino, J, Campos-Cabaleiro, V, Ruiz-Fernandez, C, Mera, A, Gonzalez-Gay, MA, Gomez, R, Gualillo, O. **Obesity, Fat Mass and Immune System: Role for Leptin. Front. Physiol.**2018;9:640-640.F.I.:3.394. [doi:10.3389/fphys.2018.00640]

9. Palmou-Fontana, N, Calvo-Río, V, Martín-Varillas, JL, Fernández-Díaz, C, Mesquida, M, Adan, A, Hernandez,

MV, Cordero-Coma, M, Maiz Alonso O, Díaz-Valle, D, Fernandez-Cid, C, Ruiz-Moreno, O, Hernández, JL, González-Gay, MA, Blanco, R. **Golimumab in refractory uveitis associated to juvenile idiopathic arthritis: multicentre study of 7 cases and literature review. Clin. Exp. Rheumatol.**2018;36:652-657.F.I.:3.201.

10. González-Gay, MA, Lopez-Mejias, R, Pina, T, Blanco, R, Castañeda S. **IgA Vasculitis: Genetics and Clinical and Therapeutic Management. Curr. Rheumatol. Rep.**2018;20:24-24.F.I.:3.079. [doi:10.1007/s11926-018-0735-3]

Projects

1. Miguel Ángel González-Gay Mantecón. **Ayuda por producción al grupo de Epidemiología Genética y Arterioesclerosis en enfermedades inflamatorias sistémicas. APG/06.** FUNDACION INSTITUTO DE INVESTIGACIÓN MARQUÉS DE VALDECILLA IDIVAL.

2. Miguel Ángel González-Gay Mantecón. **Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases.** EU13/01- PRECISEADS. COMISIÓN EUROPEA, INNOVATIVE MEDICINES INITIATIVE.

3. Ricardo Blanco Alonso. **Estudio de marcadores genéticos de susceptibilidad en pacientes con púrpura de SCHOENLEIN- HENoch.** FER14/11. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

4. María Cristina Mata Arnaiz. **Convenio de colaboración para el desarrollo de proyectos de investigación en la Unidad de Reumatología de la Dra. Cristina Mata Arnaiz del Hospital de Laredo.** C114/38. MERCK SHARP & DHOME ESPAÑA.

5. Ricardo Blanco Alonso. **Convenio de colaboración para el apoyo al Plan de publicaciones del Servicio de Reumatología del Hospital Universitario Marqués de Valdecilla 2015.** C115/14. ROCHE FARMA, S.A.U..

6. Ricardo Blanco Alonso. **Contrato de servicios de investigación para el proyecto Aterosclerosis y entesitis subclínica en pacientes con**

Hidradenitis Suppurativa. CS115/07. ABBVIE SPAIN, S.L.U..

7. Miguel Ángel González-Gay Mantecón. **Marcadores genéticos de enfermedad aterosclerótica en la Artritis Reumatoide.** PI15/00525. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

8. Ricardo Blanco Alonso. **Convenio para la gestión del ensayo con código I4V-MC-JADY. Estudio fase 3, multicéntrico para evaluar la seguridad y eficacia de Baricitinib en pacientes con artritis reumatoide.** CCI15/20.

9. Ricardo Blanco Alonso. **Contrato de apoyo a la investigación y publicación de estudios.** CS115/14.

10. José Manuel Cifrián Martínez. **Donaciones para el desarrollo de proyectos de investigación.** BDP32. GLAXOSMITHKLINE, S.A., FERRER INTERNACIONAL, S.A., ACTELION PHARMACEUTICALS ESPAÑA, S.L..

11. Miguel Ángel González-Gay Mantecón. **Donación para el desarrollo de proyectos de investigación.** C115/53. GLAXOSMITHKLINE, S.A..

12. Ricardo Blanco Alonso. **Convenio de colaboración para el desarrollo del Plan de Publicaciones de Reumatología del Hospital Universitario Marqués de Valdecilla.** C116/09. ROCHE FARMA, S.A.U., ROCHE FARMA, S.A.U..

13. Ricardo Blanco Alonso. **Convenio para la gestión del ensayo con código SL0012. Estudio en fase 3, multicéntrico, abierto y de extensión, para evaluar la seguridad y la tolerabilidad del tratamiento con epratuzumab en pacientes con lupus eritematoso sistémico (EMBODY 4).** CCI16/18.

14. Ricardo Blanco Alonso. **Contrato de apoyo a la investigación y publicación de estudios.** CS116/23. MERCK SHARP & DHOME ESPAÑA.

15. Miguel Ángel González-Gay Mantecón. **Convenio de colaboración para el desarrollo del Plan de publicaciones del Servicio de Reumatología del H.U.M de Valdecilla coordinado por el**

Dr. Miguel Ángel González-Gay Mantecón. CI16/43. ROCHE FARMA, S.A.U.

- 16.** Miguel Ángel González-Gay Mantecón. **Red temática en Inflamación y Enfermedades Reumáticas.** RD16/0012/0009. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
- 17.** Raquel López Mejías. **Cardiovascular risk assessment in patients with rheumatoid arthritis: the relevance of genetic markers.** CP16/00033. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
- 18.** Ricardo Blanco Alonso. **Convenio de Colaboración para la financiación del Plan de Publicaciones del Servicio de Reumatología del HUM de Valdecilla 2018.** CSI17/05. ROCHE FARMA, S.A.U..
- 19.** José Manuel Cifrián Martínez. **Estudio de biomarcadores genéticos, serológicos e histológicos en el síndrome antisintetasa con patología intersticial pulmonar.** SOCIALPAR17/11. SOCIEDAD CASTELLANO-LEONESA Y CÁNTABRA DE PATOLOGÍA RESPIRATORIA SOCIALPAR.
- 20.** José Manuel Cifrián Martínez. **Convenio de Colaboración para el desarrollo del proyecto de investigación Plan de publicaciones 2017 de la Unidad Multidisciplinar de Alta complejidad en EPID del Hospital Universitario Marqués de Valdecilla.** CI17/43. ROCHE FARMA, S.A.U..
- 21.** Fernanda Genre. **Estudio de nuevos biomarcadores de riesgo cardiovascular y aterosclerosis subclínica en pacientes con espondiloartritis axial.** NVAL17/10.
- 22.** Leyre Riancho Zarrabeitia. **Papel de los biomarcadores proteómicos y genéticos en la patogenia y el manejo de los abortos de repetición de causa desconocida.** NVAL17/19.
- 23.** Miguel Ángel González-Gay Mantecón. **Convenio de colaboración para el desarrollo de proyectos de investigación del Dr. Miguel**

Ángel González-Gay Mantecón en el Servicio de Reumatología del Hospital Universitario Marqués de Valdecilla. CI17/46. MERCK SHARP & DHOME ESPAÑA.

- 24.** Miguel Ángel González-Gay Mantecón. **Acuerdo de cooperación en el programa de becas de investigación científica de IDIVAL.** CI17/53/01. JANSSEN-CILAG, S.A., JANSSEN-CILAG, S.A..
- 25.** Miguel Ángel González-Gay Mantecón. **Papel de las células progenitoras endoteliales en la patofisiología de la enfermedad pulmonar intersticial asociada a artritis reumatoide.** PREVAL18/01.
- 26.** Ricardo Blanco Alonso. **Contrato de Patrocinio Jornadas formativas en Patología Reumática.** CSI18/15. BRISTOL-MYERS SQUIBB, S.A.U..
- 27.** José Manuel Cifrián Martínez. **Contrato de Patrocinio Seminario de Trasplante Pulmonar HUMV Santander.** CSI18/11.
- 28.** Miguel Ángel González-Gay Mantecón. **Molecular stratification of patients with giant cell arteritis to tailor glucocorticoid and tocilizumab therapy / START.** FOREUM18/34. FOUNDATION FOR RESEARCH IN RHEUMATOLOGY FOREUM.
- 29.** Miguel Ángel González-Gay Mantecón. **Improving the outcome in myositis spectrum diseases: core set variables harmonization and use from children to adulthood - IMPROVEMENT.** FOREUM17/31. FOUNDATION FOR RESEARCH IN RHEUMATOLOGY FOREUM.
- 30.** Raquel López Mejías. **Caracterización de las bases moleculares de la vasculitis mediada por IgA.** PI18/00042. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD, INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
- 31.** Ricardo Blanco Alonso. **Convenio de Colaboración para la financiación del Plan de Publicaciones del Servicio de Reumatología del HUM de Valdecilla 2018.** CSI18/17. ROCHE FARMA, S.A.U..
- 32.** Miguel Ángel González-Gay Mantecón. **Marcadores genéticos**

asociados a síndrome metabólico y enfermedad cardiovascular en artritis reumatoide. PI18/00043. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD, INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

- 33.** José Manuel Cifrián Martínez. **Convenio de Colaboración para regular la estancia formativa de fibrosis pulmonares en HUMV Santander.** CI18/50. BOEHRINGER INGELHEIM ESPAÑA, S.A., BOEHRINGER INGELHEIM ESPAÑA, S.A..
- 34.** Víctor Manuel Mora Cuesta. **Biomarcadores de enfermedad pulmonar intersticial: Implicación de IL-6. Estudio genético y funcional.** SEPAR18/27. RESPIRA. FUNDACION ESPAÑOLA DEL PULMON - SEPAR SEPAR.
- 35.** Víctor Manuel Mora Cuesta. **Biomarcadores de enfermedad pulmonar intersticial: Implicación de la IL-6. Estudio genético y funcional.** NVAL18/10.
- 36.** José Manuel Cifrián Martínez. **Contrato de patrocinio de las III Jornada de Trasplante Pulmonar.** CSI18/26. ASTELLAS PHARMA, S.A..
- 37.** David Iturbe Fernández. **Evaluación de la utilidad de la Osteopontina para el diagnóstico de Fibrosis Pulmonar Idiopática.** SEPAR18/32. RESPIRA. FUNDACION ESPAÑOLA DEL PULMON - SEPAR SEPAR.
- 38.** Ricardo Blanco Alonso. **Convenio de apoyo a la investigación y publicación de estudios.** CSI18/29. MERCK SHARP & DHOME ESPAÑA.
- 39.** José Manuel Cifrián Martínez. **Contrato de patrocinio III Jornadas de trasplante de pulmón.** CSI18/31. ACTELION PHARMACEUTICALS ESPAÑA, S.L.
- 40.** Natalia Palmou Fontana. **Donaciones para el desarrollo de proyectos de investigación.** BDP78. ABBVIE SPAIN, S.L.U.
- 41.** José Manuel Cifrián Martínez. **Convenio de colaboración para el desarrollo del proyecto de investigación Mejoría de la adhesión al tratamiento en pacientes SAHS.** CI18/61. OXIMESA, S.L..

42. Miguel Ángel González-Gay Mantecón. **Acuerdo de cooperación en el programa de becas de investigación científica de IDIVAL**. C118/67/01. JANSSEN-CILAG, S.A..

43. Miguel Ángel González-Gay Mantecón. **Convenio de colaboración para el desarrollo del Centro de Excelencia en Reumatología**. CSI19/03. MERCK SHARP & DHOME ESPAÑA.

44. Ricardo Blanco Alonso. **Acuerdo de colaboración para el desarrollo de las "Jornadas formativas en patología reumática"**. CSI19/13. BRISTOL-MYERS SQUIBB, S.A.U..

45. José Manuel Cifrián Martínez. **Contrato de Patrocinio de la estancia formativa de Fibrosis pulmonar en HUMV**. CSI19/12. BOEHRINGER INGELHEIM ESPAÑA, S.A..

Clinical Trials

1. Ricardo Blanco Alonso. **Estudio abierto de seguimiento a largo plazo de Tofacitinib (CP-690,550), para el tratamiento de la artritis reumatoide**. A3921024. PFIZER LIMITED.

2. Ricardo Blanco Alonso. **Estudio prospectivo, Fase IIb/III, multicéntrico, randomizado, doble ciego, controlado, de 3 grupos paralelos y 24 semanas de duración con posible extensión, para comparar la eficacia y seguridad de masitinib, a la dosis de 3 y 4.5 mg/kg/día, con metotrexato, con randomización 1:1:1, para el tratamiento de pacientes con artritis reumatoide activa y con una respuesta inadecuada a 1. metotrexato, a 2. cualquier FAME incluido al menos un fármaco biológico si previamente resultó ineficaz en pacientes tratados con metotrexato o a 3. metotrexato en combinación con cualquier FAME incluidos fármacos biológicos**. AB06012. AB SCIENCE.

3. Ricardo Blanco Alonso. **Estudio de extensión a largo plazo de los estudios WA22762 y NA25220, multicéntrico, abierto para evaluar la seguridad y eficacia de tocilizumab subcutáneo en pacientes con artritis reumatoide moderada a grave**. ML28488. ROCHE FARMA, S.A.U..

4. Ricardo Blanco Alonso. **Estudio de fase III, multicéntrico, aleatorizado, doble ciego, controlado con placebo de secukinumab subcutáneo en jeringas precargadas para demostrar la eficacia a las 16 semanas y evaluar la eficacia, seguridad y tolerabilidad a largo plazo, hasta 5 años, en pacientes con Espondilitis Anquilosante activa**. CAIN457F2310. NOVARTIS FARMACEUTICA, S.A..

5. Ricardo Blanco Alonso. **Estudio de fase 3, aleatorizado, doble ciego, controlado con placebo y un comparador activo, para evaluar la eficacia y seguridad de baricitinib en pacientes con artritis reumatoide con actividad moderada-severa y respuesta insuficiente al tratamiento con metotrexato**. I4V-MC-JADV. LILLY, S.A..

6. Ricardo Blanco Alonso. **Estudio fase 3, multicéntrico para evaluar la seguridad y eficacia de Baricitinib en pacientes con artritis reumatoide**. I4V-MC-JADY. LILLY, S.A..

7. Ricardo Blanco Alonso. **Estudio de fase II, aleatorizado, doble ciego, controlado con placebo, de búsqueda de la dosis, sobre la eficacia y seguridad de tofacitinib en pacientes con espondilitis anquilosante (EA) activa**. A3921119. PFIZER, INC.

8. Ricardo Blanco Alonso. **Estudio multicéntrico, de grupos paralelos, de seguridad y eficacia a largo plazo de CNTO 136 (sirukumab) en artritis reumatoide en sujetos que han completado el tratamiento en los estudios CNTO136ARA3002 (SIRROUND-D) y CNTO136ARA3003 (SIRROUND-T)**. CNTO136ARA3004. JANSSEN-CILAG INTERNATIONAL, NV.

9. José Manuel Cifrián Martínez. **Extensión del estudio AC-055-310, Estudio fase IIIb con Macitentan, multicéntrico, abierto, de una única rama, en pacientes con hipertensión arterial pulmonar para validar psicométricamente las versiones francesa, italiana y española de PAH-SYMPACT(tm). An extension of AC-055-310, a multi-center, open-label, single-arm, Phase 3b study of macitentan in patients with pulmonary arterial hypertension to psychometrically validate the French, Italian and Spanish versions of the**

PAH-SYMPACT(tm). AC-055-311. ACTELION PHARMACEUTICALS LTD.

10. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, doble ciego, controlado con placebo, de fase III de secukinumab subcutáneo en autoinyectores, para demostrar la eficacia a las 24 semanas y para evaluar la seguridad, tolerabilidad y eficacia a largo plazo hasta 3 años en pacientes con Artritis Psoriásica activa**. CAIN457F2318. NOVARTIS FARMACEUTICA, S.A..

11. Ricardo Blanco Alonso. **Estudio abierto, de extensión, a largo plazo, con Tofacitinib (CP-690,550) para el tratamiento de la artritis psoriásica**. A3921092. PFIZER, INC.

12. Ricardo Blanco Alonso. **Estudio de fase IIIb/IV aleatorizado, de criterios de valoración de la seguridad, de 2 dosis de Tofacitinib en comparación con un inhibidor del factor de necrosis tumoral (TNF) en pacientes con artritis reumatoide**. A3921133. PFIZER, INC.

13. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, con doble enmascaramiento, controlado con placebo, de 24 semanas de duración, seguido de una evaluación a largo plazo de la eficacia y la seguridad de ixekizumab (LY2439821) en pacientes con artritis psoriásica activa que han recibido un fármaco antirreumático modificador de la enfermedad biológico**. I1F-MC-RHBE. ELI LILLY & COMPANY.

14. Ricardo Blanco Alonso. **Estudio de fase IIb, multicéntrico, aleatorizado, doble ciego, de ALX-0061 administrado subcutáneamente como monoterapia, en sujetos con artritis reumatoide de moderada a severa con intolerancia al metotrexato o para los que el tratamiento continuado con metotrexato es inadecuado**. ALX0061-C202. ABLYNX NV.

