2015

Activity report

Valdecilla
Instituto de Investigación Sanitaria
IDIVAL

We have the research in our DNA.

Since 1929

Valdecilla
Instituto de Investigación Sanitaria IDIVAL

Editor: IDIVAL
Legal Deposit: SA 525-2015

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2015
Memoria de Actividad

Valdecilla Instituto de Investigación Sanitaria IDIVAL

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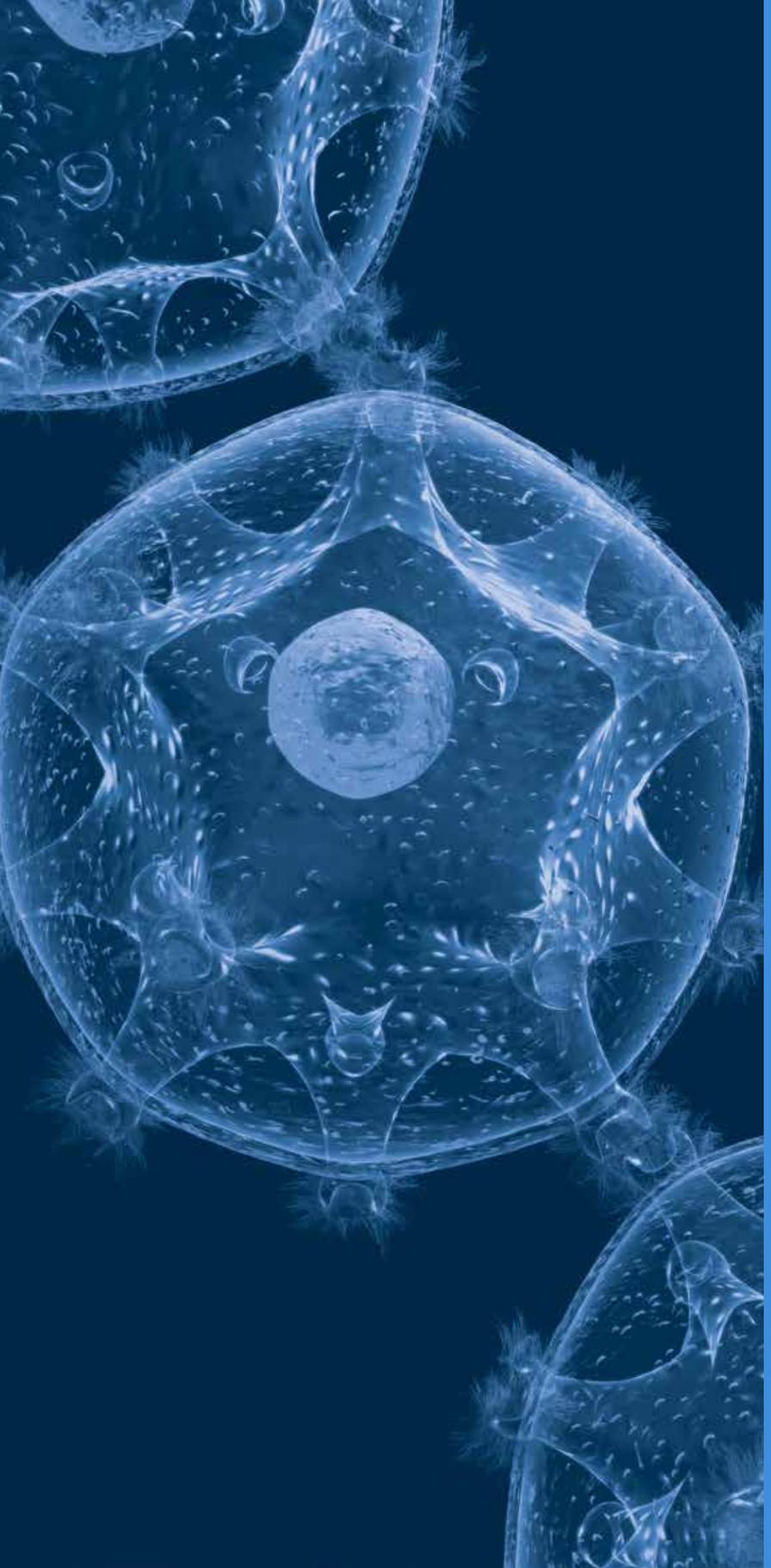


2015
Memoria de Actividad

Valdecilla
Instituto de Investigación Sanitaria IDIVAL

Prologue

The Marqués de Valdecilla Research Institute (IDIVAL) is an organisation based in Cantabria promoting excellence in research, particularly in the Marqués de Valdecilla University Hospital. IDIVAL follows the Spanish model for Health Research Institutes proposed by the Carlos III Health Institute, which encourages translational research as a basis for improving patient care.

Translational research in the Valdecilla setting is carried out by doctors in collaboration with laboratory researchers. This interaction is a key element in developing healthcare of the highest level. Moreover, research requires highly qualified professionals with advanced knowledge in disease. Following these principles, IDIVAL fosters collaborative teams comprised of basic and clinical researchers both from academia and the healthcare environment who are able to transform their discoveries into practical solutions for patients, and ultimately ensure that these discoveries are translated into benefits of the day-to-day medical practice.

Research and innovation are also a driving force for economic and social development. IDIVAL's commitment to our society is based on increasing knowledge about disease in order to not only to apply this knowledge, but to also transform our productive model into a model at least partially centred around the generation of knowledge.

The Marqués de Valdecilla University Hospital, together with the Medicine Faculty of the University of Cantabria, make up IDIVAL and the origin of translational research in Cantabria. Both seek to transform our region by improving the efficiency and quality of clinical and translational research and converting knowledge into an economic and social driving force.

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

None of IDIVAL's achievements in its short yet fruitful existence can be credited to this Managing Director of the Marqués de Valdecilla University Hospital, who has only held the position for a few months at the time of writing. To give some examples, in 2015 IDIVAL produced more than 400 indexed publications (half of which were from the first quartile), had nearly 40 active or granted research projects and participated in over 100 clinical trials. Promoting research is one of the marks of IDIVAL, as evidenced by the eight grant programmes open last year. The results of IDIVAL in a region of such a small size are undoubtedly commendable, but we should also see improving them as a goal. Therefore, in addition to strengthening initiatives with proven results, we have to continue taking steps to boost innovation and the external appeal of IDIVAL. For example, we need to improve how we capture research projects, not only in numbers but in quality and internationalisation and attract more truly competitive clinical trials, in phases 1 and 2. Innovative proposals already under way such as the EVALTEC programme, evaluation of new technologies, support for specific curricular development of medical residents who choose this hospital with a number below one hundred, or support for capturing new Heads of Department with proven track records not only demonstrate the renewed commitment of IDIVAL to innovation, but contribute to reinforcing the innate philosophy of the hospital since its first manager, the renowned Wenceslao Lopez Albo, to try to attract the best talent. Only through work coordinated with the University of Cantabria, the Virtual Hospital or institutions such as the IBBTEC will it be possible to achieve these ambitious goals.

Julio Pascual Gómez
Manager of the Marqués de Valdecilla University Hospital

Throughout 2015, IDIVAL started its undertaking as an accredited Research Institute, achieving **a number of important results:**

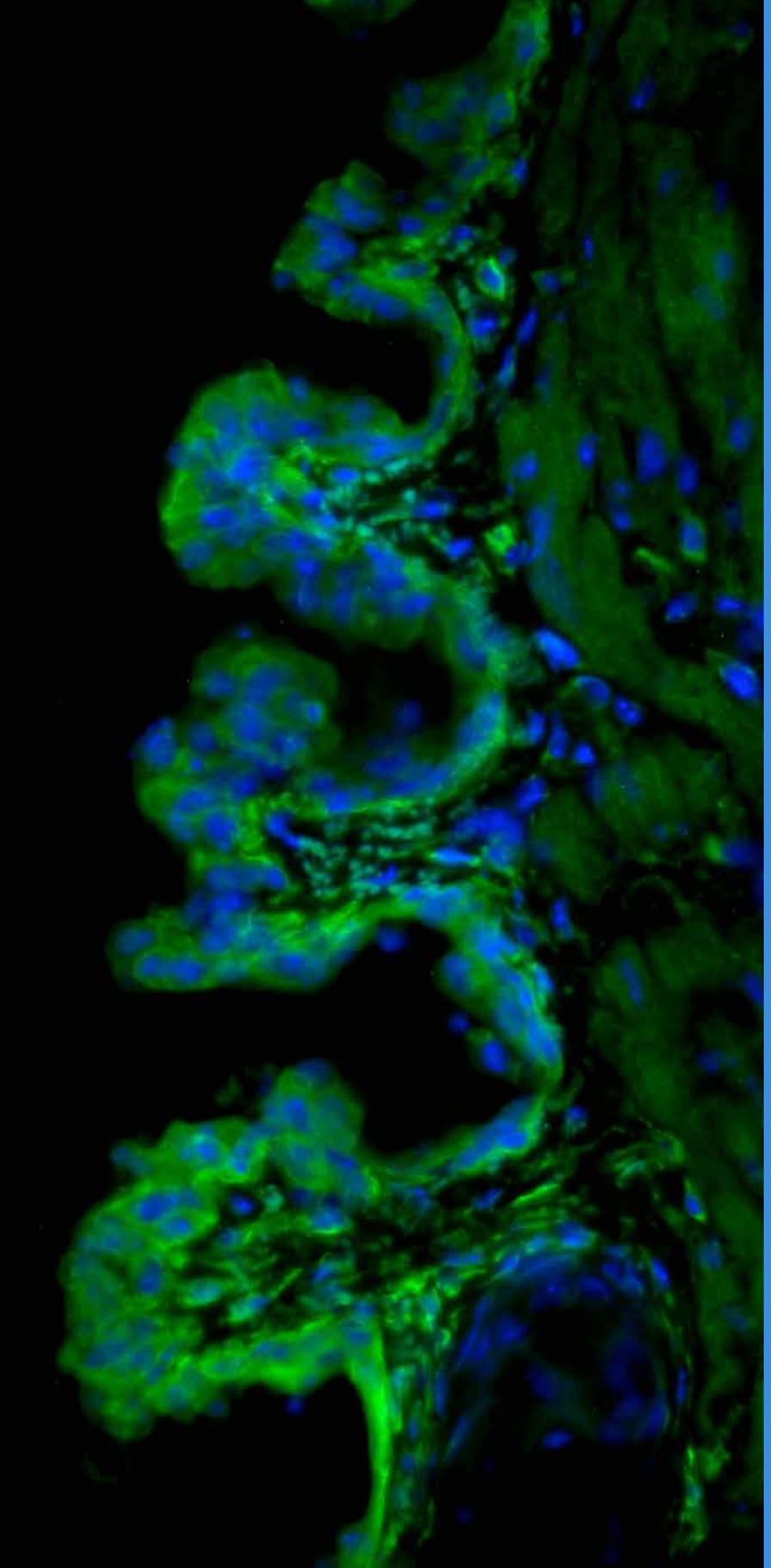
- The total volume of publications continues to increase significantly, as does their quality, with a notable presence of publications in first decile or first quartile magazines (those considered as the best and most difficult) led by IDIVAL researchers.
- It has reached unprecedented success in being granted resources through the call for projects of excellence of the ISCIII; thus IDIVAL is the only accredited research institute in Spain that has managed to receive support for two different integrated projects of excellence.
- In collaboration with the University of Cantabria, it has put out a call for predoctoral research training, allocating funds to finance seven positions.
- It announced a call for research projects for young researchers, receiving a total of around 20 projects; after external evaluation, it granted funding for five projects by novice researchers.
- It has continued the call for post-MIR training grants through the call known as Post-MIR Valdecilla contracts (ex - Lopez Albo).

These successes **should not let us forget our ongoing commitments**, such as:

- Capturing European projects.
- Consolidating research groups in areas with great clinical activity.
- Capturing and consolidating researchers of excellence.
- Publications led by IDIVAL researchers in magazines of excellence.

Management and staff at IDIVAL are committed to promoting initiatives to improve these areas in order to support researchers.

Miguel Ángel Piris
Scientific Director of IDIVAL
Head of the Anatomical Pathology Department
Marqués de Valdecilla University Hospital



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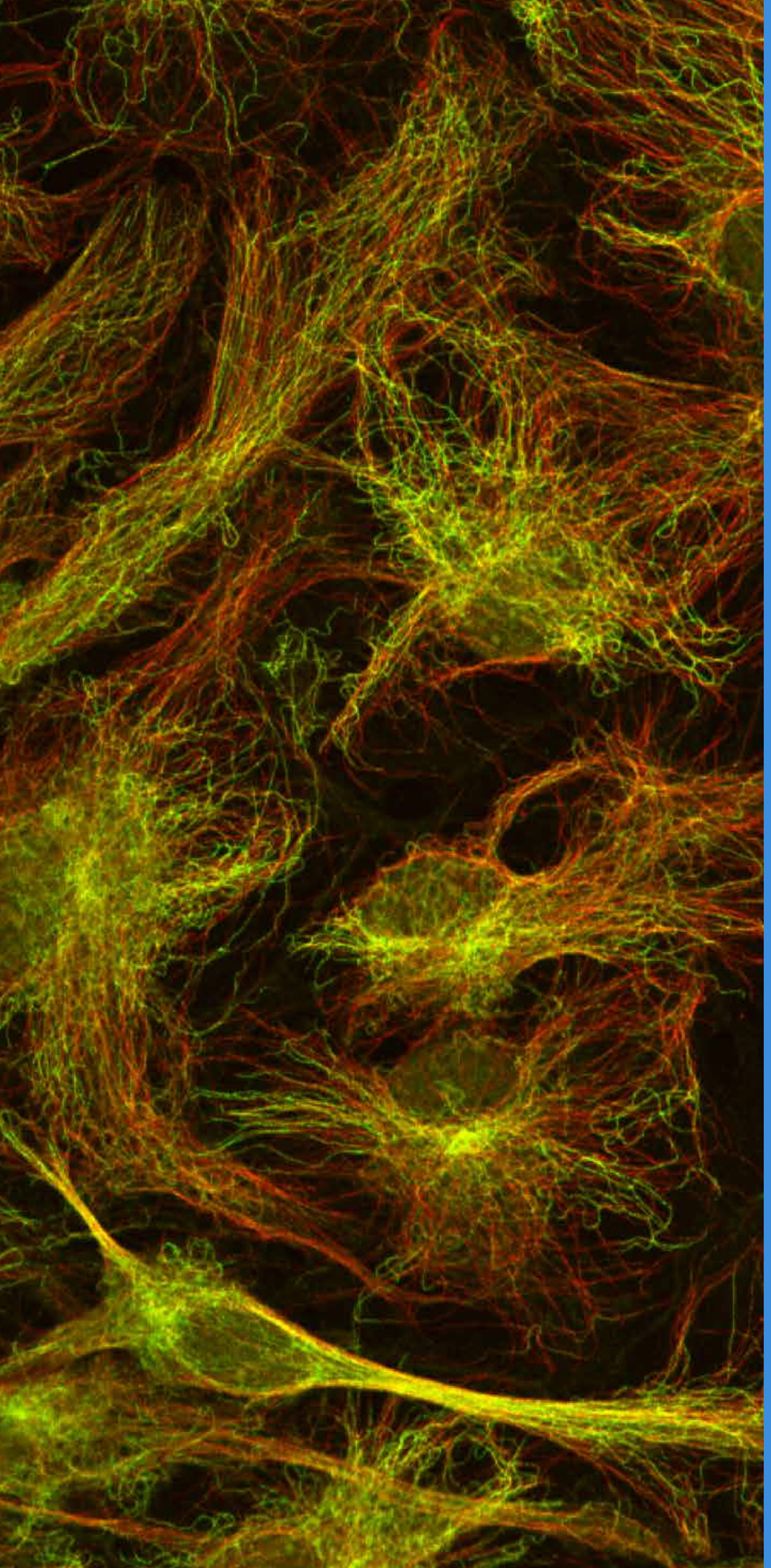
Valdecilla

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 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.



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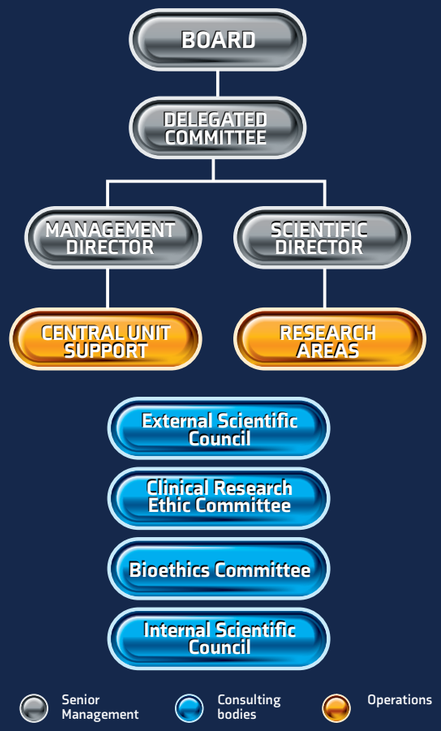
Organisational Structure

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. José Carlos Gómez Sal.
Dean of the University of Cantabria

Chairs:

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

D. Javier León Serrano.
Professor in the Department of Molecular Biology. University of Cantabria Director of the Institute of Biomedicine and Biotechnology of 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. Daniel Casanova Rituerto.
Section Head. General Surgery Department. Marqués de Valdecilla University Hospital. Professor in the Department of Medicine and Surgery. University of Cantabria

D. Javier Crespo García.
Head of the Digestive System Department. Marqués de Valdecilla University Hospital.

Professor in the Department of Medicine and Surgery. University of Cantabria

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 Board members were renewed in 2015. The IDIVAL Board met twice in 2015. At these meetings, the audited accounts and annual report for 2014 and action plans and budget for 2016 were approved.

DELEGATED COMMITTEE

President:

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

Chairs:

D. Ángel Pazos Carro.
Assistant Dean of Investigation and Knowledge Transfer. University of Cantabria Representative of the 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. 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.

EXTERNAL SCIENTIFIC COUNCIL

The External Scientific Council contributes as a scientific advisor in achieving the scientific excellence pursued by IDIVAL. The External Scientific Council offers opinions at the request of the Board or the 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.
Assistant Physician in Medicine. Diabetes Unit / Centre for Human Genetic Research. Massachusetts General Hospital. Associate Professor. Harvard Medical School.

In the meeting that took place in 2015, the activity and the financial reports of 2014 and the budget and action plan of 2015 were reviewed. In addition, the Council assessed the monitoring undertaken by the Consolidated and Emerging Groups.

INTERNAL SCIENTIFIC COUNCIL

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

It is made up of the following individuals:

President:

Miguel Ángel Piris.
Scientific Director of Idival. Head of the Pathological Anatomy Department. Marqués de Valdecilla University Hospital.

Chairs:

Manuel Arias Rodríguez.
Coordinator of the Organ and Tissue Transplant and New Therapies Area. Head of the Nephrology 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.

José Luis Fernández-Luna.
Coordinator of the Cancer Area. Head of the Molecular Genetics Area. Marqués de Valdecilla University Hospital.

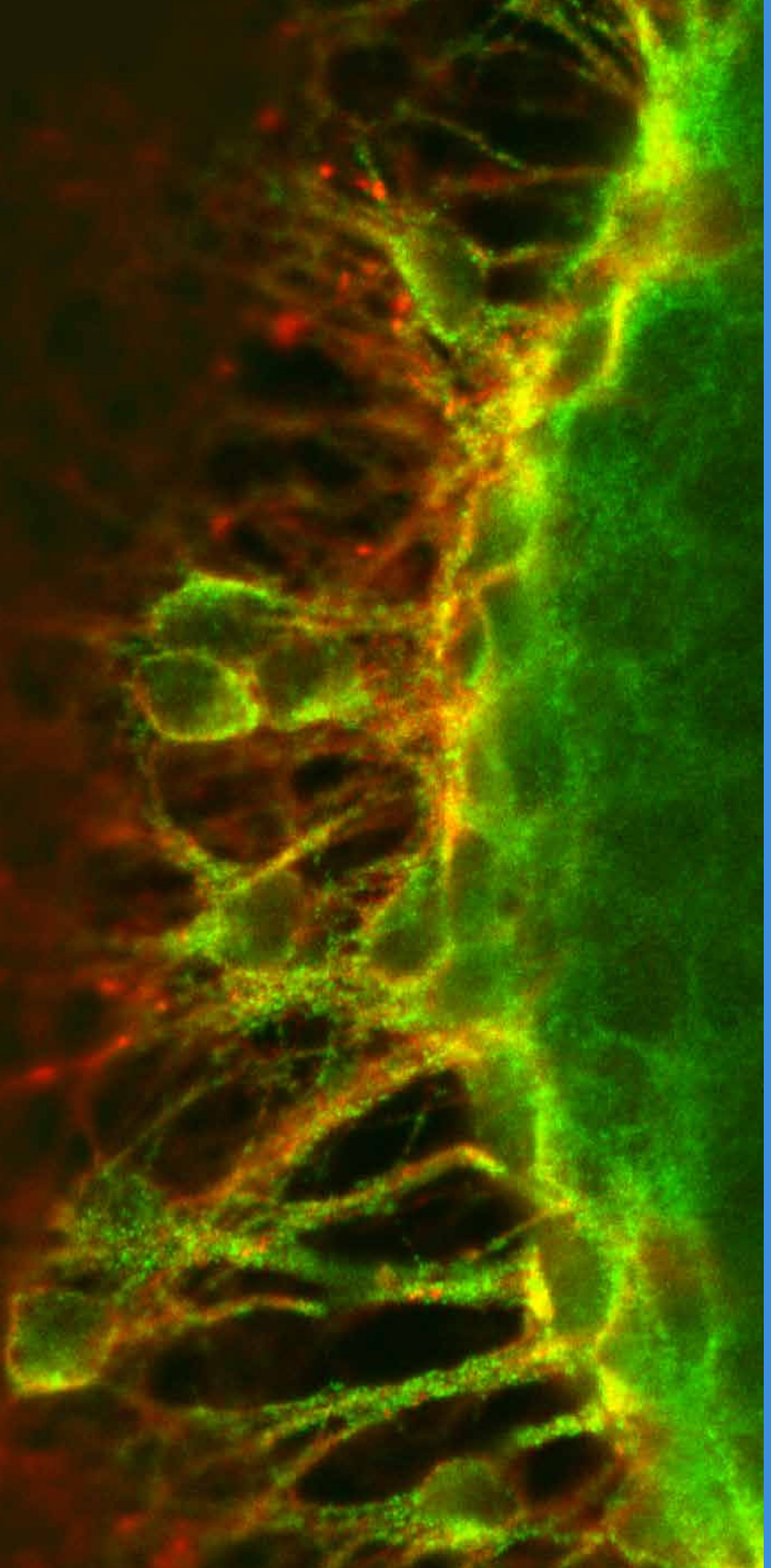
Javier Llorca Díaz.
Coordinator of the Cross-Disciplinary Area. Professor of Preventative Medicine and Public Health. University of Cantabria.

Luis Martínez Martínez.
Coordinator of the Infectious Diseases and Immune System Area. Head of the Microbiology Department. 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.



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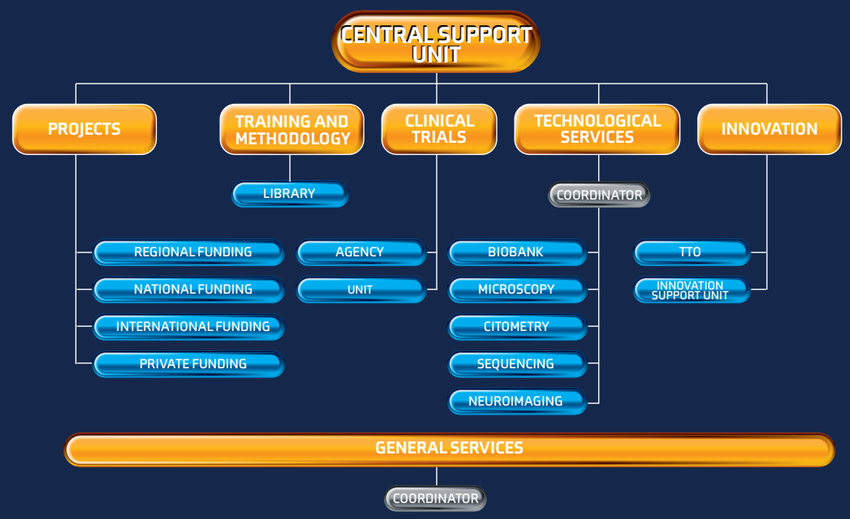
Support to Researchers

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: **Project Area,Training and Methodological Support Area, Clinical Trial Area, Technological Support Area, Innovation Area and General Services Area.**



THE IDIVAL BUILDING

IDIVAL has its own facilities, located within the 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

Coordinator
Julio Muela Carriles (IDIVAL)

Technicians:
Accounting: Javier Arce Saiz (IDIVAL)
Human Resources: Aroa Sanz Carreira (IDIVAL)

Personnel Administrator:
Billing: Laura del Río Celis (IDIVAL)
Human Resources: María José San Emeterio (IDIVAL)
Registrar: Elena Calvo (IDIVAL)

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

PROJECTS AREA

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

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.

