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Activity Report

Valdecilla
Instituto de Investigación Sanitaria
IDIVAL










Valdecilla
Instituto de Investigación Sanitaria
IDIVAL

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Valdecilla Biomedical
Research Institute
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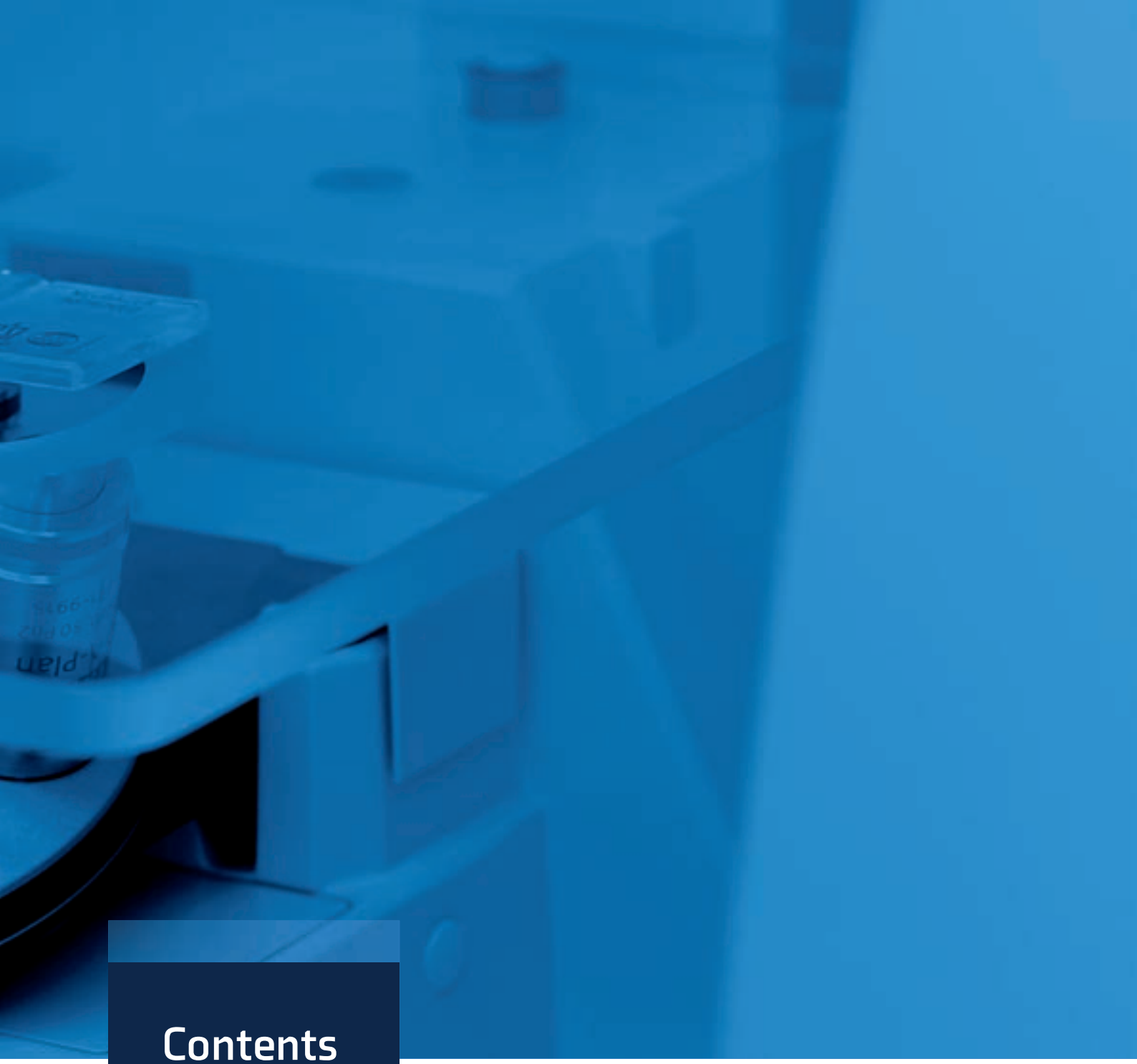

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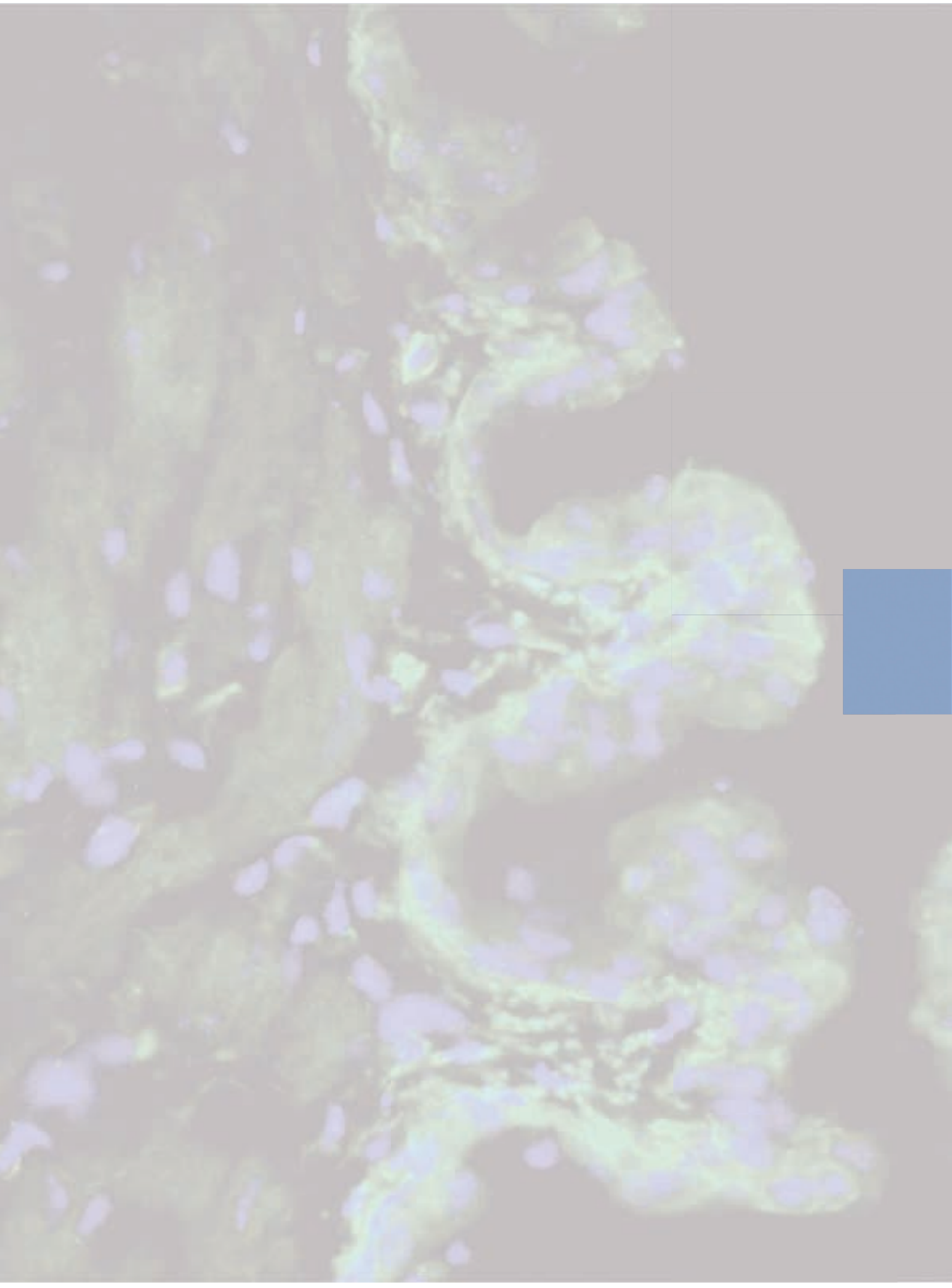
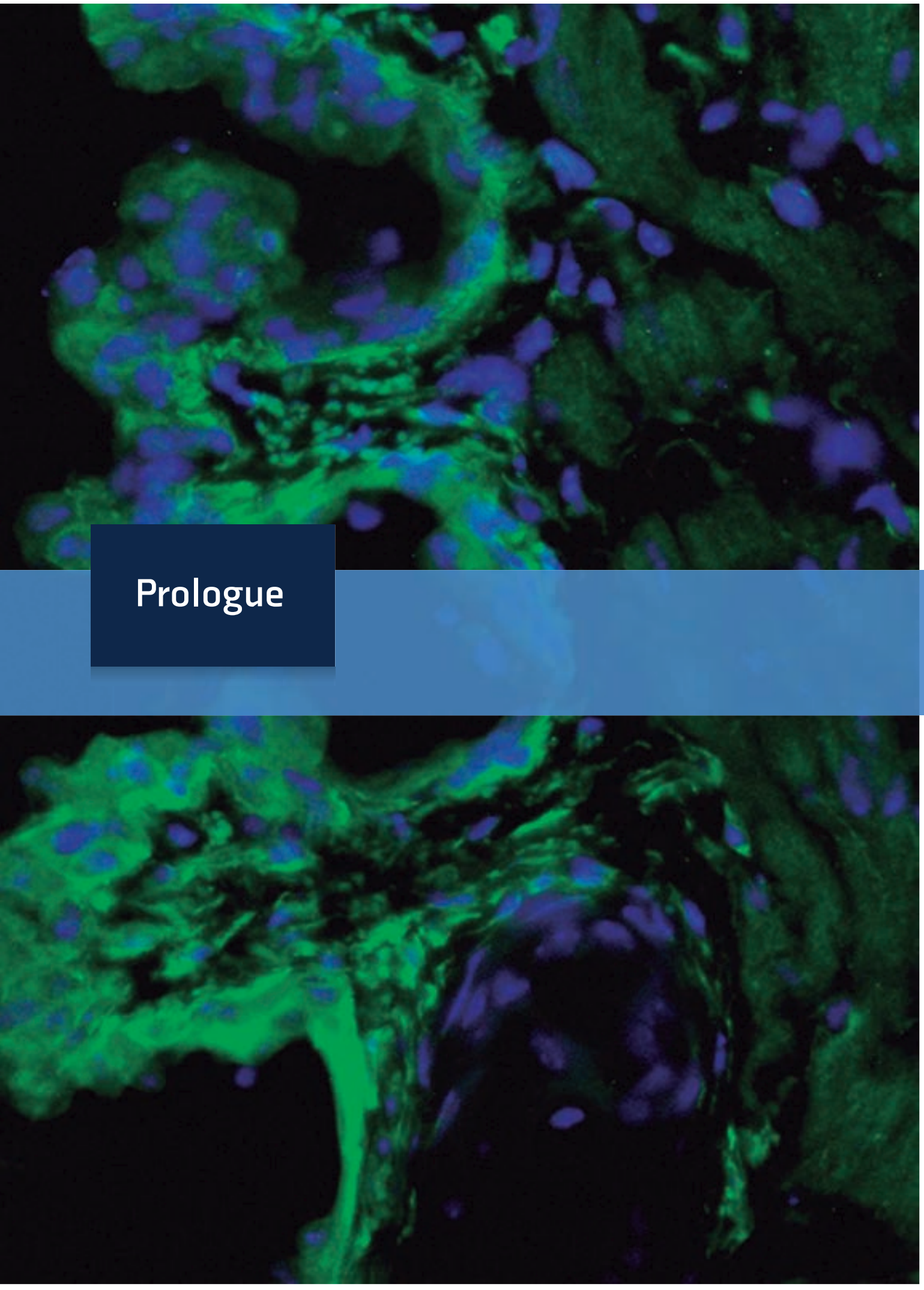




Prologue

The Marqués de Valdecilla Research Institute (IDIVAL) is established as a key actor in the generation of applied knowledge in our region. Its core engine, the Marqués de Valdecilla University Hospital, one of Spain's leading hospitals, in partnership with the University of Cantabria, promotes new solutions for patients' health problems thanks to the research and innovation of its excellent professionals. It is for this reason that we have the optimal elements to continue leading in certain fields of knowledge: expert personnel, next-generation technology and magnificent facilities, which we are committed to making the best possible use of.

Every day, the world's best healthcare centres generate wealth and solutions for patients through research and innovation. Spain as a whole hopes to move forward in this value model based on knowledge, a value that includes the application of the generated knowledge and a socioeconomic benefit. Cantabria is no exception, and has some elements that make it possible and almost necessary: its size, an important Hospital and University, and a high level of scientific expertise. Knowledge in the healthcare field generates wealth in itself, as IDIVAL demonstrates, insofar as it creates jobs and improves the approach to health problems. However, we still have a long way to go. The modern globalised world gives us unique opportunities that stem from interdisciplinary, multinational partnerships, and taking advantage of them is a key part of developing projects with real impact.

IDIVAL, as a Healthcare Research Institute accredited by the Carlos III Health Institute, encouraging translational research and innovation as a foundation for improving patient care, must have an international outlook. This cross-border vision must coexist with a integrating vision that lets the different areas that could add value to healthcare research in Cantabria contribute to IDIVAL. Patients, nurses, doctors, and personnel from other healthcare areas, whether in hospitals or in primary care, and researchers in biomedical and technological fields and other disciplines in our Autonomous Community, can and must be present in the projects designed to improve healthcare in Cantabria. We believe that IDIVAL, like Valdecilla, must be both integrated and open, and have the best among its personnel, in order to maintain a top-level healthcare system and continue to earn the support of all Cantabria's society.

Similarly, we must continue working to ensure that the public-private partnership model, based on transparency, provides greater benefits. We must see the annual expenditure of the healthcare sector in Cantabria as an investment, an opportunity, and make the most of our partnerships with business, understanding that we can add value to its products, acquiring them, but also evaluating, improving and designing them. The experience and expertise of our professionals must be given the maximum value.

Talent is one of the main keys to success. Training new generations, facilitating their professional growth, especially in research and innovation, and attracting expert professionals to help this ongoing regeneration process, are essential goals for ensuring that the high quality healthcare system we want continues to be one of the distinguishing features of our Autonomous Community. To do this, we must create mechanisms to overcome barriers, whether geographical, administrative, or sometimes cultural, requiring the collaboration of patients, healthcare professionals, managers, and society in general.

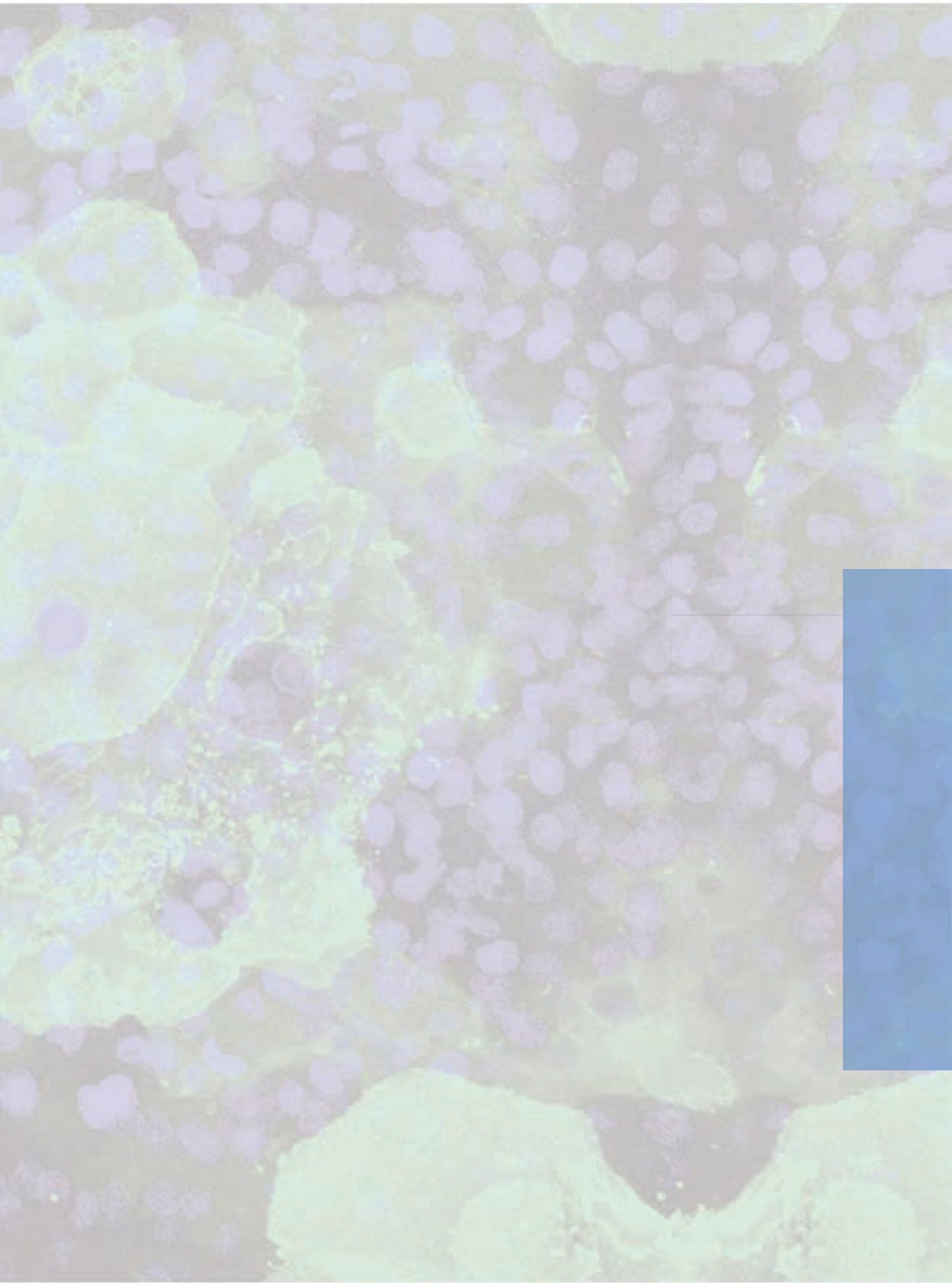
María Luisa Real González
Minister of Health of the Government of Cantabria
President of the Board of IDIVAL

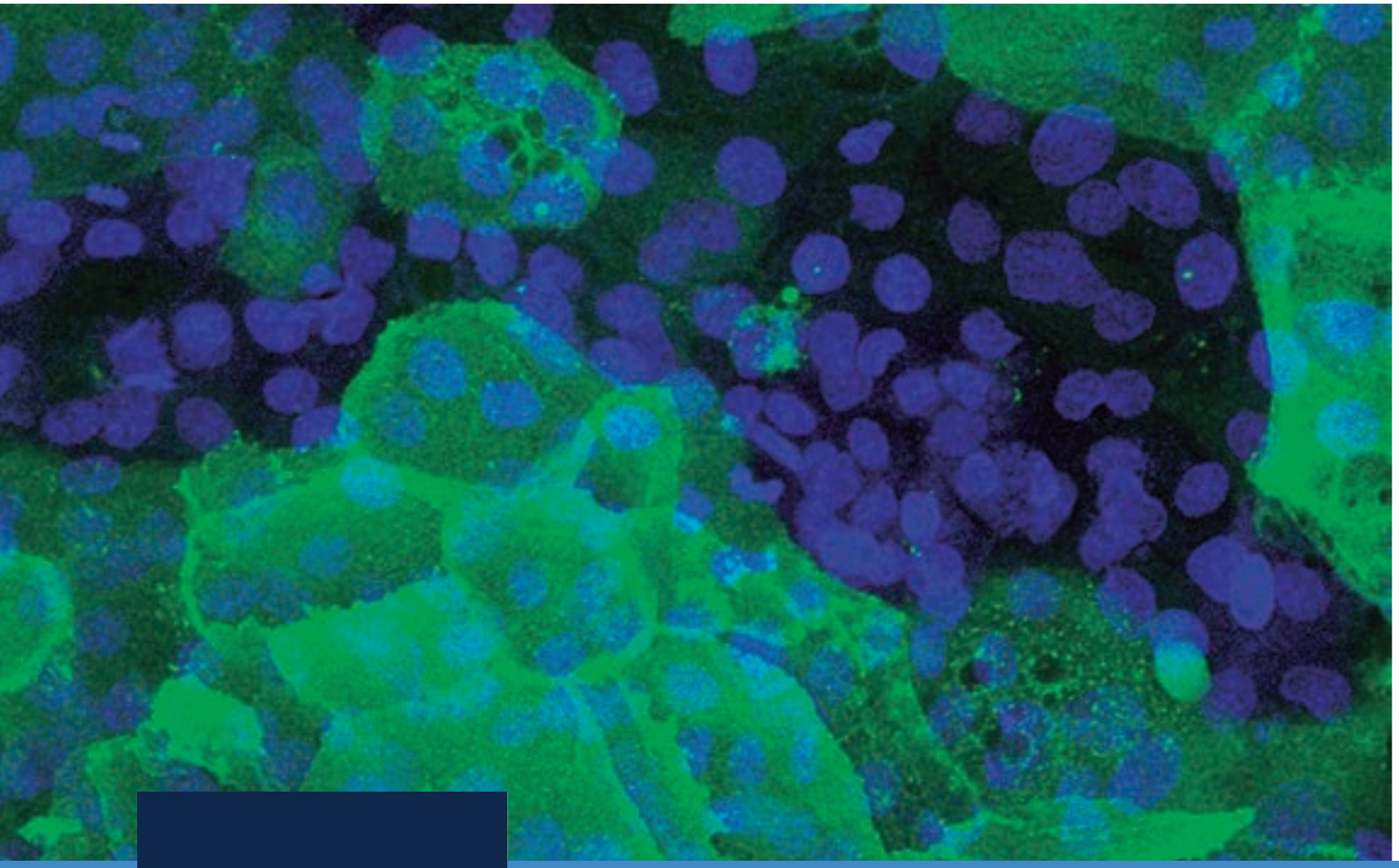
he Marqués de Valdecilla Research Institute (IDIVAL) is responsible for promoting and managing our biomedical research. IDIVAL has been recognised by the Carlos III Health Institute as a benchmark centre for research in Spain. Its main distinguishing features include the search for excellence and innovation, always focused on improving the health of our citizens.

2016 was a productive year for IDIVAL. Among its achievements, in 2016 IDIVAL produced nearly 500 indexed publications, with a very high average impact factor (3.89), and 30 articles published in journals with an impact factor higher than 10. It continued to attract external resources, with 80 competitive research projects and 175 open clinical trials. This is an important point, because it shows we are competitive and contributes to our sustainability, for example enabling us to increase the number of post-MIR contracts and grants to research groups. A significant figure was the record number of competitive research projects granted by the Carlos III Health Institute in the 2016 campaign. However, in an increasingly competitive environment, we must be aware that IDIVAL can only be sustainable and continue to expand if we consolidate repeated access to European projects. This must be one of our main challenges in the coming years.

To conclude, I will comment on some of the initiatives developed specifically in IDIVAL in 2016 that we are particularly proud of. We launched the COLABORA campaign, designed to attract altruistic, transparent donations for research, something our region was clearly lacking. The "Santander Biomedical Lectures" were a success in lecturers and attendees, and I am sure they have contributed to creating a vocation for research among some of the many young people who enjoyed them. During 2016 the new website of the Marquesa de Pelayo library was finalised. An extraordinary and necessary tool for our researchers, and to restore our library to the place its history deserves. Finally, I would like to welcome the research groups who passed a tough evaluation and have now joined IDIVAL. We all hope they settle in quickly. As an example of our commitment to inclusiveness, let me highlight the research groups in Nursing and Primary Care. In a small Autonomous Community like ours, it is only by working together (hospitals, primary care, university and private enterprise) that we can continue moving forwards to attract resources and scientific talent.

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

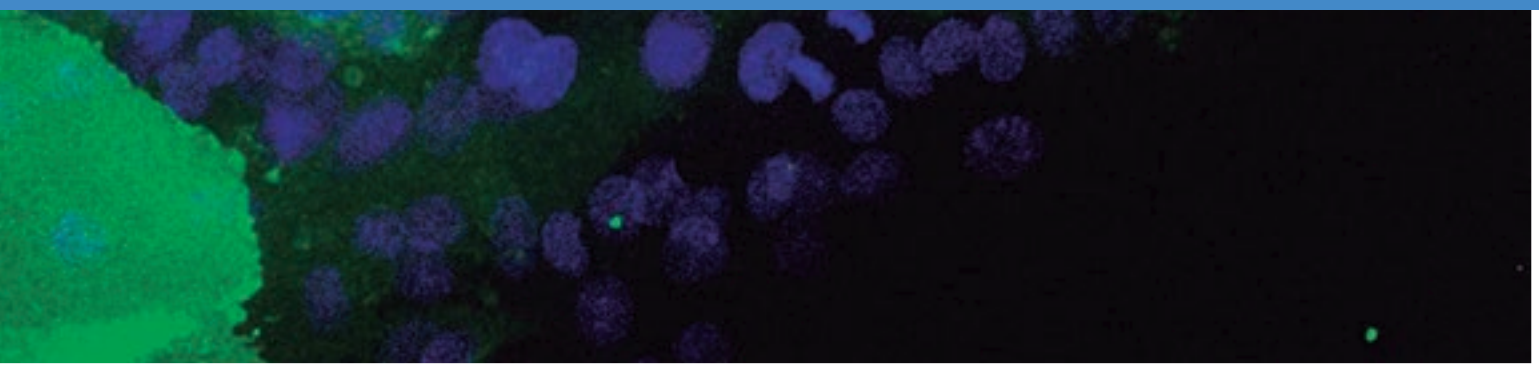
Valdecilla is the unifying mark that Ramón Pelayo de la Torriente, Marquis de Valdecilla left on the institutions that came to be during his marquessate: the Marqués de Valdecilla University Hospital, the de la Torriente, Marquis de Valdecilla left on the institutions that came to be during his marquessate: the Marqués de Valdecilla University Hospital, the Marqués de Valdecilla Research Institute (IDIVAL), and the Valdecilla Virtual Hospital, which today maintains the innovative, cross-disciplinary and philanthropic spirit with which it was created.

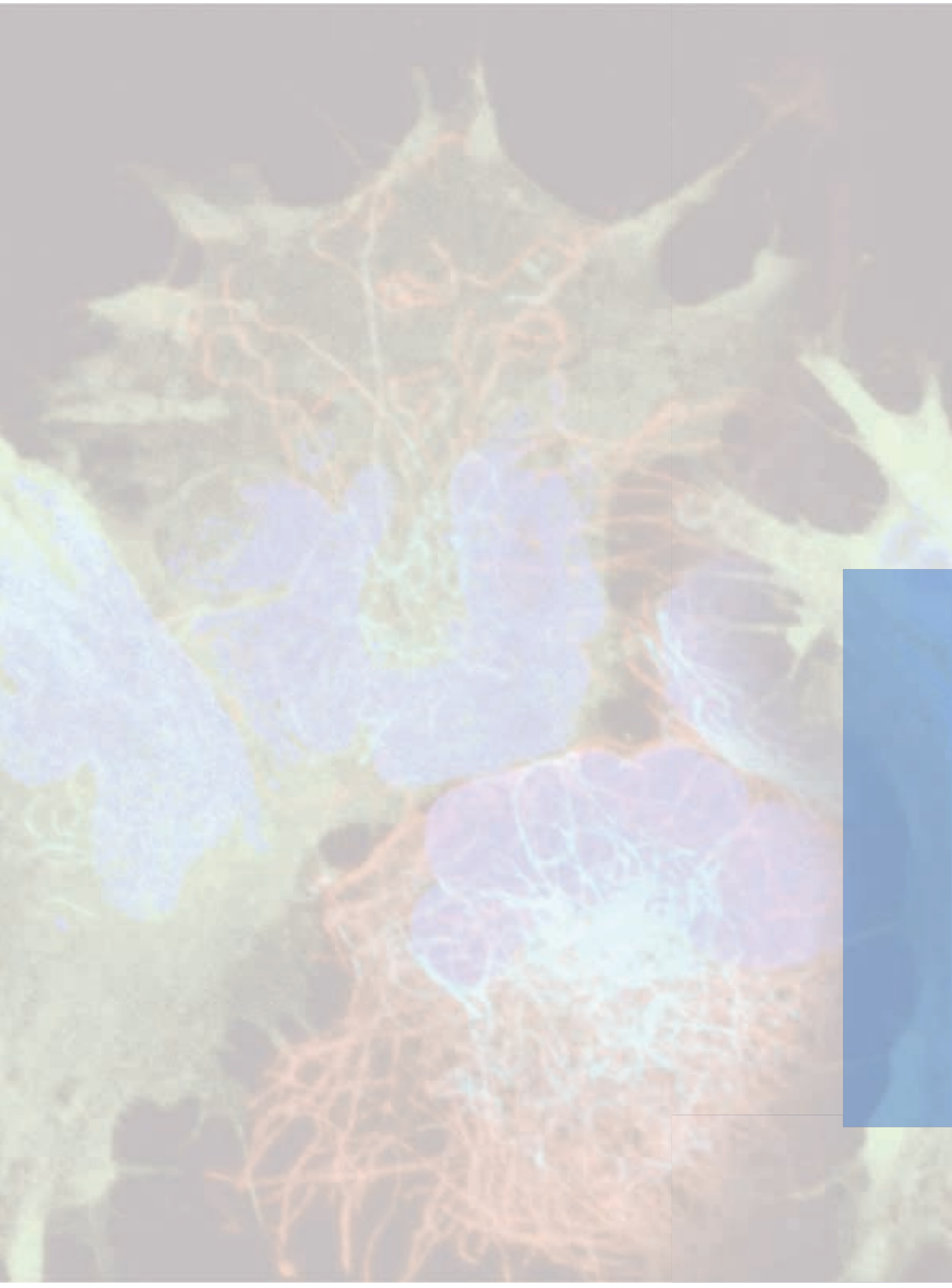
The innovative spirit of the Valdecilla mark is particularly evident in IDIVAL, conceived with the goal of promoting R&D in the field of biomedical sciences at the Marqués de Valdecilla University Hospital with the contribution of the University of Cantabria, placing it at a level of national and international excellence.

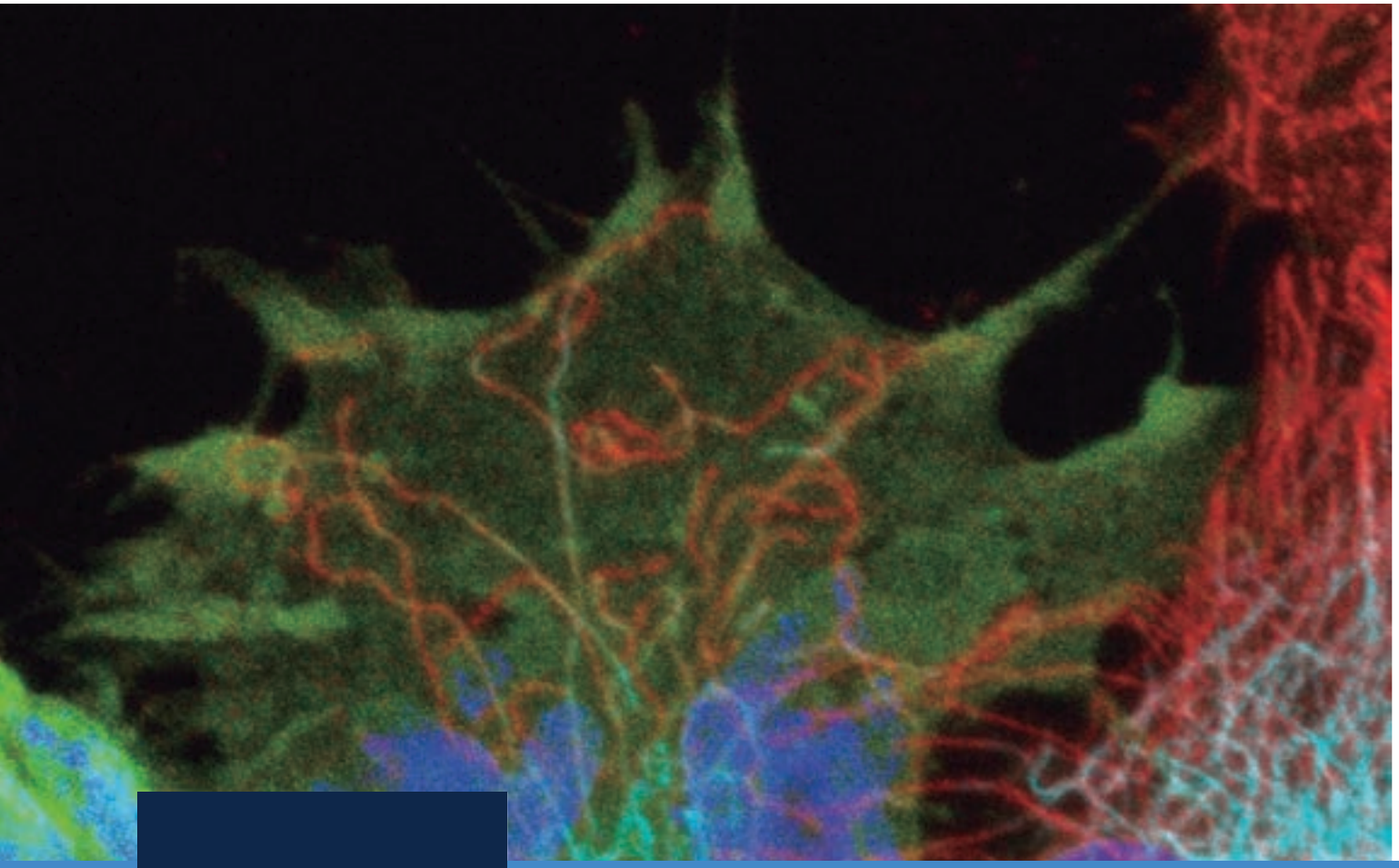
IDIVAL was conceived at the end of 2013 through an agreement between the Government of Cantabria and the University of Cantabria, as the heir of the Marqués de Valdecilla Training and Research Institute (IFIMAV).

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 the points set out in Royal Decree 339/2004 of 27 February. Therefore, the constitution of IDIVAL implies strong support of its founding institutions, the University of Cantabria and the Government of Cantabria for health research in the Valdecilla setting.

Taking over from IFIMAV, IDIVAL was launched in 2014 to harmoniously integrate basic, clinical and public health research, encouraging translational research and promoting a better transfer of the scientific progress obtained in addressing the most prevalent health problems.







IDIVAL

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

IDIVAL encourages the development of knowledge. IDIVAL promotes activities for the development of excellent scientific production, and has established 15 high-impact research groups in six areas of research: Cancer, Neuroscience, Transplants, Infection, Metabolism, and Transversal. Another 14 groups are also contributing to scientific production.

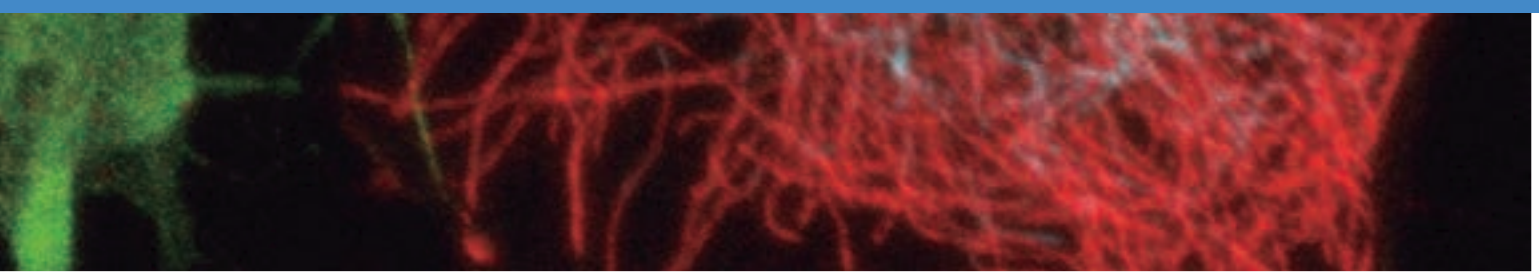
IDIVAL pursues excellence. In 2016, IDIVAL's researchers published high-impact works in collaboration with some of the world's best research groups in various biomedical disciplines. Our impact factor was over 1915 points in 2016. We have accumulated over 100,000 citations in international literature.

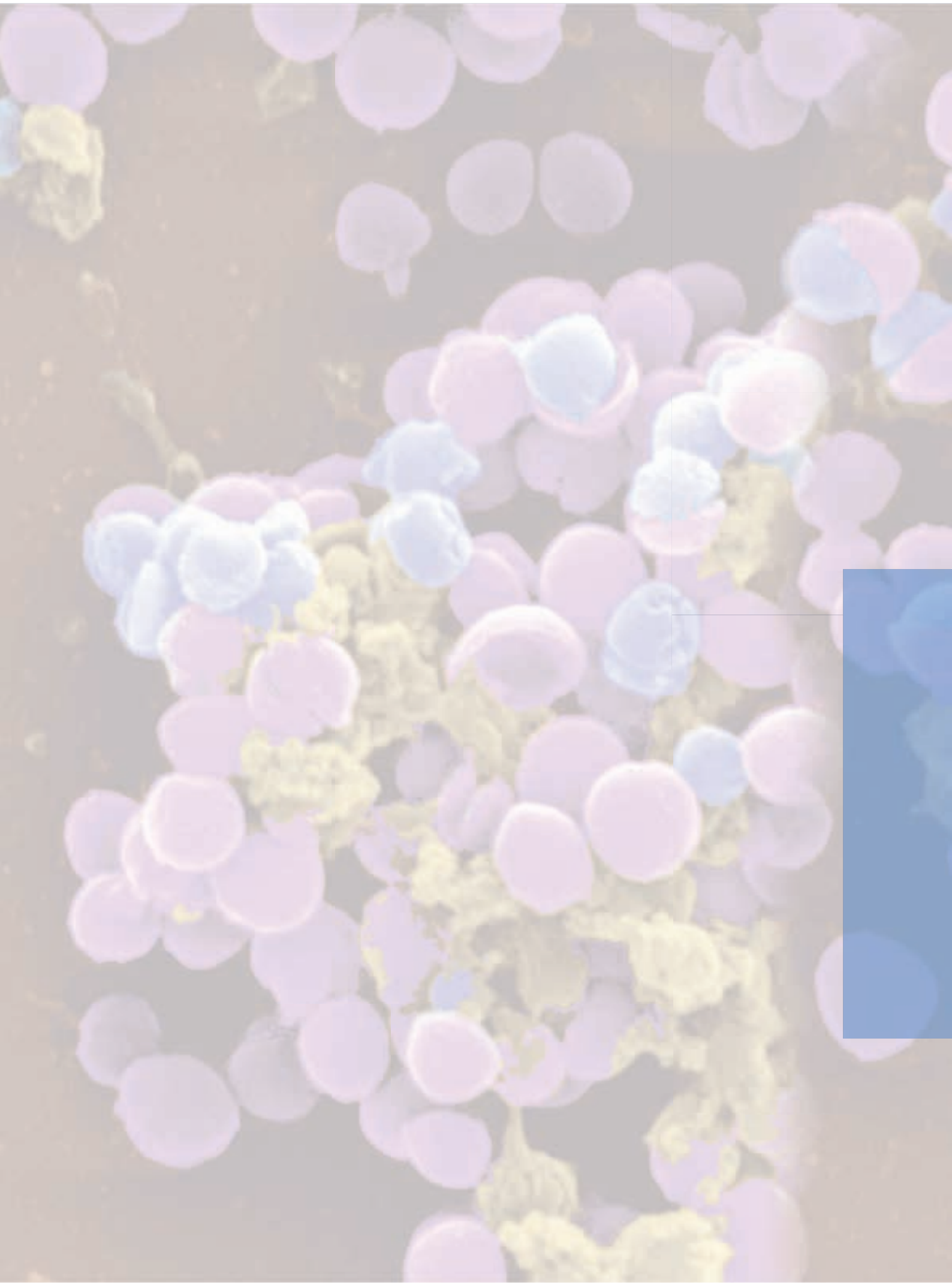
IDIVAL supports researchers. In 2016, we launched several programmes to support innovation and research. IDIVAL issued grants for healthcare research worth over a million euros in 2016.
IDIVAL is committed to society.

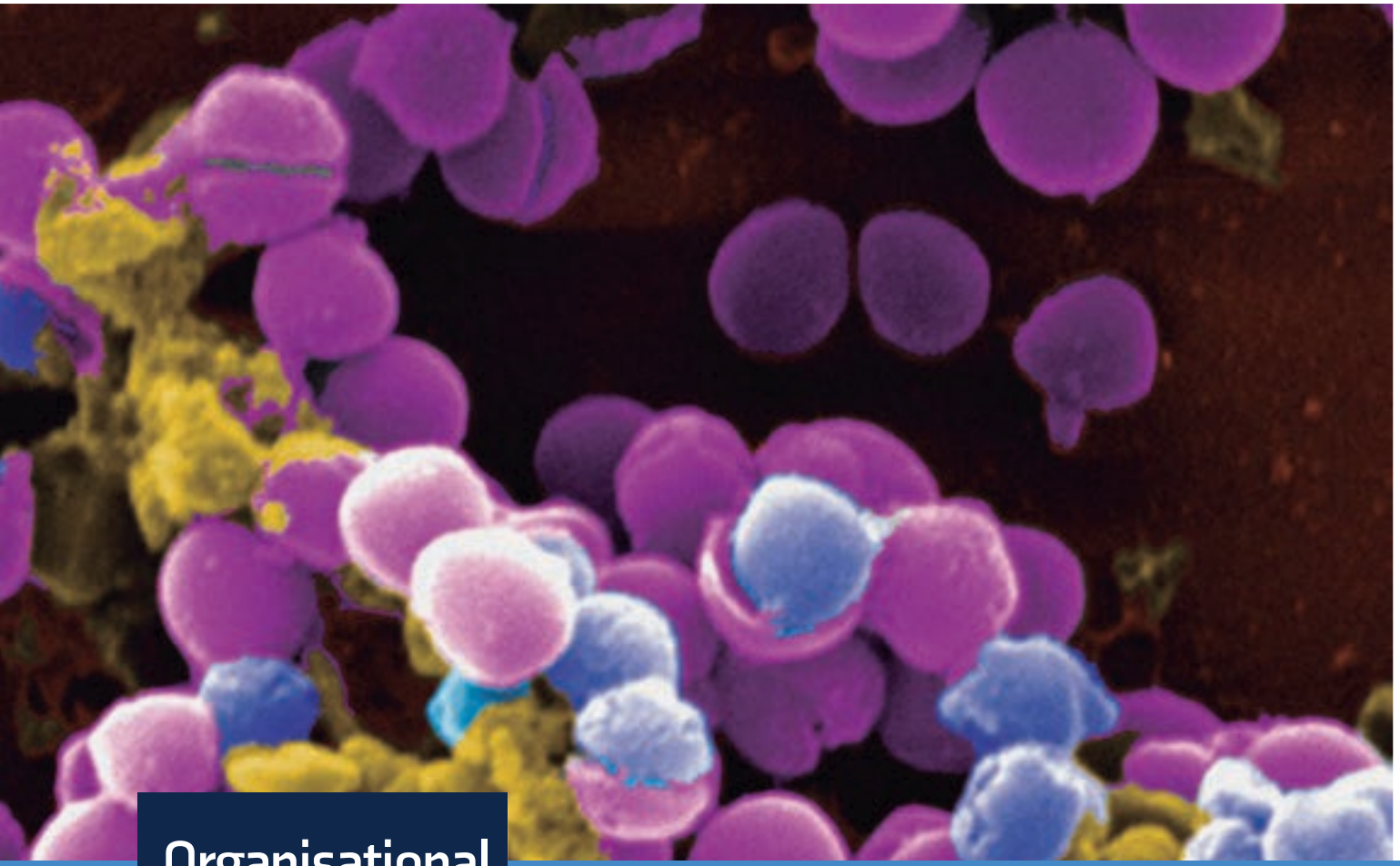
IDIVAL seeks to improve translational research and promote progress in Cantabria. Its goals include the development of knowledge, technological progress, and innovation in healthcare. IDIVAL's current challenge is to maximise the application of research results to improve healthcare.

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 accredited healthcare research institutes.





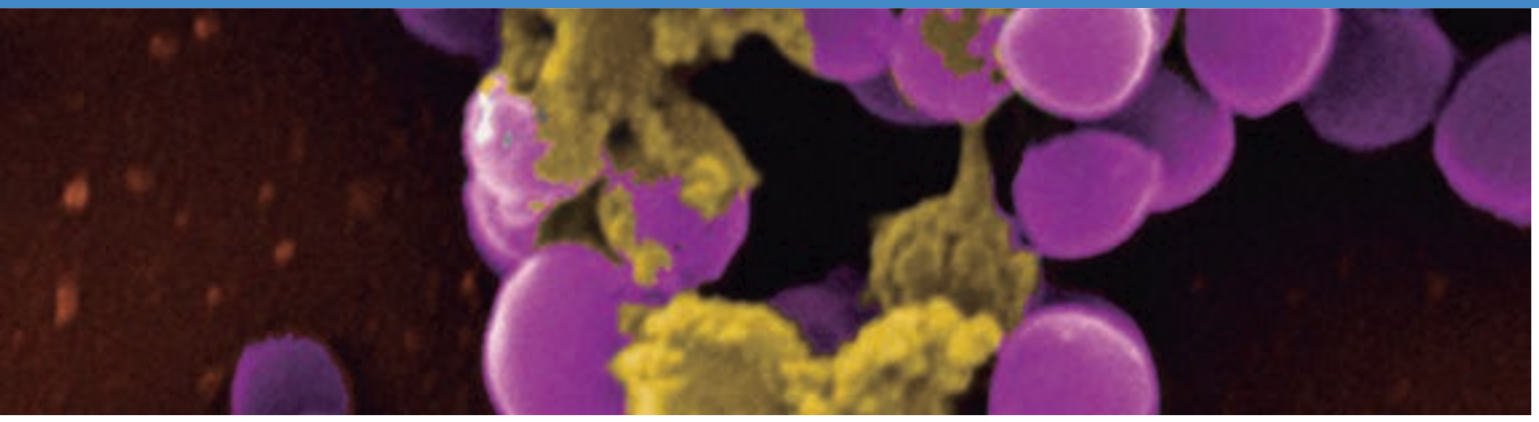


Organisational Structure

Governance and Advisory Bodies

IDIVAL is governed in accordance with its by-laws 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 Clinical Research Ethics Committee of Cantabria and the Bioethics Committee at the University of Cantabria in compliance with the requirements of clinical research and animal research, respectively



The board of IDIVAL

In accordance with the IDIVAL by-laws 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. Among its functions are 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 2015, the Board was made up of the following individuals:

President:

Dª. María Luisa Real González.
Minister of Health and Social Services of the Government of Cantabria.

Vice-president:

D. Ángel Pazos Carro.
Dean of the University of Cantabria.

Chairs:

D. Javier León Serrano.
Assistant Dean of Research and Knowledge Transfer. University of Cantabria.

Dª. María de la Cruz Reguera Andrés.
General Secretary. Ministry of Health.

D. María Antonia Mora González.
General Director of Planning and Healthcare Ministry of Health.

D. Julián Pérez Gil.
Manager director of the Cantabrian Health Service.

D. Julio Pascual Gómez.
Managing Director of the Marqués de Valdecilla University Hospital.

D. Piero Crespo Baraja.
Profesor del CSIC. Director del Instituto de Biomedicina y Biotecnología de Cantabria.

D. Manuel Gómez Fleitas.
Department Head. General Surgery Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Surgery. University of Cantabria.

D. Pedro José Prada Gómez.
Department Head. Radiation Oncology Department. Marqués de Valdecilla University Hospital.

D. 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

D. Javier Crespo García.
Professor in the Department of Molecular Biology. University of Cantabria Director of the Institute of Biomedicine and Biotechnology of Cantabria.

D. Luis Martínez Martínez.
Head of the Microbiology Department. Marqués de Valdecilla University Hospital. Tenured Professor in the Department of Molecular Biology. University of Cantabria

D. José Antonio Amado Señarís.
Section Head of the Endocrinology Department. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

Secretary, non-board:

D. Joaquín Cayón de las Cuevas.
Head of the Legal Counsel Office of the Ministry of Health

The IDIVAL Board met twice in 2016. At these meetings, the audited accounts and annual report for 2016 and action plans and budget for 2017 were approved.

Delegated Committee

President:

D. Julio Pascual Gómez.
President according to the by-laws as Managing Director of the Marqués de Valdecilla University Hospital.

Chairs:

D. Javier León Serrano.
Assistant Dean of Investigation and Knowledge Transfer. University of Cantabria Representative of the University of Cantabria.

Dª. Mª de la Cruz Reguera Andrés.
General Secretary. Ministry of Health.

D. María Antonia Mora González.
General Director of Planning and Healthcare Ministry of Health.

D. José Antonio Riancho Moral.
Section Head. Internal Medicine Department. Marqués de Valdecilla University Hospital. Representative of the University of Cantabria. Professor in the Department of Medicine and Psychiatry. University of Cantabria.

D. Luis Martínez Martínez.
Head of the Microbiology Department. Marqués de Valdecilla University Hospital. Tenured Professor in the Department of Molecular Biology. University of Cantabria Representative of the Healthcare Administration.

Governance

IDIVAL's senior management body consists of a Scientific Director and a Managing 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. The scientific director of IDIVAL in 2016 was Miguel Angel Piris, Head of the Pathological Anatomy Department, Marqués de Valdecilla University Hospital (he resigned as scientific director in February 2017).

Managing Director:
The Managing Director acts as the representative and spokesperson for the Foundation in its dealings with other institutions in relation to management activities, and manages the Institute's internal organisation and research infrastructure. The Managing Director of IDIVAL in 2016 was Galo Peralta Fernández.

Consejo científico externo

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 Directorate of IDIVAL and advises on the evaluation of the Institute's activity.

The current Council was appointed in 2009 as the advising body of the now defunct IFIMAV. Since then, some changes to its roster have been made. The appointment of its members was endorsed by the IDIVAL Board in its meeting on 25 February 2014, through a proposal from the management at IDIVAL.

It is made up of the following individuals:

President:

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

Chairs:

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

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

Juan Bernal Carrasco.
Professor of Research of the Superior Council of Scientific Researchers (CSIC), Director of the Department of Endocrine and Nervous System Pathophysiology. Alberto Sols Institute of Biomedical Research.

Miguel Delgado Rodríguez.
Professor of Preventative 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 Investigation. CSIC-University of Salamanca.

José Carlos Flórez.
Chief, Diabetes Unit. Investigator, Center for Genomic Medicine; Massachusetts General Hospital. Associate Professor; Harvard Medical School. Institute Member; Broad Institute.

Internal Scientific Council

EL Consejo Científico Interno está presidido por el Director Científico de IDIVAL y está integrado por investigadores nombrados por el Patronato. El Consejo Científico Interno de IDIVAL ha sido nombrado, a propuesta del Director Científico, por el Patronato en reunión de 25 de Febrero de 2014.

Su composición en 2016 ha sido la siguiente:

President:

Miguel Ángel Piris.
Scientific Director of IDIVAL. Head of the Pathological Anatomy Department. Marqués de Valdecilla University Hospital. (He ceases in February 2017).

Chairs:

Marcos López Hoyos.
Coordinator of the Organ and Tissue Transplant and New Therapies Area. Head of the Immunology Department. Marqués de Valdecilla University Hospital. Professor of the Department of Medicine and Psychiatry. University of Cantabria.

Benedicto Crespo Facorro.
Coordinator of the Neuroscience Area. Section Head. Psychiatry Department. Marqués de Valdecilla University Hospital. Professor of the Department of Medicine and Psychiatry. University of Cantabria.

Fernando Rivera Herrero.
Coordinator of the Cancer Area. Head of the Oncology Service. Marqués de Valdecilla University Hospital. Universitario Marqués de Valdecilla.

Javier Llorca Díaz.
Coordinator of the Cross-Disciplinary Area. Professor of Preventative Medicine and Public Health. University of Cantabria.

María Carmen Fariñas Álvarez.
Coordinator of the Infectious Diseases and Immune System Area. Head of the Infectious Diseases Service. Marqués de Valdecilla University Hospital. Tenured Professor of the Department of Molecular Biology. 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 of 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 Iidestive Disease Service. Jefe del Servicio de Digestivo. Professor of the Department of Medicine and Psychiatry. University of Cantabria.

The Internal Scientific Council of IDIVAL met in 2016 on 10 occasions, and among other aspects it has monitored the Strategic Plan 2011-2016, participated in the design of the new Strategic Plan 2017-2020, revised the program of grants of IDIVAL , The annual report and the projects presented to the Convocation of the Strategic Action in Health.

The IDIVAL Board of Trustees has approved the incorporation of two new members, Dr. Javier Crespo García, Fernando Rivera Herrero, and the renewal of the Coordinators of the Transplant and Infection and Immunity Areas to IDIVAL's Internal Scientific Council.


IFIMAV
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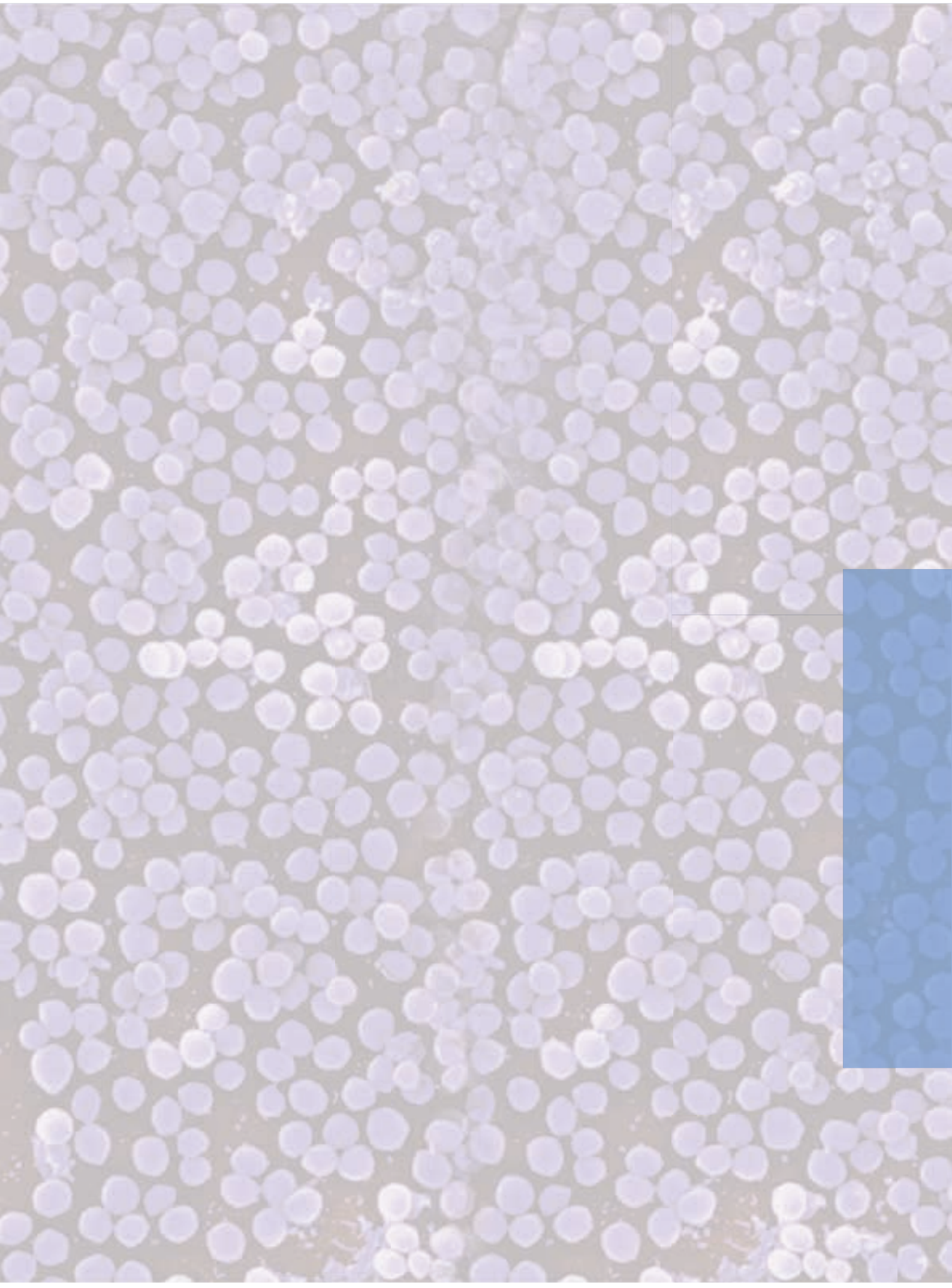
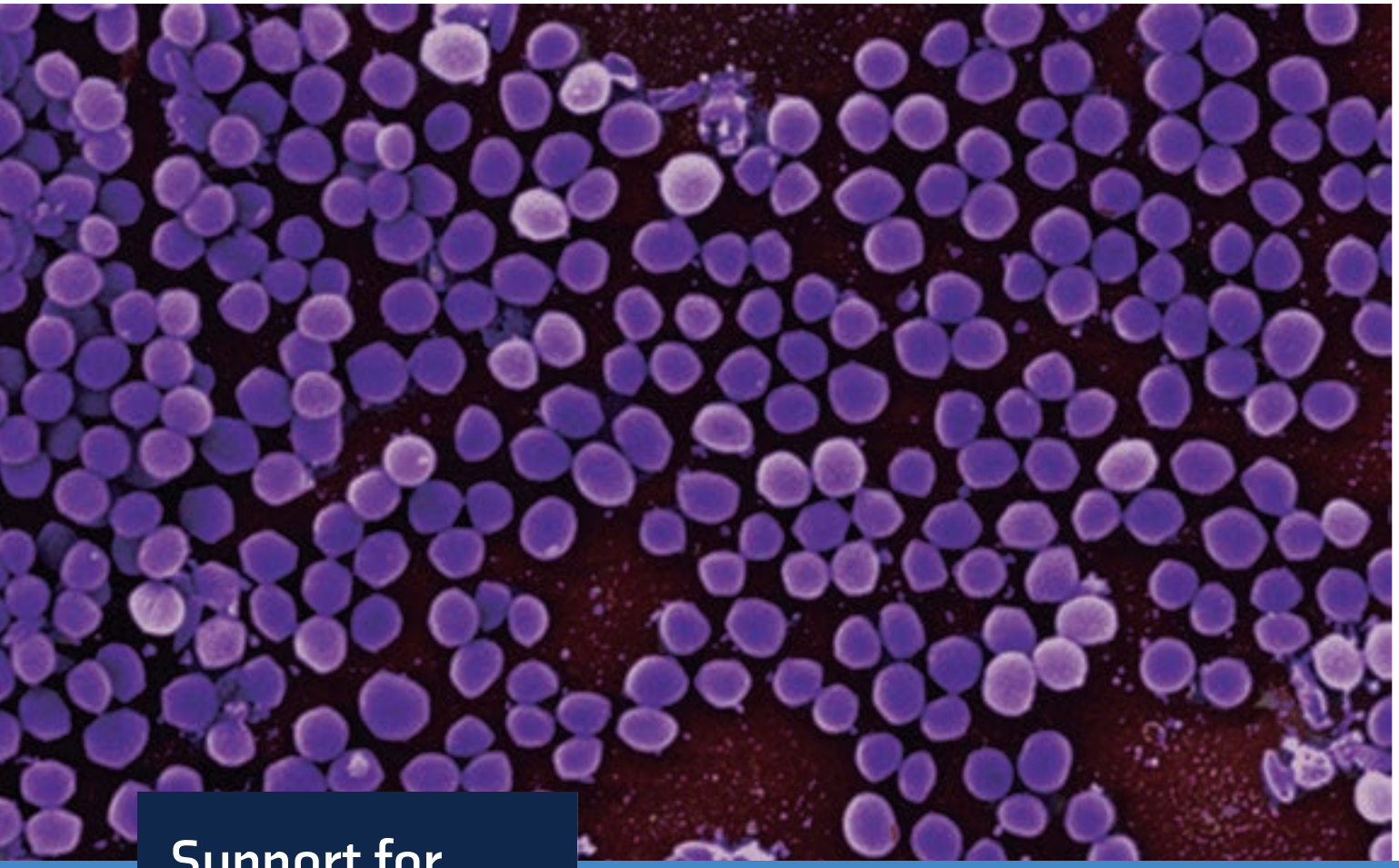
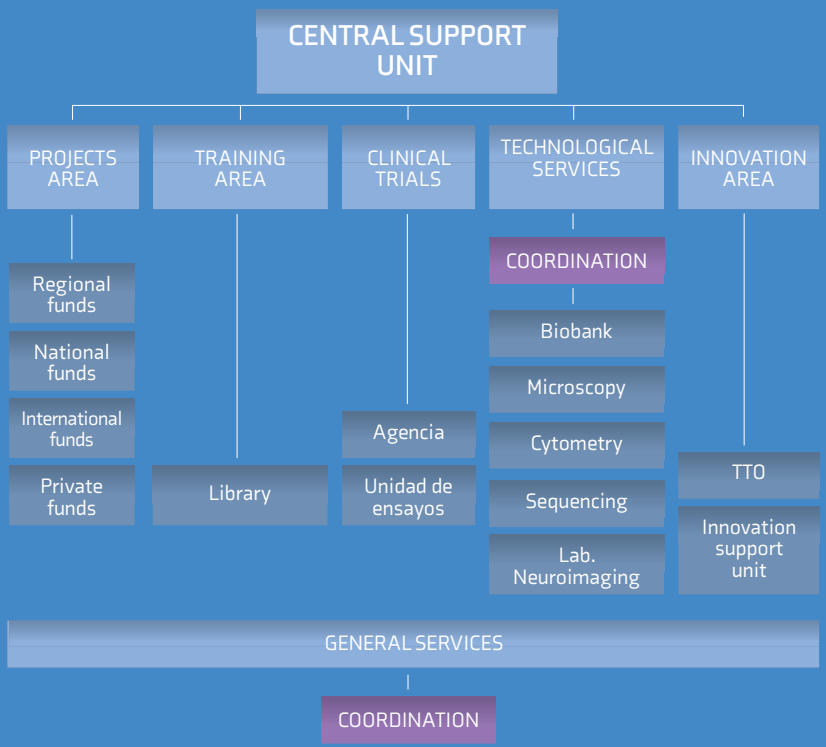
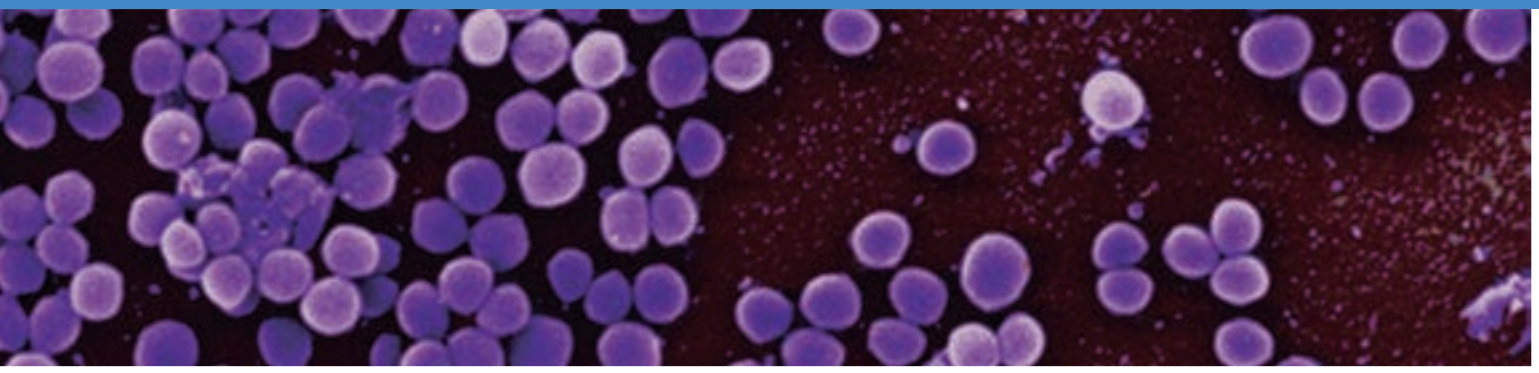




Support for researchers

Valdecilla, and in a broader sense, the entire biomedical environment of Cantabria, is able to develop its work with elements to support the research that unites IDIVAL's Central Support Research Unit. This Unit is organised into six areas: Projects Area,Training and Methodological Support Area, Clinical Trial Area, Technological Support Area, Innovation Area and General Services Area.