15. Susana Armesto Alonso. **Optimización del tratamiento de mantenimiento a largo plazo de la piel blanqueada en pacientes con psoriasis crónica en placas de moderada a grave: Estudio randomizado, multicéntrico, abierto con evaluación ciega, comparativo, de 52 semanas de seguimiento para evaluar la eficacia, seguridad y**

tolerabilidad de secukinumab 300 mg s.c. CAIN457A3302. NOVARTIS FARMACEUTICA, S.A..

16. Ricardo Blanco Alonso. **Estudio de extensión, de Fase II, multicéntrico, abierto para evaluar la eficacia y seguridad a largo plazo de ALX-0061 subcutáneo en sujetos con artritis reumatoide de moderada a severa que hayan completado uno de los estudios anteriores de Fase IIb con ALX-006.** ALX0061-C203. ABLYNX NV.

17. José Manuel Cifrián Martínez. **Evaluación de la eficacia y toxicidad del uso de Gammaglobulina intravenosa en el tratamiento de infecciones en pacientes con Hipogammaglobulinemia IGG Post-trasplante de órgano sólido.** FIBHGM-ECNC001-2012. FUNDACIÓN PARA LA INVESTIGACIÓN BIOMÉDICA DEL HOSPITAL U. GREGORIO MARAÑÓN.

18. Cristina Martínez Dubois. **Estudio de Fase 3, aleatorizado, doble ciego, controlado con placebo, multicéntrico de la seguridad y eficacia analgésicas de la administración subcutánea de Tanezumab en sujetos con artrosis de cadera o de rodilla.** A4091057. PFIZER, INC.

19. Ricardo Blanco Alonso. **Estudio de fase 3, aleatorizado, doble ciego comparando ABT-494 15 mg una vez al día en monoterapia y ABT-494 30 mg una vez al día en monoterapia frente a metotrexato (MTX) en monoterapia en sujetos no tratados previamente con MTX con artritis reumatoide activa moderada a grave.** M13-545. ABBVIE DEUTSCHLAND GMBH&CO K.G.

20. Ricardo Blanco Alonso. **Estudio de fase 3, aleatorizado, doble ciego comparando ABT-494 con placebo y con adalimumab en sujetos con artritis reumatoide activa moderada a grave en tratamiento con metotrexato (MTX) en dosis estables y que no han respondido de forma adecuada a MTX (MTX-IR).** M14-465. ABBVIE DEUTSCHLAND GMBH&CO K.G.

21. Ricardo Blanco Alonso. **Estudio de Fase 3, aleatorizado, doble ciego para comparar ABT-494 con placebo en tratamiento estable con fármacos antirreumáticos modificadores de la enfermedad sintéticos convencionales (FARMEsc) en**

sujetos con artritis reumatoide de actividad moderada a grave con respuesta insuficiente o intolerancia a los FARME biológicos (FARMEb). M13-542. ABBVIE DEUTSCHLAND GMBH&CO K.G.

22. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, doble ciego, controlado con placebo para evaluar la seguridad, tolerabilidad y eficacia de secukinumab en pacientes con spondiloartritis axial no radiográfica activa durante un periodo de 2 años.** CAIN457H2315. NOVARTIS FARMACEUTICA, S.A..

23. José Manuel Cifrián Martínez. **Estudio clínico de Fase III, controlado con placebo, doble ciego y aleatorizado para determinar la eficacia, seguridad y tolerabilidad del óxido nítrico inhalado (NOi) pulsado frente al placebo en sujetos sintomáticos con hipertensión arterial pulmonar (HAP).** PULSE-PAH-004. BELLEROPHON PULSE TECHNOLOGIES LLC.

24. José Manuel Cifrián Martínez. **Estudio de la eficacia y la seguridad de bardoxolona metilo en pacientes con hipertensión arterial pulmonar asociada a enfermedad del tejido conectivo.** 402-C-1504. REATA PHARMACEUTICALS INC..

25. Ricardo Blanco Alonso. **MAXIMISE (Tratamiento de las manifestaciones axiales en la Artritis Psoriásica con Secukinumab), estudio multicéntrico, aleatorizado, doble ciego, controlado con placebo, de 52 semanas de seguimiento para evaluar la eficacia y seguridad de secukinumab 150 mg o 300 mg s.c. en pacientes con artritis psoriásica activa y afección del esqueleto axial que no respondan adecuadamente a antiinflamatorios no esteroideos (AINEs).** CAIN457F3302. NOVARTIS FARMACEUTICA, S.A..

26. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, doble ciego, con control activo para evaluar la eficacia en la semana 52 de secukinumab en monoterapia por vía subcutánea en comparación con adalimumab en monoterapia por vía subcutánea en pacientes con artritis psoriásica activa.** CAIN457F2366. NOVARTIS FARMACEUTICA, S.A..

27. José Manuel Cifrián Martínez. **Estudio aleatorizado, doble ciego**

y controlado con placebo para evaluar la eficacia y la seguridad del tratamiento oral con nintedanib durante al menos 52 semanas en pacientes con «enfermedad pulmonar intersticial asociada a esclerosis sistémica» (SSc-ILD). 1199.214. BOEHRINGER INGELHEIM ESPAÑA, S.A..

28. José Manuel Cifrián Martínez. **Ensayo en fase II, multicéntrico, internacional, doble ciego, de dos grupos, aleatorizado y controlado con placebo, de pirfenidona en pacientes con epifibrosante progresiva inclasificable.** MA39189. ROCHE PRODUCTS LIMITED.

29. José Manuel Cifrián Martínez. **Estudio de fase IIB multicéntrico, doble ciego, randomizado, controlado con placebo para evaluar la eficacia, seguridad y tolerancia de Sildenafil en combinación con Pirfenidona en pacientes con fibrosis pulmonar idiopática avanzada y probabilidad intermedia o alta de desarrollar hipertensión pulmonar grupo 3.** MA29957. ROCHE FARMA, S.A.U..

30. José Manuel Cifrián Martínez. **Programa de acceso al estudio de extensión para evaluar la seguridad a largo plazo de bardoxolona metilo en pacientes con hipertensión pulmonar.** 402-C-1602. REATA PHARMACEUTICALS INC..

31. David Iturbe Fernández. **Ensayo clínico con enmascaramiento doble, multicéntrico y controlado con placebo para investigar la eficacia y seguridad de 12 meses de terapia con Promixin® inhalado (colistimetato de sodio) para el tratamiento de pacientes con bronquiectasia no debida a fibrosis quística con infección crónica por Pseudomonas aeruginosa (P. aeruginosa).** Z7224L01. ZAMBON SPA.

32. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, doble ciego y controlado con placebo para evaluar la seguridad y la eficacia de upadacitinib en pacientes con espondilitis anquilosante activa.** M16-098. ABBVIE DEUTSCHLAND GMBH&CO K.G.

33. Ricardo Blanco Alonso. **Estudio multicéntrico, aleatorizado, parcialmente ciego, con control**

activo para demostrar la reducción de la progresión radiográfica con secukinumab frente a GP2017 (biosimilar de adalimumab) en la semana 104 y evaluar la seguridad, tolerabilidad y eficacia a largo plazo en un periodo máximo de 2 años en pacientes con espondilitis anquilosante activa. CAIN457K2340. NOVARTIS FARMACEUTICA, S.A..

34. Ricardo Blanco Alonso. **Estudio de fase 2, multicéntrico, aleatorizado, doble ciego, controlado con placebo para evaluar la eficacia y la seguridad de CC-220 en sujetos con lupus eritematoso sistémico activo.** CC-220-SLE-002. CELGENE CORPORATION.

35. José Manuel Cifrián Martínez. **Estudio de fase 2, doble ciego, controlado con placebo y aleatorizado para comparar la eficacia y la seguridad de sotatercept (ACE-011) frente al placebo cuando se añade al tratamiento estándar de la hipertensión arterial pulmonar (HAP).** A011-09. PHARMACEUTICAL PRODUCT DEVELOPMENT SPAIN, S.L. PPD.

36. José Manuel Cifrián Martínez. **Ensayo multicéntrico de fase III aleatorizado, doble ciego, de grupos paralelos y controlado por placebo para evaluar la eficacia y la seguridad de 2 dosis de GLPG1690 en adición al tratamiento habitual durante al menos 52 semanas en sujetos con fibrosis pulmonar idiopática.** GLPG1690-CL-303. GALAPAGOS NV.

Postmarketing Studies and Other

1. M^o Enriqueta Peiró Callizo. **Evaluación del riesgo cardiovascular, y de sus determinantes, en pacientes**

con artritis reumatoide, espondilitis anquilosante y artritis psoriásica. CARMA. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

2. José Héctor Fernández Llaça. **Registro epidemiológico observacional para evaluar el perfil clínico de los pacientes con psoriasis moderada a grave en España.** Estudio ARIZONA. JAN-PSO-2010-01. JANSSEN-CILAG, S.A..

3. M^o Enriqueta Peiró Callizo. **Seguimiento y control en Reumatología-Enfermería.** SCORE-2010-01. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

4. Ricardo Blanco Alonso. **Registro observacional prospectivo a 5 años para evaluar los acontecimientos adversos de interés y la eficacia en adultos con lupus eritematoso sistémico activo, con autoanticuerpos positivos, tratados con o sin BENLYSTA (belimumab).** HGS1006-C1124. GLAXOSMITHKLINE RESEARCH & DEVELOPMENT LIMITED.

5. José Manuel Cifrián Martínez. **EXPERT: EXPosurE Registry Riociguat (registro de exposición a riociguat) en pacientes con hipertensión pulmonar.** BAY-RIO-2015-01. BAYER HISPANIA, S.L..

6. Cristina Martínez Dubois. **Estudio de prevalencia de las enfermedades reumáticas en la población adulta española.** FER-COR-2016-01. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

7. José Manuel Cifrián Martínez. **Estudio retrospectivo, posautorización de tipo observacional (EPA-OD), multicéntrico, en pacientes con HAP tratados con Opsumit[®] (macitentan) según práctica clínica habitual en España.** PRACMA. AC-055-507. ACTELION PHARMACEUTICALS ESPAÑA, S.L..

8. José Manuel Cifrián Martínez. **Estudio observacional de cohorte con pacientes HAP tratados por primera vez con Uptravi[®] (selexipag) u otra terapia específica contra la hipertensión arterial pulmonar (HAP), en la práctica clínica (EXPOSURE).** AC-065A401 (ACT-UPT-2017-01). ACTELION PHARMACEUTICALS LTD.

Collaborations

Total Impact factor 7.479

1. Dick, AD, Rosenbaum, JT, Al-Dhibi, HA, Belfort, R, Brezin, AP, Chee, SP, Davis, JL, Ramanan, AV, Sonoda, KH, Carreño E, Nascimento, H, Salah, S, Salek, S, Siak, J, Steeples, L. **Guidance on Noncorticosteroid Systemic Immunomodulatory Therapy in Noninfectious Uveitis Fundamentals Of Care for Uveitis (FOCUS) Initiative.** *Ophthalmology.* 2018;125:757-773.FI.:7.479. [doi:10.1016/j.ophtha.2017.11.017]



Pathogenic Epidemiology and Mechanisms of Infectious Diseases

Group Responsible

María Del Carmen Fariñas Álvarez

Infectious Diseases Service

Hospital Universitario Marqués de Valdecilla Universidad de Cantabria



mcarmen.farinas@scsalud.es

Itziar Chapartegui González
 M^a Concepción Fariñas Álvarez
 Marta Fernández Martínez
 Marta Fernández Sampedro
 Marina Fernández Torres
 Claudia González Rico
 Mónica Gozalo Margüello
 Manuel Gutiérrez Cuadra
 Pablo Jorrín Lozano
 María Lázaro Diez
 Jesús Navas Méndez
 Javier Gonzalo Ocejo Viñals
 Daniel Pablo Marcos
 Inmaculada Concepcion Pérez del Molino Bernal
 María José Reina Rodríguez
 María Pía Roiz Mesones
 Carlos Ruiz de Alegría Puig
 Ana Sáez López
 Carlos Antonio Salas Venero
 Borja Suberviola Cañas

Technicians

Laura Álvarez Montez



Consolidated group

Researchers

Jesús Agüero Balbín
 María Victoria Francia Gil
 Alain Antonio Campo Sosa
 José Ramos Vivas

Contributors

Carlos Armiñanzas Castillo
 Francisco Arnaiz de las Revillas Almajano
 Ana M^a Arnaiz García
 Jorge Calvo Montes
 María Eliecer Cano García

Research lines

1. Epidemiology and molecular bases of antimicrobial resistance in Gram-negative and Gram-positive bacteria of clinical interest.

Much of the research activity of our group focuses on the study of genetic and biochemical aspects of antimicrobial resistance mechanisms of greatest clinical interest (mainly beta-lactams, quinolones and aminoglycosides) in a range of resistant bacteria, particularly Gram-negative organisms such as enterobacteria (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp.) and non-fermenting organisms such as *Pseudomonas aeruginosa*,

Actinobacter baumannii and the *Burkholderia cepacia* complex, among others. In the case of the Gram-positive bacteria, the group focuses mainly on the study of characterization of the genetic elements involved in antibiotic resistance and its dissemination in multiresistant enterococci, mainly *Enterococcus faecalis* and *Enterococcus faecium*. Specifically, we are interested in the mechanism of conjugation of various mobile genetic elements including pheromone response plasmids, which are found in almost 95% of the clinical strains of *E. faecalis* associated with hospital outbreaks and that can be transferred with a frequency of 100%. Similarly, we are studying the resistance to antimicrobials in different species of corynebacteria, such as *Corynebacterium diphtheriae*, *C. amycolatum*, *C. xerosis*, and *C.*

jeikeium, since many of the clinical isolates of these species are resistant to several antibiotics.

2. New diagnostic-epidemiological methodologies and in vitro activity of new antimicrobials.

The molecular diagnosis of infectious diseases has become an indispensable tool in our group. The Microbiology Service has included the sequencing and direct detection of genes related to the microbial taxonomy and antibiotic resistance mechanisms, and has initiated the first steps for the implementation of massive sequencing techniques with promising applications in multiple fields such as analysis phylogenetic of epidemiological outbreaks or studies of human microbiomes and their possible relationship with different pathologies.

Our group also participates in multi-center projects and clinical trials for the evaluation of new antimicrobials. We also participate in the evaluation with reference methods of automated antibiogram systems, especially when these systems incorporate new antimicrobials.

3. Mechanisms of pathogenicity and pathogen / host interactions in gram-negative bacteria of clinical interest.

Responding to the need for studies on the mechanisms of interaction with host cells and resistance to antimicrobials, our group develops a multidisciplinary research on host-pathogen interactions, mainly in *Acinetobacter*, *Pseudomonas aeruginosa* and *Burkholderia cepacia* species. For this, our group is involved in the identification of the main regulators involved in the perception of environmental signals through "quorum sensing", which induce the formation of biofilms and their dispersion and also in the characterization of the molecular determinants that contribute to the virulence, as are the bacterial secretion systems.

4. Infections by multiresistant microorganisms in patients transplanted from solid organs and hematopoietic progenitors.

This line of research started in 2012 is being consolidated in our group mainly through the acquisition of competitive financing research projects (FIS - PI13 / 01191 - PI16 / 01415 and Mutua Madrileña FMM 14/01) as well as with participation in projects of Pathology Network of Investigation in Infectious Pathology (REIPI) and European Projects (Increment-SOT).

5. Epidemiology, microbiological and clinical diagnosis of Cardiovascular and Osteoarticular Infections

Among the cardiovascular infections, the creation of the Multidisciplinary Endocarditis Group in 2008, in which the Infectious Diseases, Microbiology, Cardiology, Cardiovascular Surgery, Domiciliary Hospitalization and Internal Medicine of the H.U. Marques of Valdecilla, H. Sierrallana and H. de Laredo are participating. Our group has managed since the creation of the Support Group for the Management of Endocarditis in Spain (GAMES) in 2007, one of the 7 nodes in which

the 44 participating hospitals have been divided. In these 11 years of collaboration has contributed to a better knowledge of endocarditis in Spain that is impacting on a better approach both diagnostic and therapeutic. In the case of osteoarticular infections, we have focused mainly on the study of joint prosthesis infections, which began in 2009 with the execution of the Research Project: PI 08/0609 where the study of the role of the sonicate in the diagnosis was introduced of joint prosthetic infections (in conjunction with the Traumatology and Orthopedics and Microbiology Services). The results have had as a positive consequence the incorporation into the routine of the Microbiology laboratory of said technique. Next, and thanks to API 11/09, the study of Systemic Markers is being carried out in the diagnosis and evolutionary control of Knee or Hip Prosthesis Infection (IPRC) prior to the removal of the implant.

6. Optimization of antimicrobial treatment and its impact of antibiotic consumption on cost savings and bacterial resistance.