INNOVATION AREA

Research Results Transfer Office:
Patricia Zorrilla de la Fuente (IDIVAL)

Innovation Unit
Sandra Ahedo González-Zabaleta (IDIVAL)
Laura Herrero Urigüen (IDIVAL)
Paloma Glez Álvarez (IDIVAL)

itemas isciii

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 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.

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

Librarian:
Mario Corral García (IDIVAL)

Administrators:
Rafael Lavín (HUMV)
Mª del Carmen Fuente (HUMV)

The **"Marquesa de Pelayo" Library,** located in the Marqués de Valdecilla University Hospital, is an information and documentation service that aims to offer Cantabria Healthcare Services personnel and all those with access to an updated collection to assist in maintaining the quality and improving the performance of its research functions, teachers and assistants.
The Library opened its doors in 1929 thanks to the patronage of Ms. María Luisa Gómez de Pelayo. Since its inauguration, it has been considered one of the best specialist biomedicine libraries in our country. The library, in addition to supporting the care services of the Marqués de Valdecilla University Hospital personnel, also helps teachers and students at the School of Nursing, the School of Medicine and in general, healthcare professionals. Both the library collections and the different services offered by the library are available to any clinician, teacher or researcher needing to use them.

CLINICAL TRIAL AREA

The Clinical Trial Area has a **Trial Agency and a Clinical Trial Unit** involved in the consulting, design, evaluation, management, implementation and development of clinical trials, including technical support to the Ethics Committee for Clinical Research of Cantabria.
The Clinical Trial Area **is part of the Platform for Clinical Research and Clinical Trial Units (SCREN -Spanish Clinical Research Network-) of the Carlos III Health Institute.**

Clinical Trial Agency

SCReN Spanish Clinical Research Network

Clinical Pharmacology:
María Cinta Almenara Miramón (IDIVAL)

Technician:
Blanca del Pozo Fernández (IDIVAL)
Lorena Martín Guerra (IDIVAL)

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

Clinical Trial Unit

Mª Blanca Sánchez Santiago
(Clinical Pharmacology Department, HUMV)
Mª Ángeles de Cos
(Clinical Pharmacology Department, HUMV)
Javier Adín
(Clinical Pharmacology Department, HUMV)

The IDIVAL Clinical Trial Unit, under the Clinical Pharmacology Department, located in the Marqués de Valdecilla University Hospital, measures 250 m2 and is equipped to simultaneously serve nine patients. It began operations in 2012 partially financed with funds from the Farmaindustria R&D programme.

TECHNOLOGY SUPPORT SERVICES AREA

The Technology Support Services Area is made up of six units: **Biobank, Laser Microscopy Unit, Electron Microscopy Unit, Flow Cytometry and Cell Separation Unit and Neuroimaging Unit.**
Technology Services are coordinated by Mª José Marín Vidalled (IDIVAL).

Valdecilla Biobank

Scientific Director:
Pascual Sánchez Juan
(HUMV Neurology Department)

DNA AND FLUIDS GROUP
Coordinator:
Mª José Marín Vidalled (IDIVAL)
DNA and Fluids Group Technicians:
Inés Santiuste Torcida (IDIVAL)
David Ramos Melendro (IDIVAL)

SOLID SAMPLES GROUP
Coordinator:
Santiago Montes
(Anatomical Pathology Department, HUMV)
Solid Samples Group Technicians:
José Bernardo Revert Arce (IDIVAL)
Laura Cereceda (IDIVAL)

NEUROLOGICAL TISSUES GROUP
Coordinator:
Nuria Teran Villagrá

The **VALDECILLA Biobank** 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 under the strictest conditions of quality and confidentiality. It is organised functionally into two groups: the DNA and Fluids Group and the Solid Samples Group, located on the ground floor of the IDIVAL building and in the Anatomical Pathology Department of the Marqués de Valdecilla Hospital respectively. Both groups have a wide range of sample collections of various pathologies with high scientific interest while providing a variety of services through the use of its equipment, offering comprehensive support to researchers whose projects involve the use of human biological samples.
The VALDECILLA Biobank constitutes one of the units comprising the Network of Hospital Biobanks Platform at the CARLOS III HEALTH INSTITUTE (RETICS), which has four programmes in which the Valdecilla Biobank actively participates: promotion of strategic collections, promotion of network services, R&D in biobanks and ethical, legal and social aspects. In December 2015, the unit's authorisation to operate as a biobank was renewed by the Ministry of Health of Cantabria. This authorisation implies compliance with the provisions set out in Royal Decree 1716/2011 of 18 November and its incorporation into the National Register of Biobanks of the Carlos III Health Institute.
In November 2015, the Valdecilla Biobank received the ISO9001:2015 certification for quality management.

Laser Microscopy Unit

Scientific Coordinator:
Mónica López Fanarraga (UC)

Supervising Technician:
Fidel Madrazo Toca (IDIVAL)

The IDIVAL **Laser Microscopy Unit** offers a high-end microscopy service to internal and external research groups with the ultimate goal of reaching top performance potential in their fluorescence studies in the shortest possible time. It features the latest generation equipment consisting of two sets of image systems, a confocal laser scanning microscope and a fully-automated TIRF combined Nikon A1R , which captures high-quality confocal images of cells and molecular events at high speed and sensitivity, live-cell equipment with a motorised NIKON Ti microscope and is equipped with an Epi-fluorescence module, incubation and micro-injection systems and an optical system to monitor fast processes in live cells.

Electron Microscopy Unit

Scientific Coordinator:
Miguel Lafarga (UC)

Supervising Technician:
Fidel Madrazo Toca (IDIVAL)

The Electron Microscopy Unit opened at the start of 2012. It has a JEOL transmission microscope, Model JEM-1011 equipped with a high-res Gatan digital camera, mod. SC1000 Orius, which provides excellent image quality. This microscope allows for the analysis of ultrathin sections of cells and tissues, as well as the observation of microorganism and macromolecular complex preparations contrasted with negative stain.

Both the laser microscopy and electron microscopy units organise an annual course on microscopy and preparation of samples for researchers and support personnel.

Cytometry and Cell Separation Unit

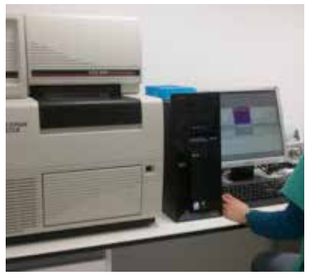
Scientific Coordinator:
Marcos López Hoyos
(Immunology Department, HUMV)

Technical coordinators:
Dr. David San Segundo Arribas
(Immunology Department, HUMV)
Dra. Lorena Álvarez Rodríguez (IDIVAL)

Laboratory technicians:
Carolina Santa Cruz Llata (IDIVAL)

The Flow Cytometry and Cell Separation Unit was created in 2005 as a support unit to IDIVAL research and operates within the Haematology Department of the Marqués de Valdecilla University Hospital. 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 AutoMACS 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.

Genomics Unit

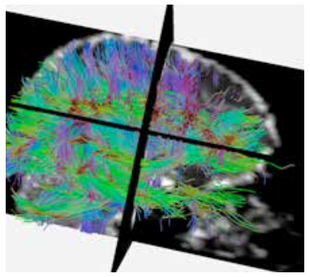


The Genomics Unit works under the Molecular Genetics Unit of the Marqués de Valdecilla University Hospital, located on the first floor of the IDIVAL building. It has functioned as such since 2002, performing care-related genetic studies for hospitals and health centres in Cantabria and other regions 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.
In 2015, space was assigned at the IDIVAL building for its physical installation.

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, stabling and animal studies services.

- Stabling and Animal Studies Services (SEEA)
- Materials Characterisation Service (SERCAMAT)
- Transmission Optical Microscopy Service (SERMET)
- Supercomputing Service
- Hydrobiology Laboratory (Hydraulic research)
- Chromotography Service
- Advanced Microscopy (IBBTEC)
- Mass Sequencing Service (IBBTEC)

IDIVAL RESEARCH GRANTS

In 2015, IDIVAL developed its line of promoting research through eight grant programmes. 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 2015, IDIVAL announced the following grants:

- **Inn-Val Grants.**
- **Next-Val Grants.**
- **Ges-Val Grants.**
- **Production Grants.**
- **Summer Internships.**
- **Pre-doctorate contracts.**
- **Complementary personnel for projects from the National R&D Plan**
- **Post-MIR Wenceslao López Albo contracts programme (described in the training section of this report).**

The total amount of IDIVAL grants awarded in 2015 was as follows:

IDIVAL Grant	Amount granted (€)
Inn-Val Grants	Pending resolution in 2016
Next-Val Grants	100,000 (five projects)
Production Grants	300,000
Research Management Grant	57,960 (one grant lasting three years)
Summer Internships	2,800 (four two-month grants)
Pre-doctorate contracts	329,600 (four four-year contracts)
Complementary personnel for projects from the National R&D+i Plan	150,000 (16 projects)
Post-MIR Wenceslao López Albo contracts programme (described in the training section of the report)	262,962 (three two-year contracts)
Total granted	**1,203,322**

Inn-Val Grants

In 2015, IDIVAL implemented the Inn-Val grant programme focussing on the development of projects in technological and healthcare innovation in collaboration with the Botín Foundation, which acted as co-financier. It seeks to promote the transfer of knowledge to society and the market, in addition to integrating agents in the area into the Valdecilla environment. The resolution of these grants is planned for 2016.

Next-Val Grants

In 2015 IDIVAL placed a call for the first NEXT-VAL (NEXT generation VALdecilla) grant programme for the development of one- or two-year research projects led by novice researchers, with the aim of promoting the inclusion of new researchers in the Valdecilla environment. This call for NEXT-VAL research projects is aimed at translational research projects led by main Researchers who have never accessed this type of competitive access grant. The five projects selected in 2015 were:

- Main researcher: Santiago Montes Moreno (Specialist in the Anatomical Pathology Department, Marqués de Valdecilla University Hospital). Project: Molecular Diagnostics in large cell B lymphoma. Duration two years. Funding: €26,000.
- Main researcher: María Sierra Peña (Specialist in the Neurology Department, Marqués de Valdecilla University Hospital). Project: Study of the usefulness of neuroimaging and olfaction biomarkers in Parkinson's disease associated with the G2019S mutation of the LRRK2 gene as predictors of the conversion to motor Parkinson's disease. Duration: Two years: €14,000.
- Main researcher: Raquel García López (Professor at the University of Cantabria). Project: Role of non-coding RNAs in the aortic abdominal aneurysm. New markers and potential therapeutic targets. Duration: One year. Funding: €20,000.
- Main researcher: Carlos Ignacio Lorda Díez (Professor at the University of Cantabria). Project: Generation, amplification and structural maturation of tendon tissue from skeletal progenitors. Duration: One year. Funding: €20,000.
- Main researcher: Ángela Puente Sánchez (Specialist in the Digestive System Department, Marqués de Valdecilla University Hospital). Project: Regression of liver fibrosis after eradication of hepatitis C. Role of LOXL2. Duration: 2 years. Funding: €20,000.

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. To this end, it aims to promote the training of technicians in this field, as they learn different aspects of management, monitoring and evaluation concerning the research promotion activities at IDIVAL, and activities of internationalisation and innovation in the field of science and health technology.

Production Grants

In 2015, IDIVAL allocated funds for group operating costs based on its 2014 production. To calculate this grant, one must consider the impact factor of each IDIVAL research group on projects in which a group's author is first or last, and differently, the impact factor of projects on those in which the group's author is neither the first nor last. The funds obtained have also been considered based on the group, the patents generated, RETIC or CIBER membership, the responsibility of any group members to any IDIVAL platform. Production grants allocated to IDIVAL groups in 2015 were as follows:

GROUP	Amount (€)
Anatomical Pathology and Molecular Pathology	6.869
Apoptosis	5.002
Cell Nucleus Biology	8.876
Cell Cycle, Determining Stem Cells and Cancer	13.136
Cytokines and growth factors in the phenomena of pathological tissue plasticity	9.398
Cephalea Clinic and Genetics	4.607
Diagnosis and Treatment Using Imaging (Radiology)	5.521
Neurodegenerative Disease	18.841
Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	32.917
Epidemiology and Pathogenic Mechanisms of Infectious Diseases	7.485
Epidemiology and Public Health	10.499
Cancer Genomics	30.639
Genomics, Proteomics and Vaccines	3.076
Haemorrhagic Telangiectasia Study Group	3.329
Cardiovascular Research Group	10.747
Immunopathology of Rheumatic Diseases	2.286
Melatonin and Breast Cancer	3.280
Mineral and Lipid Metabolism	13.079
Clinical and Molecular Microbiology	12.380
Advanced Microscopy, Protein Folding and the Cytoskeleton	1.880
Haematologic Neoplasms and Haematopoietic Progenitor Cell Transplantation	7.091
Neurophysiology in Epilepsy and Neurointensives	2.892
New techniques in Abdominal Surgery	5.415
Psychiatry	25.457
Cell signalling and therapeutic targets	7.772
Transplantation and Autoimmunity	14.653
Clinical Trials Unit, Medical Oncology and Palliative Medicine	3.756
Molecular Imaging	5.166
Digestion	14.375
Nanomedicine	9.334

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 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 2015 were:

- Alba Santos Baza. Veterinary undergraduate student. University of León. Work in the Anatomical Pathology and Molecular Pathology Group (Head researcher: Javier Gómez Román).
- Raquel García Vílchez. Biotechnology undergraduate student. University of León. Work in the Cancer Genomics Group (Head researcher: Miguel Ángel Piris).
- Laura Blanco Peña. Biomedical Sciences undergraduate student. University of Barcelona. Work in the Cell Cycle, Stem Cells and Cancer Group (Head researcher: Alberto Gandarillas).
- Marina Salmón Méndez. Biotechnology undergraduate student. University of Oviedo Work in the Cell Signalling and Therapeutic Targets in Cancer Group (Head researcher: José Luis Fernández Luna).

Pre-doctorate contracts

In 2015, IDIVAL launched, in collaboration with the University of Cantabria, a 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 objective of completing their doctoral thesis.
The selected candidates and their thesis directors were:

- Doctorate student: Esperanza Padín Gonzalez. Director: Mónica López Fanarraga (UC).
- Doctorate student: Elena Navarro Palomares. Director: Rafael Valiente Barroso (UC).
- Doctorate student: Natalia Sanz Gómez. Director: Alberto Gandarillas Solinís (IDIVAL).
- Doctorate student: Nuria García Díaz. Director: Miguel Ángel Piris (Marqués de Valdecilla University Hospital).
- Doctorate student: María Lázaro Díez. Director: José Ramos Vivas (IDIVAL).

Complementary personnel for projects from the National R&D Plan

IDIVAL, with its annual grants, has co-financed projects organised by its staff (requested but not granted) for projects by researchers at the Institute submitted to the National Plan call. The following projects started in previous years have been co-financed by IDIVAL for the hiring of complementary personnel granted. Staff recruited through this line of co-financing in 2015 have been offered their third and second contract year, respectively.

2014 Call:

RAMOS VIVAS, José.

Key host-pathogen interactions of clinical relevance in Acinetobacter species (PI13/01310). Funding: €9,375.

FARIÑAS ÁLVAREZ, Carmen.

Intestinal colonisation by multiresistant enterobacteriaceae in patients with renal and liver transplants: multicentre cohort study and randomised, controlled, open clinical trial (PI13/01191). Funding: €9,375.

FERNÁNDEZ-LUNA, José Luís.

Prognostic and therapeutic relevance in ODZ 1 glioblastoma, a new target in cancer (PI13/01760). Funding: €9,375

LÓPEZ-FANARRAGA, Mónica.

Antineoplastic development based on nanomaterials (PI13/01074). Funding: €9,375.

2013 Call:

GONZÁLEZ-GAY MANTECÓN, Miguel Ángel.

Study of genetic markers of cardiovascular disease and subclinical atherosclerosis in patients with rheumatoid arthritis (PI12/00060). Funding: €9,375.

BLANCO ALONSO, Ricardo.

Study of genetic markers of susceptibility in patients with Henoch-Schonlein vasculitis (PI12/00193). Funding: €9,375.

VAQUÉ DÍEZ, José Pedro.

Metastatic melanoma: molecular diagnosis oriented at targeted therapy (PI12/00357). Funding: €9,375.

RIANCHO MORAL, José Antonio.

DNA Methylation: pathogenic and biomarker factors in bone formation disorders (PI12/00615). Funding: €9,375.

NISTAL HERRERA, Juan Francisco.

Role of adiponectin and its relationship with TGF beta in myocardial remodelling induced by pressure overload in aortic stenosis and its post-surgical regression (PI12/00999). Funding: €9,375.

GONZÁLEZ MACÍAS, Jesús.

Osteoclast WNT-beta catenin pathway (PI12/01405). Funding: €9,375.

CRESPO GARCÍA, Javier.

Implication of different innate and adaptive immunity factors in the etiopathogenesis of liver disease caused by fatty deposits in morbidly obese patients (PI12/02026). Funding: €9,375.

SÁNCHEZ JUAN, Pascual.

Multimodal study of Alzheimer's disease biomarkers in postoperative cognitive decline (PI12/02288). Funding: €9,375.

RODRÍGUEZ REY, José Carlos.

Genetic basis of hereditary hipercolesterolemias not dependent on the LDL receptor or apolipoprotein b. Characterisation and functional analysis of variants of the 3' regulatory regions of candidate genes. PI12/00637. Funding: €9,375.

MERINO PÉREZ, Jesús.

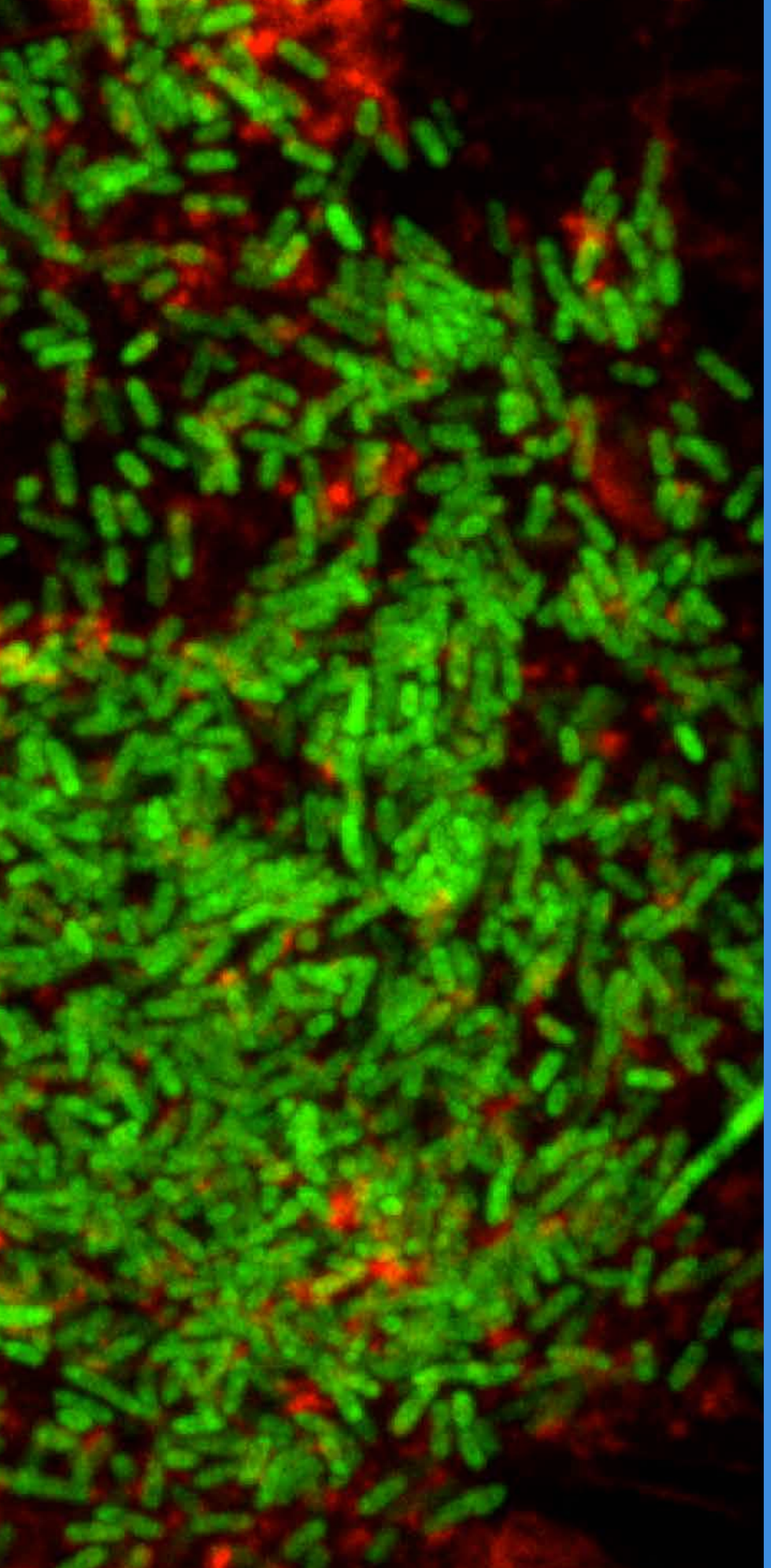
Study of the anti-inflammatory role of apolipoprotein E (APOE) in autoimmunity (SAF2012-34203). Funding: €9,375.

ÁLVAREZ DOMÍNGUEZ, Carmen.

Study of different vaccine vectors based on listeria monocytogenes against various inflammatory, infectious and cancerous processes (SAF2012-34203). Funding: €9,375.

LLORCA DÍAZ, Javier.

Genetic variants and pathways related to breast and prostate cancers, and their interaction with exposure to endogenous and exogenous sex hormones: study MCC-Spain (PI12/00715). Funding: €9,375.



2015

Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Training

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

1. HOSPITAL SESSIONS

This dissemination activity includes monthly scientific sessions which sees the participation of internationally renowned guests and IDIVAL researchers, who run sessions within the Marques de Valdecilla University Hospital (HUMV) setting.
These sessions are interspersed with weekly hospital sessions of the HUMV. The 2015 sessions were the following:

JANUARY:

15 th: **"Robotic surgery in rectal pathology".** Dr. Marcos Gómez Ruiz – Colo-rectal Surgery Unit, HUMV.

22 nd: **"Challenges in molecular diagnostics in sarcomas"**. Dr. Enrique de Álava - Head of the Anatomical Pathology Department, "Virgen del Rocío" Hospital.

29 th: **"Presentation of the Geriatric Department"**. Dr. Pérez del Molino – Geriatric Department, Liencres Hospital. HUMV.

FEBRUARY:

5 th: **"Current role of Hyperbaric oxygen therapy in a General Hospital"**. Dr. Desola – President and Medical Director of CRIS-UTH. – Professor of Medicine, University of Barcelona.

12 th: **"New therapies in rheumatoid arthritis"**. Dr. Blanco – Rheumatology Department, HUMV.

19 th: **"Multiresistant bacteria. The situation in Spain"**. Dr. Rafael Cantón – Head of the Microbiology Department, Ramón y Cajal Hospital.

26 th: **"Comprehensive care in COPD patients. Ongoing research"**. Dr. Beatriz Abascal Bolado – Pneumology Department, HUMV.

MARCH:

5 th: **"HUMV transfusion guide"**. Dr. Íñigo Román – Haematology Department, HUMV.

11 th: **"Multiple chemical sensitivity: from fiction to reality"**. Professor Dueñas Laita – Clinical Hospital and Faculty of Medicine. University of Valladolid.

19 th: **"Sonographic neural map: The future of polyneuropathy diagnosis?"**. Dr. Gallardo – Radiodiagnosis Department, HUMV.