IDIVAL Building

IDIVAL has its own facilities, located within the physical setting of the Marqués de Valdecilla University Hospital. The IDIVAL building measures 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 rooms. In 2015 the laboratory area was extended to house the Neuroimaging Laboratory.

General Services Area

The General Services Area of IDIVAL brings together the resources needed for the cross-cutting management and support of the other areas at IDIVAL.

Coordinator:

Julio Muela Carriles. (IDIVAL)

Technicians:

Accounting:
Javier Arce Saiz. (IDIVAL)
RRHH:
Aroa Sanz Carreira. (IDIVAL)

Administrative staff:

Billing:
Laura del Río Celis. (IDIVAL)
RRHH:
María José San Emeterio. (IDIVAL)
Registry:
Elena Calvo Llano. (IDIVAL)

Projects Area

The Projects Area at IDIVAL brings together the resources needed to manage the grants promoted by IDIVAL itself as well as the application, execution and justification of both public and private funds at the disposal of the IDIVAL research groups.

Technicians

Beatriz García González. (IDIVAL)
Raquel Leal García. (IDIVAL)
Charo González Cabria. (IDIVAL)
Lorena Agüero Cobo. (IDIVAL)

Innovation Area

IDIVAL has an Innovation Area, which forms part of the ITEMAS Platform of the Carlos III Health Institute (ISCIII). It also includes a Results Transfer Office (OTRI), which is part of the Spanish 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 funding, as well as all activities needed to ensure that the R&D results from IDIVAL research groups and researchers from the Cantabria Health Services reach society through public-private partnerships.

Technology Transfer Office:

Patricia Zorrilla de la Fuente. (IDIVAL)

Innovation Unit

Laura Herrero Urigüen. (IDIVAL)
Paloma Glez Álvarez. (IDIVAL)
Ana Temperán Galbán. (IDIVAL)
Health technology assessment (Evaltec®)
Marina Cano Iglesias. (IDIVAL)

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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

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. The catalogue can be accessed directly at s-hmv.c17.es

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.

Librarian:

Mario Corral García. (IDIVAL)

Administrative staff:

Rafael Lavín Fuentes. (HUMV)
Mª del Carmen Fuente San Bartolomé. (HUMV)

Clinical Trials Area

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

In 2016, Cantabria introduced a new form of contract for clinical trials, in line with national regulations and providing greater transparency, substantially improving the management of clinical trials within IDIVAL.

Clinical Trial Agency

SCReN Spanish Clinical Research Network

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.

Technician:

María Rodríguez Rodríguez. (IDIVAL)

Administrative staff:

Blanca del Pozo Fernández. (IDIVAL)
Lorena Martín Guerra. (IDIVAL)

Clinical Trials 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. It provides support for highly complex clinical trials in the Valdecilla environment.

Equipment:

Mª Blanca Sánchez Santiago. (Clinical Pharmacology Department, HUMV)
Mª Ángeles de Cos. (Clinical Pharmacology Department, HUMV)
Javier Adín Ibarra. (Clinical Pharmacology Department, HUMV)
Nuria Sánchez Avelló. (HUMV)
Amaya Riaño Laguillo. (IDIVAL)

Technology Support Services Area

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

Technology Services are Coordinator:

Mª José Marín Vidalled.
(IDIVAL).

Valdecilla Biobank

The Biobank VALDECILLA is a hospital biobank that manages human biological samples with the purpose of supporting biomedical research through the collection, storage and transfer of samples and associated clinical data, all in the strictest conditions of quality and confidentiality.

It is functionally organized in three Nodes: the DNA and Fluid Node, located on floor 0 of the IDIVAL building and the Solid Sample Nodes, and neurological tissues located in the Pathology Department of the Marqués de Valdecilla Hospital. The biobank has a large catalog of collections of samples of various pathologies of high scientific interest and also provides a variety of services derived from the use of its equipment, offering comprehensive support to researchers whose projects involve the use of human biological samples.

Biobank Valdecilla is one of the units that form part of the Hospital Biobanks Platform of the Carlos III Health Institute, which has four programs: promotion of strategic collections, promotion of network services, R & D in biobanks and ethical aspects, Legal and social.

In December of 2015 the biobank renewed the authorization of the Ministry of Health of the Government of Cantabria to function as a biobank. This authorization implies compliance with the requirements established in Royal Decree 1716/2011 of November 18 and its incorporation in the National Registry of Biobanks of the Carlos III Health Institute.

In November 2015, Biobank Valdecilla has achieved ISO9001: 2015 quality management.

Scientific Director:

Pascual Sánchez Juan.
(Neurology Service, HUMV)

DNA AND FLUIDS NODE

Coordinator:

Mª José Marín Vidalled.
(IDIVAL)

Technicians:

Inés Santiuste Torcida. (IDIVAL)
David Ramos Melendro. (IDIVAL)

TISSUES NODE

Coordinator:

Santiago Montes Moreno.
(Pathology Service, HUMV)

Technicians:

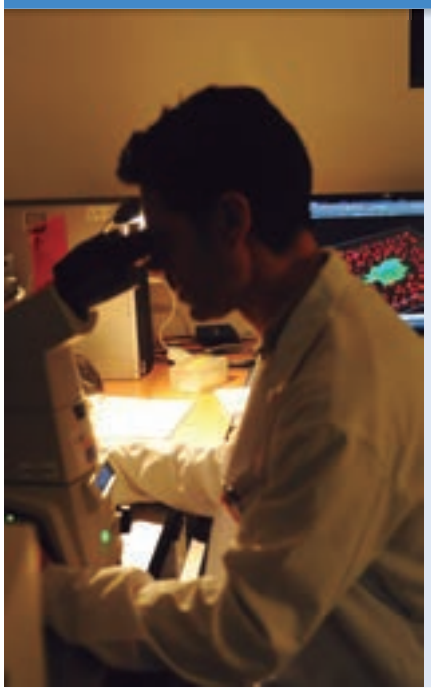
José Bernardo Revert Arce.
(IDIVAL)

NEUROLOGICAL TISSUES NODE

Coordinador:

Nuria Terán Villagrá.
(Pathology Service, HUMV)

Laser Microscopy Unit



The IDIVAL Laser Microscopy Unit offers a high-end microscopy service to its own and external research groups with the fundamental objective of obtaining a full performance in their fluorescence studies in the shortest possible time. For this purpose, it has the latest generation equipment consisting of two imaging systems, a specular confocal laser microscope (LSM) and fully automated Nikon A1R combined TIRF, which allows high-quality confocal image capture of cells and molecular events at high speed and sensitivity, And a live cell device with a motorized NIKON Ti microscope equipped with an epifluorescence module, incubation and micro-injection systems and an optical system that allow the tracking of fast processes in living cells.

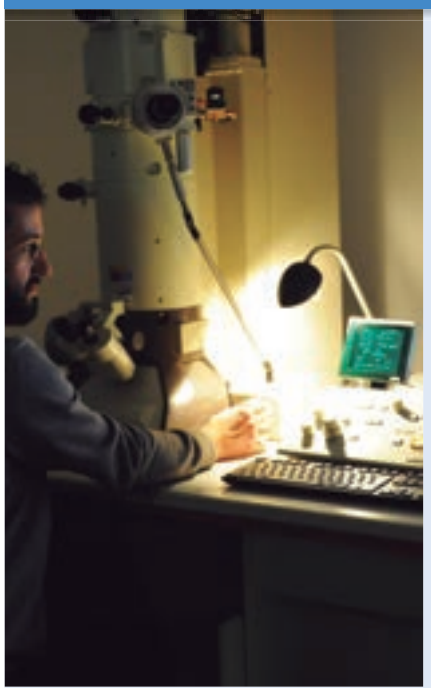
Scientific coordinator:

Mónica López Fanarraga.
(UC)

Superior Technician:

Fidel Madrazo Toca.
(IDIVAL)

Electronic Microscopy Unit



The Electronic Microscopy Unit began its activity in early 2012. It has a transmission microscope JEOL, Model JEM-1011 equipped with a Gatan digital camera, mod. SC1000 Orius high resolution solution that provides excellent image quality. This microscope allows the analysis of ultrafine sections of cells and tissues, as well as observation of microorganism preparations and macromolecular complexes contrasted with negative staining.

Each year, both laser microscopy and electron microscopy units organize a microscopy and sample preparation course for researchers and support staff.

Scientific coordinator:

Miguel Lafarga Coscojuela.
(UC)

Technician:

Fidel Madrazo Toca.
(IDIVAL)

REMOA

Cytometry and Cell Separation Unit

The Flow Cytometry and Cell Separation Unit was created in 2005 as a support unit to IDIVAL research and operates in the IDIVAL building within the Laboratory of the Research Group of Transplantation and Autoimmunity. The aim of this unit is to provide technical and methodological support regarding the use of flow cytometry and cell separation; this service is offered both to researchers at the centre and any external group that needs it. It has an upgraded FACSAria II (BD Biosciences) cytometer/sorter updated in 2013, a FACSCanto cytometer (BD Biosciences) and an Auto-MACS Pro Separator (Miltenyi Biotec) magnetic bead cell separator, which allows for the separation of cell populations in infertility.

The Unit organises an annual course on flow cytometry in collaboration with the Inbiomed Cytometry Unit intended for both researchers and health workers.

Scientific Coordinator:

Marcos López Hoyos.
(Immunology Service, HUMV)

Technical coordinator:

David San Segundo Arribas.
(Immunology Service, HUMV)

Laboratory coordinator:

David Merino Fernández.
(IDIVAL)

Genomics Unit

The Genomics Unit works under the Molecular Genetics Unit of the Marqués de Valdecilla University Hospital, located on the first floor of the IDIVAL building. It has functioned as such since 2002, performing care-related genetic studies for hospitals and health centres in Cantabria and other regions and providing primarily sequencing services.

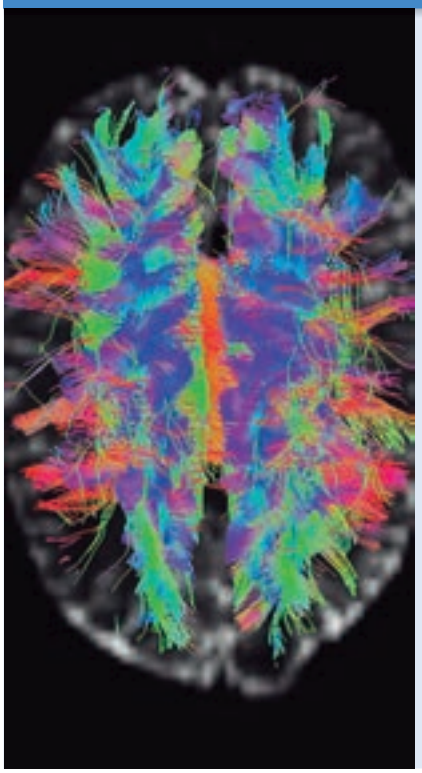
Scientific Coordinator:

José Luis Fernández Luna.
(Molecular Genetics Unit, HUMV)

Technicians:

Ana Fontalba Romero.
(HUMV)
Olga Gutiérrez Saiz.
(IDIVAL)

Neuroimaging Unit



This laboratory has implemented and developed a wide range of techniques for quantitative image analysis of the human brain obtained by magnetic resonance imaging (MRI), which is now at the service of 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 of interest (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 coordinatori:

Benedicto Crespo Facorro.
(Psychiatry Service, HUMV)

Technicians:

Diana Tordesillas Gutiérrez.
(IDIVAL)
Roberto Roiz Santibáñez.
(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.

Animal housing and experimentation services. (SEEA)

Materials characterisation service. (SERCAMAT)

Optical transmission microscopy service. (SERMET)

Supercomputing service Hydrobiology laboratory.
(I. Hidráulica)

Chromotography service.

Advanced microscopy. (IBBTEC)

Mass sequencing service.
(IBBTEC)

IDIVAL Research Grants

IDIVAL has a line of research grants focusing on fostering talent. Each of these programmes has a clear educational focus and the description of their activity is featured in the training section of this report. In 2016, IDIVAL launched the following grants:

- **Inn-Val Grants.** Awarded to Innovation projects.
- **Next-Val Grants.** Awarded to projects for young researchers.
- **Ges-Val Grants.** A research training scholarship.
- **Int-Val Grants.** For research intensification.
- **Ment-Val Grants.** Mentoring programme for resident doctors.

Production grants (support programme).

- **Summer internships.**
- **Pre-doctorate contracts.**
- **Innplant programme.** Programme to implant clinical researchers as Heads of Department at the Marqués de Valdecilla University Hospital.
- **Post-MIR** Wenceslao López Albo contracts programme (described in the training section of the report).
- **Complementary personnel** for projects from the National Plan.
- National call for **"Enfermería Valdecilla"** research projects.
- Scholarship for training in spine surgery for traumatology and orthopaedic specialists, and in neurosurgery.

The total amount of IDIVAL grants awarded in 2016 was as follows:

Grants Programme	Amount awarded (€)
Inn-Val grants	105.000 (7 projects)
Next-Val grants	100.000 (9 projects)
Ges-Val grants	57.960 (one grant lasting three years)
Int-Val grants	60.000 (2 intensification programmes over 6 months)
Ment-Val grants	8.000 (1 project)
Production grants	401.546 (one grant per group, 30 groups)
Summer internships	2.800 (4 internships of 2 months)
Predoctoral contracts	329.600 (4 contracts for 4 years)
Post-MIR Valdecilla contract programme	262.962 (3 contracts for 2 years)
Complementary personnel for National Plan projects	46.875 (cofunding 5 contracts)
National call for "Enfermería Valdecilla" research projects	7.000 (2 projects)
Scholarship for training in spine surgery for traumatology and orthopaedic specialists, and in neurosurgery	19.089 (1 scholarship)
Total awarded	1.400.832 €

INN-VAL Grants

In 2015, IDIVAL implemented the Inn-Val grant programme, in collaboration with the Botín Foundation, which acted as co-financier, focusing on the development of innovative technological and healthcare projects. The programme seeks to promote the transfer of knowledge to society and the market, and to integrate local agents in the Valdecilla environment. In 2016, the grants announced in 2015 were awarded, and a second round of grants was announced, which will be awarded in 2017. The following projects were awarded grants in 2016:

Main researcher:
Conde Portilla, Olga María.
Diagnosis of tendinous chordae of the human mitral valve using multiple approaches in analysis: optical, mechanical, micro-structural, and anatomical (DICUTEN).
Amount awarded: €15,000.

Main researcher:
Crespo Facorro, Benedicto.
Technological solution to prevent relapses and for rehabilitation in schizophrenia.
Amount awarded: €15,000.

Main researcher:
Delgado Alvarado, Manuel.
Augmented reality device combined with subsensory mechanical feedback in the treatment of motor blocks in Parkinson's disease.
Amount awarded: €15,000.

Main researcher:
Gómez Ruiz, Marcos.
Development of hardware and software applicable to stereotactic navigation of the pelvic organs.
Amount awarded: €15,000.

Main researcher:
González-Blanch Bosch, César.
Cost-effectiveness of transdiagnostic psychological group therapy for common mental disorders in a Healthcare Centre (PsicAPCantabria): a randomised controlled clinical trial.
Amount awarded: €15,000.

Main researcher:
Riancho Zarrabeitia, Javier.
New RXR agonists as a treatment of ALS.
Amount awarded: €15,000.

Main researcher:
Villegas Sordo, Juan Carlos.
Design of bio-synthetic nano-dispensers to transport treatments to the motor neuron cytoplasm.
Amount awarded: €15,000.

NEXT-VAL Grants

In 2016 IDIVAL announced the second round of NEXT-VAL (NEXT generation VALdecilla) grants for the development of one- or two-year research projects led by novice researchers, in order to encourage the recruitment of new researchers in the Valdecilla environment. This call for NEXT-VAL research projects is intended for translational research projects led by Main researchers who have never received this type of competitive access grant in such a role. The five projects selected in 2016 were:

Main researcher:
San Segundo Arribas, David.
Project: Myeloid-derived suppressor cells (MDSC) and immune regulation in kidney transplants: differential effect between calcineurin and mTOR inhibitors and evaluation as post-transplantation biomarkers.
Amount: € 20,000.

Main researcher:
Riancho Zarrabeitia, Javier.
Project: Alzheimer's disease and Down syndrome: a clinical and experimental approach.
Amount: €15,000.

Main researcher:
Mondejar Garcia, Rufino Marceliano.
Project: Directed therapy guided by molecular markers in patients with cutaneous T-cell lymphoma.
Amount: €10,000.

Main researcher:
Martín Rodríguez, Rosa.
Project: Development of multifunctional nanoparticles for cancer diagnosis and treatment.
Amount: €10,000.

Main researcher:
Fradejas Sastre, Victor.
Project: Impact on quality of life and functionality of patients with percutaneous aortic valve implantation compared to aortic valve replacement surgery.
Amount: €10,000.

Main researcher:
Collado Garrido, Luisa.
Project: Effectiveness of resistance therapy on the motion, quality of life and safety of acute stroke patients: Randomised controlled trial.
Amount: € 5,000

Main researcher:
Campos Juanatey, Felix.
Project: Etiological diagnosis and treatment of complex urinary probes using portable urethrocystoscopy.
Amount: €10,000

Main researcher:
Arias Loste, María Teresa.
Project: Effects of chronic hypercapnia, with or without hypoxia, on the hepatic level. Hepatocyte culture study and validation in a cohort of patients with fatty liver disease from normal clinical practice.
Amount: €10,000

Main researcher:
Alonso González, Carolina.
Project: Study of the sensitising effects of melatonin on neoadjuvant chemotherapy in breast cancer treatment.
Amount: €10,000

GES-VAL Grants

In 2015, IDIVAL launched a grant programme for the development of a plan for training activities in science and health technology research management to be carried out at IDIVAL over a period of two to three years, with a second round announced in 2016. This programme promotes the training of technicians in this field, as they learn different aspects of management, monitoring and evaluation of research projects.

INT-VAL Grants

In 2016, IDIVAL introduced the Int-Val programme (Intensification of research - Valdecilla) 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.
The two researchers receiving intensification grants in 2016 were:

Benedicto Crespo Facorro.
Duration: 6 months

Miguel Ángel González Gay Mantecón.
Duration: 6 months

MENT-VAL Grants

In 2016, IDIVAL launched a mentoring programme for resident doctors at Valdecilla, intended to attract new medical professionals finalising their training, young people with drive seeking excellence, and also as a way to provide personalised specialist healthcare training and an introduction to research.
The selected candidate was Teresa Borderías Villarroel, who in 2016 chose the Cardiology Department at Marqués de Valdecilla University Hospital for her residency.

Production Grants

In 2016, IDIVAL allocated funds for the operating costs of groups, based on their production in 2015. This grant was calculated considering the impact factor of each IDIVAL research group in projects in which an author in the group is first or last, differentiating them from the impact factor of 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, and the responsibility of any group members to any IDIVAL platform were also considered. The following production grants were allocated to IDIVAL groups in 2016:

Group	Total €
Pathological anatomy and molecular pathology	19.188
Apoptosis	4.018
Nuclear cell biology	6.641
Cell cycle, stem cells and cancer	4.489
Cytokines and growth factors in pathological tissue plasticity phenomena	11.760
Clinic and genetics of headaches	13.541
Diagnosis and treatment by image	8.224
Neurodegenerative diseases	20.569
Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	49.945
Epidemiology and pathogenic mechanisms of infectious diseases	9.553
Epidemiology and public health	19.185
Genomics of cancer	34.782
Nanovaccines and cellular vaccines based on listeria monocytogenes and their applications in biomedicine	4.512
Study Group on Hereditary Hemorrhagic Telangiectasia (Rendu Osler Weber)	3.213
Cardiovascular research group	6.436
Molecular image	6.488
Infection and immunity and digestive pathology	34.966
Immunopathology of rheumatic diseases	3.157
Melatonin and breast cancer	5.456
Mineral and lipid metabolism	22.201
Clinical and molecular microbiology	19.448
Advanced microscopy and folding of proteins and cytoskeleton	2.479
Nanomedicine	8.412
Hematologic Neoplasms and Hematopoietic Progenitor Transplantation	10.405
Neurophysiology in epilepsy and neurointensive	2.834
New techniques in abdominal surgery	6.025
Psychiatry	14.135
Cell signaling and therapeutic targets in cancer	19.288
Transplantation and autoimmunity	20.322
Unit for clinical trials and medical oncology	9.874

Addition of Complementary Personnel for Projects in the National R&D+I Plan

IDIVAL has co-financed personnel expenses for projects submitted to the National Plan call by researchers at the Institute. The following projects, started in previous years, were co-financed by IDIVAL for the hiring of complementary personnel. Staff recruited through this line of co-financing in 2016 have been offered their third and fourth contract years:

Principal investigator	Title	Funding
José Ramos Vivas.	Key host-pathogen interactions of clinical relevance in Acinetobacter species (PI 13/01310).	9.375€
Carmen Fariñas Álvarez.	Intestinal colonisation by multiresistant enterobacteriaceae in patients with renal and liver transplants: multicentre cohort study and randomised, controlled, open clinical trial (PI 13/01191).	9.375€
José Luís Fernandez-Luna.	Prognostic and therapeutic relevance in ODZ 1 glioblastoma, a new target in cancer (PI 13/01760).	9.375€
Mónica Lopez-Fanarraga.	Antineoplastic development based on nanomaterials (PI 13/01074).	9.375€
José Antonio Riancho Moral.	DNA Methylation: pathogenic and biomarker factors in bone formation disorders (PI 12/00615).	9.375€

Pre-Doctorate Contracts

In 2016, IDIVAL partnered with the University of Cantabria to launch the second pre-doctorate contract programme, in which seven candidates were selected (four funded by IDIVAL and three by the University of Cantabria) for a contract of up to four years with the goal of completing their doctoral theses.

The selected candidates and their thesis directors were:

Pre-doctoral contract holder:
Lourdes María Valdivia Fernández.
Director:
Mónica López Fanarraga. (UC)

Pre-doctoral contract holder:
Carmen Lage Martinez.
Director:
Pascual Jesús Sánchez Juan. (HUMV)

Pre-doctoral contract holder:
María Iglesias Escudero.
Director:
Marcos López Hoyos. (HUMV)

Pre-doctoral contract holder:
Lorenzo Joaquín Gutiérrez Avilés.
Director:
José Carlos Rodríguez Rey. (UC)

Summer internships

IDIVAL, in collaboration 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.

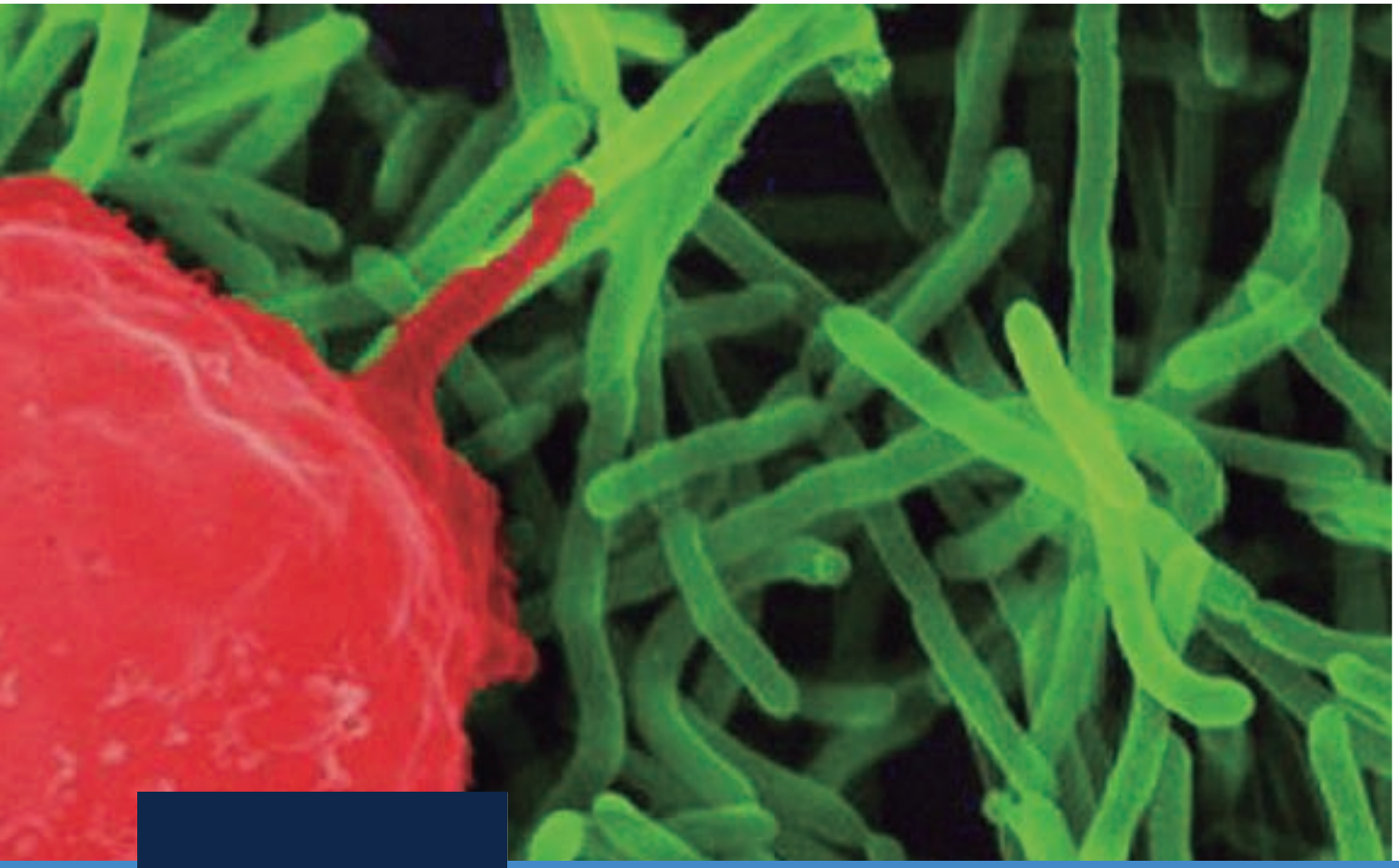
The students selected to work in the IDIVAL Group laboratories in 2016 were:

Estefanía Esteban Rodríguez.
Internship in Clinical and Molecular Microbiology.
PI: Jose Ramos Vivas.

Adriana Solís Angulo.
Internship at the Nanovaccines Group and cellular vaccines based on Listeria monocytogenes and their applications in biomedicine.
PI: Carmen Álvarez Domínguez.

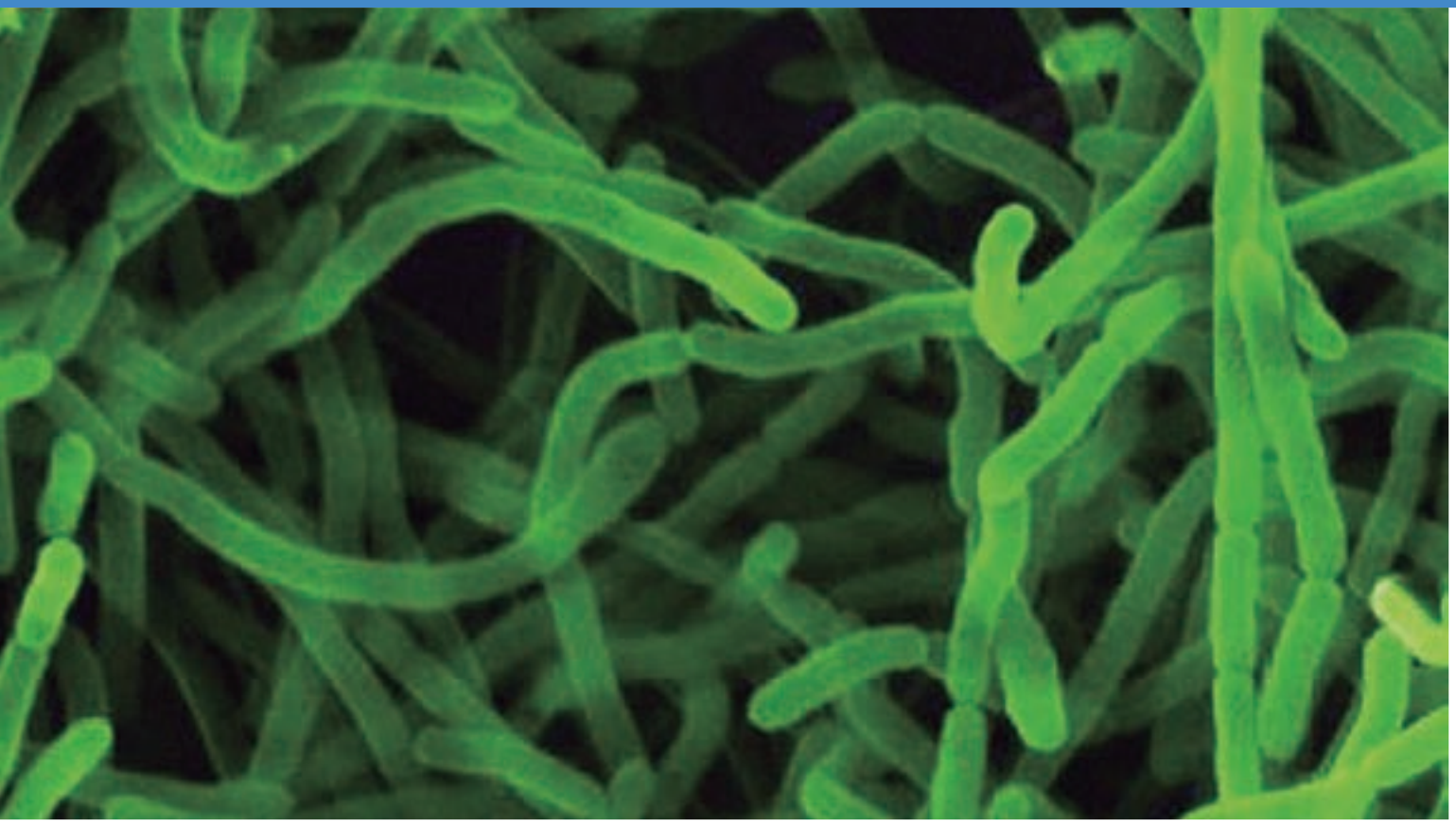
Fernando Andrés García.
Internship at the Transplantation and Autoimmunity Group.
PI: Marcos López Hoyos.

Sonia Aracil Gisbert.
Internship at the Cancer Genomics Study Group.
PI: Nerea Martínez Magunecelaya.



Training

IDIVAL considers research and innovation training and dissemination to be among the cornerstones of its activity. Therefore, it participates in a wide range of activities including ten different lines of training and dissemination.



Hospital Sessions

This dissemination activity includes monthly scientific sessions with the participation of internationally renowned guests and IDIVAL researchers, who lead sessions in the environment of the Marques de Valdecilla University Hospital (HUMV).

These sessions are interspersed with weekly hospital sessions at the HUMV. The 2016 sessions were the following:

JANUARY:

21: Commitment to quality at HUMV: Best in Class awards. Dr Julio Pascual Gómez, Managing Director. Marqués de Valdecilla University Hospital.

28: Challenges in molecular diagnostics in sarcomas. Dr Javier Crespo, Head of Department, Marqués de Valdecilla University Hospital.

FEBRUARY:

4: Contrast-induced acute renal failure. Dr A. L. Martin de Francisco. Nephrology Department. Marqués de Valdecilla University Hospital.

11: Presentation of the Chronic Disease Strategy for Cantabria. Dr I. Lapuente Heppe – SCS / Dr C. Fernández Viadero – Minister for Health.

18: The current value of the clinical autopsy. Dr Félix Arce Mateos, Pathological Anatomy Dept., Marqués de Valdecilla University Hospital.

25: Training leaders in brain health. Dr Bruce Miller, Aging and Memory Center UCSF (USA)

MARCH:

3: Clinical anatomy session: On various cases of sudden death. Dr Marta Mayorga Fernández, Pathological Anatomy Dept., Marqués de Valdecilla University Hospital.

10: Budget management at HUMV. Juan Carlos Dueñas, Deputy Director of Financial Management, Marqués de Valdecilla University Hospital.

17: New CPR guidelines? Dr Rodriguez Borregán. Intensive Care Dept., Marqués de Valdecilla University Hospital.

APRIL:

14: Multiresistant germs: the current situation at HUMV. Multiresistant workgroup, Marqués de Valdecilla University Hospital: Dr L. Martínez, Dr R Wallmann, Dr C. Fariñas.

21: Erectile dysfunction: A marker of health and quality of life. Dr J. A. Portillo Martín. Urology Dept., Marqués de Valdecilla University Hospital.

28: IDIVAL - Medical doctorate programmes. Current regulatory and operational aspects. Alberto Ruiz Jimeno, Dr B. Crespo and Dr D. Delgado. University of Cantabria.

MAY:

5: Major Outpatient Surgery: a commitment to the future Dr José María Capitán Vallvey, Head of the Surgery Dept., Jaén Hospital, National Coordinator of the National Association of Surgeons.

12: 1816-2016. The rise and fall of the art of auscultation. Dr J. Ramón Berrazueta, Cardiology Dept., Marqués de Valdecilla University Hospital.

19: Phlebitis Zero project. Multimodal strategy. Jose Luis Cobo Sánchez (Quality, Training and Research). Marqués de Valdecilla University Hospital.

26: Intraoperative neurophysiological monitoring: new horizons, new challenges. Dr Veldran Deletis / St. Luke's Hospital, N. York

JUNE:

9: The artificial heart at HUMV: seven years saving lives. Dr Virginia Burgos, Cardiology Dept., Marqués de Valdecilla University Hospital.

16: Genetics: Strategies for Translating Genetic Findings into Clinical Care. Dr David C. Glahn – Professor of Psychiatry and Psychology, University of Yale (USA)

23: Presentation of the results of the HUMV's Clinical Commissions. Dr Concepción Fariñas – Quality Coordinator. Marqués de Valdecilla University Hospital.

30: IDIVAL - Multiple Sclerosis in Cantabria: Advances and future challenges. Dr Vicente González Quintanilla; Post-MIR Valdecilla Lopez Albo contract.

OCTOBER:

6: Heart transplant with asystolic donors. Peter McDonald. Heart and Lung Transplant Unit. St. Vincent's Hospital. Sydney. Australia

13: Clinical-pathological session: neuropathology. Dr Nuria Terán. Anatomical Pathology Department, Marqués de Valdecilla University Hospital.

20: Workplace Risk Prevention Plan. Marco Antonio Gandarillas González, S. Occupational Medicine, Marqués de Valdecilla University Hospital.

NOVEMBER:

3: The Marquesa de Pelayo Library: tools for new challenges. Mario Corral García. Head Librarian of the Marquesa de Pelayo Library, IDIVAL.

10: Homage to Dr Arias. Kidney transplants: history and new breakthroughs. Dr Federico Oppenheimer. – Hospital Clinic of Barcelona.

DECEMBER:

1: Homage to Dr Castrillo. Emergency medicine: an unfinished business? Tomás Toranzo, former President of the Spanish Society of Emergency Medicine.

15: Stratified treatment in schizophrenia: integrating results of the human and cellular transcriptome in antipsychotic treatment strategies. Dr Benedicto Crespo, Psychiatry Department, Marqués de Valdecilla University Hospital.

Training Related to Support Unit Departments

Includes activities for researchers provided by Institute departments. In 2016, the following dissemination activities were provided under this line:

III Flow Cytometry Course.
Techniques and applications in clinical practice and research, 30/05/2016 - 02/06/2016

Dissemination Activities

The IDIVAL Innovation Area disseminates and promotes the culture of innovation. In 2016, there were several dissemination events in this field:

4TH INNOVATION AND DEVELOPMENT SEMINARS.

With the participation of IDIVAL. Lecture and workshop: Introduction to Design Thinking and People-Centred Innovation, by Asier Pérez, Director of Research and Creativity at Dowayo Foresight. In partnership with the Nursing Quality, Training, and R&D area at HUMV, this lecture and workshop were organised in November to introduce the Design Thinking methodology and its application to healthcare. "Generating ideas, introducing solutions" with the lecture "How to protect innovation".

SCIENCE WEEK.

Science Week was held in November 2015, an initiative coordinated by the University of Cantabria in which IDIVAL participated by opening its doors to five primary and secondary schools, with more than 100 students participating. Students got to see the IDIVAL facilities, with brief presentations by researchers including José Ramos Vivas, David San Segundo Arribas and Fidel Madrazo Toca, with whom they could talk about the research professional in the context of clinical research and learn about the tools used in their daily work, such as the Microscopy Unit, Cytometry Unit, the research laboratories, etc.

INTRODUCTORY BIOMEDICAL RESEARCH WORKSHOP.

For a third year, the IDIVAL introductory programme to Biomedicine "Long Live Science! An introduction to biomedical research" was held in collaboration with the Ministry of Education, Culture and Sport of the Government of Cantabria. There were a total of 7 classroom-based workshops in November, with the participation of 80 students from schools in Cantabria. The workshops were designed, directed and developed by IDIVAL with the main goal of encouraging the region's students to consider a career in science, in the field of biomedicine.

RESEARCHERS' NIGHT.

This European science project forms part of the PEOPLE Programme in the 7th EU Framework Programme, promoted by the Ministry of Education and Employment of the Government of Cantabria and coordinated by the Research Institutes of Physics (IFCA) and Environmental Hydraulics (IH Cantabria) of the University of Cantabria and the International Institute of Prehistoric Research (IIIPC). IDIVAL, IBBTEC and Smart Santander also participate in this initiative.

STUDENT VISITS.

During 2016 there were seven visits by students from various Cantabrian schools. The visits included the Microscopy and Flow Cytometry units and the Molecular Microbiology laboratory.

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 working 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: 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: MANAGEMENT OF HEALTHCARE AND SOCIAL SERVICES.

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). University of Cantabria.

MASTER'S DEGREE: 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.

UIMP MEETING. THE SOCIOECONOMIC EVALUATION OF HEALTHCARE RESEARCH.

Directors: Alfonso Beltrán (Deputy General Director for International Research Programmes and Institutional Relations, Carlos III Health Institute), Pedro Cortegoso (General Secretary, Carlos III Health Institute), Galo Peralta Fernández (Director of Management at IDIVAL). 29 June to 1 July 2016. 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 2016, the activities of this section directed at training on using library resources were the following:

Introduction to biomedical information for Primary Care.

Dates: 22 - 23 November.
Duration: 6 hours / seminar.
Primary Care medical **students**.
Location: Library Classroom.
Teacher: Mario Corral, Librarian.

Library immersion course for HUMV Residents.

Date: 2 July.
Duration: 1 hour.
Students: HUMV Residents-1.
Teacher: Mario Corral, Librarian.

Basic reference search using the Marquesa de Pelayo Library for midwives.

Dates: 18, 19 and 20 October.
Duration: 9h.
Location: Library classroom.
Teacher: Mario Corral, Librarian.

Reference searches in MEDLINE via PUBMED.

Date: 25 - 26 October.
Duration: 8 hours.
Location: Sierrallana Hospital - Tres Mares.
Teacher: Mario Corral, Librarian.

Web of Science advanced level.

Date: 13 October.
Location: Library classroom.
Duration: 1h.
Teacher: Rachel Mangan (FECYT).

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 2016, the Marqués de Valdecilla University Hospital offered 82 places in 39 specialisations. The Marqués de Valdecilla University Hospital also participated in the training of the 20 places offered for specialisation in Family and Community Medicine for the Santander Area, a specialist in Occupational Medicine, and 10 nurses specialising in Obstetrics and Gynaecology.

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:

Especialidad	Nº	Especialidad	Nº
Allergology	1	Intensive Medicine	3
Clinical Analysis	1	Internal Medicine	4
Pathological Anatomy	3	Nuclear Medicine	2
Anaesthesiology and Reanimation	6	Microbiology and Parasitology	1
Gastroenterologist	2	Nephrology	2
Clinical Biochemistry	3	Pneumology	2
Cardiology	3	Neurosurgery	1
Cardiovascular Surgery	1	Clinical Neurophysiology	2
General and Digestive Surgery	2	Neurology	2
Oral and Maxillofacial Surgery	1	Obstetrics and Gynaecology	3
Orthopaedic Surgery and Traumatology	2	Ophthalmology	1
Thoracic Surgery	1	Medical Oncology	1
Medical-Surgical Dermatology	1	Radiotherapeutic Oncology	1
Endocrinology and Nutrition	1	Otorhinolaryngology	1
Hospital Pharmacy	2	Paediatrics and Specific Areas	5
Clinical Pharmacology	2	Clinical Psychology	1
Haematology and Haemotherapy	3	Psychiatry	3
Immunology	2	Radiodiagnostics	4
Occupational Medicine	1	Hospital Radiophysics	1
Family and Community Medicine	20	Rheumatology	2
Physical Medicine and Rehabilitation	1	Urology	1

Training of New Clinical Researchers

IDIVAL's training programme in healthcare-related research and innovation, known as Post-MIR Wenceslao López Albo contracts, is specifically for residents who have completed their specialisation. 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 of up to three years in duration that should include a stay at one or various renowned international centres.

In 2016, IDIVAL offered grants for an 18-month contract to four specialists; the Post-MIR Valdecilla contracts of a further five specialists were active at some point during 2016.

Call 2016

ONAINDIA PÉREZ, ARANTZA.
Specialist in Pathological Anatomy formed in the HUMV.
Tutor: Miguel Ángel Piris.
Project: Application of new molecular techniques to the routine diagnosis of cancer patients.
Stay: MD Anderson Cancer Center, The University of Texas.
Duration: 18 months.

DRAKE PÉREZ, MARTA.
Specialist in Radiodiagnóstico formed in the HUMV.
Tutor: Gerardo Lopez Rasines.
Stays: Geneva University Hospital, Department of Neuroradiology National Hospital for Neurology, Neurosurgery and Psychiatry UCL Institute of Neurology (London), Johns Hopkins Hospital (Baltimore), Imaging interventionnelle oncologique et viscérale - NHC (Strasbourg).
Project: Innovation project in Neuromusculoskeletal Radiology.
Duration: 18 months.

LAS VECILLAS SÁNCHEZ, LETICIA.
Specialist in allergology trained at the HUMV.
Project: Creation of a unit of desensitization to chemotherapeutic and biological drugs. Prospective study of the risk factors in the population of patients desensitized to chemotherapy, antibiotics and biologicals.
Stay: Brigham and Women's Hospital (Boston, USA)
Duration: 18 months.

FABREGAT BORRÁS, ROSA.
Specialist in Radiation Oncology trained in the HUMV.
Tutor: Pedro Prada.
Project: Intraoperative radiotherapy as a treatment of care innovation in the Public Health System of Cantabria. Technical and clinical characteristics, methodology, dosimetry and quality control.
Stays: Gregorio Marañón University Hospital (Madrid) European Institute of Oncology (Milan).
Duration: 18 months.

Call 2015

RIANCHO ZARRABEITIA, JAVIER.

Specialist in Neurology trained in the HUMV.
Tutor: Jon Infante.
Project: Epigenetics and new technologies in dementias: a translational approach and assistance innovation.
External stay: Dr. Bruce Miller. Memory Aging Center, in San Francisco, University of California (UCSF MAC).
Duration 2 years.

KISLÍKOVÁ, MÁRIA.

Specialist in Nephrology trained in the HUMV.
Tutor: Ángel Martín de Francisco.
Project: Epigenetic Regulation of Arterial Smooth Muscle Phenotype in CKD-Associated Vascular Disease.
External stay: Dr. David Wheeler. The UCL Center for Nephrology, University College of London.
Duration: 2 years.

RIAÑO MOLLEDA, MARÍA.

Specialist in General Surgery trained at the HUMV.
Tutor: Manuel Fleitas.
Project: Training in hepatobiliary surgery and liver transplantation and study and application of solutions and machines for the preservation of solid abdominal organs for transplantation.
External stay: Professeur René ADAM, Paul Brousse Hospital in Paris and Hammersmith Hospital in London.
Duration: 2 years.

Call 2014

IRUZUBIETA COZ, PAULA.

Specialist in Digestive System formed in the HUMV.
Tutor: Javier Crespo García (Head of the Digestive S., HUMV).
Project: Role of immunity and intestinal microbiota in liver disease by non-alcoholic fatty deposit in obesity.
External stay: Cooperative Research Center on Biosciences (CIC bioGUNE 6 months), and Newcastle Freeman Hospital and Institute of Cellular Medicine at Newcastle University for 12 months.
Duration: 3 years.

Call 2013

GONZÁLEZ QUINTANILLA, VICENTE.

Specialist in Neurology trained in the HUMV.
Tutor: Agustín Oterino Durán.
Project: Evolutionary study of markers of inflammation and cerebral atrophy in patients with multiple sclerosis in Cantabria.
External stay: Dr. Pozzilli, Sant Andrea Hospital in Rome and Dr. Salvetti, University of Sapienza and Dr. Alan Thompson, National Hospital for Neurology and Neurosurgery, London.
Duration: 2 years.

Doctoral Thesis. Doctorate Programs

IDIVAL researchers participate in the two doctoral programs that the Faculty of Medicine of the University of Cantabria has assets:

> Doctorate in molecular biology and biomedicine (coordinated by Dolores Delgado, with mention of quality).

> Doctorate in health sciences (currently coordinated by a researcher at the institute, Benedict Crespo-Facorro).

The formative activity of IDIVAL has been reflected in the doctoral theses.

In 2016 the IDIVAL groups have participated in a total of 57 doctoral theses, either through its management or its authorship. The list of theses read or directed by IDIVAL staff is shown in the attached table.

AUTHOR AND DIRECTOR (S)	TITLE	UNIVERSITY
Sara Rodríguez Prado, Inés Gómez Acebo	Ocular involvement in Rendu-Osler-Weber disease: characteristics and associations	University of Cantabria
Inmaculada Hernández Bejarano, Ana Isabel Morales Martín, Marta Prieto Vicente, Mª Ángeles Ramos Barrón, Carlos Gómez Alamillo.	Analysis of the evolution of renal transplantation through the identification of risk biomarkers in the donor and in the recipient	University of Salamanca.
Rubén Gonzalo González, Manuel Gómez Fleitas.	Analysis of factors predicting remission of type 2 diabetes mellitus in morbidly obese patients after Roux-en-Y gastric bypass	Universidad de Cantabria.
Ana Machín Mave, Joaquín Cañal Villanueva, Pedro Muñoz Cacho.	Epidemiological and evolutionary analysis of open eye trauma in Cantabria	University of Cantabria
Marcos Pajarón Guerrero, María Del Carmen Fariñas Álvarez, José Ramón De Berrazueta Fernández.	Self-management of endovenous (atade) domiciliary antimicrobial treatment in infective endocarditis: a safe and efficient care model	University of Cantabria
Mª Elena Arnáiz García, Juan Francisco Nistal Herrera.	Aortic root replacement surgery with valvular preservation: analysis of early and long-term surgical outcomes, and study of predictors of survival, valvular function stability, and reoperation	University of Cantabria
Francisco Ortiz Sanjuan, Ricardo Blanco Alonso, Miguel Ángel González-Gay Mantecón, María Del Carmen González Vela.	Classification of cutaneous vasculitis	University of Cantabria
Ruth Gonzalez Sanchez, José Javier Gómez Román, Francisco Javier Freire Salinas.	Development of a diagnostic method for gastrointestinal stromal tumors (GIST)	University of Cantabria
Leyre Riancho Zarrabeitia, Miguel Ángel González-Gay Mantecón, Ricardo Blanco Alonso.	Detection of risk factors for subclinical atherosclerotic disease and cardiovascular events in patients with systemic lupus erythematosus	University of Cantabria
Diana Tordesillas Gutiérrez, Benedicto Crespo Facorro.	Differences in gray matter volume in patients with a first psychotic episode and age-onset effects using voxel-based morphometry	University of Cantabria

Autor y directores	Título	Universidad
Javier Vázquez Bourgon, Benedicto Crespo Facorro.	Disc 1 and non-affective psychosis: variations in endophenotypes and clinical characteristics in first episodes of psychosis	University of Cantabria
José Ignacio Martín Parra, Manuel Gómez Fleitas, Robert Simon, José Mª Maestre Alonso.	Design of a training program for residents of general surgery and digestive system based on competences: integration of clinical simulation and practice of care	University of Cantabria
Ana Esteban Herrera, Javier Ayesta Ayesta, Javier Llorca Díaz.	Effectiveness in the management of smoking cessation	University of Cantabria
Jorge Duerto Alvarez, Eduardo Miñambres García, María De Los Ángeles Ballesteros Sanz.	Long-term effect in renal grafts of an intensive management protocol of the multiorganic donor	University of Cantabria
Jaime Lucas Carbonero, José Antonio Vázquez De Prada Tiffe.	Efficacy and safety of corticosteroid withdrawal after cardiac transplantation	University of Cantabria
María Ruiz Soto, Miguel Ángel Lafarga Coscojuela, María Teresa Berciano Blanco.	Oxidative stress in satellite glia of the spinal ganglia induces sensory alterations in the murine HSOD1G93A model of amyotrophic lateral sclerosis (ALS)	University of Cantabria
Francisco José Amo Setien, Maria Jesús Dura Ros.	The study of social support and quality of life from personal networks: the case of chronic pain	Autonomous University of Barcelona
Marcos Gómez Ruiz, Manuel Gómez Fleitas, José Fernández-Escalante Moreno.	Comparative study of laparoscopic surgery versus robotic surgery in the treatment of rectal cancer	University of Cantabria
Jana González Gómez, Andrés Gómez Del Barrio.	Controlled study of risk factors and clinical variables associated with the development of a eating disorder in the community of Cantabria	University of Cantabria
María Toriello Suárez, Agustín Oterino Durán, Jesús Castillo Obeso.	Genetic association study of genes encoding the GABA receptor in migraine	University of Cantabria
José Javier Gómez Román, Francisco Javier Freire Salinas.	Study of markers of mesenchymal epithelium transition in renal neoplasms	University of Cantabria
José Helmut Ramírez Cuentas, Isabel De Las Cuevas Terán, Luis Gaite Pindado.	Study of parents' satisfaction in a neonatology unit	University of Cantabria
Jose Ignacio Fortea Ormaechea, Cristina Ripoll Noiseux, Rafael Bañares Cañizares.	Study of the effect of enoxaparin on cirrhosis and experimental portal hypertension	Universidad Complutense de Madrid
Javier Pérez López, José Carlos Rodríguez Rey.	Study of the role of mir-148a in the regulation of genes of lipid metabolism and adipogenesis	University of Cantabria
Ana De Juan Ferré, José Manuel López Vega, Marta Mayorga Fernández.	Phase II intramural study of neoadjuvant chemotherapy with platinum, doxorubicin and taxane salts in operable breast cancer	University of Cantabria
José Javier Gómez Román, Francisco Javier Freire Salinas.	Evaluation of biomarkers predicting peritoneal carcinomatosis in colon carcinoma	University of Cantabria

Autor y directores	Título	Universidad
Javier Rueda Gotor, Miguel Ángel González-Gay Mantecón, Javier Llorca Díaz.	Evaluation of cardiovascular risk in patients with predominantly axial spondyloarthritis	University of Cantabria
Rosalía Demetrio Pablo, Pedro Muñoz Cacho, Víctor Manuel Martínez Taboada.	Thrombotic risk assessment in asymptomatic patients with antiphospholipid antibodies	University of Cantabria
Amador Priede Diaz, César González-Blanch Bosch.	Cognitive factors associated with the development of anxiety-depressive symptoms in newly diagnosed cancer patients	University of Cantabria
Carlos López López, José Manuel López Vega, Jaime Sanz Ortíz.	Clinical-molecular prognostic factors and predictive models in glioblastoma multiforme from an intramural experience: service of medical oncology of Hospital Universitario Marqués de Valdecilla (2000-2010)	University of Cantabria
Yhivian Peñasco Martín, Alejandro González Castro, Javier Llorca Díaz.	Prognostic factors of severe thoracic trauma in the population aged over 65, 1991 - 2012	University of Cantabria
Beatriz Payá González, Jesús Ángel Artal Simón, Celso Arango López.	Premorbid functioning in early-onset psychotic disorders: differences between people diagnosed with schizophrenia, bipolar disorder and healthy population	University of Cantabria
Rosana García Díaz, Cesar Baldomero Madrazo Leal, Manuel Gómez Fleitas.	Impact of the implementation of the checklist on a general surgery service	University of Cantabria
Javier Gonzalo Ocejo Viñals, María Del Carmen Fariñas Álvarez.	Immunogenetics of pulmonary tuberculosis: influence of major histocompatibility complex polymorphisms, repertoire of KIR genes and other genes of the immune system	University of Cantabria
Arantza Onaindia Pérez, Miguel Ángel Piris Pinilla.	Peripheral T-lymphomas: study of histological, immunophenotypic and molecular markers, and selection of targeted therapy	University of Cantabria
Ana Mª Arnaiz García, José Manuel Bernal Marco, Mª Concepcion Fariñas Álvarez, María Del Carmen Fariñas Álvarez.	Morbidity and mortality in deferred sternal closure	University of Cantabria
María Isabel González Aramburu, Jon Infante Ceberio, Onofre Combarros Pascual.	Serum levels of uric acid and progranulin, genetic factors that regulate them and Parkinson's disease	University of Cantabria
Javier Aragón Valverde, Manuel Gómez Fleitas, Francisco José Vizoso Piñeiro.	Role of metalloproteinase-11 and tissue inhibitor of metalloproteinase-2 (TIMP-2) as factors of the inflammatory process and tumor invasion in non-small cell lung carcinoma	University of Cantabria
Paula Ruiz Martín, Marta Martín Millán, Jesús González Macías, Maria Ángeles Ros Lasierra.	Role of the WNT canonical pathway in osteoclast resorptive function	University of Cantabria
Marta Fernández Hernandez, José Antonio Vázquez De Prada Tiffe, Francisco Jesús González Vílchez	Guidelines for immunosuppression in heart transplantation in the medium and long term	University of Cantabria

Autor y directores	Título	Universidad
José Quintanar Lartuno, Manuel Antonio Arias Rodríguez, Luis Martínez Martínez	Peritonitis in peritoneal dialysis	University of Cantabria
Soraya Curiel Del Olmo, José Pedro Vaqué Díez, Miguel Ángel Piris Pinilla	Precision medicine in Merkel cell carcinoma and advanced cutaneous melanoma	University of Cantabria
José Alberto Sanchez Ortega, Javier Llorca Díaz, Mª Concepción Fariñas Álvarez	Prevalence of tobacco, alcohol and drug use among university students in Cantabria	University of Cantabria
José María Castillo Oti, Joaquín Cañal Villanueva, Pedro Muñoz Cacho	Prevalence and risk factors associated with diabetic retinopathy in Cantabria	University of Cantabria
José Gabriel Calcedo Giraldo, Andrés Gómez Del Barrio	Prevention in eating disorders in high school students in Cantabria	University of Cantabria
Alicia Márquez López, Luis Martínez Martínez	Quinolone resistance and hemolysin production in clinical isolates	University of Cantabria
Felipe Rodríguez Entem, José Antonio Vázquez De Prada Tiffe, José Manuel Revuelta Soba	Follow-up of the cardiac transplantation with echocardiographic rejection monitoring strategy	University of Cantabria
Laura Carral Fernández, Andrés Gómez Del Barrio	Cognitive Bias in Eating Disorders: A Case-Control Study	University of Cantabria
Liébana Maria Piedra Antón, Luis Ansorena Pool, María Del Carmen Fariñas Álvarez	Emergency information systems	University of Cantabria
Sandra Properzi, Pierpaolo Vittorini, Carmen María Sarabia Cobo	Sviluppo of a system of formazione per sustentere the cognitive capacità of the persone anziane affette of the cognitive deterioration lieve	Università Degli Studi Dell'aquila, Italia
Lorena García Hevia, Mónica López Fanarraga	Cancer therapy based on the biomimetics of carbon nanotubes with cell filaments	University of Cantabria
Gabriela Saravia Campelli, María Del Carmen Fariñas Álvarez, Mª Concepcion Fariñas Álvarez	A randomized intervention program to optimize the quality of hospital use of antibiotics	University of Cantabria
Araceli Prieto Santa-Cruz, José Javier Gómez Román	Utility of a process-based management system in the care and perceived quality of lung cancer	University of Cantabria
Juan Carlos Albarracin Castillo, Juan Carlos Rodríguez Sanjuan, Manuel Gómez Fleitas	Value of endoscopic ultrasonography and magnetic cholangioresonance in the diagnosis of choledocholithiasis	University of Cantabria
Montserrat Robustillo Villarino, Javier Llorca Díaz, Miguel Ángel González-Gay Mantecón	Evaluation of cardiovascular risk using non-invasive techniques in patients with rheumatoid arthritis	University of Cantabria
Jacqueline Maria Mayoral Van Son, Benedicto Crespo Facorro	A three-year longitudinal study of clinical evolution in patients who, after a single episode of non-affective psychosis, have achieved a complete recovery and decided to withdraw antipsychotic medication.	University of 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, that was organised in 2016 as a continuation of the programme of research seminars presented by young researchers, in collaboration with clinical and basic researchers.

The 2016 programme consisted of the following seminars, held in the Faculty of Medicine of the University of Cantabria, in the Marqués de Valdecilla University Hospital and the IDIVAL facilities.

Wednesday 02/11/2016:

Speaker:
Ana Lara Pelayo Negro.
Specialist in the Neurology Department of Marqués de Valdecilla University Hospital, former holder of a Post-MIR Wenceslao López Albo contract.
Title: Evolution of Charcot–Marie–Tooth disease type 1a duplication: a 2-year clinical-electrophysiological and lower-limb muscle MRI longitudinal study.

Wednesday 16/11/2016:

Speaker:
Ana V. Villar.
Associate Professor of the Physiology and Pharmacology department in the Faculty of Medicine, University of Cantabria.
Title: Heat shock protein 90 participates in myocardial fibrogenic response. The potential of designed biosynthetic inhibitors.

Wednesday 21/12/2016:

Speaker:
Paula Iruzubieta Coz.
Specialist in the Digestive System at Marqués de Valdecilla University Hospital. Post-MIR Wenceslao López Albo contract holder.
Title: The liver-specific deletion of the respiratory chain inhibitor MCJ attenuates NAFLD progression by enhancing hepatic beta-oxidativo

Student Training

IDIVAL's research groups include 40 of the 132 associate professors working in the Marqués de Valdecilla University Hospital. Of the 10 tenured professors and 10 other professors from the University of Cantabria working with the Marqués de Valdecilla University Hospital, 18 belong to IDIVAL groups.