The excessive and inadequate use of antimicrobials is currently an important public health problem, due to the emergence of microorganisms increasingly resistant to available antibiotics, as stated in the National Plans against Resistance to Antibiotics 2014 -2018 and 2019-2021, prepared by the Ministry of Health, Consumption and Social Welfare (MSCBS) in collaboration with the Ministry of Agriculture, Fisheries and Food (MAPA) and under the coordination of the Spanish Agency for Medicines and Health Products (AEMPS)). This line of research started in 2006 with the award of two research projects (FIS: PI06 / 90094 and API: 06/01), and that has received the award for teaching excellence Valdecilla Caja Cantabria in 2013 aims to achieve through recommendations and training on the use of antimicrobials in a standardized way, by a person with experience in this area and the result of a multidisciplinary collaboration, an appropriate use of antibiotics. The experience accumulated in the Marqués de Valdecilla Hospital has been transferred to other hospitals for 6 years by teaching specialist physicians from National hospitals who come to the Infectious Diseases Service to be trained.

PUBLICATIONS

IMPACT FACTOR | 146.890

Original articles

1. Zegri-Reiriz, I, de Alarcón, A, Muñoz P, Martínez Sellés M, Gonzalez-Ramallo, V, Miro, JM, Falces, C, González Rico C, Kortajarena Urkola X, Lepe, JA, Rodríguez Álvarez R, Reguera Iglesias JM, Navas, E, Domínguez, F, García-Pavia, P, Spanish Collaboration Endocarditis. **Infective Endocarditis in Patients With Bicuspid Aortic Valve or Mitral Valve Prolapse. J. Am. Coll. Cardiol.** 2018;71:2731-2740.F.I.:16.834. [doi:10.1016/j.jacc.2018.03.534]
2. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Álvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setián E, Lopez-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. **Microenvironment Eradication of Hepatitis C: A Novel Treatment Paradigm. Am. J. Gastroenterol.** 2018;113:1639-1648.F.I.:10.231. [doi:10.1038/s41395-018-0157-x]
3. Kumar, D, Ferreira, VH, Blumberg, E, Silveira, F, Cordero, E, Perez-Romero, P, Aydilto, T, Danziger-Isakov, L, Limaye, AP, Carratala, J, Munoz, P, Montejo, M, López-Medrano, F, Farinas, MC, Gavalda, J, Moreno, A, Levi, M, Fortun, J, Torre-Cisneros, J, Englund, JA, Natori, Y, Husain, S, Reid, G, Sharma, TS, Humar, A. **A 5-Year Prospective Multicenter Evaluation of Influenza Infection in Transplant Recipients. Clin. Infect. Dis.** 2018;67:1322-1329.F.I.:9.117. [doi:10.1093/cid/ciy294]
4. Robert-Gangneux, F, Meroni, V, Dupont, D, Botterel, F, Garcia JMA, Brenier-Pinchart, MP, Accoceberry, I, Akan, H, Abbate, I, Boggian, K, Bruschi, F, Carratala, J, David, M, Drgona, L, Djurkovic-Djakovic, O, Farinas, MC, Genco, F, Gkrania-Klotsas, E, Groll, AH, Guy, E, Hirzel, C, Khanna, N, Kurt Ö, Junie, LM, Lazzarotto, T, Len, O, Mueller, NJ, Munoz, P, Pana, ZD, ..., Manuel, O. **Toxoplasmosis in Transplant**

Recipients, Europe, 2010-2014. *Emerg. Infect. Dis.* 2018;24:1497-1504.F.I.:7.422. [doi:10.3201/eid2408.180045]

5. Oravcova, V, Peixe, L, Coque, TM, Novais, C, Francia, MV, Literak, I, Freitas, AR. **Wild corvid birds colonized with vancomycin-resistant *Enterococcus faecium* of human origin harbor epidemic vanA plasmids.** *Environ. Int.* 2018;118:125-133.F.I.:7.297. [doi:10.1016/j.envint.2018.05.039]

6. Fernández-Hidalgo, N, Ribera, A, Larrosa, MN, Viedma, E, Origen, J, de Alarcon, A, Fariñas MC, Saez, C, Peña C, Muñoz E, García López MV, Gavalda, J, Perez-Montarelo, D, Chaves, F, Almirante, B. **Impact of *Staphylococcus aureus* phenotype and genotype on the clinical characteristics and outcome of infective endocarditis. A multicentre, longitudinal, prospective, observational study.** *Clin. Microbiol. Infect.* 2018;24:985-991.F.I.:5.394. [doi:10.1016/j.cmi.2017.12.002]

7. López-Medrano, F, Fernández-Ruiz, M, Silva, JT, Carver, PL, van Delden, C, Merino, E, Pérez-Saez, MJ, Montero, M, Coussement, J, de Abreu Mazzolin M, Cervera, C, Santos, L, Sabe, N, Scemla, A, Cordero, E, Cruzado-Vega, L, Martín-Moreno, PL, Len, O, Rudas, E, Ponce de León A, Arriola, M, Lauzurica, R, David, MD, Gonzalez-Rico, C, Henriquez-Palop, F, Fortun, J, Nucci, M, Manuel, O, Paño-Pardo JR, ..., Swiss Transplant Cohort Study (STCS). **Multinational case-control study of risk factors for the development of late invasive pulmonary aspergillosis following kidney transplantation.** *Clin. Microbiol. Infect.* 2018;24:192-198.F.I.:5.394. [doi:10.1016/j.cmi.2017.06.016]

8. Llerena Santiago, Susana, García-Díaz N, Curiel del Olmo, Soraya, Agraz-Doblas A, García-Blanco A, Pisonero Fraga, Helena, Varela M, Santibáñez Margüello, Miguel, Almaraz Pro, María del Carmen, Cereceda Company, Laura, Martínez Magunacelaya, Nerea, Arias Loste, María Teresa, Puente Á, Martín-Ramos L, Rodríguez de Lope López, Carlos, Castillo Suescun, Federico, Cagigas-Fernández C, Isidro P, López-López

C, López Hoyos, Marcos, Llorca Díaz, Javier, Agüero Balbín, Jesús, Crespo Facorro, Benedicto, Varela I, Piris Pinilla, Miguel Ángel, Crespo García, Javier, Vaqué Díez, José Pedro. **Applied diagnostics in liver cancer. Efficient combinations of sorafenib with targeted inhibitors blocking AKT/mTOR.** *Oncotarget.* 2018;9:30869-30882.F.I.:5.168. [doi:10.18632/oncotarget.25766]

9. Escolà-Vergé L, Rodríguez-Pardo D, Lora-Tamayo J, Morata L, Murillo O, Vilchez H, Sorli L, Carrión LG, Barbero JM, Palomino-Nicás J, Bahamonde A, Jover-Sáenz A, Benito N, Escudero R, Sampedro MF, Vidal RP, Gómez L, Corona PS, Almirante B, Ariza J, Pigrau C, Study Group on Osteoarticular Infections of the Spanish Society of Clinical Micr. **Candida periprosthetic joint infection: A rare and difficult-to-treat infection.** *J. Infect.* 2018;77:151-157.F.I.:4.603. [doi:10.1016/j.jinf.2018.03.012]

10. Paez-Vega, A, Poyato, A, Rodríguez-Benot, A, Guirado, L, Fortun, J, Len, O, Abdala, E, Fariñas MC, Cordero, E, de Gracia, C, Hernández, D, González, R, Torre-Cisneros, J, Cantisan, S, Spanish Network for Research in Infectious Diseases (REIPI) (RD16/0016), Spanish Renal Disease Network (REDinREN, RD16/0009). **Analysis of spontaneous resolution of cytomegalovirus replication after transplantation in CMV-seropositive patients with pretransplant CD8+IFNG + response.** *Antiviral Res.* 2018;155:97-105.F.I.:4.307. [doi:10.1016/j.antiviral.2018.05.006]

11. Russo A, Falcone M, Gutiérrez-Gutiérrez B, Calbo E, Almirante B, Viale PL, Oliver A, Ruiz-Garbajosa P, Gasch O, Gozalo M, Pitout J, Akova M, Peña C, Cisneros JM, Hernández-Torres A, Farcomeni A, Prim N, Origüen J, Bou G, Tacconelli E, Tumbarello M, Hamprecht A, Karaiskos I, de la Calle C, Pérez F, Schwaber MJ, Bermejo J, Lowman W, Hsueh PR, ..., REIPI/ESGBIS/INCREMENT investigators. **Predictors of outcome in patients with severe sepsis or septic shock due to extended-spectrum β -lactamase-producing Enterobacteriaceae.** *Int. J. Antimicrob. Agents.* 2018;52:577-

585.F.I.:4.253. [doi:10.1016/j.ijantimicag.2018.06.018]

12. Hamzaoui, Z, Ocampo-Sosa, A, Martínez, MF, Landolsi, S, Ferjani, S, Maamar, E, Saidani, M, Slim, A, Martínez-Martínez, L, Boubaker IB. **Role of association of OmpK35 and OmpK36 alteration and bla(ESBL) and/or bla(AmpC) genes in conferring carbapenem resistance among non-carbapenemase-producing *Klebsiella pneumoniae*.** *Int. J. Antimicrob. Agents.* 2018;52:898-905.F.I.:4.253. [doi:10.1016/j.ijantimicag.2018.03.020]

13. Fernández-Calvet, A, Rodríguez-Arce, I, Almagro, G, Molerés, J, Euba, B, Caballero, L, Martí, S, Ramos-Vivas, J, Bartholomew, TL, Morales, X, Ortiz-de-Solórzano, C, Yuste, JE, Bengoechea, JA, Conde-Álvarez, R, Garmendia, J. **Modulation of *Haemophilus influenzae* interaction with hydrophobic molecules by the VacJ/MlaA lipoprotein impacts strongly on its interplay with the airways.** *Sci Rep.* 2018;8:6872-6872.F.I.:4.122. [doi:10.1038/s41598-018-25232-y]

14. Juncal-Ruiz, M, Riesco-Dávila, L, Ortiz García de la Foz, Víctor, Martínez-García, O, Ramírez-Bonilla, M, Oejo-Vinals, JG, Leza, JC, López-Hoyos, M, Crespo-Facorro, B. **Comparison of the anti-inflammatory effect of aripiprazole and risperidone in 75 drug-naïve first episode psychosis individuals: A3 months randomized study.** *Schizophr. Res.* 2018;202:226-233.F.I.:3.958. [doi:10.1016/j.schres.2018.06.039]

15. Bravo, Z, Chapartegui-Gonzalez, I, Lazaro-Diez, M, Ramos-Vivas, J. **Acinetobacter pittii biofilm formation on inanimate surfaces after long-term desiccation.** *J. Hosp. Infect.* 2018;98:74-82.F.I.:3.354. [doi:10.1016/j.jhin.2017.07.031]

16. Berenguer, J, Jarrin, I, Perez-Latorre, L, Hontañón V, Vivancos, MJ, Navarro, J, Tellez, MJ, Guardiola, JM, Iribarren, JA, Rivero-Juarez, A, Marquez, M, Artero, A, Morano, L, Santos, I, Moreno, J, Fariñas MC, Galindo, MJ, Hernandez, MA, Montero, M, Cifuentes, C, Domingo, P, Sanz, J,

Domínguez, L, Ferrero, OL, De la Fuente, B, Rodríguez, C, Reus, S, Hernández-Quero, J, Gaspar, G, ..., GeSIDA 8514 Study Group. **Human Immunodeficiency Virus/Hepatitis C Virus Coinfection in Spain: Elimination Is Feasible, but the Burden of Residual Cirrhosis Will Be Significant.** *Open Forum Infect. Dis.* 2018;5:F.I.:3.240. [doi:10.1093/ofid/ofx258]

17. Arnaiz de Las Revillas F, Fernández-Sampedro M, Arnaiz-García, AM, Gutiérrez-Cuadra, M, Armiñanzas C, Pulitani, I, Ponton, A, Tascon, V, García, I, Fariñas MC. **Daptomycin treatment in Gram-positive vascular graft infections.** *Int. J. Infect. Dis.* 2018;68:69-73.F.I.:3.202. [doi:10.1016/j.ijid.2018.01.009]

18. Scheuerman, O, Schechner, V, Carmeli, Y, Gutiérrez-Gutiérrez, B, Calbo, E, Almirante, B, Viale, PL, Oliver, A, Ruiz-Garbajosa, P, Gasch, O, Gozalo, M, Pitout, J, Akova, M, Peña C, Molina, J, Hernández-Torres, A, Venditti, M, Prim, N, Origen, J, Bou, G, Tacconelli, E, Tumbarello, M, Hamprecht, A, Karaiskos, I, de la Calle, C, Pérez, F, Schwaber, MJ, Bermejo, J, Lowman, W, ..., REIPI/ESGBIS/INCREMENT investigators. **Comparison of Predictors and Mortality Between Bloodstream Infections Caused by ESBL-Producing Escherichia coli and ESBL-Producing Klebsiella pneumoniae.** *Infect. Control Hosp. Epidemiol.* 2018;39:660-667.F.I.:3.084. [doi:10.1017/ice.2018.63]

19. Zboromyrska, Y, Bosch, J, Aramburu, J, Cuadros, J, García-Riestra, C, Guzman-Puche, J, Liébana Martos C, Loza, E, Muñoz-Algarra M, Ruiz de Alegría C, Sánchez-Hellin, V, Vila, J. A. **Multicentre study investigating parameters which influence direct bacterial identification from urine.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0207822]

20. Chapartegui-González, I, Lázaro-Díez, M, Bravo, Z, Navas, J, Icardo, JM, Ramos-Vivas, J. **Acinetobacter baumannii maintains its virulence after long-time starvation.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0201961]

21. Pasquau, J, Hidalgo-Tenorio, C, Montes, ML, Romero-Palacios, A, Vergas, J, Sanjoaquin, I, Hernández-Quero, J, Aguirrebengoa, K, Orihuela, F, Imaz, A, Rios-Villegas, MJ, Flores, J, Fariñas MC, Vazquez, P, Galindo, MJ, Garcia-Merce, I, Lozano, F, de los Santos, I, de Jesus, SE, Garcia-Vallecillos, C, QoLKAMON STUDY GROUP. **High quality of life, treatment tolerability, safety and efficacy in HIV patients switching from triple therapy to lopinavir/ritonavir monotherapy: A randomized clinical trial.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0195068]

22. Amado Diago, Carlos Antonio, Puente Maestu L, Abascal Bolado, Beatriz, Agüero Calvo J, Hernando, MH, Puente Bats I, AGÜERO Balbín, Ramón. **Translation and Validation of the Multidimensional Dyspnea-12 Questionnaire.** *Arch. Bronconeumol.* 2018;54:74-78.F.I.:2.633. [doi:10.1016/j.arbres.2017.08.001]

23. Aguirre-Quinonero, A, Pérez Del Molino IC, de la Fuente, CG, Sanjuan, MC, Aguero, J, Martínez-Martínez, L. **Phenotypic detection of clinical isolates of Haemophilus influenzae with altered penicillin-binding protein 3.** *Eur. J. Clin. Microbiol. Infect. Dis.* 2018;37:1475-1480.F.I.:2.537. [doi:10.1007/s10096-018-3273-z]

24. Hamzaoui Z, Ocampo-Sosa A, Maamar E, Fernández-Martínez M, Ferjani S, Hammami S, Harbaoui S, Genel N, Arlet G, Saidani M, Slim A, Boutiba-Ben Boubaker I, Martínez-Martínez L. **An Outbreak of NDM-1-Producing Klebsiella pneumoniae, Associated with OmpK35 and OmpK36 Porin Loss in Tunisia.** *Microb. Drug Resist.* 2018;24:1137-1147.F.I.:2.344. [doi:10.1089/mdr.2017.0165]

25. Fernández-Martínez M, Ruiz Del Castillo B, Lecea-Cuello MJ, Rodríguez-Baño J, Pascual Á, Martínez-Martínez L, Spanish Network for the Research in Infectious Diseases (REIPI) and the Spanish. **Prevalence of Aminoglycoside-Modifying Enzymes in Escherichia coli and Klebsiella pneumoniae Producing Extended Spectrum β -Lactamases Collected in Two**

Multicenter Studies in Spain. *Microb. Drug Resist.* 2018;24:367-376.F.I.:2.344. [doi:10.1089/mdr.2017.0102]

26. Cerezales, M, Ocampo-Sosa, AA, Álvarez Montes L, Díaz Ríos C, Bustamante, Z, Santos, J, Martínez-Martínez, L, Higgins, PG, Gallego, L. **High Prevalence of Extensively Drug-resistant Acinetobacter baumannii at a Children Hospital in Bolivia.** *Pediatr. Infect. Dis. J.* 2018;37:1118-1123.F.I.:2.305. [doi:10.1097/INF.0000000000001962]