26 th: **"Presentation of the results of clinical commissions"**. Dr. Concepción Fariñas – Quality Coordinator, HUMV.

APRIL:

16 th: **Solid organ transplantation: current trends"**. Dr. Manuel Pascual- Director, Romand de Transplantatión Lausanne University Medical Centre.

22 nd: **"Electrophysiology from Frankenstein to nonconvulsive status epilepticus"**. Dr. Peter Wolfe Kaplan.- Professor of Neurology and serves as the Director of Epilepsy and EEG, Johns Hopkins Bayview Medical Center.

30 th: **"Multidisciplinary approach to pain"**. Dr. Natalia Royuela – Cardiology Department, HUMV. Dr. Maldonado – Anaesthesia Department, HUMV.

MAY:

7 th: **"Organ donation and transplantation activity in the HUMV 2014"**. Dr. Miñambres – Transplant coordinator, HUMV.

14 th: **"Implementing quality management systems in the Hospital"**. Dr. Conchepción Fariñas – Quality Coordinator, HUMV.

21 st: **Hepatocellular management protocol in the HUMV"**. Dr. Rodríguez López – Digestive System Department, HUMV. Dr. Rodríguez San Juan – General and Digestive Surgery Department, HUMV.

28 th: **"Light as a driver of medical innovation"**. Mr. José Miguel López-Higuera / Professor of Electronics and Photonics; Olga M. Conde / Doctor of Telecommunications Engineering, University of Cantabria.

JUNE:

4 th: **"Becoming a surgeon in the 21st Century: international collaboration in research, clinical education and quality control"**. Dr. Andres Bergenfelz. – Professor Consultant Surgeon in Endocrine-and sarcoma Surgery , Director Practicum Clinic Skills Centre.

11 th: **"Original and biosimilar drugs. Clinical use experience."** Dr. Fernando de Mora – Director of the Pharmacology Department, GUAP (Autonomous University of Barcelona).

18 th: **"Liaison psychiatry at the HUMV"**. Dr. Artal.- Head of the Psychiatry Department, HUMV.

25 th: **"Nanomedicine for cancer. Antitumour effect of carbon nanotubes in animal models"**. Mónica López Fanarraga–Professor, University of Cantabria. Head of the Nanomedicine Group - IDIVAL.

SEPTEMBER:

24: **"A New Understanding on Asthma"**. Dr.Young J. Juhn (Mayo Clinic – Rochester - EE.UU.)

OCTOBER:

1 st. **"Soft tissue sarcoma care protocol in the HUMV"**. Dr. Santiago Montes Moreno – Anatomical Pathology Department, HUMV.

8 th. **"Systematic approach to oral mucositis after chemotherapy from Día Médico Hospital"**. Dr. Manuel F. Fernández Miera Nurse Ángeles Marquínez Carrión. Home Hospitalisation Service, HUMV.

15 th. **"Implementing a point of care analysis plan in a University Hospital"**. Dr. María Ortiz Espejo – Clinical Analysis Department, HUMV.

22 nd. **"Inducing Transplant Tolerance Using DC-SIGN+ Macrophages"**. Dr. Jordi Cano Ochando" - CARLOS III Health Institute.

29 th. **"Medicine from a legal standpoint"**. Dr. Javier Adín Ibarra. Clinical Pharmacology Department, HUMV.

NOVEMBER:

5 th. **"Eating disorders and obesity: interaction of neuro-biological-environmental risk factors and the therapeutic implications"**. Dr. Fernando Fernández Aranda – Bellvitge IDIBELL University Hospital.

12 th. **"Adequacy of therapeutic effort"**. Mortality Commission - Healthcare Ethics Committee, HUMV.

19 th. **"Biochemical mechanisms at the start of human birth"**. Dr. J. R. De Miguel Sesmero – Obstetrics-Gynaecology Department, HUMV.

26 th: **"Early identification of schizophrenia. Fantasy or future reality?**. Dr. Benedicto Crespo Facorro – Psychiatry Department, HUMV.

DECEMBER:

3 rd: **"Action protocol for pancreatic adenocarcinoma at the HUMV"**. Dr. Rodríguez San Juan – General Surgery Department, HUMV.

10 th: **"The rise of sarcopenia. A cake for many diners"**. Dr. Mª José Sánchez Pérez – Rehabilitation Department, HUMV.

17 th: **"IDIVAL and the model of health research institutes"**. Dr. Galo Peralta - Director of Management of the IDIVAL.

2. TRAINING RELATED TO SUPPORT UNIT DEPARTMENTS

Includes activities for researchers disseminated by Institute departments. In 2015, the following dissemination activities were carried out under this line:

II FLOW CYTOMETRY COURSE. CLINICAL AND RESEARCH TECHNIQUES AND APPLICATIONS. Co-organised with Inbiomed. 9-12 June 2015 (20 hours). Accredited by the Commission on Continuing Education of Health Professions of the Government of Cantabria with 4.1 credits (File: 4.847-143/2015).

FUNDAMENTALS OF OPTICAL AND ELECTRONIC MICROSCOPY. SAMPLE PREPARATION. II Edition. 23-27 November 2015 (20 hours). Accredited by the Commission on Continuing Education of Health Professions of the Government of Cantabria with 4.3 credits (File: 14.200-399/2015).

3. DISSEMINATION ACTIVITIES

The IDIVAL Innovation Area carries out dissemination and promotion activities concerning the culture of innovation. In 2015, various events in this field were carried out:

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 like 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 WORKSHOP FOR BIOMEDICAL RESEARCH . For the second 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. Between 4 and 12 of November, a total of 80 students from educational centres around Cantabria took part in biomedicine workshops designed, directed and developed by the IDIVAL Foundation.

RESEARCHERS' NIGHT. This European science project forms part of the PEOPLE Programme of 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.

4. COLLABORATIONS WITH UNIVERSITIES

As part of its research groups, 40 of the 132 associate professors at IDIVAL work 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 masters programmes:

MASTERS IN MOLECULAR BIOLOGY AND BIOMEDICINE. University of Cantabria and University of Basque Country Director: Dolores Delgado (Professor of Immunology. Department of Molecular Biology. University of Cantabria).

MASTERS IN MANAGEMENT OF HEALTHCARE AND SOCIAL SERVICES . DDirector: 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.

MASTERS IN THE STUDY AND TREATMENT OF PAIN. Rey Juan Carlos University and University of Cantabria.

MASTERS IN THE 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 SOCIO-ECONOMIC IMPACT OF BIOMEDICAL RESEARCH AND INNOVATION. 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). 1-3 July 2015. Annual landmark meeting in which IDIVAL collaborates with the Carlos III Health Institute.

5. RESEARCH METHODOLOGY

This section includes in-house training activities and programmes organised and financed directly by IDIVAL. In 2015, the activities of this section oriented towards training on using library resources were the following:

Introduction to biomedical information for Primary Care. Dates: 22 and 23 September, 27 and 29 October, 24 and 25 November. Duration: 18 hours / seminar. Primary Care medical students. Location: Library Training Room. Teacher: Mario Corral, Librarian.

Library immersion course for HUMV Residents. Date: 28 May. Duration: 1 hour. Students: HUMV Residents-1. Teacher: Mario Corral, Librarian.

Basic reference search using the Marquesa de Pelayo Library for Nursing. Dates: 4 and 11 May and 19 and 26 October Location: Library Training Room. Teacher: Mario Corral, Librarian.

Basic reference search using the Marquesa de Pelayo Library for midwives. Dates: 20, 21 and 22 October. Location: Library Training Room. Teacher: Mario Corral, Librarian.

Reference search in PubMed. 3 and 4 September. Teacher: Mario Corral, Librarian.

Reference search strategies in Health. Dates: 10, 11, 17, 18 and 26 November and 15 December (HUMV), 3 and 5 February (Laredo Hospital).

6. RESIDENT 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 2015, the Marqués de Valdecilla University Hospital offered 80 places in 39 specialisations. Furthermore, the Marqués de Valdecilla University Hospital participated in the training of the 20 places offered for a specialisation in Family and Community Medicine for the Santander Area.

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:

- ALLERGOLOGY: 1
- CLINICAL ANALYSIS: 1
- ANATOMICAL PATHOLOGY: 3
- ANAESTHESIOLOGY AND RESUSCITATION: 4
- DIGESTIVE SYSTEM 2
- CLINICAL BIOCHEMISTRY 1
- CARDIOLOGY 3
- GENERAL AND DIGESTIVE SURGERY: 2
- ORAL AND MAXILLOFACIAL SURGERY: 1
- ORTHOPAEDIC SURGERY AND TRAUMATOLOGY: 2
- THORACIC SURGERY: 1
- MEDICAL-SURGICAL DERMATOLOGY:..... 1
- ENDOCRINOLOGY AND NUTRITION: 1
- HOSPITAL PHARMACY: 2
- CLINICAL PHARMACY: 1
- HAEMATOLOGY AND HAEMOTHERAPY: 2
- IMMUNOLOGY: 1
- OCCUPATIONAL MEDICINE 2
- FAMILY AND COMMUNITY MEDICINE 20
- PHYSICAL MEDICINE AND REHABILITATION: 1
- INTENSIVE MEDICINE: 3
- INTERNAL MEDICINE: 4
- NUCLEAR MEDICINE: 1
- MICROBIOLOGY AND PARASITOLOGY: 1
- NEPHROLOGY 2
- PNEUMOLOGY: 2
- NEUROSURGERY: 1
- CLINICAL NEUROPHYSIOLOGY: 2
- NEUROLOGY: 2
- OBSTETRICS AND GYNAECOLOGY: 3
- OPHTHALMOLOGY: 1
- MEDICAL ONCOLOGY: 2
- RADIATION ONCOLOGY:..... 1
- OTOLARINGOLOGY: 1
- PEDIATRICS AND SPECIFIC AREAS: 5
- CLINICAL PSYCHOLOGY: 1
- PSYCHIATRY: 3
- RADIODIAGNOSTICS: 3
- HOSPITAL RADIOPHYSICS 1
- RHEUMATOLOGY: 2
- UROLOGY: 1

7. 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 which should include a stay at one or various renowned international centres. In 2015, IDIVAL offered grants for a two-year contract to three specialists; the Post-MIR Valdecilla contracts of a further seven specialists were active at some point during 2015.

2015 CALL

RIANCHO ZARRABEITIA, JAVIER. Neurology Specialist, trained at HUMV. Tutor: Jon Infante. Project: Epigenetics and new technologies in dementia: a translational approach and innovation in care. Stay abroad: Dr. Bruce Miller. Memory Ageing Centre in San Francisco, University of California (UCSF MAC). Duration: two years.

KISLÍKOVÁ, MÁRIA. Nephrology Specialist, trained at HUMV. Tutor: Ángel Martín de Francisco. Project: Epigenetic Regulation of Arterial Smooth Muscle Phenotype in CKD-Associated Vascular Disease. Stay abroad: Dr. David Wheeler. The UCL Centre for Nephrology, University College of London. Duration: two years.

RIAÑO MOLLEDA, MARÍA. General Surgery Specialist, trained at HUMV. Tutor: Manuel Fleitas, Project: Training in hepatobiliary surgery and liver transplantation and the study and application of solutions and machines for preserving abdominal solid organs for transplantation. Stay abroad Professeur René ADAM, Paul Brousse Hospital in Paris and the Hammersmith Hospital in London. Duration: two years.

2014 CALL

IRUZUBIETA COZ, PAULA. Digestive System Specialist, trained at HUMV. Tutor: Javier Crespo García (Head of Digestive System Dept., HUMV). Project: Role of immunity and intestinal microbiota in liver disease due to non-alcoholic fatty deposits in obesity. Stay Abroad: Cooperative Research Centre in Biosciences (CIC bioGUNE 6 months) and Freeman Hospital in Newcastle and the Institute of Cellular Medicine at the University of Newcastle for 12 months. Duration: 3 years.

2013 CALL

GONZÁLEZ QUINTANILLA, VICENTE. Neurology Specialist, trained at HUMV. Tutor: Agustín Oterino Durán. Project: Evolutionary study of markers of inflammation and brain atrophy in patients with multiple sclerosis in Cantabria. Stay abroad: Dr. Pozzilli, Sant Ándrea Hospital in Roma and Dr. Salvetti, University of Sapienza and Dr. Alan Thompson, National Hospital for Neurology and Neurosurgery, London. Duration: 2 years.

PÉREZ DEL MOLINO BERNAL, INMACULADA. Microbiology and Parasitology Specialist, trained at HUMV. Tutor: Jesús Agüero Balbín. Project: Molecular characterisation of the Mycobacterium tuberculosis complex in Cantabria, its importance in the clinical and epidemiological context of our region. Stay abroad: Dr. Troels Lillebaek, Microbacteria laboratory, Statens Serum Institut. Copenhagen (Denmark). Duration: 2 years.

CAMPOS JUANATEY, FÉLIX. Urology Specialist, trained at HUMV. Tutor: José A. Portillo Martín (Urology Dept. HUMV). Project: Specific training for reconstructive urologic pathology and andrology. Centre abroad: Dr. Anthony Mundy and Dr. David Ralp, University College London Hospitals. London. Duration: 2 years.

2012 CALL

ABASCAL BOLADO, BEATRIZ. Specialisation: Pneumology. Tutor: Dr. Ramón Agüero Balbín. Project: To determine the relationship between the exercise capacity and physical activity of patients with chronic obstructive pulmonary disease and the use of new technologies for measurement. Medical intervention to reduce rates of rehospitalisation after exacerbation in COPD patients. Centre abroad: Mayo Clinic, Rochester, Minnesota. Director: Roberto P Benzo. Duration: 2 years.

PELAYO NEGRO, ANA LARA. Specialisation: Neurology. Tutor: Dr. José Ángel Berciano Blanco. Project: Atrophy of the lower extremities in Charcot-Marie-Tooth disease type 1A: findings in muscle MRI and the clinical-neurophysiological correlation. Centre abroad: Centre for Neuromuscular Disease (UCL Institute of Neurology in Queen Square, London, UK). Director: Mary Reilly. Duration: 2 years.

SUÁREZ PINILLA, PAULA. Specialisation: Psychiatry. Tutor: Dr. Benedicto Crespo Facorro. Project: Development and implementation of a protocol for early diagnosis and prevention of psychosis based on proteomic analysis. Centre abroad: Centre for Neuropsychiatry Research, Cambridge. Duration: 2 years.

8. DOCTORAL THESES. DOCTORAL PROGRAMMES

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

- Doctorate in Molecular biology and biomedicine (coordinated by Dolores Delgado. The programme is quality accredited).
- Doctorate in Health Sciences (currently coordinated by institute researcher Benedicto Crespo-Facorro).

IDIVAL training activity is reflected in doctoral theses. **In 2015, IDIVAL groups participated in a total of 37 doctoral theses, either through their direction or authorship.**

DOCTORATE	DIRECTOR(S)	TITLE	UNIVERSITY
Alfonso Fernando Corrales Martínez	Javier Llorca Díaz José Antonio Parra Blanco Miguel Á. González-Gay Mantecón	Cardiovascular risk assessment in patients with rheumatoid arthritis	Cantabria
Ana Canga Villegas	Juan Antonio García-Porrero Pérez Juan Antonio Montero Simón	Round ligament of the hip: an anatomical, radiological, functional and molecular study	Cantabria
Andrea Corrales Pardo	Noemí Rueda Revilla	Study of the protective effects of chronic treatment with melatonin on cognitive deficits of the TS65DN mouse, a model of Down syndrome	Cantabria
Carlos Antonio Amado Diago	Mª Teresa García Unzueta, Mª Del Carmen Fariñas Álvarez	Nutritional status of vitamin D and vitamin D-dependent antimicrobial peptides (cathelicidin and beta-defensin-2) in blood and pleural fluid, possible pathophysiological and diagnostic implications in pleural effusions	Cantabria
Carlos Renero Lecuna	Rafael Valiente Barroso	Optical properties of doped wide band gap binary oxides with luminescent ions: the effects of high pressure	Cantabria
Carmen María Montes Gaisán	Eulogio Conde García	Long-term survival of patients with transplants for acute myelogenous leukaemia. Analysis of risk factors	Cantabria
Carmen María Rodríguez Gómez	José Manuel Bernal Marco, Dieter José Morales García	Rheumatic mitral stenosis. Very long-term results of surgical treatment involving commissurotomy and Duran annuloplasty	Cantabria
Clara Caridad Michel Rollock	Dieter José Morales García, Francisco José Herrero Fernández	Incidence of traumatic injuries of the hand and wrist with an occupational origin: a study of quality of life	Cantabria
Elisabeth Coll Torres	Gil Rodriguez Carvaca Eduardo Miñambres García	Treatment protocol for a multiorgan donor for increased pulmonary donation. Multi-centre national study	Rey Juan Carlos
Javier Loricera García	Miguel Á. González-Gay Mantecón Mª Del Carmen Glez Vela Ricardo Blanco Alonso	Clinical characterisation of cutaneous vasculitis	Cantabria

DOCTORANDO	DIRECTOR (ES)	TÍTULO	UNIVERSIDAD
Javier Riancho Zarrabeitia	Mª Teresa Berciano Blanco, Miguel Ángel Lafarga Coscojuela, José Ángel Berciano Blanco	Effect of bexarotene in transgenic mice with amyotrophic lateral sclerosis (ALS). A histological and molecular study	Cantabria
José Antonio Amado Señaris, Francisco Jesús González Vílchez	Cristina Ruisánchez Villar	Impact of new echocardiographic techniques on the detection of myocardial dysfunction in asymptomatic type 1 diabetes mellitus. Role of myocardial deformation and three-dimensional echocardiography	Cantabria
José Luis González Fernández	José Luís Hernández Hernández José Manuel Olmos Martínez	Secular trend in the hip fracture rate in Cantabria (1988-2010)	Cantabria
José Luis González Fernández	José Luís Hernández Hernández José Manuel Olmos Martínez	Validation of the FRAX predictive model for osteoporotic fracture in postmenopausal women and men over 50 years old	Cantabria
Juan Crespo Del Pozo	Daniel Casanova Rituerto	Diagnosis and staging of rectal cancer: the influence of post chemo and radiotherapy changes in the assessment of the mesorectal fascia using MRI	Cantabria
Laura Sánchez Moreno	Manuel Gómez Fleitas Juan Carlos Rodríguez Sanjuan	Analysis of survival after pulmonary and hepatic metastasis in colorectal carcinoma	Cantabria
Lourdes Calera Urbizu	Jesús González Macías, Fernando Rivera Herrero	Colorectal cancer and liver metastasis: a new staging system. Analysis of prognostic and predictive factors	Cantabria
Lucrecia Yáñez San Segundo	Eulogio Conde García José Luís Hernández Hernández	The impact of changes in the procedure of the allogeneic transplant of haematopoietic progenitor cells on the evolution, morbidity and mortality of infectious complications	Cantabria
Luis Cadelo Gomez	Luís García- Castrillo Riesgo.	Early markers of severe sepsis in hospital emergency departments	Cantabria
Mª Ascensión Jorrin Moreno	Pedro Muñoz Cacho, José Antonio Amado Señaris	Diagnostic utility of the audit questionnaire and carbohydrate-deficient transferrin to detect risk-associated alcohol consumption in the working female population.	Cantabria
Mª Del Carmen Manzanares Campillo	Daniel Casanova Rituerto, Jesus Martin Fernandez.	Strategies to optimise results in elective surgery for colorectal cancer: preoperative oral immunonutrition	Cantabria
María de Pedro de Cardenas,	Marina Pollan Santamaria, Javier Llorca Díaz	Influence of non-steroidal anti-inflammatory drug use and breast cancer incidence	Cantabria
María Soledad Holanda Peña	Álvaro Castellanos Ortega Javier Llorca Díaz	Measuring the satisfaction of patients admitted to the ICU and their families	Cantabria
María Victoria Jiménez Moreno	Mónica López Fanárraga	Study of cofactors of tubulin in human gametes	Cantabria
Marta Garcia Hoyos	José Antonio Riancho Moral Carmen Valero Díaz de Lamadrid	Study of bone mass and remodelling markers in individuals with Down syndrome	Cantabria
Natalia Palmou Fontana	Joaquin Jordan Bueso Julian Eloy Solis Garcia Del Pozo	Effect of inhibitor drugs for the tumour necrosis factor alpha on the quality of life in patients with ankylosing spondylitis and psoriatic arthritis	Castilla-La Mancha
Paula Suarez Pinilla	Benedicto Crespo Facorro	Cerebral morphological changes in first-episode non-affective psychosis: the implication of changes in BDNF, NRG1 and CNR1 polymorphisms	Cantabria
Pilar Alonso Lecue	Alberto Gandarillas Solinis	Changes in mitosis-differentiation control in carcinoma of the skin	Cantabria
Roberto Garrastazu Lopez	Miguel Santibáñez Margüello Javier Llorca Díaz	Predictors of morbidity and mortality in COPD patients annually	Cantabria
Roberto Zarrabeitia Puente	José Antonio Parra Blanco, María del Carmen Fariñas Álvarez	Epidemiology of hereditary haemorrhagic telangiectasia in Spain: experience of the specialised unit in the Sierrallana hospital (2003-2013)	Cantabria
Santiago Montes Moreno	Miguel Ángel Piris Pinilla	Identification of markers with diagnostic and prognostic use in aggressive large B-cell lymphoma	Cantabria
Sara Diaz Angulo	Marcos Antonio González López Marcos López Hoyos	Study of the prevalence of thyroid dysfunction and autoimmunity in patients with chronic urticaria, vitiligo and alopecia areata in the autonomous region of Cantabria	Cantabria
Sara Velategui Camus	Mª Amor Hurlé González, Mónica Tramullas Fernández	Role of microRNA-30c in pain perception	Cantabria
Susana García Cerro	Carmen Martínez-Cue Pesini Noemí Rueda Revilla	Study of the effect of reducing the number of copies of the DYRK1A gene on different functional and neuromorphologic phenotypes found in a mouse model with Down syndrome and euploid mice	Cantabria
Trinitario Pina Murcia	Javier Llorca Díaz Miguel Ángel González-Gay Mantecón	Modification of cardiovascular risk markers in psoriasis after anti-TNF therapy	Cantabria
Vanesa Calvo del Río	Miguel Á. González-Gay Mantecón María del Carmen González Vela Ricardo Blanco Alonso	Clinical characterisation of Henoch–Schönlein purpura	Cantabria
Vicente González Quintanilla	Agustín Oterino Durán Jesús Castillo Obeso	Endothelial function in multiple sclerosis and migraines. A cross-sectional study with active comparator	Cantabria

9. RESEARCH SEMINARS

The Biomedical Research Forum of Cantabria, consisting of researchers from IDIVAL, the University of Cantabria and the Institute of Biology and Biomedicine of Cantabria, has organised an ambitious programme of research seminars in collaboration with clinical and basic researchers. The researchers who have coordinated the development of this programme are as follows: Dr. Ana Batlle (HUMV), Dr. Carlos López (HUMV), Dr. Ramón Merino (IBBTEC-UC), Dr. Juan Antonio Montero (UC), Dr. Félix Sangari (IBBTEC-UC) and Dr. José Pedro Vaqué (IDIVAL).

The 2015 programme consisted of the following seminars that were held in the Faculty of Medicine of the University of Cantabria, in the Marqués de Valdecilla University Hospital and the IDIVAL facilities.