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 whose training involves the Marqués de Valdecilla University Hospital (in the last five academic years) is as follows: 4th year of Medical Studies: 132, 5th year of Medical Studies: 157, 6th year of Medical Studies: 100.

2. Summer internship programme. In 2013, IDIVAL launched a grant programme for five students studying for 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 been continued into 2014, 2015 and 2016. The students awarded the grant and the research group in which they worked during the summer of 2016 appear in the IDIVAL grants section.

3. Spanish for Health Programme with the Comillas Foundation. IDIVAL, in collaboration with the Comillas Foundation, hosts four medical students from New York University Langone for six weeks so they can study Spanish for Health.

FUNDACIÓN COMILLAS

Oncology

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 have launched 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 on subjects such as Oncology, Neurology, Immunology, Regenerative Medicine, and Microbiology.

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 2016 were:

Thursday 29/09/2016:

Speaker:
Pilar Garrido.
Section Head of the Medical department at Ramón y Cajal University Hospital.
Title: Current and future challenges in lung cancer.

Thursday 27/10/2016:

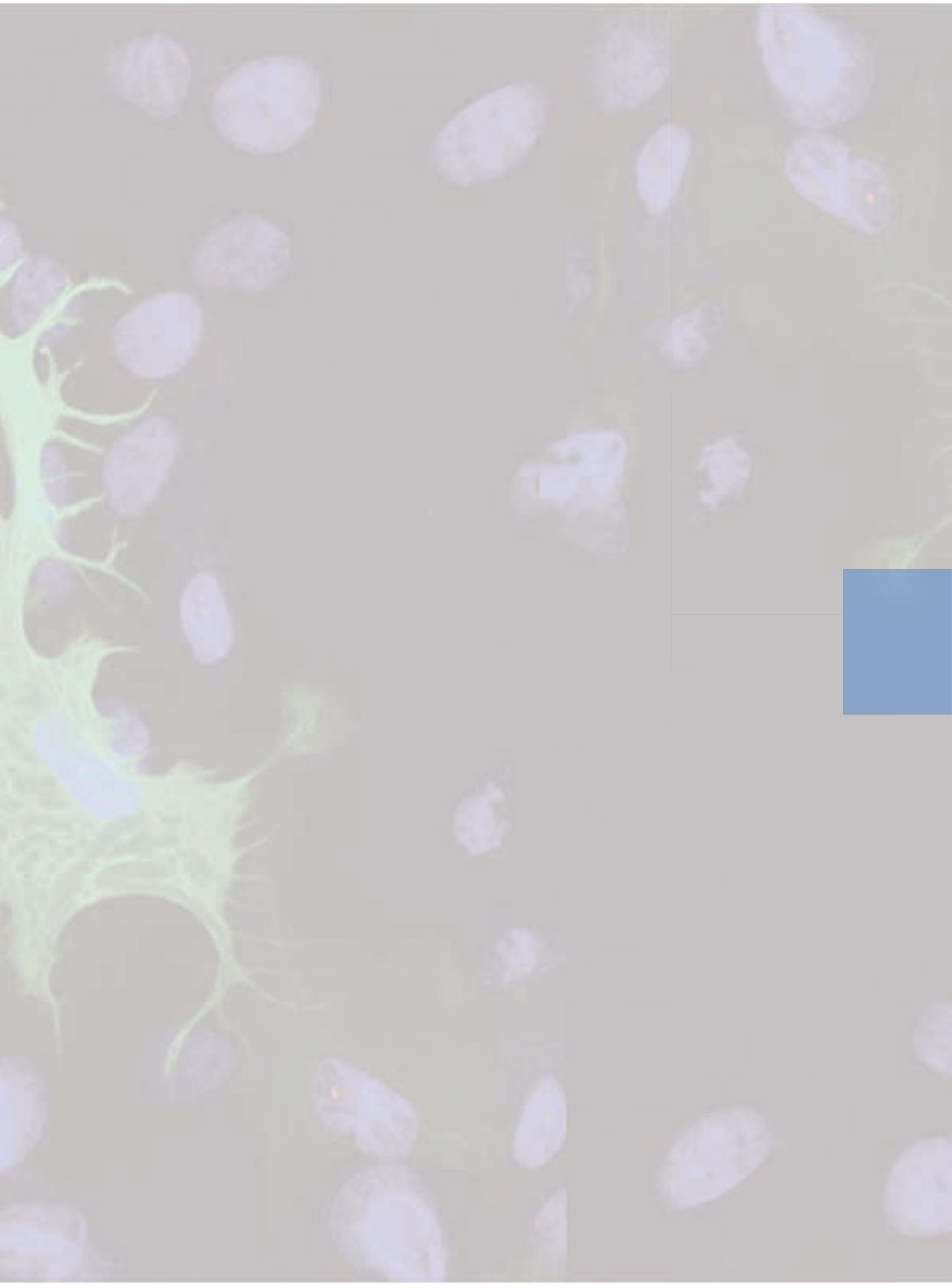
Speaker:
Francesc Artigas.
Director of the Neurochemistry and Neuropharmacology Department of the Insitut d'Investigacions Biomèdiques de Barcelona.
Title: Fast-acting antidepressants: Are they possible?

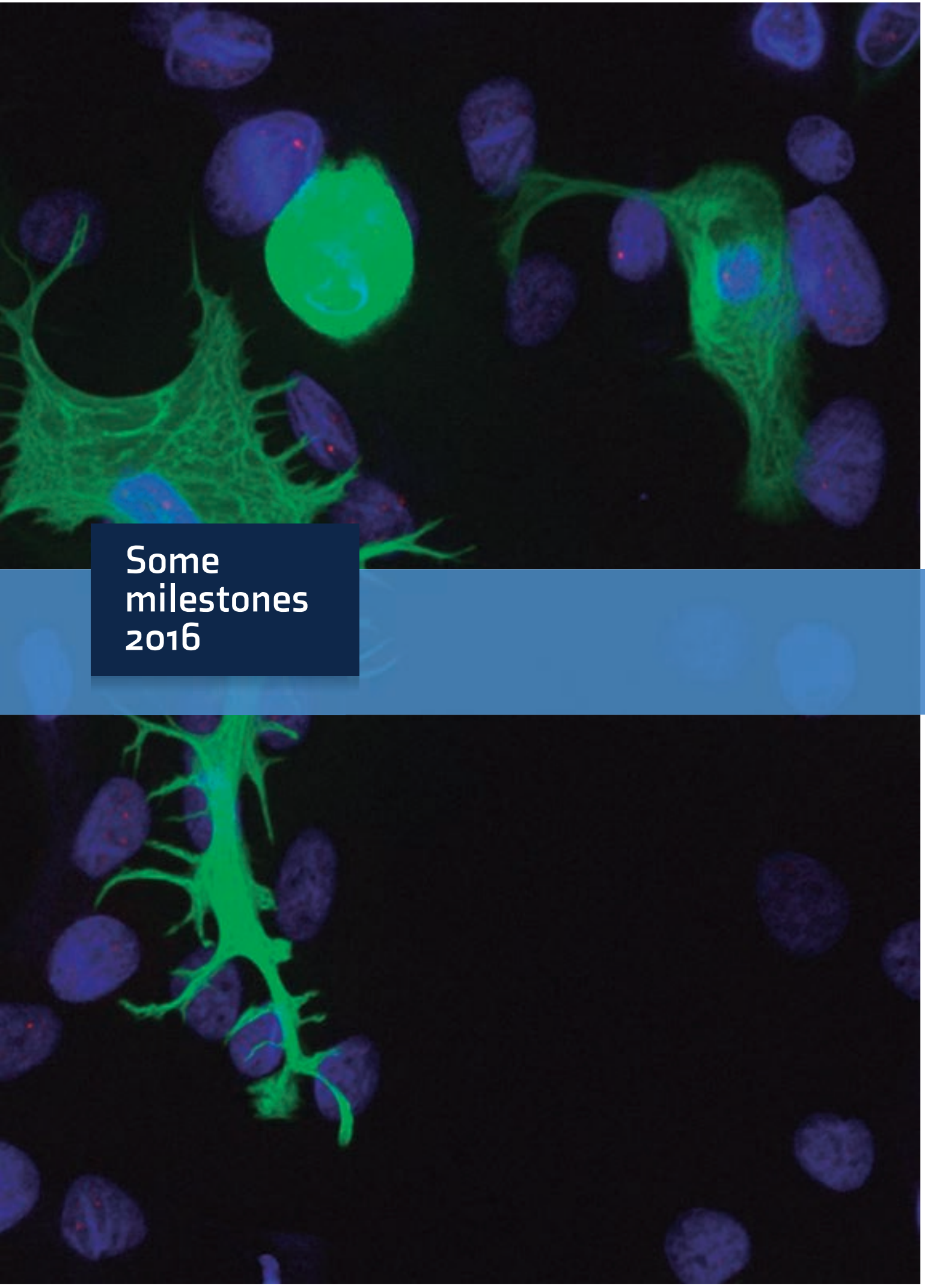
Thursday 17/11/2016:

Speaker:
Jesús San Miguel.
Medical Director of the University Clinic of Navarre. Specialist in Haematology and Haemotherapy.
Title: Multiple myeloma, from biology to therapy.

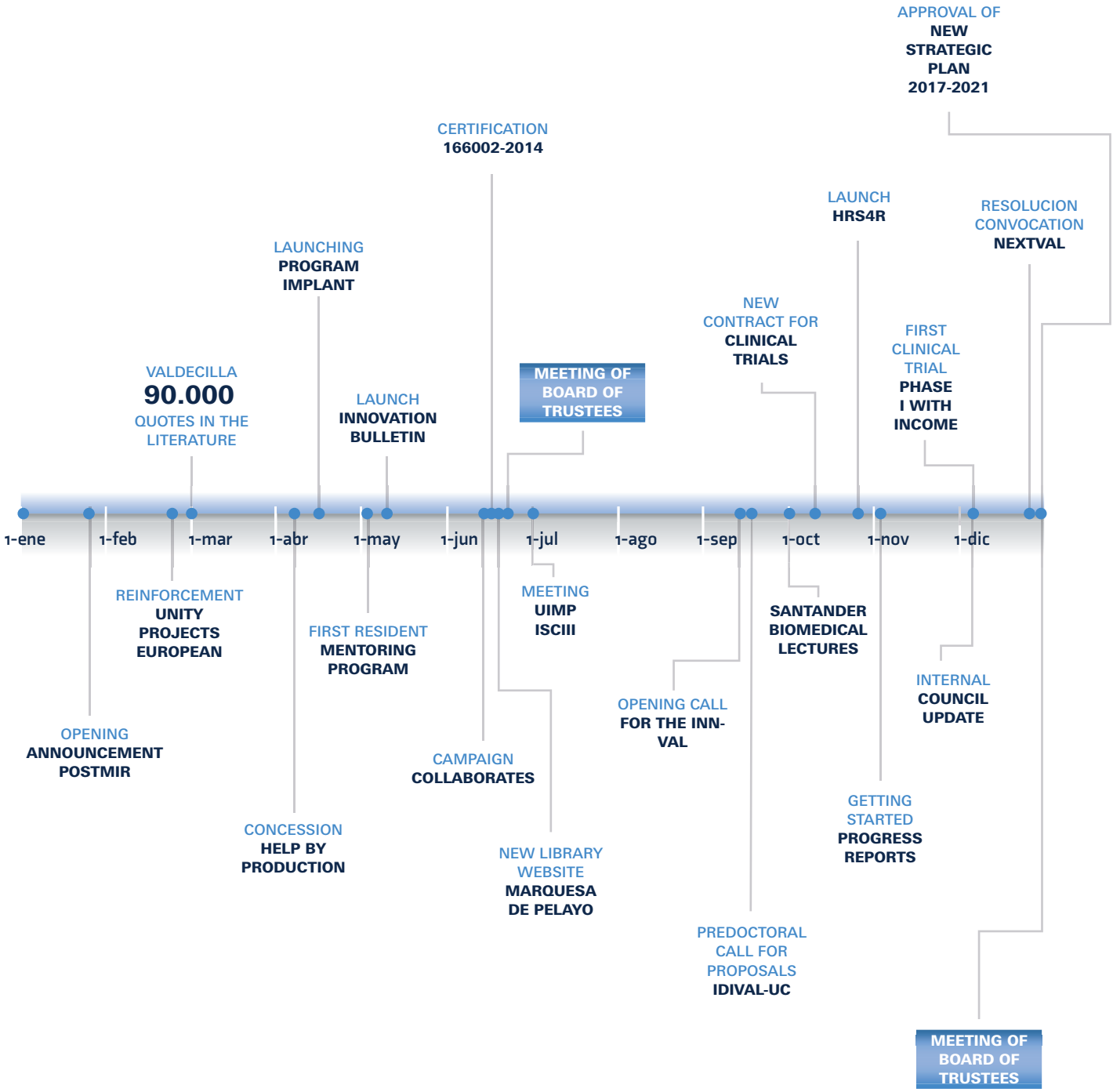
Thursday 24/11/2016:

Ponente:
Giuseppe Del Giudice.
Translational Science Leader at GSK Vaccines Srl, Siena, Italy.
Título: The quest of early biomarkers of vaccine safety and long-term immunity.





Some milestones 2016


APPROVAL OF NEW STRATEGIC PLAN 2017-2021
CERTIFICATION 166002-2014
LAUNCH HRS4R
RESOLUCION CONVOCATION NEXTVAL
LAUNCHING PROGRAM IMPLANT
NEW CONTRACT FOR CLINICAL TRIALS
FIRST CLINICAL TRIAL PHASE I WITH INCOME
VALDECILLA 90.000 QUOTES IN THE LITERATURE
LAUNCH INNOVATION BULLETIN
MEETING OF BOARD OF TRUSTEES
1-ene
1-feb
1-mar
1-abr
1-may
1-jun
1-jul
1-ago
1-sep
1-oct
1-nov
1-dic
REINFORCEMENT UNITY PROJECTS EUROPEAN
FIRST RESIDENT MENTORING PROGRAM
MEETING UIMP ISCIII
SANTANDER BIOMEDICAL LECTURES
INTERNAL COUNCIL UPDATE
OPENING ANNOUNCEMENT POSTMIR
CAMPAIGN COLLABORATES
OPENING CALL FOR THE INN-VAL
CONCESSION HELP BY PRODUCTION
NEW LIBRARY WEBSITE MARQUESA DE PELAYO
GETTING STARTED PROGRESS REPORTS
PREDOCTORAL CALL FOR PROPOSALS IDIVAL-UC
MEETING OF BOARD OF TRUSTEES

News Stories from 2016

Valdecilla launches the COLABORA campaign

The biomedical research of the Valdecilla environment is only possible thanks to the help of everyone involved. Patients, nurses, researchers, doctors, citizens, companies, patients' associations, all work together to defeat more diseases thanks to breakthroughs in the understanding of their causes, symptoms and behaviour, and the emergence of new treatments. For this reason IDIVAL is launching a campaign to inform society about the research projects in the Valdecilla environment that seek solutions for health problems, and that anyone can support.

IDIVAL participates in the largest ever genetic study of schizophrenia

After analysing over 41,000 people (21,000 individuals with schizophrenia and 20,000 without), the largest genetic study of schizophrenia to date was able to isolate the rare genetic variants that increase the risk of this illness.
The work, recently published in Nature Genetics, was led by the University of San Diego (USA) and the Psychiatric Genomic Consortium (PGC) with data from over 43 research groups, including the CIBERSAM research group coordinated by Benedicto Crespo-Facorro at UC-IDIVAL.

Very good results for IDIVAL in the Strategic Action for Health 2016

The strategic action is a set of annual programmes to encourage biomedical research, promoted by the Carlos III Health Institute, which are essential for research in Spain's healthcare system. As a healthcare research institute accredited by the Carlos III Health Institute, IDIVAL's researchers at the University of Cantabria and the Marqués de Valdecilla University Hospital attend these annual aid programmes every year. The results in 2016 were excellent. The total grants awarded in the 2016 round were worth €2,307,508. The success rate of the projects was notably high at 50%.

Charcot-Marie-Tooth disease type 2G redefined by a new mutation in LRSAM1

IDIVAL's Neurodegenerative Diseases Group participated and made key contributions to this multinational work, which has concluded that this sub-type of the disease, based on the mutation causing it, should be reclassified, and that studies of the magnetic resonance imaging of the leg muscles can be used to detect minimal signs of the disease. Meanwhile, a transcriptomic analysis of the cells of several patients enabled the identification of new factors associated with LRSAM1 dysfunction, which offer new therapeutic targets shared with amyotrophic lateral sclerosis and Alzheimer's disease.

Robotic surgery to treat colorectal cancer

In the Colorectal Surgery Unit at Marqués de Valdecilla University Hospital, robotics has been the preferred approach since 2010 for treating rectal cancer in all patients who can benefit from it, and has been used on over 500 colorectal cancer patients so far. This is the longest series in Spain and one of the longest experiments in Europe; this Unit is one of just a few groups teaching other teams at the national and international levels.

Recently, this team published its short-term and medium-term results in the European Journal of Surgical Oncólogy. This publication revealed that very satisfactory results had been obtained overall. Using the da Vinci robot, there is much less need for large incisions, and there are far fewer serious post-surgical complications.

Stratification of patients with diffuse large B-cell lymphoma treated with chemoimmunotherapy: GCB/non-GCB by immunohistochemistry is still a robust and feasible marker

IDIVAL's Cancer Genomics Group coordinates an international multicentre study that validates the effectiveness of a method based on immunohistochemistry. The work is a retrospective international multicentre study coordinated by the Pathological Anatomy and Haematology departments of Marqués de Valdecilla University Hospital/IDIVAL. It confirms the prognostic validity of this method based on the immunohistochemical study of tumoral samples from patients diagnosed with diffuse large B-cell lymphoma. It also demonstrates the utility of a diagnostic approach combining immunohistochemical and fluorescent in situ hybridisation techniques to assign the biological risk of each tumour more precisely.

Valdecilla researchers develop new treatment strategies to preserve donor organs

This prospective study led by Eduardo Miñambres, transplant coordinator at Hospital Valdecilla and IDIVAL researcher, demonstrates the benefits of a triple therapy to conserve donated tissues, based on protective mechanical ventilation, invasive haemodynamic monitoring with water restriction, and the use of hormone therapy. The study included 618 multi-organ donors, and it demonstrated that this proposed intensive treatment of the donor does not affect the availability of the other donated organs (heart, liver, pancreas, and kidneys); in fact, it increases the availability of cardiac inserts.

A Valdecilla study concludes that teenage binge drinking alters cognitive functions

The Cognitive Deterioration Unit at Hospital Valdecilla, directed by Pascual Sánchez-Juan, neurologist at Marqués de Valdecilla University Hospital and IDIVAL researcher, carried out a study to assess the effects of the "botellón" custom on some cognitive functions. The results obtained show that young people with a pattern of binge drinking at the weekends present poorer performance in neuropsychological tests that assess attention span and mental agility. The deficit observed is more marked in women and in subjects who began consuming alcohol at an earlier age.

This study, the largest of this type performed to date, was published in the journal Plos One and studied 206 university students at the Gimbernat-Cantabria School, a centre attached to the University of Cantabria.

Doctor Sánchez-Juan highlighted that "these results are an alarm call on the effects of binge drinking on the immature brain, which is particularly significant given the high prevalence of this habit among young Spaniards"

Deconstructing schizophrenia: new discoveries reveal altered cerebral physiological processes

The article published recently in the journal Nature by Sekar et al. is an outstanding genetic and neurobiological study representing a major breakthrough, demonstrating that genetic anomalies (gen C4) and functional anomalies in immunological processes (major histocompatibility complex) could be causing alterations in normal brain development. Professor Crespo-Facorro's group (University of Cantabria-IDIVAL-CIBERSAM) collaborated in this international research project. "Changes in the structure of a gene associated with schizophrenia could lead to excessive loss of inter-neuron connections in adolescence. Synaptic pruning is a normal physiological process during brain development, in which surplus connections are eliminated in order to optimise brain function. But excessive paring during this period alters mental functions."

Based on powerful genome-wide analyses, a zone in chromosome 6 had been identified that includes various genes relating to the immune function, which is very significantly related to schizophrenia. "This research is a step forward, not just for its discoveries, but also for the research model, working from genetic finds and gene expressions to the altered biological process." "Having a specific variant of the C4 gene apparently facilitates an immunological trigger that would lead to a faulty synaptic pruning, eliminating too many connections in the patients."

The Valdecilla brand has over 90,000 citations in international literature

The Valdecilla brand, created in 1929, has been cited over 90,000 times in the international biomedical literature, according to data from the Web of Science platform. The Valdecilla is not just a consolidated brand in our region and in Spain, having earned the respect and affection of the people of Cantabria, and regarded as a benchmark in certain medical fields by Spanish doctors. It is also well-known internationally, as attested by data from the scientific literature.

The citations were calculated using the search term "Valdecilla" in the "address" field of the Web of Science (WOS) search engine. Remarkably, 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.

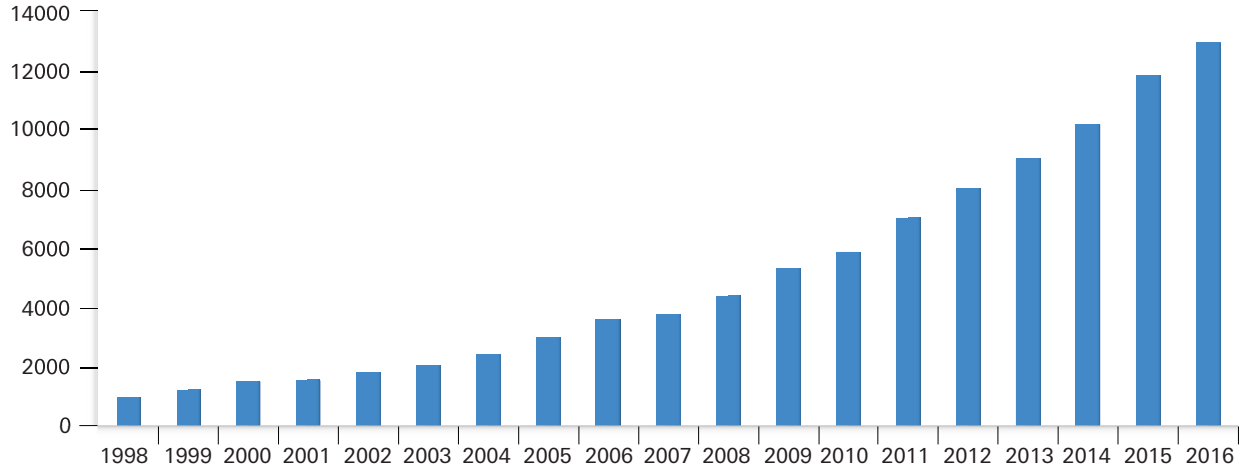
IDIVAL launches the innovation newsletter

On 5 May IDIVAL launched a R&D newsletter for biomedical professionals in Cantabria. The weekly newsletter covers the main news in the field, with information on R&D conferences and funding opportunities in national and international grant announcements. It also gathers the latest high-impact publications in national and international journals. The weekly newsletter is designed and published by IDIVAL's Innovation department and emailed to professionals on request. It is also available on the IDIVAL website.

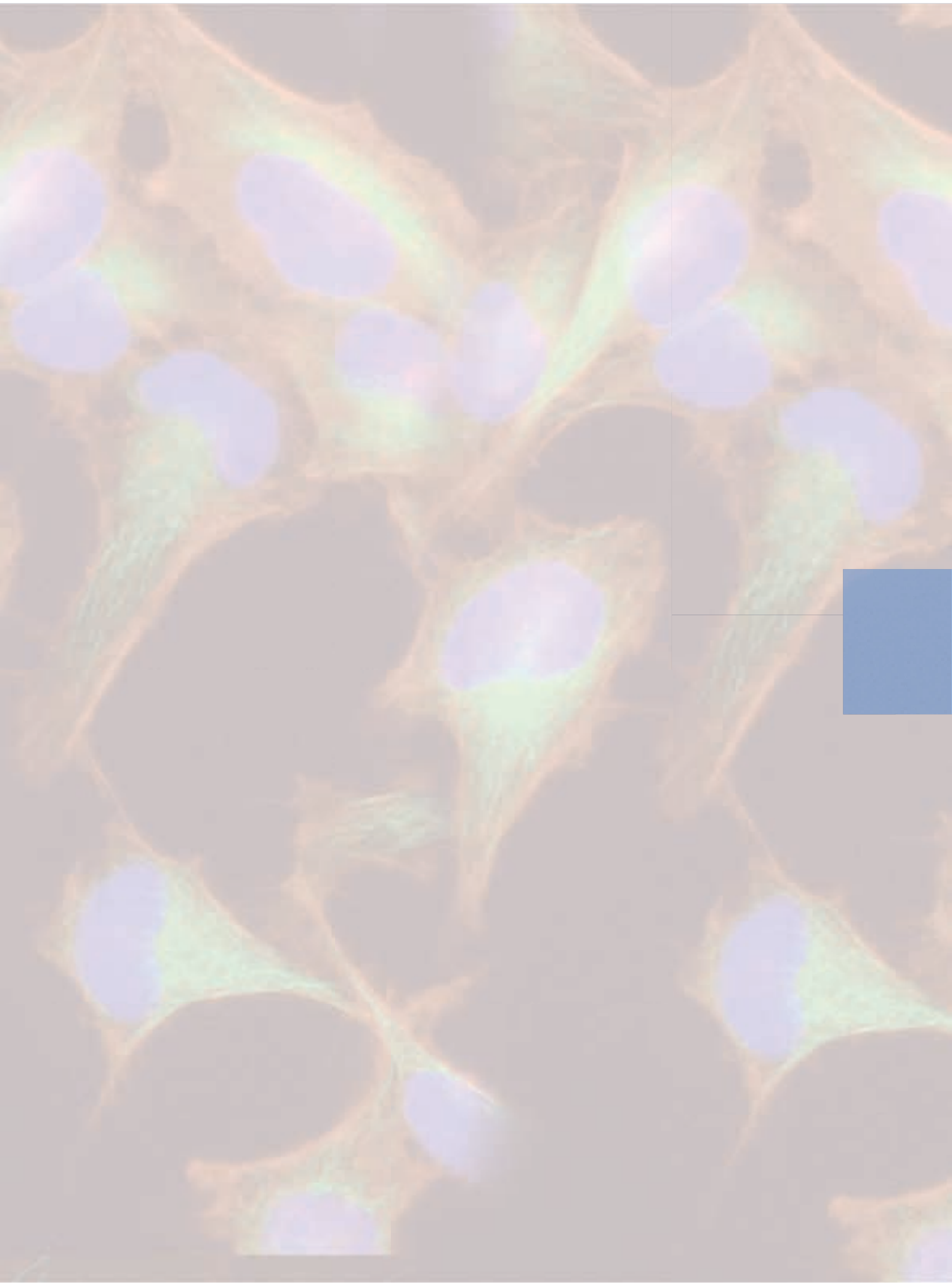
IDIVAL, in partnership with the University of Cantabria and IBBTEC, launches the Santander Biomedical Lectures

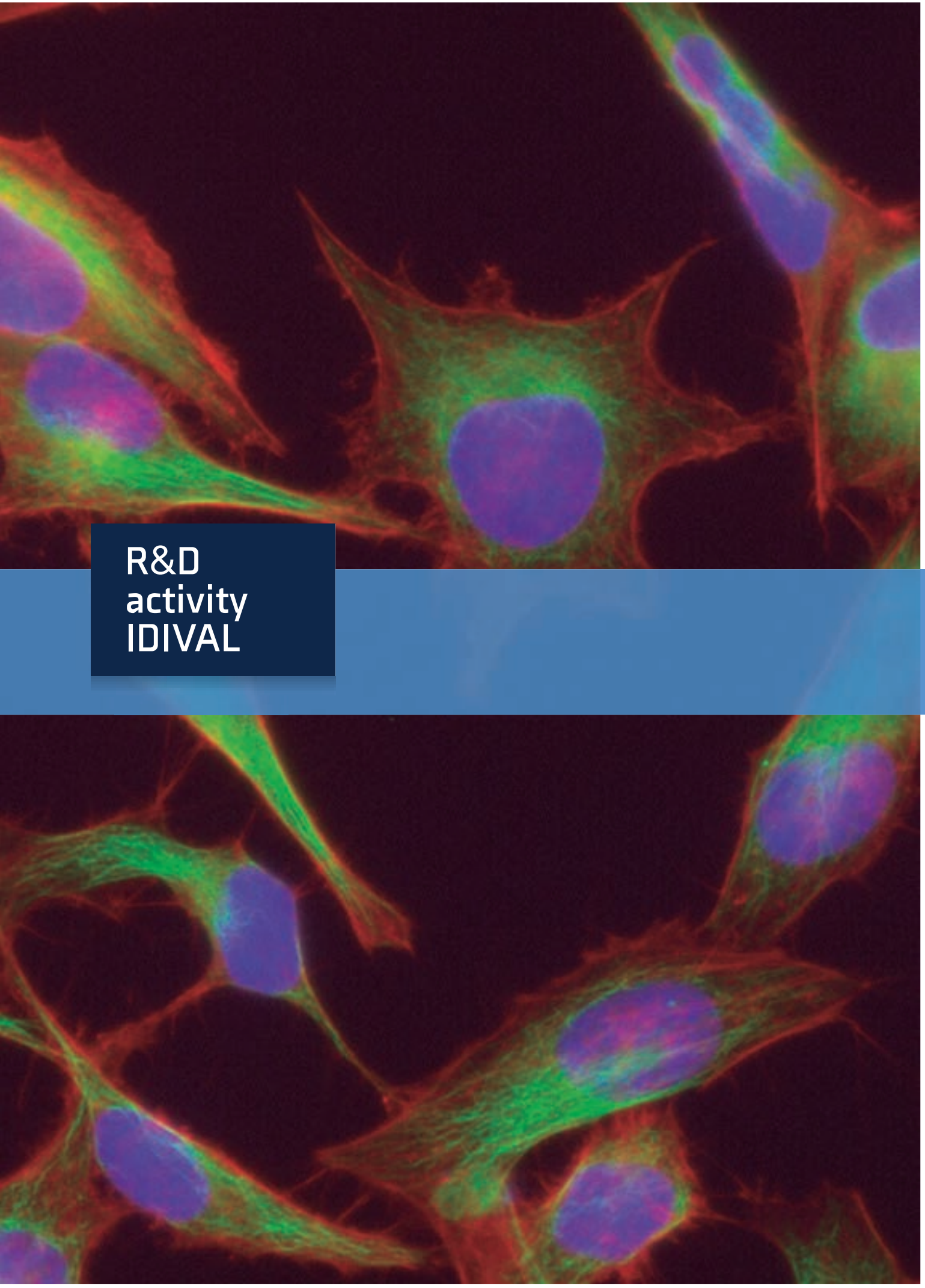
The Biomedical Research Forum of Cantabria, consisting of Cantabria Healthcare Services, the Marqués de Valdecilla Research Institute (IDIVAL), the University of Cantabria and the Institute of Biomedicine and Biotechnology of Cantabria have launched the SANTANDER BIOMEDICAL LECTURES programme, a series of lectures intended to advance worldwide Biomedical knowledge. The lectures bring to Santander prestigious international researchers in fields such as Oncology, Neurology, Immunology, Regenerative Medicine, and Microbiology. 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.

Annual citations in the period 1998-2016 of works identified with the descriptor "Valdecilla" in filiation



(fuente: WOS)





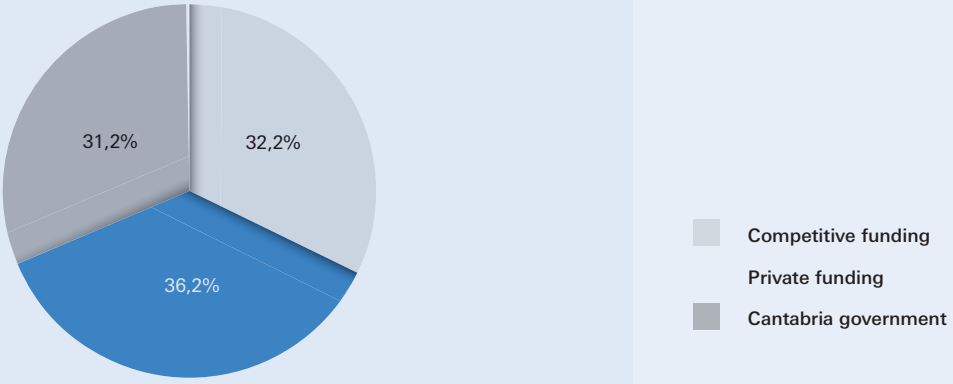
R&D activity IDIVAL

IDIVAL FUNDING IN 2016

Revenue

IDIVAL recorded total revenue of €6.98 million in 2016. The revenue pertaining to the Government of Cantabria was €2.18 million, representing 31.2% of total revenue. The remaining revenue (68.8%) pertains to the public and private competitive programmes at national and international levels (€2.53 million) and to the private agreements and contracts signed during the year (€2.25 million)

ORIGIN OF REVENUES 2016 IDIVAL	2016
Government of Cantabria	2.178.554,00
Competitive calls	2.526.390,63
Regional programs	22.586,49
National R & D & I Plan	2.306.428,24
Programs European Commission	16.648,79
Private Competitive Aid	180.727,11
Private contracts and agreements	2.249.767,36
Clinical Trials	583.914,86
Service Contracts	584.655,10
Collaboration Agreements	356.652,80
Donations	724.544,60
Provision of services	20.521,49
Total income	**6.975.233,48 €**



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 2016, it allocated a total of €2.84 million to developing projects with specific funding, €1.93 million to structural, costs and €230,000 to investments.

The IDIVAL grant programme represented expenditure of €760,000 (Post-MIR Valdecilla López Albo contracts, pre-doctoral contracts, co-financing of projects and contracts, etc.).

Personnel

In 2016, IDIVAL had 29 Research Groups, consisting of researchers, collaborators and technical personnel, all belonging to the Marqués de Valdecilla University Hospital and the University of Cantabria. Of these research groups, 16 are consolidated, 2 emerging, 8 clinical, 1 newly created and 2 cross-disciplinary. Of these, 20 are directed by head researchers involved with clinical activity, 7 by researchers of the University of Cantabria and 2 by Institute researchers.

In 2016, these groups had a total of 650 members, of which 59 were Main researchers on projects developed through competitive funding in active national or international calls over the last five years (2011-2015).

Personnel contracted by IDIVAL during 2016 belong to the following programmes:

Researcher Programmes	**Number**
Miguel Servet Programme (ISCIII)	2
IDIVAL Researchers	6
Research Training Programme	**Number**
Rio Hortega Programme (ISCIII)	1
Sara Borell Programme (ISCIII)	2
Wenceslao López Albo Programme (IDIVAL)	9
IDIVAL Predoctoral programme	5
MINECO Predoctoral programme	1
Contracts for Research Projects	**Number**
IDIVAL-funded contracts	21
ISCIII contracts	20
MICINN contracts	3
Privately-funded contracts	45
Support Services	**Number**
Scren Programme (ISCIII)	2
Biobank network (ISCIII)	1
ITEMAS Platform (ISCIII)	3
Infrastructure technicians (ISCIII)	1
IDIVAL support personnel	12
ISCIII Healthcare Research Manager	1
Research Management Training Programme	**Number**
IDIVAL Healthcare Research Manager	2

Publications

In terms of production activity, IDIVAL researchers have published 493 indexed papers in 2016 (excluding conference papers published in journals). In 246 papers (49.9%), the first or last author belongs to IDIVAL.

Impact factor

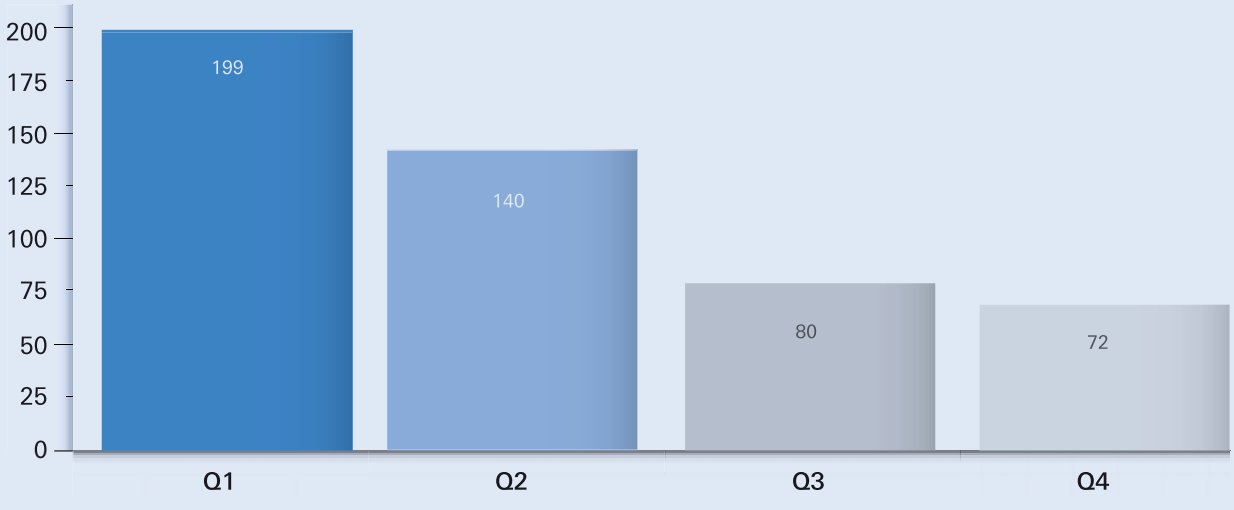
In 2016. the cumulative impact factor of IDIVAL group publications was 1915 (JCR 2015), the percentage of publications with an impact factor in the first quartile was 40%, and 70 papers published in 2016 had an impact factor in the first decile of the subject category..

Citations

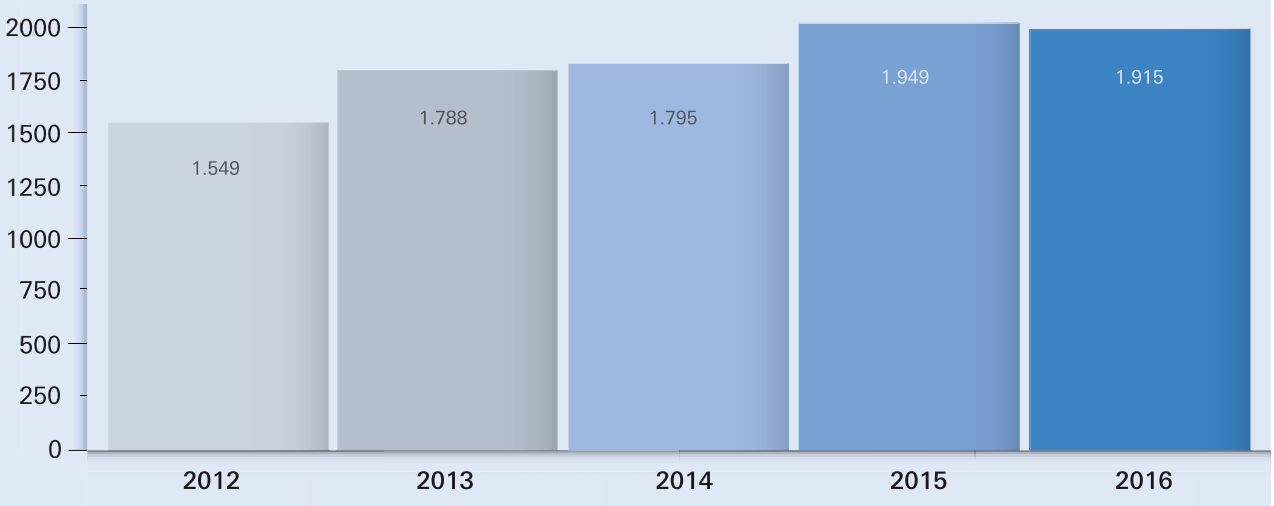
The first article by Valdecilla researchers was cited in 1930 and 1941. This was the paper published by Dr González Aguilar: González-Aguilar J. Contribution to the pathogeny of tendon tumours of giant cells. Journal of Bone and Joint Surgery, 1930; 12: 280-288.

Throughout 2016, the Valdecilla brand obtained 12,711 citations, according to data from the ISI Web of Knowledge platform (using the descriptor "Valdecilla" in the affiliation field). Thus, in 2016 the Valdecilla brand exceeded an accumulated 101,000 citations, and more than 150 works exceeded 100 citations, with the number of citations obtained annually continuing to increase.

2016 IDIVAL PUBLICATIONS, DISTRIBUTED BY QUARTILE

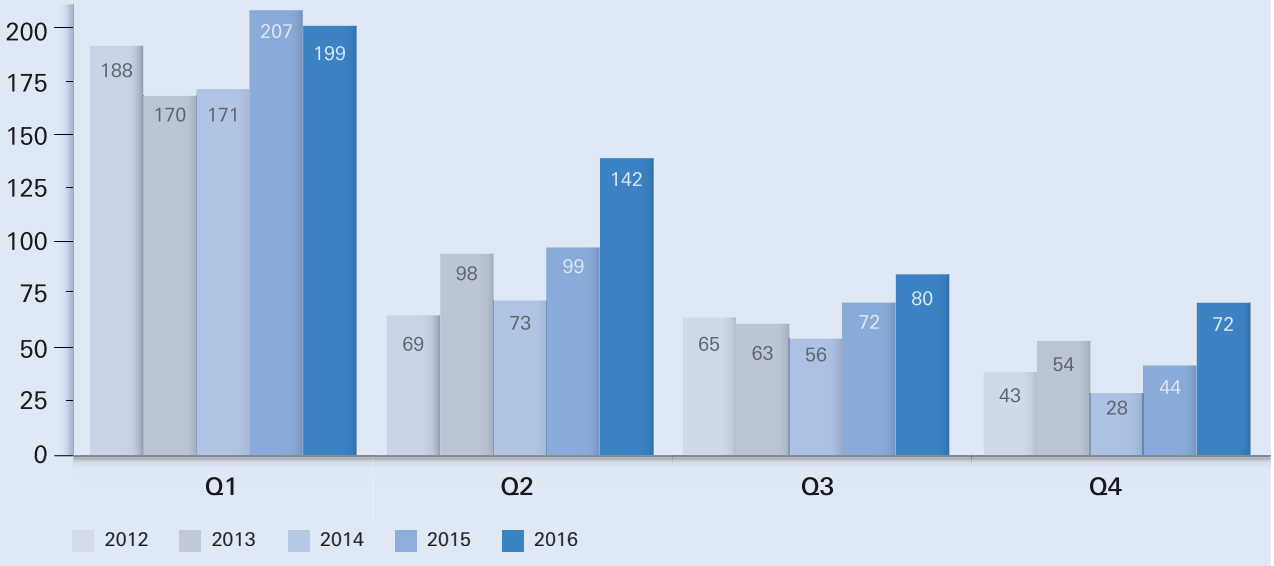


EVOLUTION OF THE TOTAL IMPACT FACTOR AND THE AVERAGE IMPACT FACTOR



EVOLUTION OF THE DISTRIBUTION BY QUARTERS OF THE IMPACT FACTOR. DISTRIBUTION BY CUARTILES

Year	Q1		Q2		Q3		Q4		Total
	N	%	N	%	N	%	N	%	
2012	188	51,6%	69	19,0%	64	17,6%	43	11,81%	**364**
2013	170	44,2%	98	25,5%	63	16,4%	54	14,0%	**385**
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**



IDIVAL PUBLICATIONS IN 2016 ACCORDING TO IMPACT FACTOR

(Excluding those derived from multicentre collaborations)

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
ACTA DIABETOL	3,074	1	3,074	2	5
ACTAS UROL ESP	0,964	5	4,82	4	9
ADV HEALTHC MATER	5,76	1	5,76	1	1
ADV THER	2,503	1	2,503	2	5
AGING (ALBANY NY)	3,979	3	11,937	2	4
AIDS REV	2,068	1	2,068	4	8
ALLERGOL IMMUNOPATHOL (MADR)	1,689	1	1,689	4	8
ALLERGY	6,335	3	19,005	1	1
AM J CARDIOL	3,154	4	12,616	2	4
AM J CRIT CARE	2,053	1	2,053	3	7
AM J DERMATOPATHOL	1,396	1	1,396	3	7
AM J RESPIR CRIT CARE MED	13,118	4	52,472	1	1
AM J SURG PATHOL	4,951	2	9,902	1	2
AM J TRANSPLANT	5,669	3	17,007	1	1
AN PEDIATR (BARC)	0,773	3	2,319	4	9
ANN HEMATOL	3,022	2	6,044	2	5
ANN NEUROL	9,638	1	9,638	1	1
ANN ONCOL	9,269	1	9,269	1	1
ANN RHEUM DIS	12,384	1	12,384	1	1
ANTICANCER RES	1,895	1	1,895	3	8
ANTIMICROB AGENTS CHEMOTHER	4,415	3	13,245	1	2
APPL PHYSIOL NUTR METAB	1,91	1	1,91	3	7
ARCH BRONCONEUMOL	1,771	3	5,313	3	8
ARCH ESP UROL	0,307	2	0,614	4	10
ARTHRITIS CARE RES (HOBOKEN)	3,229	1	3,229	2	4
ARTHRITIS RES THER	3,979	1	3,979	1	3
ARTHRITIS RHEUMATOL	6,009	4	24,036	1	2
ATHEROSCLEROSIS	3,942	1	3,942	1	2
AUTOIMMUN REV	8,49	1	8,49	1	1
BEST PRACT RES CLIN RHEUMATOL	3,267	2	6,534	2	4
BIOL BLOOD MARROW TRANSPLANT	3,98	1	3,98	1	2
BIOMED OPT EXPRESS	3,344	1	3,344	2	3

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
BLOOD	11,847	2	23,694	1	1
BMC CANCER	3,265	3	9,795	2	4
BMC MED	8,005	1	8,005	1	1
BMC NEUROL	1,961	1	1,961	3	6
BMC PULM MED	2,329	1	2,329	3	6
BMJ OPEN	2,562	1	2,562	1	3
BONE	3,736	1	3,736	2	3
BONE MARROW TRANSPLANT	3,636	2	7,272	2	3
BR J CANCER	5,569	1	5,569	1	2
BR J HAEMATOL	5,812	1	5,812	1	2
BR J NEUROSURG	1,063	1	1,063	4	9
BRAIN BEHAV IMMUN	5,874	1	5,874	1	2
BRAIN IMAGING BEHAV	3,667	1	3,667	2	3
BREAST CANCER RES	5,211	1	5,211	1	2
BREAST CARE (BASEL)	1,645	1	1,645	3	7
CALCIF TISSUE INT	3,052	1	3,052	2	5
CANCER EPIDEMIOL	2,644	2	5,288	3	6
CANCER LETT	5,992	1	5,992	1	2
CANCER MED	2,915	1	2,915	3	6
CARDIOVASC DIABETOL	4,534	1	4,534	1	2
CARDIOVASC RES	5,465	1	5,465	1	2
CATHETER CARDIOVASC INTERV	2,181	2	4,362	3	6
CELL SIGNAL	4,191	1	4,191	2	4
CELL TISSUE RES	2,948	1	2,948	3	6
CEPHALALGIA	6,052	1	6,052	1	1
CEREBELLUM	2,429	1	2,429	3	6
CHEST	6,136	1	6,136	1	2
CIR ESP	1	1	1	3	7
CIRC CARDIOVASC INTERV	5,706	1	5,706	1	2
CIRC J	4,124	1	4,124	1	3
CIRCULATION	17,202	1	17,202	1	1
CLIMACTERIC	2,492	1	2,492	2	3
CLIN CANCER RES	8,738	2	17,476	1	1
CLIN CARDIOL	2,431	1	2,431	2	5
CLIN CHEM LAB MED	3,017	1	3,017	1	2
CLIN CHIM ACTA	2,799	1	2,799	1	3

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
CLIN EXP IMMUNOL	3,148	1	3,148	2	5
CLIN EXP RHEUMATOL	2,495	25	62,375	2	5
CLIN GASTROENTEROL HEPATOL	7,68	2	15,36	1	1
CLIN IMMUNOL	4,034	1	4,034	2	3
CLIN MICROBIOL INFECT	4,575	2	9,15	1	2
CLIN NEUROPHYSIOL	3,426	1	3,426	2	3
CLIN NEUROPSYCHOL	1,556	1	1,556	3	8
CLIN NUCL MED	4,278	1	4,278	1	2
CLIN PHYSIOL FUNCT IMAGING	1,869	1	1,869	3	7
CLIN SCI (LOND)	5,016	1	5,016	1	2
CLIN TRANSL ONCOL	2,075	3	6,225	3	8
CNS DRUGS	4,91	1	4,91	1	2
COLORECTAL DIS	2,452	1	2,452	3	6
COMPUT BIOL MED	1,521	1	1,521	2	5
DERMATOLOGY	1,449	1	1,449	3	6
DIABETES CARE	8,934	1	8,934	1	1
DIAGN MICROBIOL INFECT DIS	2,45	3	7,35	3	6
DIS MODEL MECH	4,316	1	4,316	2	4
DRUG RESIST UPDAT	7,95	1	7,95	1	1
EARLY INTERV PSYCHIATRY	2,889	1	2,889	2	4
ELECTROPHORESIS	2,482	1	2,482	2	5
EMERG MICROBES INFECT	4,012	1	4,012	2	4
EMERGENCIAS	2,917	1	2,917	1	2
ENDOCRINOL NUTR	1,314	3	3,942	4	9
ENDOSCOPY	5,634	1	5,634	1	2
ENFERM INFECC MICROBIOL CLIN	1,53	3	4,59	3	8
ENVIRON. HEALTH PERSPECT.	8,443	2	16,886	1	1
EPIDEMIOL PSYCHIATR SCI	2,847	1	2,847	2	4
EUR ARCH PSYCHIATRY CLIN NEUROSCI	4,113	1	4,113	1	2
EUR EAT DISORD REV	2,912	1	2,912	2	4
EUR HEART J	15,064	5	75,32	1	1
EUR HEART J CARDIOVASC IMAGING	4,293	1	4,293	1	3
EUR J APPL PHYSIOL	2,328	1	2,328	2	5
EUR J CANCER	6,163	1	6,163	1	2
EUR J CARDIOTHORAC SURG	2,803	2	5,606	2	5
EUR J EPIDEMIOL	7,105	1	7,105	1	1

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
EUR J HAEMATOL	2,544	2	5,088	3	6
EUR J HUM GENET	4,58	1	4,58	1	3
EUR J INTERN MED	2,591	2	5,182	1	2
EUR J NUCL MED MOL IMAGING	5,537	3	16,611	1	1
EUR J SURG ONCOL	2,94	1	2,94	2	5
EUR UROL	14,976	1	14,976	1	1
EUROINTERVENTION	3,863	2	7,726	2	3
EUROPACE	4,021	1	4,021	2	3
EXP HEMATOL	2,303	1	2,303	3	6
EXP. OPIN. ORPHAN DRUGS	0,464	1	0,464	4	10
EXPERT OPIN DRUG METAB TOXICOL	2,598	2	5,196	3	6
EXPERT REV ANTICANCER THER	2,094	1	2,094	3	8
EXPERT REV CLIN IMMUNOL	2,596	1	2,596	3	6
FREE RADIC BIOL MED	5,784	1	5,784	1	2
FRONT AGING NEUROSCI	4,348	1	4,348	1	2
FRONT IMMUNOL	5,695	1	5,695	1	2
FRONT NEUROL	3,184	1	3,184	2	4
FRONT PSYCHOL	2,463	2	4,926	1	0
FUTURE MICROBIOL	3,637	1	3,637	2	3
GAC SANIT	1,509	1	1,509	3	7
GASTROENTEROL HEPATOL	0,8	1	0,8	4	9
GASTROINTEST ENDOSC	6,217	1	6,217	1	2
GENE	2,319	1	2,319	3	6
GENES CHROMOSOMES CANCER	3,96	1	3,96	1	3
GENES GENOM	0,692	1	0,692	4	10
HAEMATOLOGICA	6,671	1	6,671	1	1
HEADACHE	2,961	3	8,883	2	4
HEART	5,693	1	5,693	1	2
HEPATOL INT	1,125	1	1,125	4	9
HIPPOCAMPUS	4,074	1	4,074	1	3
HORM RES PAEDIAT	1,661	1	1,661	2	5
HUM IMMUNOL	2,127	1	2,127	3	8
IMMUNOBIOLOGY	2,781	1	2,781	3	6
IMMUNOLOGY	4,078	1	4,078	2	3
IMMUNOTHERAPY	2,083	1	2,083	3	8
INFLAMM BOWEL DIS	4,358	1	4,358	1	3

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
INJURY	1,91	1	1,91	3	8
INT BRAZ J UROL	0,871	2	1,742	4	9
INT IMMUNOL	3,031	1	3,031	2	5
INT J ANTIMICROB AGENTS	4,097	1	4,097	1	2
INT J CANCER	5,531	3	16,593	1	2
INT J CARDIOL	4,638	5	23,19	1	2
INT J COLORECTAL DIS	2,383	1	2,383	3	6
INT J INFECT DIS	2,229	1	2,229	3	6
INT J MOL SCI	3,257	1	3,257	2	4
INT J NEUROPSYCHOPHARMACOL	4,333	1	4,333	1	2
INTENSIVE CARE MED	10,125	1	10,125	1	1
J ACAD NUTR DIET	3,609	1	3,609	1	3
J ALZHEIMERS DIS	3,92	1	3,92	1	3
J AM ACAD DERMATOL	5,621	1	5,621	1	1
J ANTIMICROB CHEMOTHER	4,919	4	19,676	1	2
J CARDIOVASC SURG (TORINO)	1,632	1	1,632	3	7
J CLIN GASTROENTEROL	3,163	1	3,163	2	4
J CLIN LIPIDOL	4,906	1	4,906	1	1
J CLIN NEUROPHYSIOL	1,337	1	1,337	4	8
J CLIN ONCOL	20,982	2	41,964	1	1
J CLIN PSYCHIATRY	5,408	1	5,408	1	2
J CLIN SLEEP MED	2,71	1	2,71	2	4
J CLIN VIROL	2,647	2	5,294	2	5
J CRANIOFAC SURG	0,7	1	0,7	4	9
J CROHNS COLITIS	6,585	1	6,585	1	2
J CUTAN PATHOL	1,409	2	2,818	3	7
J DERMATOL	1,577	2	3,154	2	5
J EUR ACAD DERMATOL VENEREOL	3,029	2	6,058	1	2
J EXP MED	11,24	1	11,24	1	1
J GERONTOL A BIOL SCI MED SCI	5,476	1	5,476	1	1
J HEART LUNG TRANSPLANT	7,509	1	7,509	1	1
J HUM GENET	2,487	1	2,487	3	6
J IMMUNOL RES	2,812	1	2,812	3	6
J INFECT	4,382	3	13,146	1	2
J INVEST DERMATOL	6,915	1	6,915	1	1
J LARYNGOL OTOL	0,736	1	0,736	4	9

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
J LUMIN	2,693	1	2,693	1	2
J MATER CHEM C MATER OPT ELECTRON DEVICES	5,066	1	5,066	1	2
J NATL COMPR CANC NETW	4,262	1	4,262	1	3
J NEUROL	3,408	3	10,224	2	3
J NEUROL SCI	2,126	2	4,252	3	6
J NEUROONCOL	2,754	1	2,754	2	4
J NON-CRYST SOLIDS	1,825	1	1,825	1	2
J PHYS CHEM C	4,509	1	4,509	1	3
J PINEAL RES	9,314	1	9,314	1	1
J PLAST RECONSTR AESTHET SURG	1,743	1	1,743	2	5
J PROTEOMICS	3,867	1	3,867	1	2
J RHEUMATOL	3,236	2	6,472	2	4
J THERM ANAL CALORIM	1,781	1	1,781	2	4
J THORAC CARDIOVASC SURG	3,494	2	6,988	2	3
J TRANSL MED	3,694	1	3,694	1	3
J VASC SURG VENOUS LYMPHAT DISORD	0,882	1	0,882	3	8
J. NEUROL. NEUROSURG. PSYCHIATRY	6,431	2	12,862	1	1
JACC CARDIOVASC INTERV	7,63	2	15,26	1	1
JAMA PSYCHIATRY	14,417	1	14,417	1	1
LANCET NEUROL	23,468	1	23,468	1	1
LANGENBECKS ARCH SURG	2,149	1	2,149	2	4
LEUK LYMPHOMA	3,093	2	6,186	2	4
LEUK RES	2,606	1	2,606	3	6
LEUKEMIA	12,104	2	24,208	1	1
LIFE SCI	2,685	1	2,685	2	5
LIVER TRANSPL	3,951	1	3,951	1	3
MATURITAS	3,12	1	3,12	2	4
MED CLIN (BARC)	1,267	12	15,204	2	5
MED INTENSIVA	1,193	5	5,965	4	10
MEDIATORS INFLAMM	3,418	1	3,418	2	4
MEDICINE (BALTIMORE)	2,133	4	8,532	2	3
MICROBES INFECT	2,291	1	2,291	3	7
MOL NEUROBIOL	5,397	1	5,397	1	2
MOL PSYCHIATRY	13,314	1	13,314	1	1
MOV DISORD	6,01	1	6,01	1	1

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
NANO LETT	13,779	1	13,779	1	1
NANOMATERIALS (BASEL)	2,69	1	2,69	1	3
NANOSCALE	7,76	1	7,76	1	2
NAT COMMUN	11,329	1	11,329	1	1
NAT NEUROSCI	16,724	2	33,448	1	1
NAT REV GASTROENTEROL HEPATOL	14,435	1	14,435	1	1
NAT REV RHEUMATOL	10,531	1	10,531	1	1
NEFROLOGIA	1,207	7	8,449	4	8
NEPHROL DIAL TRANSPLANT	4,085	1	4,085	1	2
NEUROBIOL AGING	5,153	2	10,306	1	2
NEUROCHEM RES	2,472	1	2,472	3	6
NEURODEGENER DIS	2,937	1	2,937	2	4
NEUROENDOCRINOLOGY	2,583	6	15,498	3	6
NEUROIMAGING CLIN N AM	1,557	1	1,557	3	7
NEUROL SCI	1,783	1	1,783	3	7
NEUROLOGY	8,166	1	8,166	1	1
NEUROMUSCUL DISORD	3,107	1	3,107	2	4
NEUROPATHOL APPL NEUROBIOL	4,483	1	4,483	1	2
NEUROSCI BIOBEHAV REV	8,58	1	8,58	1	1
NEUROSURGERY	3,78	1	3,78	1	3
NEUROTOX RES	3,14	1	3,14	2	4
NPJ PRIM CARE RESPIR MED	1,447	1	1,447	3	6
NUCL MED COMMUN	1,453	1	1,453	3	8
NUTR HOSP	1,497	1	1,497	3	8
OCCUP ENVIRON MED	3,745	1	3,745	1	2
OCUL IMMUNOL INFLAMM	2,481	2	4,962	2	4
ONCOGENE	7,932	1	7,932	1	1
ONCOL. RES. TREAT.	1,333	2	2,666	4	9
ONCOTARGET	5,008	6	30,048	1	3
OPT LASER TECHNOL	1,879	1	1,879	2	4
OSTEOPOROS INT	3,445	1	3,445	2	4
PATHOL RES PRACT	1,388	4	5,552	3	7
PATIENT EDUC COUNS	2,232	1	2,232	2	4
PHYS CHEM CHEM PHYS	4,449	1	4,449	1	3
PLOS ONE	3,057	11	33,627	1	2
POLYMERS-BASEL	2,944	1	2,944	1	3

Journa	IF (JCR 2015)	Nº	IF Suma	Cuartil	Decil
PROG NEUROBIOL	13,177	1	13,177	1	1
PSYCHOPHARMACOLOGY (BERL)	3,54	1	3,54	2	4
QJM	2,824	2	5,648	1	2
RADIOTHER ONCOL	4,817	1	4,817	1	2
RESPIR MED	3,036	1	3,036	2	4
REV ESP ENFERM DIG	1,455	2	2,91	4	9
REV ESP MED NUCL IMAGEN MOL	0,983	3	2,949	4	9
REV ESP QUIMIOTER	1,014	5	5,07	4	9
REV NEUROL	0,684	11	7,524	4	10
REV PSIQUIATR SALUD MENT	1,65	1	1,65	3	7
RHEUMATOL INT	1,702	1	1,702	3	8
RHEUMATOLOGY (OXFORD)	4,524	3	13,572	1	2
ROM J MORPHOL EMBRYOL	0,811	1	0,811	4	10
SCAND J GASTROENTEROL	2,199	1	2,199	3	7
SCI REP	5,228	8	41,824	1	2
SEIZURE	2,109	2	4,218	3	6
SEMIN ARTHRITIS RHEUM	3,946	3	11,838	2	3
SIMUL HEALTHC	1,685	1	1,685	3	6
SKELETAL RADIOL	1,527	1	1,527	2	5
SLEEP BREATH	2,332	1	2,332	2	5
SOL ENERGY MATER SOL CELLS	4,732	1	4,732	1	2
THER DRUG MONIT	2,094	3	6,282	2	4
THORAX	8,121	1	8,121	1	1
THROMB HAEMOST	5,255	3	15,765	1	2
THROMB RES	2,32	2	4,64	3	7
TRANSPL IMMUNOL	1,317	1	1,317	4	10
TRANSPL INT	2,835	2	5,67	1	2
TRANSPLANT PROC	0,867	10	8,67	4	10
TRANSPLANT REV (ORLANDO)	3,915	1	3,915	2	4
TRANSPLANTATION	3,69	2	7,38	2	4
UROLOGY	2,187	1	2,187	2	4
WOMEN HEALTH	1,294	1	1,294	1	2
WORLD J GASTROENTEROL	2,787	2	5,574	2	5
WORLD J UROL	2,397	1	2,397	2	4
WORLD NEUROSURG	2,685	3	8,055	2	4
Total general					