27. Parra, JA, Hernández, L, Muñoz P, Blanco, G, Rodríguez-Álvarez, R, Vilar, DR, de Alarcón, A, Goenaga, MA, Moreno, M, Fariñas MC, Spanish Collaboration Endocarditis. **Detection of spleen, kidney and liver infarcts by abdominal computed tomography does not affect the outcome in patients with left-side infective endocarditis.** *Medicine (Baltimore).* 2018;97:F.I.:2.028. [doi:10.1097/MD.0000000000001952]

28. Aguado, R, Paez-Vega, A, Aguera, ML, Montejo, M, Guirado, L, Fortun, J, Suarez-Benjumea, A, Len, O, Fariñas MC, de Gracia, C, Hernández, D, Cobos-Ceballos, MJ, Torre-Cisneros, J, Cantisan, S, Spanish Network Res Infect Dis, Spanish Renal Disease Network. **Spanish Transplantation Infection Study Group (GE). Lack of evidence of association between IFNG and IL28B polymorphisms and QuantiFERON-CMV test results in seropositive transplant patients.** *Hum. Immunol.* 2018;79:499-505.F.I.:1.994. [doi:10.1016/j.humimm.2018.03.009]

29. Ramos-Martínez A, Muñoz Serrano A, de Alarcón-González A, Muñoz P, Fernández-Cruz A, Valerio M, Fariñas MC, Gutiérrez-Cuadra M, Miró JM, Ruiz-Morales J, Sousa-Regueiro D, Montejo JM, Gálvez-Acebal J, Hidalgo-Tenorio C, Domínguez F, Spanish Collaboration on Endocarditis – Grupo de Apoyo al Manejo de la Endocardia. **Gentamicin may have no effect on mortality of staphylococcal prosthetic valve endocarditis.** *J. Infect. Chemother.* 2018;24:555-562.F.I.:1.777. [doi:10.1016/j.jiac.2018.03.003]

30. Chaves F, Garnacho-Montero J, Del Pozo JL, Bouza E, Capdevila JA, de Cueto M, Domínguez MÁ, Esteban J, Fernández-Hidalgo N, Fernández Sampedro M, Fortún J, Guembe M, Lorente L, Paño JR, Ramírez P, Salavert M, Sánchez M, Vallés J. **Diagnosis and treatment of catheter-related bloodstream infection: Clinical guidelines of the Spanish Society of Infectious Diseases and Clinical Microbiology and (SEIMC) and the Spanish Society of Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC).** *Med. Intensiv.* 2018;42:5-36.F.I.:1.755. [doi:10.1016/j.medin.2017.09.012]

31. Rodríguez, A, Reyes, LF, Monclou, J, Suberviola, B, Bodi, M, Sirgo, G, Sole-Violan, J, Guardiola, J, Barahona, D, Díaz, E, Martín-Loeches, I, Restrepo, MI, on behalf GETGAG study group. **Relationship between acute kidney injury and serum procalcitonin (PCT) concentration in critically ill patients with influenza infection.** *Med. Intensiv.* 2018;42:399-408.F.I.:1.755. [doi:10.1016/j.medin.2017.12.004]

32. Rodríguez-Lozano, J, de Malet, A, Cano, ME, de la Rubia, L, Wallmann, R, Martínez-Martínez, L, Calvo, J. **Antimicrobial susceptibility of microorganisms that cause urinary tract infections in pediatric patients.** *Enferm. Infec. Microbiol. Clin.* 2018;36:417-422.F.I.:1.707. [doi:10.1016/j.eimc.2017.08.003]

33. Chaves, F, Garnacho-Montero, J, del Pozo, JL, Bouza E, Capdevila, JA, de Cueto, M, Domínguez, MA, Esteban, J, Fernández-Hidalgo, N, Fernández Sampedro M, Fortun, J, Guembe, M, Lorente, L, Paño JR, Ramirez, P, Salavert, M, Sánchez, M, Valles, J. **Executive summary: Diagnosis and Treatment of Catheter-Related Bloodstream Infection: Clinical Guidelines of the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC) and the Spanish Society of Intensive Care Medicine and Coronary Units (SEMICYUC).** *Enferm. Infec. Microbiol. Clin.* 2018;36:112-119.F.I.:1.707. [doi:10.1016/j.eimc.2017.10.019]

34. Toresano-Lopez, D, Arnaiz-García, AM, Arnaiz-García, ME. **Gastric wall and splenic abscess in the background of an invasive salmonellosis caused by Salmonella enteritidis.** *Med. Clin.* 2018;150:31-32.F.I.:1.168. [doi:10.1016/j.medcli.2017.10.003]

35. Ruiz de Alegría Puig C, Agüero-Balbin, J, Fernández-Mazarrasa, C, Martínez-Martínez, L. **Evaluation of the Vitek-MS (TM) system in the identification of Candida isolates from bloodstream infections.** *Rev. Iberoam. Micol.* 2018;35:130-133.F.I.:0.989. [doi:10.1016/j.riam.2018.02.001]

36. Fernández Torres M, Angulo López I, Ruiz Bueno P, González Martínez M, Ruiz de Alegría Puig C, Rodríguez Lozano J, Agüero Balbín J, Crespo García J, Calvo Montes J. **Spontaneous bacterial peritonitis caused by Listeria monocytogenes: eight case reports (1992-2017) and literature review.** *Rev. Esp. Quim.* 2018;31:532-536.F.I.:0.605.

Reviews

1. Duque, JCR, Rubín, PG, Humara, BG, Sanz, AAQ, Vallina, MBB, Fernández-Sampedro, M. **Fusobacterium nucleatum prosthetic hip infection: Case report and review of the literature of unusual anaerobic prosthetic joint infection.** *ANAEROBE.* 2018;54:75-82.F.I.:2.742. [doi:10.1016/j.anaerobe.2018.08.003]

2. Aguado, JM, Silva, JT, Fernández-Ruiz, M, Cordero, E, Fortun, J, Gudiol, C, Martínez-Martínez, L, Vidal, E, Almenar, L, Almirante, B, Canton, R, Carratala, J, Caston, JJ, Cercenado, E, Cervera, C, Cisneros, JM, Crespo-Leiro, MG, Cuervas-Mons, V, Elizalde-Fernández, J, Fariñas MC, Gavalda, J, Goyanes, MJ, Gutiérrez-Gutiérrez, B, Hernández, D, Len, O, Lopez-Andujar, R, Lopez-Medrano, F, Martín-Davila, P, Montejo, M, ..., Spanish Network for Research in Infectious Diseases (REIPI) (RD16/0016). **Management of multidrug resistant Gram-negative bacilli infections in solid organ transplant recipients: SET/GESITRA-SEIMC/REIPI**

recommendations. *Transplant. Rev.* 2018;32:36-57.F.I.:2.364. [doi:10.1016/j.trre.2017.07.001]

3. Candel, FJ, Borges Sá M, Belda, S, Bou, G, Del Pozo, JL, Estrada, O, Ferrer, R, González Del Castillo J, Julián-Jiménez, A, Martín-Loeches, I, Maseda, E, Matesanz, M, Ramirez, P, Ramos, JT, Rello, J, Suberviola, B, Suárez de la Rica A, Vidal, P. **Current aspects in sepsis approach. Turning things around.** *Rev. Esp. Quim.* 2018;31:298-315.F.I.:0.605.

Projects

1. Jorge Calvo Montes. **Ayuda por Producción al Grupo de Microbiología Clínica y Molecular. APG/14.** FUNDACION INSTITUTO DE INVESTIGACION MARQUES DE VALDECILLA IDIVAL.

2. María del Carmen Fariñas Álvarez. **Ayuda por Producción al Grupo de Epidemiología y Mecanismos Patogénicos en Enfermedades Infecciosas.** APG/22.

3. Jorge Calvo Montes. **Tigecycline European Surveillance Trial (TEST). CSI13/01.** INTERNATIONAL HEALTH MANAGEMENT ASSOCIATES, INC..

4. María del Carmen Fariñas Álvarez. **Colonización intestinal por enterobacterias multiresistentes en pacientes con trasplante renal y hepático: estudio multicéntrico de cohortes y ensayo clínico aleatorizado y abierto.** PI13/01191. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

5. María del Carmen Fariñas Álvarez. **Convenio para la gestión del ensayo con código PFI-PRE-2013-01. Estudio epidemiológico, prospectivo, multicéntrico para la caracterización de la neumonía asociada a cuidados sanitarios e implicación de la colonización por Streptococcus Pneumoniae o Staphylococcus Aureus resistente a Meticilina.** Estudio Sócrates. CC114/04.

6. María del Carmen Fariñas Álvarez. **Contrato de servicios de investigación para el Estudio de la**

eficacia de daptomicina (Cubicin) versus otros antibióticos activos frente a infecciones de prótesis vasculares por microorganismos grampositivos. CSI14/04.

7. María del Carmen Fariñas Álvarez. **Convenio de colaboración para el desarrollo del proyecto de investigación Influenza virus infections in transplant recipients: a multicenter registry.** C114/60. FUNDACIÓN PÚBLICA ANDALUZA PARA LA GESTIÓN DE LA INVESTIGACIÓN EN SALUD DE SEVILLA FISEVI.

8. Jorge Calvo Montes. **Contrato de servicios de investigación para el Estudio SMART.** CSI15/06.

9. Jorge Calvo Montes. **Contrato de servicios de investigación para el proyecto AstraZeneca Global Surveillance Study.** CSI15/11.

10. María del Carmen Fariñas Álvarez. **Convenio de colaboración para el desarrollo del programa de Estrategias de Optimización en Terapéutica Antibiótica.** C114/59/01. MERCK SHARP & DHOME ESPAÑA.

11. Alain Antonio Ocampo Sosa. **Identificación y caracterización funcional de nuevos componentes de sistemas de secreción tipo VI y las bases moleculares de su regulación en cepas clínicas de Pseudomonas aeruginosa.** PI15/00009. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

12. Jorge Calvo Montes. **Contrato de servicios de investigación para el proyecto Ceftaroline MIC Methods Study.** CSI15/09.

13. Borja Suberviola Cañas. **Convenio para la gestión del ensayo con código IC43-202. Estudio en fase II/III confirmatorio para evaluar la eficacia, inmunogenicidad y seguridad de la vacuna recombinante IC43 contra pseudomonas en pacientes con cuidados intensivos.** CC115/21.

14. María del Carmen Fariñas Álvarez. **Convenio de colaboración para el desarrollo del programa de Estrategias de Optimización en Terapéutica Antibiótica.** C115/50/01. MERCK SHARP &

DHOME ESPAÑA, MERCK SHARP & DHOME ESPAÑA.

15. Mónica Gozalo Margüello. **Contrato de servicios de investigación para el Ensayo del rendimiento del Panel Respiratorio FilmArray para el Diagnóstico Rápido de Síndrome Respiratorio de Vía Alta en pacientes graves de estación de Gripe.** CSI16/03. BIOMERIEUX ESPAÑA, S.A..

16. José Ramos Vivas. **Biología integrada de la infección y la resistencia antimicrobiana de Acinetobacter baumannii y A. pittii.** PI16/01103. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

17. María del Carmen Fariñas Álvarez. **Impacto de la colonización intestinal por enterobacterias multirresistentes en las infecciones sistémicas, enfermedad de injerto contra huésped (EICH) y mortalidad de pacientes receptores de trasplante alogénico de progenitores hematopoyéticos (Alo-TPH).** PI16/01415. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

18. María Victoria Francia Gil. **Inducción de la transferencia conjugativa de los plásmidos de respuesta a feromonas.** PI16/01535. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

19. María del Carmen Fariñas Álvarez. **Red Temática de Enfermedades Infecciosas.** RD16/0016/0007. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

20. Jorge Calvo Montes. **Contrato de servicios de investigación para el proyecto In vitro study ceftolozane/tazobactam susceptibility in Pseudomonas aeruginosa and Enterobacteriaceae isolates recovered from ICU patines with cUITs and CIAls in Spain.** Estudio SUPERIOR. CSI16/17.

21. María del Carmen Fariñas Álvarez. **Convenio de Colaboración para el desarrollo del programa de Estrategias de Optimización en Terapéutica Antibiótica.**

CSI16/26/01. MERCK SHARP & DHOME ESPAÑA.

22. Jorge Calvo Montes. **Contrato de Patrocinio Ciclo de sesiones clínicas en el Servicio de Microbiología e infecciosas del HUMV.** CSI17/18. MERCK SHARP & DHOME ESPAÑA.

23. Jorge Calvo Montes. **Convenio de colaboración para el desarrollo del proyecto de investigación Validación de la citometría de flujo UF-series asociado a EM MALDI-TOF como sistema de identificación rápida de microorganismos en infecciones del tracto urinario Estudio RIPU.** C117/27. SYSMEX ESPAÑA, S.L..

24. María del Carmen Fariñas Álvarez. **Contrato de servicios de investigación para el proyecto Estrategias de optimización en terapéutica antibiótica PROA.** CSI17/26. MERCK SHARP & DHOME ESPAÑA.

25. Daniel Pablo Marcos. **MTVAL17/05 PABLO MARCOS DANIEL.** MTVAL17/05.

26. Jorge Calvo Montes. **Convenio de colaboración para la inscripción al Congreso ECCMID.** C118/03. ALERE HEALTHCARE, S.L.U..

27. Jorge Calvo Montes. **Convenio de colaboración para la asistencia de dos profesionales de la salud al XXII Congreso de la SEIMC.** C118/11. ABBOTT LABORATORIES, S.A..

28. Jorge Calvo Montes. **Convenio de colaboración para la asistencia de dos profesionales de la salud al 28º Congreso de la ECCMID.** C118/12. ABBOTT LABORATORIES, S.A..

29. Jorge Calvo Montes. **Convenio de colaboración para la asistencia al XXII Congreso Nacional SEIMC y a 28th ECCMID.** C118/02. BECTON DICKINSON, S. A. U..

30. Jorge Calvo Montes. **Convenio de colaboración para la asistencia al 28th Congreso ECCMID.** C118/22. BIOMERIEUX ESPAÑA, S.A..

31. Jorge Calvo Montes. **Donación para el desarrollo de proyectos de investigación en el Servicio de Microbiología del Hospital Universitario Marqués de**

SOBRE 94

SOBRE 91

V121480FTA1

V121484FTA1

V121488FTA1

V121492FTA1

V121

V121200FTA1

V121200FTA1

Valdecilla. CI18/24. VIRCELL SPAIN S.L.U..

32. Alain Antonio Ocampo Sosa. **El sistema de secreción tipo VI y la exolisina ExIA como marcadores de virulencia de Pseudomonas aeruginosa en la neumonía asociada a ventilación mecánica.** PI18/00380. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

33. José Ramos Vivas. **Donación para el desarrollo de proyectos de investigación del Grupo de Investigación de IDIVAL Epidemiología y Mecanismos Patogénicos y Moleculares de Enfermedades Infecciosas y Microbiología Clínica.** CI18/55. NUÑEZ GIL, ELISA ISABEL, NUÑEZ GIL, ELISA ISABEL.

34. Mónica Gozalo Margüello. **El complejo Burkholderia cepacia en la fibrosis quística: contribución de los mecanismos de resistencia antibiótica y factores de virulencia.** NVAL18/08.

35. José Ramos Vivas. **Búsqueda y caracterización de fagos líticos frente a patógenos nosocomiales de relevancia clínica.** INVAL18/22.

36. Borja Suberviola Cañas. **Transcripción génica de neutrófilos humanos como herramienta para el diagnóstico en pacientes con sepsis.** INVAL18/27.

37. María del Carmen Fariñas Álvarez. **Convenio de colaboración para el desarrollo del Programa de Optimización de uso de Antimicrobianos.** CS119/04. MERCK SHARP & DHOME ESPAÑA, MERCK SHARP & DHOME ESPAÑA.

38. Jorge Calvo Montes. **Contrato de Servicios de investigación para el desarrollo del estudio ATLAS: Antimicrobial Testing Leadership and Surveillance.** CS119/02. INTERNATIONAL HEALTH MANAGEMENT ASSOCIATES, INC..

Clinical Trials

1. María del Carmen Fariñas Álvarez. **Ensayo prospectivo, aleatorizado, comparativo de la eficacia y seguridad del levofloxacino versus isoniazida en el tratamiento de**

la infección latente tuberculosa del trasplante hepático. FLISH-ILT. FUNDACIÓN PÚBLICA ANDALUZA PARA LA GESTIÓN DE LA INVESTIGACIÓN EN SALUD DE SEVILLA FISEVI.

2. María del Carmen Fariñas Álvarez. **Ensayo clínico prospectivo aleatorizado comparativo de la eficacia y seguridad de una dosis de vacuna estacional respecto a dos dosis de vacunas como prevención de la gripe en receptores de trasplante de órgano sólido.** TRANSGRIPE 1-2. FUNDACIÓN PÚBLICA ANDALUZA PROGRESO Y SALUD.