DATE (LOCATION)	SESSION	SPEAKER
20 January (IBBTEC)	**12:30h.** A clinical focus on breast cancer: "What do we expect from molecular research?"	**Dr. J. Manuel López-Vega** *HUMV-IDIVAL*
3 February (IBBTEC)	**12:30h.** Brucellosis in Subsaharan Africa: practical and scientific challenges	**Dr. Ignacio Moriyon** *U. Navarra*
24 February (IBBTEC)	**12:30h.** In search of therapeutic strategies to effectively block K-Ras driven lung and pancreatic tumours	**Dr. Mariano Barbacid** *CNIO, Madrid*
17 March (IBBTEC)	**12:30h.** Fuelling gene therapy research with next generation lentiviral vectors	**Dr. J. Carlos Ramírez** *CNIO, Madrid*
31 March (IBBTEC)	**12:30h.** Molecular diagnosis of cancer	**Dr. Miguel A. Piris** *HUMV-IDIVAL*
14 April (IBBTEC)	**12:30h.** "Role and Therapeutic Potential of the Endocannabinoid System in Myelin Diseases"	**Dra. Susana Mato** *UPV, Bilbao*
28 April (IBBTEC)	**12:30h.** Mutational and functional studies on PTEN tumor suppressor / Estudio mutacional-funcional del supresor tumoral PTEN	**Dr. Rafael Pulido** *CIPF-BioCruces*
4 May (UC-F.MEDICINE)	**13:00h.** The role of microglia in the immune response against Listeria monocytogenes	**Dra. Elisabet Frande** *(IDIVAL)*
11 May (UC-F.MEDICINE)	**13:00h.** HCV in Spain	**Dr. Javier Crespo** *Head of the Digestive System Department HUMV-IDIVAL*
13 May (Téllez-Plasencia Room, Pavilion 16, HUMV)	**14:00h.** Next Generation Sequencing (NGS). Mass DNA sequencing has revolutionised research and will have a major impact on clinical care	**Dr. Eduardo Pareja** *Era7 Bioinformatics*
18 May (UC-F.MEDICINA)	**13:00h.** Metabolic programs in prostate cancer progression	**Dr. Arkaitz Carracedo** *Group leader, Molecular Oncology program CIC bioGUNE*
25 May (UC-F.MEDICINE)	**13:00h.** Ovarian cancer: towards a personalised treatment	**Dra. Ana de Juan** *Oncology Department Marqués de Valdecilla University*
1 June (UC-F.MEDICINE)	**13:00h.** Biomedical applications of DNA origamis: the potential of DNA nanotechnology	**Lda. Sandra Sagredo** *Protein Engineering Group*
8 June (UC-F.MEDICINE)	**13:00h.** Hepatocellular carcinoma: Therapy guided by mutational signatures	**Dra. Susana Llerena** *Digestive System Department, HUMV* and **Lda. Nuria García** *Cancer Genomics Group, IDIVAL*
15 June (UC-F.MEDICINE)	**13:00h.** Cytotoxic effects of nanomaterials and their application in the biomedical area	**Lda. Lorena García Hevia** *Department of Molecular Biology. University of Cantabria*
22 June (UC-F.MEDICINE)	**13:00h.** Bioinformatics: Advances, applications and services for research	**Dr. Carlos Prieto** *Head of the Bioinformatics Department University of Salamanca*
29 June (UC-F.MEDICINE))	**13:00h.** Hacking the master transcriptional program of prostate cancer metabolism	**Dra. Verónica Torrano** *Post doctorate Researcher Molecular Oncology*
21 September (Anatomical Pathology Seminar Hall)	**13:00h.** Understanding ambiguous pathological models in oncogenesis	**Alejandro A Gru, MD** *Pathology and Laboratory Medicine University Of Virginia Health System*
5 October (Sala de Seminarios IDIVAL)	**13:00h.** Subthalamic nucleus: a critical point of cortical projection for mediating sensorimotor, cognitive and limbic functions	**Dr. Juan Martino** *Neurosurgery Department - Raquis Unit Marqués de Valdecilla Marqués de Valdecilla*
19 October (IDIVAL Seminar Hall)	**13:00h.** The role of BAMBI in humoral immunity	**Dr. Juan Jesús Augustín** *Chronic Inflammation and Autoimmune Diseases*
26 October (IDIVAL Seminar Hall)	**13:00h.** MCJ/DNACJ15 in Acetaminophen Induced	**Dra. Paula Iruzubieta** *Digestive System Department HUMV*
9 November (Sala de Seminarios IDIVAL)	**14:00h.** Frequency and characteristics of familial melanoma in Spain: results of the FAM-GEM-1 study	*Medical Oncology Department Healthcare Research Institute Gregorio Marañón Madrid*
10 November (IDIVAL Seminar Hall)	**14:00h.** PTPR-K IN ZEBRAFISH: A new model of tumour	**Dr. Iñaki Jiménez Gómez** *Spatial regulation of Ras-ERK signals IBBTEC*
24 November (Sala de Seminarios IDIVAL)	**14:00h.** Myc roles in proliferation and erythroid differentiation	**Dra. Lucía García-Gutiérrez** *MYC Oncoprotein in cell differentiation and leukemia IBBTEC*
01 December (IDIVAL Seminar Hall)	**14:00h.** New antidepressant therapies: the role of the old players	**Dr. Albert Adell** *Systems Neurobiology IBBTEC*
21 December (Téllez Plasencia Room. HUMV)	**10:00h.** Novel mechanisms of extracellular intrinsic antimicrobial resistance	**Miguel A. Valvano, M.D.** *Professor of Microbiology and Infectious Diseases The Wellcome-Wolfson Institute for Experimental Medicine*

10. STUDENT TRAINING

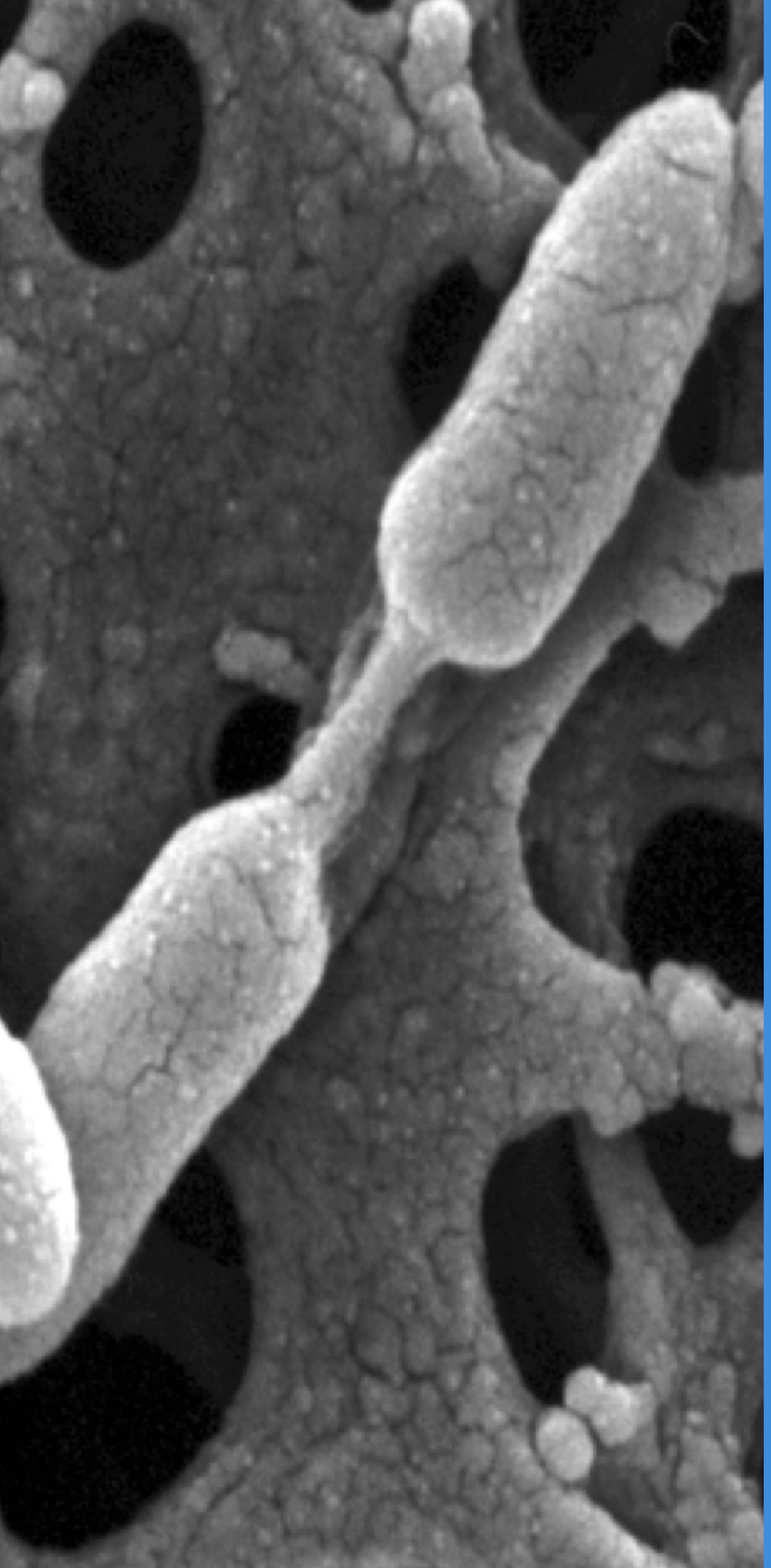
As part of its research groups, 40 of the 132 associate professors at IDIVAL work in the Marqués de Valdecilla University Hospital. Of the 10 tenured professors and 10 other professors from the University of Cantabria working with the Marqués de Valdecilla University Hospital, 18 belong to IDIVAL groups.

1. Undergraduate Studies in Medicine at the University of Cantabria. The Marqués de Valdecilla University Hospital develops training which teaches 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 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 and 2015. The students awarded the grant and the research group in which they worked during the summer of 2015 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



2015

Activity report

IDIVAL R&D activity

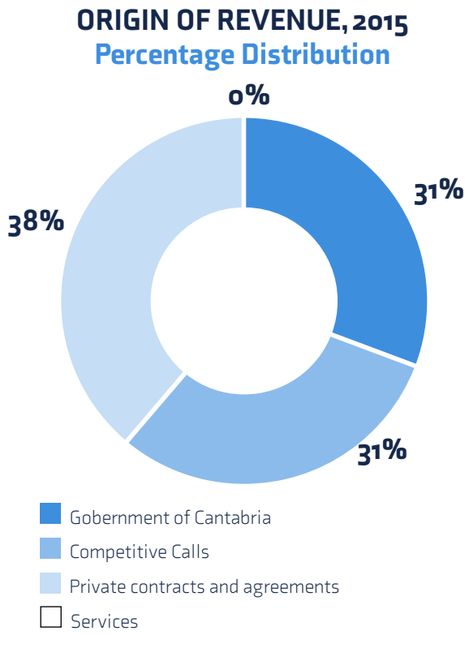
Valdecilla Instituto de Investigación Sanitaria IDIVAL

IDIVAL FUNDING IN 2015

Revenue

IDIVAL recorded total revenue of €7.05 million in 2015. The revenue pertaining to the Government of Cantabria increased to €2.18 million, representing 30.5% of total revenue. The remaining revenue (69.5%) pertains to both the public and private competitive programmes at a national and international level (€2.20 million) and to the private agreements and contracts signed during the year (€2.65 million).

ORIGIN OF IDIVAL REVENUE, 2015	AMOUNT
Government of Cantabria	2,178,554
Regional Ministry of Health	
Competitive calls 2,182,866	2.182.866
Regional programmes	92.534
R&D National Plan	2.019.891
European Commission Programmes	70.441
Private competitive grants	18.873
Private contracts and agreements	2.651.383
Clinical Trials	613.086
Service contracts	542.329
Collaboration agreements	953.369
Donations	542.599
Revenue from service provision	15.669
TOTAL REVENUE	7.047.344



Spending

IDIVAL spending is essentially allocated towards developing research projects using its own financing, to the IDIVAL research grant programme and to organisational spending (support personnel, in-house research personnel and operational costs)
In 2015, it allocated a total of €3.09 million to developing projects with specific funding, €1.89 million to structural costs and €350,000 to investments.
The IDIVAL grant programme has represented expenditure of €970,000 (Post-MIR Valdecilla López Albo contracts, productivity, co-financing of projects and contracts, etc.).

PERSONNEL

In 2015, IDIVAL had 29 Research Groups made up of researchers, collaborators and technical personnel, all pertaining 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 2015, these groups had a total of 538 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 2015 pertain to the following programmes:

Researcher Programmes
Miguel Servet Programme (ISCIII): 2
IDIVAL Researchers: 6
Research Training Programme
Rio Hortega Programme (ISCIII): 0
Sara Borell Programme (ISCIII): 2
Wenceslao López Albo Programme (IDIVAL): 10
Contracts for Research Projects
IDIVAL-funded contracts 28
ISCIII contracts: 32
MICINN contracts: 6
Privately-funded contracts: 41
Support Services
Scren Platform (ISCIII): 2
Biobank Platform (ISCIII): 2
ITEMAS Platform (ISCIII): 3
Infrastructure technicians (ISCIII): 1
IDIVAL support personnel: 12

Three individuals contracted through CIBER must be added to this list.

PUBLICATIONS

Production activity originated by IDIVAL researchers is at 422 indexed papers in 2015 (excluding conference papers published in journals). In 200 papers (47%), the first or last author pertains to IDIVAL. In 78 publications (18%), there was collaboration with authors from other countries.

IMPACT FACTOR

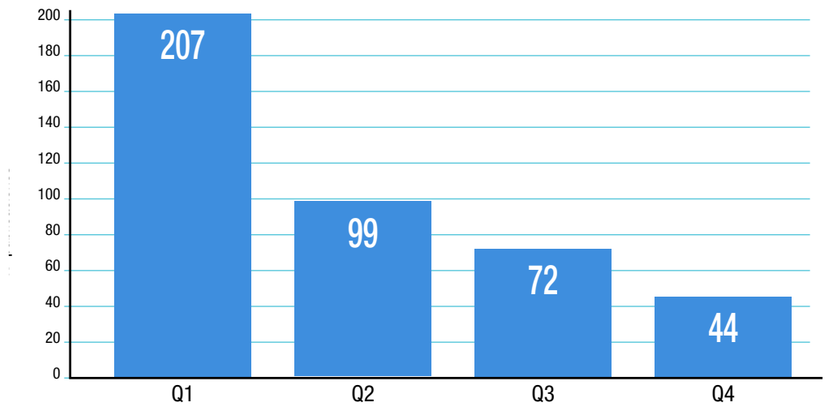
In 2015. the cumulative impact factor of IDIVAL group publications was 1949 (SCI 2014), the percentage of publications with an impact factor in the first quartile was 49%, and the 107 papers published in 2015 had an impact factor in the first decile of the specialisation of 25%.

QUOTATIONS

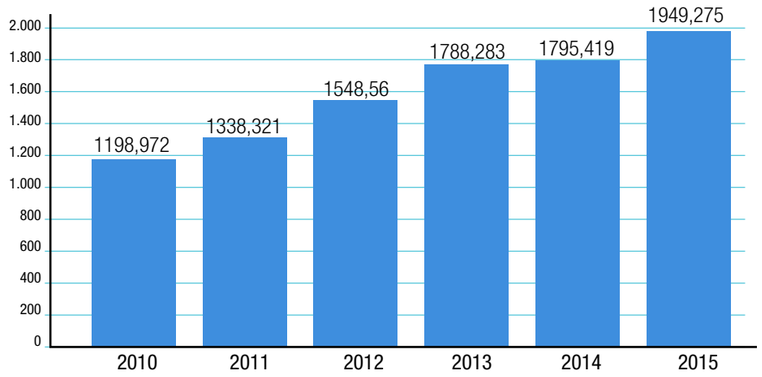
The first article authored by Valdecilla researchers was quoted in 1930 and 1941. It concerned the paper published by Dr. González Aguilar: **González-Aguilar J. Contribution to the pathogeny of tendon tumors of giant cells. Journal of Bone and Joint Surgery 1930; 12: 280-288.**

Throughout 2015, the Valdecilla mark obtained 11,183 featured quotations according to data from the ISI web of knowledge platform (using the descriptor "valdecilla" in the corresponding affiliation field). Therefore, in 2015 the Valdecilla mark exceeded an accumulated 87,000 citations, as more than a hundred references exceeded 100 citations, with the number of citations obtained annually continuing to increase.

2015 IDIVAL PUBLICATIONS, DISTRIBUTED BY QUARTILE



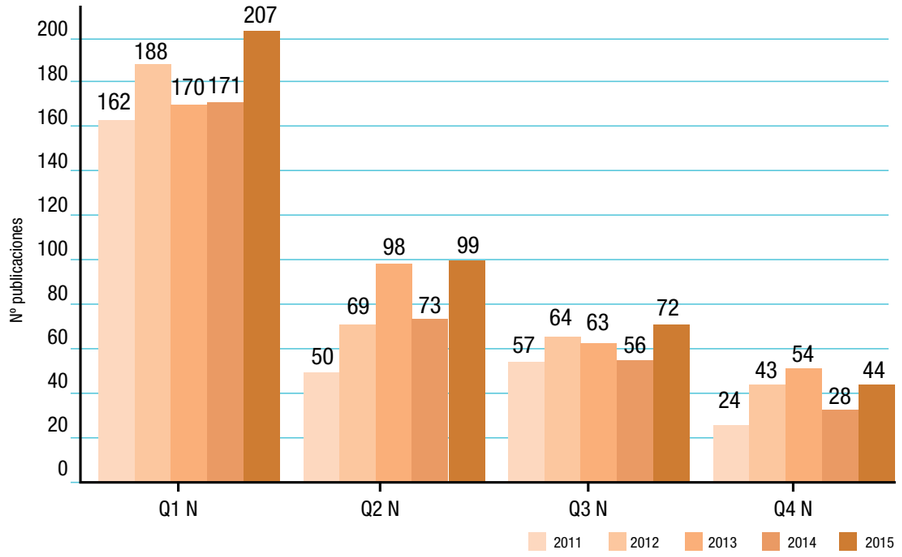
EVOLUTION OF THE TOTAL IMPACT FACTOR



EVOLUTION OF IMPACT FACTOR DISTRIBUTION BY QUARTILE

Año	Q1		Q2		Q3		Q4		Total
	n	%	n	%	n	%	n	%	
2011	162	55,3%	50	17,1%	57	19,5%	24	8,2%	293
2012	188	51,6%	69	19,0%	64	17,6%	43	11,8%	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

IMPACT FACTOR DISTRIBUTION BY QUARTILE OVER THE LAST 5 YEARS



IDIVAL PUBLICATIONS IN 2015 ACCORDING TO IMPACT FACTOR

(Excluding those derived from multi-centre collaborations)

REVISTA	FI (JCR 2014)	Nº	Suma FI	Cuartil	Decil
ACTA RADIOL	1,603	1	1,603	3	6
ACTAS UROL ESP	1,022	2	2,044	4	8
ADICCIONES	1,154	1	1,154	4	9
ADVANCED HEALTHCARE MATERIALS	5,797	1	5,797	1	1
ADVANCED OPTICAL MATERIALS	4,062	1	4,062	1	2
AGING-US	6,432	2	12,864	1	2
ALLERGY	6,028	1	6,028	1	1
ALZHEIMERS DEMENT	12,407	1	12,407	1	1
AM J CARDIOL	3,276	1	3,276	2	4
AM J HUM GENET	10,931	1	10,931	1	1
AM J MED GENET B	3,416	1	3,416	2	4
AM J PSYCHIAT	12,295	1	12,295	1	1
AM J RESP CRIT CARE	12,996	1	12,996	1	1
AM J ROENTGENOL	2,731	1	2,731	2	3
AM J SURG PATHOL	5,145	1	5,145	1	1
AM J TRANSPLANT	5,683	2	11,366	1	1
AMERICAN JOURNAL OF HEMATOLOGY	3,798	1	3,798	1	3
ANAESTHESIA	3,382	1	3,382	1	2
ANGEW CHEM INT EDIT	11,261	1	11,261	1	1
ANN ALLERG ASTHMA IM	2,599	1	2,599	2	5
ANN HEPATOL	2,065	1	2,065	3	7
ANN NEUROL	9,977	1	9,977	1	1
ANN RHEUM DIS	10,377	8	83,016	1	1
ANN SURG ONCOL	3,93	1	3,93	1	1
ANN TRANSPL	1,261	1	1,261	3	6
ANN VASC SURG	1,17	1	1,17	4	9
ANNALS OF ONCOLOGY	7,04	2	14,08	1	1
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY	4,476	3	13,428	1	2
APMIS	2,042	1	2,042	3	8
APPL ENVIRON MICROB	3,668	1	3,668	1	3
ARCH BRONCONEUMOL	1,823	3	5,469	3	7
ARTHRIT CARE RES	4,713	1	4,713	1	2
ARTHRITIS RESEARCH & THERAPY	3,753	4	15,012	2	3
AUSTRALAS J DERMATOL	1,106	1	1,106	3	7
BBA-MOL BASIS DIS	4,882	1	4,882	1	2
BEHAV BRAIN RES	3,028	1	3,028	2	4
BIOMED RESEARCH INTERNATIONAL	1,579	5	7,895	3	7
BIOSCIENCE REP	2,637	1	2,637	3	7
BLOOD	10,452	1	10,452	1	1
BMC CANCER	3,362	2	6,724	2	4
BMC FAM PRACT	1,669	1	1,669	2	4
BMC GENET	2,397	1	2,397	3	6
BMC GENOMICS	3,986	1	3,986	1	2
BMC INFECTIOUS DISEASES	2,613	2	5,226	2	5
BMC PUBLIC HEALTH	2,264	1	2,264	2	4
BRAIN	9,196	1	9,196	1	1
BREAST CANCER RESEARCH AND TREATMENT	3,94	1	3,94	2	3
BRITISH JOURNAL OF HAEMATOLOGY	4,711	1	4,711	1	2
BRITISH JOURNAL OF OPHTHALMOLOGY	2,976	1	2,976	1	3
BURNS	1,88	1	1,88	4	8
CALCIFIED TISSUE INT	3,272	1	3,272	2	5
CANCER CELL	23,523	1	23,523	1	1
CANCER CHEMOTHERAPY AND PHARMACOLOGY	2,769	2	5,538	2	4
CARDIOL J	1,062	1	1,062	4	8
CELL DEATH DIFFER	8,184	1	8,184	1	1
CELL STRESS CHAPERON	3,163	1	3,163	3	6
CEPHALALGIA	4,891	3	14,673	1	2
CHEST	7,483	1	7,483	1	1
CHRONOBIOL INT	3,343	1	3,343	1	2
CIR ESPAN	0,743	4	2,972	4	8
CLIN EXP RHEUMATOL	2,724	12	32,688	2	5
CLIN GASTROENTEROL H	7,896	1	7,896	1	1
CLIN LAB	1,129	1	1,129	3	7
CLIN NEUROPHYSIOL	3,097	1	3,097	2	4
CLIN NUCL MED	3,931	1	3,931	1	2
CLIN TRANSPLANT	1,522	1	1,522	2	5
CLINICA CHIMICA ACTA	2,824	1	2,824	1	2
CLINICAL & TRANSLATIONAL ONCOLOGY	2,077	6	12,462	3	7
CLINICAL CHEMISTRY AND LABORATORY MEDICINE	2,707	1	2,707	1	2
CLINICAL INFECTIOUS DISEASES	8,886	2	17,772	1	1
CLINICAL MICROBIOLOGY AND INFECTION	5,768	2	11,536	1	1
COGN NEUROPSYCHIATRY	1,912	1	1,912	3	6
CRIT CARE MED	6,312	1	6,312	1	2
CURR GENOMICS	2,342	3	7,026	3	7
CURR OPIN RHEUMATOL	4,886	1	4,886	1	2
CURRENT NEUROPHARMACOLOGY	3,049	1	3,049	2	3
CURRENT PHARMACEUTICAL DESIGN	3,452	2	6,904	1	3
CURRENT RHEUMATOLOGY REPORTS	2,871	1	2,871	2	4
DERMATOLOGY	1,569	1	1,569	2	5
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE	2,457	1	2,457	3	6
DIS COLON RECTUM	3,749	1	3,749	2	3
DRUGS	4,343	1	4,343	1	2
EMERGENCIAS	2,895	2	5,79	1	2