Impact Factor of Research Groups

The number of works by IDIVAL research groups and their impact factors are shown in the following table:

GROUP	Nº of works	IF Total
Pathological anatomy and molecular pathology	18	36,4555
Apoptosis	3	12,492
Nuclear Cell Biology	7	24,839
Cell cycle, stem cells and cancer	4	21,835
Cytokines and growth factors in pathological tissue plasticity phenomena	11	47,704
Clinic and genetics of headaches	11	43,673
Diagnosis and treatment by image	8	32,138
Neurodegenerative diseases	33	123,897
Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	72	264,243
Epidemiology and pathogenic mechanisms of infectious diseases	30	98,636
Epidemiology and public health	36	145,435
Transplantation hemopathology	37	164,141
Nanovaccines and cellular vaccines based on listeria monocytogenes and its applications in biomedicine	6	25,070
Group of cardiovascular investigation	21	140,623
Molecular image	21	61,852
Infection and immunity and digestive pathology	26	116,186
Immunopathology of rheumatic diseases	13	56,390
Melatonin and breast cancer	3	9,331
Mineral and lipid metabolism	36	103,717
Clinical and molecular microbiology	31	94,143
Advanced microscopy and folding of proteins and cytoskeleton	1	4,348
Nanomedicine	13	58,565
Hematological neoplasms and hematopoietic progenitors transplantation	14	51,393
Neurophysiology in epilepsy and neurointensive	5	18,524
New techniques in abdominal surgery	11	21,292
Psychiatry	23	130,588
Cellular signaling and therapeutic targets in cancer	11	30,862
Transplantation and autoimmunity	48	118,768
Unit of clinical trials and medical oncology and palliative medicine	29	104,217

Some of the most Representative Articles

1. Adams HH, Hibar DP, Chouraki V, Stein JL, Nyquist PA, Rentería ME, Trompet S, Arias-Vasquez A, Seshadri S, Desrivières S, Beecham AH, Jahanshad N, Wittfeld K, Van der Lee SJ, Abramovic L, Alhusaini S, Amin N, Andersson M, Arfanakis K, Aribisala BS, Armstrong NJ, Athanasiu L, Axelsson T, Beiser A, Bernard M, Bis JC, Blanken LM, Blanton SH, Bohlken MM, ..., Thompson PM.
Novel genetic loci underlying human intracranial volume identified through genome-wide association.
Nat Neurosci 2016. 19: 1569-1582.
FI: 16,724(Q1)

2. Berciano J, Gallardo E, Orizaola P, Marco de Lucas E, García A, Pelayo-Negro AL, Sedano MJ.
Early axonal Guillain-Barré syndrome with normal peripheral conduction: imaging evidence for changes in proximal nerve segments.
J Neurol Neurosurg Psychiatry 2016. 87: 563-565. FI: 6,431(Q1)

3. Cabezas J, Sampedro B, Hernández C, Crespo J.
Computerized Physician Order Entry-Based System Improves Hepatitis B Virus Screening in Patients Undergoing Chemotherapy.
J Clin Oncol 2016. 34: 290-0.
FI: 20,982(Q1)

4. Campos-Rodriguez F, Queipo-Corona C, Carmona-Bernal C, Jurado-Gamez B, Cordero-Guevara J, Reyes-Nuñez N, Troncoso-Acevedo F, Abad-Fernandez A, Teran-Santos J, Caballero-Rodriguez J, Martin-Romero M, Encabo-Motiño A, Sacristan-Bou L, Navarro-Esteva J, Somoza-Gonzalez M, Masa JF, Sanchez-Quiroga MA, Jara-Chinarro B, Orosa-Bertol B, Martinez-Garcia MA.
Spanish Sleep Network. Continuous Positive Airway Pressure Improves Quality of Life in Women with Obstructive Sleep Apnea. A Randomized Controlled Trial.
Am J Respir Crit Care Med 2016. 194: 1286-1294. FI: 13,118(Q1)

5. García-Hevia L, Valiente R, Martín-Rodríguez R, Renero-Lecuna C, González J, Rodríguez-Fernández L, Aguado F, Villegas JC, Fanarraga ML.
Nano-ZnO leads to tubulin macrotube assembly and actin bundling, triggering cytoskeletal catastrophe and cell necrosis.
NANOSCALE 2016. 8: 10963-10973.
FI: 7,760(Q1)

6. Márquez A, Vidal-Bralo L, Rodríguez-Rodríguez L, González-Gay MA, Balsa A, González-Álvaro I, Carreira P, Ortego-Centeno N, Ayala-Gutiérrez MM, García-Hernández FJ, González-Escribano MF, Sabio JM, Tolosa C, Suárez A, González A, Padyukov L, Worthington J, Vyse T, Alarcón-Riquelme ME, Martín J.
A combined large-scale meta-analysis identifies COG6 as a novel shared risk locus for rheumatoid arthritis and systemic lupus erythematosus.
Ann Rheum Dis 2017. 76: 286-294.
FI: 12,384(Q1)

7. Masa JF, Corral J, Caballero C, Barrot E, Terán-Santos J, Alonso-Álvarez ML, Gomez-Garcia T, González M, López-Martín S, De Lucas P, Marin JM, Marti S, Díaz-Cambriles T, Chiner E, Egea C, Miranda E, Mokhlesi B, Spanish Sleep Network, García-Ledesma E, Sánchez-Quiroga MÁ, Ordax E, González-Mangado N, Troncoso MF, Martinez-Martinez MÁ, Cantalejo O, Ojeda E, Carrizo SJ, Gallego B, Pallero M, ..., Bengoa M.
Non-invasive ventilation in obesity hypoventilation syndrome without severe obstructive sleep apnoea.
Thorax 2016. 71: 899-906.
FI: 8,121(Q1)

8. Orta-Mascaró M, Consuegra-Fernández M, Carreras E, Roncagalli R, Carreras-Sureda A, Alvarez P, Girard L, Simões I, Martínez-Florensa M, Aranda F, Merino R, Martínez VG, Vicente R, Merino J, Sarukhan A, Malissen M, Malissen B, Lozano F.
CD6 modulates thymocyte selection and peripheral T cell homeostasis. J Exp Med 2016. 213: 1387-1397.
FI: 11,240(Q1)

9. Peeters K, Palaima P, Pelayo-Negro AL, García A, Gallardo E, García-Barredo R, Mateiu L, Baets J, Menten B, De Vriendt E, De Jonghe P, Timmerman V, Infante J, Berciano J, Jordanova A.
Charcot-Marie-Tooth disease type 2G redefined by a novel mutation in LRSAM1.
Ann Neurol 2016. 80: 823-833.
FI: 9,638(Q1)

10. Perelló CS, Fernández-Carrillo C, Londoño MC, Arias-Loste T, Hernández-Conde M, Llerena S, Crespo J, Forns X, Calleja JL.
Reactivation of Herpesvirus in Patients With Hepatitis C Treated With Direct-Acting Antiviral Agents.
Clin Gastroenterol Hepatol 2016.
FI: 7,680(Q1)

11. Robles EF, Mena-Varas M, Barrio L, Merino-Cortes SV, Balogh P, Du MQ, Akasaka T, Parker A, Roa S, Panizo C, Martin-Guerrero I, Siebert R, Segura V, Agirre X, Macri-Pellizeri L, Aldaz B, Vilas-Zornoza A, Zhang S, Moody S, Calasanz MJ, Tousseyn T, Broccardo C, Brousset P, Campos-Sanchez E, Cobaleda C, Sanchez-Garcia I, Fernandez-Luna JL, Garcia-Muñoz R, Pena E, ..., Martinez-Climent JA.
Homeobox NKX2-3 promotes marginal-zone lymphomagenesis by activating B-cell receptor signalling and shaping lymphocyte dynamics.
Nat Commun 2016. 7: 11889-0.
FI: 11,329(Q1)

12. Roncero AM, López-Nieva P, Cobos-Fernández MA, Villa-Morales M,

González-Sánchez L, López-Lorenzo JL, Llamas P, Ayuso C, Rodríguez-Pinilla SM, María Del CA, Piris M, Fernández-Navarro P, Fernández AF, Fraga MF, Santos J, Fernández-Piqueras J.
Contribution of JAK2 mutations to T-cell lymphoblastic lymphoma development.
Leukemia 2016. 30: 94-103.
FI: 12,104(Q1)

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13. Sanchez-Barcelo EJ, Mediavilla MD, Vriend J, Reiter RJ.
Constitutive photomorphogenesis protein 1 (COP1) and COP9 signalosome, evolutionarily conserved photomorphogenic proteins as possible targets of melatonin.
J Pineal Res 2016. 61: 41-51.
FI: 9,314(Q1)

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14. Sanz B, Calatayud MP, Torres TE, Fanarraga ML, Ibarra MR, Goya GF.
Magnetic hyperthermia enhances cell toxicity with respect to exogenous heating.
BIOMATERIALS 2017. 114: 62-70.
FI: 8,387(Q1)

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15. Spaliviero M, Poon BY, Karlo CA, Guglielmetti GB, Di Paolo PL, Beluco Corradi R, Martin-Malburet AG, Campos-Juanatey F, Escudero-Fontano E, Sjoberg DD, Russo P, Coleman JA, Akin O, Touijer KA.
An Arterial Based Complexity (ABC) Scoring System to Assess the Morbidity Profile of Partial
Nephrectomy. Eur Urol 2016. 69: 72-79. FI: 14,976(Q1)

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16. van Erp TG, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreassen OA, Agartz I, Westlye LT, Haukvik UK, Dale AM, Melle I, Hartberg CB, Gruber O, Kraemer B, Zilles D, Donohoe G, Kelly S, McDonald C, Morris DW, Cannon DM, Corvin A, Machielsen MW, Koenders L, de Haan L, Veltman DJ, Satterthwaite TD, Wolf DH, Gur RC, Gur RE, ...,
Turner JA. Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium.
Mol Psychiatry 2016. 21: 547-553.
FI: 13,314(Q1)

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17. Zufiría M, Gil-Bea FJ, Fernández-Torrón R, Poza JJ, Muñoz-Blanco JL, Rojas-García R, Riancho J, de Munain AL.**ALS: A bucket of genes, environment, metabolism and unknown ingredients.**
Prog Neurobiol 2016. 142: 104-129.
FI: 13,177(Q1)

18. Setién-Suero E, Suárez-Pinilla M, Suárez-Pinilla P, Crespo-Facorro B, Ayesa-Arriola R.
Homocysteine and cognition: A systematic review of 111 studies.
Neurosci Biobehav Rev 2016. 69: 280-298. FI: 8,580(Q1)

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19. López-Mejías R, Castañeda S, González-Juanatey C, Corrales A, Ferraz-Amaro I, Genre F, Remuzgo-Martínez S, Rodriguez-Rodriguez L, Blanco R, Llorca J, Martín J, González-Gay MA.
Cardiovascular risk assessment in patients with rheumatoid arthritis: The relevance of clinical, genetic and serological markers.
Autoimmun Rev 2016. 15: 1013-1030. FI: 8,490(Q1)

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20. Remuzgo-Martínez S, Genre F, López-Mejías R, Ubilla B, Mijares V, Pina T, Corrales A, Blanco R, Martín J, Llorca J, González-Gay MA.
Expression of osteoprotegerin and its ligands, RANKL and TRAIL, in rheumatoid arthritis.
Sci Rep 2016. 6: 29713-0.
FI: 5,228(Q1)

Research Projects

R&D+I NATIONAL PLAN PROJECTS ACTIVE OR GRANTED IN 2016

Active Grants

Throughout 2016, IDIVAL groups maintained 34 active projects in the R&D+i National Plan, 7 research contracts, and two European projects.

Projects

PI12/02605
María Victoria Mier Ruiz.
Epidemiological aspects, variability and survival in cardiac arrest care outside hospital by emergency services in Spain (sub-project Cantabria). CARLOS III HEALTH INSTITUTE. 2013-2016.

PI12/02288
Juan Pascual Sánchez.
Multimodal study of Alzheimer's disease biomarkers in postoperative cognitive decline. CARLOS III HEALTH INSTITUTE. 2013-2016.

PI12/00060
Miguel Ángel González-Gay Mantecón.
Study of genetic markers of cardiovascular disease and subclinical atherosclerosis in rheumatoid arthritis patients. CARLOS III HEALTH INSTITUTE. 2013-2016.

PI12/01405
Jesús González Macías.
The canonical WNT pathway in osteoclast: study of its intervention in the regulation of bone mass. CARLOS III HEALTH INSTITUTE. 2013-2016.

PI12/00999
Juan Francisco Nistal Herrera.
Role of adiponectin and its relationship with TGF beta in myocardial remodelling induced by pressure overload in aortic stenosis and its post-surgical regression. CARLOS III HEALTH INSTITUTE. 2013-2016.

PI12/00615.
José Antonio Riancho Moral.
DNA Methylation: The pathogenic and biomarker factor in bone formation disorders. CARLOS III HEALTH INSTITUTE. 2013-2017.

SAF2013-46292-R
Benedicto Crespo Facorro. New candidate genes for the response to antipsychotic treatment in schizophrenia: evidence from gene expression studies. MINECO. 2014-2017.

SAF2013-47416-R
Miguel Ángel Piris Pinilla.
Aggressive lymphomas: treatment guided by molecular diagnosis. MINECO. 2014-2016.

SAF2013-42012-P.
Samuel Cos Corral.
Sensitising effects of melatonin for chemotherapy and radiotherapy: a study of the molecular changes that modulate this process. MINECO. 2014-2016.

SAF2013-47434-R.
María amor Hurle González.
MicroRNAs in neuropathic pain: molecular biomarkers and targeted therapies. MINECO. 2014-2016..

PI13/01008
Eloy Manuel Rodríguez Rodríguez.
Alzheimer's disease biomarkers as prognostic factors in idiopathic normal pressure hydrocephalus. CARLOS III HEALTH INSTITUTE. 2014-2016.

PI13/01310.
José Ramos Vivas.
Clinically relevant host-pathogen key interaction in Acinetobacter species. CARLOS III HEALTH INSTITUTE. 2014-2016.

PI13/01760.
José Luis Fernández Luna.
Prognostic and therapeutic relevance in ODZ 1 glioblastoma, a new target in cancer. CARLOS III HEALTH INSTITUTE. 2014-2016.

PI13/01884.
Eugenio Carrasco Marín.
Defects in innate immunity and coinfection with respiratory viruses: the perfect storm to develop invasive pneumococcal disease in children? CARLOS III HEALTH INSTITUTE. 2014-2016.

PI13/01249.
Juan Martino González.
Preservation of areas involved in the verbal working memory to prevent sequelae in glioma surgery in eloquent areas. CARLOS III HEALTH INSTITUTE. 2014-2016.

PI13/01191.
María del Carmen Fariñas Álvarez.
Intestinal colonisation by multiresistant enterobacteriaceae in patients with renal and liver transplants: multicentre cohort study and randomised, controlled, open clinical trial CARLOS III HEALTH INSTITUTE. 2014-2016.

BFU2014-54754-P.
Mª Teresa Berciano Blanco, Miguel Ángel Lafarga Coscojuela.
Acetylation regulation of the survival factor of motoneurons: its importance in snRNP biogenesis and the assembly of CAJAL nuclear bodies. MINECO. 2015-2017.

BFU2014-54026-P.
Juan Hurle González.
Biological mechanism and new significance of the interdigital cell death responsible for the separation of the fingers during limb development. MINECO. 2015-2017.

PI14/00378.
Manuel Antonio Árias Rodríguez.
Study of serological factors and cellular activation as potential early markers of chronic antibody-mediated rejection in renal transplants. CARLOS III HEALTH INSTITUTE. 2015-2017.

PI14/00900.
Alberto Gandarillas Solinis.
New Routes and Strategies Towards Squamous Cell Cancer. CARLOS III HEALTH INSTITUTE. 2015-2017.

PI14/00918.
Rosa Ayesa Arriola.
PAFIP neurocognition: Long-term longitudinal study (10 years) of cognitive functioning in patients with schizophrenia spectrum psychosis. CARLOS III HEALTH INSTITUTE. 2015-2017.

PI14/01911.
Luis Martínez Martínez.
Heteroresistance and Persistence in carbapenem-resistant Klebsiella pneumoniae. CARLOS III HEALTH INSTITUTE. 2015-2017.

PI15/00009.
Alain Antonio Ocampo Sosa.
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.

PI15/00521.
José Manuel Olmos Martínez.
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.

PI15/00525.
Miguel Ángel González-Gay Mantecón.
Genetic markers of atherosclerotic disease in Rheumatoid Arthritis. CARLOS III HEALTH INSTITUTE. 2016-2018.

PI15/01224.
Juan Francisco Nistal Herrera.
Bone morphogenetic protein 7 (BMP7): Potential therapeutic target in the pathological remodelling of the cardiovascular system. CARLOS III HEALTH INSTITUTE. 2016-2018.

PI15/02138.
Javier Crespo García.
Endothelial dysfunction, subclinical atheromatous disease and cardiomyopathy in patients with HCV infection. Characterisation and potential reversibility with direct antiviral agents. CARLOS III HEALTH INSTITUTE. 2016-2018..

PI15/01285.
Agustín Oterino Durán.
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.

PI15/00069.
Javier Llorca Díaz.
Integration of genetic big data and clinical data: survival with breast cancer in the MCC-Spain study. CARLOS III HEALTH INSTITUTE. 2016-2018.

PIE15/00079.
Javier Crespo García.
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.

PIE15/00081.
Miguel Ángel Piris Pinilla.
Discovery, Validation and Implementation of Biomarkers for Precision Oncology. CARLOS III HEALTH INSTITUTE. 2016-2019.

RTC-2015-3786-1.
Javier Gómez Román.
Development of anti-CCR9 therapeutic antibodies for the personalised treatment of tumours-TERPERAN. CARLOS III HEALTH INSTITUTE. 2016-2018.

DTS15/00238
Olga María Conde Portilla.
Fusioderm, fusion of photonic technologies for dermatological diagnosis. CARLOS III HEALTH INSTITUTE 2016-2017.

Research and Mobility Contracts

CP12/03149
Alain Antonio Ocampo Sosa.
OprD analysis in clinical strains of Pseudomonas aeruginosa with different carbapenem sensitivity levels and study of the molecular bases of OprD regulation mechanisms. CARLOS III HEALTH INSTITUTE. 2013-2016.

MS12/03149
Alain Antonio Ocampo Sosa.
Miguel Servet Type I contracts, CARLOS III HEALTH INSTITUTE. 2013-2017.

CD13/00088
Cristina Pérez Menéndez. Sara Borrell contracts. CARLOS III HEALTH INSTITUTE. 2014-2017.

CPII14/00016
José Ramos Vivas.
Miguel Servet Type II contracts. CARLOS III HEALTH INSTITUTE. 2015-2017.

BES-2014-070615
Fulgencio Ruso Julve.
Grants for pre-doctorate contracts. MINECO 2015-2019.

GIS15/00017
Aroa Sanz Carreira.
Healthcare Research Management Contracts in IIS. CARLOS III HEALTH INSTITUTE 2016-2018.

CD15/00095
Fernanda Genre.
Sara Borrell contracts. CARLOS III HEALTH INSTITUTE 2016-2019.

CM15/00186
Rufino Mondejar García.
Rio Hortega contracts. CARLOS III HEALTH INSTITUTE 2016-2018.

INT15/00096
Benedicto Crespo Facorro.
Contracts for intensification of research activity in the SNS CARLOS III HEALTH INSTITUTE 2016.

BA15/00053
Santiago Montes Moreno.
CARLOS III HEALTH INSTITUTE 2016.

Active European Projects in 2016

EU12/01- PSYSCAN.
Benedicto Crespo Facorro.
Translating neuroimaging findings from research into clinical practice. 7PM. European Commission.

EU13/01- Precisesads.
Miguel Ángel González-Gay.
Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases. FP7, Innovative Medicines Initiative. European Commission.

Grants awarded

In 2016, IDIVAL researchers received a positive response on 13 projects in the National Plan:

Proyectos

PI16/00156
José Pedro Vaque Díez.
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.

PI16/00915
José Antonio Riancho Moral.
Study of mesenchymal stem cells in osteoporosis: Role of long non-coding RNAs (lncRNAs) and regenerative potential. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01103
José Ramos Vivas.
Integrated biology of infection and antimicrobial resistance of Acinetobacter baumannii and A. pittii. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01294
Miguel ángel Piris Pinilla.
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.

PI16/01397
Santiago Montes Moreno.
Targeted exonic next generation sequencing for the molecular diagnosis and cell free tumor DNA analysis as a screening method for patients with DLBCL. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01415
María del Carmen Fariñas Álvarez.
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.

PI16/01535
María Victoria Francia Gil.
Induction of conjugative pheromone-induced plasmid transfer. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01585
Marcos López Hoyos.
Utility of the study of Myeloid-Derived Suppressor Cells (MDSC) when monitoring kidney transplants. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01652
Juan Pascual Sánchez.
Study of rare variant genes associated with Alzheimer's disease in the Spanish population. CARLOS III HEALTH INSTITUTE. 2017-2019.

PI16/01656
Julio Francisco Jimenez Bonilla.
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.

PI16/01717
Víctor Manuel Martínez Taboada.
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.

CP16/00033
Raquel López Mejías.
Cardiovascular risk assessment in patients with rheumatoid arthritis: the relevance of genetic markers. CARLOS III HEALTH INSTITUTE 2017-2019.

PI16-00496
Mónica López Fanarraga.
Design and evaluation of multi-therapeutic nano-dispensers based on carbon nanotubes to treat tumours. CARLOS III HEALTH INSTITUTE. 2017-2019.

SAF2016-76046-R
Benedicto Crespo Facorro.
Stratified treatment in schizophrenia: integrating results of the human and cellular transcriptome in antipsychotic treatment strategies. MINECO. 2017-2019.

SAF2016-75195-R
Jesús Merino Pérez.
BAMBI, a regulator of TGF beta signalling, in cutaneous inflammation and differentiation of Human CD4 T Lymphocytes.

PTA2015-11501-I
Saray Pereda Marcos.
Research Technical Support Contract MINECO 2017-2019.

There were also positive resolutions of the following programmes in 2016:

Ciber

CB16/12/00291
Miguel Ángel Piris Pinilla.
Cancer subject area, CARLOS III HEALTH INSTITUTE 2017-2021.

Human Resources

MS16/00033
Raquel López Mejías.
Miguel Servet Type I contract. CARLOS III HEALTH INSTITUTE 2017-2021.

CM16/00051
Javier Riancho Zarrabeitia.
Rio Hortega contract. CARLOS III HEALTH INSTITUTE 2017-2018.

CM16/00034
Manuel Delgado Alvarado.
Rio Hortega contract. CARLOS III HEALTH INSTITUTE 2017-2018..

INT16/00133
Miguel Ángel González-gay Mantecón.
CARLOS III HEALTH INSTITUTE 2017.

Mobility

BA16/00021
Jose María De la Torre Hernández.
CARLOS III HEALTH INSTITUTE 2017.

Clinical Trials

During 2016, IDIVAL authorised a total of 57 clinical trials and 49 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 2016 is shown in the attached table.

Notably, in 2016 a Phase I clinical trial was begun for the first time with an admission to the Valdecilla Clinical Trial Unit.

List of clinical trials whose contracts were signed in 2016

Clinical trial	Leader researcher
EECC for the suspension of valganciclovir prophylaxis in CMV-seropositive kidney transplant recipients who develop CMV-specific CD8 + cellular immunity after receiving thymoglobulin.	**María del Carmen Fariñas Álvarez.**
Telavancin open-label multicenter, open-label clinical trial in comparison to conventional intravenous therapy in the treatment of patients with Staphylococcus aureus bacteremia, including endocarditis.	**María del Carmen Fariñas Álvarez.**
A randomized, double-blind, placebo-controlled, active-controlled (fluoxetine) and fixed-dose vortioxetine trial in pediatric patients 7 to 11 years of age with major depressive disorder (MDD).	**Beatriz Payá González.**
A multicenter, randomized, placebo-controlled, double-blind study to evaluate the efficacy and tolerability of 2% diltiazem hydrochloride in the treatment of chronic anal fissure, and a 24-week follow-up period.	**Julio Jose Castillo Diego.**
A 24-week randomized, double-blind, phase IIIb study comparing "closed" triple therapy (ff / umec / vi) with "open" triple therapy (ff / vi + umec) in subjects with pulmonary disease Chronic obstructive pulmonary disease (COPD).	**Juan García Rivero.**
A randomized, multicenter, open-label, parallel-group Phase III study to evaluate the efficacy, safety, and tolerability of a long-acting intramuscular regimen of cabotegravir and rilpivirine in maintenance of virologic suppression following induction with Single-blocker with an integrase inhibitor in a randomized, multicenter, open-label, parallel-group study to assess the efficacy, safety, and tolerability of a long-acting intramuscular regimen with cabotegravir and rilpivirine in maintenance of suppression After induction with a single tablet treatment with an integrase inhibitor in HIV-1 infected adult patients who have not received prior antiretroviral therapy	**María del Carmen Fariñas Álvarez.**
Osmo study: multicenter, open-label study with a treatment arm of 32 weeks in subjects with severe eosinophilic asthma not optimally controlled with their current treatment with omalizumab, who are switched from omalizumab to mepolizumab 100 mg subcutaneously.	**Juan García Rivero.**
A 29-day, double-blind, placebo-controlled, multicenter, parallel-group study to evaluate the efficacy, safety, and pharmacokinetics of three-weekly GSK1278863 administration in hemodialysis-dependent subjects with anemia associated with chronic nephropathy Who received a stable dose of an erythropoiesis-stimulating drug.	**Ángel Luis Martín De Francisco Hernández.**
Phase II, multicenter, randomized, double-blind (non-blind to the promoter), placebo-controlled, parallel-group study to evaluate the efficacy and safety of sirukumab in subjects with poorly controlled severe asthma.	**Fernando Rodríguez Fernández.**

Ensayo	Investigador principal
Active, parallel group, double-blind, phase III study to compare the efficacy, safety, and tolerability of the FF / UMEC / VI fixed dose combination versus the fixed dose dual FF / VI combination administered Once daily with dry powder inhaler, in subjects with inadequately controlled asthma	**Fernando Rodríguez Fernández.**
Study of the efficacy and safety of bardoxolone methyl in patients with pulmonary arterial hypertension associated with connective tissue disease.	**José Manuel Cifrián Martínez.**
Protocol for the use of open treatment for daratumumab in subjects with multiple myeloma who have received at least 3 previous treatment lines (including a proteasome inhibitor and an immunomodulatory drug) or have double resistance to a proteasome inhibitor and an immunomodulatory drug.	**Andrés Insunza Gaminde.**
First-administration, double-blind, randomized, placebo-controlled, phase I study of jnj-56136379 administered orally to examine safety, tolerability and pharmacokinetics after ascending single doses and a multiple dose regimen in healthy volunteers (part i) , And after multiple multiple dose regimens in subjects with chronic hepatitis b (part ii).	**Javier Crespo García.**
Phase 3b, double-blind, randomized, placebo-controlled, multicenter study evaluating the effect of obeticolic acid on clinical outcomes in patients with primary biliary cirrhosis.	**Javier Crespo García.**
Phase 3 multicenter, randomized, double masked, long-term, placebo-controlled study to evaluate the safety and efficacy of obeticolic acid in subjects with non-alcoholic steatohepatitis.	**Javier Crespo García.**
Multivessel, prospective, non-safety-related, clinical efficacy and pharmacokinetic properties of normal human immunoglobulin for intravenous administration of bts95 as a restitution treatment in patients with primary immunodeficiency (ip).	**Marcos López Hoyos.**
Phase 3, randomized, double-blind, placebo-controlled, multicenter study of the safety and efficacy of analgesic subcutaneous administration of Tanezumab in subjects with osteoarthritis of the hip or knee.	**Cristina Martínez Dubois.**
Obinutuzumab in combination with Clorambucilo, ACP 196 in combination with Obinutuzumab and ACP 196 in monotherapy, in subjects with chronic non-treated lymphocytic leukemia.	**Lucrecia Yáñez San Segundo.**
A Randomized, Multicenter, Open-Label, Phase 3 Study of Acalabrutinib (ACP-196) Versus Investigator Choice of Either Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in Subjects with Relapsed or Refractory Chronic Lymphocytic Leukemia.	**Lucrecia Yáñez San Segundo.**
Randomized controlled trial of maintenance therapy with S-1 in metastatic esophageal-gastric cancer.	**Fernando Rivera Herrero.**
Randomized clinical trial to compare the efficacy of the Angiolite stent versus a second-generation drug-eluting stent such as Xience in patients with indication for percutaneous coronary intervention.	**Jose Javier Zueco Gil.**
Phase II study of plitidepsin in patients with relapsed or refractory T cell angioinmunoblastic lymphoma.	**Isabel Fernández González de Villambrosia.**
Phase III prospective, randomized, double-blind, multicentre study of the efficacy and safety of lanreotide autogel / depot 120 mg plus the best supportive treatment (mts) versus placebo plus the best supportive treatment for tumor control in subjects with Well differentiated metastatic and / or unresectable, typical or atypical lung neuroendocrine tumors.	**Carlos López López.**
A randomized controlled study on the safety and efficacy of low molecular weight heparins in the prevention of thrombotic events in hospitalized cirrhotic patients.	**Ángela María Puente Sánchez.**

Ensayo	Investigador principal
Open, multicenter clinical trial with subcutaneous immunotherapy at depot presentation in patients with allergic rhinoconjunctivitis sensitized to domestic mites.	**Fernando Rodríguez Fernández.**
Phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of crenezumab in patients with mild to prodromal Alzheimer's disease.	**Eloy Manuel Rodríguez Rodríguez.**
A multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and efficacy of secukinumab in patients with active non-radiographic axial spondyloarthritis over a 2-year period.	**Ricardo Blanco Alonso.**
Comparison between the absorbable bioreabsorbable framework and the xience metal stent in the prevention of restenosis following percutaneous coronary intervention in patients at high risk of restenosis.	**José María De La Torre Hernández.**
Phase II clinical trial demonstrating viability to evaluate the efficacy and safety of MEDI3902 in the prevention of nosocomial pneumonia caused by Pseudomonas aeruginosa in patients undergoing mechanical ventilation.	**Borja Suberviola Cañas.**
A randomized, double-blind, double-simulated, 24-week, parallel-group, multicenter clinical trial to evaluate the efficacy and safety of the fixed-dose combination of aclidinium bromide 400 mcg / formoterol fumarate 12 mcg twice a Day as compared to each active ingredient in monotherapy (aclidinium bromide 400 mcg twice daily and formoterol fumarate 12 mcg twice daily) and with tiotropium 18 mcg once daily in its administration to patients with chronic obstructive pulmonary disease.	**Juan García Rivero.**
A randomized, double-blind, placebo-controlled phase II study of neoadjuvant chemotherapy with carboplatin and paclitaxel with or without debio 1143 in patients with newly diagnosed advanced ovarian epithelial cancer.	**Ana De Juan Ferré.**
Dexmedetomidine versus usual clinical practice during non-invasive mechanical ventilation: Randomized clinical trial.	**Mª Isabel Rubio Lopez.**
Closure of mucosal defects with clips after endoscopic mucosal resection of large colorectal lesions as prophylaxis of delayed hemorrhage.	**Joaquin De La Peña García.**
Double-blind, randomized, placebo-controlled phase II / III study to evaluate the safety and efficacy of induction and maintenance therapy with GS-5745 in patients with moderate to severe active ulcerative colitis.	**Montserrat Rivero Tirado.**
A randomized, multicenter, open-label Phase II study to evaluate the efficacy and safety of the fixed-dose combination (cdf) of sofosbuvir / velpatasvir and the sofosbuvir / velpatasvir cdf plus ribavirin in patients with chronic HCV genotype 3 infection cirrhosis.	**Javier Crespo García.**
Phase II, randomized, double-blind, placebo-controlled trial of the combination of the monoclonal antibody MHAA4549A with oseltamivir versus oseltamivir alone for the treatment of influenza-to-severe infection.	**Borja Suberviola Cañas.**
A 36-week open-label multicentre phase III study followed by a double-blind, randomized withdrawal period from week 36 to week 104 to assess the long-term efficacy and safety of ixekizumab (LY2439821) 80 mg Every 2 weeks in patients with active psoriatic arthritis who have never received a disease-modifying biological antirheumatic drug.	**Ricardo Blanco Alonso.**
Phase II randomized trial evaluating alternative doses of ramucirumab in combination with paclitaxel as second line treatment in patients with gastric or locally advanced or metastatic and unresectable gastroesophageal adenocarcinoma.	**Rivera Herrero, Fernando.**
Phase III, randomized, double-blind, placebo-controlled study evaluating LY2951742 in patients with episodic migraine - EVOLVE-2 study.	**Agustín Oterino Durán.**

Ensayo	Investigador principal
Phase III, randomized, double-blind, placebo-controlled study evaluating LY2951742 in patients with chronic migraine - REGAIN study.	**Agustín Oterino Durán.**
A multicenter, randomized, double-blind, placebo-controlled trial to evaluate emsartan (idn 6556), an oral caspase inhibitor, in subjects with nonalcoholic steatohepatitis (ehna) fibrosis).	**Javier Crespo García.**
A multicenter, randomized, double-blind, placebo-controlled trial to evaluate emsartan, an oral caspase inhibitor, in subjects with non-alcoholic steatohepatitis (NASH) cirrhosis and severe portal hypertension.	**Javier Crespo García.**
"TWILIGHT-Ticagrelor Study with Aspirin or Alone in High-Risk Patients After Coronary Intervention"	**José María De La Torre Hernández.**
A 12-week parallel-group, randomized, double-blind, placebo-controlled, phase-II clinical trial to evaluate the efficacy and safety of three ultra-low estriol vaginal gel formulations (estriol vaginal gel 0.005%, 0.27% estriol vaginal gel, 0.0008% estriol vaginal gel) in the treatment of vaginal dryness in postmenopausal women with vaginal atrophy.	**José Estévez Tesouro.**
Phase III, randomized, double-blind study comparing abt-494 with placebo in stable treatment with conventional synthetic disease modifying antirheumatic drugs (farmesc) in subjects with moderate to severe rheumatoid arthritis with insufficient response or intolerance to biological farms (Farmeb).	**Ricardo Blanco Alonso.**
Phase III, randomized, double-blind study comparing ABT-494 15 mg once daily in monotherapy and ABT-494 30 mg once daily in monotherapy versus methotrexate (MTX) monotherapy in subjects not previously treated with MTX with arthritis Moderate to severe active rheumatoid.	**Ricardo Blanco Alonso.**
ABT 493 / ABT 530 in adults with chronic hepatitis C virus genotype 1, 2, 4, 5 or 6 and compensated cirrhosis (EXPEDITION- 1).	**Javier Crespo García.**
A randomized, double-blind phase III study comparing ABT-494 with placebo and with adalimumab in subjects with moderate to severe active rheumatoid arthritis treated with methotrexate (MTX) in stable doses and who did not respond adequately to MTX (MTX-GO).	**Ricardo Blanco Alonso.**
Multicenter clinical trial of maintenance treatment based on biomarkers for first line metastatic colorectal cancer (Modul).	**Fernando Rivera Herrero.**
A multicenter, randomized, phase 2b study to evaluate the efficacy, safety, and tolerability of ocr-002 (ornithine phenylacetate) in hospitalized patients with cirrhosis and hyperamoniaemia associated with an episode of hepatic encephalopathy. Studio stop-he.	**Javier Crespo García.**
Ib / 2 phase study of combined treatment with Ibrutinib in selected gastrointestinal and genitourinary tumors.	**Fernando Rivera Herrero.**
Phase III, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of qpi-1002 in preventing delayed graft function in recipients of a kidney transplant of elderly donors with brain death.	**Emilio Rodrigo Calabia.**
A randomized, multicenter, open-label, controlled, Phase III trial to demonstrate non-inferiority of targeted narrow-spectrum antibiotic treatment versus broad-spectrum anti-pseudomonal beta-lactam treatment in the treatment of patients with Enterobacteriaceae bacteremia.	**María Del Carmen Fariñas Álvarez.**
Phase 2 randomized study comparing different dose-induction treatment regimens (first cycle) regorafenib in patients with metastatic colorectal cancer (mcrc).	**Fernando Rivera Herrero.**
Phase II study to evaluate the efficacy of FOLFIRI + aflibercept in patients with metastatic colorectal cancer previously treated with oxaliplatin with or without ACE polymorphisms.	**Fernando Rivera Herrero.**

Clinical Practice Guidelines

IDIVAL researchers have participated in 2016 in the following clinical practice guidelines and consensus documents. The relevance of these guidelines is undoubtedly as systematically developed recommendations to help professionals and patients make the most appropriate health care decisions and to select the most appropriate diagnostic or therapeutic options when addressing a health problem.

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En representación del Comité Científico del trabajo de Recomendaciones de la Sociedad Española de Reumatología para el manejo clínico del paciente con artritis reumatoide que no puede utilizar metotrexato.. Recommendations by the Spanish Rheumatology Society for the management of patients diagnosed with rheumatoid arthritis who cannot be treated with methotrexate.
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Retics and Ciber with the Participation of IDIVAL

The Carlos III Health Institute has promoted various Thematic Networks for Cooperative Research (RETIC) Platforms and Biomedical Research Centre Networks (CIBER) in which IDIVAL groups participate. 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 three CIBERs, seven RETICS and three other platforms Three of the RETICs in which IDIVAL participates (ITEMAS Platform, the Biobank Platform and the Scren Platform) have a supportive and cross-disciplinary nature, making up part of the researcher support services.

CIBER/RETIC/Platform	IDIVAL Group	IP
CIBER of Mental Health (CIBERSAM)	Psychiatry	**Benedicto Crespo Facorro**
CIBER of Neurodegenerative Diseases (CIBERNED)	Neurodegenerative Diseases	**José Ángel Berciano Blanco**
CIBER of Epidemiology and Public Health (CIBERESP)	Epidemiology and Public	**Javier Llorca Díaz**
Spanish Infectious Pathology Research Network (REIPI)	Clinical Microbiology and Molecule	**Luis Martínez Martínez**
Maternal and Child Health and Development Network (SAMID NETWORK)	University Hospital Marqués de Valdecilla	**Maria Jesús Cabero**
Thematic Network of Cooperative Research in Aging and Fragility (RETICEF)	Mineral and Lipid Metabolism	**Jesús González Macías**
Renal Research Network (REDinREN)	Transplantation and autoimmunity	**Manuel Arias Rodríguez**
Red Temática de Investigación Cooperativa de Cáncer (RTICC)	Cell Signaling and Therapeutic Targets in Cancer	**José Luis Fernández Luna**
Research Network Cooperative Cancer Research (RTICC)	Hematologic Neoplasms and Hematopoietic Progenitor Transplantation	**Eulogio Conde García**
Thematic Network of Cooperative Cancer Research (RTICC)	Genomic Cancer	**Miguel Ángel Piris Pinilla**
Cardiovascular Research Network (RIC)	Cytokines and growth factors in pathological tissue plasticity phenomena	**Juan Francisco Nistal**
Research Network on Inflammation and Rheumatic Diseases (RIER)	Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	**Miguel Angel Glez Gay**
Biobanks Platform	IDIVAL	**Pascual Sánchez Juan**
Platform for Innovation in Health Technologies (ITEMAS)	IDIVAL	**Galo Peralta Fernández**
Platform of Clinical Research Units and Clinical Trials (Scren)	IDIVAL	**Galo Peralta Fernández**

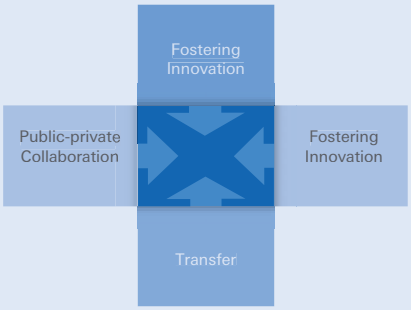
Innovation

Introduction

IDIVAL has an Innovation Area that includes a Research Results Transfer Office (OTRI) and an Innovation Unit, which forms part of the ITEMAS network.

The current context of market globalisation is guiding European countries towards innovation as a major driver of continued growth.

At IDIVAL, we believe that innovation and knowledge transfer can become drivers of the economy in the region of Cantabria, and therefore we are committed to the activities of the Innovation Unit.



ITEMAS Platform

IDIVAL is the node of the Platform for Innovation in Medical and Health Technologies (ITEMAS) promoted by the Carlos III Health Institute (ISCIII).

ITEMAS promotes innovation in health technology as a crucial tool to make the National Healthcare System more sustainable, supporting development of the innovative culture needed to integrate scientific and industrial systems in the field of medical technology. The core of ITEMAS currently comprises the innovation units of large hospitals in the National Healthcare System.

IDIVAL participates in the ITEMAS platform through the IDIVAL Innovation Unit, which throughout 2016 worked on related activities linked to its participation in different work groups and its Assembly. Specifically, it leads the Alliances working group within the Platform.

Innovative Culture

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.

Transfer

At present, innovation is considered to be a fundamental factor for growth and competitiveness in the economic and business sphere. 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.

For the transfer of research results from our environment to the market to be effective and have an impact on society, an economic and legal environment conducive to innovation and economic development must be created. In relation to this, 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:

Nineteen patent applications to the Spanish Office of Patents and Brands (OEPM).

Twelve international patent applications through the Patent Cooperation Treaty (PCT).

One European patent application to the European Patent Office (EPO).

A utility model application to the Spanish Office of Patents and Brands (OEPM).

A Community Design application to the Office for Harmonization in the Internal Market (OHIM).

Three Spanish trademark applications to the Spanish Office of Patents and Brands (OEPM).

Of these, the following were processed in 2016:

Nº Solicitud	Título	Solicitantes	Inventor
National patent-P201600160	"Uso de un complejo GNP-LLO91-99 para el tratamiento y la prevención del cáncer"	IDIVAL-SCS	Carmen Álvarez Domínguez Ricardo Calderón González Elisabet Frande Cabanes Eva Ferrández Fernández Sonsoles Yáñez Díaz Soledad Penadés Ullate Marco Marradi Isabel García Martín
National patent-P201600636	"Método para predecir la respuesta clínica a un tratamiento con agentes antiinflamatorios"	IDIVAL-UC-SCS-VHIR-IdiPAZ	José Luis Fernández Luna Víctor Manuel Martínez Taboada Silvia Torices del Val Marcos López Hoyos Pedro Muñoz Cacho Ignacio Varela Egocheaga Alejandro Balsa Criado Sara Marsal Barril Antonio Julià Cano
European Patent – 14721426.6	"Device and method for the detection of biomarkers"	SCS-IDIVAL-UC-TEKNIKER-CELLBIOCAN	José Luis Fernández Luna Ana Talamillo Cancelo Fernando Moreno García Francisco González Fernández Ruth Díez Ahedo Santos Merino Álvarez Deitze Otaduy del Paso

Nº Solicitud	Título	Solicitantes	Inventor
National Utility Model -U201600872	"Dispositivo de tracción dinámica de pared para abdomen abierto"	SCS	Federico Castillo Suescun
National patent -P201601099	"Uso del gen PRKACA para predecir la respuesta de un sujeto al tratamiento con un análogo de purina"	IDIVAL-SCS	Carlos Pipaón González Lucrecia Yáñez San Segundo

Para todas ellas se han llevado, o se realizan en la actualidad, labores de transferencia y contacto con posibles licenciatarios.

Innovation Funnel

In 2016, 12 new ideas were analysed. The projects were classified into FIVE phases, as defined below:

1. Capturing ideas.
In this phase, the ideas that Innovation Areas captured in 2016 are considered, as well as those captured in previous years that did not advance to a later stage.

2. Analysis.
In this phase, proposals for which market research, patentability reports, or product value or technical feasibility reports are being carried out are considered.

3. Development.
This includes the development of prototypes, approvals and testing.

4. Transfer.
Ideas that have generated some type of commercial activity, e.g., contact with companies or potential licensees.

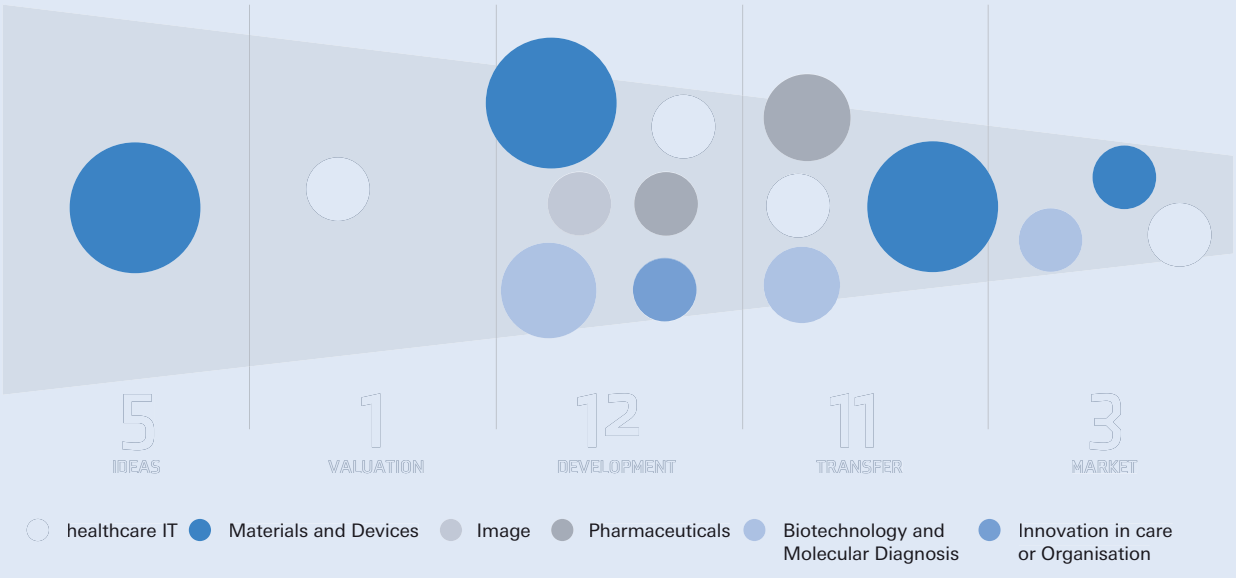
5. Market.
cases where innovation is found in one of the following situations:

a) Licensed to industry

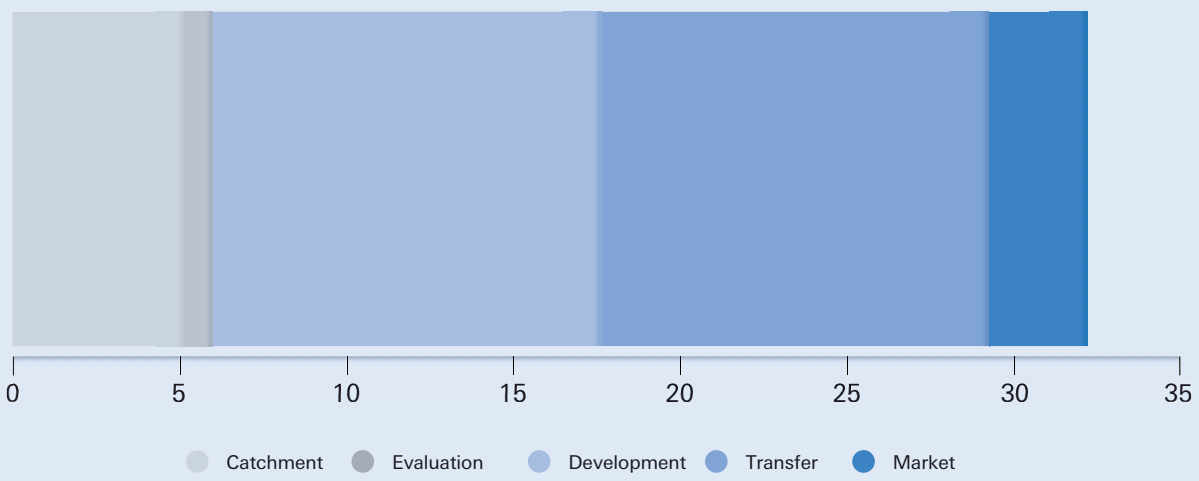
b) Generated a spin-off

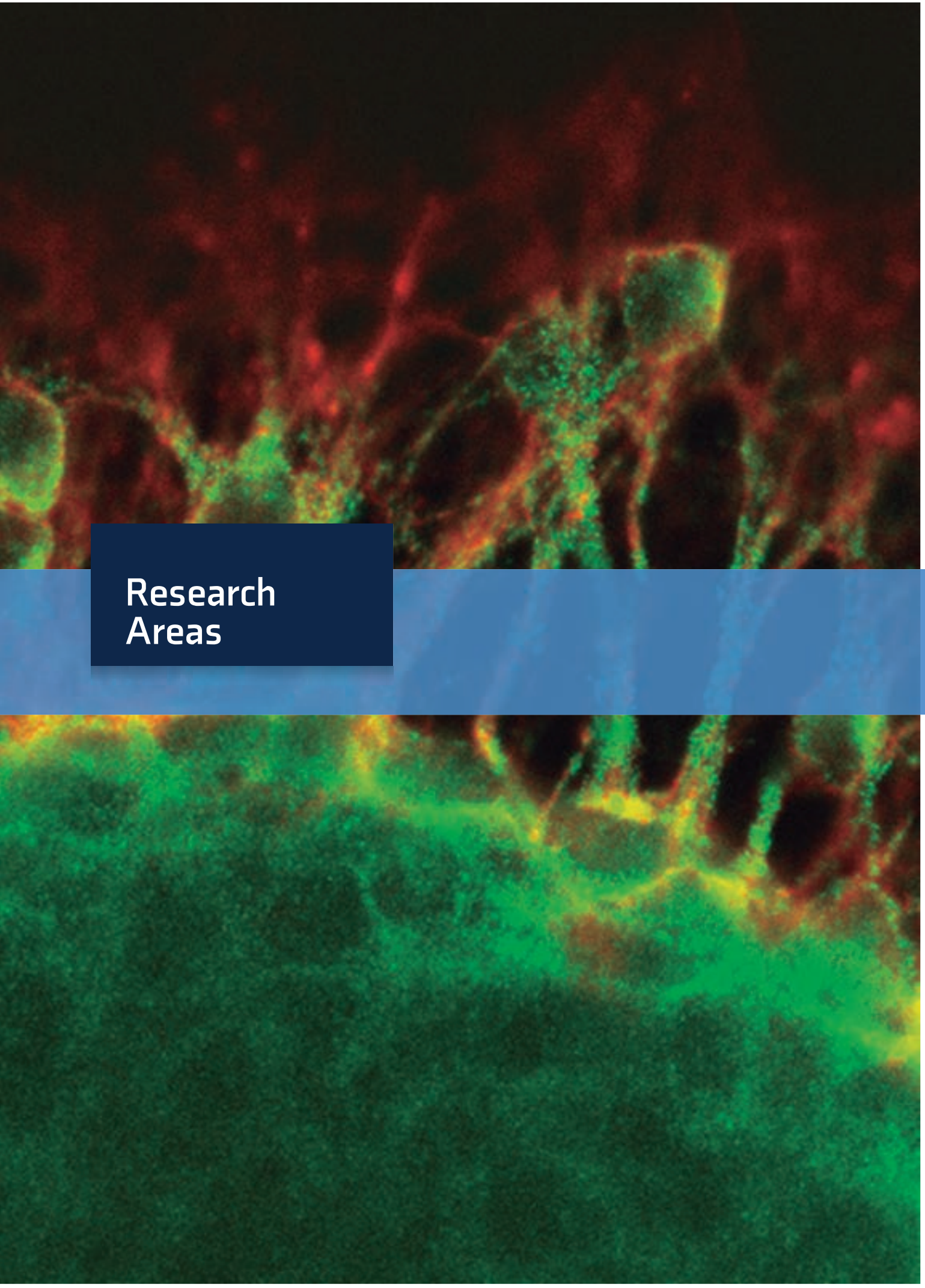
c) Forms part of an exclusive agreement with a company

d) Implemented in a healthcare centre (in the case of healthcare and organisational innovations).

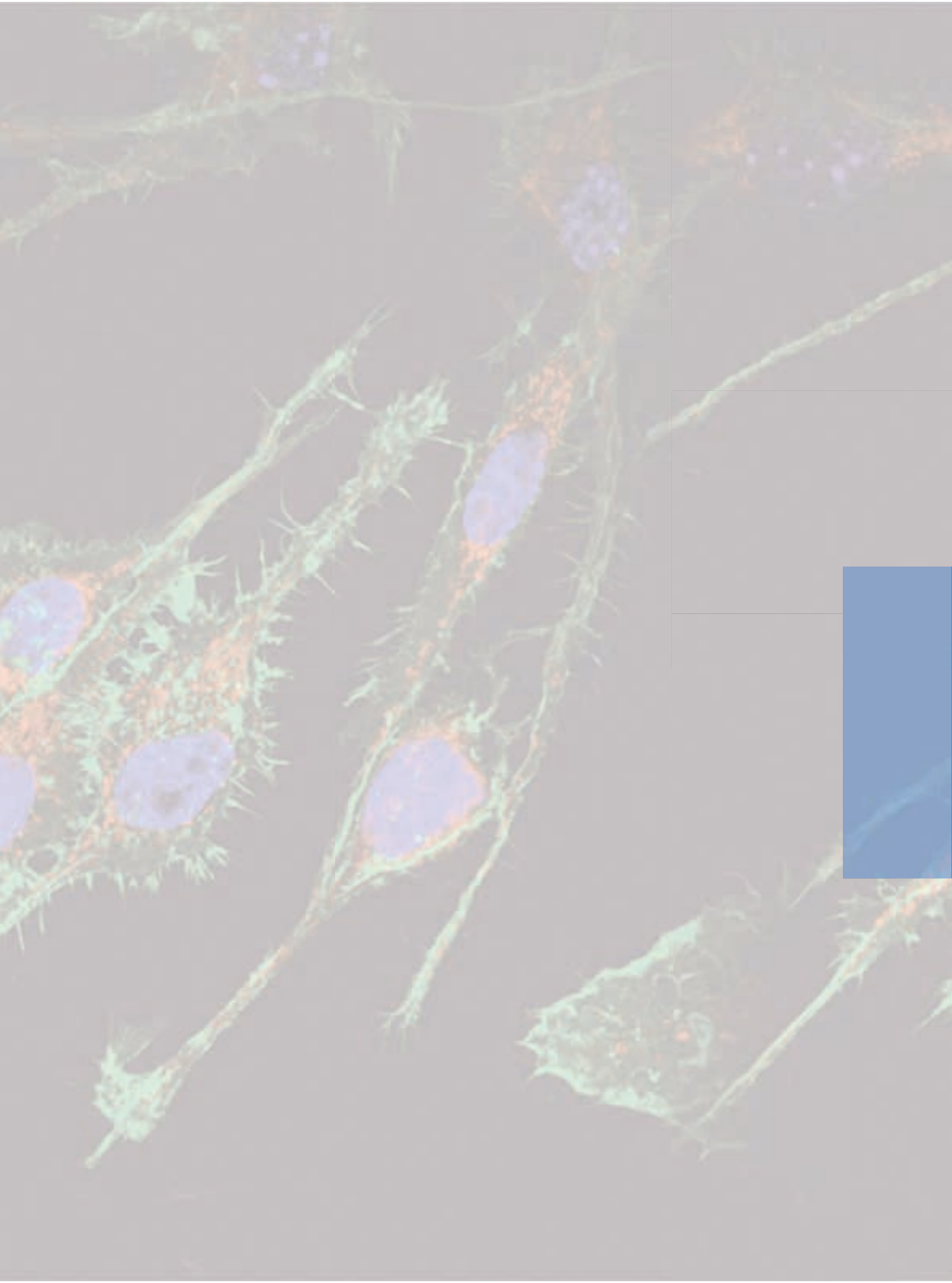


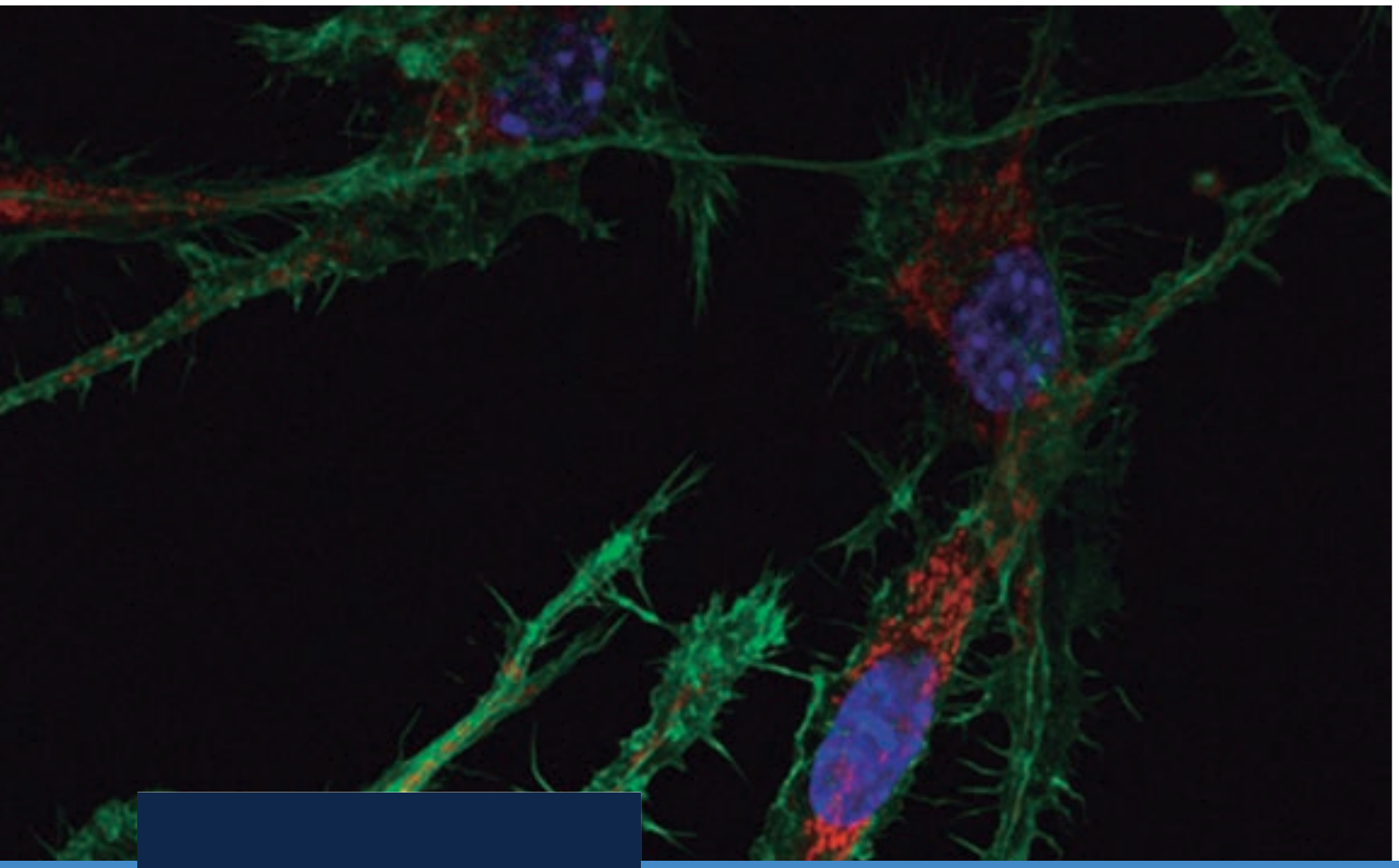
In 2016, the Innovation Area managed 32 ideas, distributed among the five stages as follows:





Research Areas

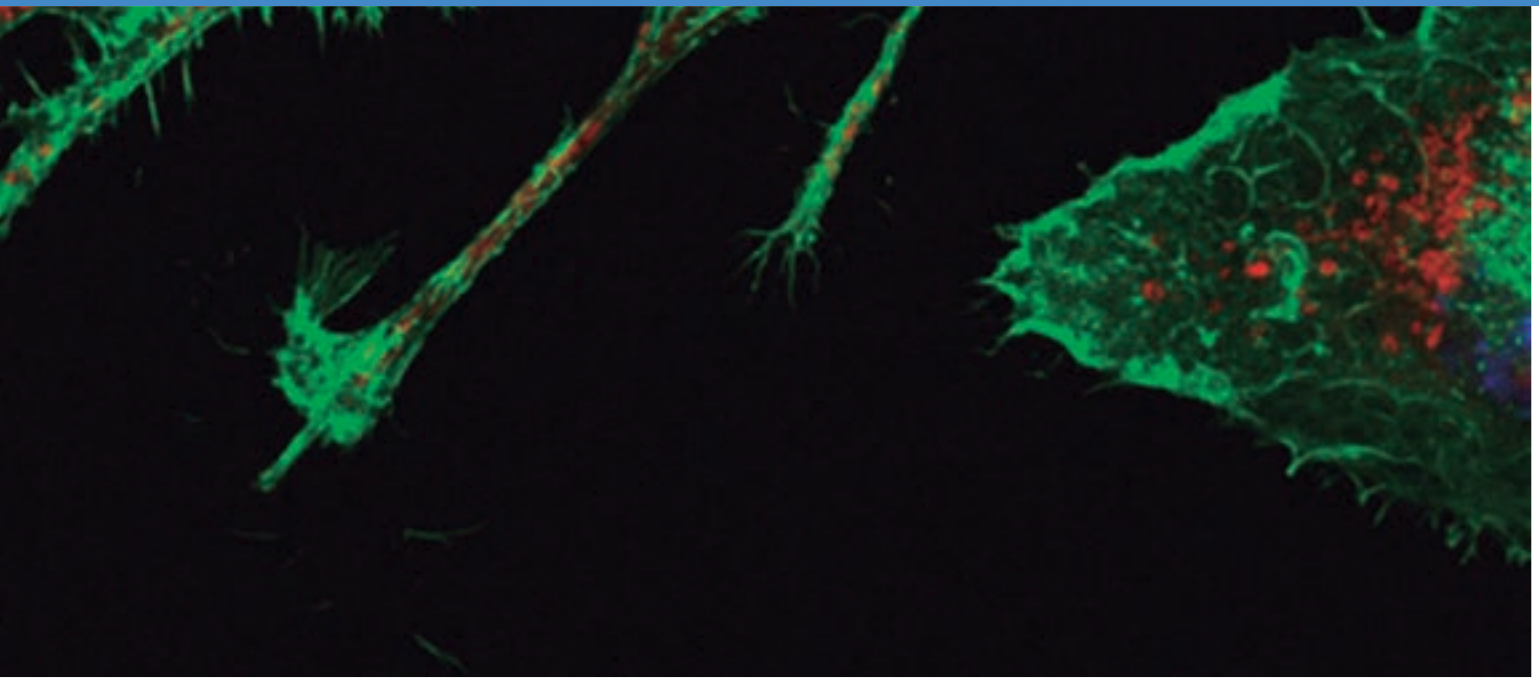




Organ Transplants and Tissue and New Therapies Area

Marcos López Hoyos.
Coordinator of the Transplant Area of Organs and Tissues and New Therapies.