3. María del Carmen Fariñas Álvarez. **Ensayo clínico de fase III multicéntrico, aleatorizado, abierto de Telavancina en comparación con la terapia intravenosa convencional en el tratamiento de pacientes con bacteriemia por Staphylococcus aureus, incluyendo la endocarditis infecciosa.** 0112. THERAVANCE BIOPHARMA ANTIBIOTICS, INC.

4. María del Carmen Fariñas Álvarez. **Ensayo clínico aleatorizado, multicéntrico, abierto, controlado, en fase III, para demostrar la no inferioridad del tratamiento antibiótico dirigido de espectro reducido frente al tratamiento de amplio espectro con un betalactámico antipseudomónico en el tratamiento de pacientes con bacteriemia por Enterobacteriaceae.** SIMPLIFY. FUNDACIÓN PÚBLICA ANDALUZA PARA LA GESTIÓN DE LA INVESTIGACIÓN EN SALUD DE SEVILLA FISEVI.

5. Borja Suberviola Cañas. **Ensayo clínico de fase II de demostración de viabilidad para evaluar la eficacia y la seguridad de MEDI3902 en la prevención de la neumonía nosocomial causada por Pseudomonas aeruginosa en pacientes sujetos a ventilación mecánica.** D5470C00004. MEDIMMUNE, INC.

6. María del Carmen Fariñas Álvarez. **Estudio Fase III, aleatorizado, multicéntrico, abierto, de grupos paralelos, para evaluar la eficacia, seguridad y tolerabilidad de una pauta de tratamiento intramuscular de acción prolongada con cabotegravir y rilpivirina en el**

mantenimiento de la supresión virológica, tras una inducción con un tratamiento de comprimido único con un inhibidor de la integrasa en pacientes adultos infectados por el VIH-1 que no han recibido un tratamiento antirretroviral previo. 201584. LABORATORIOS VIIV HEALTHCARE, S.L..

7. María del Carmen Fariñas Álvarez. **Estudio de fase Ib, aleatorizado, doble ciego, controlado con placebo, de dosis múltiples ascendentes, para investigar la seguridad, la tolerabilidad y la farmacocinética de DSTA4637S en pacientes con bacteriemia por Staphylococcus aureus que reciben tratamiento antibiótico convencional.** GV39131. GENENTECH, INC.

Postmarketing Studies and Other

1. María del Carmen Fariñas Álvarez. **Estudio epidemiológico no intervencionista para conocer el perfil del paciente naive que inicia el tratamiento antirretroviral en España.** JAN-VIH-2009-04/TMC114HIV4051. JANSSEN-CILAG, S.A..

2. María del Carmen Fariñas Álvarez. **Caracterización de las infecciones urinarias bacteriémicas relacionadas con la asistencia sanitaria y comparación con infecciones urinarias bacteriémicas nosocomiales en la era de la resistencia múltiple a fármacos.** MSD-CEF-2017-01. MERCK SHARP & DHOME ESPAÑA.

Authorship Thesis 2018

1. María Lázaro Diez. **Interacciones clave Hospedador-Patógeno en especies de Acinetobacter de relevancia clínica.** Director/s: José Ramos Vivas, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.

Other Publications

1. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecoechea, E, Faripasevare, C, Fontalba, A, Zarauza, J, Ojeda, L, Parra, JA. **Nailfold capillaroscopy in hereditary hemorrhagic telangiectasia.** ANGIOGENESIS. 2018;21:144-144.

Nanovaccines and cellular vaccines based on *Listeria monocytogenes* and their applications in biomedicine



Emerging group

Group Responsible

Carmen Álvarez Domínguez

Fundación Instituto de Investigación Marqués de Valdecilla IDIVAL



carmen.alvarezd@scsalud.es

Contributors

Ricardo Calderón González
Susana Gómez Salces
Hector Terán Navarro
Sonsoles Yáñez Díaz

Technicians

Milagros González Toca

Research lines

1.- Cerebral listeriosis and neonatal listeriosis models:

(PI: Dr. C. Alvarez Domínguez/ Grants: SAF2006- 08968, SAF2009-08695, SAF2012-34203). To establish cerebral and neonatal listeriosis models to analyze specific virulence factors of the pathogen targeted

to microglia and design a cerebral listeriosis vaccine. This study implies the characterization of microglia phagosomes using differential proteomics (col. C. Gil. UCM) and examine new adjuvants for neonatal vaccines (col. M. Fresno, CBMSO).

2.- *Listeria* based dendritic vaccines loaded with peptides against infectious agents.

(PI: Dr. C. Alvarez Dominguez and Co-PI: Dra. S. Yáñez Díaz/Grants: SAF2009-08695 y SAF2012-34203

and Approved Clinical Study: CEIC-Acta 19/2014- 2014.228). A *Listeria* based dendritic vaccine loaded with peptides from virulence factors specific of *Listeria* (LLO) and common to *Mycobacterium smegmatis* (GAPDH) will be used to examine experimental prophylactic measures against both bacteria. Moreover, we are performing a clinical study with listeriosis patients from a 2014 outbreak with Dr. C. Fariñas (Infectious Section-HUMV) and Dr. Martinez (Microbiology Dpt-HUMV) and Biodonostia Group of Microbiologists (col. Dr. E. Trallero,

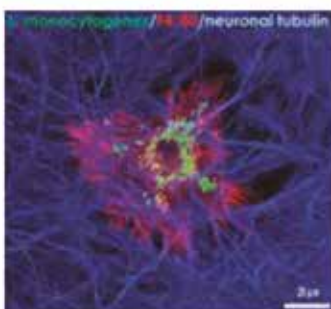


Figure 1. Dendritic vaccine with a new *Listeria monocytogenes* antigen: GAPDH.



Figure 2. Dendritic vaccine with a new *Listeria monocytogenes* antigen.

Dr. J. Marimon and Dr. CG. Cilla) to elaborate a human vaccine for patients at high risk of listeriosis.

3.- Listeria based dendritic vaccines loaded with peptides against melanoma

(IP: Dr. C. Alvarez Dominguez y Dra. S. Yañez Diaz/Proyectos: SAF2009-08695 y SAF2012-34203 y Estudio Clínicos aprobado: CEIC-Acta 30/2012). Se utiliza una vacuna DC basada en *Listeria* cargada con el péptido LLO91-99 como terapia anti-adhesiva para el melanoma en modelos murinos (col. Dr. J. Gomez-Roman, S. Anatomía Patológica) y preparar en pacientes con melanomas una vacuna DC anti-melanoma en colaboración con los Servicios de Oncología y Dermatología del HUMV (melanoma metastático) (cols. Dr. H. Fernandez-Llaca y Dra. A. Garcia) y el Grupo de Melanoma Humano de UPV (col. Dra. D. Boyano Lopez).

4.- Listeria based Nanovaccines and their applications.

(PI: Dr. C. Alvarez Dominguez, Dr. S. Gomez Salces and Dr. S. Yañez Diaz/Grants: SAF2012-34203, and Approved Clinical Study: CEIC-Acta 1/2016-2015.177). In this study we used as vaccine vectors gold glyconanoparticles (AuGNP) of 2 nm size conjugated to *Listeria* peptides, LLO91-99 and

GAPDH1-22. The group of CIC-biomaGUNE collaborates with our group preparing AuGNP (cols. Dr. M. Marradi, Dr. I. Garcia and Dr. S. Penades). We have performed studies with a prophylactic experimental nanovaccine against listeriosis and a non-pathogenic tuberculosis model. The efficiency of nanovaccine is based in their targeting to dendritic cells, lack of toxicity, biocompatibility and induction of a cytotoxic cellular immune response. Other applications with these Nanovaccines and their modifications are tumor therapies.

3. Carmen Álvarez Domínguez. **Proyecto de la Asociación Estelas Rosas con referencia: BDP77 de la Título: Nanovacunas basadas en *Listeria* como inmunoterapia frente a tumores sólidos.** (Proyecto externo conseguido en el 2018).

4. Carmen Álvarez Domínguez. **Proyecto INNVAL17/01 de la Título: Validación de una nueva inmunoterapia para tumores sólidos con nanopartículas de oro basadas en *Listeria monocytogenes* como terapia combinatoria.** (Proyecto IDIVAL vigente en el 2018).

Projects

1. Carmen Álvarez Domínguez. **Validación de las nanovacunas basadas en *Listeria* como inmunoterapia de combinación en tumores sólidos.** DTS18/00022. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
2. Carmen Álvarez Domínguez. **Nanovacunas basadas en *Listeria* y su aplicación como terapia tumoral.** CI-08-09. Asociación Luchamos por la vida con referencia.

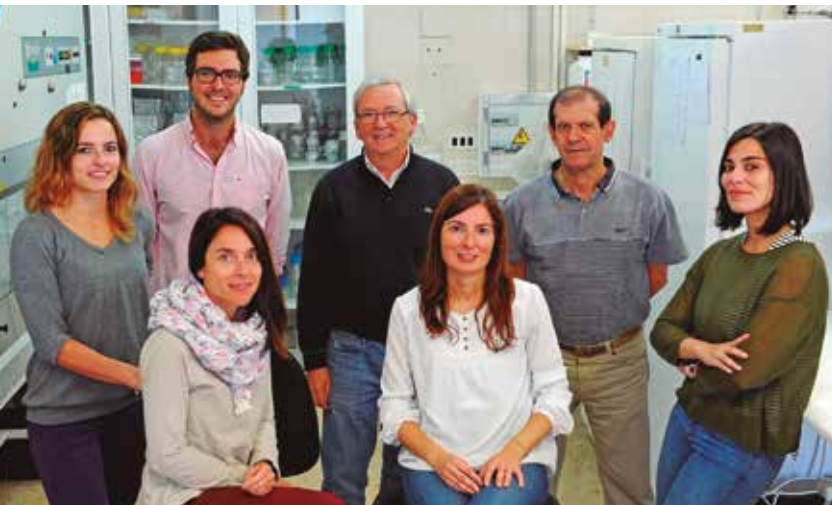
Authorship Thesis 2017

1. Ricardo Calderón González. **Vacunas basadas en *Listeria Monocytogenes*.** Director/s: Carmen Álvarez Domínguez, Mónica López Fanárraga. UNIVERSIDAD DE CANTABRIA.

Thesis Addressed 2017

1. Elisabet Frande Cabanes. **Listeriosis cerebral en el modelo murino: Patogénesis y Prevención.** Director/s: Carmen Álvarez Domínguez, Mónica López Fanárraga. UNIVERSIDAD DE CANTABRIA.

Immunopathology of Rheumatic Diseases



Consolidated group

Group Responsible

**Jesús
Merino Pérez**

Department of Molecular
Biology

School of Medicine
Universidad de Cantabria



merinoj@unican.es

Contributors

Elena Aurrecoechea Aguinaga
Manuel Ignacio González Carreró
Marcos Iglesias Lozano
Marta Muñoz Ruiz
Jorge Postigo Fernández
Teresa Ruiz Jimeno
Esther Tamayo Revuelta
Juan Ignacio Villa Blanco

Technicians

María Aramburu Landeras
Yordana Vega Miranda

Research lines

The research activity of our group focuses on the study of the cellular and molecular mechanisms involved in rheumatic inflammatory diseases. Our final aims are the

identification and characterization of potential therapeutic targets for the treatment of these diseases. We undertake these tasks from a basic approach, coordinated by Dr. Jesus Merino at the University of Cantabria, and a clinical approach coordinated by Dr. Jaime Calvo at the Hospital Sierrallana of Torrelavega. Jesus Merino, in close collaboration with Dr. Ramon Merino (IBBTEC), is studying several molecules involved in the

control of inflammatory responses, such as BAMBI (BMP and activin membrane bound inhibitor) and BCL2A1 (a cell death regulator). We maintain also collaborations with other Spanish groups to evaluate the role in inflammation of the immunomodulatory molecules, CD38 (Dr. Jaime Sancho, Granada), CD5 and CD6 (Dr Francisco Lozano, Barcelona), the transcriptional factors E2F1 and E2F2 (Dr. Ana Zubiaga, UPV) and GPBP

(Goodpasture antigen binding protein), a protein-kinase that forms quaternary protein structures (Dr Juan Saus, Fibrostatin SL, Valencia).

Overall, this research activity pretends to validate these molecules as therapeutic targets in inflammation and autoimmune diseases. For this purpose we use murine models of these diseases, such as the collagen-II-induced arthritis, adriamycin or bleomycin-induced pulmonary fibrosis, the colitis induced by sodium dextran sulphate, or the psoriasis caused by local application of Imiquimod or i.p. injection of *Saccharomyces cerevisiae* mannan.

- Impact of gender on prognosis of rheumatoid arthritis, with particular emphasis on quality of life.
- Influence of treatment with TNF inhibitors in the oxidative phenotype of HDL cholesterol and its influence on their anti-atherogenic capacity in patients with rheumatoid arthritis.
- Lipoprotein profiles and HDL phenotypes in patients with systemic lupus erythematosus (SLE) in correlation with inter-ethnic differences, in collaboration with the University of Puebla (Mexico).
- Prospective evaluation of individuals with high titers of antinuclear antibodies (>1280) without clinical symptoms of autoimmune diseases.
- Evaluation of new criteria for clinical classification of SLE patients (SLICC criteria), in collaboration with Dr. Luis Ines (University of Coimbra, Portugal).
- Co-chairman in the RELESSER-PROS registration for the follow-up of SLE patients.
- Phase 3 Clinical trials: two trials in rheumatoid arthritis and one in psoriatic arthritis.

PUBLICATIONS

IMPACT FACTOR | 21.159

Original articles

1. Martín-Varillas, JL, Calvo-Río, V, Beltran, E, Sánchez-Burson, J, Mesquida, M, Adan, A, Hernandez, MV, Garfella, MH, Pascual, EV, Martínez-Costa, L, Sellas-Fernández, A, Cordero-Coma, M, Díaz-Llopis, M, Gallego, R, Salom, D, Ortego, N, García-Serrano, JL, Callejas-Rubio, JL, Herreras, JM, García-Aparicio, A, Maiz, O, Blanco, A, Torre, I, Díaz-Valle, D, Pato, E, Aurrecochea, E, Caracuel, MA, Gamero, F, Minguez, E, ..., Blanco, R. **Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behcet's Disease.** *Ophthalmology.* 2018;125:1444-1451.FI.:7.479. [doi:10.1016/j.ophtha.2018.02.020]
2. Rueda, N, Vidal, V, García-Cerro, S, Narcis, JO, Llorens-Martin, M, Corrales, A, Lantigua, S, Iglesias, M, Merino, J, Merino, R, Martínez-Cue, C. Anti-IL17 treatment ameliorates **Down syndrome phenotypes in mice.** *Brain Behav. Immun.* 2018;73:235-251.FI.:6.306. [doi:10.1016/j.bbi.2018.05.008]
3. Álvarez-Rodríguez, L, Riancho-Zarrabeitia, L, Calvo-Alen, J, López-Hoyos, M, Martínez-Taboada, V. **Peripheral B-Cell Subset Distribution in Primary Antiphospholipid Syndrome.** *Int. J. Mol. Sci.* 2018;19:FI.:3.687. [doi:10.3390/ijms19020589]

Reviews

1. Tamayo, E, Álvarez, P, Merino, R. **TGF Superfamily Members as Regulators of B Cell Development and Function Implications for Autoimmunity.** *Int. J. Mol. Sci.* 2018;19:FI.:3.687. [doi:10.3390/ijms19123928]

Projects

1. Elena Aurrecochea Aguinaga. **KF6005/03. Estudio Fase IIA, randomizado, de 4 semanas, en el que se evalúa la eficacia seguridad y tolerabilidad de**

GRT6005, un nuevo analgésico de acción central, en pacientes con dolor moderado a severo, debido a osteoartritis (OA) de rodilla. CCI1203.

2. Jesús Merino Pérez. **Ayuda por Producción al Grupo de Investigación de Inmunopatología de las enfermedades reumáticas.** APG/05.
3. Elena Aurrecochea Aguinaga. **Convenio de Colaboración para el desarrollo del Plan de investigación y publicaciones del Servicio de Reumatología del Hospital de Sierrallana de Torrelavega.** CI15/29. ROCHE FARMA, S.A.U..
4. Jesús Merino Pérez. **Identificación de Dianas Terapéuticas en el Cáncer Colorrectal.** CI17/03. ASOCIACION LUCHAMOS POR LA VIDA.
5. Elena Aurrecochea Aguinaga. **Convenio de colaboración para el desarrollo de proyectos de investigación en el Servicio de Reumatología del Hospital Comarcal de Sierrallana.** CI18/73. MERCK SHARP & DHOME ESPAÑA.
6. Jesús Merino Pérez. **Donación persona física por el importe de los beneficios derivados de la venta del libro titulado "El espíritu de la mariposa" destinado a contribuir en un porcentaje del cincuenta por ciento (50%) Carmen Álvarez y (50%) Jesús Merino.** CI19/12/02. MARTIN HORGA, MARIA LUISA.