REVISTA	FI (JCR 2014)	Nº	Suma FI	Cuartil	Decil
ENFERMEDADES INFECCIOSAS Y MICROBIOLOGIA CLINICA	2,172	5	10,86	3	7
EPILEPSY BEHAV	2,257	1	2,257	2	5
EUR CHILD ADOLES PSY	3,336	3	10,008	1	1
EUR J DERMATOL	1,99	1	1,99	2	4
EUR J MED CHEM	3,447	1	3,447	1	2
EUR NEUROPSYCHOPHARM	4,369	1	4,369	1	2
EUR PSYCHIAT	3,439	3	10,317	2	3
EUR RESPIR J	7,636	1	7,636	1	1
EUR UROL	13,938	2	27,876	1	1
EUROINTERVENTION	3,769	3	11,307	2	3
EUROPEAN JOURNAL OF CANCER	5,417	2	10,834	1	2
EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY	2,966	1	2,966	2	4
EUROPEAN JOURNAL OF INTERNAL MEDICINE	2,891	1	2,891	1	2
EUROSURVEILLANCE	5,722	1	5,722	1	1
EXPERT REV HEMATOL	2,07	1	2,07	3	7
EXPERT REV NEUROTHER	2,783	1	2,783	2	4
EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH	1,669	1	1,669	3	6
FISH SHELLFISH IMMUN	2,674	1	2,674	1	1
FORENSIC SCI INT-GEN	4,604	1	4,604	1	1
FRONT CELL NEUROSCI	4,289	1	4,289	1	3
FRONTIERS IN PHYSIOLOGY	3,534	1	3,534	1	3
GAC SANIT	1,186	1	1,186	3	8
GASTROENT HEPAT-BARC	0,838	2	1,676	4	10
GASTROINTEST ENDOSC	5,369	1	5,369	1	2
GENOME RES	14,63	1	14,63	1	1
HAEMATOLOGICA	5,814	4	23,256	1	1
HEPATOLOGY	11,055	2	22,11	1	1
HISTOL HISTOPATHOL	2,096	1	2,096	3	8
HISTOPATHOLOGY	3,453	2	6,906	1	2
HUM VACC IMMUNOTHER	2,366	1	2,366	2	5
IEEE ELECTR INSUL M	1,643	1	1,643	2	4
IMMUNOLOGIC RESEARCH	3,098	1	3,098	2	5
INFECTIOUS AGENTS AND CANCER	2,358	1	2,358	3	7
INJURY	2,137	1	2,137	1	2
INT IMMUNOPHARMACOL	2,472	1	2,472	3	6
INT J CARDIOL	4,036	3	12,108	1	3
INT J DERMATOL	1,312	3	3,936	3	7
INT J DEV BIOL	1,903	1	1,903	4	9
INT J MED ROBOT COMP	1,526	1	1,526	2	5
INT J NEUROPSYCHOPH	4,009	1	4,009	1	2
INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS	4,296	1	4,296	1	2
INTERNATIONAL JOURNAL OF CANCER	5,085	2	10,17	1	2
INTERNATIONAL JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE	3,141	1	3,141	2	3
INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE	2,088	1	2,088	3	6

REVISTA	FI (JCR 2014)	Nº	Suma FI	Cuartil	Decil
J AFFECT DISORDERS	3,383	1	3,383	2	3
J AM COLL CARDIOL	16,503	2	33,006	1	1
J AM GERIATR SOC	4,572	1	4,572	1	2
J APPL ANIM RES	0,435	1	0,435	4	8
J BIOL CHEM	4,573	1	4,573	1	3
J CARDIOTHOR VASC AN	1,463	1	1,463	3	7
J CELL SCI	5,432	1	5,432	1	3
J CHILD PSYCHOL PSYC	6,459	1	6,459	1	1
J CLIN ENDOCR METAB	6,209	1	6,209	1	2
J CLIN PSYCHIAT	5,498	1	5,498	1	2
J CLIN VIROL	3,016	1	3,016	2	5
J DERMATOL TREAT	1,669	1	1,669	2	5
J EUR ACAD DERMATOL	2,826	2	5,652	1	2
J GEN VIROL	3,183	1	3,183	2	3
J HEADACHE PAIN	2,801	1	2,801	2	4
J HEART LUNG TRANSPL	6,65	1	6,65	1	1
J HEPATOL	11,336	3	34,008	1	1
J HYPERTENS	4,72	1	4,72	1	2
J IMMUNOL METHODS	1,82	1	1,82	3	7
J INVASIVE CARDIOL	0,949	1	0,949	4	9
J INVEST ALLERG CLIN	2,596	3	7,788	2	5
J NEUROL	3,377	1	3,377	2	3
J NEUROL NEUROSUR PS	6,807	2	13,614	1	1
J NEUROSURG	3,737	1	3,737	1	2
J NON-CRYST SOLIDS	1,766	1	1,766	1	2
J PARKINSON DIS	1,91	1	1,91	3	8
J PERIPHER NERV SYST	2,758	1	2,758	2	4
J PHYS CHEM C	4,772	1	4,772	1	3
J PINEAL RES	9,6	1	9,6	1	1
J PSYCHIATR PRACT	1,344	1	1,344	3	8
J RHEUMATOL	3,187	2	6,374	2	4
J VIRAL HEPATITIS	3,909	1	3,909	2	3
JACC-CARDIOVASC INTE	7,345	1	7,345	1	1
JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION	35,289	2	70,578	1	1
JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY	5,313	6	31,878	1	1
JOURNAL OF CLINICAL MICROBIOLOGY	3,993	1	3,993	1	3
JOURNAL OF CLINICAL ONCOLOGY	18,428	2	36,856	1	1
JOURNAL OF IMMUNOLOGY	4,922	1	4,922	1	2
JOURNAL OF INFECTION	4,441	2	8,882	1	2
JOURNAL OF NEUROSCIENCE	6,344	1	6,344	1	1
KIDNEY INT	8,563	1	8,563	1	1
LANCET INFECT DIS	22,433	1	22,433	1	1
LANCET NEUROL	21,896	2	43,792	1	1
LANCET RESPIRATORY MEDICINE	9,629	1	9,629	1	1

REVISTA	FI (JCR 2014)	Nº	Suma FI	Cuartil	Decil
LEUKEMIA & LYMPHOMA	2,891	1	2,891	2	5
LEUKEMIA RESEARCH	2,351	1	2,351	3	6
LIGHT-SCIENCE & APPLICATIONS	14,603	1	14,603	1	1
LIVER INT	4,85	3	14,55	1	2
LUPUS	2,197	1	2,197	3	6
MATURITAS	2,942	1	2,942	1	2
MED INTENSIVA	1,336	5	6,68	4	9
MEDICINA CLINICA	1,417	9	12,753	2	5
MEDICINE	5,723	7	40,061	1	1
MEM I OSWALDO CRUZ	1,592	1	1,592	2	5
MENOPAUSE-THE JOURNAL OF THE NORTH AMERICAN MENOPAUSE SOCIETY	3,361	1	3,361	1	2
MICROBES AND INFECTION	2,861	1	2,861	2	5
MIDWIFERY	1,573	1	1,573	1	2
MODERN PATHOLOGY	6,187	3	18,561	1	1
MOL CELL BIOCHEM	2,393	1	2,393	3	7
MOL GENET METAB	2,625	1	2,625	3	6
MOVEMENT DISORD	5,68	1	5,68	1	1
MUSCLE NERVE	2,283	2	4,566	3	6
NANO LETT	13,592	1	13,592	1	1
NATURE	41,456	2	82,912	1	1
NATURE COMMUNICATIONS	11,47	1	11,47	1	1
NEFROLOGIA	1,223	2	2,446	3	8
NEPHROL DIAL TRANSPL	3,577	1	3,577	2	3
NEUROBIOL AGING	5,013	2	10,026	1	1
NEUROL MED-CHIR	0,724	1	0,724	4	10
NEUROLOGIA	1,381	1	1,381	4	8
NEUROLOGY	8,286	1	8,286	1	1
NEUROMUSCULAR DISORD	2,638	1	2,638	2	5
NEUROPSYCHOBIOLOGY	2,261	1	2,261	3	7
NEUROUROL URODYNAM	2,873	1	2,873	1	3
NEW ENGLAND JOURNAL OF MEDICINE	55,873	1	55,873	1	1
NUCL MED COMMUN	1,669	1	1,669	3	6
NUTRICION HOSPITALARIA	1,04	1	1,04	4	9
ONCOGENE	8,459	1	8,459	1	1
ONCOTARGET	6,359	8	50,872	1	1
OPT MATER EXPRESS	2,844	1	2,844	1	2
OSTEOPOROSIS INT	4,169	2	8,338	2	3
PAIN	5,213	1	5,213	1	1
PANCREAS	2,959	1	2,959	2	5
PARKINSONISM RELAT D	3,972	1	3,972	1	2
PATHOLOGY RESEARCH AND PRACTICE	1,397	2	2,794	4	8
PHARMACOEPIDEMIOLOGY AND DRUG SAFETY	2,939	1	2,939	2	4
PLASMID	1,578	1	1,578	3	8
PLOS ONE	3,234	14	45,276	1	2
PROTEOMICS	3,807	1	3,807	1	3
PSYCHIAT RES-NEUROIM	2,424	3	7,272	2	5
PSYCHOL MED	5,938	1	5,938	1	1
REV ESP CARDIOL	3,792	5	18,96	2	3
REV ESP ENFERM DIG	1,414	5	7,07	4	9
REV ESP MED NUCL IMA	1,054	4	4,216	4	9
REV NEUROLOGIA	0,83	1	0,83	4	9
REVISTA CLINICA ESPANOLA	1,063	4	4,252	3	6
REVISTA ESPANOLA DE QUIMIOTERAPIA	0,797	2	1,594	4	9
REVISTA IBEROAMERICANA DE MICOLOGIA	1,056	1	1,056	4	9
RHEUMATOL INT	1,516	2	3,032	3	7
RHEUMATOLOGY	4,475	2	8,95	1	2
ROM J MORPHOL EMBRYO	0,659	1	0,659	4	10
RSC ADV	3,84	1	3,84	1	3
SCHIZOPHR RES	3,923	3	11,769	1	3
SCI TOTAL ENVIRON	4,099	1	4,099	1	1
SEMIN ARTHRITIS RHEU	3,925	5	19,625	1	3
SKELETAL RADIOL	1,51	2	3,02	2	5
SLEEP	4,591	1	4,591	1	2
SLEEP MED	3,154	1	3,154	2	3
TEX HEART I J	0,649	1	0,649	4	10
TISSUE ANTIGENS	2,137	1	2,137	2	5
TRANSLATIONAL PSYCHIATRY	5,62	1	5,62	1	2
TRANSPL INFECT DIS	2,064	2	4,128	3	6
TRANSPL INT	2,599	2	5,198	2	3
TRANSPL P	0,982	6	5,892	3	7
TRANSPLANTATION	3,828	2	7,656	1	1
UNITED EUROPEAN GASTROENTEROLOGY JOURNAL	2,08	1	2,08	3	7
VACCINE	3,624	1	3,624	2	4
WORLD J GASTROENTERO	2,369	2	4,738	3	6
WORLD NEUROSURG	2,878	1	2,878	1	2
XENOTRANSPLANTATION	2,84	1	2,84	2	4
TOTAL GENERAL		**422**	**1949,271**		

RESEARCH IDIVAL GROUPS' IMPACTFACTOR

Scientific production of the 29 research IDIVAL groups descibed by impact factor is as follows:

GROUP	Impact
ADVANCED MICROSCOPY, PROTEIN FOLDING AND THE CYTOSKELETON	5,432
ANATOMICAL PATHOLOGY AND MOLECULAR PATHOLOGY	61,338
APOPTOSIS	13,582
CANCER GENOMICS	178,58
CARDIOVASCULAR RESEARCH GROUP	70,533
CELL CYCLE, DETERMINING STEM CELLS AND CANCER	1,392
CELL NUCLEUS BIOLOGY	18,318
CELL SIGNALLING AND THERAPEUTIC TARGETS	21,51
CEPHALEA CLINIC AND GENETICS	60,187
CLINICAL AND MOLECULAR MICROBIOLOGY	118,462
CLINICAL TRIALS UNIT, MEDICAL ONCOLOGY AND PALLIATIVE MEDICINE	114,805
CYTOKINES AND GROWTH FACTORS IN THE PHENOMENA OF PATHOLOGICAL TISSUE PLASTICITY	29,135
DIAGNOSIS AND TREATMENT USING IMAGING (RADIOLOGY)	30,269
EPIDEMIOLOGY AND PATHOGENIC MECHANISMS OF INFECTIOUS DISEASES	70,38
EPIDEMIOLOGY AND PUBLIC HEALTH	108,201
GENETIC EPIDEMIOLOGY AND ATHEROSCLEROSIS IN SYSTEMIC INFLAMMATORY DISEASES	255,614
GENOMICS, PROTEOMICS AND VACCINES	11,044
HAEMATOLOGIC NEOPLASMS AND HAEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION	39,631
IMMUNOPATHOLOGY OF RHEUMATIC DISEASES	34,272
INFECTION,IMMUNITY AND DIGESTIVE DISEASES	131,808
MELATONIN AND BREAST CANCER	18,939
MINERAL AND LIPID METABOLISM	140,119
MOLECULAR IMAGING	62,65
NANOMEDICINE	59,605
NEURODEGENERATIVE DISEASE	241,745
NEUROPHYSIOLOGY IN EPILEPSY AND NEUROINTENSIVES	10,353
NEW TECHNIQUES IN ABDOMINAL SURGERY	11,003
PSYCHIATRY	146,272
TRANSPLANTATION AND AUTOIMMUNITY	122,285

RESEARCH PROJECTS

Active or granted R&D National Plan projects in 2015

Active

Throughout 2015, IDIVAL groups maintained 29 active projects from the R&D National Plan and two European projects.

PI12/00715. LLORCA DÍAZ, JAVIER. Genetic variants and pathways related to breast and prostate cancers, and their interaction with exposure to endogenous and exogenous sex hormones: study MCC-Spain. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/00637. RODRÍGUEZ REY, JOSÉ CARLOS. Genetic basis of hereditary hipercolesterolemias not dependent on the LDL receptor or apolipoprotein b. Characterisation and functional analysis of variants of the 3' regulatory regions of candidate genes. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/02288. SÁNCHEZ JUAN, PASCUAL. Multimodal study of Alzheimer's disease biomarkers in postoperative cognitive decline. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/02605. MIER RUIZ, MARÍA VICTORIA. Epidemiological aspects, variability and survival in cardiac arrest care outside of the hospital for emergency services in Spain (subproject Cantabria). CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/00060. GONZÁLEZ-GAY MANTECÓN, MIGUEL ÁNGEL. Study of genetic markers of cardiovascular disease and subclinical atherosclerosis in rheumatoid arthritis patients. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/02026. CRESPO GARCÍA, JAVIER. Implication of different factors of innate and adaptive immunity in the etiopathogenesis of liver disease from fatty deposits in morbidly obese patients. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/01405. GONZÁLEZ MACÍAS, JESÚS. The canonical Wnt pathway in osteoclast: 2012*study of its intervention in the regulation of bone mass. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/00193. BLANCO ALONSO, RICARDO. Study of genetic markers of susceptibility in patients with Henoch-Schönlein vasculitis. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/00357. VAQUE DÍEZ, JOSÉ PEDRO. Metastatic melanoma: Molecular diagnosis oriented towards targeted therapy. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/00615. RIANCHO MORAL, JOSÉ ANTONIO. DNA Methylation: The pathogenic and biomarker factor in bone formation disorders. CARLOS III HEALTH INSTITUTE 2013-2016.

PI12/00999. NISTAL HERRERA, JUAN FRANCISCO Role of adiponectin and its relationship with TNF-ß in myocardial remodelling induced by pressure overload in aortic stenosis and its postsurgical regression. CARLOS III HEALTH INSTITUTE 2013-2015.

PI12/01433. FERNÁNDEZ MIERA, MANUEL FRANCISCO. Multichannel preview: Contribution of telemedicine to care continuity for complex chronic patients. CARLOS III HEALTH INSTITUTE 2013-2015.

PSI2012-33652. MARTÍNEZ-CUÉ, CARMEN. Pharmacological and genetic inhibition of the GABAA R alpha 5 receptor and inhibition of the Dyrk1A gene in the Down syndrome Ts65Dn mouse model: therapeutic action. MINECO. 2013-2015.

SAF2012-34059. MERINO PÉREZ, JESÚS. Study of the anti-inflammatory role of apolipoprotein E (APOE) in autoimmunity. MINECO. 2013-2015.

SAF2012-34203. ÁLVAREZ DOMÍNGUEZ, CARMEN. Study of different vaccine vectors based on Listeria monocytogenes against various inflammatory, infectious and cancerous processes. MINECO. 2013-2015.

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. HURLÉ GONZÁLEZ, MARÍA AMOR. MicroRNAs in neuropathic pain: molecular biomarkers and targeted therapies. MINECO. 2014-2016.

PI13/01008. RODRÍGUEZ RODRÍGUEZ, ELOY MANUEL. Alzheimer's disease biomarkers as prognostic factors in idiopathic normal pressure hydrocephalus. CARLOS III HEALTH INSTITUTE 2014-2016.

PI13/01310. RAMOS VIVAS, JOSÉ. Clinically relevant host-pathogen key interaction in Acinetobacter species. CARLOS III HEALTH INSTITUTE 2014-2016.

PI13/01760. FERNÁNDEZ LUNA, JOSÉ LUIS. Prognostic and therapeutic relevance in ODZ 1 glioblastoma, a new target in cancer. CARLOS III HEALTH INSTITUTE 2014-2016.

PI13/01884. CARRASCO MARÍN EUGENIO. 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. MARTINO GONZÁLEZ, JUAN. 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. FARIÑAS ÁLVAREZ, MARÍA DEL CARMEN. 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. BERCIANO BLANCO, Mª TERESA, MIGUEL ÁNGEL LAFARGA COSCOJUELA Acetylation regulation of the survival factor of motoneurons: its importance in snRNP biogenesis and the assembly cajal nuclear bodies. MINECO. 2015-2017.

BFU2014-54026-P. HURLÉ GONZÁLEZ, JUAN. 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. ARIAS RODRÍGUEZ, MANUEL ANTONIO. 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. GANDARILLAS SOLINÍS, ALBERTO. New Routes and Strategies Towards Squamous Cell Cancer. CARLOS III HEALTH INSTITUTE 2015-2017.

PI14/00918. AYESA ARRIOLA, ROSA. 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. MARTÍNEZ MARTÍNEZ, LUIS. Heteroresistance and Persistence in carbapenem-resistant Klebsiella pneumoniae. CARLOS III HEALTH INSTITUTE 2015-2017.

Granted

In 2015, IDIVAL researchers received a positive response on 10 projects in the National Plan.

PI15/00009. OCAMPO SOSA, ALAIN ANTONIO. Functional identification and characterisation of new components of type VI secretion systems and the molecular basis of their regulation in clinical strains of Pseudomonas aeruginosa. CARLOS III HEALTH INSTITUTE 2016-2018.

PI15/00521. OLMOS MARTÍNEZ, JOSÉ MANUEL. Study of bone and mineral metabolism of the post-menopausal female and male population aged 50 and over receiving care from a health centre in Cantabria. CARLOS III HEALTH INSTITUTE 2016-2018.

PI15/00525. GONZÁLEZ-GAY MANTECÓN, MIGUEL ÁNGEL. Genetic markers of atherosclerotic disease in Rheumatoid Arthritis. CARLOS III HEALTH INSTITUTE 2016-2018.

PI15/01224. NISTAL HERRERA, JUAN FRANCISCO. Protein morphogenetic of bone 7 (BMP7): Potential therapeutic target in the pathological remodelling of the cardiovascular system. CARLOS III HEALTH INSTITUTE 2016-2018.

PI15/02138. CRESPO GARCÍA, JAVIER. 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. 2016-2018.

PI15/01285. OTERINO DURÁN, AGUSTÍN. 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. LLORCA DÍAZ, JAVIER. Integration of genetic big data and clinical data: survival with breast cancer in the MCC-Spain study. CARLOS III HEALTH INSTITUTE 2016-2018.

PIE15/00079. CRESPO GARCÍA, JAVIER. Personalized Medicine in HCV infection: understanding and predicting hepatic and systemic responses in the era of the new antiviral drugs. CARLOS III HEALTH INSTITUTE 2016-2018.

PIE15/00081. PIRIS PINILLA, MIGUEL ÁNGEL. Discovery, Validation and Implementation of Biomarkers for Precision Oncology. CARLOS III HEALTH INSTITUTE 2016-2019.

RTC-2015-3786-1. GOMEZ ROMÁN, JAVIER. Development of anti-CCR9 therapeutic antibodies for the personalised treatment of tumours- TERPERAN. CARLOS III HEALTH INSTITUTE 2016-2018.

Active European Projects in 2015

EU12/01- PSYSCAN. CRESPO FACORRO, BENEDICTO. Translating neuroimaging findings from research into clinical practice. 7PM. European Commission.

EU13/01- PRECISESADS. GONZÁLEZ-GAY MIGUEL ÁNGEL. Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases. FP7, Innovative Medicines Initiative. European Commission.

CLINICAL TRIALS

During 2015, the Ethics Committee for Clinical Research of Cantabria (CEIC) authorised a total of 54 clinical trials and 49 post-authorisation studies to be developed at the Marqués de Valdecilla University Hospital and its area of influence. Of the 54 clinical trials approved in 2015 by the CEIC of Cantabria, one is Phase I, 14 are Phase II, 23 are Phase III, six are Phase IV, four concern healthcare products and six concern procedures (without drugs or healthcare products). The list of major clinical trials approved in 2015 is as follows.

LIST OF TRIALS AUTHORISED BY CEIC IN 2015

CODE	MAIN RESEARCHER	FULL TITLE
UTS-2014	MARTA MARÍA CABELLO NÁJERA	Cost-effectiveness of diagnosis and treatment in the syndrome of sleep apnea hypopnea using home respiratory polygraphy.
SLICE	RAMÓN AGÜERO BALBÍN	Clinical efficacy and safety in the active search and treatment of PE in patients hospitalised for the exacerbation of COPD of an unknown cause.
SURMOUNT_ P.Sanitario	ANDRÉS GONZÁLEZ MANDLY	Prospective international register: observational, multicentre, of a single group, with consecutive inscription and subsequent to the marketing of the Surpass flow diverter in intracranial arteries.
WRAP-IT_Ensayo con P. Sanitario	JUAN JOSÉ OLALLA ANTOLÍN	Randomised global study on the prevention of infection envelope antibiotics.
2015.077	ENRIQUE RAMOS BARSELO	Randomised study on Laparoscopic Radical Prostatectomy with preservation of neurovascular bundles. Conventional technique versus hydrodissection technique.
201378_2014-002253-19	FERNANDO RODRÍGUEZ FERNÁNDEZ	A multicentre, randomised, double-blind, double dummy study using parallel groups with Fluticasone Furoate/Vilanterol 100/25 mcg powder for inhalation once daily, Fluticasone Propionate/Salmeterol 250/50 mcg powder for inhalation twice daily and Fluticasone Propionate 250 mcg powder for inhalation twice daily, for the treatment of asthma persistent in adults and adolescents who are already adequately controlled with an inhaled corticosteroid treatment and a long-acting beta2 agonist twice daily.
RGB-03-104_2014-003255-54	JAIME CALVO ALÉN	Randomised, double-blind study to assess the pharmacokinetics, pharmacodynamics, efficacy and safety of RGB-03 compared with MabThera®, combined with methotrexate, in patients with rheumatoid arthritis.
POL7080-003_2013-001596-21	CARMEN BLANCO HUELGA	Multicentre open study of phase II to evaluate the pharmacokinetics (PK), safety and efficacy of POL7080 administered together with the standard treatment in patients with ventilator associated pneumonia (VAP) secondary to infection, suspected or confirmed, due to Pseudomonas aeruginosa.
TMC435HPC2019_2014-003413-28	JAVIER CRESPO GARCÍA	Phase 2 open study to research the efficacy and safety of the combination of simeprevir and daclatasvir in patients chronically infected with the hepatitis C virus genotype 1b with advanced liver disease.
8232-CL-0004_2014-002349-23	GEMA FERNÁNDEZ FRESNEDO	Phase II, double-blind, randomised, placebo-controlled study to evaluate the efficacy and safety of ASP8232 as complementary therapy for angiotensin converting enzyme (ACE) inhibitors or receptor antagonist blockers (ARBs) in reducing albuminuria in patients with type 2 diabetes and chronic kidney disease.
DIA-Der-02-14_2014 004429-42	FERNANDO RODRÍGUEZ FERNÁNDEZ	Multicentre open clinical trial to confirm the nonreactive (endpoint titration) maximum dose with the allergoid polymerised Dermatophagoides pteronyssinus administered intradermally in patients with allergic rhinoconjunctivitis or mild or moderate asthma sensitised to the mite Dermatophagoides pteronyssinus.
GETNE-1408_2014-004072-30	CARLOS LÓPEZ LÓPEZ	Phase II study to assess the activity and safety of TH-302 in combination with sunitinib in patients with previously untreated highly or moderately differentiated metastatic pancreatic neuroendocrine tumours (pNET). .
ABI-007-PANC-007_2014-001408-23	FERNANDO RIVERA HERRERO	Nab-paclitaxel (Abraxane®) and gemcitabine in patients with locally advanced pancreatic cancer (LAPC): phase 2, international, open multicentre study (LAPACT).
ALX0061-C202_2014-003012-36	RICARDO BLANCO ALONSO	Phase IIb, multicentre, randomised, double-blind study of ALX-0061 as monotherapy administered subcutaneously in subjects with rheumatoid arthritis with moderate to severe intolerance to methotrexate or for whom continued treatment with methotrexate is unsuitable.
ALX0061-C202_2014-003012-36 (SIERRALLANA)	JAIME CALVO ALÉN	Phase IIb, multicentre, randomised, double-blind study of ALX-0061 as monotherapy administered subcutaneously in subjects with rheumatoid arthritis with moderate to severe intolerance to methotrexate or for whom continued treatment with methotrexate is unsuitable.
CA209-171_2014-001285-10	MARTA FRANCISCA LÓPEZ-BREA PIQUERAS	Open multicentre clinical trial of nivolumab (BMS-936558) as monotherapy in subjects with advanced or metastic squamous non-small-cell lung carcinoma (NSCLC) who have received at least one prior line of systemic therapy for the treatment of stage IIIb/IV squamous NSCLC .
TMC435HPC2018_2014-004250-34	JAVIER CRESPO GARCÍA	Phase II open study with only one line of treatment to study the efficacy, safety, tolerability and pharmacokinetics of 12 weeks of treatment with Simeprevir and Daclatasvir in patients chronically infected with genotype 1b or 4 of the hepatitis C virus and with severe renal dysfunction or terminal renal disease on haemodialysis.
ACE-011-REN-002_2012-003788-23	ÁNGEL LUIS MARTÍN DE FRANCISCO HERNÁNDEZ	Phase 2 multicentre, randomised, open study with multiple doses of sotatercept (ACE-011) administered intravenously and subcutaneously, replacing haematopoiesis stimulating agents in patients with terminal renal nephropathy on hemodialysis using groups with doses increasing in steps in part 1, followed by a study of parallel groups with an active control of the dose(s) and regimen selected in part 2, to evaluate the pharmacokinetics, safety, tolerability, efficacy, dosing regimen and pharmacodynamics of sotatercept.
ALX0061-C203_2014-003034-42	RICARDO BLANCO ALONSO	hemodialysis using groups with doses increasing in steps in part 1, followed by a study of parallel groups with an active control of the dose(s) and regimen selected in part 2, to evaluate the pharmacokinetics, safety, tolerability, efficacy, dosing regimen and