Head of Immunology Service.
University Hospital Marqués de Valdecilla.



Cytokines and Growth Factors in Pathological Tissue Plasticity Phenomena

Group Leader

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Cardiovascular Surgery Service

University Hospital Marqués de Valdecilla
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María Navarro Rego

Research Lines

1. Pathological plasticity of myocardium.

We are analysing the involvement of transforming growth factors beta (TGF-Ðs, 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 cause of surgery in our setting, and it associates a left ventricular hypertrophy that is a response of pathological significance in these patients. We studied the molecular mechanisms of myocardial remodeling in this context using myocardial samples from patients with aortic stenosis, a murine experimental model of said pathology

1.2. Alteraciones del desarrollo y plasticidad miocárdica patológica en el síndrome de Down. The Ts65Dn mouse (trisomy of an area of chromosome 16 homologous to the human 21) is an experimental model of Down syndrome that reproduces its phenotypic characteristics. We are studying the involvement of the TGF-ß family in cardiac development variations found in this model.

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-ßs 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- ßs 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-ß family in processing the physiological nociceptive signal. We intend to study: a) Molecular mechanisms involving TGF-ß in neuropathic pain, and experimental inflammatory pain; b) The interaction between TGF-ßs and the endogenous opioid system; c) The involvement of TGF-ßs in adaptive processes in chronic opioid therapy; d) The involvement of TGF-ßs 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-ß 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-ß family is involved in the pathophysiology of experimental Alzheimer's disease. We intend to evaluate the role of TGF-ß in the cognitive variations found in the Ts65Dn mouse and evaluate different therapeutic strategies.

PUBLICATIONS:

IMPACT FACTOR | 47,704

Original articles

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2. Merino D, Villar AV, García R, Tramullas M, Nistal JF, Hurlé MA.
BMP-7 attenuates left ventricular remodelling under pressure overload and facilitates reverse remodelling and functional recovery.
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4. Expósito V, Rodríguez-Mañero M, González-Enríquez S, Arias MA, Sánchez-Gómez JM, Andrés La Huerta A, Bertomeu-González V, Arce-León Á, Barrio-López MT, Arguedas-Jiménez H, Seara JG, Rodriguez-Entem F.
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EUROPACE. 2016;18:1203-1210. F.I.:4,021. [doi:10.1093/europace/euv337]

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PLoS One. 2016;11:F.I.:3,057. [doi:10.1371/journal.pone.0155367]

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Chronic Melatonin Administration Reduced Oxidative Damage and Cellular Senescence in the Hippocampus of a Mouse Model of Down Syndrome.
Neurochem Res. 2016;41:2904-2913. F.I.:2,472. [doi:10.1007/s11064-016-2008-8]

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7. Expósito V, Rodríguez-Entem F, González-Enríquez S, Veiga G, Olavarri I, Olalla JJ.
Stroke and Systemic Embolism After Successful Ablation of Typical Atrial Flutter.
Clin Cardiol. 2016;39:347-351. F.I.:2,431. [doi:10.1002/clc.22538]

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8. Santurtún A, Villar A, López-Delgado L, Riancho J.
Amyotrophic lateral sclerosis and richness: A correlation study across Spain.
J Neurol Sci. 2016;367:380-381. F.I.:2,126. [doi:10.1016/j.jns.2016.06.050]

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9. Santurtún A, Villar A, Delgado-Alvarado M, Riancho J. **Trends in motor neuron disease: association with latitude and air lead levels in Spain.**
Neurol Sci. 2016;37:1271-1275. F.I.:1,783. [doi:10.1007/s10072-016-2581-2]

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10. Angulo López, Itziar, Nistal Herrera, Juan Francisco.
Infestation of a diabetic foot by Wohlfahrtia Magnifica.
J Vasc Surg Venous Lymphat Disord. 2016;2:119-122.F.I.:0,882.

Reviews

1. García R, Merino D, Gómez JM, Nistal JF, Hurlé MA, Cortajarena AL, Villar AV.
Extracellular heat shock protein 90 binding to TGFß receptor I participates in TGFß-mediated collagen production in myocardial fibroblasts.
Cell Signal. 2016;28:1563-1579. F.I.:4,191. [doi:10.1016/j.cellsig.2016.07.003]

Doctoral thesis

1. Mª Elena Arnáiz García.
Aortic root replacement surgery with valvular preservation: analysis of early and long-term surgical outcomes, and study of predictors of survival, valvular function stability, and reoperation.
Director/a: **Juan Francisco Nistal Herrera.** University of Cantabria.

PROJECTS

Projects

1. María Amor Hurlé González.
MicroRNAs in neuropathic pain: molecular biomarkers and targeted therapies.
SAF2013-47434-R.

2. Juan Francisco Nistal Herrera. **Bone morphogenetic protein 7 (BMP7): possible therapeutic target in the pathological remodeling of the cardiovascular system.** PI15/01224. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

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3. Juan Francisco Nistal Herrera. **Thematic Network for Research in Cardiovascular Diseases.** RD12/0042/0018. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Cardiovascular Research Group

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Cardiology Service
Marqués de Valdecilla
University of Cantabria

Clinic group

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Manuel Jesús Zarauza Navarro
José Javier Zueco Gil

Technicians
María Cristina Obregón Rodríguez

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:

1. 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.

Percutaneous Structural Heart Disease Interventions

c. Atrial septal defects closure

d. Transcatheter aortic valve implantations (TAVI)

e. Prosthetic leaks closure -Left atrial appendage closure

f. Preconditioning in acute coronary syndromes.

2. Multimodality Cardiac Imaging:

a. Diagnosis and characterization of Cardiac Allograft

b. Vasculopathy with intravascular ultrasonography (IVUS), optical coherence and virtual histology.

c. Transesophageal three-dimensional echocardiography in atrial septal defects and mitral valve prolapse.

d. Three-dimensional echocardiography evaluation of the mitral annulus.

e. Strain and strain-rate in diabetic and oncologic cardiomyopathy.

f. Genetic study of prolapse Mitral valve.

g. Evaluation of response to Ischemic preconditioning.

During myocardial infarction with magnetic resonance.

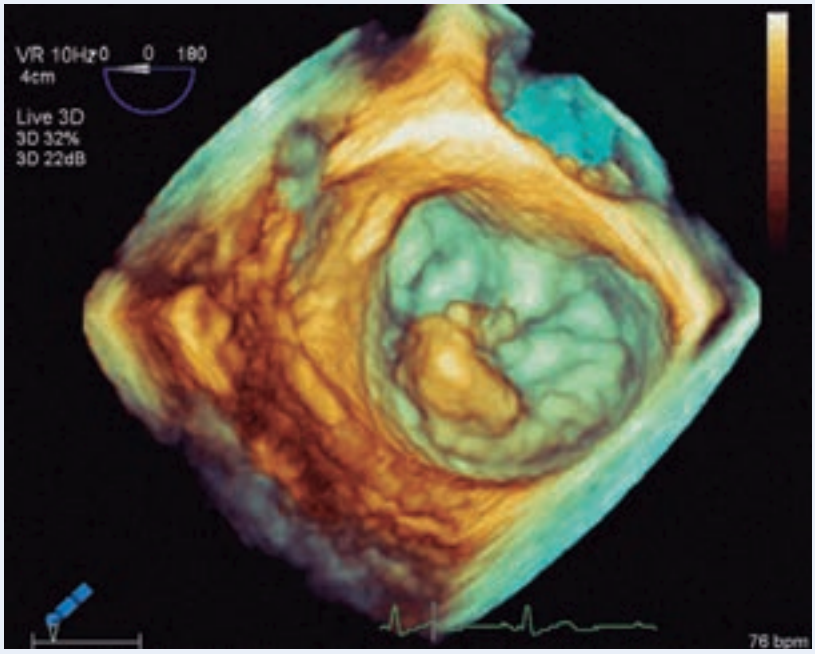

Figure. Three-dimensional echocardiogram demonstrating mitral valve prolapse

PUBLICATIONS:

IMPACT FACTOR | 80,367

Original articles

1. Crespo-Leiro MG, Muñiz J, Gonzalez-Vilchez F. **Spanish Post-Heart Transplant Tumor Registry Investigators. Comment on: Post-transplant lymphoproliferative disease in heart and lung transplantation: Defining risk and prognostic factors.** J Heart Lung Transplant. 2016;35:693-694.F.I.:7,509. [doi:10.1016/j.healun.2016.01.006]

2. Alfonso F, Pérez-Vizcayno MJ, García Del Blanco B, García-Touchard A, López-Mínguez JR, Masotti M, Zueco J, Melgares R, Mainar V, Moreno R, Domínguez A, Sanchís J, Bethencourt A, Moreu J, Cequier A, Martí V, Otaegui I, Bastante T, Gonzalo N, Jiménez-Quevedo P, Cárdenas A, Fernández C. **Under the auspices of the Interventional Cardiology Working Group of the Spanish. Everolimus-Eluting Stents in Patients With Bare-Metal and Drug-Eluting In-Stent Restenosis: Results From a Patient-Level Pooled Analysis of the RIBS IV and V Trials.** Circ Cardiovasc Interv. 2016;9: F.I.:5,706. [doi:10.1161/CIRCINTERVENTIONS.115.003479]

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6. Sambola, Antonia, Mutuberria, Maria, del Blanco, Bruno Garcia,

Alonso, Albert, Barrabes, Jose A., Alfonso, Fernando, Bueno, Hector, Cequier, Angel, Zueco, Javier, Rodriguez-Leor, Oriol, Bosch, Eduard, Tornos, Pilar, Garcia-Dorado, David. **Effects of Triple Therapy in Patients With Non-Valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention Regarding Thromboembolic Risk Stratification.** CIRC J. 2016;80:354-362. F.I.:4,124. [doi:10.1253/circj.CJ-15-0923]

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12. Sambola A, Mutuberría M, García Del Blanco B, Alonso A, Barrabés JA, Bueno H, Alfonso F, Cequier A, Zueco J, Rodríguez-Leor O, Tornos P, García-Dorado D. **Impact of Triple Therapy in Elderly Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention.** PLoS One. 2016;11:F.I.:3,057. [doi:10.1371/journal.pone.0147245]

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Martin JC, Serra Garcia V, Gaviria K, Garcia Blas S, Garcia I, Zueco J. **The routine use of surgical exposure approach for trans-femoral implantation of the balloon expandable aortic prosthesis is associated to a low rate of vascular complications.** J Cardiovasc Surg (Torino). 2016;57:615-619.F.I.:1,632.

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1. Alfonso F, De la Torre Hernández JM. **Vasa vasorum and coronary artery disease progression: optical coherence tomography findings.** Eur Heart J Cardiovasc Imaging. 2016;17:280-282.F.I.:4,293. [doi:10.1093/ehjci/jev318]

Doctoral Thesis

1. Marta Fernández Hernández. **Dosing schedule for immunosuppression in heart transplantation in the medium and long term.** Directors: **José Antonio Vázquez de Prada, Francisco Jesús González Vilchez.** University of Cantabria

2. Jaime Lucas Carbonero. **Efficacy and safety of corticosteroid withdrawal after cardiac transplantation.** Director: **José Antonio Vázquez De Prada Tiffe.** University of Cantabria.

—

3. Felipe Rodríguez Entem. **Follow-up of the cardiac transplantation with a echocardiography-based rejection monitoring strategy.** Directors: **José Antonio Vázquez De Prada Tiffe, José Manuel Revuelta Soba.** University of Cantabria.

Infection, Immunity and Digestive Diseases

Group Leader

Javier Crespo García

Digestive Service

Marqués de Valdecilla
University of Cantabria

Emerging group

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José Pedro Vaqué Díez

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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).

PUBLICATIONS:

IMPACT FACTOR | 116,186

Original articles

1. Cabezas J, Sampedro B, Hernández C, Crespo J.
Computerized Physician Order Entry-Based System Improves Hepatitis B Virus Screening in Patients Undergoing Chemotherapy.
J Clin Oncol. 2016;34:290-290. F.I.:20,982. [doi:10.1200/JCO.2015.63.6779]

2. Cabezas J, Bataller R.
Alcoholic liver disease: New UK alcohol guidelines and Dry January: enough to give up boozing?.
Nat Rev Gastroenterol Hepatol. 2016;13:191-192.F.I.:14,435. [doi:10.1038/nrgastro.2016.39]

3. Albéniz E, Fraile M, Ibáñez B, Alonso-Aguirre P, Martínez-Ares D, Soto S, Gargallo CJ, Ramos Zabala F, Álvarez MA, Rodríguez-Sánchez J, Múgica F, Nogales Ó, de Tejada AH, Redondo E, Guarner-Argente C, Pin N, León-Brito H, Pardeiro R, López-Roses L, Rodríguez-Téllez M, Jiménez A, Martínez-Alcalá F, García O, de la Peña J, Ono A, Alberca de Las Parras F, Pellisé M, Rivero L, Saperas E, ...,
Endoscopic Mucosal Resection Endoscopic Spanish Society Group. A Scoring System to Determine Risk of Delayed Bleeding After Endoscopic Mucosal Resection of Large Colorectal Lesions.
Clin Gastroenterol Hepatol. 2016;14:1140-1147.F.I.:7,680. [doi:10.1016/j.cgh.2016.03.021]

4. Perelló CS, Fernández-Carrillo C, Londoño MC, Arias-Loste T, Hernández-Conde M, Llerena S, Crespo J, Forns X, Calleja JL.
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5. Carpio D, Jauregui-Amezaga A, de Francisco R, de Castro L, Barreiro-de Acosta M, Mendoza JL, Mañosa M, Ollero V, Castro B, González-Conde B, Hervías D, Sierra Ausin M, Sancho Del Val L, Botella-Mateu B, Martínez-Cadilla J, Calvo M, Chaparro M, Ginard D, Guerra I, Maroto N, Calvet X, Fernández-Salgado E, Gordillo J, Rojas Feria M, GETECCU.
Tuberculosis in Anti-Tumour Necrosis Factor-treated Inflammatory Bowel Disease Patients After the Implementation of Preventive Measures: Compliance With Recommendations and Safety of Retreatment.
J CROHNS COLITIS. 2016;10:1186-1193.F.I.:6,585. [doi:10.1093/ecco-jcc/jjw022]

6. Vila JJ, Martín L, Prieto C, Urman J, de la Peña J.
Challenging combined EUS-and-ERCP-endoscopic retrieval of proximally migrated pancreatic stent.
Gastrointest Endosc. 2016;84:187-188. F.I.:6,217. [doi:10.1016/j.gie.2016.01.032]

7. Cubiella J, Carballo F, Portillo I, Cruzado Quevedo J, Salas D, Binefa G, Milà N, Hernández C, Andreu M, Terán Á, Arana-Arri E, Ono A, Valverde MJ, Bujanda L, Hernández V, Morillas JD, Jover R, Castells A.
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8. Gallego-Durán R, Cerro-Salido P, Gomez-Gonzalez E, Pareja MJ, Ampuero J, Rico MC, Aznar R, Vilar-Gomez E, Bugianesi E, Crespo J, González-Sánchez FJ, Aparcero R, Moreno I, Soto S, Arias-Loste MT, Abad J, Ranchal I, Andrade RJ, Calleja JL, Pastrana M, Iacono OL, Romero-Gómez M.
Imaging biomarkers for steatohepatitis and fibrosis detection in non-alcoholic fatty liver disease.
Sci Rep. 2016;6:31421-31421. F.I.:5,228. [doi:10.1038/srep31421]

9. Guerra I, Pérez-Jeldres T, Iborra M, Algaba A, Monfort D, Calvet X, Chaparro M, Mañosa M, Hinojosa E, Minguez M, Ortiz de Zarate J, Márquez L, Prieto V, García-Sánchez V, Guardiola J, Rodriguez GE, Martín-Arranz MD, García-Tercero I, Sicilia B, Masedo Á, Lorente R, Rivero M, Fernández-Salazar L, Gutiérrez A, Van Domselaar M, López-SanRomán A, Ber Y, García-Sepulcre M, Ramos L, ..., Gisbert JP.
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INT J MOL SCI. 2016;17: F.I.:3,257. [doi:10.3390/ijms17111878]

13. Rodríguez-Nóvoa S, García-Samaniego J, Prieto M, Calleja JL, Pascasio JM, Delgado Blanco M, Crespo J, Buti M, Bonet Vidal ML, Arenas Ruiz Tapiador J, Fernández-Rodríguez C, Solá R, Fraga E, González Diéguez L, Núñez O, Praga M, Del Pino-Montes J, Romero-Gómez M, Morillas R, Diago M, Castro Á, MENTE Study Group.
Altered Underlying Renal Tubular Function in Patients With Chronic Hepatitis B Receiving Nucleos(t)ide Analogs in a Real-World Setting: The MENTE Study.
J Clin Gastroenterol. 2016;50:779-789.F.I.:3,163. [doi:10.1097/MCG.0000000000000569]

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Predictors of Hospitalized Exacerbations and Mortality in Chronic Obstructive Pulmonary Disease.
PLoS One. 2016;11:F.I.:3,057. [doi:10.1371/journal.pone.0158727]

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Int Immunol. 2016;28:55-64.F.I.:3,031. [doi:10.1093/intimm/dxv048]

16. Boix F, Millan O, Segundo DS, Mancebo E, Rimola A, Fabrega E, Fortuna V, Mrowiec A, Castro-Panete MJ, Peña J, Llorente S, Minguela A, Bolarin JM, Paz-Artal E, Lopez-Hoyos M, Brunet M, Muro M.
High expression of CD38, CD69, CD95 and CD154 biomarkers in cultured peripheral T lymphocytes correlates with an increased risk of acute rejection in liver allograft recipients.
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Colon Cancer Study Group. Ferric carboxymaltose reduces transfusions and hospital stay in patients with colon cancer and anemia.
INT J COLORECTAL DIS. 2016;31:543-551.F.I.:2,383. [doi:10.1007/s00384-015-2461-x]

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Scand J Gastroenterol. 2016;51:186-195.F.I.:2,199. [doi:10.3109/00365521.2015.1070900]

19. Cabezas, Joaquin, Llerena, Susana, Puente, Angela, Fabrega, Emilio, Crespo, Javier.
Causes of treatment failure for hepatitis C in the era of direct-acting antiviral therapy.
Rev Esp Enferm Dig. 2016;108:421-430.F.I.:1,455.

20. Díaz-González Á, Forner A, Rodríguez de Lope C, Varela M.
New challenges in clinical research on hepatocellular carcinoma.
Rev Esp Enferm Dig. 2016;108:485-493. F.I.:1,455. [doi:10.17235/reed.2015.4012/2015]

21. San Segundo D, Alonso C, Ruiz P, Roman I, Arias-Loste MT, Cuadrado A, Puente A, Casafont F, López-Hoyos M, Crespo J, Fábrega E.
De Novo Donor-Specific Anti-Human Leukocyte Antigen Antibody Detection in Long-Term Adult Liver Transplantation.
Transplant Proc. 2016;48:2980-2982. F.I.:0,867. [doi:10.1016/j.transproceed.2016.08.037]

22. San Segundo D, Ruiz P, Irure J, Arias-Loste MT, Cuadrado A, Puente A, Casafont F, López-Hoyos M, Crespo J, Fábrega E.
Serum Levels of Interleukin-34 During Acute Rejection in Liver Transplantation.
Transplant Proc. 2016;48:2977-2979. F.I.:0,867. [doi:10.1016/j.transproceed.2016.08.038]

23. Gisbert JP, Molina-Infante J, Amador J, Bermejo F, Bujanda L, Calvet X, Castro-Fernández M, Cuadrado-Lavín A, Elizalde JI, Gene E, Gomollón F, Lanas Á, Martín de Argila C, Mearin F, Montoro M, Pérez-Aisa Á, Pérez-Trallero E, McNicholl AG.
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Gastroenterol Hepatol. 2016;39:697-721.F.I.:0,800. [doi:10.1016/j.gastrohep.2016.05.003]

Reviews

1. Calleja JL, Llerena S, Perelló C, Crespo J.
NS5A Resistance: Clinical Implications and Treatment Possibilities.
AIDS REV. 2016;18:15-22.F.I.:2,068.

2. Val-Bernal JF, Mayorga M, Cagigal ML, Cabezas-González J.
Gastric pyogenic granuloma: Report of two cases and review of the literature. Pathol Res Pract. 2016;212:68-71.F.I.:1,388. [doi:10.1016/j.prp.2015.11.001]

Editorials

1. Cabezas J, Bataller R.
Alcoholic hepatitis: should we combine old drugs for better results?.
HEPATOL INT. 2016;10:851-853. F.I.:1,125. [doi:10.1007/s12072-016-9768-8]

Tesis doctorales

1. Jose Ignacio Fortea Ormaechea.
Study of the effect of enoxaparin on cirrhosis and experimental portal hypertension.
Directors: **Cristina Ripoll Noiseux, Rafael Bañares Cañizares**.
Complutense University of Madrid.

PROJECTS

Projects

1.. Javier Crespo García.
Endothelial dysfunction, subclinical atheromatosis and cardiomyopathy in patients with HCV infection. Characterization and potential reversibility with direct antiviral agents.
Instituto de Salud Carlos III. Ministerio de Economía y Competitividad.

2.. 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.

3.. José Pedro Vaqué Díez.
New mechanisms in aggressive skin cancers: applications to the diagnosis, prognosis and therapy of melanoma resistant to Merkel cell therapy and carcinoma.
PI16/00156. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad.

Haematologic Neoplasms and Haematopoietic Stem Cells Transplantation

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Hematology Service

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Consolidated group

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Lucrecia Yáñez San Segundo

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María del Carmen García Casquero

Technicians

María Pilar González Echezarreta

Research Lines

LINE 1. CELLULAR BIOLOGY OF HEMOPATHIES.

Prognostic significance of BCL6 and MYC expression in lymphomas. The expression of MYC and BCL6 seems to have a prognostic and therapeutic importance in NHL. This line is being developed in collaboration with the group of Pathological Anatomy and group of Molecular Biology of Faculty of Medicine of UC of Cantabria.

Chronic lymphatic leukemia: Analysis of post-transduction modifications, prognostic value study and therapeutic applications. Study of resistance to purine analogs mediated by kinases.

Molecular biology and genetics of SMD: prospective tracking of alterations in the FA-BRACA pathway.

LINE 2. DIAGNOSTIC AND THERAPEUTIC INNOVATION

Research on the application of new drugs in relapsed / refractory chronic lymphatic leukemia or with high-risk cytogenetic alterations (17p13 and / or 11q23). Phase II and Phase III trials.

Research on treatment regimens in patients with newly diagnosed myeloma as well as application of new drugs in multiple myeloma in refractory relapse. Phase III trials

Application of new treatment regimens in patients with elderly myeloblastic leukemia. Phase III trials

Application of new treatment regimens including proteasome inhibitors, monoclonal antibodies and liposomal formulations in lymphoid pathology.

LINE 3. TRANSPLANTATION OF HEMATOPOYETIC PROGENITORS.

Clinical results of allo-TPH in patients with different neoplastic pathologies

Extracorporeal phototherapy as treatment of acute or chronic steroid-resistant CHF.

Investigate the usefulness of the CMN infusion of the patient treated with metopsipsoralen and submitted to extracorporeal phototherapy.

Cooperative clinical research on TCPH. Our casuistry is incorporated into national and international databases, allowing a large number of cases to be accumulated for retrospective studies.

Investigation on the application of specific anti-CMV vaccine in patients with hematopoietic allograft to reduce complications associated with it. Phase III trial.

Study of different modalities of immunosuppression, including post-transplant cyclophosphamide in high-risk allogeneic transplantation.

PUBLICATIONS:

IMPACT FACTOR | 51,393

Original articles

1. Batlle, Javier, Perez-Rodriguez, Almudena, Corrales, Irene, Fernanda Lopez-Fernandez, Maria, Rodriguez-Trillo, Angela, Loures, Esther, Rosa Cid, Ana, Bonanad, Santiago, Cabrera, Noelia, Moret, Andres, Parra, Rafael, Eva Mingot-Castellano, Maria, Balda, Ignacia, Altisent, Carmen, Perez-Montes, Rocio, Maria Fisac, Rosa, Iruin, Gemma, Herrero, Sonia, Soto, Inmaculada, de Rueda, Beatriz, Jimenez-Yuste, Victor, Alonso, Nieves, Vilarino, Dolores, Arija, Olga, Campos, Rosa, Jose Paloma, Maria, Bermejo, Nuria, Toll, Teresa, Mateo, Jose, ..., Vidal, Francisco.
Molecular and clinical profile of von Willebrand disease in Spain (PCM-EVW-ES): Proposal for a new diagnostic paradigm.
Thromb Haemost. 2016;115:40-50. F.I.:5,255. [doi:10.1160/TH15-04-0282]

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Oncotarget. 2016;7:30492-30503. F.I.:5,008. [doi:10.18632/oncotarget.9026]

3. Batlle-López A, González de Villambrosía S, Mazorra F, Malatxeberria S, Sáez A, Montalban C, Sánchez L, Garcia JF, González-Barca E, López A, Ruiz-Marcellan MC, Mollejo M, Grande C, Richards KL, Hsi ED, Tzankov A, Visco C, Xu-Monette ZY, Cao X, Young KH, Angel Piris M, Conde E, Montes-Moreno S.
Stratifying diffuse large B-cell lymphoma patients treated with chemoimmunotherapy: GCB/non-GCB by immunohistochemistry is still a robust and feasible marker.
Oncotarget. 2016;7:18036-18049. F.I.:5,008. [doi:10.18632/oncotarget.7495]

4. Bermudez G, González de Villambrosía S, Martínez-López A, Batlle A, Revert-Arce JB, Cereceda Company L, Ortega Bezanilla C, Piris MA, Montes-Moreno S.
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Am J Surg Pathol. 2016;40:943-949. F.I.:4,951. [doi:10.1097/PAS.0000000000000628]

5. Orti G, Sanz J, Bermudez A, Caballero D, Martinez C, Sierra J, Cabrera Marin JR, Espigado I, Solano C, Ferrà C, García-Noblejas A, Jimenez S, Sampol A, Yañez L, García-Gutiérrez V, Pascual MJ, Jurado M, Moraleda JM, Valcarcel D, Sanz MA, Carreras E, Duarte RF.
Outcome of Second Allogeneic Hematopoietic Cell Transplantation after Relapse of Myeloid Malignancies following Allogeneic Hematopoietic Cell Transplantation: A Retrospective Cohort on Behalf of the Grupo Español de Trasplante Hematopoyetico.
Biol Blood Marrow Transplant. 2016;22:584-588.F.I.:3,980. [doi:10.1016/j.bbmt.2015.11.012]

6. Nomdedeu M, Calvo X, Pereira A, Carrió A, Solé F, Luño E, Cervera J, Vallespí T, Muñoz C, Gómez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardanaz MT, Hernández-Rivas JM, Azaceta G, Álvarez S, Sánchez J, Martín ML, Bargay J, Gómez V, Cervero CJ, Allegue MJ, Collado R, Campo E, Esteve J, ...,
Spanish Group of Myelodysplastic Syndromes. Prognostic impact of chromosomal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemia patients. A study by the spanish group of myelodysplastic syndromes.
Genes Chromosomes Cancer. 2016;55:322-327.F.I.:3,960. [doi:10.1002/gcc.22333]

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Outcome of patients with chronic myeloid leukemia and a low-risk score: allogeneic hematopoietic stem cell transplantation in the era of targeted therapy. A report from the EBMT Chronic Malignancies Working Party.
Bone Marrow Transplant. 2016;51:1259-1261.F.I.:3,636. [doi:10.1038/bmt.2016.97]

8. De La Serna J, Sanz J, Bermúdez A, Cabrero M, Serrano D, Vallejo C, Gómez V, Moraleda JM, Perez SG, Caballero MD, Conde E.
Lahuerta JJ, Sanz G. Toxicity and efficacy of busulfan and fludarabine myeloablative conditioning for HLA-identical sibling allogeneic hematopoietic cell transplantation in AML and MDS.
Bone Marrow Transplant. 2016;51:961-966.F.I.:3,636. [doi:10.1038/bmt.2016.42]

9. Kelleher N, Gallardo D, González-Campos J, Hernández-Rivas JM, Montesinos P, Sarrá J, Gil C, Barba P, Guàrdia R, Brunet S, Bernal T, Martínez MP, Abella E, Bermúdez A, Sánchez-Delgado M, Antònia C, Gayoso J, Calbacho M, Ribera JM,
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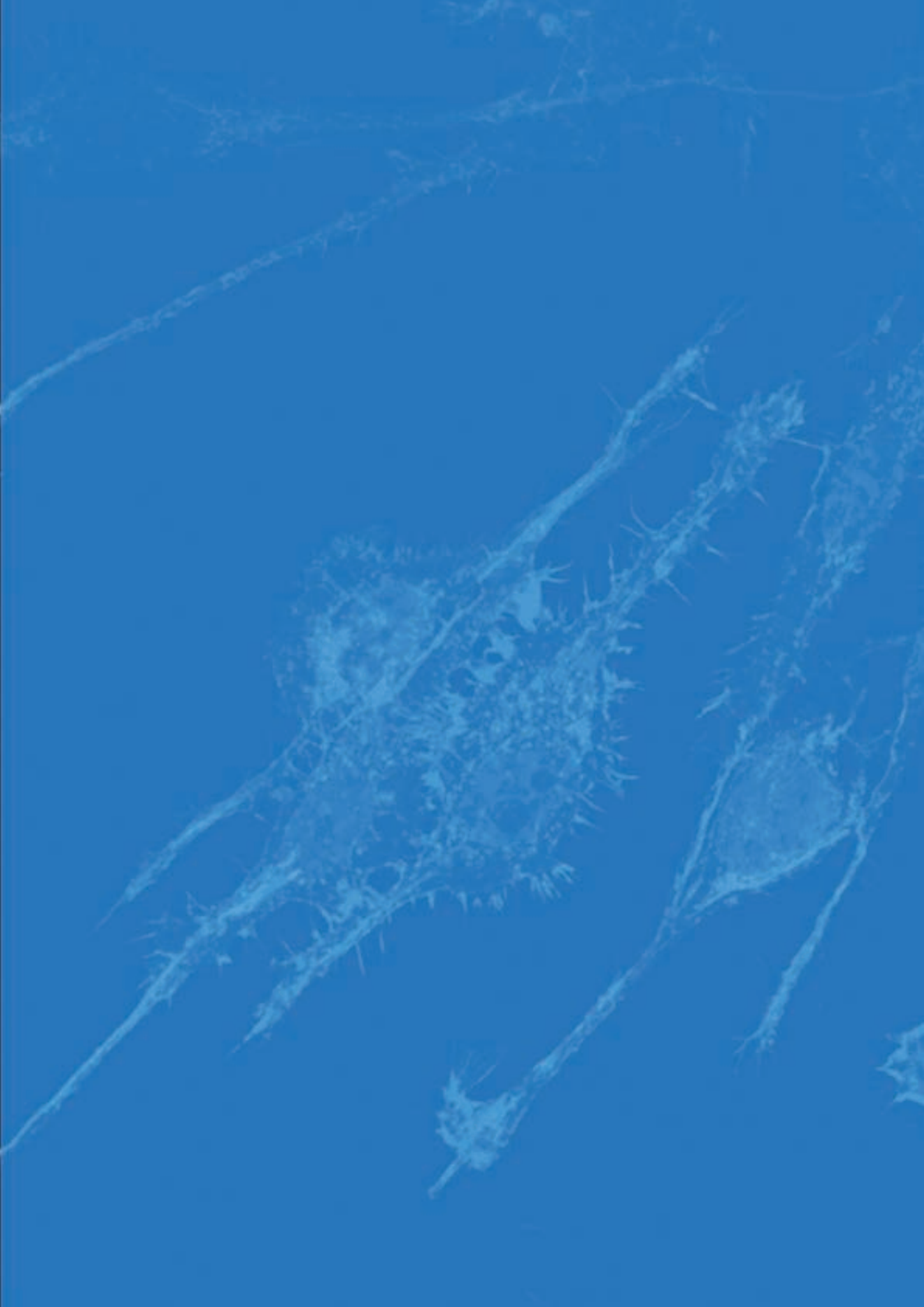

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Research Lines

LINE 1: TRANSPLANTATION OF SOLID ORGANS

1. Non-invasive blood and urine biomarkers of clinical events related to solid organ transplantation (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 plays 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 transplant-able 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.

PUBLICATIONS:

IMPACT FACTOR | 118,768

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Transplant Proc. 2016;48:2980-2982. F.I.:0,867. [doi:10.1016/j.transproceed.2016.08.037]

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working group PATHI. Implementation of a National Priority Allocation System for Hypersensitized Patients in Spain, Based on Virtual Crossmatch: Initial Results.
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42. Belmar Vega L, Rodrigo Calabia E, Gómez Román JJ, Ruiz San Millán JC, Martín Penagos L, Arias Rodríguez M.
Relationship Between Albuminuria During the First Year and Antibody-Mediated Rejection in Protocol Biopsies in Kidney Transplant Recipients.

Transplant Proc. 2016;48:2950-2952. F.I.:0,867. [doi:10.1016/j.transproceed.2016.09.012]

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Reviews

1. García R, Merino D, Gómez JM, Nistal JF, Hurlé MA, Cortajarena AL, Villar AV. **Extracellular heat shock protein 90 binding to TGFß receptor I participates in TGFß-mediated collagen production in myocardial fibroblasts.** Cell Signal. 2016;28:1563-1579. F.I.:4,191. [doi:10.1016/j.cellsig.2016.07.003]

2. Brunet M, Shipkova M, van Gelder T, Wieland E, Sommerer C, Budde K, Haufroid V, Christians U, López-Hoyos M, Barten MJ, Bergan S, Picard N, Millán López O, Marquet P, Hesselink DA, Noceti O, Pawinski T, Wallemacq P, Oellerich M. **Barcelona Consensus on Biomarker-Based Immunosuppressive Drugs Management in Solid Organ Transplantation.** Ther Drug Monit. 2016;38 Suppl 1:1-20. F.I.:2,094. [doi:10.1097/FTD.0000000000000287]

3. López-Hoyos M, San Segundo D, Brunet M. **Regulatory T Cells as Biomarkers for Rejection and Immunosuppression Tailoring in Solid Organ Transplantation.** Ther Drug Monit. 2016;38 Suppl 1:36-42. F.I.:2,094. [doi:10.1097/FTD.0000000000000265]

4. Mercè B, Olga M, Marcos LH. **T-Cell Cytokines as Predictive Markers of the Risk of Allograft Rejection.** Ther Drug Monit. 2016;38 Suppl 1:21-28. F.I.:2,094. [doi:10.1097/FTD.0000000000000253]

Editorials

1. Cuervas-Mons V, López-Hoyos M. **Preface.** Transplant Proc. 2016;48:2855-2855. F.I.:0,867. [doi:10.1016/j.transproceed.2016.10.004]

Doctoral thesis

1. Jorge Duerto Alvarez. **Long-term effect in renal grafts of an intensive management protocol of the multiorganic donor.** Directors: **Eduardo Miñambres García, María De Los Ángeles Ballesteros Sanz.** University of Cantabria.

2. Rosalía Demetrio Pablo. **Evaluation of thrombotic risk in asymptomatic patients with antiphospholipid antibodies.** Directors: **Pedro Muñoz Cacho, Victor Manuel Martínez Taboada.** University of Cantabria.

3. Inmaculada Hernandez Bejarano. **Analysis of the evolution of renal transplantation by identifying risk biomarkers in the donor and recipient.** Directors: **Ana Isabel Morales Martin, Marta Prieto Vicente, Mª Ángeles Ramos Barrón, Carlos Gómez Alamillo.** University of Salamanca.

4. José Quintanar Lartuno. **Peritonitis in peritoneal dialysis. Experience over a decade: evolution, microbiological profile, antimicrobial sensitivity and differences according to age.** Directors: **Manuel Antonio Arias Rodríguez, Luis Martínez Martínez.** University of Cantabria.

PROYECTOS

Proyectos

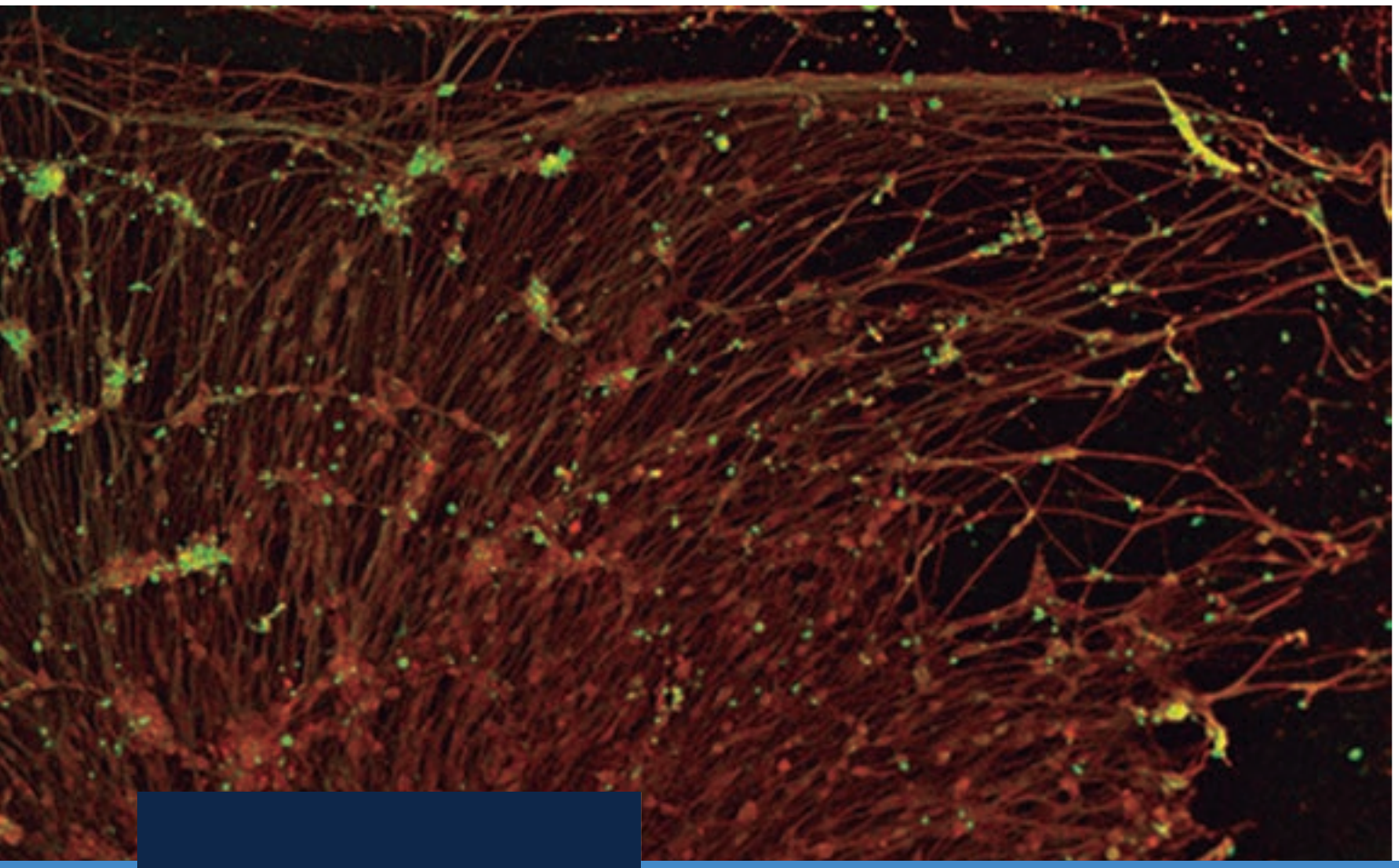
1. Manuel Antonio Arias Rodríguez. **Research Network on Kidney Diseases.** RD12/0021/0007. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. Manuel Antonio Arias Rodríguez. **Study of serological and cell activation factors as possible early markers of chronic kidney-mediated rejection in renal transplantation.** PI14/00378. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. Marcos López Hoyos. **Usefulness of the study of suppressor myeloid cells (MDSC) in renal transplant monitoring.** PI16/01585. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

4. Víctor Manuel Martínez Taboada. **Study of the role BAMBI, a regulator of TGF beta signaling, as a pathogenic factor and prognostic marker in rheumatoid arthritis.** PI16/01717. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

5. Marcos López Hoyos. **Research Network for Kidney Diseases.** RD16/0009/0027. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.



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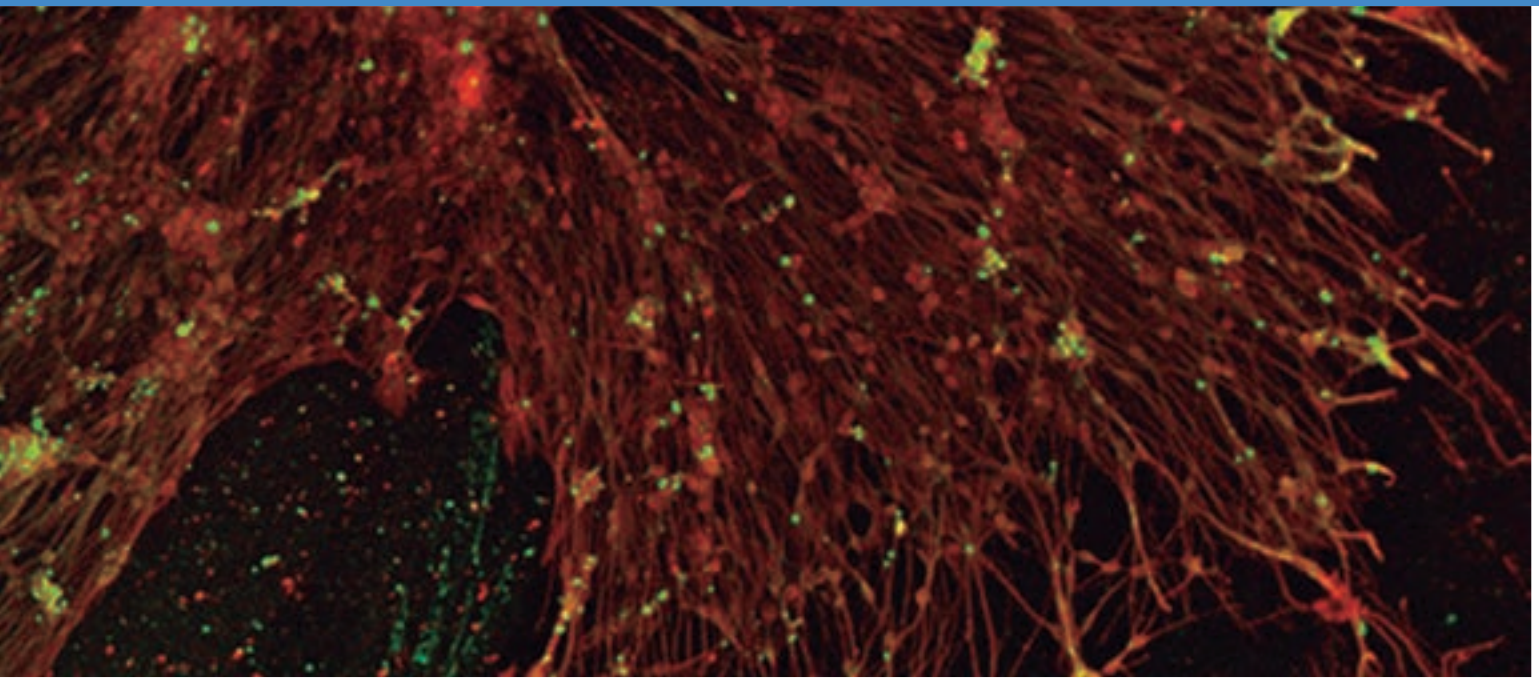

Nuclear Cell Biology

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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 acetyltranferase 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 | 24,839

Original articles

1. García-Hevia L, Villegas JC, Fernández F, Casafont Í, González J, Valiente R, Fanarraga ML.
Multiwalled Carbon Nanotubes Inhibit Tumor Progression in a Mouse Model.
Adv Healthc Mater. 2016;5:1080-1087. F.I.:5,760. [doi:10.1002/adhm.201500753]

2. Casafont I, Palanca A, Lafarga V, Mata-Garrido J, Berciano MT, Lafarga M.
Dynamic Behavior of the RNA Polymerase II and the Ubiquitin Proteasome System During the Neuronal DNA Damage Response to Ionizing Radiation.
Mol Neurobiol. 2016;53:6799-6808. F.I.:5,397. [doi:10.1007/s12035-015-9565-8]

3. Lafita-Navarro MC, Blanco R, Mata-Garrido J, Liaño-Pons J, Tapia O, García-Gutiérrez L, García-Alegría E, Berciano MT, Lafarga M, León J.
MXD1 localizes in the nucleolus, binds UBF and impairs rRNA synthesis.
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4. Riancho J, Berciano MT, Berciano J, Lafarga M.
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J Neurol. 2016;263:177-178.F.I.:3,408. [doi:10.1007/s00415-015-8004-0]

5. Romero AM, Palanca A, Ruiz-Soto M, Llorca J, Marín MP, Renau-Piqueras J, Berciano MT, Lafarga M.
Chronic Alcohol Exposure Decreases 53BP1 Protein Levels Leading to a Defective DNA Repair in Cultured Primary Cortical Neurons.
Neurotox Res. 2016;29:69-79. F.I.:3,140. [doi:10.1007/s12640-015-9554-8]

Reviews

1. Riancho J, Berciano MT, Ruiz-Soto M, Berciano J, Landreth G, Lafarga M.
Retinoids and motor neuron disease: Potential role in amyotrophic lateral sclerosis.
J Neurol Sci. 2016;360:115-120. F.I.:2,126. [doi:10.1016/j.jns.2015.11.058]

Doctoral thesis

1. Maria Ruiz Soto.
El estrés oxidativo en la glia satélite de los ganglios raquídeos induce alteraciones sensitivas en el modelo murino HSOD1g93a de esclerosis lateral amiotrófica (ELA).
Director/es: **Miguel Ángel Lafarga Coscojuela, María Teresa Berciano Blanco.** UNIVERSIDAD DE CANTABRIA.

Projects

1. María Teresa Berciano Blanco.
Regulación por acetilación del factor de supervivencia de las neuronas motoras: su importancia en la biogénesis de snrnps y en el ensamblaje de cuerpos nucleares de cajal.
BFU2014-54754-P. MINISTERIO DE ECONOMIA Y COMPETITIVIDAD.

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Clinic group

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 estrogen metabolism in migraines (estrogen 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.

In this line of research, we are developing sub-programmes which include:

> 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.

PUBLICACIONES:

IMPACT FACTOR | 42,989

Original articles

1. Ramos ML, Pascual J.
AMG 334 CGRP antibody for migraine: time to celebrate?.
Lancet Neurol. 2016;15:347-349.
F.I.:23,468. [doi:10.1016/S1474-4422(16)00040-5]

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2. González-Quintanilla V, Toriello M, Palacio E, González-Gay MA, Castillo J, Montes S, Martínez-Nieto R, Fernandez J, Rojo A, Gutiérrez S, Pons E, Oterino A.
Systemic and cerebral endothelial dysfunction in chronic migraine. A case-control study with an active comparator.
Cephalalgia. 2016;36:552-560.
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3. Cernuda-Morollón E, Riesco N, Martínez-Camblor P, Serrano-Pertierra E, García-Cabo C, Pascual J.
No Change in Interictal PACAP Levels in Peripheral Blood in Women With Chronic Migraine.
Headache. 2016;56:1448-1454.
F.I.:2,961. [doi:10.1111/head.12949]

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4. Larrosa D, Ramón C, Alvarez R, Martínez-Camblor P, Cernuda E, Pascual J.
No Relationship Between Patent Foramen Ovale and Migraine Frequency.
Headache. 2016;56:1466-1473.
F.I.:2,961. [doi:10.1111/head.12945]

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5. Martínez-Rodríguez L, Pascual J. **Negligencia de afeitado en la hemicara izquierda por isquemia parietal.**
Med Clin (Barc). 2016;147:93-93.
F.I.:1,267. [doi:10.1016/j.medcli.2015.11.035]

6. Oterino, Agustin, Uria, Dionisio F., Pena, Joaquin, Solar, Dulce, Villafani, Javier, Oliva-Nacarino, Pedro, Suarez-Moro, Roberto, Quintanilla, Vicente G. **Fingolimod: efectividad y seguridad en la practica clinica habitual. Estudio observacional, retrospectivo y multicentrico en Asturias y Cantabria.**
Rev Neurol. 2016;63:19-26.
F.I.:0,684.

—

7. Palacio E, Viadero-Cervera R, Revilla M, Larrosa-Campo D, Acha-Salazar O, Novo-Robledo F, Oterino A.
Utilidad del tratamiento con atorvastatina 40 mg más ezetimiba 10 mg frente a atorvastatina 80 mg en la reducción de los niveles de colesterol LDL en pacientes con ictus isquémico o ataque isquémico transitorio.
Rev Neurol. 2016;62:203-210.
F.I.:0,684.

—

8. Palacio, Enrique, Viadero-Cervera, Raquel, Revilla, Marian, Larrosa-Campo, Davinia, Acha-Salazar, Olga, Novo-Robledo, Francisco, Oterino, Agustin.
Utility of treatment with atorvastatin 40 mg plus ezetimibe 10 mg versus atorvastatin 80 mg in reducing the levels of LDL cholesterol in patients with ischaemic stroke or transient ischaemic attack.
Rev Neurol. 2016;62:203-210.
F.I.:0,684.

Reviews

1. Riesco N, García-Cabo C, Pascual J.
Migraña.
Med Clin (Barc). 2016;146:35-39.
F.I.:1,267. [doi:10.1016/j.medcli.2015.07.003]

Editorials

1. Purdy AR, Pascual J.
Don't Bring Me Down--Too Fast!.
Headache. 2016;56:223-224.
F.I.:2,961. [doi:10.1111/head.12761]

Doctoral thesis

1. María Toriello Suárez.
Genetic association study of genes encoding the GABA-A receptor in migraine.
Un estudio de asociación familiar.
Director/es: **Agustín Oterino Durán, Jesús Castillo Obeso.**
University of Cantabria.

PROJECTS

Projects

1. Agustín Oterino Durán.
Epigenetic modifications induced by childhood adverse experiences and endothelial damage in chronic migraine.
a case-control study. Creation of murine experimental model.
PI15/01285. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

—

2. Agustín Oterino Durán.
Thematic Network of Multiple Sclerosis.
RD16/0015/0023. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Neurodegenerative Diseases

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Research Lines

1. Peripheral neuropathy.

In a prospective study of six early Guillain-Barre syndrome (GBS) patients, we have demonstrated the pathogenic relevance of inflammatory oedema in proximal nerves, particularly in spinal nerves. This notion is applicable to both demyelinating and axonal forms of the syndrome (figure 1). Our contributions to GBS nosology have been compiled in a monographic textbook (see publications 2015).

In two pedigrees of Charcot-Marie-Tooth disease (CMT) harboring NEFL mutations, either E397K or N98S, we have re-defined the corresponding phenotypes, which should be classified in the category of dominant intermediate CMT. We have reported the first electrophysiological recording of T reflex in CMT1A duplication, which is a simple and painless diagnostic method, particularly useful for at-risk children. In collaboration with Dr Albena Jordanova (Department of Genetics, University of Antwerp, Belgium), we have continue evaluating a large CMT2 pedigree, categorized as CMT2G by linkage analysis. Using next-generation sequencing technology, we have found a pathogenic LRSAM1 missense mutation indicating that the syndrome should be reclassified as a novel CMT2P phenotype. In two review papers, we have addressed the role of imaging techniques in the diagnosis of inflammatory and inherited neuropathies.

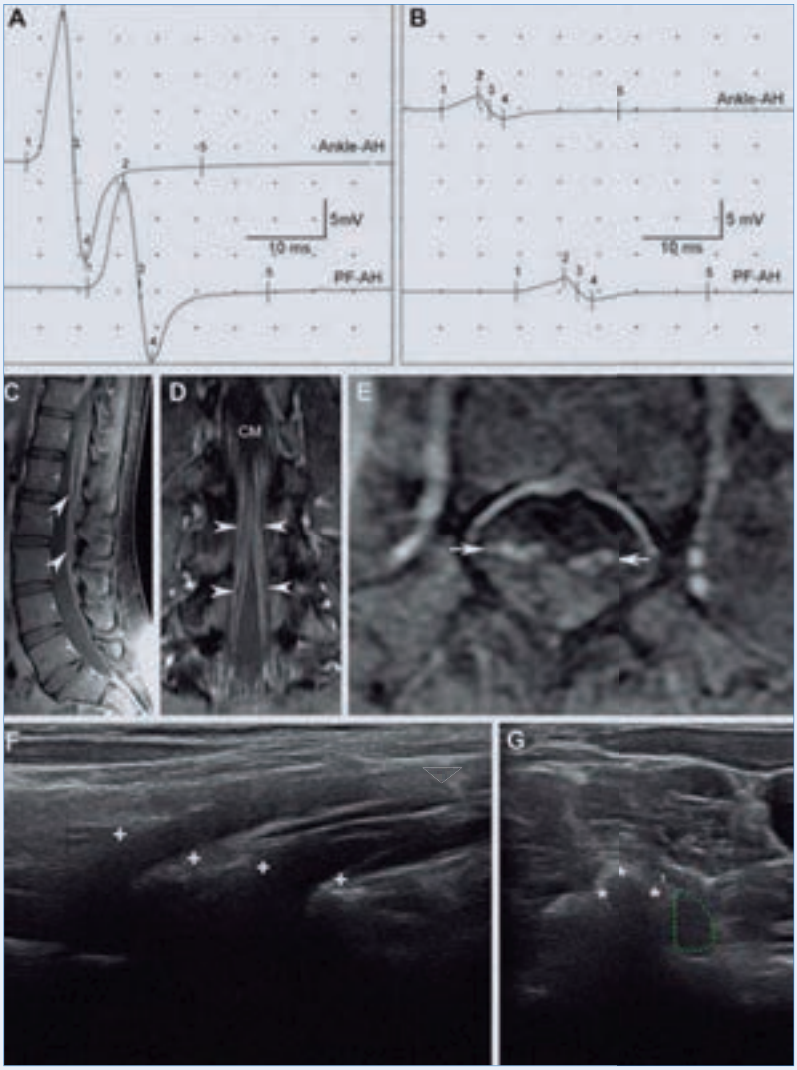

Figure 1. Picture taken from the paper by Berciano et al (JNNP 2016; 87: 563-5. Epub 2015 May 13) showing electrophysiological and imaging findings in a patient with the paraparetic and axonal form of GBS. (A) Tibial nerve motor conduction velocity (MCV) study on day 4 after onset showing normal compound 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)2. Note blurred margins and the absence of the physiologic hyperechoic rim. Asterisks indicate the posterior tubercle of the seventh transverse vertebral process.

2. Hereditary Ataxias.

We have continued with the SCANatural History Study within the EUROSCA project (for more details http:// www.ataxia-study-group.net/html/studies/eurosca). Also, within the EUROSCA group we have continued with the prospective follow-up of patients with dominant ataxia included in the RISCA project we have participated in a follow-up study of a longitudinal cohort of patients with SCA1, 2, 3 and 6 (see references of our group published in 2005).

3. Parkinson's disease. We have demonstrated that serum uric acid levels are not associated with the risk of dementia in Parkinson's disease. We have participated in two international collaborative studies analyzing the temporal profile of non-motor symptoms in idiopathic and LRRK2G2019S associated Parkinson's disease (PD). Through a blood transcriptomic analysis, we have identified 13 candidate genes for PD in sporadic cases, asymptomatic carriers of the G2019S mutation and controls.

As member of the EMSA-SG group (www.emsa-sg. org/), we have participated in a study that discards the pathogenic role of mutations in COQ2 in MSA

In collaboration with the Neurology Department of Toulouse Purpam Hospital (INSERM), we are participating in an ongoing project to identify clinical and preclinical (multimodal MRI) biomarkers in LRRK2- PD 4.Alzheimer's disease.

4. Alzheimer's disease. Our group is a founder member of the Spanish consortium of dementia (DEGESCO). As a consequence of this collaboration, in the framework of CIBERNED, we have published in 2015 an association between MAPT gene variants and different neurodegenerative conditions in a sample of 11572 subjects. In the line of Alzheimer's disease biomarkers, we are carrying out PET-PIB and PET-FDG studies to: 1) patients with AD,2) patients with mild cognitive impairment and 3) healthy controls. We are preparing an article describing our clinical experience in the use of amyloid-PET and we have collaborated with our data in international consortiums producing a double publication in JAMA describing the prevalence of brain amyloid deposits in healthy subjects and subjects with mild cognitive impairment.

5. Prionopathies.

In 2015, we have published a genome wide association study (GWAs) with the largest sample of patients recruited so far (1543 samples from patients with sporadic Creutzfeldt Jakob disease, coming from 7 European countries and Australia, and 4203 controls). This study has been carried out in the framework of a collaborative European project, JPND DEMTEST.

PUBLICATIONS:

IMPACT FACTOR | 42,989

Original articles

1. Peeters K, Palaima P, Pelayo-Negro AL, García A, Gallardo E, García-Barredo R, Mateiu L, Baets J, Menten B, De Vriendt E, De Jonghe P, Timmerman V, Infante J, Berciano J, Jordanova A.
Charcot-Marie-Tooth disease type 2G redefined by a novel mutation in LRSAM1.
Ann Neurol. 2016;80:823-833. F.I.:9,638. [doi:10.1002/ana.24775]

2. Sailer A, Scholz SW, Nalls MA, Schulte C, Federoff M, Price TR, Lees A, Ross OA, Dickson DW, Mok K, Mencacci NE, Schottlaender L, Chelban V, Ling H, O'Sullivan SS, Wood NW, Traynor BJ, Ferrucci L, Federoff HJ, Mhyre TR, Morris HR, Deuschl G, Quinn N, Widner H, Albanese A, Infante J, Bhatia KP, Poewe W, Oertel W.
European Multiple System Atrophy Study Group and the UK Multiple System Atrophy. A genome-wide association study in multiple system atrophy.
Neurology. 2016;87:1591-1598. F.I.:8,166. [doi:10.1212/WNL.0000000000003221]

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PROJECTS

Projects

1. Eloy Manuel Rodríguez Rodríguez. **Alzheimer's disease biomarkers as prognostic factors in idiopathic normal pressure hydrocephalus.** PI13/01008. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD, INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. Pascual Jesús Sánchez Juan. **Biobanks Platform.** PT13/0010/0024. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

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3. Pascual jesús sánchez juan. **Study of rare variants in genes associated with Alzheimer's disease in Spanish population.** PI16/01652. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE CONOMÍA Y COMPETITIVIDAD.

Neurophysiology in Epilepsy and Neurointensive Care

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Research Lines

> Refractory nonconvulsive status epilepticus

> Super-refractory or malignant nonconvulsive status epilepticus.

> Multimodal neuromonitoring including intracortical electrodes in acute brain injury patients.

> EEG patterns and prognosis in hipoxic-ischemic encephalopathy.