Clinical Trials

1. Elena Aurrecochea Aguinaga. **Estudio fase 3, multicéntrico, aleatorizado, doble ciego, controlado con placebo y de grupos paralelos para evaluar la eficacia y la seguridad de dos dosis de Apremilast (CC-10004) en pacientes con artritis psoriásica activa.** CC-10004-PSA-003. CELGENE CORPORATION.
2. Elena Aurrecochea Aguinaga. **Estudio Fase IIIb para evaluar la eficacia, seguridad y tolerabilidad de Tocilizumab (TCZ) subcutáneo (SC) administrado en monoterapia o en combinación con metotrexato (MTX) en pacientes con artritis reumatoide.** ML28709. ROCHE FARMA, S.A.U..

3. Juan Ignacio Villa Blanco. **Estudio multicéntrico, aleatorizado, doble ciego, controlado con placebo para demostrar la eficacia de secukinumab subcutáneo hasta 1 año en el tratamiento de la entesitis del tendón de Aquiles en pacientes adultos con Artritis Psoriásica (APs) activa y Espondiloartritis axial (EspA axial) (ACHILLES).** CAIN457F3301. NOVARTIS FARMACEUTICA, S.A..

4. Juan Ignacio Villa Blanco. **SKIPPAIN (Rapidez en el alivio del dolor en pacientes con espondiloartritis axial inducido por secukinumab) Estudio multicéntrico, aleatorizado, doble ciego, controlado con placebo, de 24 semanas de duración para evaluar la eficacia y seguridad de secukinumab en el control del dolor espinal en pacientes con espondiloartritis axial.** CAIN457H3301. NOVARTIS FARMACEUTICA, S.A..

Postmarketing Studies and Other

1. Elena Aurrecochea Aguinaga. **Evaluación del riesgo cardiovascular, y de sus determinantes, en pacientes con artritis reumatoide, espondilitis anquilosante y artritis psoriásica.** CARMA. FUNDACIÓN ESPAÑOLA DE REUMATOLOGÍA F.E.R..

2. Juan Ignacio Villa Blanco. **Estudio retrospectivo sobre la eficacia en práctica clínica de golimumab tras el fracaso de un primer anti-TNF- α en pacientes con espondiloartritis (Go-Beyond Spain).** MSD-GOL-2016-01. MERCK SHARP & DHOME ESPAÑA.

3. Juan Ignacio Villa Blanco. **Estudio de cohortes observacional y prospectivo (ECOP) sobre el lupus eritematoso sistémico (LES).** D3461R00001. ASTRAZENECA AB.

Authorship Thesis

1. Marta Muñoz Ruiz. **Papel de BAMBI en la respuesta inmune de las mucosas y en el desarrollo de Patología inflamatoria intestinal y de neoplasias secundarias.**

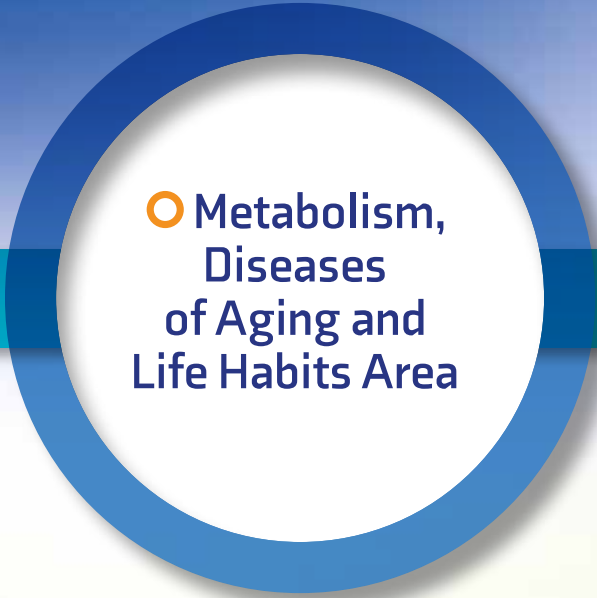
Director/s: Ramón Merino Pérez, Jesús Merino Pérez. UNIVERSIDAD DE CANTABRIA.

Other Publications


1. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecochea, E, Faripas-elvarez, C, Fontalba, A, Zaruza, J, Ojeda, L, Parra, JA. **Nailfold capillaroscopy in hereditary hemorrhagic telangiectasia.** ANGIOGENESIS. 2018;21:144-144.





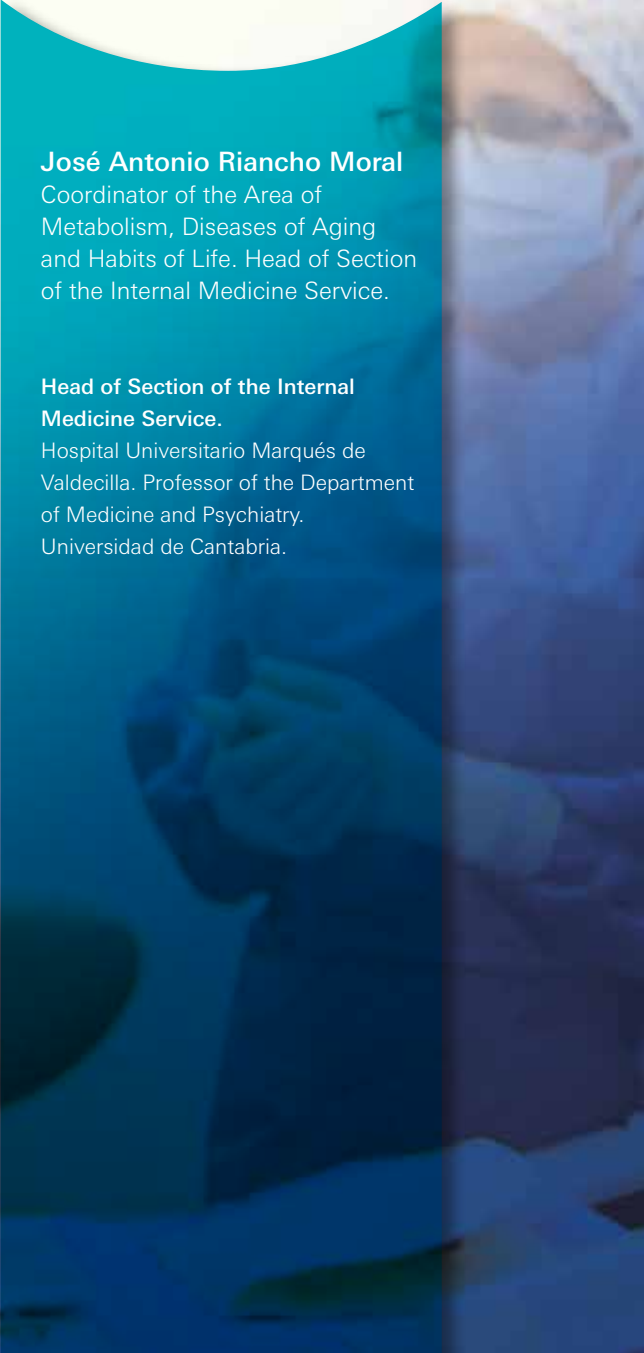


**○ Metabolism,
Diseases
of Aging and
Life Habits Area**



José Antonio Riancho Moral
Coordinator of the Area of
Metabolism, Diseases of Aging
and Habits of Life. Head of Section
of the Internal Medicine Service.

**Head of Section of the Internal
Medicine Service.**



Hospital Universitario Marqués de
Valdecilla. Professor of the Department
of Medicine and Psychiatry.
Universidad de Cantabria.

○ Diagnosis and Treatment Using Imaging (Radiology)



Associated group

Contributors

María Mercedes Acebo García
María Pilar Alonso Bartolomé
Eva Alonso Fernández
Javier Azcuna Saez
Ana Belén Barba Arce
Gerardo Blanco Rodríguez
Ana Canga Villegas
Adrián Alberto Cardin Pereda
Juan Crespo del Pozo

Alexandra de Diego Diez
María Rosa de la Puente Formoso
Marta Drake Pérez
Alejandro Fernández Flórez
Ana García Bolado
M^a del Rosario García-Barredo Pérez
Vanessa Gómez Demit
Francisco González Sánchez
Carmen González-Carrero Sixto
Eduardo Herrero Romero

Group Responsible

José Antonio Parra Blanco

Radiology Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



joseantonio.parra@scsalud.es

Juan Jordá Lope
Angélica Lamagrande Obregón
Yasmina Lamprecht
Rosa María Landeras Álvaro
Pedro Lastra García-Barón
Gerardo López Rasines
Enrique Marco de Lucas
Elena Marín Diez
Paula Merino Rasillo
Enrique Montes Figueroa
Estrella Ortega García
Luis Antonio Ortiz Rivas
María Macarena Otero Fernández
Marta Pelaz Esteban
Rául Pellón Daben
María Elena Peña Gómez
Francisco Pozo Piñón
Mariano Rico Gutiérrez
Eva Ruiz Pérez
Sonia Sánchez Gómez
Elena Sánchez Salmón
Eduardo Torres Díez
Natalia Valle San Román
Alfonso Vega Bolivar
Héctor Vidal Trueba
Elena Yllera Contreras

○ Research lines

Active research lines:

1. Evaluation of new low percutaneous breast biopsy devices Image control.
2. Study of arteriovenous malformations in patients with
3. Quantification of coronary calcium and carotid ultrasonography and as predictors of cardiovascular risk.
4. Development of hybrid techniques: surgical-radiological in the treatment of Vascular pathology.
5. Evaluation of the usefulness and
6. Ultrasonic contrasts in the study of hepatic, renal and intestinal pathology.
7. Study of cerebral connectivity with diffusion tensor MRI.
8. Anatomic-radiological correlation studies in cutaneous pathology.

Telangiectasia Hemorrhagic Hereditary (THH).

complications of thermoablation treatments In patients with neoplastic disease

9. Ultrasound in the diagnosis and follow-up of hidradenitis suppurativa.
10. Anatomical-radiological (MR) correlation in corpse.
11. Contribution of multi-cut CT in the evaluation of perforating arteries prior to Plastic reconstructive surgery.
12. Imaging study of diffuse liver disease (NASH)

PUBLICATIONS

PUBLICATIONS | 39.030

Original articles

1. Cuadrado A, Llerena S, Cobo C, Pallás JR, Mateo M, Cabezas J, Fortea JI, Álvarez S, Pellón R, Crespo J, Echevarría S, Ayesa R, Setién E, López-Hoyos M, Crespo-Facorro B, Agüero J, Chueca N, García F, Calleja JL, Crespo J. **Microenvironment Eradication of Hepatitis C: A Novel Treatment Paradigm. Am. J. Gastroenterol.** 2018;113:1639-1648.FI.:10.231. [doi:10.1038/s41395-018-0157-x]
2. Martino, J, Gómez, E, de Lucas, EM, Mato, D, Vázquez-Bourgon, J. **Intraoperative Identification and Preservation of Verbal Memory in Diffuse Gliomas: A Matched-Pair Cohort Study. Neurosurgery.** 2018;83:1209-1218.FI.:4.475. [doi:10.1093/neuros/nyx617]
3. Infante, J, García, A, Serrano-Cardenas, K, González-Aguado, R, Gazulla, J, de Lucas, EM, Berciano, J. **Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS) with chronic cough and preserved muscle stretch reflexes: evidence for selective sparing of afferent la fibres. J. Neurol.** 2018;265:1454-1462.FI.:3.783. [doi:10.1007/s00415-018-8872-1]
4. Fernández-Torre, JL, Banzo, I, Ortega-Valin, F, Orozco-Sevilla, E, Martínez-Rodríguez, I, Marco de Lucas E. **Subacute encephalopathy with seizures in alcoholics (SESA) syndrome: further evidence supporting that may lie on the ictal-interictal continuum. J. Neurol.** 2018;265:2448-2450.FI.:3.783. [doi:10.1007/s00415-018-9010-9]
5. Vargas, MI, Drake-Perez, M, Delattre BMA, Boto, J, Lovblad, KO, Boudabous, S. **Feasibility of a Synthetic MR Imaging Sequence for Spine Imaging. Am. J. Neuroradiol.** 2018;39:1756-1763.FI.:3.653. [doi:10.3174/ajnr.A5728]
6. Drake-Perez, M, Delattre BMA, Boto, J, Fitsiori, A, Lovblad, KO, Boudabous, S, Vargas, MI. **Normal Values of Magnetic Relaxation Parameters of Spine Components with the Synthetic MRI Sequence. Am. J. Neuroradiol.** 2018;39:788-795.FI.:3.653. [doi:10.3174/ajnr.A5566]
7. Rueda-Gotor, J, Llorca, J, Corrales, A, Parra, JA, Portilla, V, Genre, F, Blanco, R, Agudo, M, Fuentesvilla, P, Expósito, R, Mata, C, Pina, T, González-Juanatey, C, González-Gay, MA. **Cardiovascular risk stratification in axial spondyloarthritis: carotid ultrasound is more sensitive than coronary artery calcification score to detect high-cardiovascular risk axial spondyloarthritis patients. Clin. Exp. Rheumatol.** 2018;36:73-80.FI.:3.201.
8. Martínez-Dubarbie, F, Herrera-Calvo, G, Drake-Pérez, M, Riancho, J. **Unilateral isolated hypoglossal neuropathy associated to jugular paraganglioma. Neurol. Sci.** 2018;39:971-972.FI.:2.285. [doi:10.1007/s10072-018-3256-y]
9. Parra, JA, Hernández, L, Muñoz P, Blanco, G, Rodríguez-Álvarez, R, Vilar, DR, de Alarcón, A, Goenaga, MA, Moreno, M, Fariñas MC, Spanish Collaboration Endocarditis. **Detection of spleen, kidney and liver infarcts by abdominal computed tomography does not affect the outcome in**

patients with left-side infective endocarditis. **Medicine (Baltimore).** 2018;97:FI.:2.028. [doi:10.1097/MD.00000000000011952]

Reviews

1. Martín-Laez, R, Valle-San Román, N, Rodríguez-Rodríguez, EM, Marco-de Lucas, E, Berciano Blanco JA, Vazquez-Barquero, A. **Current concepts on the pathophysiology of idiopathic chronic adult hydrocephalus: Are we facing another neurodegenerative disease?. Neurologia.** 2018;33:449-458.FI.:1.938. [doi:10.1016/j.nrl.2016.03.010]

Clinical Trials

1. Ana Canga Villegas. **Estudio de seguridad poscomercialización en pacientes con insuficiencia renal moderada a los que se administra Omniscan™ (inyección de gadodiamida) para la adquisición de imágenes de RM (IRM) realizada con contraste. Version 1.0 de 03.Mar.2009.**, GE-041-075. GE HEALTHCARE LTD..

Other Publications

1. Zarrabeitia, R, Salcedo, M, Farithas-elvarez, C, SantibAthez, M, Pascual, C, Limia, C, Setharis, B, Fontalba, A, Recio-Poveda, L, Marua Botella, Luisa, Antonio Parra, Jose. **Euroqol 5D test to evaluate quality of life in patients with hereditary haemorrhagic telangiectasia (HHT) in Spain. ANGIOGENESIS.** 2018;21:167-167.
2. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecoechea, E, Faripas-elvarez, C, Fontalba, A, Zarauza, J, Ojeda, L, Parra, JA. **Nailfold capillaroscopy in hereditary hemorrhagic telangiectasia. ANGIOGENESIS.** 2018;21:144-144.

○ Mineral and Lipid Metabolism



Consolidated group

Group Responsible

**Jesús
González Macías**

Internal Medicine Service

Hospital Universitario
Marqués de Valdecilla
Universidad de Cantabria



mirgmj47@gmail.com



Researchers

José Luís Hernández Hernández
José Manuel Olmos Martínez
José Antonio Riancho Moral
José Carlos Rodríguez Rey

Contributors

Alvaro del Real Bolt
M^a Carmen García Ibarbia
Marta Martín Millán
Josefina Micaela Martínez García
Daniel Narcis Nan Nan
Flor María Pérez Campo
Ana Santurtun Zarrabeitia
Carmen Valero Díaz De Lamadrid
María Teresa Zarrabeitia Cimiano

Nurses

Isabel Sierra Setién

Predoctoral

Daniel García Sánchez

Technicians

Estefanía Escalante Lanza
María Luisa Junco Martín
Carolina Sañudo Campo

Research lines

1. Line of genetics/genomics. It studies the genetic and epigenetic mechanisms involved in prevalent skeletal diseases like osteoarthritis and osteoporosis. The following issues are addressed:

- Genetic polymorphisms that influence bone mass, the risk of fractures and large joint osteoarthritis, using candidate genes and genome-wide association studies.
- The role of DNA methylation in the differentiation of bone cells as well as in the modulation of the expression of genes which play a key role in skeletal homeostasis.
- The possible role of the differential expression of microRNAs in bone changes that characterize these disorders.
- Molecular and functional study of mesenchymal stem cells as precursors of bone-forming cells.