CODE	MAIN RESERACHER	FULL TITLE
ALX0061-C203_2014-003034-42 (SIERRALLANA)	JAIME CALVO ALÉN	Extension, Phase II, multicentre, open study to evaluate the efficacy and safety in long-term subcutaneous ALX-0061 use in patients with moderate to severe rheumatoid arthritis who have completed one of the above Phase IIb studies with ALX-006.
MK-3475-164_2015-001852-32	FERNANDO RIVERA HERRERO	Phase II study of Pembrokeshire (MK 3475) as monotherapy in patients previously treated for declarant locally advanced or metastatic (stage IV) colorectal carcinoma with high micro satellite instability or repair of deficient pairing errors. (KEYNOTE 164).
DS5565-A-E312_2013-005164-26	ROSA SANTILLAN FERNANDEZ	Open extension 52-week study of DS-5565 for the treatment of pain associated with fibromyalgia.
BAMI-01_2012-001495-11	JOSÉ MARÍA DE LA TORRE HERNÁNDEZ	Effect of intracoronary infusion of mononuclear stem cells derived from bone marrow (BM-MNCs) on all-cause mortality in acute myocardial infarction.
I1F-MC-RHBE_2011-002328-42	RICARDO BLANCO ALONSO	Multicentre, randomised, double-blind, placebo-controlled 24-week study followed by a long-term evaluation of the efficacy and safety of ixekizumab (LY2439821) in patients with active psoriatic arthritis who received a modifying antirheumatic drug for the biological disease.
CAIN457F2320_2013-005575-41	RICARDO BLANCO ALONSO	Phase III, multicentre, randomised, double-blind, placebo-controlled study of secukinumab (150 mg) administered subcutaneously with or without a loading dose administered subcutaneously to evaluate the efficacy, safety and tolerability in patients with active ankylosing spondylitis for up to two years.
CAIN457A3302_2014-005339-15	SUSANA ARMESTO ALONSO	Optimising treatment of long-term maintenance of whitened skin in patients with moderate to severe chronic plaque psoriasis: randomised, multicentre, open-blind, comparative 52-week monitoring study to evaluate the efficacy, safety and tolerability of secukinumab 300 mg s.c.
MK3475-061_2014-005241-45	FERNANDO RIVERA HERRERO	Phase III, randomised, open clinical trial on Pembrokeshire (MK 3475) versus paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma who have displayed progression after first-line treatment with platinum and fluoropyrimidine.
200862_2014-002513-27	FERNANDO RODRÍGUEZ FERNÁNDEZ	Multicentre, randomised, double-blind, placebo-controlled 24-week study with parallel groups to evaluate the efficacy and safety of a complementary treatment with mepolizumab in subjects with severe eosinophilic asthma on markers of asthma control.
CIRROXABAN_2014-005523-27	ÁNGELA PUENTE SÁNCHEZ	Prospective, multicentre, randomised study on the effect of Rivaroxaban on the survival and development of complications of portal hypertension in patients with cirrhosis.

CODE	MAIN RESERACHER	FULL TITLE
H-030-014_2013-000775-32	JAVIER CRESPO GARCÍA	Study on the efficacy, immunogenicity and safety of the Clostridium difficile toxoid vaccine in subjects at risk of developing the C. difficile infection.
02044190615-01_2013-005428-41	FERNANDO RIVERA HERRERO	Phase III study of regorafenib versus placebo as maintenance therapy after first-line treatment of metastatic colorectal cancer with wild-type RAS (RAVELLO trial).
GO29436_2014-003207-30	MARTA FRANCISCA LÓPEZ-BREA PIQUERAS	Phase III, open, randomised study of MPDL3280A (Anti-PD-L1 antibody) in combination with Carboplatin + Paclitaxel with or without Bevacizumab compared with Carboplatin + Paclitaxel + Bevacizumab in patients with squamous non-small-cell stage IV lung cancer who have not received prior chemotherapy.
GO29437_2014-003208-59	MARTA FRANCISCA LÓPEZ-BREA PIQUERAS	Phase III, open, multicentre, randomised study evaluating the efficacy and safety of MPDL3280A (ANTI PD L1antibody) in combination with Carboplatin + Paclitaxel or MPDL3280A in combination with Carboplatin + Nab Paclitaxel compared with Carboplatin + Nab Paclitaxel in patients with squamous non-small-cell stage IV lung cancer who have not received prior chemotherapy.
42160443PAI3007_2014-003224-40	JAIME CALVO ALÉN	Randomised 16-week, multi-phase, double-blind, placebo-controlled study to evaluate the safety, tolerability and efficacy of fulranumab as complementary therapy in patients with signs and symptoms of osteoarthritis of the hip or knee.
42160443PAI3003_2014-002598-13	RICARDO BLANCO ALONSO	Randomised 16-week, multi-phase, double-blind, placebo-controlled study to evaluate the safety, tolerability and efficacy of fulranumab as monotherapy in patients with signs and symptoms of osteoarthritis of the hip or knee.
I4T-MC-JVDE_2014-005068-13	CARLOS LÓPEZ LÓPEZ	Phase 3, randomised, double-blind, placebo-controlled study of ramucirumab and the best complementary measures against a placebo and the best complementary measures as a second-line treatment in patients with hepatocellular carcinoma and a high alpha-fetoprotein (AFP) basal after first-line treatment with sorafenib.
ACE-CL-006_2014-005530-64	LUCRECIA YÁÑEZ SAN SEGUNDO	Phase 3, randomised, multicentre open study to assess the non-inferiority of ACP 196 with Ibrutinib in subjects with previously treated high-risk chronic lymphocytic leukaemia.
ACE-CL-007_2014-005582-73	LUCRECIA YÁÑEZ SAN SEGUNDO	Phase 3, randomised, multicentre, open study with three groups of Obinutuzumab in combination with Chlorambucil, ACP 196 in combination with Obinutuzumab and ACP 196 as monotherapy in patients with chronic lymphocytic leukaemia without previous treatment.
B1481022_2013-002646-36	JOSÉ RAMÓN DE BERRAZUETA FERNÁNDEZ	Phase III, multicentre, double-blind, randomised, placebo-controlled study with parallel groups to assess the efficacy, safety and tolerability of bococizumab (PF-04950615) in reducing the number of major cardiovascular episodes in high risk patients.
B1481038_2013-002795-41	JOSÉ RAMÓN DE BERRAZUETA FERNÁNDEZ	Phase III, multicentre, double-blind, randomised, placebo-controlled study with parallel groups to assess the efficacy, safety and tolerability of bococizumab in reducing the number of major cardiovascular episodes in high risk patients.

CODE	MAIN RESERACHER	FULL TITLE
GETNE1509_2015-001467-39	CARLOS LÓPEZ LÓPEZ	Trial to evaluate the efficacy of lenvatinib in metastatic neuroendocrine tumours (Talent Study).
MK3475-062_2015-000972-88	FERNANDO RIVERA HERRERO	Phase III, randomised, partially-blind clinical study with control of the active treatment and biomarker detection of Pembrokeshire in monotherapy and in combination with cisplatin + 5-fluorouracil versus placebo + cisplatin + 5-fluorouracil as first-line treatment in patients with advanced gastric or gastroesophageal junction adenocarcinoma (GEJ).
20120297_2014-004463-20	AGUSTÍN OTERINO DURÁN	Phase III, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of AMG 334 in migraine prevention.
M14-172_2015-003797-32	JAVIER CRESPO GARCÍA	Open study with a single-treatment branch to assess the efficacy and safety of ABT 493/ABT 530 in adults chronically infected with hepatitis C virus genotypes 1, 2, 4, 5 or 6 and compensated cirrhosis (EXPEDITION-1).
FOBRALOC	PEDRO JOSÉ PRADA GÓMEZ	Focused treatment with brachytherapy on localised unifocal and multifocal prostate tumours.
FOCUSED_BQT_2013	PEDRO JOSÉ PRADA GÓMEZ	Phase II clinical trial of focused Brachytherapy in the management of prostate cancer in early stages.
ABR49490_2014-002765-30	BENEDICTO CRESPO FACORRO	European study of long-acting antipsychotic drugs in schizophrenia.
GO28399_2012-003144-80	ALMUDENA GARCÍA CASTAÑO	Extension (transfer) open study on Vemurafenib in patients with malignant neoplasia with the BRAFV600 mutation previously included in a prior Vemurafenib protocol.
M-34273-46_2014-004715-37	JUAN GARCÍA RIVERO	Randomised, double-blind, placebo-controlled study with parallel groups to evaluate the benefits of aclidinium bromide in improving COPD symptoms, including a cough, in its administration to patients with COPD.
AP105162012_2013-001955-11	CÉSAR GONZÁLEZ-BLANCH BOSCH	Pilot project to treat emotional disorders in primary care using psychological techniques based on evidence: a randomised controlled trial.
VPH-GXL-2013-01_2015-001181-26	PEDRO LUIS FERNÁNDEZ GIL	Evaluation of the impact of the LacTEST on diagnostic thinking and therapeutic management of the patient, and of reproducibility (Test-Retest) for the diagnosis of hypolactasia in adults and the elderly population showing clinical symptoms of lactose intolerance.
CCD-06235AA1-01_2014-004314-29	JUAN CARLOS RUÍZ SAN MILLÁN	Multicentre, open, randomised study with two parallel groups to evaluate the efficacy and safety of Envarsus® compared to tacrolimus, used according to current clinical practice as initial maintenance therapy in patients with de novo kidney transplantation.
ANCHOR_Ensayo con P. Sanitario	JOSÉ MARÍA DE LA TORRE HERNÁNDEZ	Percutaneous Coronary Intervention with the Angiolite drug-eluting stent: Tomography Study of Optical Coherence.
ANGIOLITE	JOSE JAVIER ZUECO GIL	Randomised clinical trial to compare the efficacy of the Angiolite Stent versus a second-generation drug-eluting stent such as Xience in patients with an indication for percutaneous coronary intervention.

CLINICAL PRACTICE GUIDELINES

In 2015, IDIVAL researchers participated in the following clinical practice guidelines and consensus documents. The relevance of these guidelines as recommendations developed systematically to help professionals and patients make decisions about the most suitable healthcare and to select the most appropriate diagnostic or therapeutic options when addressing a health problem is unquestionable..

1 Sastre J, Díaz-Beveridge R, García-Foncillas J, Guardeño R, López C, Pazo R, Rodriguez-Salas N, Salgado M, Salud A, Feliu J. Clinical guideline SEOM: hepatocellular carcinoma. Clin Transl Oncol 2015; 17:988-95.

2 Guillén-Ponce C, Serrano R, Sánchez-Heras AB, Teulé A, Chirivella I, Martín T, Martínez E, Morales R, Robles L. Clinical guideline seom: hereditary colorrectal cancer. Clin Transl Oncol 2015; 17:962-71.

3 Dejaco C, Singh YP, Perel P, Hutchings A, Camellino D, Mackie S, Abril A, Bachta A, Balint P, Barraclough K, Bianconi L, Buttgereit F, Carsons S, Ching D, Cid M, Cimmino M, Diamantopoulos A, Docken W, Duftner C, Fashanu B, Gilbert K, Hildreth P, Hollywood J, Jayne D, Lima M, Maharaj A, Mallen C, Martinez-Taboada V, Maz M, Merry S, Miller J, Mori S, Neill L, Nordborg E, Nott J, Padbury H, Pease C, Salvarani C, Schirmer M, Schmidt W, Spiera R, Tronnier D, Wagner A, Whitlock M, Matteson EL, Dasgupta B; European League Against Rheumatism; American College of Rheumatology. 2015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis 2015;74:1799-807.

4 Mingot-Castellano ME, Álvarez-Román MT, López-Fernández MF, Roca CA, Hirnyk MI, Jiménez-Yuste V, Haro AR, Pérez-Garrido R, Sedano Balbas C. Spanish consensus guidelines on prophylaxis with bypassing agents for surgery in patients with haemophilia and inhibitors. Eur J Haematol. 2015 Dec 29.

5 Plaza AM, Ibáñez MD, Sánchez-Solís M, Bosque-García M, Cabero MJ, Corzo JL, García-Hernández G, de la Hoz B, Korta-Murua J, Sánchez-Salguero C, Torres-Borrego J, Tortajada-Girbés M, Valverde-Molina J, Zapatero L, Nieto A. [Consensus-based approach for severe paediatric asthma in routine clinical practice]. An Pediatr (Barc) 2015 Oct 26. pii: S1695-4033(15)00362-8.

6 Campistol JM, Arias M, Ariceta G, Blasco M, Espinosa L, Espinosa M, Grinyó JM, Macía M, Mendizábal S, Praga M, Román E, Torra R, Valdés F, Vilalta R, Rodríguez de Córdoba S. An update for atypical haemolytic uraemic syndrome: Diagnosis and treatment. A consensus document. Nefrologia. 2015; 35:421-447.

7 Dejaco C, Singh YP, Perel P, Hutchings A, Camellino D, Mackie S, Abril A, Bachta A, Balint P, Barraclough K, Bianconi L, Buttgereit F, Carsons S, Ching D, Cid M, Cimmino M, Diamantopoulos A, Docken W, Duftner C, Fashanu B, Gilbert K, Hildreth P, Hollywood J, Jayne D, Lima M, Maharaj A, Mallen C, Martinez-Taboada V, Maz M, Merry S, Miller J, Mori S, Neill L, Nordborg E, Nott J, Padbury H, Pease C, Salvarani C, Schirmer M, Schmidt W, Spiera R, Tronnier D, Wagner A, Whitlock M, Matteson EL, Dasgupta B. 2015 recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Arthritis Rheumatol 2015 ;67:2569-80.

RETICS AND CIBER PARTICIPATING WITH IDIVAL

The Carlos III Health Institute has promoted various Thematic Network 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..

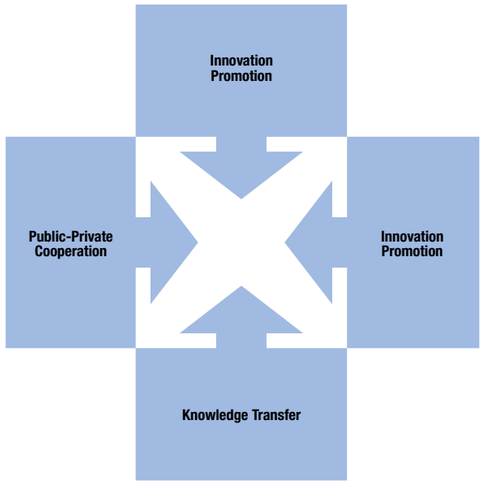
IDIVAL participates in three CIBERs, seven RETICS and three other platforms. Three of the RETICs in which IDIVAL participates (ITEMAS Platform, the Biobank Platform and the Scren Platform) have a supportive and cross-disciplinary nature, making up part of the researcher support services.

CIBER/RETIC	GRUPO/UNIDAD	IP
Mental Health CIBER (CIBERSAM)	Psychiatry	Benedicto Crespo Facorro
Neurodegenerative Disease CIBER (CIBERNED)	Neurodegenerative Disease	José Ángel Berciano Blanco
Epidemiology and Public Health CIBER (CIBERESP)	Epidemiology and Public Health	Javier Llorca Díaz
Spanish Network for Research in Infectious Diseases (REIPI)	Clinical and Molecular Microbiology	Luis Martínez Martínez
Network for Maternal and Children's Health and Development (RED SAMID)	Marqués de Valdecilla University Hospital	Maria Jesús Cabero
Thematic Network for Cooperative Research in Ageing and Fragility (RETICEF)	Mineral and Lipid Metabolism	Jesús González Macías
Renal Research Network (REDinREN)	Transplantation and autoimmunity	Manuel Arias Rodríguez
Thematic Network for Cooperative Research in Cancer (RTICC)	Cell Signalling and Therapeutic Targets in Cancer	José Luis Fernández Luna
Thematic Network for Cooperative Research in Cancer (RTICC)	Haematologic Neoplasms and Haematopoietic Progenitor Cell Transplantation	Eulogio Conde Garcia
Thematic Network for Cooperative Research in Cancer (RTICC)	Cancer Genomics	Miguel Ángel Piris Pinilla
Cardiovascular Research Network (RIC)	Cytokines and growth factors in the phenomena of pathological tissue plasticity	Juan Francisco Nistal
Research Network for Inflammation and Rheumatic Disease (RIER)	Genetic epidemiology and atherosclerosis in systemic inflammatory diseases	Miguel Angel Glez Gay
Biobank Platform	IDIVAL	Pascual Sánchez Juan
Platform for Innovation in Healthcare (ITEMAS)	IDIVAL	Galo Peralta Fernández
Platform for Clinical Research and Clinical Trials (Scren)	IDIVAL	Galo Peralta Fernández

INNOVATION

INTRODUCTION

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



The current context of market globalisation guides the course of the economy of neighbouring countries towards innovation activity as a major aspect of continued growth.
At IDIVAL, we believe that innovation and knowledge transfer can become drivers of the economy in the region of Cantabria; therefore we are committed to the activities carried out by 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 aims to promote innovation as a fundamental tool in health technology to make the National Healthcare System more sustainable, supporting development of the innovative culture necessary to facilitate the integration of a science-industry system in the field of medical technology. The core of ITEMAS currently comprises the innovation units of large hospitals in the National Healthcare System.
IDIVAL is part of ITEMAS through the IDIVAL Innovation Unit, which throughout 2015 developed related activities and those linked to participation in different working and Assembly groups. Specifically, it leads the alliances working group within the Platform.

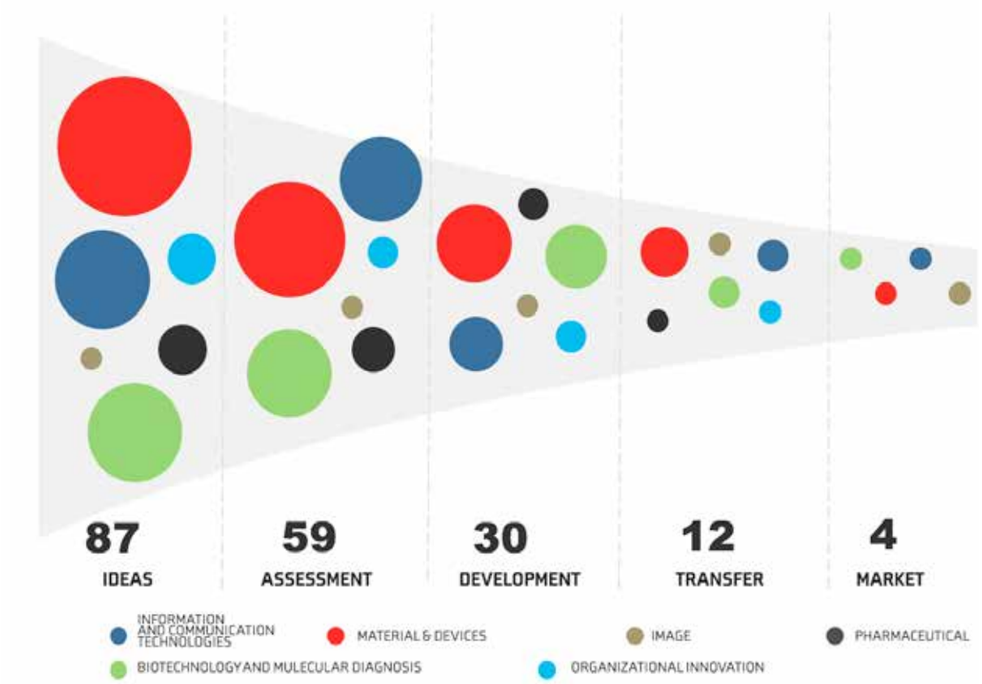
INNOVATIVE CULTURE

With the aim of promoting the culture of innovation in HUMV and our environment, IDIVAL organises a series of courses and workshops that encourage creativity, teamwork, reporting and forms of specific aspects of the innovation process, etc.
The Innovation Unit has participated in various activities presented in the training section.

TRANSFER

The need for a change in the production model in our country has meant that government measures support science-company collaboration as a driver of this change in model. For the transfer of research results to the market to be effective and have an impact on society, it is necessary to create an economic and legal environment conducive to innovation and economic development.
Since the establishment of the OTRI, the following have been presented:

- 15 patent applications to the Spanish Office of Patents and Brands (OEPM).
- 10 of which have been expanded internationally through the Patent Cooperation Treaty (PCT- Patent Cooperation Treaty).
- A Euro – PCT application
- Eight of the applications are in co-ownership with the University of Cantabria, two with the Centre for Higher Scientific Research (CSIC), one with the Scientific Foundation of the Spanish Association Against Cancer (AECC), the Foundation for Biomedical Research of the 12 de Octubre University Hospital (FIBH120) and the Biomedical Research foundation of the Puerta de Hierro University Hospital of Majadahonda (FIBHUPH) and another, with the TEKNIKER Foundation and Cellbiocan S.L.