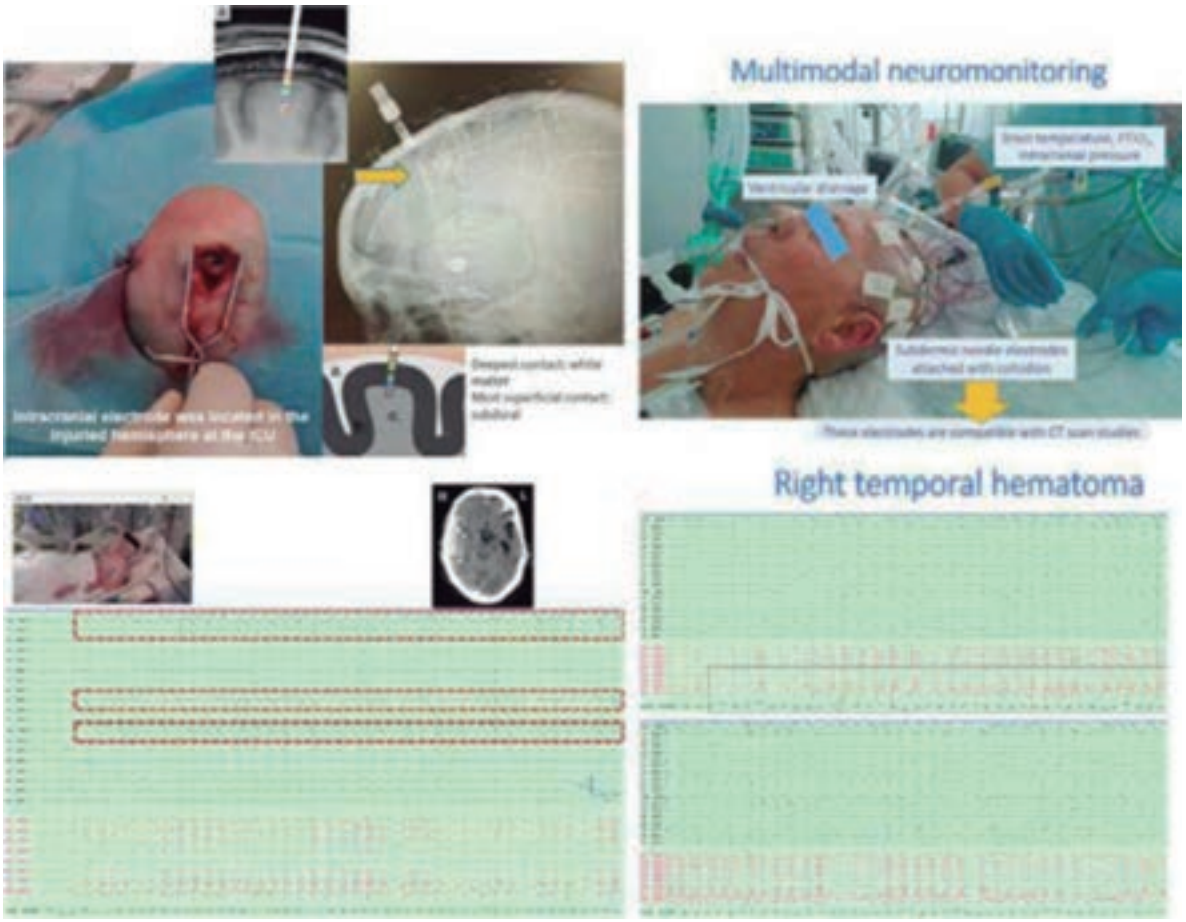
> Post-anoxic myoclonic status epilepticus. Stimulus-induced postanoxic myoclonus.

> Utility of EEG in the diagnosis of brain death.

> Toxic encephalopathy in neurocritical patients.

> The use of bilateral bispectral index (BIS) in the diagnosis of nonconvulsive status epilepticus in comatose patients.

> Experimental models of status epilepticus. EEG phases of status epilepticus in humans.



PUBLICATIONS:

IMPACT FACTOR | 18,524

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Subacute progressive aphasia: a rare presentation of Creutzfeldt-Jakob disease.
J Neurol. 2016;263:600-602. F.I.:3,408. [doi:10.1007/s00415-016-8054-y].

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3. Hernández-Hernández MA, Fernández-Torre JL.
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Seizure. 2016;34:18-25. F.I.:2,109. [doi:10.1016/j.seizure.2015.11.001].

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4. Hernández-Hernández MA, Iglesias-Posadilla D, Ruiz-Ruiz A, Gómez-Marcos V, Fernández-Torre JL.
Matriz de densidad espectral de color del BIS bilateral en estado epiléptico.
An Pediatr (Barc). 2016;85:44-47. F.I.:0,773. [doi:10.1016/j.anpedi.2015.09.021].

Reviews

1. Drake-Pérez M, Marco de Lucas E, Lyo J, Fernández-Torre JL.
Neuroimaging features in subacute encephalopathy with seizures in alcoholics (SESA syndrome).
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Psychiatry

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Research Lines

1- Brain Neuroimaging in Non-Affective Psychosis (NAP).

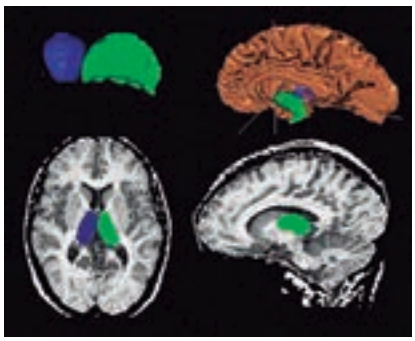
Responsible: **R. Roiz Santiáñez** y **D. Tordesillas Gutiérrez.** The techniques of brain imaging, such as magnetic resonance imaging (MRI), allow exploring the presence of structural alterations from the first clinical phases of the disease (neurodevelopmental anomalies) and also study the onset of morphological changes during the course of the disease (neurodegeneration processes). Our work in this area aims to:

a. To compare the volume of gray and white matter in the cortex between patients and controls

b. To determine the existence of differences in volume of the basal ganglia between patients and controls

c. study to detect structural changes over time in people with schizophrenia, and

d. 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.** Entre los objetivos de esta línea desarrollada por nuestro grupo, se encuentran:

a. To investigate the incidence of psychosis in Cantabria and likely related factors.

a. To identify the profile of symptoms during early phases of the illness.

a. To describe predictors of outcome.

a. To advance in the knowledge of biological markers (neuroimaging, biochemical, genetic) of Schizophrenia.

a. 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: **Dra. R. Ayesa Arriola.** The main objectives of this research are:

a. To evaluate the course of early cognitive function in a sample of first episodes of psychosis individuals.

b. To examine the relationship between cognitive functions and clinical variables.

c. 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:

a. Implement an early, multi-disciplined and multi-factorial evaluation and intervention protocol for all patients that develop an eating disorder in the area referenced by the Psychiatric Service of University Hospital Marqués de Valdecilla.

b. Research the early phases of the disease— the psychological, biological, and social components of eating disorders.

c. Identify and define the risk factors of developing eating disorders, as well as the nature and characteristics of prodromal symptoms and earliest clinical manifestations.

d. Evaluate the response to

interventions, as well as the evolutionary course of the disease, researching bio-psycho-social factors that condition them.

e. 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. Responsible: Dra. Jana Gonzalez Gomez and Dr. J.A. Gomez del Barrio. This program integrates DETECTA (DEtecion TEmprana 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.

Responsible: **Dra. S. Otero Cuesta** y **Dra. 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.

Responsible: **Dr. L. Gaite Pindado** y **Dra. S. Herrera Castanedo.** Since the inception of the UIPC, one of the areas of greatest interest has been the development and dissemination of the evaluation methodology in mental health, along with the adaptation to our environment of tools and strategies for the evaluation of mental health services. In this sense, the Unit has collaborated with the European Network for Mental Health Evaluation Service (ENMESH), which integrates European experts in the field of evaluation of mental health services and has as main objectives:

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.

Responsible: **Dra. 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.

Responsible: **Dra. 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 Development Project for the Spanish version of the WHO International Standard Classification of Functioning, Disability and Health-Children and Youth Version has been culminated with its definitive publication and the beginning of the dissemination work Same.

PUBLICATIONS:

IMPACT FACTOR | 130,588

Original articles

1. Franke B, Stein JL, Ripke S, Anttila V, Hibar DP, van Hulzen KJ, Arias-Vasquez A, Smoller JW, Nichols TE, Neale MC, McIntosh AM, Lee P, McMahon FJ, Meyer-Lindenberg A, Mattheisen M, Andreassen OA, Gruber O, Sachdev PS, Roiz-Santiañez R, Saykin AJ, Ehrlich S, Mather KA, Turner JA, Schwarz E, Thalamuthu A, Yao Y, Ho YY, Martin NG, Wright MJ, ..., Sullivan PF.
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NAT NEUROSCI. 2016;19:420-431. F.I.:16,724. [doi:10.1038/nn.4228]

2. Adams HH, Hibar DP, Chouraki V, Stein JL, Nyquist PA, Rentería ME, Trompet S, Arias-Vasquez A, Seshadri S, Desrivières S, Beecham AH, Jahanshad N, Wittfeld K, Van der Lee SJ, Abramovic L, Alhusaini S, Amin N, Andersson M, Arfanakis K, Aribisala BS, Armstrong NJ, Athanasiu L, Axelsson T, Beiser A, Bernard M, Bis JC, Blanken LM, Blanton SH, Bohlken MM, ..., Thompson PM.
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NAT NEUROSCI. 2016;19:1569-1582. F.I.:16,724. [doi:10.1038/nn.4398]

3. Mehta D, Tropf FC, Gratten J, Bakshi A, Zhu Z, Bacanu SA, Hemani G, Magnusson PK, Barban N, Esko T, Metspalu A, Snieder H, Mowry BJ, Kendler KS, Yang J, Visscher PM, McGrath JJ, Mills MC, Wray NR, Lee SH, Schizophrenia Working Group of the Psychiatric Genomics Consortium, LifeLines Co, Andreassen OA, Bramon E, Bruggeman R, Buxbaum JD, Cairns MJ, Cantor RM, Cloninger CR, Cohen D, ..., Wu JQ.
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Reviews

1. Setién-Suero E, Suárez-Pinilla M, Suárez-Pinilla P, Crespo-Facorro B, Ayesa-Arriola R.
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F.I.:4,910. [doi:10.1007/s40263-016-0331-x]

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3. Apostolo J, Holland C, O'Connell MD, Feeney J, Tabares-Seisdedos R, Tadros G, Campos E, Santos N, Robertson DA, Marcucci M, Varela-Nieto I, Crespo-Facorro B, Vieta E, Navarro-Pardo E, Selva-Vera G, Balanzá-Martínez V, Cano A.
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Maturitas. 2016;83:83-93.
F.I.:3,120. [doi:10.1016/j.maturitas.2015.10.008]

Doctoral thesis

1. Amador Priede Diaz.
Cognitive factors associated with the development of anxiety-depressive symptoms in newly diagnosed cancer patients.
Director: **César González-Blanch Bosch.**
University of Cantabria.

—

2. Beatriz Payá González. **Predicted functioning in psychotic disorders of early onset: differences between people diagnosed with schizophrenia, bipolar disorder and healthy population.**
Directors: **Jesús Ángel Artal Simón, Celso Arango Lopez.**
University of Cantabria.

—

3. Diana Tordesillas Gutiérrez.
Differences in gray matter volume in patients with a first psychotic episode and age-onset effects using voxel-based morphometry.
Director: **Benedicto Crespo Facorro.**
University of Cantabria.

—

4. Jacqueline Maria Mayoral Van Son.
A three-year longitudinal study of clinical evolution in patients who, after a single episode of non-affective psychosis, have achieved a complete recovery and decided to withdraw antipsychotic medication.
Directoa: **Benedicto Crespo Facorro.**
University of Cantabria.

5. Jana González Gómez.
Controlled study of risk factors and clinical variables associated with the development of a eating disorder in the community of Cantabria.
Director: **Andrés Gómez Del Barrio.**
University of Cantabria.

6. Javier Vázquez Bourgon.
DISC1 and non-affective psychosis: variations in endophenotypes and clinical characteristics in the first episodes of psychosis.
Director: **Benedicto Crespo Facorro.**
University of Cantabria.

7. José Gabriel Calcedo Giraldo.
Prevention in eating disorders in high school students in cantabria.
Director: **Andrés Gómez Del Barrio.**
University of Cantabria.

8. Jose Helmut Ramirez Cuentas.
Study of parents' satisfaction in a neonatal unit.
Directors: **Isabel De Las Cuevas Terán, Luis Gaite Pindado.**
University of Cantabria..

9. Laura Carral Fernández.
Cognitive bias in eating disorders: a case-control study.
Director/a: **Andrés Gómez Del Barrio.**
University of Cantabria.

PROJECTS

Projects

1. Benedicto Crespo Facorro.
Center for Biomedical Research in Mental Health Network. CIBERSAM.
CIBERSAM. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

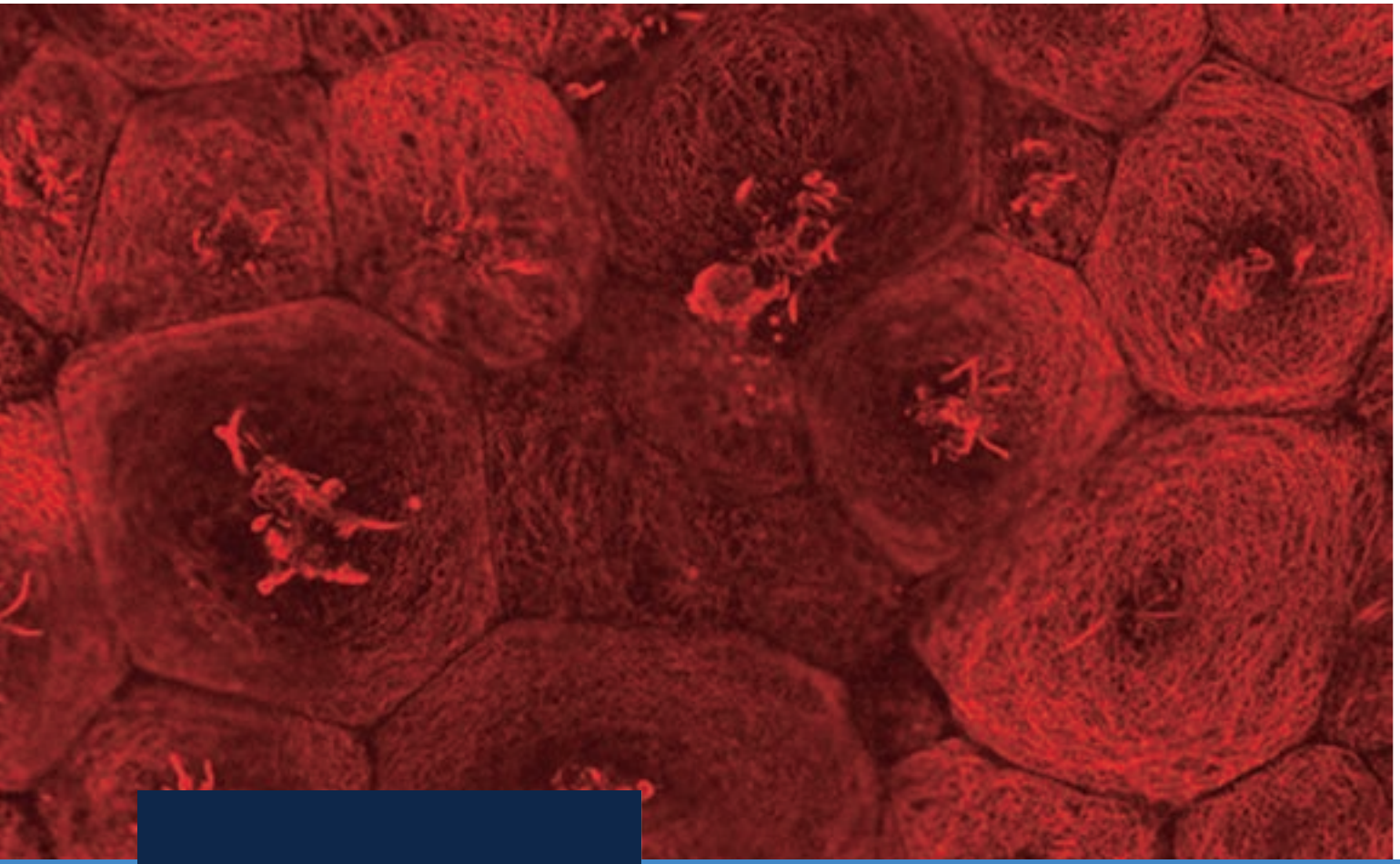
2. Benedicto Crespo Facorro.
Translating neuroimaging findings from research into clinical practice.
EU12/01- PSYSCAN.
COMISIÓN EUROPEA.

3. Diana Tordesillas Gutiérrez.
10PAFIP neurocognition: long-term longitudinal study (10 years) of cognitive functioning in patients with schizophrenia spectrum psychosis.
PI14/00918. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

4. Benedicto Crespo Facorro.
Aid for predoctoral contracts for the training of doctors.
BES-2014-070615.
MINISTERIO DE ECONOMIA Y COMPETITIVIDAD.

5. Benedicto Crespo Facorro.
Contracts for the intensification of the research activity in the SNS.
INT15/00096.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

6. Benedicto Crespo Facorro.
Stratified treatment in schizophrenia: integrating human and cellular transcriptome results in antipsychotic treatment strategies.
SAF2016-76046-R.
MINISTERIO DE ECONOMIA Y COMPETITIVIDAD.



Cancer Area

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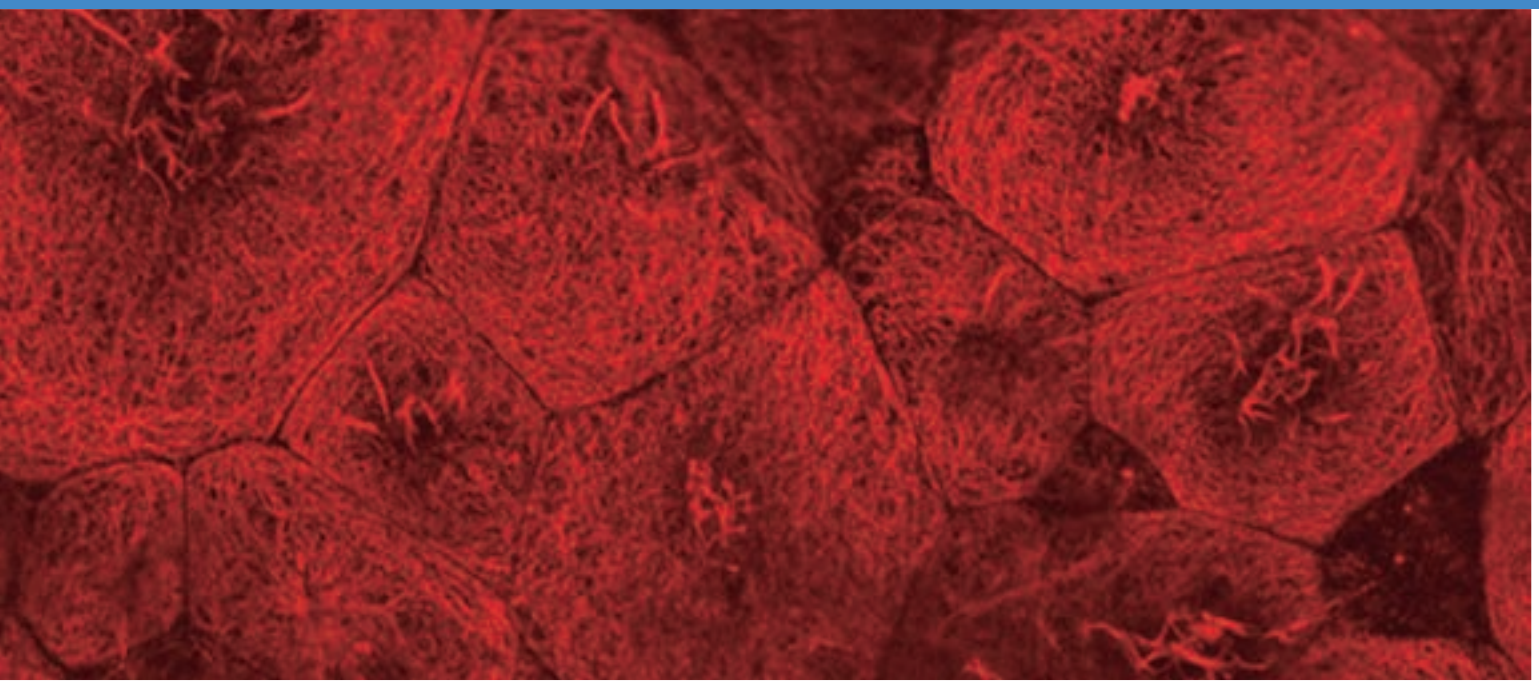
Head of the Oncology Service.
University Hospital Marqués de Valdecilla.



Anatomical and Molecular Pathology

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Consolidated group

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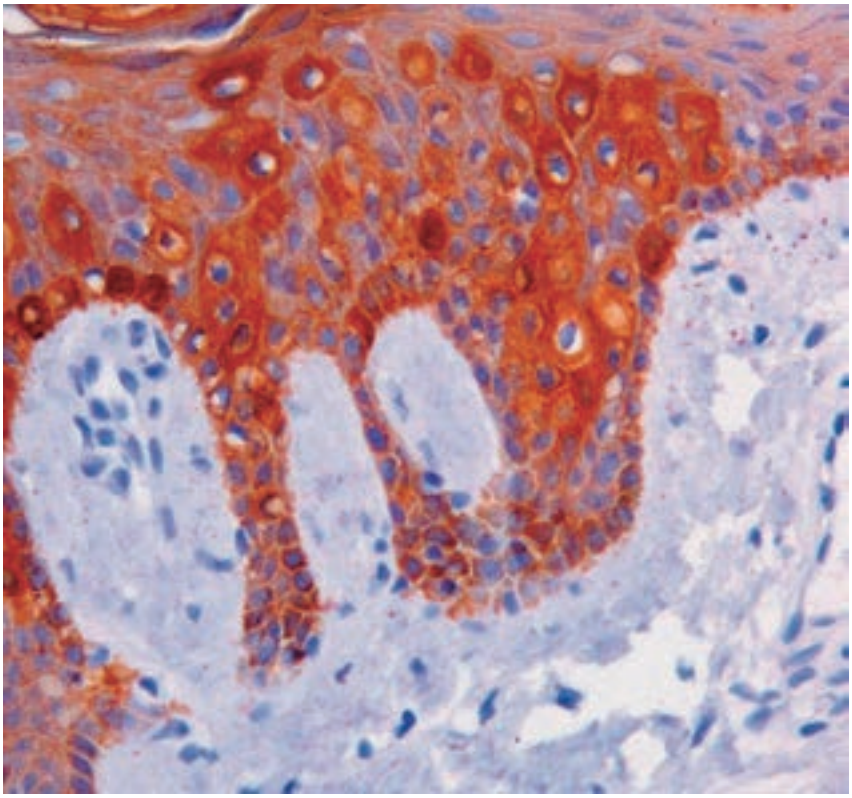
Research Lines

Research on cancer is one of the most important and we can distinguish the following lines:

1. Diagnostic and predictive biomarkers in solid tumors.

Our main task remains to establish a model of translational medicine, which is to be the bridge between basics and applied investigation. We are basically implied in all the new biomarkers that are necessary to obtain a correct diagnosis at the right time with a strong predictive response value (Mamacan project). This project is designed to find stromal based biomarkers capable to be transformed in therapeutic targets in breast carcinomas. The same methodology is being applied to urinary bladder carcinomas, lung carcinomas, renal cell carcinomas and gastrointestinal stromal tumors (GIST).



2. We have developed systems to diagnose hereditary cancer in clinical routine based in Next generation sequencing and we have incorporated the epithelial-mesenchymal transition program to our biomarker's discovery plan.

3. Our most important role as pathologists is to incorporate our results to clinical routine, mainly in oncology.

We believe the basic investigation results are very difficult to use in our day-to-day work. We try to streamline the process to give the oncologist the data he needs to treat the patient with the biomarkers that have been accepted by the international community and the agencies.

Thus, we use the EGFR and ALK and ROS1 rearrangements in non-small cell lung carcinomas, the KRAS and NRAS mutations in colon adenocarcinomas by several techniques, including liquid biopsy, and several other biomarkers that are the key to precision medicine establishment.

4. Development of Immunotherapy in cancer.

Immunotherapy is one of the most promising fields in new cancer therapies. The use of so-called "companion tests" are mandatory according to the regulatory agencies for prescription. Our interest is to develop all of the markers associated with specific therapies anti PD1 and anti PD-L1. To do this we are involved in the clinical establishment and in new models of anti-PD1-L1 antibodies SP142, SP263, 22C3 and 28-8. The availability of all antibodies allows the participation in clinical trials of new development in new tumor models. The research line in non-tumoral pathology is reflected by the existence of several doctoral theses in development that explore the detection of viral infectious agents in Immunosuppressed patients in the tissue and its relation to graft failures in the case of organ transplantation. We collaborate actively with Nephrology groups (gene expression project in transplant patients' biopsies) in this sense. Our collaboration extends to the University of Cantabria with active projects in relation to Legal Medicine (utility of DNA extraction methods in ancient samples) and IBBTEC in Genomics (Dr Ignacio Varela with several projects underway using mass sequencing procedures). 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 epithelial-mesenchymal transition in breast cancer We received rotating professionals from different hospitals of the national network to deepen teaching. The collaboration extends to European countries as with the group of Dr Julian Downward of the London Research Institute investigating factors of resistance to drugs inhibiting the tyrosine kinase activity in lung cancer. We also collaborated with MD Anderson Hospital on a neuroendocrine evaluation project and its new classification (Dr César Morán).

PUBLICATIONS:

IMPACT FACTOR | 33,960

Artículos originales

1. Villalba M, Diaz-Lagares A, Redrado M, de Aberasturi AL, Segura V, Bodegas ME, Pajares MJ, Pio R, Freire J, Gomez-Roman J, Montuenga LM, Esteller M, Sandoval J, Calvo A.
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Exceptional antineoplastic activity of a dendritic-cell-targeted vaccine loaded with a Listeria peptide proposed against metastatic melanoma.
Oncotarget. 2016;7:16855-16865. F.I.:5,008. [doi:10.18632/oncotarget.7806]

3. Real, Eusebio, Fernando Val-Bernal, Jose, Revuelta, Jose M., Ponton, Alejandro, Calvo Diez, Marta, Mayorga, Marta, Lopez-Higuera, Jose M., Conde, Olga M.
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QJM. 2016;109:345-346. F.I.:2,824. [doi:10.1093/qjmed/hcw008]

5. Calderon-Gonzalez, Ricardo, Teran-Navarro, Hector, Frande-Cabanes, Elisabet, Ferrandez-Fernandez, Eva, Freire, Javier, Penades, Soledad, Marradi, Marco, Garcia, Isabel, Gomez-Roman, Javier, Yanez-Diaz, Sonsoles, Alvarez-Dominguez, Carmen.
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6. Loricera J, González-Vela C, Blanco R, Hernández JL, Armesto S, González-López MA, Calvo-Río V, Ortiz-Sanjuán F, Val-Bernal JF, Hermana S, Onaindia-Pérez A, González-Gay MA.
Histopathologic differences between cutaneous vasculitis associated with severe bacterial infection and cutaneous vasculitis secondary to other causes: study of 52 patients.
Clin Exp Rheumatol. 2016;34:93-97. F.I.:2,495.

7. Val-Bernal JF, Mayorga M, Val D.
Incidental Melanocytic Nevi in Hemorrhoidectomy Specimens.
Am J Dermatopathol. 2016;38:278-282.F.I.:1,396. [doi:10.1097/DAD.0000000000000419]

8. Val-Bernal JF, Hermana S.
Arteriovenous malformation of the uterine cervix.
Pathol Res Pract. 2016;212:226-228. F.I.:1,388. [doi:10.1016/j.prp.2015.08.010]

9. Val-Bernal JF, Mayorga M, Terán-Villagrá N.
Extracutaneous intravascular histiocytosis of the aortic valve: Report of two cases.
Pathol Res Pract. 2016;212:258-263. F.I.:1,388. [doi:10.1016/j.prp.2015.12.016]

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Incidental vaginal müllerianosis.
Pathol Res Pract. 2016;212:568-572. F.I.:1,388. [doi:10.1016/j.prp.2016.02.023]

11. Val-Bernal JF. **Respuesta.**
Med Clin (Barc). 2016;146:186-187. F.I.:1,267. [doi:10.1016/j.medcli.2015.09.001]

12. Velilla G, Carrión CJ, Portillo JA, Truán D, Azueta A, Fuentes J, Herrero E, Gala L.
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14. Sango C, Merino D, San Segundo D, Rodrigo E, Lopez-Hoyos M, Benito A, Ángeles Ramos M, Gómez-Román J, Arias M.
B-Cell-Activating Factor Levels Are Associated With Antibody-Mediated Histological Damage in Kidney Transplantation. Transplant Proc. 2016;48:2910-2912. F.I.:0,867. [doi:10.1016/j.transproceed.2016.09.019]

15. Belmar Vega L, Rodrigo Calabia E, Gómez Román JJ, Ruiz San Millán JC, Martín Penagos L, Arias Rodríguez M.
Relationship Between Albuminuria During the First Year and Antibody-Mediated Rejection in Protocol Biopsies in Kidney Transplant Recipients.
Transplant Proc. 2016;48:2950-2952. F.I.:0,867. [doi:10.1016/j.transproceed.2016.09.012]

16. Val-Bernal JF, Hermana S.
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Rom J Morphol Embryol. 2016;57:875-878.F.I.:0,811.

Reviews

1. Val-Bernal JF, Mayorga M, Cagigal ML, Cabezas-González J.
Gastric pyogenic granuloma: Report of two cases and review of the literature.
Pathol Res Pract. 2016;212:68-71. F.I.:1,388. [doi:10.1016/j.prp.2015.11.001]

Doctoral thesis

1. Ruth Gonzalez Sanchez.
Development of a diagnostic method for gastrointestinal stromal tumors (GIST).
Directors: **José Javier Gómez Román, Francisco Javier Freire Salinas.**
University of Cantabria.

—

2. Araceli Prieto Santacruz.
Utility of a process-based management system in the care and perceived quality of lung cancer.
Director: **José Javier Gómez Román**.
University of Cantabria.

—

3. Víctor Jacinto Ovejero Gómez.
Evaluation of biomarker predictors of peritoneal carcinomatosis in colon carcinoma.
Directors: **José Javier Gómez Román, Francisco Javier Freire Salinas.**
University of Cantabria.

—

4. Nuria E. Cadenas González.
Study of mesenchymal epithelial transition markers in renal neoplasms.
Directors: **José Javier Gómez Román, Francisco Javier Freire Salinas.**
University of Cantabria.

—

5. Ana De Juan Ferré.
Phase II intramural study of neoadjuvant chemotherapy with platinum, doxorubicin and taxane salts in operable breast cancer. Experience of the medical oncology service of the University Hospital Marqués de Valdecilla.
Directors: **José Manuel López Vega, Marta Mayorga Fernández.**
University of Cantabria.

PROYECTS

Proyects

1. José Javier Gómez Román.
Development of anti-CCR9 therapeutic antibodies for the personalized treatment of tumors-TERPERAN.
RTC-2015-3786-1.
MINISTERIO DE ECONOMIA Y COMPETITIVIDAD.

Apoptosis

Group Leader
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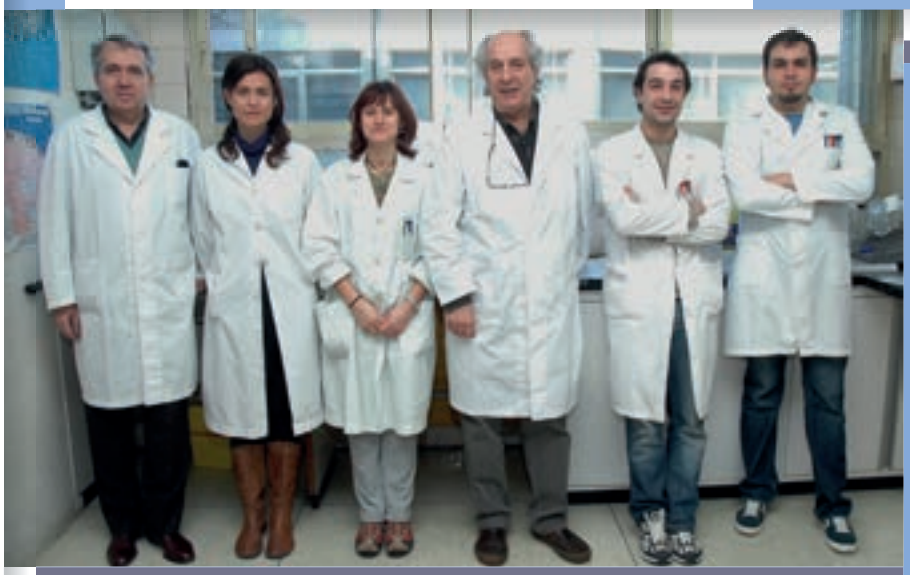

Consolidated group

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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. Gens identified by different molecular strategies are functionally analyzed through gain-of- and lossof-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 | 12,492

Original articles

1. Montero, Juan A., Sanchez-Fernandez, Cristina, Lorda-Diez, Carlos I., Garcia-Porrero, Juan A., Hurle, Juan M.
DNA damage precedes apoptosis during the regression of the interdigital tissue in vertebrate embryos.
Sci Rep. 2016;6:35478-35478.
F.I.:5,228. [doi:10.1038/srep35478]

2. Arroba AI, Rosa LR, Murillo-Cuesta S, Vaquero-Villanueva L, Hurlé JM, Varela-Nieto I, Valverde ÁM.
Autophagy resolves early retinal inflammation in Igf1-deficient mice.
Dis Model Mech. 2016;9:965-974.
F.I.:4,316. [doi:10.1242/dmm.026344]

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3. Lorda-Diez CI, Montero JA, Garcia-Porrero JA, Hurle JM. **The tumor suppressor BTG1 is expressed in the developing digits and regulates skeletogenic differentiation of limb mesodermal progenitors in high density cultures.**
Cell Tissue Res. 2016;364:299-308.
F.I.:2,948. [doi:10.1007/s00441-015-2331-4]

PROYECTOS

Proyectos

1. Juan M. Hurlé Gonzalez.
Mechanism and new biological significance of interdigital cell death responsible for the separation of the fingers during the development of the extremities. BFU2014-54026-P.
MINISTERIO DE ECONOMIA Y COMPETITIVIDAD.

Cell cycle, Determining stem Cells and Cancer

Group Leader
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Fundación Instituto de Investigación
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Predoctoral

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Natalia Sanz Gómez

Technicians

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Contributors

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Ernesto de Diego García
Isabel de Pedro González
Inmaculada Fernández Jiménez

Research Lines

Among the many skin conditions that affect the health and life expectancy of the population and that pose a growing problem in public health (psoriasis, xerodermas, keratosis), skin cancer is the most common cancer. This stems from variations in DNA caused primarily by ultraviolet radiation (UV) from the sun and the Human Papillomavirus (HPV). It is also the cancer with the most increasing frequency within our societies, due to the aesthetic tendencies that induce tanning, which is making it the leading cause of cancer death in women aged 20-30 years (*National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2008/index.html. Cancer Epidemiology in Older Adolescents & Young Adults. 2007. SEER AYA Monograph, pages 53–57).

For these reasons, the skin needs powerful cellular and molecular mechanisms to protect itself from continued mutagenic risk. These mechanisms go through the proper control of Stem Cells and homoeostasis. The main goal of our group is to research these mechanisms and their variations in hyperproliferative skin problems, mainly those leading to cancer. The

objective is the reciprocal transfer between the laboratory (molecular mechanisms of the cell cycle), the industry (exploitation of results) and the hospital (obtaining biopsies, characterisation, monitoring, new diagnostics or therapies).

The main lines that are currently active are:

1) Functional control mechanisms of mitosis and differentiation in the skin.

2) Epidermal protection and repair mechanisms against genetic damage.

3) Variations in mitosis control and differentiation in epidermoid cancer.

4) Stem Cell applications in the repair and regeneration of tissue.

PUBLICATIONS:

IMPACT FACTOR | 21,835

Original articles

1. Stoll SW, Stuart PE, Swindell WR, Tsoi LC, Li B, Gandarillas A, Lambert S, Johnston A, Nair RP, Elder JT.
The EGF receptor ligand amphiregulin controls cell division via FoxM1.
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J Invest Dermatol. 2016;136:444-452. F.I.:6,915. [doi:10.1016/j.jid.2015.10.061]

Editorials

1. Bernal JM, Mestres CA.
Epicardial adipose hypertrophy: The Phantom of the Opera.
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J Thorac Cardiovasc Surg. 2016;151:110-111.F.I.:3,494. [doi:10.1016/j.jtcvs.2015.10.055]

PROJECTS

Projects

1. Alberto Gandarillas Solinis.
New Routes and Strategies for Squamous Cell Cancer. PI14/00900. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

OTHER PUBLICATIONS

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1. Ana Mª Arnaiz García.
Morbidity and mortality in deferred sternal closure.
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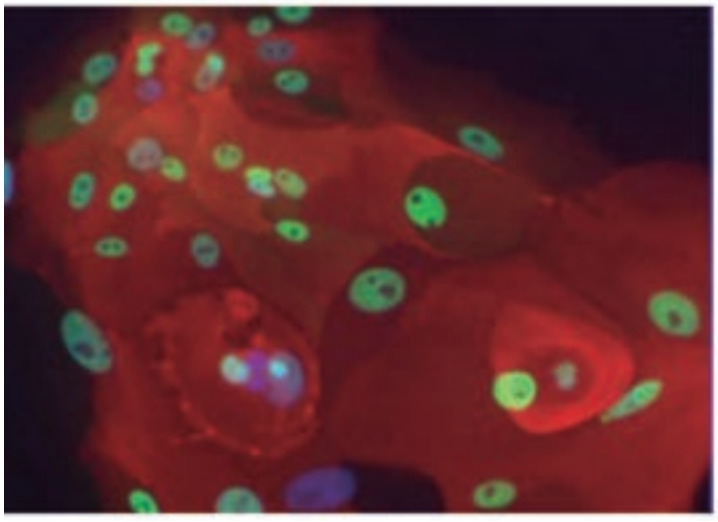

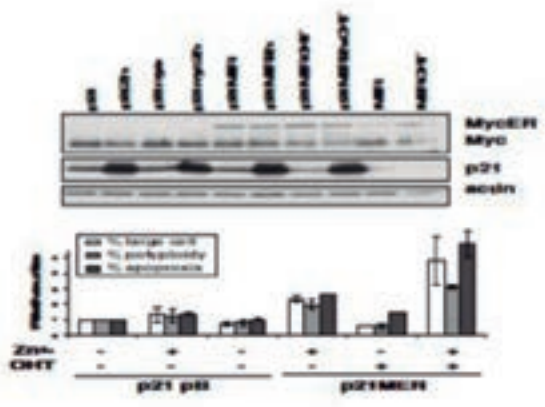

Translational Hematopathology

Group Leader
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Pathology Service
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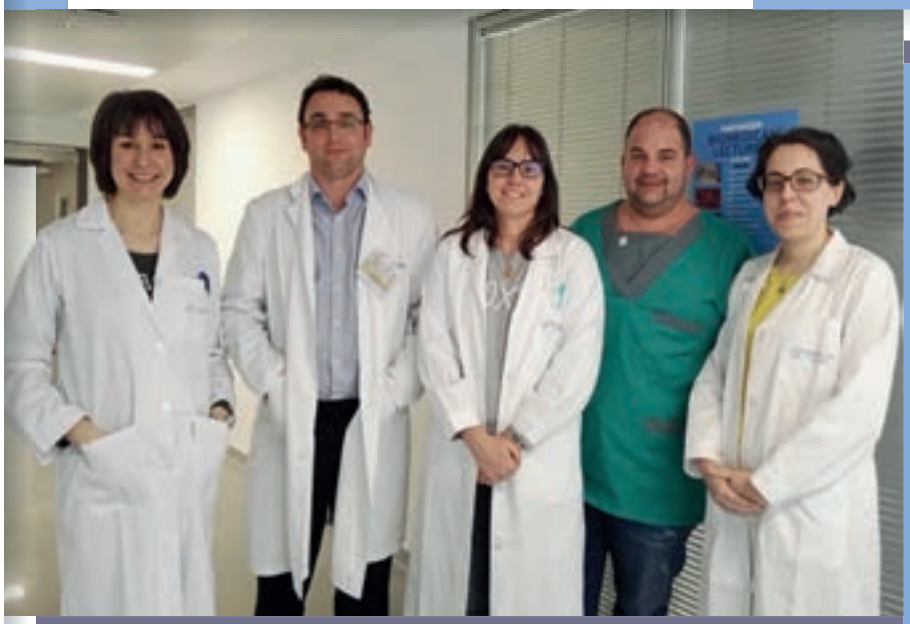

Consolidated group

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Research Lines

1. New technologies useful for the molecular diagnosis of patients with hematolymphoid neoplasms.

The field of hematopathology is in continuous development regarding the identification of new molecular markers of clinical utility. The use of phenotyping techniques, new technologies such as mass sequencing, high sensitivity expression analysis techniques (ie digital quantitative PCR), detection of circulating plasma DNA (liquid biopsy) requires rigorous preclinical validation for use as clinical diagnostic tools. Our group generates and validates clinical molecular diagnostic tools useful in the area of hematolymphoid pathology. He has participated in the validation of monoclonal antibodies useful in the diagnosis (ie GCET1, SPI-B), validation and standardization of the protocols of analysis and interpretation of lymphoid B and T clonality of the European consortium Biomed2 and recently generated a protocol Of clinical diagnosis of somatic mutation MYD88L265P, useful for small cell B-cell lymphomas with

differentiation (lymphoplasma B lymphoplasmacytic / Waldestrom disease) and diffuse large cell lymphoma of the ABC phenotype that is applied in the clinical diagnostic field. Currently a line of advance is the optimization of a protocol for the identification of somatic mutations in free circulating tumor DNA in plasma of patients with LBDCG that serves as screening for the diagnosis of the disease and clinical follow-up of patients.

2. Clinical validation of biomarkers in translational research projects linked to multicenter clinical trials for patients with hematolymphoid neoplasms.

The clinical validation of molecular markers is concretized by analyzing the impact of these biomarkers in clinical trials designed to test their predictive value of response and prognosis. The design of protocols of biological study of the samples, linked to clinical trials with new drugs is the method that allows to accelerate the translation of results and to demonstrate its potential clinical utility. In this sense, our group, integrated with the HUMV Pathology Service, leads a centralized anatomical and molecular diagnostic platform for the samples of patients included in clinical trials of the cooperative national group GELTAMO (Spanish Group of Lymphomas and Bone Marrow Transplant) , As responsible for the centralized diagnosis and generation of protocols of molecular studies of the different open-label clinical trials in large cell lymphoma (GEL-BRCAP21 (EudraCT No: 2012-005138-12), GEL-RCOMP 2013 (EudraCT No: 2013- 001065-17), LR-ESHAP (EudraCT No.: 2010-018463-41) This collaboration involves several clinical groups at the national level and other groups specialized in laboratory diagnosis, mainly at the Hospital Clínico Universitario de Salamanca and at the Hospital The platform integrates clinical groups responsible for the development of clinical trials with subjects and groups of translational research, responsible for the study of the samples and the Laboratory development, more experimental. A small group of pathologists who are experts in the area are also included, who validate the diagnoses of the patients included in the EECC and process the samples appropriately for the laboratory studies. The incorporation of Biobank Valdecilla into the network facilitates and normalizes the use of biological samples from patients.

3. Identification of biomarkers of diagnostic, prognostic and predictive usefulness of response to therapy in patients with large cell B-cell lymphoma.

Diffuse large cell lymphoma (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 of about 93,000 new cases per year in Europe (BLOBOCAN (IARC)) The precise subclassification of the different LBDCG entities is clinically relevant from a prognostic and therapeutic selection point of view, as there are a number of aggressive clinical behavioral phenotypes (high grade B lymphoma with "double / LBDCG of ABC subtype, plasmablast lymphoma) for which standard therapy is ineffective or inadequate Recent studies using massive genome and exome sequencing are identifying recurrent genetic alterations in the NFkB, BCR, JAK / STAT pathways, Histone-modifying genes and genes related to the immune response, among others in LBDCG. In aggressive variants such as plasmablast lymphoma, a relevant role of the MYC oncogene has been identified, with gene translocation occurring in about 60% of the cases. Recent data from our group demonstrate that in this type of lymphomas there is overexpression of the MYC protein in the majority of cases of plasmablast lymphoma, associated with marked overexpression of the alpha isoform of PRDM1 / Blimp1, a key tumor suppressor gene in induction of the plasmocellular phenotype and inhibitor of MYC under physiological conditions. Additionally, we have demonstrated a high frequency of recurrent point mutations in PRDM1 / Blimp1 regulatory domains, by targeted sequencing of the PRDM1 / Blimp1 exome. These results reinforce the relevance of the MYC oncogene in this type of neoplasia and describe, for the first time, somatic mutations in PRDM1 / blimp1 in plasmablast lymphoma, which would explain the apparent paradox, biologically, involving the coexpression of MYC and PRDM1 / Blimp1. These preliminary data confirm the intrinsic heterogeneity of LBDCG and lead to the need to specifically identify those functionally biologically relevant events and, on the other hand, predictors of response to specific therapies or prognoses in a specific therapeutic context.

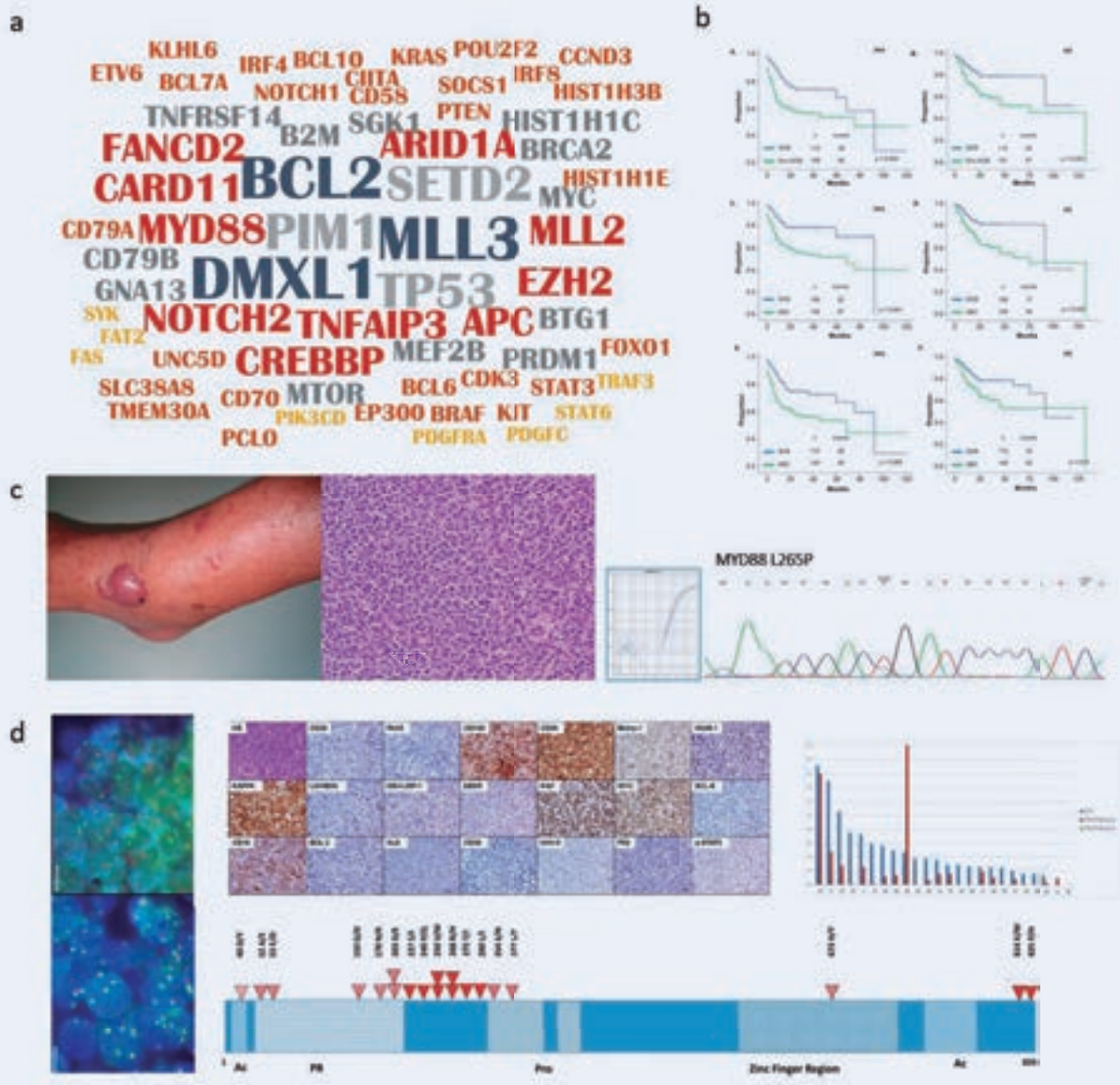

Figura a. Image depicting recurrent mutated genes in LBDCG. The new methods of directed sequencing of the exoma allow generating mapping of the cases in order to identify profiles that guide the optimal therapy in each subject. .

Figura b. The correlation of expression data with global survival and progression-free survival in LBDCG allows the identification of patients who could benefit from inclusion in clinical trials with new, more selective drugs (Stratifying diffuse large B-cell lymphoma patients treated with chemoimmunotherapy: GCB / Non-GCB by immunohistochemistry is still a robust and feasible marker. Oncotarget 2016).

Figura c. Clinical validation of new molecular diagnostic techniques (identification of the mutation of MYD88L265P by AS-PCR and direct sequencing in large cell type B lymphoma is shown as an example) is useful for proper subclassification of each case.

Figura d. The complete molecular characterization (genotype and phenotype) of aggressive B-cell subtypes such as plasmablastic lymphoma allows explaining the interaction between neoplastic driver genes (MYC) and other regulatory genes (PRDM1 / Blimp1) revealing new molecular mechanisms of disease (Plasmablastic Lymphoma phenotype is determined by genetic alterations in MYC and PRDM1, Modern Pathology 2017).

PUBLICATIONS:

IMPACT FACTOR | 159,151

Original articles

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Editorials

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PROJECTS

Projects

1. Santiago Montes Moreno.
Thematic Network of Cooperative Cancer Research.
RD12/0036/0060.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

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.

Molecular Imaging

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Pedro José Prada Gómez
Remedios Quirce Pisano
María Ángeles Revilla García

Clinic group

Research Lines

1. Molecular Imaging and Glucose Metabolism in Oncology.

a. Imaging Criteria for measuring the Metabolic Response to treatment in Oncology.

b. Assessment of the role of 18F-FDG PET/CT on the effect of biologic therapy in solid tumors.

c. Tissue characterization of pulmonary lesions by 18F-FDG PET/CT.

d. 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.

a. To define an acquisition protocol of 18F-FDG PET/CT to study the carotid plaque metabolism.

b. To assess the inflammation process of the carotid plaque by 18F-FDG PET/CT

c. To assess the calcification process of the carotid plaque by 18FNa PET/CT

d. To monitor the response to anti-inflammatory treatment by 18F-FDG PET/CT

e. 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.

a. To establish an acquisition protocol for 18F-FNa PET/CT and 18F-FDG PET/CT for the study of atherosclerosis in diabetic patients

b. To identify uptake patterns in different vascular territories of the body in diabetic patients

c. 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.

a. Identification of patients with Alzheimer´s disease

b. To establish an acquisition protocol for b-amyloid imaging using 11C-PIB PET/CT

c. To determine the 11C-PIB retention patterns in the brain

d. To study the contribution of 11C-PIB PET/CT in the study of cognitive impairment

e. To identify the patients with b amyloid deposit in the brain

f. To assess the role of 11C-PIB in differential diagnose of dementias

g. To evaluate quantitatively the contribution of 11C-PIB

5. Molecular Imaging in the early diagnosis and extension of vasculitis.

a. ETo establish an acquisition protocol for 18F-FDG in patients with suspicion of large vessel vasculitis.

b. To determine the biokinetics of FDG in the large vessels was, to establish the optimum time for image acquisition

c. To identify the normal uptake patterns in different vascular territories

d. To quantify the arterial wall activity in relation to the global vascular activity

e. 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.

a. ETo study the application of radiotracers for prostate cancer recurrence

b. To assess the role of 11C-methionine in primary hyperparathyroidism

c. To evaluate the role of 11C-methionine in the suspicion of brain tumor recurrence

d. To carry out the synthesis and clinical and to assess the clinical contribution of 18F-FLT

e. To carry out the synthesis and develop

PUBLICATIONS:

IMPACT FACTOR | 60,981

Original articles

1. Dominguez Rodriguez, F., Ramos, A., Bouza, E., Munoz, P., Valerio, M. C., Farinas, C., De Berrazueta, J. R., Zarauza, J., Pericas Pulido, J. M., Pare, J. C., De Alarcon, A., Sousa, D., Rodriguez Bailon, I., Montejo-Baranda, M., Garcia-Pavia, P.
Infective endocarditis in hypertrophic cardiomyopathy: should antibiotic prophylaxis be reconsidered?.
Eur Heart J. 2016;37:1015-1015. F.I.:15,064.

2. Jimenez-Bonilla, J. F., Quirce, R., De Arcocha-Torres, M., Martinez-Rodriguez, I., Carril, J. M., Jimenez-Alonso, M., Banzo, I., Pozueta, A., Martin-Laez, R., Rodriguez-Rodriguez, 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.F.I.:5,537.

3. Lopez-Defillo, J. L., Martinez-Rodriguez, I., De Arcocha-Torres, M., Jimenez-Bonilla, J., Quirce, R., Jimenez-Alonso, M., Gomez-De La Fuente, F., Lavado-Perez, C., Martinez-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.F.I.:5,537.

4. Jimenez-Alonso, M., Martinez-Rodriguez, I., Lavado-Perez, C., Lopez-Defillo, J., Quirce, R., Jimenez-Bonilla, J., De Arcocha-Torres, M., Meza-Escobar, D., Loricera, J., Gonzalez-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.F.I.:5,537.

5. Prada PJ, Cardenal J, Blanco AG, Anchuelo J, Ferri M, Fernández G, Arrojo E, Vázquez A, Pacheco M, Fernández J.
High-dose-rate interstitial brachytherapy as monotherapy in one fraction for the treatment of favorable stage prostate cancer: Toxicity and long-term biochemical results.
RADIOTHER ONCOL. 2016;119:411-416.F.I.:4,817. [doi:10.1016/j.radonc.2016.04.006]

6. Jiménez-Bonilla JF, Banzo I, De Arcocha-Torres M, Quirce R, Martínez-Rodríguez I, Sánchez-Juan P, Carril JM.
Amyloid Imaging With 11C-PIB in Patients With Cognitive Impairment in a Clinical Setting: A Visual and Semiquantitative Analysis.
Clin Nucl Med. 2016;41:18-23. F.I.:4,278. [doi:10.1097/RLU.0000000000000934]

7. Riancho-Zarrabeitia L, García-Unzueta M, Tenorio JA, Gómez-Gerique JA, Ruiz Pérez VL, Heath KE, Lapunzina P, Riancho JA.
Clinical, biochemical and genetic spectrum of low alkaline phosphatase levels in adults.
Eur J Intern Med. 2016;29:40-45. F.I.:2,591. [doi:10.1016/j.ejim.2015.12.019]

8. Amado CA, García-Unzueta MT, Fariñas MC, Santos F, Ortiz M, Muñoz-Cacho P, Amado JA.
Vitamin D nutritional status and vitamin D regulated antimicrobial peptides in serum and pleural fluid of patients with infectious and noninfectious pleural effusions.
BMC Pulm Med. 2016;16:99-99. F.I.:2,329. [doi:10.1186/s12890-016-0259-4]

9. Dominguez F, Ramos A, Bouza E, Muñoz P, Valerio MC, Fariñas MC, de Berrazueta JR, Zarauza J, Pericás Pulido JM, Paré JC, de Alarcón A, Sousa D, Rodriguez Bailón I, Montejo-Baranda M, Noureddine M, García Vázquez E, Garcia-Pavia P.
Infective endocarditis in hypertrophic cardiomyopathy: A multicenter, prospective, cohort study.
Medicine (Baltimore). 2016;95: F.I.:2,133. [doi:10.1097/MD.0000000000004008]

10. Quirce R, Martínez-Rodríguez I, Banzo I, Jiménez-Bonilla J, Martínez-Amador N, Ibáñez-Bravo S, López-Defilló J, Jiménez-Alonso M, Revilla MA, Carril JM.
New insight of functional molecular imaging into the atheroma biology: 18F-NaF and 18F-FDG in symptomatic and asymptomatic carotid plaques after recent CVA.
Preliminary results. Clin Physiol Funct Imaging. 2016;36:499-503. F.I.:1,869. [doi:10.1111/cpf.12254]

11. Moran Lopez, Jesus Manuel, Luengo Perez, Luis Miguel, Beneitez Moralejo, Belen, Piedra Leon, Maria, Gonzalez Aguado, Rocio, Enclso Izquierdo, Fldel Jesus, Amado Senaris, Jose Antonio.
Impact of adequate coding of undernutrition and nutritional procedures on case-mix index in medical and surgical pathologies.
Nutr Hosp. 2016;33:64-69. F.I.:1,497.

12. Jiménez-Bonilla JF, Banzo I, De Arcocha-Torres M, Quirce R, Martínez-Rodríguez I, Lavado-Pérez C, Bravo-Ferrer Z, Rodríguez-Rodríguez E, Sánchez-Juan P, Carril JM.
Diagnostic role of 11C-Pittsburgh compound B retention patterns and glucose metabolism by fluorine-18-fluorodeoxyglucose PET/CT in amnestic and nonamnestic mild cognitive impairment patients. Nucl Med Commun. 2016;37:1189-1196. F.I.:1,453. [doi:10.1097/MNM.0000000000000569]

13. Amado Diago CA, García-Unzueta MT, Fariñas MD, Amado JA.
Calcitriol-modulated human antibiotics: New pathophysiological aspects of vitamin D.
Endocrinol Nutr. 2016;63:87-94. F.I.:1,314. [doi:10.1016/j.endonu.2015.09.005]

14. Morán López JM, Piedra León M, Enciso Izquierdo FJ, Luengo Pérez LM, Amado Señaris JA.
Differences in quality standards when prescribing nutritional support: Differences between specialist and non-specialist physicians.
Endocrinol Nutr. 2016;63:27-31. F.I.:1,314. [doi:10.1016/j.endonu.2015.08.002]

15. Belmar Vega L, de Francisco A, Albines Fiestas Z, Serrano Soto M, Kislikova M, Seras Mozas M, Unzueta MG, Arias Rodríguez M.
Investigation of iron deficiency in patients with congestive heart failure: A medical practice that requires greater attention. Nefrologia. 2016;36:249-254. F.I.:1,207. [doi:10.1016/j.nefro.2016.03.001]

16. Banzo I, Jiménez-Bonilla JF, Martínez-Rodríguez I, Quirce R, de Arcocha-Torres M, Bravo-Ferrer Z, Lavado-Pérez C, Sánchez-Juan P, Rodríguez E, Jiménez-Alonso M, López-Defilló J, Carril JM.
Patterns of 11C-PIB cerebral retention in mild cognitive impairment patients.
Rev Esp Med Nucl Imagen Mol. 2016;35:171-174.
F.I.:0,983. [doi:10.1016/j.remn.2015.09.008]

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17. Ibáñez-Bravo S, Banzo I, Quirce R, Martínez-Rodríguez I, Jiménez-Bonilla J, Martínez-Amador N, Parra JA, González-Macías J, Carril JM.
Ventilation/Perfusion SPECT lung scintigraphy and computed tomography pulmonary angiography in patients with clinical suspicion of pulmonary embolism.
Rev Esp Med Nucl Imagen Mol. 2016;35:215-220.
F.I.:0,983. [doi:10.1016/j.remn.2015.12.008]

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18. Prada PJ, Anchuelo J, Blanco AG, Paya G, Cardenal J, Acuna E, Ferri M, Vazquez A, Pacheco M, Sanchez J.
Low-dose-rate brachytherapy for patients with transurethral resection before implantation in prostate cancer. Longterm results.
INT BRAZ J UROL. 2016;42:47-52.
F.I.:0,871.

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19. Palacio E, Viadero-Cervera R, Revilla M, Larrosa-Campo D, Acha-Salazar O, Novo-Robledo F, Oterino A.
Utilidad del tratamiento con atorvastatina 40 mg más ezetimiba 10 mg frente a atorvastatina 80 mg en la reducción de los niveles de colesterol LDL en pacientes con ictus isquémico o ataque isquémico transitorio.
Rev Neurol. 2016;62:203-210.
F.I.:0,684.

Editorials

1. Banzo I.
Un trabajo apasionante.
Rev Esp Med Nucl Imagen Mol. 2016;35:1-2.
F.I.:0,983. [doi:10.1016/j.remn.2015.10.008]

Doctoral thesis

1. Marcos Pajaron Guerrero.
Self-management of intravenous antimicrobial (a-tade) treatment in infective endocarditis: a safe and efficient care model.
Directors: **María Del Carmen Fariñas Álvarez, José Ramón De Berrazueta Fernández.**
University of Cantabria.