2. Clinical and epidemiological line. Its objective is to study in Cantabria, as well as in the whole Spain (the latter by means of

multicenter studies), the prevalence and incidence of different aspects of mineral and bone metabolism diseases, mainly (but not only) osteoporosis. This includes the prevalence of osteoporosis, the incidence of osteoporotic fractures (vertebral and hip fractures), and the prevalence of low vitamin D levels and secondary hyperparathyroidism, as well as the analysis of those factors influencing the response to treatment. The relationship between osteoporosis and other disorders, such as dyslipidemias, diabetes, obesity, and metabolic syndrome should also be studied. Of particular interest is the follow-up of the cohort of Camargo, which allows the analysis of the association between various manifestations of bone and mineral metabolism diseases with their risk factors. Mortality rate will be considered in the study. Prominent among the factors to be analyzed is the trabecular bone score (TBS), a new tool to evaluate the risk of osteoporotic fractures. On the other hand, we have participated in the Spanish Registry of Osteoporotic Fractures of Fémur, sponsored by SEFRAOS, which has already concluded and we will participate in the new National Fracture Registry in which more than 90 Hospitals have been registered Spanish people.

3. Mineral metabolism and cardiovascular risk in systemic inflammatory diseases.

A line of collaboration has been initiated with the Rheumatology Service for the study of mineral metabolism and cardiovascular risk in systemic inflammatory diseases.

4. Line of lipid metabolism genomic. The Group of Molecular Biology (Prof. Rodriguez Rey) investigates on the molecular mechanisms of mesenchymal stem cells differentiation into adipose tissue. Firstly, the group studies the role of epigenetic regulation in the process of progenitor cell differentiation into adipocytes and its possible relationship with obesity, with particular emphasis on the role of microRNAs (in collaboration with Dr Carlos Fernandez of Yale University). Secondly, the group investigates the role of other epigenetic mechanism, the methylation of DNA, in the modulation of gene expression during the process of adipocyte differentiation. Besides that, and in collaboration with the Group of Professor Carmen Évora (Pharmaceutical Technology Department, Univesidad de la Laguna) and Dr. Gomez-Cimiano (Servicio de Traumatología del HUMV) it is developing an experimental model consisting of using mesenchymal stem cells modified in the treatment of fractures of critical size.

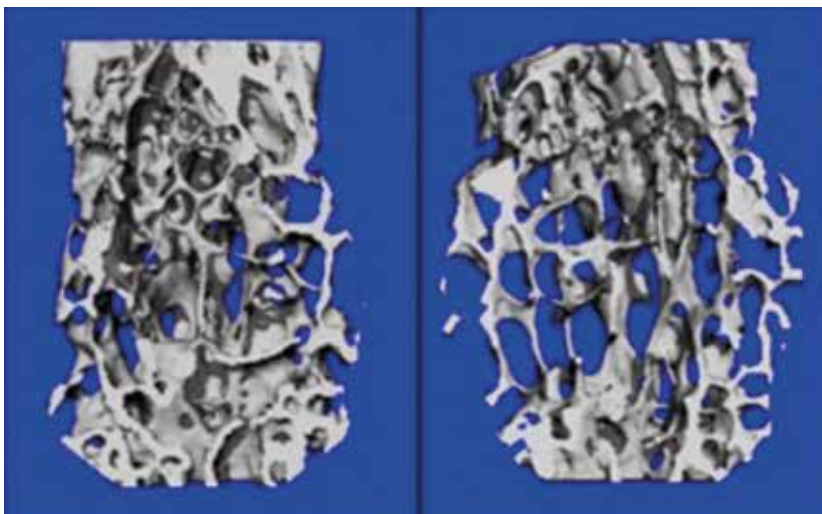


Figure 1.
Micro CT bone images of OVX animals and control.

PUBLICATIONS

IMPACT FACTOR | 126.105

Original articles

1. Lipps, C, Klein, F, Wahlicht, T, Seiffert, V, Butueva, M, Zauers, J, Truschel, T, Luckner, M, Köster M, MacLeod, R, Pezoldt, J, Huhn, J, Yuan, QG, Muller, PP, Kempf, H, Zweigerdt, R, Dittrich-Breiholz, O, Pufe, T, Beckmann, R, Drescher, W, Riancho, J, Sañudo C, Korff, T, Opalka, B, Rebmann, V, Göthert JR, Alves, PM, Ott, M, Schucht, R, ..., May, T. **Expansion of functional personalized cells with specific transgene combinations.** *Nat. Commun.* 2018;9:994-994.F.I.:12.353. [doi:10.1038/s41467-018-03408-4]

2. Alonso, N, Estrada, K, Albagha OME, Herrera, L, Reppe, S, Olstad, OK, Gautvik, KM, Ryan, NM, Evans, KL, Nielson, CM, Hsu, YH, Kiel, DP, Markozannes, G, Ntzani, EE, Evangelou, E, Feenstra, B, Liu, XP, Melbye, M, Masi, L, Brandi, ML, Riches, P, Daroszewska, A, Olmos, JM, Valero, C, Castillo, J, Riancho, JA, Husted, LB, Langdahl, BL, Brown, MA, ..., Ralston, SH. **Identification of a novel locus on chromosome 2q13, which predisposes to clinical vertebral fractures independently of bone density.** *Ann. Rheum. Dis.* 2018;77:378-385.F.I.:12.350. [doi:10.1136/annrheumdis-2017-212469]

3. Martín-Varillas, JL, Calvo-Río, V, Beltrán, E, Sánchez-Burson, J, Mesquida, M, Adan, A, Hernandez, MV, Garfella, MH, Pascual, EV, Martínez-Costa, L, Sellas-Fernández, A, Cordero-Coma, M, Diaz-Llopis, M, Gallego, R, Salom, D, Ortego, N, García-Serrano, JL, Callejas-Rubio, JL, Herreras, JM, Garcia-Aparicio, A, Maiz, O, Blanco, A, Torre, I, Díaz-Valle, D, Pato, E, Aurrecochea, E, Caracuel, MA, Gamero, F, Minguez, E, ..., Blanco, R. **Successful Optimization of Adalimumab Therapy in Refractory Uveitis Due to Behcet's Disease.** *Ophthalmology.* 2018;125:1444-1451.F.I.:7.479. [doi:10.1016/j.ophtha.2018.02.020]

4. del Real, A, Riancho-Zarrabeitia, L, Riancho, JA. **Epigenetic Aging**

in Osteoporosis. *J. Bone Miner. Res.* 2018;33:1902-1903.F.I.:6.314. [doi:10.1002/jbmr.3567]

5. Pereira, R, Alves, C, Aler, M, Amorim, A, Arévalo, C, Betancor, E, Braganholi, D, Bravo, ML, Brito, P, Builes, JJ, Burgos, G, Carvalho, EF, Castillon, A, Citanesi, CI, Cicarelli RMB, Coufalova, P, Dario, P, D'Amato, ME, Davison, S, Ferragut, J, Fondevila, M, Furfuro, S, García, O, Gaviria, A, Gomes, I, González, E, González-Linan, A, Gross, TE, Hernández, A, ..., Gusmão L. **A GHEP-ISFG collaborative study on the genetic variation of 38 autosomal indels for human identification in different continental populations.** *Forensic Sci. Int.-Genet.* 2018;32:18-25.F.I.:5.637. [doi:10.1016/j.fsigen.2017.09.012]

6. Delgado-Calle, J, Hancock, B, Likine, EF, Sato, AY, McAndrews, K, Sanudo, C, Bruzzaniti, A, Riancho, JA, Tonra, JR, Bellido, T. **MMP14 is a novel target of PTH signaling in osteocytes that controls resorption by regulating soluble RANKL production.** *Faseb J.* 2018;32:2878-2890.F.I.:5.595. [doi:10.1096/fj.201700919RRR]

7. Atienza-Mateo, B, Calvo-Río, V, Beltrán, E, Martínez-Costa, L, Valls-Pascual, E, Hernández-Garfella, M, Atanes, A, Cordero-Coma, M, Miquel Nolla J, Carrasco-Cubero, C, Loricera, J, González-Vela, MC, Vegas-Revenga, N, Fernández-Díaz, C, Demetrio-Pablo, R, Domínguez-Casas, LC, Luis Martín-Varillas J, Palmou-Fontana, N, Hernández, JL, González-Gay, MA, Blanco, R. **Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behcet's disease: multicentre retrospective study.** *RHEUMATOLOGY.* 2018;57:856-864.F.I.:5.245. [doi:10.1093/rheumatology/kex480]

8. Fernández-Díaz, C, Loricera, J, Castañeda S, López-Mejias, R, Ojeda-García, C, Olive, A, Rodríguez-Muguruza, S, Carreira, PE, Pérez-Sandoval, T, Retuerto, M, Cervantes-Pérez, EC, Flores-Robles, BJ, Hernández-Cruz, B, Urruticochea, A, Maiz-Alonso, O, Arbolea, L, Bonilla, G, Hernández-Rodríguez, I, Palma, D, Delgado, C, Expósito-Molinero, R, Ruibal-Escribano, A, Álvarez-Rodríguez,

B, Blanco-Madrugal, J, Bernal, JA, Vela-Casasempere, P, Rodríguez-Gómez, M, Fito, C, Ortiz-Sanjuan, F, ..., Blanco, R. **Abatacept in patients with rheumatoid arthritis and interstitial lung disease: A national multicenter study of 63 patients.** *Semin. Arthritis Rheum.* 2018;48:22-27.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.12.012]

9. Vilanova, I, Hernández, JL, Mata, C, Duran, C, García-Unzueta, MT, Portilla, V, Fuentes-Villa, P, Corrales, A, González-Vela, MC, González-Gay, MA, Blanco, R, González-Lopez, MA. **Insulin resistance in hidradenitis suppurativa: a case-control study.** *J. Eur. Acad. Dermatol. Venereol.* 2018;32:820-824.F.I.:4.287. [doi:10.1111/jdv.14894]

10. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Mijares, V, Expósito, R, Mata, C, Portilla, V, Blanco, R, Hernández, JL, Llorca, J, Gualillo, O, López-Mejias, R, González-Gay, MA. **Association of circulating calprotectin with lipid profile in axial spondyloarthritis.** *Sci Rep.* 2018;8:13728-13728.F.I.:4.122. [doi:10.1038/s41598-018-32199-3]

11. Olmos, JM, Hernández, JL, Pariente, E, Martínez, J, González-Macías, J. **Serum 25-Hydroxyvitamin D in Obese Spanish Adults: the Camargo Cohort Study.** *Obes. Surg.* 2018;28:3862-3871.F.I.:3.895. [doi:10.1007/s11695-018-3430-6]

12. López-Delgado, L, Riancho-Zarrabeitia, L, García-Unzueta, MT, Tenorio, JA, Garcia-Hoyos, M, Lapunzina, P, Valero, C, Riancho, JA. **Abnormal bone turnover in individuals with low serum alkaline phosphatase.** *Osteoporosis Int.* 2018;29:2147-2150.F.I.:3.856. [doi:10.1007/s00198-018-4571-0]

13. Urbina-Soto, L, Hernández-Martínez, P, Ortiz-Flores, F, Hernández, JL. **Thyrotoxic hypokalemic periodic paralysis.** *QJM-An Int. J. Med.* 2018;111:887-889.F.I.:3.204. [doi:10.1093/qjmed/hcy186]

14. Ferraz-Amaro, I, López-Mejias, R, Tejera-Segura, B, de Vera-González, AM, Ubilla, B, Olmos, JM, Hernández, JL, González-Gay, MA. **Amylin in the insulin resistance of**

patients with rheumatoid arthritis. *Clin. Exp. Rheumatol.*2018;36:421-427.F.I.:3.201.

15. Genre, F, Rueda-Gotor, J, Remuzgo-Martínez, S, Corrales, A, Ubilla, B, Mijares, V, Fernandez-Díaz, C, Portilla, V, Blanco, R, Hernández, JL, Llorca, J, López-Mejias, R, González-Gay, MA.

Implication of osteoprotegerin and sclerostin in axial spondyloarthritis cardiovascular disease: a study of 163 Spanish patients. *Clin. Exp. Rheumatol.*2018;36:302-309.F.I.:3.201.

16. Loricera J, Hernández JL, García-Castaño A, Martínez-Rodríguez I, González-Gay MÁ, Blanco R. **Subclinical aortitis after starting nivolumab in a patient with metastatic melanoma. A case of drug-associated aortitis?.** *Clin. Exp. Rheumatol.*2018;36 Suppl 111:171-171.F.I.:3.201.

17. González-López, MA, Lacalle, M, Mata, C, López-Escobar, M, Corrales, A, López-Mejias, R, Rueda, J, González-Vela, MC, González-Gay, MA, Blanco, R, Hernández, JL. **Carotid ultrasound is useful for the cardiovascular risk stratification in patients with hidradenitis suppurativa.** *PLoS One.* 2018;13:F.I.:2.766. [doi:10.1371/journal.pone.0190568]

18. Villar, A, Zarrabeitia, MT, Fdez-Arroyabe, P, Santurtun, A. **Integrating and analyzing medical and environmental data using ETL and Business Intelligence tools.** *Int. J. Biometeorol.*2018;62:1085-1095.F.I.:2.577. [doi:10.1007/s00484-018-1511-9]

19. Santurtun, A, Villar, A, Zarrabeitia, MT. **Who is legally responsible for deaths caused by air pollution?.** *Int. J. Biometeorol.*2018;62:2063-2064.F.I.:2.577. [doi:10.1007/s00484-018-1616-1]

20. Olmos, JM, Hernández, JL, Martínez, J, Pariente, E, Castillo, J, Prieto-Alhambra, D, González-Macías, J. **Prevalence of vertebral fracture and densitometric osteoporosis in Spanish adult men: The Camargo Cohort Study. J. Bone Miner. Metab.**2018;36:103-110.F.I.:2.472. [doi:10.1007/s00774-017-0812-0]

21. Prieto-Alhambra, D, Reyes, C, Sainz, MS, González-Macías, J, Delgado, LG, Bouzon, CA, Gañan SM, Miedes, DM, Vaquero-Cervino, E, Bardaji MFB, Herrando, LE, Baztan, FB, Ferrer, BL, Pérez-Coto, I, Bueno, GA, Mora-Fernández, J, Doñate TE, Blasco, JMI, Aguado-Maestro, I, Saez-López, P, Domenech, MS, Climent-Peris, V, Rodríguez, AD, Sardiñas HK, Gómez, OT, Serra, JT, Caeiro-Rey, JR, Cano, IA, Carsi, MB, ..., Díez-Pérez, A. **In-hospital care, complications, and 4-month mortality following a hip or proximal femur fracture: the Spanish registry of osteoporotic femur fractures prospective cohort study.** *Arch Osteoporos.* 2018;13:96-96.F.I.:2.382. [doi:10.1007/s11657-018-0515-8]

22. Santurtún M, Santurtún A, Zarrabeitia MT. **Does the environment affect suicide rates in Spain? A spatiotemporal analysis.** *Rev. Psiquiatr. Salud Ment.*2018;11:192-198.F.I.:2.233. [doi:10.1016/j.rpsm.2017.05.001]

23. Riancho-Zarrabeitia, L, Rasilla, DF, Roye, D, Fdez-Arroyabe, P, Santurtun, A. **Kawasaki disease in Spanish paediatric population and synoptic weather types: an observational study.** *Rheumatol. Int.*2018;38:1259-1266.F.I.:1.952. [doi:10.1007/s00296-018-4066-5]

24. Li, HG, Song, XN, Yang, F, Bao, HX, Lu, XL, Perez-Campo, FM, Zhao, JS. **Application of oligonucleotides to construct a conditional targeting vector for porcine IB.** *Mol. Med. Rep.*2018;17:653-659.F.I.:1.922. [doi:10.3892/mmr.2017.7917]

25. Suárez Fernández C, Castilla-Guerra, L, Cantero Hinojosa J, Suriñach JM, Acosta de Bilbao F, Tamarit, JJ, Diaz, JLD, Hernández, JL, Pose, A, Montero-Pérez-Barquero, M, Roquer, J, Gallego, J, Vivancos, J, Mostaza, JM. **Satisfaction with oral anticoagulants in patients with atrial fibrillation.** *Patient Prefer. Adherence.* 2018;12:267-274.F.I.:1.733. [doi:10.2147/PPA.S152109]

26. Suárez Fernández C, Mostaza, JM, Castilla Guerra L, Cantero Hinojosa J, Suriñach JM, Acosta de Bilbao F, Tamarit, JJ, Diaz, JLD, Hernández, JL, Cazorla, D, Ràfols C, en nombre de los

Investigadores del Estudio ESPARTA. **Adherence to recommendations of the Therapeutic Positioning Report about treatment with oral anticoagulants in elderly patients with atrial fibrillation. The ESPARTA study.** *Med. Clin.*2018;151:8-15.F.I.:1.168. [doi:10.1016/j.medcli.2017.07.025]

27. Santurtún M, Sánchez-Lorenzo A, Del Real Á, Zarrabeitia, M., Santurtún, A.. **Association Between Suicide and Environmental Variables in the North of Spain: A 14-Year Analysis.** *Cult. Med. Psychiatr.*2018;42:647-653.F.I.:0.983. [doi:10.1007/s11013-018-9578-7]

Reviews

1. Riancho-Zarrabeitia, L, Cuberia, M, Muñoz P, López-Hoyos, M, García-Canale, S, García-Unzueta, M, Hernández, JL, Martínez-Taboada, VM. **Vitamin D and antiphospholipid syndrome: A retrospective cohort study and meta-analysis.** *Semin. Arthritis Rheum.*2018;47:877-882.F.I.:4.356. [doi:10.1016/j.semarthrit.2017.10.007]

2. del Real, A, Riancho-Zarrabeitia, L, López-Delgado, L, Riancho, JA. **Epigenetics of Skeletal Diseases.** *Curr. Osteoporos. Rep.*2018;16:246-255.F.I.:3.726. [doi:10.1007/s11914-018-0435-y]

3. Palmou-Fontana, N, Calvo-Río, V, Martín-Varillas, JL, Fernández-Díaz, C, Mesquida, M, Adan, A, Hernández, MV, Cordero-Coma, M, Maiz Alonso O, Díaz-Valle, D, Fernández-Cid, C, Ruiz-Moreno, O, Hernández, JL, González-Gay, MA, Blanco, R. **Golimumab in refractory uveitis associated to juvenile idiopathic arthritis: multicentre study of 7 cases and literature review.** *Clin. Exp. Rheumatol.*2018;36:652-657.F.I.:3.201.