Of these, two PCT applications were processed in 2015:

APPLICATION Nº	TITLE	APPLICANT	INVENTOR
PCT/ ES2015/070608	Monitoring method for antipsychotic treatment	**UC-SCS-CSIC**	Benedicto Crespo Facorro, Jesús Vicente Sainz Maza
ES201500469	Controlled liquid waste evacuation system	**SCS**	Inés Cuesta Guerrero
ES201500530	Ergonomic handle and system as a surgical instrument	**UC-SCS**	Ramón Sancibrián Herrera, Marta López Azcue, Mari Cruz Gutiérrez Díez, José Carlos Manuel Palazuelos, Carlos Redondo Figuero, Mª Asunción Benito González

For all applications, transfer and contact work with potential licensees has been performed or is currently under way. Moreover, at least eleven other possible innovative ideas were studied. Some lacked innovation and/or inventive activity, while others are in the evaluation and development phase.
Other industrial property rights were also processed during 2015:

APPLICATION Nº	TITLE	APPLICANT	INVENTOR
Community design – no. K2737254	Ergonomic handle and system as a surgical instrument	**UC-SCS**	Ramón Sancibrián Herrera, Marta López Azcue, Mari Cruz Gutiérrez Díez, José Carlos Manuel Palazuelos, Carlos Redondo Figuero, Mª Asunción Benito González
Marca Nacional – M3555620	EVALTEC	**IDIVAL**	

INNOVATION FUNNEL

In 2015, 13 new ideas were analysed. The projects were classified into FIVE phases, as defined below:

1. Capturing ideas. In this phase, those ideas are considered that Innovation Areas captured in 2015, as well as those captured in previous years that did not advance to a later stage.
2. Evaluation. 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 process: This includes the development of prototypes, approvals and testing.
4. Transfer: The ideas for which some type of commercial activity has been carried out, i.e. some contact with companies or potential licensee entities.
5. Market: involving cases where innovation is found in one of the following situations:

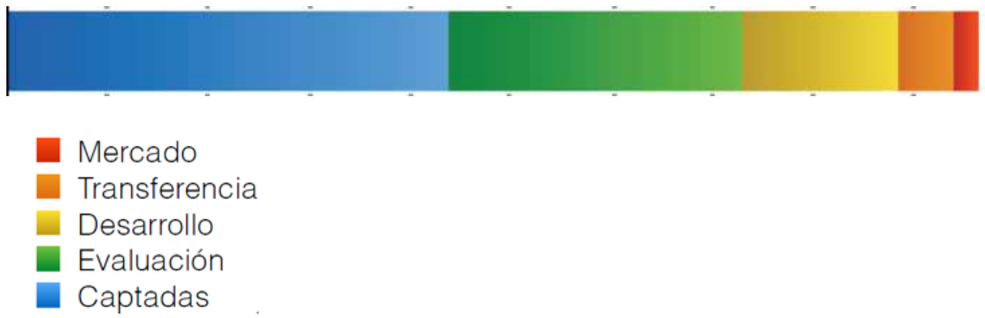
a) Licensed to industry

b) Generated a spin-off

c) Forms part of an exclusive agreement with a company

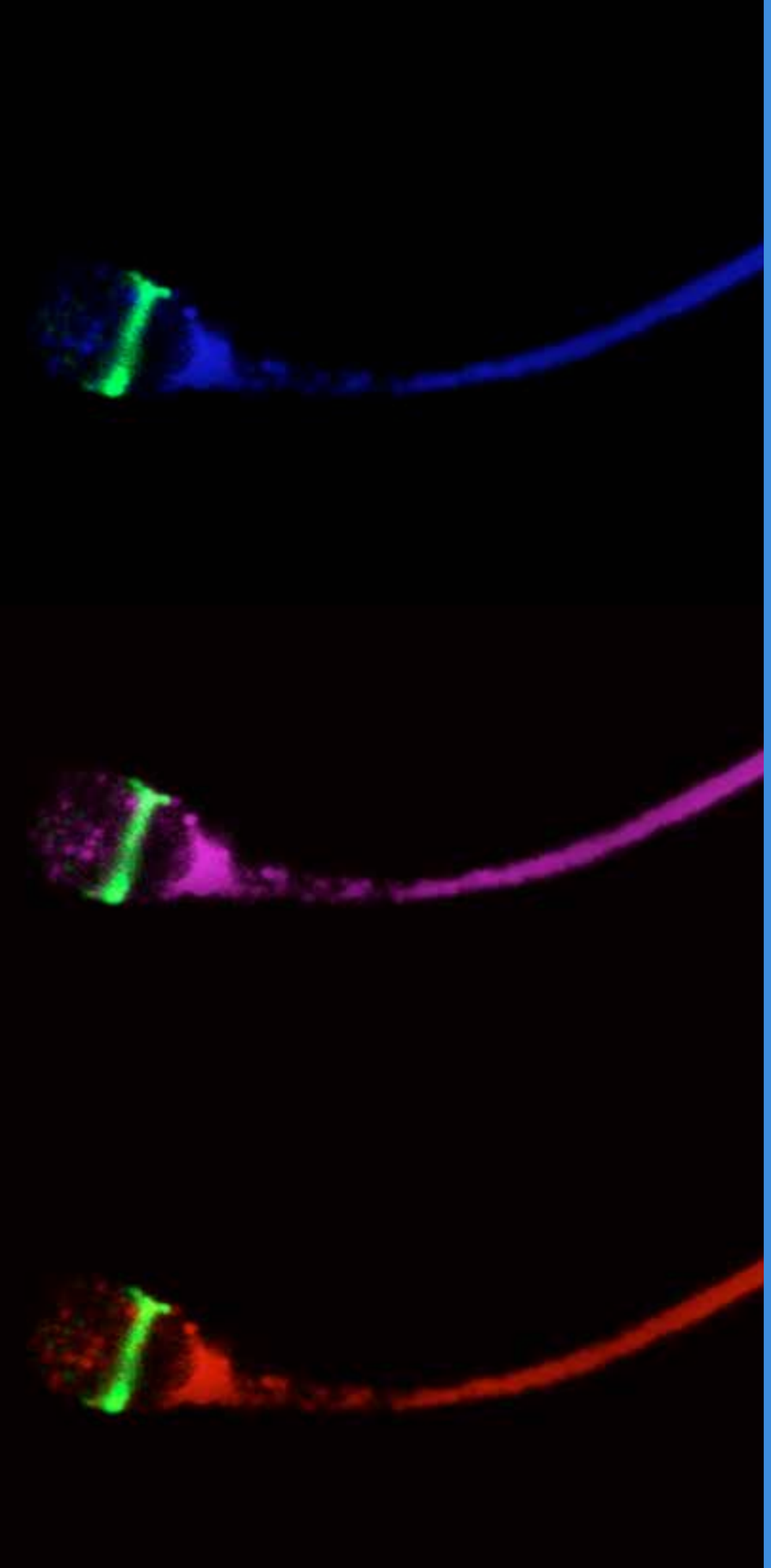
d) Implemented in a healthcare centre (in the case of healthcare and organisational innovations).

Idea 1: ITEMAS indicators



HUMAN FACTOR. EVALUATION OF TECHNOLOGY.

The innovation area working to support the development of innovative health technologies (healthcare devices, diagnostic tools, medical software and management of new therapies) based on the application of the study of human factors set out in the development of technologies and their later use; as well as the usability and ergonomics of them. To this end, the Marqués de Valdecilla Research Institute (IDIVAL), through its innovation area together with the Marqués de Valdecilla University Hospital (HUMV) and the Valdecilla Virtual Hospital (HvV), has launched eValTec.
EVALTEC is comprised of a multidisciplinary team belonging to the three institutions mentioned above: IDIVAL, HUMV, and HvV. They work on proposals from the hospital itself (HUMV) as well as from external entities that hope to acquire better knowledge surrounding the use, design and development of healthcare technology devices.

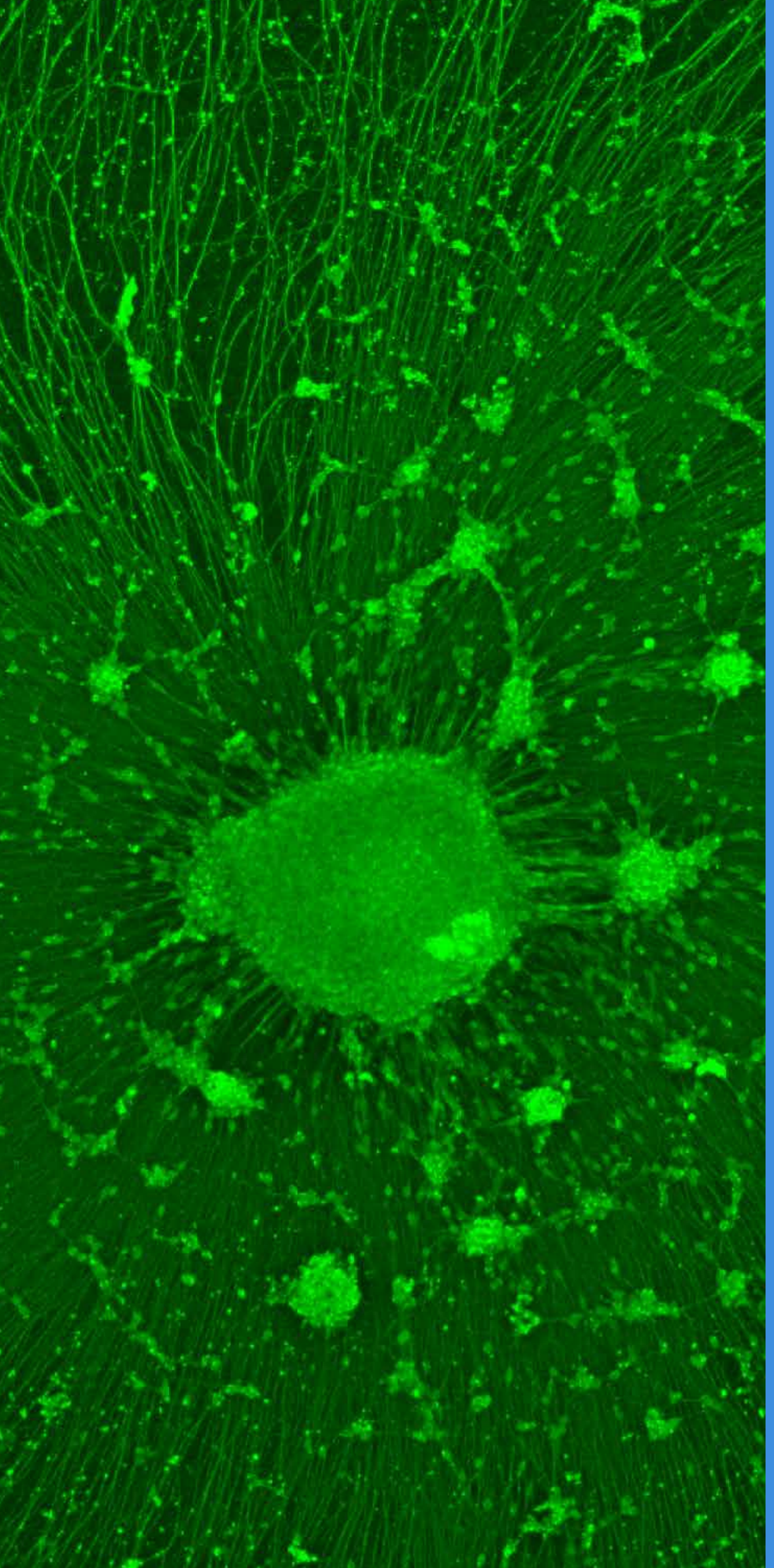


2015

Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Research Areas



2015

Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Cross-Disciplinary Area

Epidemiology and Public Health

Head:
LLORCA DÍAZ, JAVIER
Departamento de Medicina Preventiva y Salud Pública
Facultad de Medicina
Universidad de Cantabria

Email: llorcaj@unican.es

Researchers:

Dierssen Sotos, Trinidad (UC)
Rodríguez Cundín, Paz (HUMV)

Collaborators:

Gómez Acebo, Inés (UC)
Pérez Vázquez, Germán (IDIVAL)

Predoctorals:

Palazuelos Calderón, Camilo (UC)

Research lines

1. Epidemiological method

Development of methods for estimating confidence intervals of the population attributable fraction (Stat Med) and its asignation when risk factors are not aditive (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).

Inequality in the year of death using the Gini index and the Lorenz curve (J Epidemiol Community Health; Med Sci Mon).

Quality of published clinical trials and meta-analysis (J Asthma; Arch Bronconeumol; J Glaucoma; Pharmacopsychiatry; J Epidemiol Community Health). Publication bias and heterogeneity in meta-analysis (J Epidemiol Community Health).

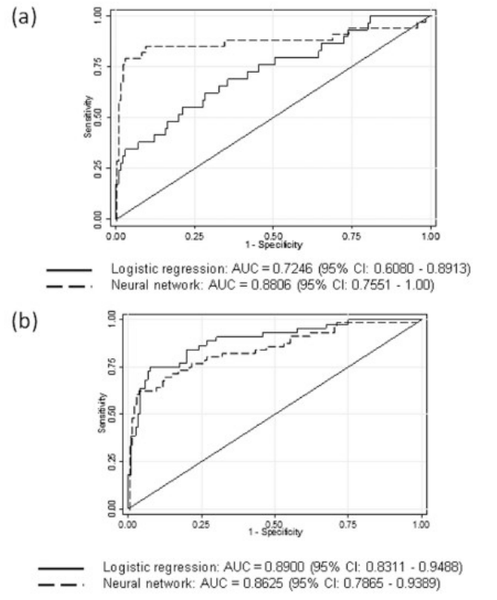


Figure 1. ROC curves for the death outcomes at: (a) 30 days after transplantation, and (b) 90 days after transplantation. Solid lines: logistic regression (area under ROC curve [AUC] is 0.7246 [95% CI 0.6080 to 0.8913] for 30-day mortality and 0.8900 [95% CI 0.8311 to 0.9488] for 90-day mortality). Dashed 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).

Artificial Neural Networks (J Heart Lunt Transplant).

Estimating the NNT in multivariate settings (Med Clin).

Isotemporal substitution analysis: It was developed by Mekara et al (2009) in order to analyze the effect of physical activity on continuous variables, and it was eventually applied (Mekara et al, 2013) to dichotomous variables. Our group has been the first one in applying it to survival analysis.

2. Cancer epidemiology

In 2010, we opened a new line on cancer epidemiology by leading a coordinated FIS project (2010-2012). This research includes prostate, breast, gastric and colorectal cancers as well as chronic linfoid leukemia. En 2011, we participated in four new projects no this subject, headed by Manolis Kogevinas (CREAL), Cristina Villanueva (CREAL), Silvia San José (ICO) and Nuria Aragonés (ISCIII). En 2012 we obtained a new project intended to genotype samples obtained in the previous project. Samples and environmental information on more than 10,000 cases and controls are available, and about 7,000 have been genotyped for 300,000 exome SNPs. Our group participates in PRACTICAL, an international consortium on prostate cancer funded by EU and NIH. In 2015, we obtained a new FIS project on integrating genetic and environmental factors in analysing breast cancer survivorship.

3. Clinical epidemiology

Rheumatic diseases: Our group has published a great number of papers on clinical and population epidemiology in rheumatoid arthritis, giant cell arteritis, ankylosing spondylitis, Schönlein-Henoch purple, lupus and other rheumatic diseases. This line has recently changed its focus to, by one hand, genetic factors associated with rheumatic disease incidence / cardiovascular events; by other hand, to the relationship among inflammation level / inflammation treatment and endothelial function / development of carotid plaques / cardiovascular events.

FUNDING

Llorca Díaz, Javier. Variantes genéticas y pathways relacionadas con cánceres de mama y próstata, y su interacción con la exposición a hormonas sexuales endógenas y exógenas: estudio MCC-Spain. PI12/00715. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Duración: 2013- 2015.

PUBLICATIONS

IMPACT FACTOR: 108,201

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Sex disparities in systemic lupus erythematosus in Northwestern Spain are not due to ethnic diversity.

Rheumatol Int. 2015;35:939-940.F.I.:1,516. [doi:10.1007/s00296-014-3124-x]

Doctoral Thesis

• Alfonso Fernando Corrales Martínez.

Evaluación del riesgo cardiovascular en pacientes con artritis reumatoide.

Director/es: Javier Llorca Díaz, José Antonio Parra Blanco, Miguel Ángel González-Gay Mantecón. UNIVERSIDAD DE CANTABRIA.

• Trinitario Pina Murcia.

Modificación de marcadores de riesgo cardiovascular en psoriasis tras terapia anti-TNF.

Director/es: Javier Llorca Díaz, Miguel Ángel González-Gay Mantecón. UNIVERSIDAD DE CANTABRIA.

• María de Pedro de Cárdenas.

Influencia del consumo de antiinflamatorios no esteroideos sobre la incidencia de cáncer de mama - Influence of non-steroidal anti-inflammatory drug use and breast cancer incidence.

Director/es: Marina Pollán Santamaria, Javier Llorca Díaz. UNIVERSIDAD DE CANTABRIA.

• Roberto Garrastazu López.

Factores predictivos de morbimortalidad al año en pacientes EPOC.

Director/es: Miguel Santibáñez Margüello, Javier Llorca Díaz. UNIVERSIDAD DE CANTABRIA.

• María Soledad Holanda Peña.

Medición de la satisfacción de los pacientes ingresados en UCI y sus familiares.

Director/es: Álvaro Castellanos Ortega, Javier Llorca Díaz.

UNIVERSIDAD DE CANTABRIA.

Advanced Microscopy, Protein Folding and the Cytoskeleton

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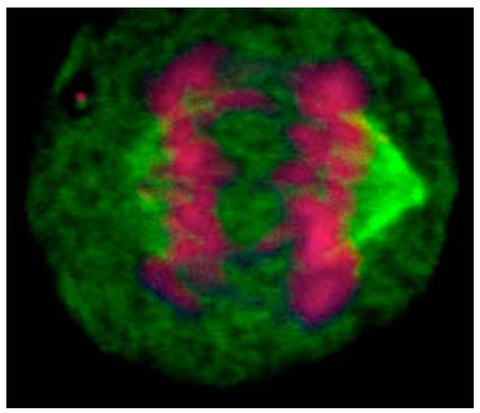
Research lines

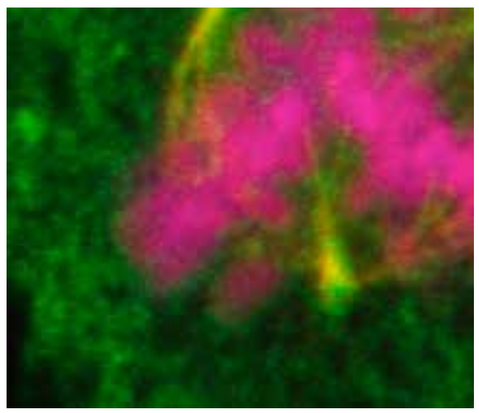
1. Tubulin folding cofactors.

Microtubules are polymers composed of globular subunits of α- and β-tubulin. Both proteins, with an approximate molecular mass of 50 kDa, form an α, β-tubulin heterodimer which represents the structural and functional unit of the microtubule. Tubulins represent one of the largest families of genes and proteins. Folding of tubulins follows a sophisticated pathway involving several molecular chaperones. Tubulin Folding cofactors (TBCs) are molecular chaperones specifically required for tubulin dimer formation. In addition, TBCs are involved in tubulin proteostasis through dimer dissociation and tagging for proteasome recognition. In fact, the importance of tubulin proteostasis is revealed by the number of human syndromes and diseases associated with TBCs malfunction such as lissencephaly, hypoparathyroidism-retardation dysmorphism and AR-Kenny–Caffey syndrome; giant axonal neuropathy, retinitis pigmentosa and also cancer. Despite the importance of the tubulin recycling and degradation pathway in maintaining the dynamicity required for the proper MT function as well as the tight quality control requirements of the cytoskeletal proteins, many aspects of their function remain unknown. The goal of our work is to achieve a better understanding of the structure and function of the mammalian tubulin folding cofactors as well as the molecular pathology of the above mentioned diseases.

Psychrophilic organisms, such as the Antarctic notothenioid fish, are threatened by protein denaturation at both the upper and lower limits of their narrow thermal regimes (+2 to −2°C). To assess the capacity of these fish to maintain protein homeostasis as the Southern Ocean warms due to climate change, we have analyzed assisted protein folding by the cytoplasmic chaperonin CCT of the Antarctic fish, Gobionotothen gibberifrons. We conclude that the thermal scope of G. gibberifrons CCT is sufficient to tolerate temperatures as much as 5 °C above their present habitat norm. Furthermore, our observations support the hypothesis that CCT (cytoplasmic chaperonin) and some of its client proteins have co-evolved to maintain productive chaperonin-assisted folding reactions in a psychrothermal environment. Our next goal is the sequencing and analysis of the genome of the Antarctic fish, Gobionotothen gibberifrons, as well as the transcriptome analysis from RNA-seq experiments conducted to explore temperature challenges involved in cold-adapted evolution to understand these evolutionary mechanisms.



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.

PUBLICATIONS

IMPACT FACTOR: 5,432

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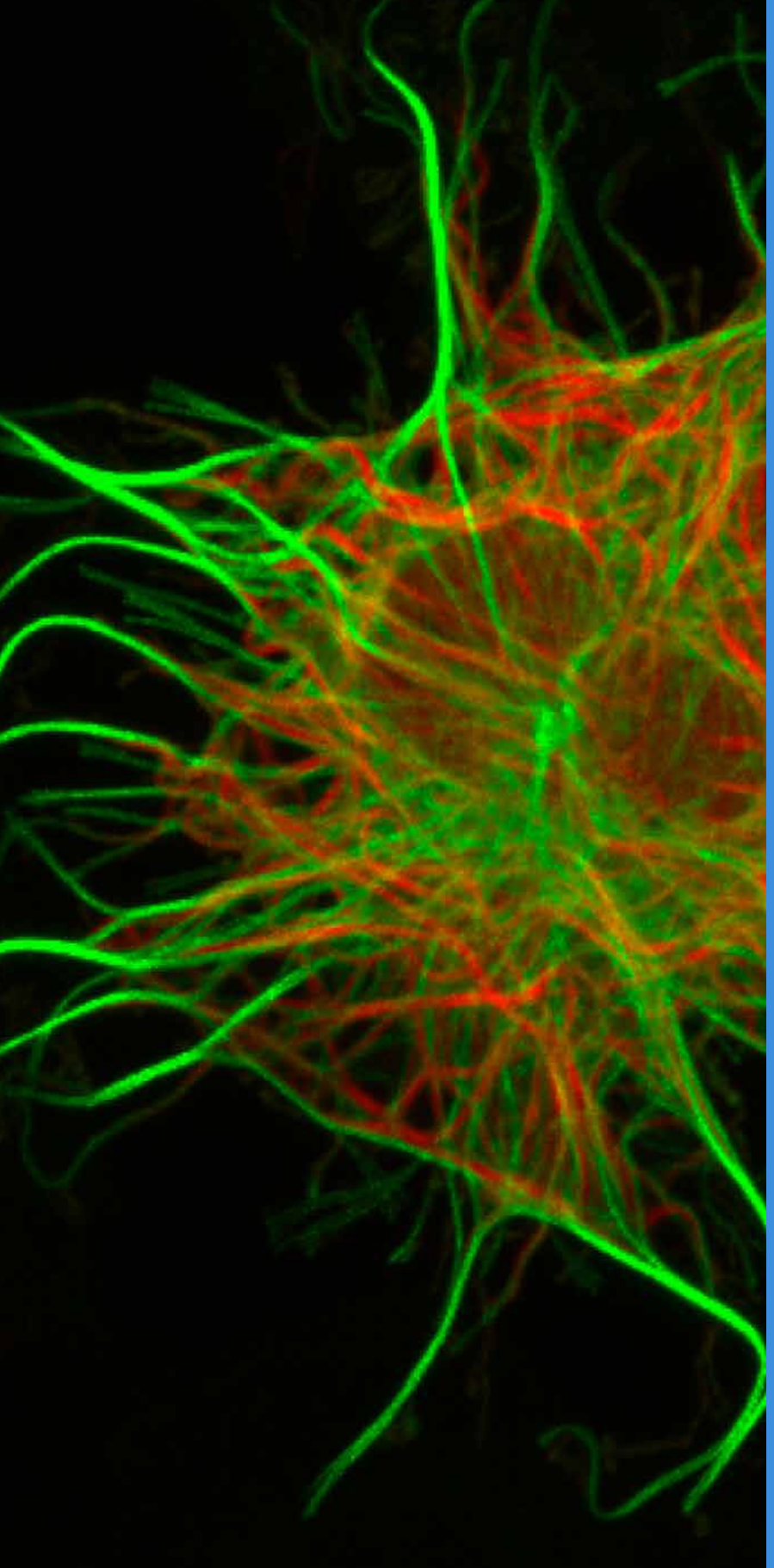


2015
Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Cancer Area

Consolidated Groups

- Cancer Genomics
- Cell Signalling and Therapeutic Targets in Cancer
- Melatonin and Breast Cancer
- Apoptosis
- Anatomical and Molecular Pathology
- Cell Cycle, Determining Stem Cells and Cancer

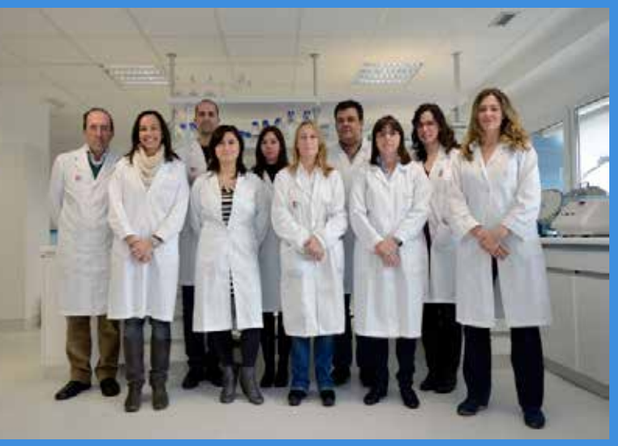
Clinical Groups

- Clinical Trials Unit, Medical Oncology and Palliative Medicine
- New Techniques in Abdominal Surgery
- Molecular Imaging

Newly Created Groups

- Nanomedicine

Cancer Genomics



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RTICC Red Temática de Investigación Cooperativa en Cáncer

Research lines

Over the last decade we have witnessed a boom in the techniques of mass molecular analysis, including transcriptomics, epigenomics, microRNA expression profiles, matrix CGH and mutational studies on a large scale, offering researchers an array of opportunities for the molecular analysis of cancer.