PROJECTS

Projects

1. Julio Francisco Jiménez Bonilla.
Five-year evolution study in a population with mild Cognitive Impairment (DCL) previously evaluated with 11C-PIB and 18F-FDG PET/ CT.
PI16/01656.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Melatonin and Breast Cancer

Group Leader
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Consolidated group

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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, 17Đ-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 | 9,331

Original articles

1. Alonso-González C, González A, Martínez-Campa C, Menéndez-Menéndez J, Gómez-Arozamena J, García-Vidal A, Cos S.
Melatonin enhancement of the radiosensitivity of human breast cancer cells is associated with the modulation of proteins involved in estrogen biosynthesis.
Cancer Lett. 2016;370:145-152. F.I.:5,992. [doi:10.1016/j.canlet.2015.10.015]

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2. Parisotto EB, Vidal V, García-Cerro S, Lantigua S, Wilhelm Filho D, Sanchez-Barceló EJ, Martínez-Cué C, Rueda N.
Chronic Melatonin Administration Reduced Oxidative Damage and Cellular Senescence in the Hippocampus of a Mouse Model of Down Syndrome.
Neurochem Res. 2016;41:2904-2913. F.I.:2,472. [doi:10.1007/s11064-016-2008-8]

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3. San Segundo D, Alonso C, Ruiz P, Roman I, Arias-Loste MT, Cuadrado A, Puente A, Casafont F, López-Hoyos M, Crespo J, Fábrega E.
De Novo Donor-Specific Anti-Human Leukocyte Antigen Antibody Detection in Long-Term Adult Liver Transplantation.
Transplant Proc. 2016;48:2980-2982. F.I.:0,867. [doi:10.1016/j.transproceed.2016.08.037]

Doctoral thesis

1. Andrea Corrales Pardo.
EStudy of the protective effects of chronic treatment with melatonin on the cognitive deficits of TS65DN mouse, a model of Down syndrome.
Director: **Noemí Rueda Revilla.**
University of Cantabria.

—

2. Susana García Cerro.
Study of the effect of the reduction of copy number of the dyrk1a gene on different functional and neuromorphological phenotypes found in a murine model of down syndrome and in euploid mice.
Directors: **Carmen Martínez-Cue Pesini, Noemí Rueda Revilla.**
University of Cantabria.

PROYECTS

Proyects

1. Samuel Cos Corral.
Sensitizing effects of melatonin to chemotherapy and radiotherapy: study of the molecular changes that modulate this process.
SAF2013-42012-P.

Nanomedicine

Group Leader
Mónica López Fanárraga
Departamento de Biología Molecular
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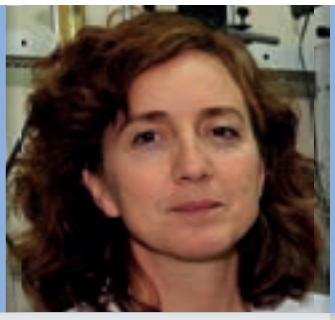

Group of new establishment

Researchers
Rafael Valiente Barroso

Contributors
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Carmen Pesquera González
Ciro Luis Salcines Suárez
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Juan Carlos Villegas Sordo

Predoctoral
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Elena María Navarro Palomares
Esperanza Padín González
Lourdes María Valdivia Fernández

Research Lines

The group of Nanomedicine-IDIVAL studies the biological response to different nanomaterials. The main activity of our group focuses on the study of nanomaterials as treatments for cancer, nanotoxicity and the development of fluorescent probes for in vivo imaging with up-conversion particles, without stopping to explore other possibilities offered by nanomaterials (Nano-drugs, injectable nanovectors, functional polymer nano-systems), regenerative medicine, as contrast agents for imaging techniques and detection of tumor borders for surgery, nanobiocides, etc.
Our studies demonstrate how carbon nanotubes (NTC) can penetrate cells, interfering with microtubule dynamics and behaving like microtubule stabilizing drugs, acting as mitotic spindle disrupters. NTC interacts biomimetically with microtubules causing aberrant or catastrophic mitosis, and triggering cell death. The advantage of NTC versus traditional cytotoxic chemotherapy (taxol and its derivatives, epothilones, colchicine or vinca derivatives) is its large surface area of interaction with the microtubule, which makes resistance quite unlikely.
Our most immediate objectives are to provide a topical NTC-based treatment for cancer treatment, for example for use as an adjuvant or neoadjuvant treatment in cancers affecting the skin, head neck cancers or topically accessible or by injection) in the zone. This development we already have a patent. Currently we work on the functionalisation of the surface of the NTC to preferentially target them to the target cells and develop in the medium / long term a parenteral treatment and in the biocompatibilization of the NTC so

that they are more biodegradable through different treatments. Together with this line of research we are investigating a series of biological applications of upconversion luminescent nanoparticles, synthesized by the physicists and chemists of the group, which we will try to adapt (modifying diameters and composition) for use as intracellular nano-thermometers and as contrast systems Based on the application of infrared light (not harmful to living tissue) for diagnosis and tumor detection.

PUBLICATIONS:

IMPACT FACTOR | 58,565

Original articles

1. Almonacid G, Martín-Rodríguez R, Renero-Lecuna C, Pellicer-Porres J, Agouram S, Valiente R, González J, Rodríguez F, Nataf L, Gamelin DR, Segura A.
Structural Metastability and Quantum Confinement in Zn1-xCoxO Nanoparticles.
NANO LETT. 2016;16:5204-5212. F.I.:13,779. [doi:10.1021/acs.nanolett.6b02230]

2. García-Hevia L, Valiente R, Martín-Rodríguez R, Renero-Lecuna C, González J, Rodríguez-Fernández L, Aguado F, Villegas JC, Fanarraga ML.
Nano-ZnO leads to tubulin macrotube assembly and actin bundling, triggering cytoskeletal catastrophe and cell necrosis.
NANOSCALE. 2016;8:10963-10973. F.I.:7,760. [doi:10.1039/c6nr00391e]

3. García-Hevia L, Villegas JC, Fernández F, Casafont Í, González J, Valiente R, Fanarraga ML.
Multiwalled Carbon Nanotubes Inhibit Tumor Progression in a Mouse Model.
Adv Healthc Mater. 2016;5:1080-1087. F.I.:5,760. [doi:10.1002/adhm.201500753]

4. Gomez-Salces, Susana, Antonio Barreda-Argueso, Jose, Valiente, Rafael, Rodrigueza, Fernando.
A study of Ce3+ to Mn2+ energy transfer in high transmission glasses using time-resolved spectroscopy.
J Mater Chem C Mater Opt Electron Devices. 2016;4:9021-9026. F.I.:5,066. [doi:10.1039/c6tc01408a]

5. Gomez-Salces, Susana, Barreda-Argueso, Jose A., Valiente, Rafael, Rodriguez, Fernando.
Solarization-induced redox reactions in doubly Ce3+/Mn2+-doped highly transmission glasses studied by optical absorption and photoluminescence.
Sol Energy Mater Sol Cells. 2016;157:42-47.F.I.:4,732. [doi:10.1016/j.solmat.2016.05.010]

6. Antonio Barreda-Argueso, J., Aguado, Fernando, Gonzalez, Jesus, Valiente, Rafael, Nataf, Lucie, Sanz-Ortiz, Marta N., Rodriguez, Fernando.
Crystal-Field Theory Validity Through Local (and Bulk) Compressibilities in CoF2 and KCoF3.
J PHYS CHEM C. 2016;120:18788-18793.F.I.:4,509. [doi:10.1021/acs.jpcc.6b06132]

7. Villanueva-Delgado P, Krämer KW, Valiente R, de Jong M, Meijerink A.
Modeling blue to UV upconversion in ß-NaYF4:Tm(3).
PHYS CHEM CHEM PHYS. 2016;18:27396-27404. F.I.:4,449. [doi:10.1039/c6cp04347j]

8. Dikhtiarenko, Alla, Villanueva-Delgado, Pedro, Valiente, Rafael, Garcia, Jose R., Gimeno, Jose.
Tris(bipyridine)Metal(II)-Templated Assemblies of 3D Alkali-Ruthenium Oxalate Coordination Frameworks: Crystal Structures, Characterization and Photocatalytic Activity in Water Reduction.
POLYMERS-BASEL. 2016;8: F.I.:2,944. [doi:10.3390/polym8020048]

9. Valiente, Rafael, Renero-Lecuna, Carlos, Rodriguez, Fernando, Gonzalez, Jesus.
Role of high pressure for understanding luminescent phenomena.
J LUMIN. 2016;169:410-414.F.I.:2,693. [doi:10.1016/j.jlumin.2014.11.043]
Vazquez, G. V., Valiente, R., Gomez-Salces, S., Flores-Romero, E., Rickards, J., Trejo-Luna, R.
Carbon implanted waveguides in soda lime glass doped with Yb3+ and Er3+ for visible light emission.
OPT LASER TECHNOL. 2016;79:132-136.F.I.:1,879. [doi:10.1016/j.optlastec.2015.12.002]

10. Kaur, Amandeep, Khanna, Atul, Gonzalez, Fernando, Pesquera, Carmen, Chen, Banghao.
Structural, optical, dielectric and thermal properties of molybdenum tellurite and borotellurite glasses.
J NON-CRYST SOLIDS. 2016;444:1-10. F.I.:1,825. [doi:10.1016/j.jnoncrysol.2016.04.033]

11. Fernandez, Josefa, Gonzalez, Fernando, Pesquera, Carmen, Neves, Alex, Jr., Viana, Marcelo Mendes, Dweck, Jo.
Qualitative and quantitative characterization of a coal power plant waste by TG/DSC/MS, XRF and XRD.
J THERM ANAL CALORIM. 2016;125:703-710. F.I.:1,781. [doi:10.1007/s10973-016-5270-8]

12. Val-Bernal JF, Mayorga M, Terán-Villagrá N. **Extracutaneous intravascular histiocytosis of the aortic valve: Report of two cases.**
Pathol Res Pract. 2016;212:258-263. F.I.:1,388. [doi:10.1016/j.prp.2015.12.016]

Doctoral thesis

1. Lorena García Hevia.
Cancer therapy based on the biomimetics of carbon nanotubes with cell filaments.
Director: **Mónica López Fanárraga.**
University of Cantabria.

PROJECTS

Projects

1. Mónica López Fanárraga.
Development of antineoplastics based on nanomaterials.
PI13/01074.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

New Techniques in Abdominal Surgery

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University Hospital Marqués de Valdecilla
University of Cantabria

Clinic group

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Antonio López Useros
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José Carlos Manuel Palazuelos
José Ignacio Martín Parra
Dieter José Morales García
Carlos Ortega Morales
Rodrigo Perea Muñoz
Maria Riaño Molleda
Juan Carlos Rodríguez Sanjuan
Isabel Seco Olmedo
Mª Soledad Trugeda Carrera

Research Lines

a. **Liver tumor pathology.** Staging, new diagnosis and therapeutic techniques.

b. **Pancreatic tumor pathology**. Staging, new diagnosis and therapeutic techniques.

c. **Biliary tumor pathology and non-neoplastic pathology.** Implementing new clinical surgical procedures (Laparoscopic choledocholithotomy).

d. **Results in tumor pathology.** Thermal ablation of hepatocellular carcinoma as a bridge to transplantation and Xenotransplantation.

e. **Obesity surgery.** Effects of bariatric surgery on the morbidity factors of obesity in steatohepatitis and ghrelin levels. Evaluation of results.

f. **Breast cancer.** Tumor excision using image-guided techniques. Oncoplastic surgical techniques for breast cancer surgery.

g. **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 | 21,292

Original articles

1. Arias-Loste MT, Iruzubieta P, Puente Á, Ramos D, Santa Cruz C, Estébanez Á, Llerena S, Alonso-Martín C, San Segundo D, Álvarez L, López Useros A, Fábrega E, López-Hoyos M, Crespo J.
Increased Expression Profile and Functionality of TLR6 in Peripheral Blood Mononuclear Cells and Hepatocytes of Morbidly Obese Patients with Non-Alcoholic Fatty Liver Disease.
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Sacral nerve stimulation lead implantation in partial sacral agenesis using intra-operative computerized tomography.
COLORECTAL DIS. 2016;18:923-923. F.I.:2,452. [doi:10.1111/codi.13437]

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Role of bacteriobilia in postoperative complications.
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Reviews

1. Rodriguez-Sanjuan, Juan C., Gomez-Ruiz, Marcos, Trugeda-Carrera, Soledad, Manuel-Palazuelos, Carlos, Lopez-Useros, Antonio, Gomez-Fleitas, Manuel.
Laparoscopic and robot-assisted laparoscopic digestive surgery: Present and future directions.
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Bacteriobilia: un problema sin resolver.
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Doctoral thesis

1. Javier Aragon Valverde.
Role of metalloproteinase-11 and tissue inhibitor of metalloproteinase-2 (timp-2) as factors of the inflammatory process and tumor invasion in non-small cell lung carcinoma.
Directors: **Manuel Gómez Fleitas, Francisco Jose Vizoso Piñeiro.**
University of Cantabria.

—

2. José Ignacio Martín Parra.
Design of a training program for residents of general surgery and digestive system based on competences: integration of clinical simulation and practice of care.
Directors: **Manuel Gómez Fleitas, Robert Simon, José Mª Maestre Alonso.**
University of Cantabria.

—

3. Juan Carlos Albarracin Castillo.
Value of endoscopic ultrasonography and magnetic cholangioresonance in the diagnosis of choledocholithiasis.
Directors: **Juan Carlos Rodríguez Sanjuan, Manuel Gómez Fleitas.**
University of Cantabria.

—

4. Marcos Gómez Ruiz.
Comparative study of laparoscopic surgery versus robotic surgery in the treatment of rectal cancer.
Directors: **Manuel Gómez Fleitas, José Fernández-Escalante Moreno.**
University of Cantabria.

—

5. Rosana García Díaz.
Impact of the implementation of the checklist on a general surgery service.
Directors: **Cesar Baldomero Madrazo Leal, Manuel Gómez Fleitas.**
University of Cantabria.

—

6. Rubén Gonzalo Gonzalez.
Analysis of factors predicting remission of type 2 diabetes mellitus in morbidly obese patients after gastric bypass at Roux-en-Y.
Director: **Manuel Gómez Fleitas.**
University of Cantabria.

Cell Signalling and Therapeutic Targets in Cancer

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Molecular Genetics Unit
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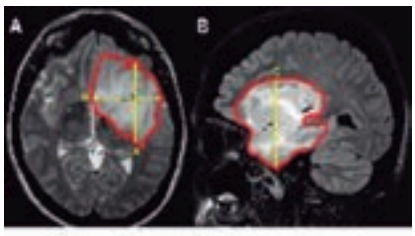
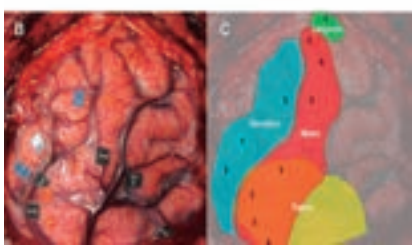
Research Lines

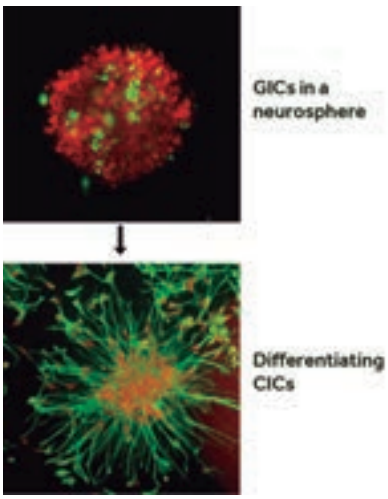
1. Study of the invasive capacity of glioblastoma stem cells (GSCs).

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 biophysical features of the microenvironment in cellular processes studied in vitro (differentiation, migration, survival). In order to optimize more physiological in vitro models of chemotherapy response, closer to in vivo models, we are studying the behavior 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 collaboration 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.

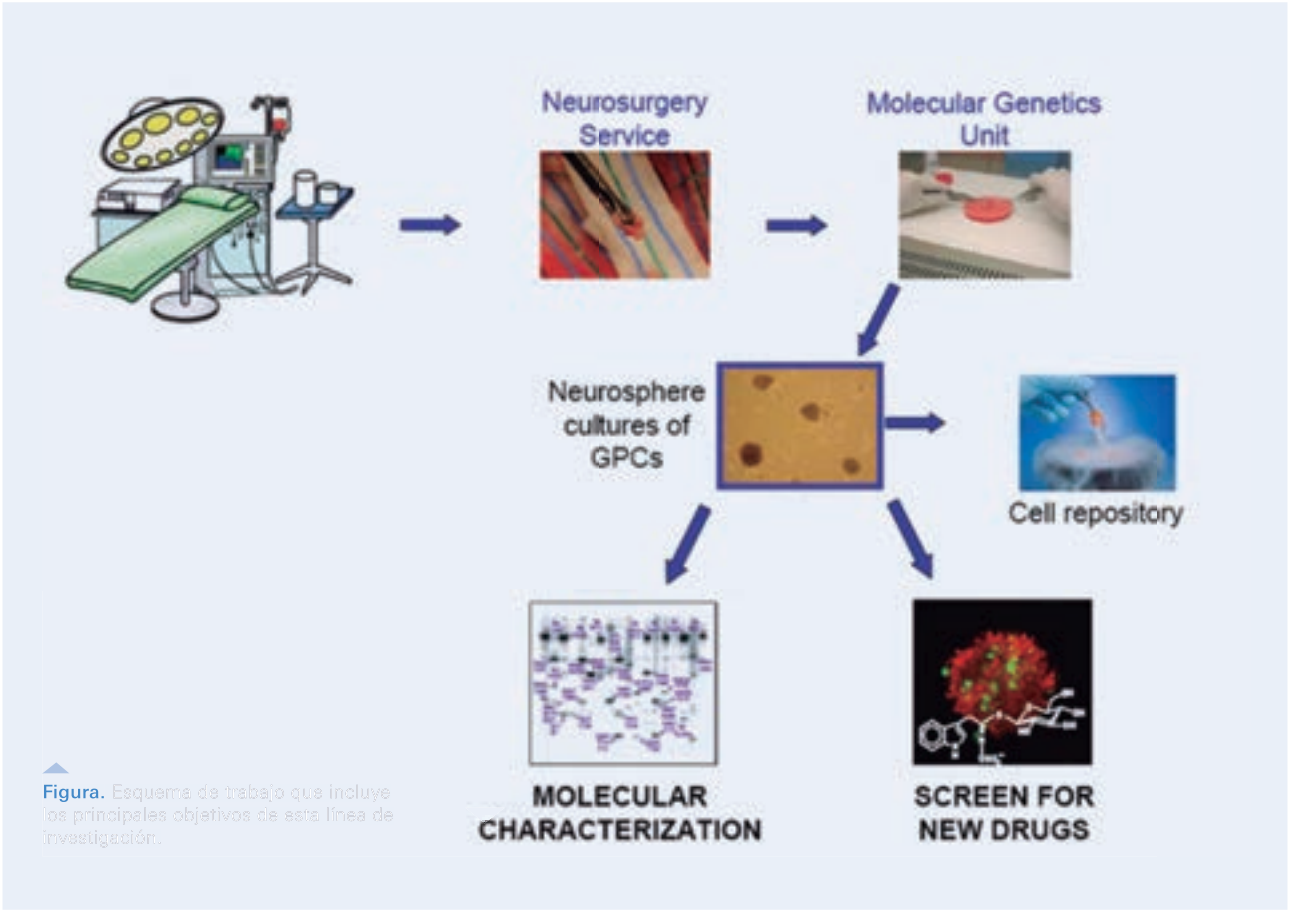


Figura. Esquema de trabajo que incluye los principales objetivos de esta línea de investigación.

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.

PUBLICATIONS:

IMPACT FACTOR | 30,862

Original articles

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Projects

1. José Luis Fernández Luna.
Thematic Network of Cooperative Cancer Research.
RD12/0036/0022.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. José Luis Fernández Luna.
Prognostic and therapeutic relevance in glioblastoma of ODZ1, a new target in cancer.
PI13/01760.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. Juan Martino González.
Preservation of the areas involved in verbal work memory to avoid sequelae in gliomas surgery in eloquent areas.
PI13/01249.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Oncology Clinical trials Unit

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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.

PUBLICACIONES:

IMPACT FACTOR | 104,217

Original articles

1. iMartin-Broto J, Pousa AL, de Las Peñas R, García Del Muro X, Gutierrez A, Martinez-Trufero J, Cruz J, Alvarez R, Cubedo R, Redondo A, Maurel J, Carrasco JA, López-Martin JA, Sala Á, Meana JA, Ramos R, Martinez-Serra J, Lopez-Guerrero JA, Sevilla I, Balaña C, Vaz Á, De Juan A, Alemany R, Poveda A.
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Validation of the International Metastatic Renal-Cell Carcinoma Database Consortium (IMDC) prognostic model for first-line pazopanib in metastatic renal carcinoma: the Spanish Oncologic Genitourinary Group (SOGUG) SPAZO study.
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Br J Cancer. 2016;114:1191-1198. F.I.:5,569. [doi:10.1038/bjc.2016.118]

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5. Perez EA, López-Vega JM, Petit T, Zamagni C, Easton V, Kamber J, Restuccia E, Andersson M.
Safety and efficacy of vinorelbine in combination with pertuzumab and trastuzumab for first-line treatment of patients with HER2-positive locally advanced or metastatic breast cancer: VELVET Cohort 1 final results.
Breast Cancer Res. 2016;18:126-126. F.I.:5,211. [doi:10.1186/s13058-016-0773-6]

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6. Carmona-Bayonas A, Jiménez-Fonseca P, Lorenzo ML, Ramchandani A, Martínez EA, Custodio A, Garrido M, Echavarría I, Cano JM, Barreto JE, García TG, Manceñido FÁ, Lacalle A, Cardona MF, Mangas M, Visa L, Buxó E, Azkarate A, Díaz-Serrano A, Montes AF, Rivera F.
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Impact on clinical practice of the implementation of guidelines for the toxicity management of targeted therapies in kidney cancer.
The protect-2 study. BMC Cancer. 2016;16:135-135. F.I.:3,265. [doi:10.1186/s12885-016-2084-9]

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Balana C, De Las Penas R, Sepúlveda JM, Gil-Gil MJ, Luque R, Gallego O,

Carrato C, Sanz C, Reynes G, Herrero A, Ramirez JL, Pérez-Segura P, Berrocal A, Vieitez JM, Garcia A, Vazquez-Estevez S, Peralta S, Fernandez I, Henriquez I, Martinez-Garcia M, De la Cruz JJ, Capellades J, Giner P, Villà S. **Bevacizumab and temozolomide versus temozolomide alone as neoadjuvant treatment in unresected glioblastoma: the GENOM 009 randomized phase II trial.** J Neurooncol. 2016;127:569-579. F.I.:2,754. [doi:10.1007/s11060-016-2065-5]

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11. Crespo, G. H., Jimenez-Fonseca, P., Custodio, A., Lopez, C., Carmona-Bayonas, A., Alonso, V, Navarro, M., Aller, J., Sevilla, I, Gajate, P., Alonso, T., Matos, I, Capdevila, J., Nieto, B., Barriuso, J. **Capecitabine and Temozolomide in NETs G1-2: The Experience of Various Hospitals in Spain.** Neuroendocrinology. 2016;103:66-66. F.I.:2,583.

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17. Munoz Martin, A. J., Ziyatdinov, A., Castellon Rubio, V., Pachon Olmos, V., Morejon Huerta, B., Calzas Rodriguez, J., Salgado Fernandez, M., Martinez de Castro, E., Luque Caro, R., Soria Fernandez, J. M. **A new genetic risk score for predicting venous thromboembolic events in cancer patients receiving chemotherapy.** Thromb Res. 2016;140:177-178. F.I.:2,320.

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21. Martin-Richard M, Díaz Beveridge R, Arrazubi V, Alsina M, Galan Guzmán M, Custodio AB, Gómez C, Muñoz FL, Pazo R, Rivera F. **SEOM Clinical Guideline for the diagnosis and treatment of esophageal cancer (2016).** Clin Transl Oncol. 2016;18:1179-1186. F.I.:2,075. [doi:10.1007/s12094-016-1577-y]

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An exploratory analysis evaluating the effect of sequence of biologic therapies on overall survival (OS) in patients (pts) with RAS wild-type (WT) metastatic colorectal carcinoma (mCRC).
Oncol. Res. Treat.2016;39:94-94.
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Oncol. Res. Treat.2016;39:93-94.
F.I.:1,333.

Reviews

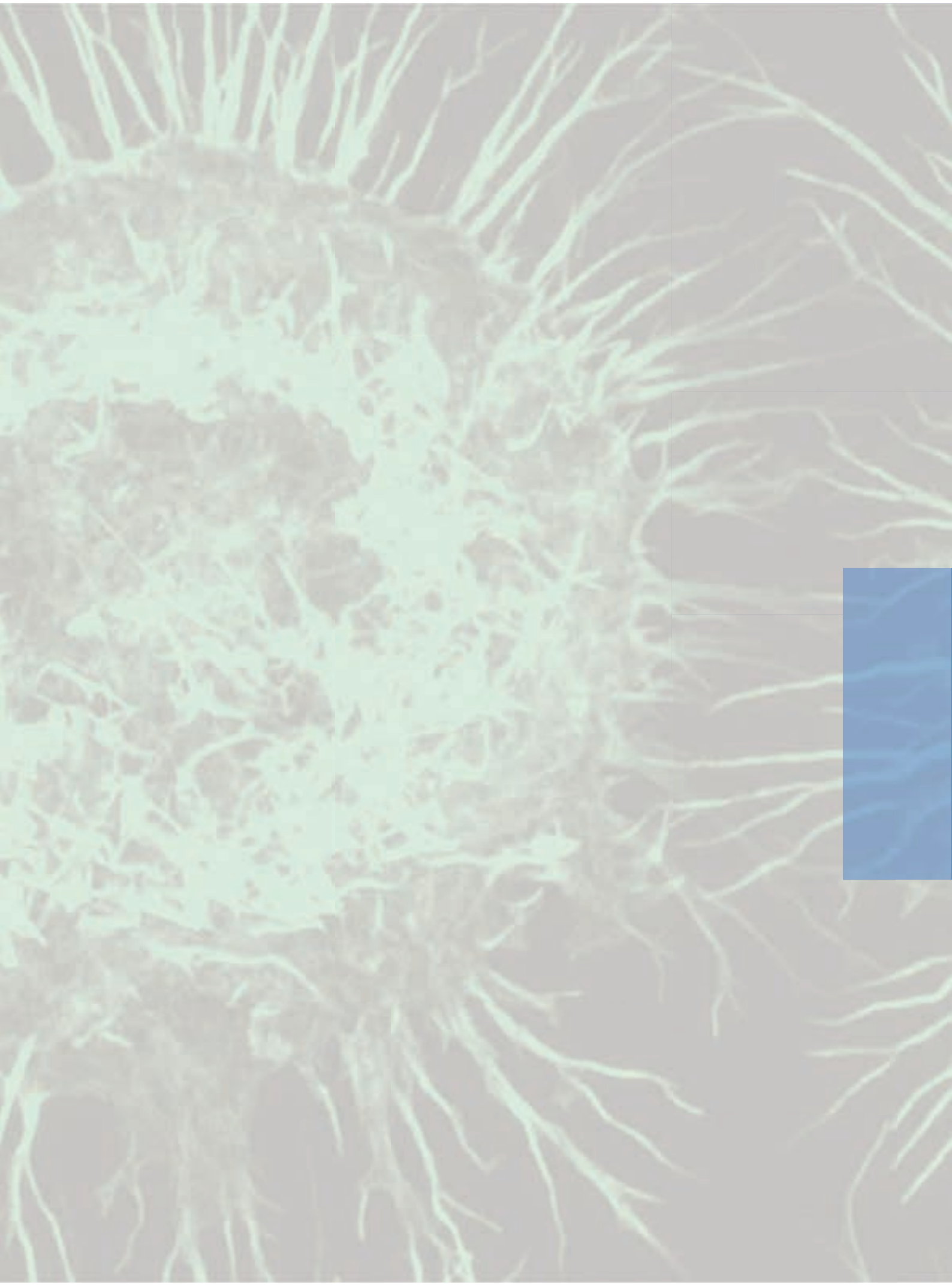
1. Pericay C, Rivera F, Gomez-Martin C, Nuñez I, Cassinello A, Imedio ER.
Positioning of second-line treatment for advanced gastric and gastroesophageal junction adenocarcinoma.
Cancer Med. 2016;5:3464-3474.
F.I.:2,915. [doi:10.1002/cam4.941]

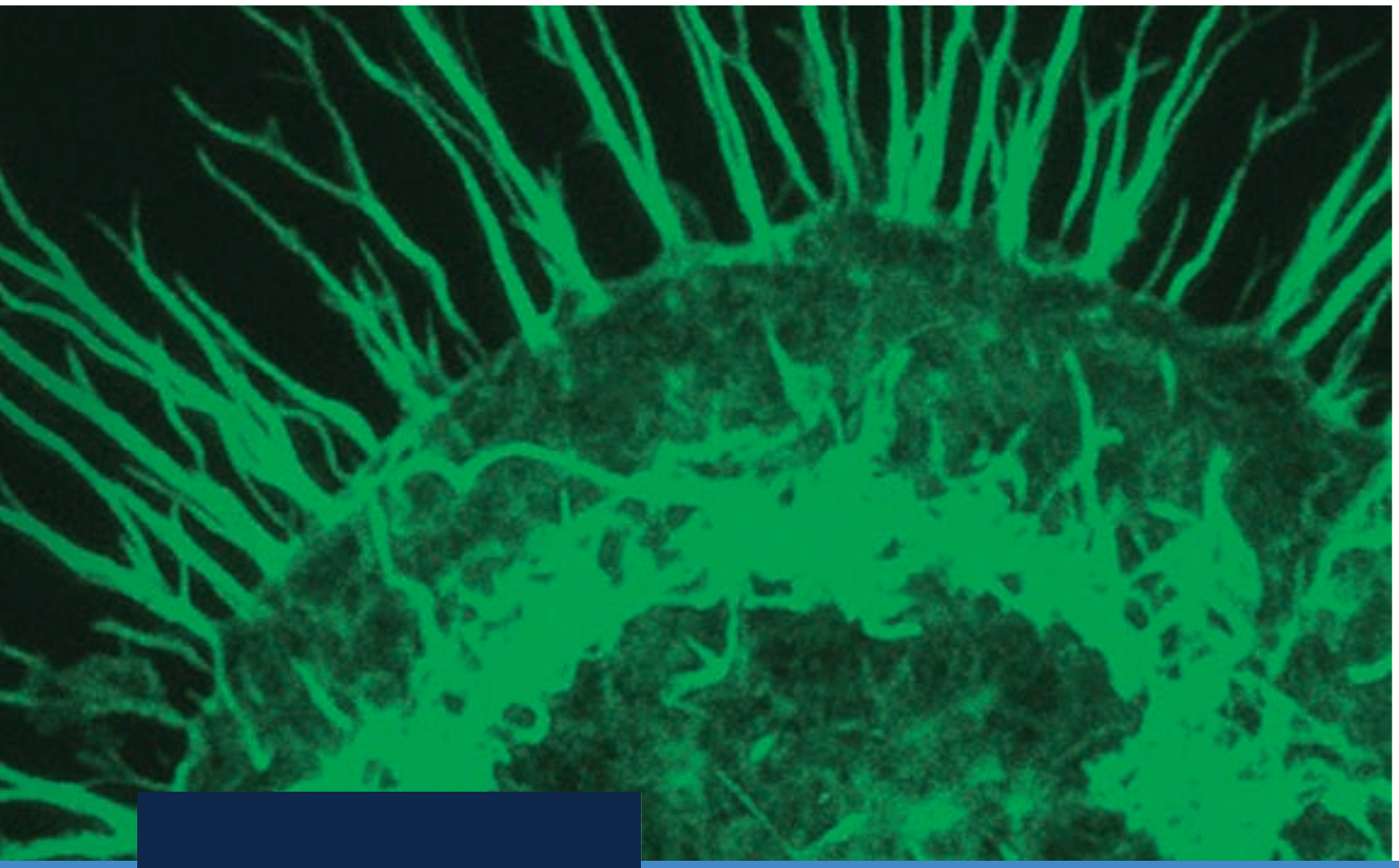
Doctoral thesis

1. Ana De Juan Ferré.
Phase II intramural study of neoadjuvant chemotherapy with platinum, doxorubicin and taxane salts in operable breast cancer. Experience of the medical oncology service of the University Hospital Marqués de Valdecilla.
Directors: **José Manuel López Vega, Marta Mayorga Fernández.**
University of Cantabria.

—

2. Carlos López López.
Clinical-molecular prognostic factors and predictive models in glioblastoma multiforme from an intramural experience: service of medical oncology at University Hospital Marqués de Valdecilla (2000-2010).
Directors: **José Manuel López Vega, Jaime Sanz Ortíz.**
University of Cantabria.





Transversal Area

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Coordinator of the Transversal Area.

Professor of Preventive Medicine and Public Health.
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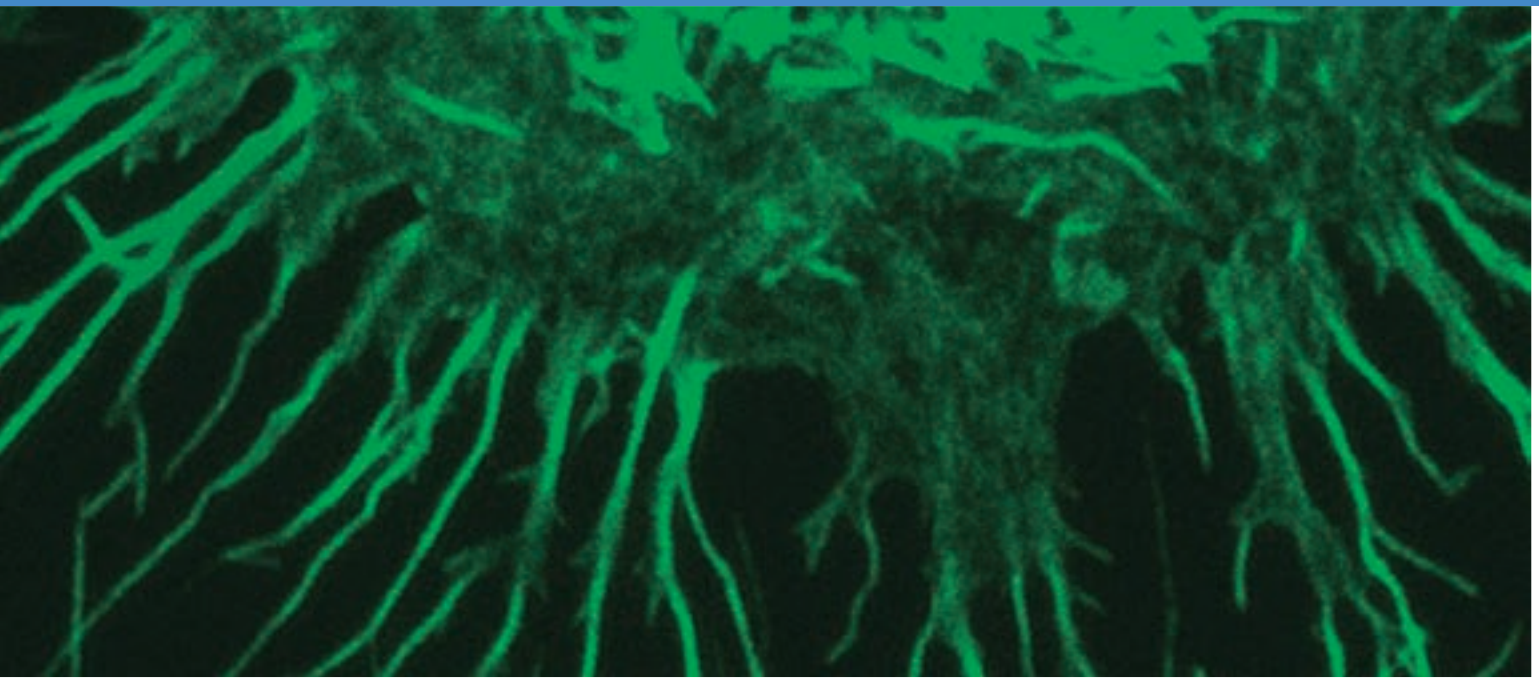

Epidemiology and Public Health

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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 assignation 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).

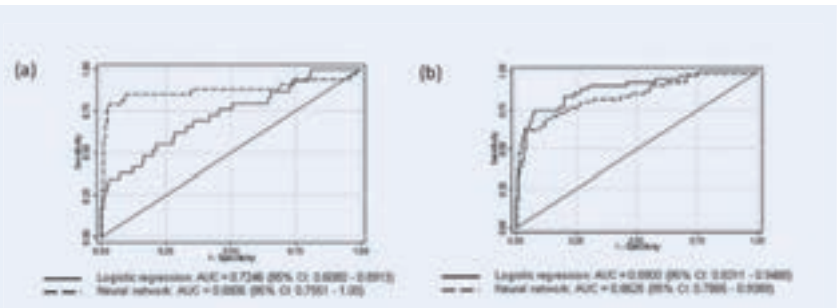

Figura. ROC Curves for the death outcomes at: (a) 30 days after transplantation, and (b) 90 days after transplantation. Solid lines: logistic regression (area under ROC curve [AUC] is 0.7246 [95% CI 0.6080 to 0.8913] for 30-day mortality and 0.8900 [95% CI 0.8311 to 0.9488] for 90-day mortality). Dashed 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

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, 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 old 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 | 140,445

Original articles

1. González-Gay MA, Llorca J.
Clinical guidelines: Best practices and uncertainties in the management of PMR.
Nat Rev Rheumatol. 2016;12:3-4.
F.I.:10,531. [doi:10.1038/nrrheum.2015.142]

2. Espejo-Herrera N, Gracia-Lavedan E, Pollan M, Aragonés N, Boldo E, Perez-Gomez B, Altzibar JM, Amiano P, Zabala AJ, Ardanaz E, Guevara M, Molina AJ, Barrio JP, Gómez-Acebo I, Tardón A, Peiró R, Chirlaque MD, Palau M, Muñoz M, Font-Ribera L, Castaño-Vinyals G, Kogevinas M, Villanueva CM.
Ingested Nitrate and Breast Cancer in the Spanish Multicase-Control Study on Cancer (MCC-Spain).
Environ. Health Perspect.2016;124:1042-1049.
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3. Pastor-Barriuso R, Fernández MF, Castaño-Vinyals G, Whelan D, Perez-Gomez B, Llorca J, Villanueva CM, Guevara M, Molina JM, Artacho-Cordon F, Barriuso-Lapresa L, Tusquets I, Dierssen-Sotos T, Aragonés N, Olea N, Kogevinas M, Pollan M.
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4. Papantoniou K, Castaño-Vinyals G, Espinosa A, Aragonés N, Pérez-Gómez B, Ardanaz E, Altzibar JM, Sanchez VM, Gómez-Acebo I, Llorca J, Muñoz D, Tardón A, Peiró R, Marcos-Gragera R, Pollan M, Kogevinas M.
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Eur J Epidemiol. 2016;31:867-878.
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5. Butt J, Romero-Hernández B, Pérez-Gómez B, Willhauck-Fleckenstein M, Holzinger D, Martin V, Moreno V, Linares C, Dierssen-Sotos T, Barricarte A, Tardón A, Altzibar JM, Moreno-Osset E, Franco F, Olmedo Requena R, María Huerta J, Michel A, Waterboer T, Castaño-Vinyals G, Kogevinas M, Pollán M, Boleij A, de Sanjosé S, Del Campo R, Tjalsma H, Aragonés N, Pawlita M.
Association of Streptococcus gallolyticus subspecies gallolyticus with colorectal cancer: Serological evidence.
Int J Cancer. 2016;138:1670-1679.
F.I.:5,531. [doi:10.1002/ijc.29914]

6. Espejo-Herrera N, Gràcia-Lavedan E, Boldo E, Aragonés N, Pérez-Gómez B, Pollán M, Molina AJ, Fernández T, Martín V, La Vecchia C, Bosetti C, Tavani A, Polesel J, Serraino D, Gómez Acebo I, Altzibar JM, Ardanaz E, Burgui R, Pisa F, Fernández-Tardón G, Tardón A, Peiró R, Navarro C, Castaño-Vinyals G, Moreno V, Righi E, Aggazzotti G, Basagaña X, Nieuwenhuijsen M, ..., Villanueva CM.
Colorectal cancer risk and nitrate exposure through drinking water and diet.
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9. López-Mejías R, Genre F, Remuzgo-Martínez S, González-Juanatey C, Robustillo-Villarino M, Llorca J, Corrales A, Vicente E, Miranda-Filloy JA, Magro C, Tejera-Segura B, Ramírez Huaranga MA, Pina T, Blanco R, Alegre-Sancho JJ, Raya E, Mijares V, Ubilla B, Mínguez Sánchez MD, Gómez-Vaquero C, Balsa A, Pascual-Salcedo D, López-Longo FJ, Carreira P, González-Álvaro I, Rodríguez-Rodríguez L, Fernández-Gutiérrez B, Ferraz-Amaro I, Castañeda S, ...,

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19. Lope V, Fernández de Larrea N, Pérez-Gómez B, Martín V, Moreno V, Costas L, Longo F, Jiménez-Moleón JJ, Llorca J, Ascunce N, Peiró-Pérez R, Altzibar JM, Tardón A, Alguacil J, Navarro C, Sierra Á, Vega AB, Villafañe A, Castaño-Vinyals G, Kogevinas M, Pollán M, Aragonés N.
Menstrual and Reproductive Factors and Risk of Gastric and Colorectal Cancer in Spain.
PLoS One. 2016;11:
F.I.:3,057. [doi:10.1371/journal.pone.0164620]

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The Use of Antihypertensive Medication and the Risk of Breast Cancer in a Case-Control Study in a Spanish Population: The MCC-Spain Study.
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Anti-TNF-a therapy reduces retinol-binding protein 4 serum levels in non-diabetic patients with psoriasis: a 6-month prospective study.
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Perinatal and childhood factors and risk of prostate cancer in adulthood: MCC-Spain case-control study.
Cancer Epidemiol. 2016;43:49-55.
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Carotid ultrasound in the cardiovascular risk stratification of patients with ankylosing spondylitis: results of a population-based study.
Clin Exp Rheumatol. 2016;34:885-892. F.I.:2,495.

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Decreased expression of methylene tetrahydrofolate reductase (MTHFR) gene in patients with rheumatoid arthritis.
Clin Exp Rheumatol. 2016;34:106-110. F.I.:2,495.

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Subclinical atherosclerosis is not increased in patients with non-radiographic axial spondyloarthritis.
Clin Exp Rheumatol. 2016;34:159-160. F.I.:2,495.

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Asymmetric dimethylarginine but not osteoprotegerin correlates with disease severity in patients with moderate-to-severe psoriasis undergoing anti-tumor necrosis factor-a therapy.
J Dermatol. 2016;43:389-394. F.I.:1,577. [doi:10.1111/1346-8138.13094]

Reviews

1. López-Mejías R, Castañeda S, González-Juanatey C, Corrales A, Ferraz-Amaro I, Genre F, Remuzgo-Martínez S, Rodriguez-Rodriguez L, Blanco R, Llorca J, Martín J, González-Gay MA.
Cardiovascular risk assessment in patients with rheumatoid arthritis: The relevance of clinical, genetic and serological markers.
Autoimmun Rev. 2016;15:1013-1030. F.I.:8,490. [doi:10.1016/j.autrev.2016.07.026]

Editorials

1. Gonzalez-Gay MA, Castañeda S, Llorca J.
Giant Cell Arteritis: Visual Loss Is Our Major Concern.
J Rheumatol. 2016;43:1458-1461. F.I.:3,236. [doi:10.3899/jrheum.160466]

Doctoral thesis

1. Javier Rueda Gotor.
Evaluation of cardiovascular risk in patients with predominantly axial spondyloarthritis.
Directors: **Miguel Ángel González-Gay Mantecón, Javier Llorca Díaz.**
University of Cantabria.

2. Montserrat Robustillo Villarino.
Evaluation of cardiovascular risk using non-invasive techniques in patients with rheumatoid arthritis.
Directors: **Javier Llorca Díaz, Miguel Ángel González-Gay Mantecón.**
University of Cantabria.

3. Yhivian Peñasco Martín.
Prognostic factors of severe thoracic trauma in the population aged over 65, 1991-2012.
Directors: **Alejandro González Castro, Javier Llorca Díaz.** University of Cantabria.

4. Sara Rodríguez Prado.
Ocular involvement in rendu-osler-weber disease: characteristics and associations.
Director: **Inés Gómez Acebo.**
University of Cantabria.

5. Ana Esteban Herrera.
Effectiveness in the management of smoking cessation. Cohort study in a primary care context. Directors: **Javier Ayesta Ayesta, Javier Llorca Díaz.**
University of Cantabria.

6. Jose Alberto Sanchez Ortega.
Prevalence of tobacco, alcohol and drug use among university students in Cantabria.
Directors: **Javier Llorca Díaz, Mª Concepcion Fariñas Álvarez.**
University of Cantabria.

PROJECTS

Projects

1. Javier Llorca Díaz.
Integration of genetic big data and clinical data: survival with breast cancer in the MCC-Spain study.
PI15/00069.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Advanced Microscopy and Protein Folding and Citoesqueleto

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Researchers
Jorge Alfonso Díaz Gómez

Research Lines

1. Study of tubulin folding cofactors (TBCs).

Protease of tubulin. Development of biochemical and biophysical techniques to study the interactions of these proteins with others, identify their "partners" in the cell and dissect each and every one of their functions using, among others, electron microscopy and confocal techniques.

2. Study of the folding of proteins in organisms living between -1 and -2 ° C (Antarctic fish).

3. Study of protein folding in organisms living between -1 and -2 ° C (Antarctic fish).

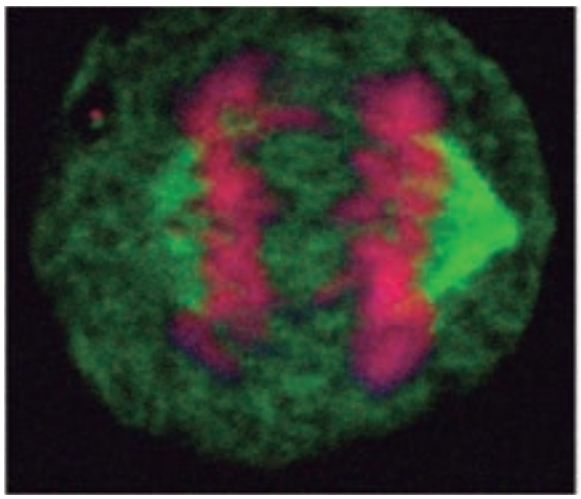
The research of our group, since its creation, has been articulated around the study of the Microtubule Cytoskeleton and specifically in the characterization of any activity of a family of proteins intimately linked to tubulins such as co-factors of folding (TBCs) in addition to Other chaperones involved in their folding as the cytosolic chaperonin CCT. Our studies have also focused on the role of these proteins in different diseases but we are mainly trying to characterize the molecular mechanism leading to Kenny-Caffey syndrome in which the TBCE cofactor has a deletion of four amino acids. The approach used is multidisciplinary.

PUBLICACIONES:

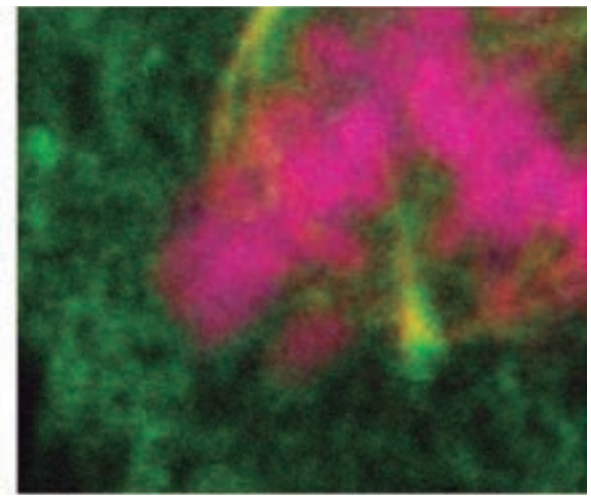
FACTOR DE IMPACTO | 4,348.

Artículos Originales

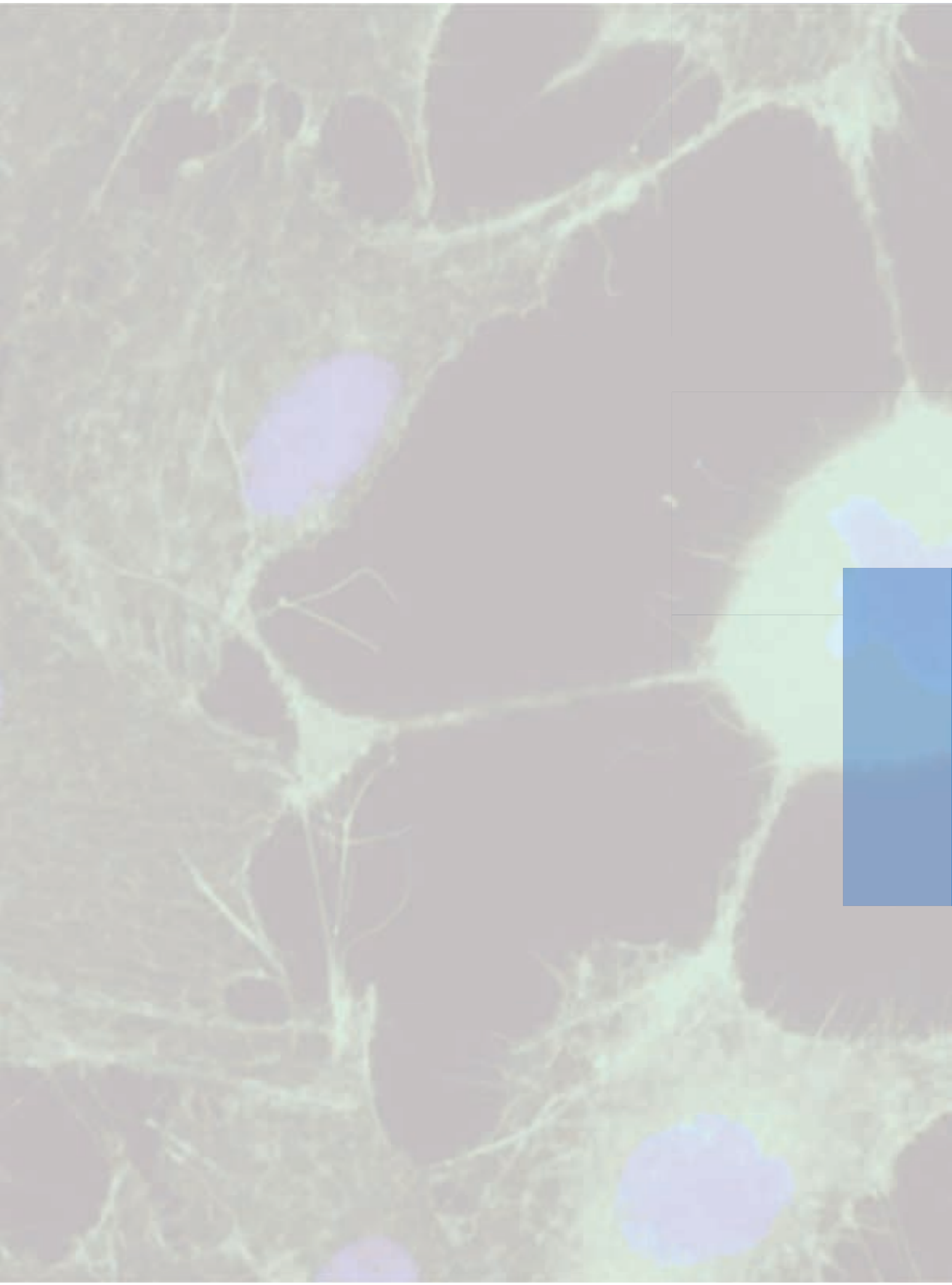
1.. Avila J, Jiménez JS, Sayas CL, Bolós M, Zabala JC, Rivas G, Hernández F. **Tau Structures.** FRONT AGING NEUROSCI 2016. 8: 262-0.FI: 4,348.

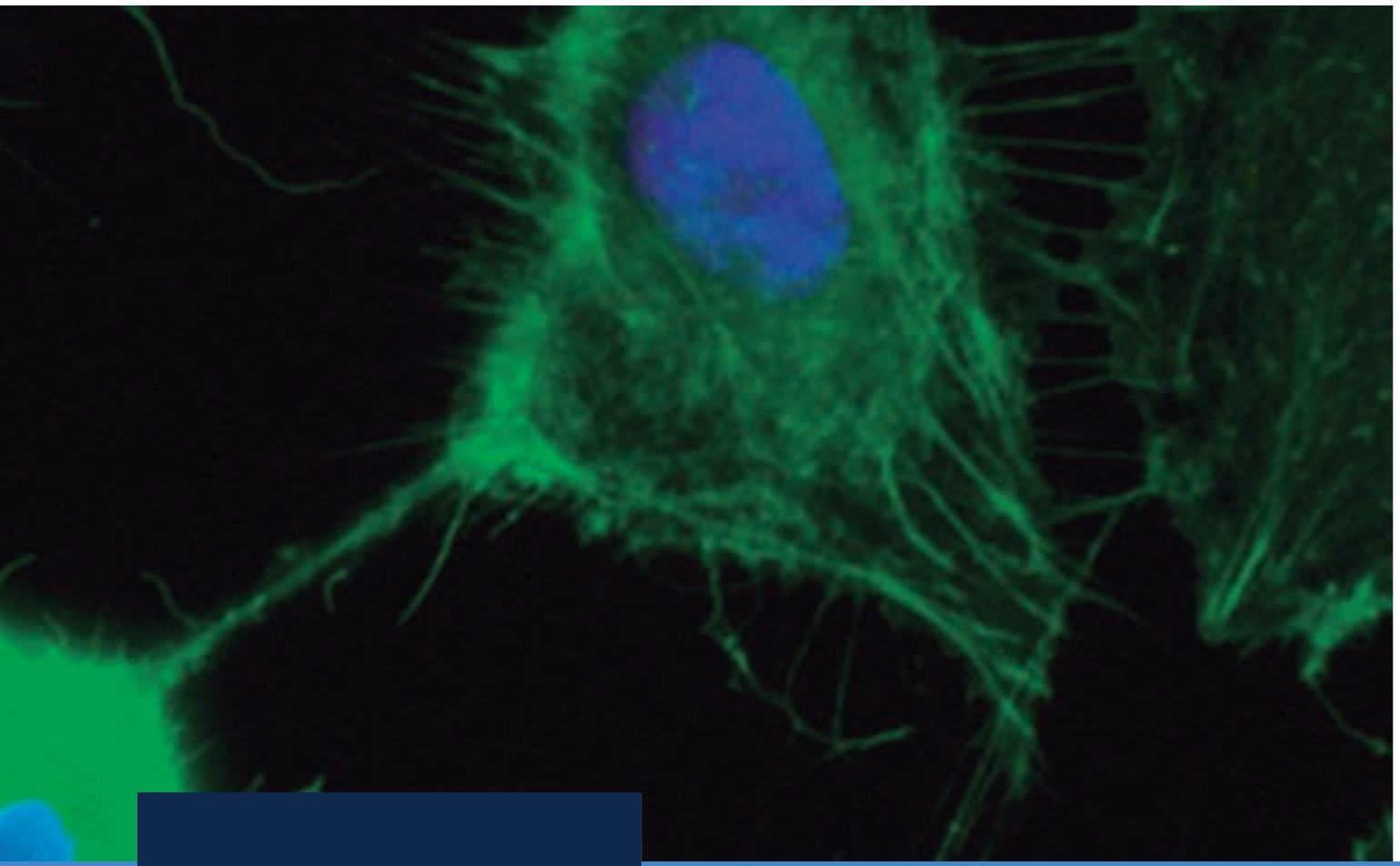


Anafase en célula humana. DNA en violeta, microtúbulos en amarillo y TBCB en verde.



Metafase aberrante en célula humana de 3 polos. DNA en violeta, microtúbulos en amarillo y TBCB en verde.





Infectious Diseases and Immune System Area

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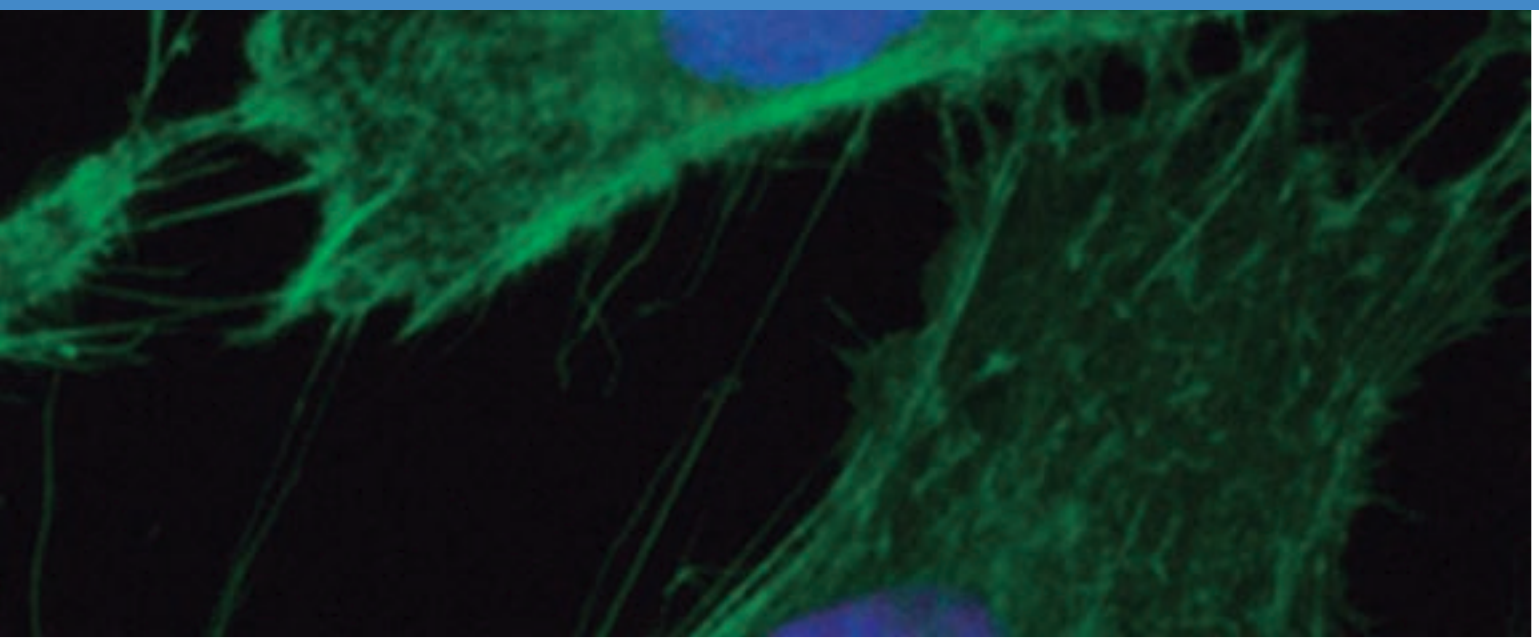

Epidemiología Genética y Arterioesclerosis en Enfermedades Inflamatorias Sistémicas

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Research Line

1. Epidemiology of autoimmune diseases (mainly rheumatoid arthritis (RA), giant cell arteritis, scleroderma, spondyloarthropathies (EspA), systemic lupus erythematosus (SLE), psoriasis, anti-synthetase syndrome, interstitial lung disease, Schönlein-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, anti-synthetase 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.

PUBLICACIONES:

IMPACT FACTOR | 251,768

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2. Castañeda S, Vicente EF, González-Gay MA.
Additional proposals to reduce comorbidity in patients with chronic inflammatory rheumatic diseases: comment on 'Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative' by Baillet et al.
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7. Rodríguez-Carrio J, López-Mejías R, Alperi-López M, López P, Ballina-García FJ, González-Gay MÁ, Suárez A.
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Doctoral thesis

1. Ana Machin Mave.
Epidemiological and evolutionary analysis of open eye trauma in cantabria. 2007-2014. Directors: **Joaquín Cañal Villanueva, Pedro Muñoz Cacho.**
University of Cantabria.

2. Francisco Ortiz Sanjuan.
Classification of cutaneous vasculitis. Cutaneous vasculitis by drugs.
Directors: **Ricardo Blanco Alonso, Miguel Ángel González-Gay Mantecón, María Del Carmen González Vela.**
University of Cantabria.

3. Javier Rueda Gotor.
Evaluation of cardiovascular risk in patients with predominantly axial spondyloarthritis.
Directors: **Miguel Ángel González-Gay Mantecón, Javier Llorca Díaz.**
University of Cantabria.

4. Jose Maria Castillo Oti.
Prevalence and risk factors associated with diabetic retinopathy in Cantabria.
Directors: **Joaquín Cañal Villanueva, Pedro Muñoz Cacho.**
University of Cantabria.

5. Leyre Riancho Zarrabeitia.
Detection of risk factors for subclinical atherosclerotic disease and cardiovascular events in patients with systemic lupus erythematosus.
Directors: **Miguel Ángel González-Gay Mantecón, Ricardo Blanco Alonso.**
University of Cantabria.

6. Montserrat Robustillo Villarino.
Evaluation of cardiovascular risk using non-invasive techniques in patients with rheumatoid arthritis.
Directors: **Javier Llorca Díaz, Miguel Ángel González-Gay Mantecón.**
University of Cantabria.