4. Riancho, J, Bosque-Varela, P, Pérez-Pereda, S, Povedano, M, de Munain, AL, Santurtun, A. **The increasing importance of environmental conditions in amyotrophic lateral sclerosis.** *Int. J. Biometeorol.*2018;62:1361-1374.F.I.:2.577. [doi:10.1007/s00484-018-1550-2]

Editorials

1. Olmos, JM, González-Macías, J. **The trabecular bone index: a new tool for assessing osteoporosis.** *Rev. Clin. Esp.* 2018;218:135-136.F.I.:1.184. [doi:10.1016/j.rce.2018.01.007]

Projects

- Jesús González Macías. **Ayuda por Producción al Grupo de Metabolismo Mineral y Lípico.** APG/13.
- José Manuel Olmos Martínez. **Estudio del metabolismo óseo y mineral de la población femenina postmenopáusica y masculina mayor de 50 años atendida por un Centro de Salud en Cantabria.** PI15/00521. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
- Carmen Valero Díaz de Lamadrid. **Estudio del metabolismo óseo en pacientes tratados con oxígeno a alto flujo en una cama hiperbárica.** FEIOMM2015. FUNDACIÓN ESPAÑOLA DE INVESTIGACIÓN ÓSEA Y DEL METABOLISMO MINERAL.
- José Manuel Olmos Martínez. **Donaciones para el desarrollo de proyectos de investigación.** BDP57. AMGEN, S.A.
- José Antonio Riancho Moral. **Estudio de las células troncales mesenquimales en la osteoporosis: Papel de los RNAs largos no codificantes (lncRNAs) y potencial regenerativo.** PI16/00915. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.
- José Luis Hernández Hernández. **Donación para el desarrollo de proyectos de investigación en la Unidad de Lípidos del Servicio de Medicina Interna del HUMV.** CI16/35. CASEN RECORDATI, S.L.
- José Manuel Olmos Martínez. **Contrato de servicios de investigación para el proyecto Niveles de 25(OH)D en pacientes osteoporóticos tratados con Calcifediol.** CSI17/03. FAES FARMA, S.A.

8. José Antonio Riancho Moral. **PREVAL17/06 Álvaro del Real Bolt.** PREVAL17/06.

9. José Carlos Rodríguez Rey. **Efectividad de la Inyección Intra-articular de ASOs con Efecto Condrogénico en el Tratamiento de la Osteoartritis: Prueba de Concepto.** INVAL17/15.

10. José Antonio Riancho Moral. **Beca de investigación de FEIOMM al proyecto Proteoma óseo en suero de pacientes osteoporóticos.** FEIOMM17/25. FUNDACIÓN ESPAÑOLA DE INVESTIGACIÓN ÓSEA Y DEL METABOLISMO MINERAL.

11. José Manuel Olmos Martínez. **Contrato de servicios de investigación para el Estudio multicéntrico, internacional, aleatorizado, doble ciego, controlado con alendronato para determinar la eficacia y seguridad de AMG 785 en el tratamiento de mujeres con osteoporosis postmenopáusica.** CSI18/05. AMGEN, S.A.

12. José Antonio Riancho Moral. **COST Action: GEMSTONE "Genomics of MusculoSkeletal traits Translational Network".** EU18/12. COMISIÓN EUROPEA.

13. José Carlos Rodríguez Rey. **Efectividad de la inyección intra-articular de ASOs con efecto condrogénico en el tratamiento de la osteoartritis.** PREVAL19/02.

Clinical Trials

1. Jesús González Macías. **Estudio multicéntrico, internacional, aleatorizado, doble ciego, controlado con alendronato para determinar la eficacia y seguridad de AMG 785 en el tratamiento de mujeres con osteoporosis postmenopáusica.** 20110142. AMGEN, S.A..

2. José Manuel Olmos Martínez. **Efecto de la administración de diferentes regímenes de tratamiento de Hidroferol® Cápsulas de Gelatina Blanda (calcifediol) y colecalciferol (Dibase®) en los niveles de 25(OH)D y marcadores de remodelado óseo en mujeres**

postmenopáusicas con deficiencia de 25(OH)D. Influencia de factores clínicos y genéticos en la población osteoporótica y no-osteoporótica. HIDR-0217/OST. FAES FARMA, S.A..

Postmarketing Studies and Other

1. José Luis Hernández Hernández. **XALIA - Xarelto® para la Anticoagulación a Largo plazo e Inicial en el Tromboembolismo Venoso (TEV).** BAY-RIV-2012-01. BAYER HISPANIA, S.L..

2. José Antonio Riancho Moral. **Registro internacional prospectivo y multicéntrico de pacientes hombres y mujeres que han sido diagnosticados recientemente con fibrilación auricular y reciben tratamiento con Rivaroxabán.** TRI08890. THE TROMBOSIS RESEARCH INSTITUTE.

Collaborations

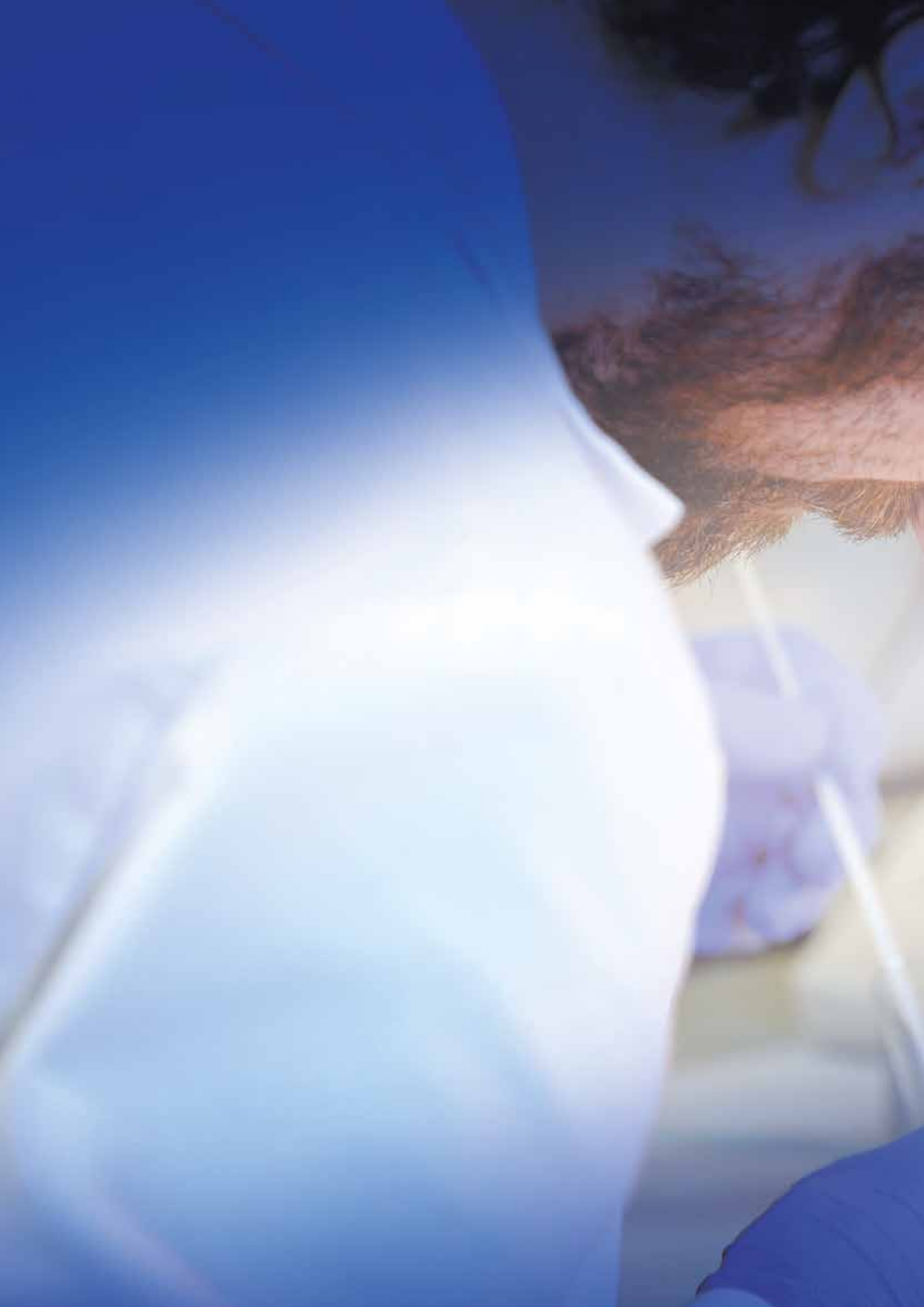
Total Impact factor 23.259

1. Trajanoska K, Morris JA, Oei L, Zheng HF, Evans DM, Kiel DP, Ohlsson C, Richards JB, Rivadeneira F. **Assessment of the genetic and clinical determinants of fracture risk: genome wide association and mendelian randomisation study.** *BMJ.* 2018;362:F.I.:23.259. [doi:10.1136/bmj.k3225]



IFIMAV

Valdecilla Instituto de Investigación Valdecilla **IDIVAL**





○ **Associated
groups**

Roberto Zarrabeitia Puente

Hereditary Hemorrhagic
Telangiectasia Unit
Hospital de Sierrallana

Hereditary hemorrhagic telangiectasia (Rendu Osler Weber) Study Group

Group Responsible

Roberto Zarrabeitia Puente

Hereditary Hemorrhagic Telangiectasia Service
Hospital de Sierrallana



roberto.zarrabeitia@scsalud.es

Colaboradores

Jesús Bueno López
Ana José Bustamante Ruiz
Manuel Secundino Bustamante Sánchez
José Luis Fernández Forcelledo
José Luis Martín Gurpegui
Roberto Megía López
Cristina Menéndez García
Julio Rodríguez Iglesias
Sara Rodríguez Prado,
Blanca Señaris González

Enfermeras

Elena Barahona Bustamante
Mar Rodriguez Garrido
María Valdor Arriaran

Técnicos

Teresa Dosal
Josefa Hernández



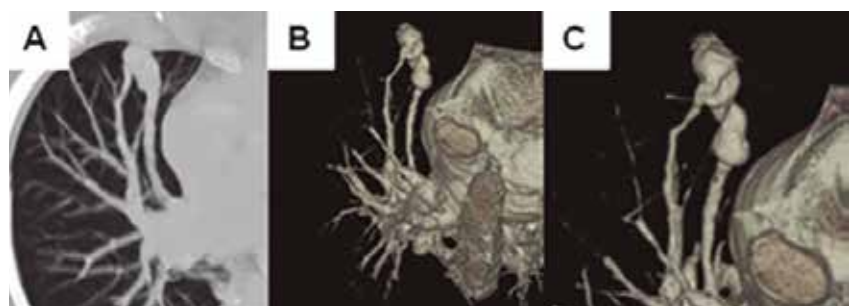
Associated group

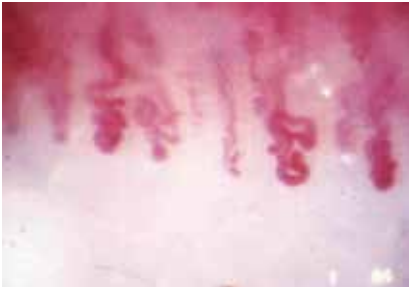
Research lines

1. Epidemiology of hereditary haemorrhagic telangiectasia in Spain (phenotype-genotype

correlation, validity of diagnostic tests, radiological and clinical findings).

2. Study of new therapies for HHT: selective modulators of estrogen





receptors and beta-blockers, in collaboration with the Center for Biological Research (CIB) of the Center for Scientific Research (CSIC) in the basic area.

PUBLICATIONS

IMPACT FACTOR | 9.090

Original articles

1. Rodríguez-García, J, Zarrabeitia-Puente, R, Fernández-Santos, R, García-Erce, JA. **Infection prevention in patients with hereditary hemorrhagic telangiectasia.** *Haematologica*. 2018;103:491-492.F.I.:9.090. [doi:10.3324/haematol.2018.200873]

Clinical Trials

1. Ana José Bustamante Ruiz. **Estudio fase III, aleatorizado, doble ciego, con 3 grupos paralelos, de 52 semanas de duración para comparar la eficacia, seguridad y tolerabilidad de la combinación triple de**

dosis fija FF/UMEC/VI con las combinaciones dobles de dosis fija FF/VI y UMEC/VI, administradas una vez al día por la mañana mediante un inhalador de polvo seco en sujetos con enfermedad pulmonar obstructiva crónica. CTT116855. GLAXOSMITHKLINE, S.A..

2. Ana José Bustamante Ruiz. **Evaluación, en pacientes con procesos médicos, de rivaroxaban frente a placebo en la reducción del riesgo de tromboembolismo venoso después del alta hospitalaria.** (MARINER). BAY59-7939/17261/RIVAROXDVT3002. JANSSEN-CILAG INTERNATIONAL, NV.

Postmarketing Studies and Other

1. Ana José Bustamante Ruiz. **Estudio Observacional del impacto socioeconómico de la FPI en España. (Estudio Oasis).** BOE-MAC-2017-01/1199-0296.

Other Publications

1. Zarrabeitia, R, Salcedo, M, Bueno, J, Marqués, S, Setharis, B, Coduras, A, González-Pascual, A, Anta, M, Cuesta, M, Rodríguez Prado, Sara. **Epidemiology of hereditary haemorrhagic telangiectasia in Spain: experience of the HHT unit in hospital Sierrallana.** *ANGIOGENESIS*. 2018;21:166-167.

2. Zarrabeitia, R, Salcedo, M, Farithas-elvarez, C, SantibAthez, M, Pascual, C, Limia, C, Setharis, B, Fontalba, A, Recio-Poveda, L, Marua Botella, Luisa, Antonio Parra, José. **Euroqol 5D test to evaluate quality of life in patients with hereditary haemorrhagic telangiectasia (HHT) in Spain.** *ANGIOGENESIS*. 2018;21:167-167.

3. Botella, LM, Zarrabeitia, R, Recio-Poveda, L, Bernabeu, C, Albipana, V. **Mutation affecting the proximal promoter of Endoglin as the origin of hereditary hemorrhagic telangiectasia type 1.** *ANGIOGENESIS*. 2018;21:146-146.

4. Zarrabeitia, R, Salcedo, M, Esles, M, Portilla, R, Aurrecochea, E, Faripas-elvarez, C, Fontalba, A, Zarauza, J, Ojeda, L, Parra, JA. **Naifold capillaroscopy in hereditary hemorrhagic telangiectasia.** *ANGIOGENESIS*. 2018;21:144-144.

5. Riera-Mestre, A, Patier, JL, Gómez-Del Olmo, V, SAchez, R, Lopez-Wolf, D, Torralba, MA, Ojeda, A, Zarrabeitia, R, Juyol, MC, Fernández-García, A, Gómez-Cerezo, J, López-Rodríguez, M. **RiTHHa registry: a national computerized regisry of patients with hemorrhagic hereditary telangiectasia in Spain.** *ANGIOGENESIS*. 2018;21:164-164.