PROJECTS

Projects

1. Miguel Ángel González-Gay Mantecón.
Research Network on Inflammation and Rheumatic Diseases.
RD12/0009/0013.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. Miguel Ángel González-Gay Mantecón.
Sara Borrell Contracts.
CD15/00095.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. Miguel Ángel González-Gay Mantecón.
Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases.
EU13/01- PRECISESADS.
COMISIÓN EUROPEA, INNOVATIVE MEDICINES INITIATIVE.

4. Miguel Ángel González-Gay Mantecón.
Genetic markers of atherosclerotic disease in rheumatoid arthritis.
PI15/00525.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

5. Miguel Ángel González-Gay Mantecón.
Thematic Network in Inflammation and Rheumatic Diseases.
RD16/0012/0009.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

6. Raquel López Mejías.
Project associated to the Miguel Servet Posdoctoral Contract Type. CV risk assessment in patients with rheumatoid arthritis: the relevance of genetic marker.
CP16/00033.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Pathogenic Epidemiology and Mechanisms of Infectious Diseases

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Clinic group

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Research Lines

1. Infections in Transplanted Solid Organs.

This line of research started in 2012 is being consolidated in our group mainly through the acquisition of competitive funding research projects (FIS - PI13 / 01191 - PI16 / 01415 and Mutua Madrileña FMM 14/01. Research in Infectious Pathology (REIPI) and European Projects (Increment-SOT).

2. The study of Articular Prosthesis Infections.

This line began in 2009 with the execution of the Research Project: PI 08/0609 where the study of the role of sonication in the diagnosis of joint prosthesis infections was introduced. The results have had as a positive result the incorporation into the laboratory routine of Microbiology of this technique. Then, and thanks to API 11/09, are there more accurate Systemic Markers in the diagnosis of Knee Prosthesis Infection (IPRC) prior to Implant withdrawal? the study of Systemic Markers is being carried out in the diagnosis of Infection of Knee Prosthesis or Hip (IPRC) prior to the withdrawal of the Implant such as ILA6, Procalcitonin, VEGF (Vascular Endothelial Growth Factor) or NETs (Neutrophils extracellular traps).

3. Optimization of antimicrobial treatment and its impact of antibiotic consumption on cost savings and bacterial resistance.

Initiated in 2006 with the granting of two research projects (FIS: PI06 / 90094 and API: 06/01). This project has received the Valdecilla-Caja Cantabria Teaching Excellence Award in 2013. Since then, the experience accumulated at the Marqués de Valdecilla Hospital is being transferred to other hospitals through the teaching of professional specialists of staff from National Hospitals that go to Diseases Infectious.

The excessive and inadequate use of antimicrobials is currently an important economic and

public health problem due to the emergence of microorganisms that are increasingly resistant to available antibiotics. This study is part of an attempt to achieve these objectives through recommendations on the use of antimicrobials in a standardized way by a person with experience in this area, the result of a multidisciplinary collaboration.

4. Epidemiology of Infective Endocarditis.

With the creation of the Endocarditis Management Assistance Group in Spain (GAMES) in 2007, which comprises 35 hospitals, a better knowledge of this disease is being achieved, which is having an impact on a better diagnostic and therapeutic approach. Our group manages one of the 7 nodes in which the participating Hospitals have been divided and has contributed to the formation of the HUMV Multidisciplinary Endocarditis Group, H. Sierrallana and H. de Laredo, in which the Cardiology, Cardiovascular Surgery, Home Hospitalization, Internal Medicine and Microbiology.

5. Research in the field of sepsis.

Study of sepsis in a global way, both from the point of view of predisposing factors and the optimization of its treatment and the identification of prognostic factors. This line of research began with research projects with competitive funding: PI07 / 0723, PI10 / 01497 and API11 / 35.

6. Tuberculosis (Infection / Disease) and Genetic Alterations.

The study of alleles and haplotypes of the major histocompatibility complex between healthy controls, individuals with latent tuberculosis and individuals with active pulmonary tuberculosis in the population of Cantabria, is one of the lines initiated in 2008 and later consolidated with the obtaining Of an API1010 Grant. Currently still active. Likewise, the search for other genes for susceptibility or resistance to progression, from a latent state of tuberculosis infection to disease, is another objective of the group.

PUBLICACIONS:

IMPACT FACTOR | 98,636

Original articles

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Rev Esp Quimioter. 2016;29:230-238. F.I.:1,014.

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Rev Esp Quimioter. 2016;29:123-129. F.I.:1,014.

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Reviews

1. Torre-Cisneros J, Aguado JM, Caston JJ, Almenar L, Alonso A, Cantisán S, Carratalá J, Cervera C, Cordero E, Fariñas MC, Fernández-Ruiz M, Fortún J, Frauca E, Gavaldá J, Hernández D, Herrero I, Len O, Lopez-Medrano F, Manito N, Marcos MA, Martín-Dávila P, Monforte V, Montejo M, Moreno A, Muñoz P, Navarro D, Pérez-Romero P, Rodriguez-Bernot A, Rumbao J, ..., **Spanish Network for Research in Infectious Diseases (REIPI). Management of cytomegalovirus infection in solid organ transplant recipients: SET/GESITRA-SEIMC/REIPI recommendations.**
Transplant Rev (Orlando). 2016;30:119-143.F.I.:3,915. [doi:10.1016/j.trre.2016.04.001]

2. Armiñanzas C, Herrera LA, Fariñas MC. **Bacteriobilia: un problema sin resolver.**
Rev Esp Quimioter. 2016;29:113-118. F.I.:1,014.

Doctoral thesis

1. Ana Mª Arnaiz García. **Morbidity and mortality in deferred sternal closure.**
Directors: **José Manuel Bernal Marco, Mª Concepcion Fariñas Álvarez, María Del Carmen Fariñas Álvarez.**
University of Cantabria.

2. Gabriela Saravia Campelli. **A randomized intervention program to optimize the quality of antibiotic use in the hospital.**
Directors: **María Del Carmen Fariñas Álvarez, Mª Concepcion Fariñas Álvarez.**
University of Cantabria.

3. Javier Gonzalo Ocejo Viñals. **Immunogenetics of pulmonary tuberculosis: influence of major histocompatibility complex polymorphisms, repertoire of kir genes and other genes of the immune system.**
Director: **María Del Carmen Fariñas Álvarez.**
University of Cantabria.

4. Jose Alberto Sanchez Ortega. **Prevalence of tobacco, alcohol and drug use among university students in Cantabria.**
Directors: **Javier Llorca Díaz, Mª Concepcion Fariñas Álvarez.**
University of Cantabria.

5. Liebana Maria Piedra Anton. **Information systems of urgency services. Application to the Sierrallana Hospital.**
Directors: **Luis Ansorena Pool, María Del Carmen Fariñas Álvarez.**
University of Cantabria.

6. Marcos Pajaron Guerrero. **Self-management of intravenous antimicrobial treatment (a-tade) in infective endocarditis: a safe and efficient care model.**
Director/es: **María Del Carmen Fariñas Álvarez, José Ramón De Berrazueta Fernández.**
University of Cantabria.

PROJECTS

Projects

1. María del Carmen Fariñas Álvarez. **Spanish Network of Research in Infectious Pathology.**
RD12/0015/0019.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

2. María del Carmen Fariñas Álvarez. **Intestinal colonization by multiresistant enterobacteria in patients with renal and hepatic transplantation: multicenter cohort study and randomized, controlled and open clinical trial.**
PI13/01191.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. María del Carmen Fariñas Álvarez. **Impact of intestinal colonization by multiresistant enterobacteria on systemic infections, graft versus host disease (GVHD), and mortality of patients receiving allogeneic transplantation of haematopoietic progenitors (Alo-TPH).**
PI16/01415.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

4. María del Carmen Fariñas Álvarez. **Thematic Network on Infectious Diseases.**
RD16/0016/0007.
INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

Nanovaccines and Cellular Vaccines Based on Listeria Monocytogenes and their Applications in Biomedicine

Group Leader

Carmen Álvarez Domínguez

Valdecilla Biomedical Research Institute

Marqués de Valdecilla
IDIVAL

Emerging group

Contributors

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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. Yañez Diaz/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

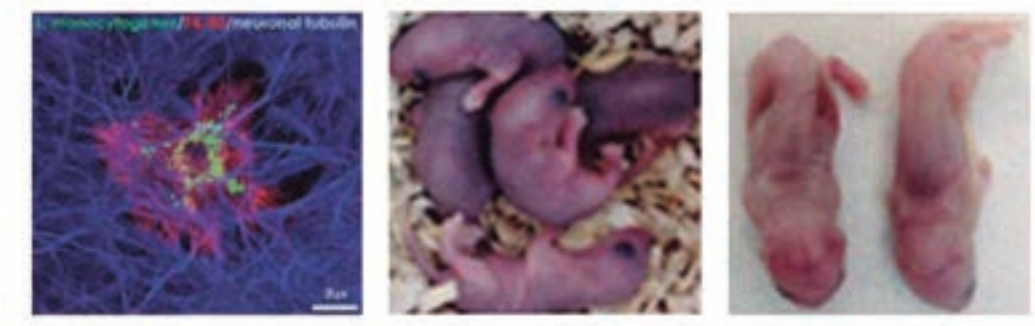

Figura1. Listeriosis cerebral neonatal y papel de microglía

Figura 2.
Vacuna dendrítica con un nuevo antígeno de Listeria monocytogenes: GAPDH.

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, 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/Proyects: SAF2009-08695 y SAF2012-34203 y Estudio Clínicos aprobado: CEIC-Acta 30/2012). A Listeria-based DC vaccine loaded with the peptide LLO91-99 is used as anti-adhesive therapy for melanoma in murine models (Dr. J. Gomez-Roman, S. Anatomia Patologica) and to prepare in melanoma patients a vaccine DC in combination with the HUMV Oncology and Dermatology Services (metastatic melanoma) (Dr. H. Fernandez-Llaca and Dr. A. Garcia) and the UPV Human Melanoma Group (Dr. 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.

PUBLICACIONS:

IMPACT FACTOR | 25,070

Original articles

1. Calderon-Gonzalez R, Teran-Navarro H, Marimon JM, González-Rico C, Calvo-Montes J, Frande-Cabanes E, Alkorta-Gurrutxaga M, Fariñas MC, Martínez-Martínez L, Perez-Trallero E, Alvarez-Dominguez C.
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2. Gomez-Salces, Susana, Antonio Barreda-Argueso, Jose, Valiente, Rafael, Rodrigueza, Fernando.
A study of Ce3+ to Mn2+ energy transfer in high transmission glasses using time-resolved spectroscopy. J Mater Chem C Mater Opt Electron Devices. 2016;4:9021-9026. F.I.:5,066. [doi:10.1039/c6tc01408a]

3. Calderon-Gonzalez R, Bronchalo-Vicente L, Freire J, Frande-Cabanes E, Alaez-Alvarez L, Gomez-Roman J, Yañez-Diaz S, Alvarez-Dominguez C.
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Oncotarget. 2016;7:16855-16865. F.I.:5,008. [doi:10.18632/oncotarget.7806].

4. Gomez-Salces, Susana, Barreda-Argueso, Jose A., Valiente, Rafael, Rodriguez, Fernando.
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Pregnancy Vaccination with Gold Glyco-Nanoparticles Carrying Listeria monocytogenes Peptides Protects against Listeriosis and Brain- and Cutaneous-Associated Morbidities.
Nanomaterials (Basel). 2016;6: F.I.:2,690. [doi:10.3390/nano6080151].

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Carbon implanted waveguides in soda lime glass doped with Yb3+ and Er3+ for visible light emission.
OPT LASER TECHNOL. 2016;79:132-136. F.I.:1,879. [doi:10.1016/j.optlastec.2015.12.002].

Immunopathology of Rheumatic Diseases

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Jointly Responsible
Jaime Calvo Alén

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.

> PImpact 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 erithematosus (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 | 56,390

Original articles

1. Orta-Mascaró M, Consuegra-Fernández M, Carreras E, Roncagalli R, Carreras-Sureda A, Alvarez P, Girard L, Simões I, Martínez-Florensa M, Aranda F, Merino R, Martínez VG, Vicente R, Merino J, Sarukhan A, Malissen M, Malissen B, Lozano F.
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2. Postigo J, Iglesias M, Álvarez P, Augustin JJ, Buelta L, Merino J, Merino R.
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Arthritis Rheumatol. 2016;68:1551-1562.
F.I.:6,009. [doi:10.1002/art.39557]

3. López-Hoyos M, Álvarez-Rodríguez L, Mahler M, Torices S, Calvo-Alén J, Villa I, Seaman A, Yee A, Martínez-Taboada V.
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4. Pego-Reigosa JM, Lois-Iglesias A, Rúa-Figueroa Í, Galindo M, Calvo-Alén J, de Uña-Álvarez J, Balboa-Barreiro V, Ibáñez Ruan J, Olivé A, Rodríguez-Gómez M, Fernández Nebro A, Andrés M, Erausquin C, Tomero E, Horcada Rubio L, Uriarte Isacelaya E, Freire M, Montilla C, Sánchez-Atrio AI, Santos-Soler G, Zea A, Díez E, Narváez J, Blanco-Alonso R, Silva-Fernández L, Ruiz-Lucea ME, Fernández-Castro M, Hernández-Beriain JÁ, Gantes-Mora M, ..., López-Longo FJ.
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6. Alvarez P, Jensen LE.
Imiquimod Treatment Causes Systemic Disease in Mice Resembling Generalized Pustular Psoriasis in an IL-1 and IL-36 Dependent Manner.
Mediators Inflamm. 2016;2016:6756138-6756138.
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7. Alvarez P, Genre F, Iglesias M, Augustin JJ, Tamayo E, Escolà-Gil JC, Lavín B, Blanco-Vaca F, Merino R, Merino J.
Modulation of autoimmune arthritis severity in mice by apolipoprotein E (ApoE) and cholesterol.
CLIN EXP IMMUNOL. 2016;186:292-303.
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8. Iglesias M, Augustin JJ, Alvarez P, Santiuste I, Postigo J, Merino J, Merino R.
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9. Torrente-Segarra V, Salman-Monte TC, Rúa-Figueroa Í, Pérez-Vicente S, López-Longo FJ, Galindo-Izquierdo M, Calvo-Alén J, Olivé-Marqués A, Ibañez-Ruán J, Horcada L, Sánchez-Atrio A, Montilla C, Rodríguez-Gómez M, Díez-Álvarez E, Martinez-Taboada V, Andreu JL, Fernández-Berrizbeitia O, Hernández-Beriain JA, Gantes M, Hernández-Cruz B, Pecondón-Español Á, Marras C, Bonilla G, Pego-Reigosa JM.
RELESSER Study Group of the Spanish Society of Rheumatology (SER) and the Study. Fibromyalgia prevalence and related factors in a large registry of patients with systemic lupus erythematosus.
Clin Exp Rheumatol. 2016;34:40-47.
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10. Rua-Figueroa, I., Castro, M. Fernandez, Pego-Reigosa, J. M., Sanchez-Piedra, C., Lopez-Longo, J., Taboada, V. Martinez, Calvo-Alen, J., Olive, A., Galindo, M., Blanco, R., Alonso, F., Erausquin, C., Andreu, J. L.
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11. Galindo-Izquierdo M, Rodriguez-Almaraz E, Pego-Reigosa JM, López-Longo FJ, Calvo-Alén J, Olivé A, Fernández-Nebro A, Martinez-Taboada V, Vela-Casasempere P, Freire M, Narváez FJ, Rosas J, Ibáñez-Barceló M, Uriarte E, Tomero E, Zea A, Horcada L, Torrente V, Castellvi I, Calvet J, Menor-Almagro R, Zamorano MA, Raya E, Díez-Álvarez E, Vázquez-Rodríguez T, García de la Peña P, Movasat A, Andreu JL, Richi P, ...,
RELESSER Group, from the Spanish Society of Rheumatology

Systemic Autoimmune Dis. Characterization of Patients With Lupus Nephritis Included in a Large Cohort From the Spanish Society of Rheumatology Registry of Patients With Systemic Lupus Erythematosus (RELESSER).
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12. Canut-Blasco A, Calvo J, Rodríguez Díaz JC, Martínez-Martínez L.
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Enferm Infecc Microbiol Clin. 2016;34:524-530.
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Reviews

1. Rodríguez-Martínez JM, Machuca J, Cano ME, Calvo J, Martínez-Martínez L, Pascual A.
Plasmid-mediated quinolone resistance: Two decades on.
Drug Resist Updat. 2016;29:13-29.
F.I.:7,950. [doi:10.1016/j.drup.2016.09.001]

Clinical and Molecular Microbiology

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Líneas de investigación

1. Resistencia a los antimicrobianos en bacterias Gram-negativas de interés médico.

La resistencia a los antimicrobianos es un problema importante desde el punto de vista de la salud pública. Gran parte de la actividad investigadora de nuestro grupo se centra en el estudio de aspectos genéticos y bioquímicos de los mecanismos de resistencia a los antimicrobianos de mayor interés clínico (fundamentalmente, beta-lactámicos, quinolonas y aminoglucósidos) en una gama de bacterias resistentes, particularmente los organismos Gramnegativos como enterobacterias (Escherichia coli, Klebsiella pneumoniae, Enterobacter spp.) y los no fermentadores como Pseudomonas aeruginosa, Actinetobacter baumannii y el complejo de Burkholderia cepacia, entre otros. En relación con ello, los dos aspectos a los que se ha prestado particular atención son la multirresistencia y el bajo nivel de resistencia. El impacto clínico de los organismos multirresistentes es profundo ya que existen pocos fármacos nuevos en desarrollo que sean eficaces contra estas cepas. El grupo forma parte del Programa de Resistencia a los Antimicrobianos de la Red de Investigación en Patología Infecciosa (REIPI, http://reipi.org/) financiada por el ISCIII. Esta Red ha desarrollado y está desarrollando diversos estudios

multicéntricos sobre aspectos clínicos y microbiológicos de infecciones causadas por microorganismos resistentes de interés clínico, un grave problema sanitario en muchos hospitales españoles. Nuestra colaboración en el estudio de las bases moleculares de la resistencia ha permitido obtener nueva información sobre aspectos clínicos de las infecciones causadas, entre otros, por Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa y Acinetobacter baumannii. El grupo colabora también activamente en el otro programa, de infecciones en trasplantados, de la REIPI. Nuestros objetivos incluyen la caracterización de genes y elementos móviles (plásmidos, transposones, integrones, casetes genéticos) implicados en la resistencia a los antimicrobianos. Nuestros estudios han contribuido también a descubrir y caracterizar nuevas beta-lactamasas, como es el caso de la nueva oxacilinasa OXA-207 en cepas de Acinetobacter pittii, un microorganismo relacionado con A. baumannii, que también está implicado en infecciones nosocomiales. Los beta-lactámicos siguen siendo la clase más prescrita de antibióticos. Dentro de estos, los carbapenémicos, los más nuevos y potentes beta-lactámicos, se han convertido en los fármacos de elección para el tratamiento de infecciones por bacterias patógenas oportunistas Gram-negativas. Sin embargo, la resistencia a estos antimicrobianos ha surgido en varias especies de Gram-negativos, fundamentalmente mediada por enzimas que contrarrestan la acción de los carbapenémicos llamadas carbapenemasas. Entre nuestros objetivos está el uso métodos fenotípicos y genotípicos para estudiar y caracterizar y los mecanismos de resistencia a carbapenémicos conferida por una gama de metalo-beta-lactamasas (MBL) (incluyendo el IMP, VIM, SPM y tipos NDM) y por serina-betalactamasas de las clases A y D de Ambler. Nuestros intereses se extienden también a la caracterización de dichas enzimas aisladas de microorganismos ambientales, como es el caso de Pseudomonas putida y otras especies relacionadas taxonómicamente como P. monteilii, que constituyen reservorios de genes de multirresistencia, en particular MBL, de las cuales se han reportado infecciones nosocomiales causadas por estas cepas portando VIM-2 en pacientes gravemente enfermos o inmunocomprometidos con frecuencia hospitalizados en unidades de cuidados intensivos. Las fluoroquinolonas como ciprofloxacino son antibióticos de amplio espectro de una gran utilidad para tratar infecciones por varias especies de Gram-negativos y Gram-positivos. Debido a que estos son agentes totalmente sintéticos se pensó que la resistencia transferible era poco probable, ya que no hay ningún organismo ambiental productor que proporcionara una fuente de genes de resistencia. Sin embargo, numerosos genes qnr (resistencia a quinolonas) se han diseminado horizontalmente en todo el mundo en una extensa gama de patógenos bacterianos (principalmente Gram-negativos). Por tanto, nuestro grupo continúa con la línea de trabajo sobre el estudio de los mecanismos plasmídicos de resistencia a quinolonas.

La resistencia a los aminoglucósidos en Gram-negativos, principalmente en enterobacterias, es otra de las líneas de trabajo del grupo, específicamente 1) la resistencia debida a la presencia de enzimas modificadoras de aminoglucósidos del tipo N-acetiltransferasas (AAC), Ofosfotransferasas (APH) y O-nucleotidiltransferasas (ANT) que provocan que su fijación al ARN 16S se vea afectada y de esta forma pierdan su actividad, y 2) a la presencia de metilasas de ARN 16S, que como su nombre lo indica metilan esta molécula en determinadas posiciones confiriendo resistencia de alto nivel a los aminoglucósidos. Los genes que codifican dichas enzimas suelen encontrarse en elementos genéticos móviles llevados por plásmidos, lo cual favorece en gran medida su dispersión intra- e inter-especies.

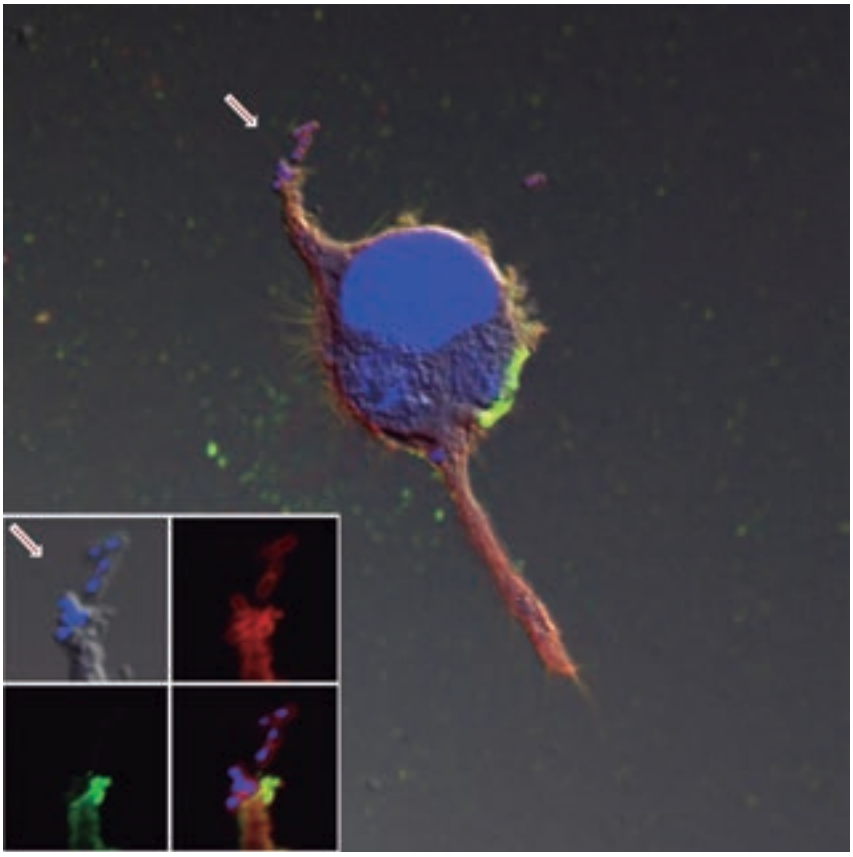
Otros de nuestros objetivos es evaluar la importancia de las bombas de expulsión activa en la resistencia intrínseca de bacterias Gram-negativas a antibióticos utilizados en la clínica, como los mencionados beta-lactámicos, quinolonas y aminoglucósidos, así como estudiar el papel de las porinas de enterobacterias (fundamentalmente K. pneumoniae, E. coli, Enterobacter spp.) en la resistencia de bajo nivel a los antibióticos y el estudio de los mecanismos de regulación de la porina OprD de P. aeruginosa en la resistencia a carbapenémicos.

2. Mecanismos de patogenicidad e interacciones patógeno/hospedador en bacterias gram-negativas de interés clínico.

Pseudomonas aeruginosa y Burkholderia cepacia son capaces de liberar una gran variedad de enzimas hidrolíticas e inyectarlas dentro de las células del hospedador mediante complejos sistemas de secreción (SST) que involucran diversos complejos de proteínas que están parcialmente embebidas dentro de la envoltura celular bacteriana. Uno de estos sistemas es el SST6, recientemente descubierto, el cual secreta proteínas que están implicadas tanto en la interacción con células eucariotas como procariotas. La secreción de proteínas es fundamental en muchos aspectos de la patogénesis bacteriana. Muchas de las proteínas efectoras del SST6 se relacionan con las capacidades de adhesión e invasión a la célula hospedadora, así como la inducción de crecimiento y la supervivencia intracelular en macrófagos. Nuestro grupo se centra en la caracterización de nuevos efectores de SST6 en Pseudomonas aeruginosa y diferentes especies dentro del complejo de Burkholderia cepacia. Por otro lado, se ha visto que los SST6 de P. aeruginosa también están relacionado con la producción de biofilms y la resistencia específica de estos a ciertos antibióticos como los aminoglucósidos. Los biofilms o biopelículas son comunidades microbianas formadas por una o varias especies de microorganismos asociadas a superficies vivas o inertes. La mayoría de los

microorganismos existen en la naturaleza formando biopelículas, lo cual constituye un medio eficaz mediante el cual estos se mantienen en un nicho protegido. En el hombre, el establecimiento de las biopelículas puede conducir a una infección bacteriana crónica. Se ha demostrado que las biopelículas presentan una mayor resistencia al tratamiento con antibióticos y son resistentes a la erradicación por el sistema inmune. Nuestro grupo también está implicado en la identificación de los principales reguladores que intervienen en la percepción de las señales ambientales mediante "quórum sensing", que inducen la formación de biopelículas y su dispersión. Y también en la caracterización de los determinantes moleculares que contribuyen a la virulencia y a la resistencia a los antibióticos en estos microorganismos. Para nuestros estudios, disponemos de un amplio abanico de herramientas de genómica y transcriptómica. Varias especies del género Acinetobacter se han vuelto muy importantes como patógenos asociados a infecciones hospitalarias, especialmente en las unidades de cuidados intensivos. Estas bacterias pueden sobrevivir en el ambiente hospitalario durante largos periodos de tiempo y tienen una gran propensión a desarrollar resistencias a múltiples clases de antibióticos. Esta tendencia al aumento de resistencias se ha convertido en una gran preocupación, al reducir las opciones terapéuticas para combatir estas cepas multirresistentes. Mientras que la epidemiología y los mecanismos de resistencia de Acinetobacter baumannii han recibido especial atención durante los últimos años, las bases moleculares, genéticas y fenotípicas de la virulencia de A. baumannii, A. pittii, y A. nosocomialis son escasamente conocidas, y tampoco se ha incrementado de manera importante la información sobre la respuesta del hospedador a estas bacterias.

Respondiendo a la necesidad de estudios sobre los mecanismos de interacción con células del



hospedador y la resistencia a los antimicrobianos, nuestro grupo desarrolla una investigación multidisciplinar sobre interacciones hospedador-patógeno en estas tres especies de Acinetobacter.

Los objetivos de nuestro grupo en este campo son: (1) Desarrollar nuevas herramientas para el estudio de interacciones hospedador-patógeno en Acinetobacter. (2) Estudiar el impacto de diferentes antibióticos a concentraciones sub-inhibitorias (sub-CMIs) sobre la producción de biocapas en Acinetobacter, y sobre las interacciones hospedador-patógeno in vitro. (3)

Desenmarañar la dinámica y el papel de las vesículas extracelulares producidas por las especies de Acinetobacter. (4) Realizar un análisis detallado de la respuesta de células inmunitarias y no inmunitarias humanas frente a cepas de Acinetobacter de diferentes fenotipos.

3. Mecanismos de resistencia en bacterias Gram positivas.

El grupo está interesado en la caracterización de los elementos genéticos implicados en la resistencia a antibióticos y en su diseminación en enterococos multirresistentes, principalmente Enterococcus faecalis y
Enterococcus faecium. Ambos son patógenos oportunistas asociados a bacteriemia, endocarditis e infecciones urinarias y postoperatorias que normalmente habitan en el intestino humano. Y son, además, uno de los organismos más comunes implicados en infecciones nosocomiales a nivel mundial. En concreto, estamos interesados en el mecanismo de conjugación de diversos elementos genéticos móviles enterococales, entre ellos, los plásmidos de respuesta a feromonas, que son plásmidos que se encuentran en casi un 95% de las cepas clínicas de E. faecalis asociadas a brotes hospitalarios y que pueden

transferirse con una frecuencia del 100%.

En Enterococcus faecalis Se está analizando la regulación transcripcional del plásmido conjugativo pAD1, que codifica múltiples resistencias a antibióticos y se encuentra en el 90% de las cepas clínicas de E. faecalis asociadas a brotes hospitalarios. El promotor de la relaxasa del plásmido se ha caracterizado y se ha visto que tanto la relaxasa como una proteína codificada por un gen adyacente regulan negativamente su propia expresión. Además se ha analizado la regulación de la transferencia del plásmido, de forma que una región de unos 25- 30 Kb se induce en respuesta a la feromona específica cAD1. Para que esta inducción tenga lugar es clave TraE1, de forma que mutaciones dentro de este gen impiden la transferencia del plásmido. Nuestro objetivo inmediato es la caracterización del mecanismo molecular por el que TraE1 regula la expresión del resto de los genes de conjugación.

Se están analizando tanto los clones de E. faecium como los plásmidos que han diseminado la resistencia a vancomicina en nuestro hospital durante el periodo 2002-2012. Principalmente 3 clones (ST132, ST18 y ST192, todos E. faecium CC17) son responsables de la transmisión de la resistencia a glucopéptidos. Todos estos clones llevan múltiples plásmidos que se están caracterizando. La resistencia a vancomicina se localiza en variantes del transposón Tn1546que contienen principalmente ISEf1 e IS1216. Otra parte importante de nuestro trabajo se centra en la identificación y caracterización de plásmidos en cepas hospitalarias de E. faecium multirresistentes, sobre todo en lo que respecta a plásmidos implicados en la aparición y diseminación de la resistencia a vancomicina, aunque sin olvidar otros genes de resistencia a antibióticos importantes en enterococos (resistencia a aminoglucósidos y macrólidos, principalmente) y su asociación a determinados elementos genéticos móviles.

Nuestro grupo también está estudiando la resistencia a antimicrobianos en distintas especies de corinebacterias. Estas bacterias están ampliamente distribuidas en la naturaleza, encontrándose en el suelo, agua y también en la piel y mucosas de hombres y animales. Algunas especies son patógenas para el hombre. La especie más importante es C. diphteriae, pero también estudiamos otras como, C. amycolatum, C. xerosis, y C. jeikeium, ya que buena parte de los aislados clínicos de estas especies son resistentes a varios antibióticos.

En los últimos años hemos realizado además, estudios sobre las resistencias a antibióticos en cepas de las especies C. striatum y C. urealyticum aisladas en el hospital Marqués de Valdecilla y su entorno cercano. Nos centramos en los mecanismos de resistencia y propagación, y también realizamos estudios de su interacción con el hospedador.

El grupo trabaja además en el desarrollo y aplicación de nuevos métodos para diagnóstico en Microbiología Clínica basados en la genómica y la proteómica, principalmente orientados a su aplicación a las actinobacterias.

4. Metodología diagnóstica y epidemiológica.

El diagnóstico molecular de las enfermedades infecciosas se ha vuelto una herramienta indispensable en nuestro Servicio de Microbiología, incluyendo la secuenciación y la detección directa de genes relacionados con la taxonomía microbiana y los mecanismos de resistencia a antibióticos. Durante más de 100 años, los agentes causantes de enfermedades infecciosas han sido identificados directamente tras el aislamiento y crecimiento en cultivo gracias a su fenotipo. En la era de la biología molecular, tenemos la oportunidad de detectar patógenos de forma más rápida y más precisa basándonos en su huella genética. Los métodos moleculares, esencialmente los pasados en la reacción en cadena de la polimerasa (PCR) se han vuelto indispensables para el diagnóstico de las enfermedades infecciosas. En la última década, ha habido un incremento extraordinario de la utilización de test moleculares para diagnosticar y controlar las enfermedades infecciosas. Como resultado, nuestro laboratorio de Microbiología Clínica en el Hospital Universitario Marqués de Valdecilla ofrece un número creciente y consolidado de técnicas de amplificación de ácidos nucleicos para la detección e identificación de patógenos bacterianos, víricos y fúngicos. Un buen ejemplo de nuestra experiencia es laamplificación y secuenciación del 16S rDNA, genes de resistencia y mutaciones relacionadas con la resistencia a antibióticos.

Dada la complejidad del mundo microbiano y del aumento y sofisticación de las técnicas de amplificación de ácidos nucleicos, hemos adquirido no solo experiencia para desarrollar ensayos sino también para la rutina clínica, lo que mejora la atención al paciente, reduce la utilización de antibióticos, optimiza la utilización de pruebas diagnósticas y aumenta la eficiencia nuestro laboratorio y del hospital.

Recientemente hemos incorporado un sistema de espectrometría de masas automatizado para la identificación microbiana (Matrix Assisted Laser Desorption Ionization Time-of-Flight, MALDI-TOF) con una amplia base de datos de especies clínicamente importantes, que nos permite obtener resultados en minutos.

Por otra parte, es interesante analizar aislados múltiples pertenecientes a una especie para determinar si representan una cepa única o múltiples cepas. El proceso de diferenciar cepas basado en sus diferencias genotípicas y fenotípicas se conoce como “tipificación”. Los métodos de genotipificación implican el estudio del ADN microbiano.

El desarrollo de métodos de genotipipificación molecular ha revolucionado la posibilidad de

clasificar los microorganismos a nivel de subespecie, lo que es crucial para descifrar la relación molecular entre los aislados, para estudios epidemiológicos. Para ello, los nuevos métodos de tipado basados en PCR han supuesto un avance importante para determinar la epidemiología molecular de los microorganismos.

Las principales ventajas de estos métodos son la flexibilidad, la simplicidad técnica y el alto poder discriminatorio. Aunque la mayoría de estos métodos basados en PCR son más rápidos, sencillos y de fácil interpretación, en algunos casos (dependiendo de la especie estudiada) se requieren otras aproximaciones para estudiar la relación clonal entre los aislados. Estas incluyen la electroforesis en campo pulsado (PFGE) técnica principal para el tipificación de la mayoría de bacterias y hongos, el tipado de secuencias multilocus (MLST), y el tipificación VNRT. Estos métodos de tipificación son realizados en las distintas áreas de nuestro laboratorio y son muy útiles para el control de las infecciones en el hospital, para estudios epidemiológicos y para la comprensión de la patogénesis y las infecciones.

Mediante la utilización de esta metodología, los principales objetivos de nuestro grupo incluyen: estudiar la epidemiología molecular de las bacterias resistentes, y en particular del problema de la multirresistencia en el entorno hospitalario, e implementar el uso de herramientas de secuenciación masiva para una mejor integración de la información sobre resistencia y virulencia.

5. Actividad in vitro de nuevos antimicrobianos.

Diversos organismos mundiales, incluida la OMS, han alertado que la resistencia a antimicrobianos constituye uno de los principales problemas de salud en todo el mundo, y una de las estrategias prioritarias para afrontarlo es el desarrollo de nuevos antimicrobianos. Nuestro grupo participa en proyectos multicéntricos de evaluación de nuevos antimicrobianos, consistentes en medir la actividad in vitro de los mismos frente a la amplia colección de cepas de la que dispone nuestro grupo. Asimismo, participamos en la evaluación con métodos de referencia de los sistemas automatizados de antibiograma, especialmente cuando estos sistemas incorporan antimicrobianos nuevos. En los últimos años hemos estudiado la actividad de daptomicina, linezolid, chelocardina y ceftarolina. Con algunos de ellos, nuestro grupo ha colaborado también en el establecimiento de puntos de corte de sensibilidad para definir categorías clínicas.

Nuestro grupo ha colaborado además en el estudio de las variables que influyen en la actividad in vitro de una nueva cefalosporina (ceftarolina) con actividad frente a Staphylococcus aureus resistente a meticilina (MRSA). Para este mismo compuesto, hemos analizado la idoneidad de los puntos de corte para definir categorías clínicas. Hemos contribuido al estudio in vitro de un nuevo antimicrobiano, chelocardina, cuya síntesis se ha mejorado mediante ingeniería genética y cuya actividad in vitro frente a diversas especies de bacterias multirresistentes resulta prometedora. Los estudios en este ámbito se han desarrollado en colaboración con miembros de la Universidad de Cantabria y de la Universidad de Lubljana (Eslovenia). Recientemente, hemos coordinado y participado en la elaboración de una guía sobre la preparación de datos acumulados de antibiograma. Esta guía ayudará al proceso de estandarización de los estudios locales y nacionales de seguimiento y evaluación de la resistencia a los antimicrobianos. EL grupo está iniciando su colaboración con otros grupos de IDIVAL en la desarrollar las bases que permitan la aplicación de la nanomedicina en terapia antimicrobiana.

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F.I.:1,014.

27. Arminanzas, Carlos, Tigera, Teresa, Ferrer, Diego, Calvo, Jorge, Antonio Herrera, Luis, Pajaron, Marcos, Gomez-Fleitas, Manuel, Carmen Farinas, Maria.
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Rev Esp Quimioter. 2016;29:123-129.
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Reviews

1. Rodríguez-Martínez JM, Machuca J, Cano ME, Calvo J, Martínez-Martínez L, Pascual A.
Plasmid-mediated quinolone resistance: Two decades on.
Drug Resist Updat. 2016;29:13-29.
F.I.:7,950. [doi:10.1016/j.drup.2016.09.001]

Doctoral Thesis

1. Alicia Márquez López.
Resistance to quinolones and production of hemolysins in clinical isolates of E. coli.
Director: **Luis Martínez Martínez.**
University of Cantabria.

2. José Quintanar Lartuno. Peritonitis en diálisis peritoneal.
Peritonitis in peritoneal dialysis. Experience over a decade: evolution, microbiological profile, antimicrobial sensitivity and differences according to age.
Directors: **Manuel Antonio Arias Rodríguez, Luis Martínez Martínez.**
University of Cantabria.

PROJECTS

Projects

1. José Ramos Vivas.
Host-pathogen key interactions in Acinetobacter species of clinical relevance.
PI13/01310.
INSTITUTO DE SALUD CARLOS III.
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

—

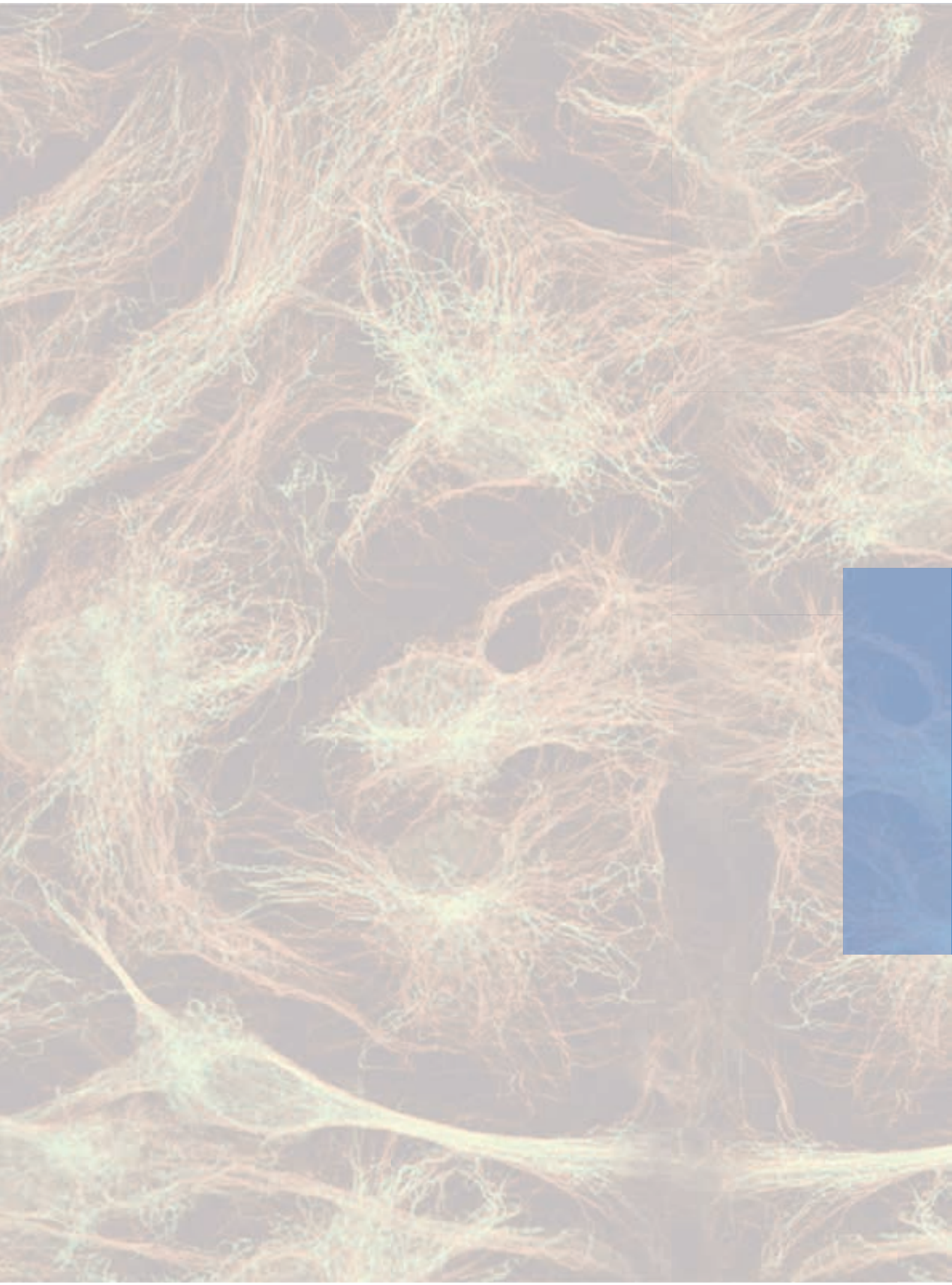
2. Alain Antonio Ocampo Sosa.
Identification and functional characterization of new components of type VI secretion systems and the molecular bases of their regulation in clinical strains of Pseudomonas aeruginosa. PI15/00009.
INSTITUTO DE SALUD CARLOS III.
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

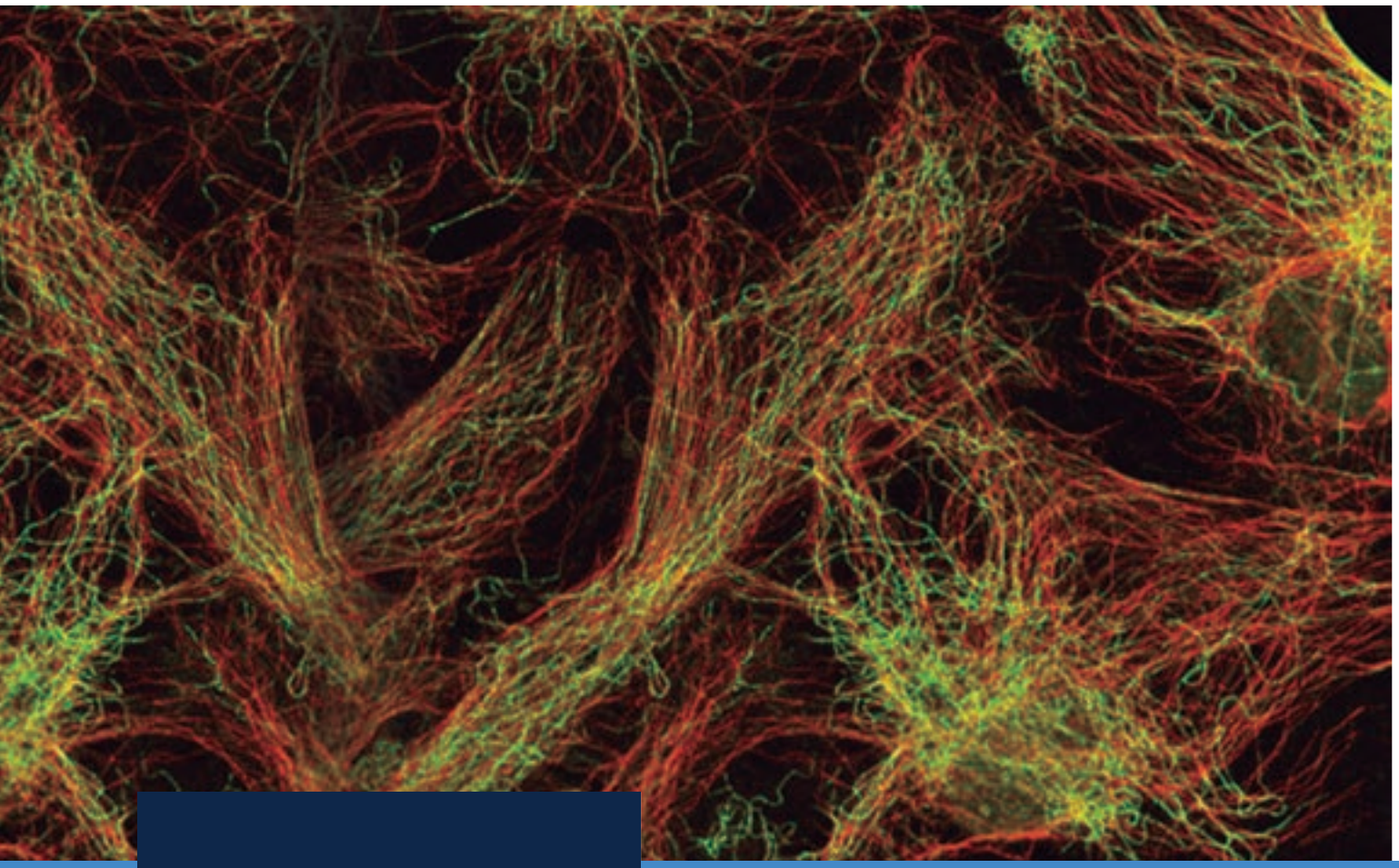
—

3. José Ramos Vivas.
Integrated biology of infection and antimicrobial resistance of Acinetobacter baumannii and A. PITTII.
PI16/01103.
INSTITUTO DE SALUD CARLOS III.
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

—

4. María Victoria Francia Gil.
Induction of the conjugative transfer of the pheromone response plasmids.
PI16/01535.
INSTITUTO DE SALUD CARLOS III.
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.





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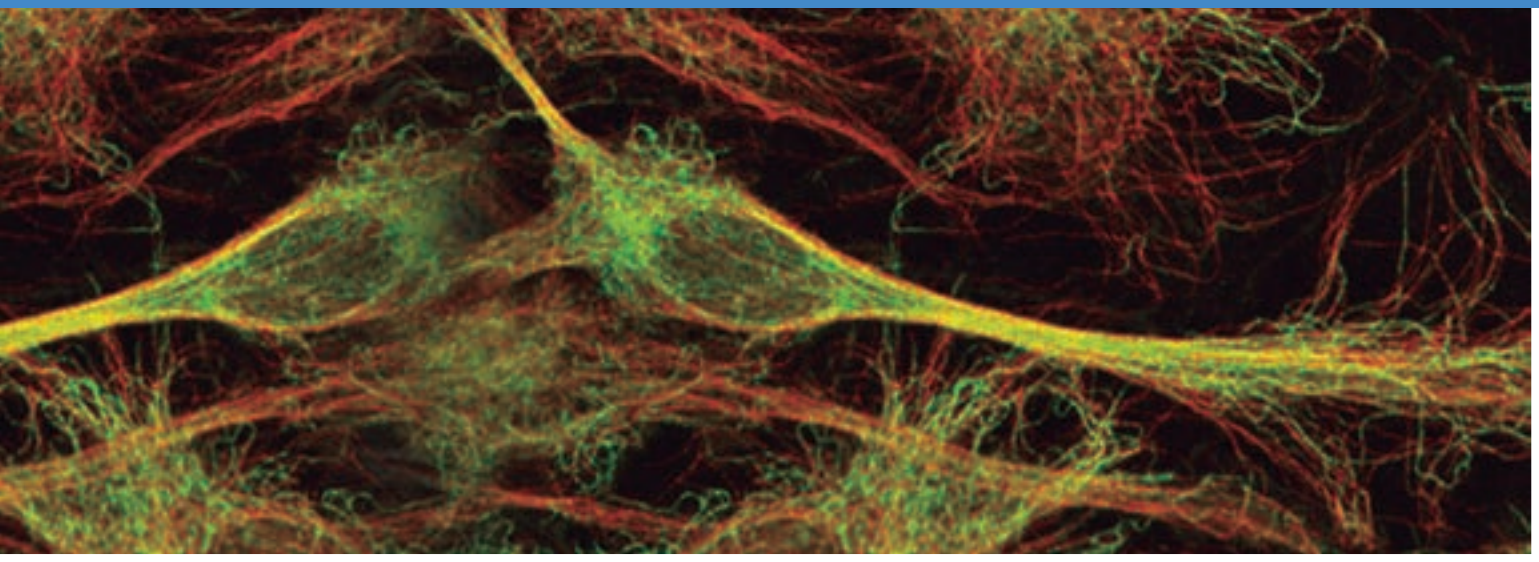

Diagnosis and Treatment Using Imaging (radiology)

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Clinic group

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Research Lines

Active research lines:

> Evaluation of new low percutaneous breast biopsy devices Image control.

> Study of arteriovenous malformations in patients with Telangiectasia Hemorrhagic Hereditary (THH).

> Quantification of coronary calcium and carotid ultrasonography and as predictors of cardiovascular risk.

> Development of hybrid techniques: surgical-radiological in the treatment of Vascular pathology.

> Evaluation of the usefulness and complications of thermoablation treatments in patients with neoplastic disease

> Ultrasonic contrasts in the study of hepatic, renal and intestinal pathology.

> Study of cerebral connectivity with diffusion tensor MRI.

> Anatomic-radiological correlation studies in cutaneous pathology.

> Ultrasound in the diagnosis and follow-up of hidradenitis suppurativa.

> Anatomical-radiological (MR) correlation in corpse.

> Contribution of multi-cut CT in the evaluation of perforating arteries prior to Plastic reconstructive surgery.

PUBLICATIONS:

IMPACT FACTOR | 32,138

Original articles

1. Peeters K, Palaima P, Pelayo-Negro AL, García A, Gallardo E, García-Barredo R, Mateiu L, Baets J, Menten B, De Vriendt E, De Jonghe P, Timmerman V, Infante J, Berciano J, Jordanova A.
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2. Berciano J, Gallardo E, Orizaola P, Marco de Lucas E, García A, Pelayo-Negro AL, Sedano MJ.
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J. Neurol. Neurosurg. Psychiatry. 2016;87:563-565.
F.I.:6,431. [doi:10.1136/jnnp-2015-310601]

3. Zarrabeitia, Roberto, Ojeda-Fernandez, Luisa, Recio, Lucia, Bernabeu, Carmelo, Parra, Jose A., Albinana, Virginia, Botella, Luisa M.
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Thromb Haemost. 2016;115:1167-1177.
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4. Parra JA, Cuesta JM, Zarrabeitia R, Fariñas-Álvarez C, Bueno J, Marqués S, Parra-Fariñas C, Botella ML, Bernabéu C, Zarauza J.
Screening pulmonary arteriovenous malformations in a large cohort of Spanish patients with hemorrhagic hereditary telangiectasia.
Int J Cardiol. 2016;218:240-245.
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5. Ibáñez-Bravo S, Banzo I, Quirce R, Martínez-Rodríguez I, Jiménez-Bonilla J, Martínez-Amador N, Parra JA, González-Macías J, Carril JM.
Ventilation/Perfusion SPECT lung scintigraphy and computed tomography pulmonary angiography in patients with clinical suspicion of pulmonary embolism.
Rev Esp Med Nucl Imagen Mol. 2016;35:215-220.
F.I.:0,983. [doi:10.1016/j.remn.2015.12.008]

Reviews

1. Drake-Pérez M, Marco de Lucas E, Lyo J, Fernández-Torre JL.
Neuroimaging features in subacute encephalopathy with seizures in alcoholics (SESA syndrome).
Seizure. 2016;40:102-107.
F.I.:2,109. [doi:10.1016/j.seizure.2016.06.009]

2. Drake-Pérez M, Smirniotopoulos JG.
Extraparenchymal Lesions in Adults.
Neuroimaging Clin N Am. 2016;26:621-646.
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3. Hernando MF, Cerezal L, Pérez-Carro L, Canga A, González RP.
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Mineral and Lipid Metabolism

Group Leader

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red envejecimiento y fragilidad

Consolidated group

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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. Because of the actuality of the topic, bone and mineral metabolism changes in patients with hepatitis C virus infection will be tackled too. All these aspects will be approached by both cross-sectional and longitudinal studies.

3. Animal models (mainly mouse).

This line focuses on studying the Wnt/b-catenin pathway in osteoclasts, using models with conditional changes of the b-catenin gene in these cells. Animal models with gain or loss of function of b-catenin in cells of osteoclastic lineage are generated by means of the CRE/loxP technology. The Cre recombinase is placed under the control of the promoter of lysozyme M or cathepsin K, so that the osteoclast can be analyzed at different evolutive moments. Studies in other animal models assess the effect of certain therapeutic agents such as PTH and strontium ranelate on bone strength.

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, Universidad de la Laguna) and Dr. Gomez-Cimiano (Orthopedics and trauma Service, HUMV) it is developing an experimental model consisting of using mesenchymal stem cells modified in the treatment of fractures of critical size.

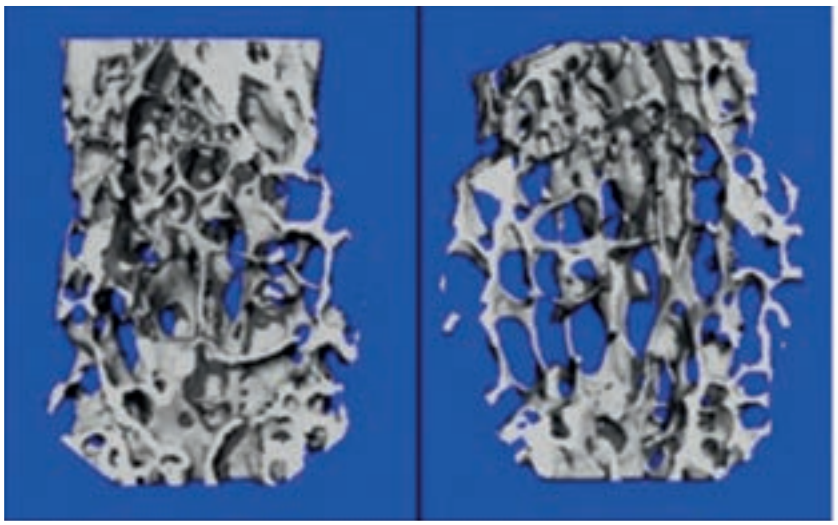

Figura.
Imágenes de hueso por micro TC de animales OVX y control.

PUBLICATIONS:

IMPACT FACTOR | 98,727

Original articles

1. González-López MA, Hernández JL, Lacalle M, Mata C, López-Escobar M, López-Mejías R, Portilla V, Fuentevilla P, Corrales A, González-Vela MC, González-Gay MA, Blanco R. **Increased prevalence of subclinical atherosclerosis in patients with hidradenitis suppurativa (HS).**
J Am Acad Dermatol. 2016;75:329-335.
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2. Martin-Cano FE, Camello-Almaraz C, Macías JG, Pozo MJ, Camello PJ. **Propagation of Intracellular Ca2+ Signals in Aged Exocrine Cells.**
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3. Ruiz P, Martin-Millan M, Gonzalez-Martin MC, Almeida M, González-Macias J, Ros MA. **CathepsinKCre mediated deletion of ßcatenin results in dramatic loss of bone mass by targeting both osteoclasts and osteoblastic cells.**
Sci Rep. 2016;6:36201-36201.
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J CLIN LIPIDOL. 2016;10:790-797.
F.I.:4,906. [doi:10.1016/j.jacl.2016.02.010]

5. Valverde L, Illescas MJ, Villaescusa P, Gotor AM, García A, Cardoso S, Algorta J, Catarino S, Rouault K, Férec C, Hardiman O, Zarrabeitia M, Jiménez S, Pinheiro MF, Jarreta BM, Olofsson J, Morling N, de Pancorbo MM. **New clues to the evolutionary history of the main European paternal lineage M269: dissection of the Y-SNP S116 in Atlantic Europe and Iberia.**
Eur J Hum Genet. 2016;24:437-441.
F.I.:4,580. [doi:10.1038/ejhg.2015.114]

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Aging (Albany NY). 2016;8:2222-2231
F.I.:3,979. [doi:10.18632/aging.101053]

7. Calvo-Río V, Blanco R, Santos-Gómez M, Rubio-Romero E, Cordero-Coma M, Gallego-Flores A, Veroz R, Torre I, Hernández FF, Atanes A, Loricera J, González-Vela MC, Palmou N, Hernández JL, González-Gay MA. **Golimumab in refractory uveitis related to spondyloarthritis. Multicenter study of 15 patients.**
Semin Arthritis Rheum. 2016;46:95-101.
F.I.:3,946. [doi:10.1016/j.semarthrit.2016.03.002]

8. Toraño EG, Bayón GF, Del Real Á, Sierra MI, García MG, Carella A, Belmonte T, Urdinguio RG, Cubillo I, García-Castro J, Delgado-Calle J, Pérez-Campo FM, Riancho JA, Fraga MF, Fernández AF. **Age-associated hydroxymethylation in human bone-marrow mesenchymal stem cells.**
J TRANSL MED. 2016;14:207-207.
F.I.:3,694. [doi:10.1186/s12967-016-0966-x]

9. Olmos JM, Hernández JL, García-Velasco P, Martínez J, Llorca J, González-Macías J. **Serum 25-hydroxyvitamin D, parathyroid hormone, calcium intake, and bone mineral density in Spanish adults.**
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F.I.:3,445. [doi:10.1007/s00198-015-3219-6]

10. Pérez-Campo FM, Santurtún A, García-Ibarbia C, Pascual MA, Valero C, Garcés C, Sañudo C, Zarrabeitia MT, Riancho JA. **Osterix and RUNX2 are Transcriptional Regulators of Sclerostin in Human Bone.**
Calcif Tissue Int. 2016;99:302-309.F.I.:3,052. [doi:10.1007/s00223-016-0144-4]

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Neurodegener Dis. 2016;16:337-341.
F.I.:2,937. [doi:10.1159/000445750]

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QJM. 2016;109:345-346.
F.I.:2,824. [doi:10.1093/qjmed/hcw008]

13. Napal JJ, Neila S, Pérez-Montes R, Sierra I, Ruiz S, Hernández JL. **The role of coagulation disorders in patients with retinal vein occlusion.**
QJM. 2016;109:97-102.
F.I.:2,824. [doi:10.1093/qjmed/hcv088]

14. Riancho-Zarrabeitia L, García-Unzueta M, Tenorio JA, Gómez-Gerique JA, Ruiz Pérez VL, Heath KE, Lapunzina P, Riancho JA. **Clinical, biochemical and genetic spectrum of low alkaline phosphatase levels in adults.**
Eur J Intern Med. 2016;29:40-45.
F.I.:2,591. [doi:10.1016/j.ejim.2015.12.019]

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Adv Ther. 2016;33:658-669.
F.I.:2,503. [doi:10.1007/s12325-016-0314-9]

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Histopathologic differences between cutaneous vasculitis associated with severe bacterial infection and cutaneous vasculitis secondary to other causes: study of 52 patients.
Clin Exp Rheumatol. 2016;34:93-97. F.I.:2,495.

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17. Ferraz-Amaro I, López-Mejías R, Ubilla B, Genre F, Tejera-Segura B, de Vera-González AM, González-Rivero AF, Olmos JM, Hernández JL, Llorca J, González-Gay MA.
Proprotein convertase subtilisin/kexin type 9 in rheumatoid arthritis.
Clin Exp Rheumatol. 2016;34:1013-1019.
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2. Javier Pérez López. **Study of the role of mir-148a in the regulation of genes of lipid metabolism and adipogenesis.** Director: **José Carlos Rodríguez Rey.** University of Cantabria.

PROJECTS

Projects

1. Jesús González Macías. **Thematic Network of Cooperative Research in Aging and Fragility.** RD12/0043/0009. INSTITUTO DE SALUD

2. José Manuel Olmos Martínez. **Study of the bone and mineral metabolism of the postmenopausal and male female population over 50 years of age attended by a Health Center in Cantabria.** PI15/00521. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD.

3. José Antonio Riancho Moral. **Study of mesenchymal stem cells in osteoporosis: Role of long non-coding RNAs (lncRNAs) and regenerative potential.** PI16/00915. INSTITUTO DE SALUD CARLOS III. MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD, INSTITUTO DE SALUD CARLOS III.

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