Until now, the lack of integrated genomic analysis has hampered the discovery of tumorigenesis molecular mechanisms and has delayed the clinical application of the results of these molecular studies.

There is a dramatic contrast between the number of compounds in early clinical trials in cancer (about 800) and the number of molecular markers that allow therapy to be guided using targeted drugs.

Hipótesis.

In cancer, the integration of highly-complex molecular studies with those focused on the use of drugs aimed at chosen targets can facilitate recognition of the pathways and genes essential for the survival of neoplastic cells, enabling the identification of molecular markers to guide therapy. This knowledge will facilitate the identification of actionable molecular targets (against which a drug to block its action can be generated) and the efficient use of drugs designed from molecular knowledge.

Proposals.

Based on the integrated analysis of data obtained by various large-scale molecular study techniques, we will try to obtain information regarding the molecular mechanisms of pathogenesis in neoplasms in general, including the common mechanisms and specific events of each type of tumour. We hope that this can contribute to a more precise classification of them and to the identification of new therapeutic targets.

The integrated analysis of the data obtained by mass molecular studies in different types of neoplasms can be addressed using the following strategies:

- Genomic studies for routes and genes. Hypothesis: Integrated genomic studies allow us to identify critical survival pathways in different types of neoplasms, revealing in them essential genes. Method: aCGH + RNA expression + miRNAs + Phosphoproteomics and integrated analysis using tumour-specific gene sets.

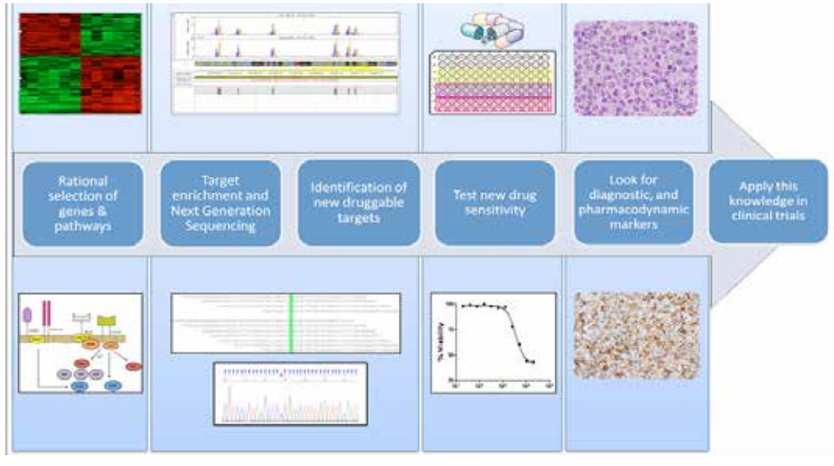
- Mutational studies. Hypothesis: Alterations of the neoplastic cell may be dependent on the acquisition of mutations in several key genes in tumour development. Method: aCGH and high-capacity mutational studies (NGS, massive parallel sequencing).

- Functional genomics. Hypothesis: Gene silencing using siRNA libraries will allow us to identify essential genes for the survival of neoplastic cells. Method: Using siRNA to silence selected pathways including survival, apoptosis and signal transduction pathways.

- New drugs/models. Hypothesis: Molecular "gene signatures" can be used to identify new drugs in the treatment of neoplasms. Method: In vivo and in vitro models allow us to identify synergies and shorten the time needed to introduce new drugs into the clinic.

Currently this approach is being performed on various lymphoid neoplasms, including the most common types of B-cell and T-cell lymphoma.

A similar approach has been considered for Colorectal Cancer, Melanoma, Merkel cell carcinoma and Hepatocellular carcinoma in a project that aims to set out the basis for the development of an experimental genomics platform to individually, quickly and cheaply identify/study possible altered therapeutic targets for each case.



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Doctoral Thesis

• Santiago Montes Moreno.

Identificación de marcadores de utilidad diagnóstica y pronóstica en linfoma B de célula grande agresivo.

Director: Miguel Ángel Piris Pinilla. UNIVERSIDAD DE CANTABRIA.

• Javier Loricera García.

Caracterización clínica de las vasculitis cutáneas.

Directores: Miguel Ángel González-Gay Mantecón, María del Carmen González Vela, Ricardo Blanco Alonso. UNIVERSIDAD DE CANTABRIA.

• Vanesa Calvo Del Río.

Caracterización clínica de la púrpura de Schoenlein-Henoch.

Directores: Miguel Ángel González-Gay Mantecón, María del Carmen González Vela, Ricardo Blanco Alonso. UNIVERSIDAD DE CANTABRIA.

Cell Signalling and Therapeutic Targets in Cáncer

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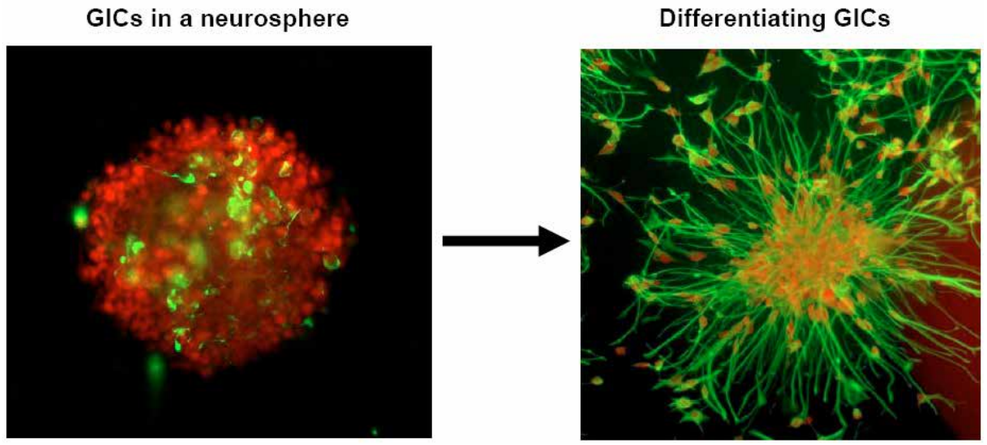
Red Temática de Investigación Cooperativa en Cáncer

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Research lines

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

The capacity of glioblastoma (GBM) cells to invade the surrounding parenchyma is one of the main problems for an efficient therapeutic strategy because it makes complete resection nearly impossible. Among the GBM cells there is a small population (<5%) with the capacity to regenerate the tumor and with features similar to those found in adult stem cells. They are the so-called cancer stem cells. If the current hypothesis is right, this cell population is the proper target for new therapeutic strategies. We aim to identify molecular mediators of migration and invasion of GSCs.



2. Development of in vitro models to study the response of GBM cells to chemotherapy in physiological environments.

Most in vitro studies to measure the cellular response to chemotherapy use cell cultures on 2D surfaces. There are many evidences about the role of the biophysic features of the microenvironment in cellular processes studied in vitro (diferentiation, migration, survival). In order to optimize more physiological in vitro models of chemotherapy response, closer to in vivo models, we are studying the behaviour of GBM cells (GSCs and tumor parenchymal cells) following exposure to chemotherapeutic agents in different microenvironments.

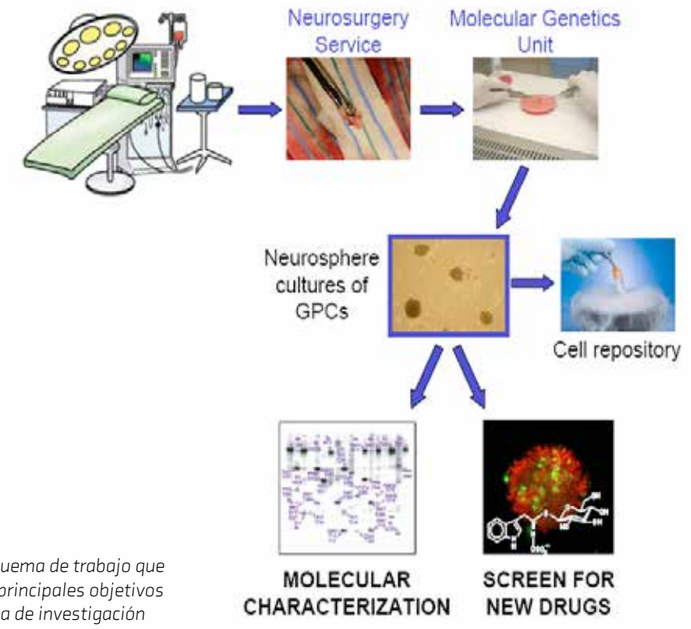


Figura . *Esquema de trabajo que incluye los principales objetivos de esta línea de investigación*

3. Screening of novel compounds addressed to cancer stem cells by using computational and biologic platforms.

Currently, there are different undergoing clinical trials addressed to kill cancer stem cells. However, a lack of proof of concept still persist, which means that there are no drugs approved for this indication. This novel therapeutic area is open to different experimental approaches including combinatorial chemistry, re-profiling and virtual screening, among others. In co-llaboration with a start-up from the Bioinformatics Unit at Centro de Biologia Molecular Severo Ochoa (CSIC), we have established a platform that joints computational screening of 5 million compounds with the validation of candidates in biological models in vitro and in vivo. Target cells are cancer stem cells from GBM and colon cancer.

FUNDING

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PUBLICATIONS

IMPACT FACTOR 21,510

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J Neurosurg. 2015;123:1081-1092.F.I.:3,737. [doi:10.3171/2014.11.JNS141992]

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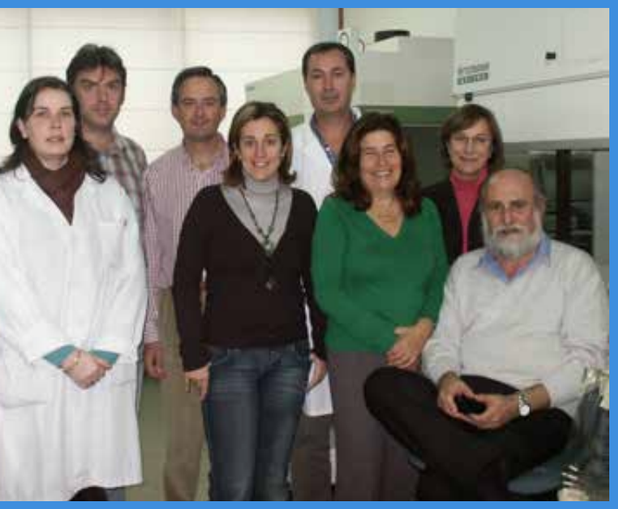
Melatonin and Breast Cancer



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Consolidated Group

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:

- To study, on the one hand, the ability of melatonin to modulate the activity of some enzymes (aromatase, sulfatase, 17β-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.

- 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.

- 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.

- To study the protective effects of melatonin on the molecular changes induced by chemotherapy used in the treatment of breast cancer.

- To study the protective effects of chronic treatment with melatonin on cognitive and neuromorphological deficits in Ts65Dn mouse, a model of Down syndrome.

Doctoral Thesis

- Andrea Corrales Pardo.

Estudio de los efectos protectores del tratamiento crónico con melatonina sobre los déficits cognitivos del ratón TS65DN, un modelo de síndrome de Down.

Director/a: Noemí Rueda Revilla. UNIVERSIDAD DE CANTABRIA.

- Susana García Cerro.

Estudio del efecto de la reducción del número de copias del gen DYRK1A sobre distintos fenotipos funcionales y neuromorfológicos encontrados en un modelo murino de síndrome de Down y en ratones euploides.

Director/es: Carmen Martínez-Cue Pesini, Noemí Rueda Revilla. UNIVERSIDAD DE CANTABRIA.

FUNDING

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PUBLICATIONS

IMPACT FACTOR 18,939

Original articles

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J Pineal Res. 2015;58:189-197.F.I.:9,600. [doi:10.1111/jpi.12205]

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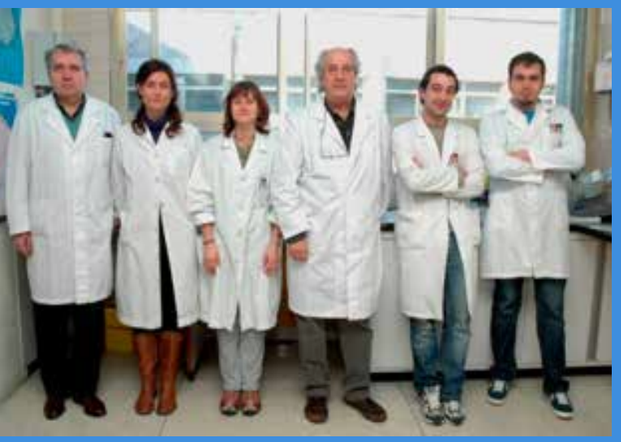
Melatonin affects the dynamic steady-state equilibrium of estrogen sulfates in human umbilical vein endothelial cells by regulating the balance between estrogen sulfatase and sulfotransferase.

Int J Mol Med. 2015;36:1671-1676.F.I.:2,088. [doi:10.3892/ijmm.2015.2360]

Apoptosis



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Research lines

We are interested in the development of the vertebrate limb using avian and mouse embryos as experimental models. The aim of our research is to uncover molecular signals which regulate the differentiation of skeletal progenitors and also to provide information about limb morphogenesis. Genes identified by different molecular strategies are functionally analyzed through gain-of- and loss-of-function experiments. Gain-of-function experiments are performed through the overexpression of the selected genes employing viral infections or plasmid electroporation. Loss-of-function experiments are made with short hairpin RNAi or CRISPR-Cas9 approaches.

Our major research field is the formation of the digits. During this process mesodermal progenitors of the embryonic limb bud follow two alternative fates: in the future digit regions, mesodermal cells aggregate and differentiate into cartilage, joints and fibrous tissues such as tendons or ligaments; in the interdigital regions, cells do not condense and instead undergo massive cell death. The goal of these studies is to obtain information of relevance in regenerative medicine to direct the differentiation of stem cells into skeletal tissues and to provide basic information about the mechanisms accounting for programmed cell death.

FUNDING

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PUBLICATIONS

IMPACT FACTOR 13,582

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J Neurosurg. 2015;123:1081-1092.F.I.:3,737. [doi:10.3171/2014.11.JNS141992]

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Anatomical and Molecular Pathology

Consolidated Group

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Lines of Research

1. Diagnostic and predictive biomarkers in solid tumors.

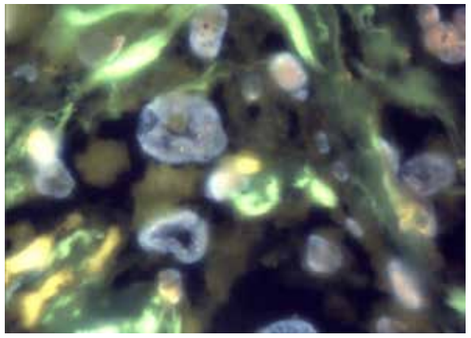
Our main task remains to establish a model of translational medicine, that is to be the bridge between basics and applied investigation. We are basically implied in all the new biomarkers that are necessary to obtain a correct diagnosis at the right time with a strong predictive response value (Mamacan 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-mesenchimal 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.



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Reviews

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Biomarker testing in advanced non-small-cell lung cancer: a National Consensus of the Spanish Society of Pathology and the Spanish Society of Medical Oncology.
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Cell Cycle, Determining Stem Cells and Cancer

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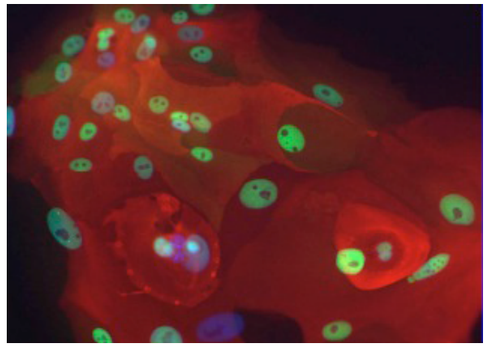
Research lines

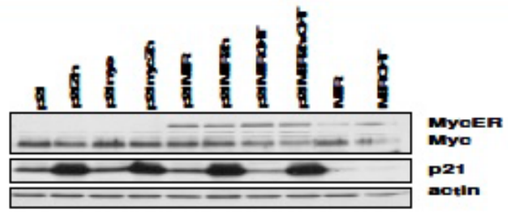
Among the many skin conditions that affect the health and life expectancy of the population and that pose a growing problem in public health (psoriasis, xerodermas, keratosis), skin cancer is the most common cancer. This stems from variations in DNA caused primarily by ultraviolet radiation (UV) from 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).

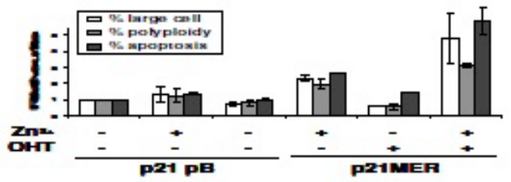
For these reasons the skin needs powerful cellular and molecular mechanisms to protect itself from continued mutagenic risk. These mechanisms go through the proper control of Stem Cells and homoeostasis. The main goal of our group is to research these mechanisms and their variations in hyperproliferative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







FUNDING

Gandarillas Solinis, Alberto. Nuevas Rutas y Estrategias Hacia el Cáncer de Células Escamosas. PI14/00900. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Duración: 2015-2017.

PUBLICATIONS

IMPACT FACTOR 1,392

Original articles

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Iliac Artery Aneurysm Repair with Preservation of a Single Ectopic Pelvic Kidney.
Tex Heart Inst J. 2015;42:61-62.F.I.:0,649. [doi:10.14503/THIJ-13-3724]

Doctoral Thesis

• Pilar Alonso Lecue.
Alteraciones del control mitosis-diferenciación en el carcinoma de piel.
Director/a: Alberto Gandarillas Solinis. UNIVERSIDAD DE CANTABRIA.

• Carmen María Rodríguez Gómez.
Estenosis mitral reumática. Resultados a muy largo plazo del tratamiento quirúrgico mediante comisurotomía y anuloplastia de Durán.
Director/es: José Manuel Bernal Marco, Dieter José Morales García. UNIVERSIDAD DE CANTABRIA.

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Clinical Group

Research lines

Clinical trials in solid tumors

Nowadays our Unit starts around thirty new clinical trials every year, many of them in Phases II and III, becoming a leading center in Spain on development of some lines of new drugs, particularly anti-EGFR therapies, anti-VGF and anti-PD-L1.

This line of research is well established, it is the basis of the group's publications and has an intense activity.

PUBLICATIONS

IMPACT FACTOR 114,805

Original articles

1 Martín M, Ruiz Simón A, Ruiz Borrego M, Ribelles N, Rodríguez-Lescure Á, Muñoz-Mateu M, González S, Margelí Vila M, Barnadas A, Ramos M, Del Barco Berrón S, Jara C, Calvo L, Martínez-Jáñez N, Mendiola Fernández C, Rodríguez CA, Martínez de Dueñas E, Andrés R, Plazaola A, de la Haba-Rodríguez J, López-Vega JM, Adrover E, Ballesteros AI, Santaballa A, Sánchez-Rovira P, Baena-Cañada JM, Casas M, Del Carmen Cámara M, Carrasco EM, Lluch A.

Epirubicin Plus Cyclophosphamide Followed by Docetaxel Versus Epirubicin Plus Docetaxel Followed by Capecitabine As Adjuvant Therapy for Node-Positive Early Breast Cancer: Results From the GEICAM/2003-10 Study.

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2 Carmona-Bayonas A, Jiménez-Fonseca P, Virizuela Echaburu JA, Font M, Biosca M, Ramchandani A, Martínez, J, Hernando Cubero J, Espinosa J, Martínez de Castro E, Ghanem I, Beato C, Blasco A, Garrido M, Bonilla Y, Mondejar R, Arcusa Lanza MA, Aragón Manrique I, Manzano A, Sevillano E, Castanón E, Cardona M, Gallardo Martín E, Pérez Armillas Q, Sánchez Lasheras F, Ayala de la Pena F.

Prediction of Serious Complications in Patients With Seemingly Stable Febrile Neutropenia: Validation of the Clinical Index of Stable Febrile Neutropenia in a Prospective Cohort of Patients From the FINITE Study.

J Clin Oncol. 2015;33:465-124.F.I.:18,428. [doi:10.1200/JCO.2014.57.2347]

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Ann Oncol. 2015;26:132-140.F.I.:7,040. [doi:10.1093/annonc/mdu474]

4 Sotelo MJ, Sastre J, Maestro ML, Veganzones S, Vieitez JM, Alonso V, Grávalos C, Escudero P, Vera R, Aranda E, García-Alfonso P, Gallego-Plazas J, López C, Pericay C, Arrivi A, Vicente P, Ballesteros P, Elez E, López-Ladron A, Díaz-Rubio E.

Role of circulating tumor cells as prognostic marker in resected stage III colorectal cancer.

Ann Oncol. 2015;26:535-541.F.I.:7,040. [doi:10.1093/annonc/mdu568]

5 Estévez-García P, Rivera F, Molina-Pinelo S, Benavent M, Gómez J, Limón L, Pastor MD, Martínez-Pérez J, Paz-Ares L, Carnero A, García-Carbonero R.

Gene expression profile predictive of response to chemotherapy in metastatic colorectal cancer.

Oncotarget. 2015;6:6151-6159.F.I.:6,359. [doi:10.18632/oncotarget.3152]

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Regorafenib plus modified FOLFOX6 as first-line treatment of metastatic colorectal cancer: A phase II trial.

Eur J Cancer. 2015;51:942-949.F.I.:5,417. [doi:10.1016/j.ejca.2015.02.013]

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Panitumumab in Metastatic Colorectal Cancer: The Importance of Tumour RAS Status.

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Role of Surgery in Patients with Recurrent, Metastatic, or Unresectable Locally Advanced Gastrointestinal Stromal Tumors Sensitive to Imatinib: A Retrospective Analysis of the Spanish Group for Research on Sarcoma (GEIS).

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12 Capdevila J, Sevilla I, Alonso V, Antón Aparicio L, Jiménez Fonseca P, Grande E, Reina JJ, Manzano JL, Alonso Lájara JD, Barriuso J, Castellano D, Medina J, López C, Segura Á, Carrera S, Crespo G, Fuster J, Munarriz J, García Alfonso P.

Evaluation of the efficacy and safety of lanreotide in combination with targeted therapies in patients with neuroendocrine tumours in clinical practice: a retrospective cross-sectional analysis.

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14 Rivera F, Massuti B, Salcedo M, Sastre J, Martínez Galán J, Valladares-Ayerbes M, Serrano R, García de Paredes ML, Manzano JL, Galán M, Alsina M, Yuste Izquierdo AL, López C, Díaz-Rubio E, Conde V, Reboredo M, Cano MT, Pachón V, Aranda E.

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Cancer Chemother Pharmacol. 2015;75:319-324.F.I.:2,769. [doi:10.1007/s00280-014-2641-3]

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Clin Transl Oncol. 2015;17:988-995.F.I.:2,077. [doi:10.1007/s12094-015-1451-3]

16 Guillén-Ponce C, Serrano R, Sánchez-Heras AB, Teulé A, Chirivella I, Martín T, Martínez E, Morales R, Robles L.
Clinical guideline seom: hereditary colorectal cancer.
Clin Transl Oncol. 2015;17:962-971.F.I.:2,077. [doi:10.1007/s12094-015-1439-z]

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Clin Transl Oncol. 2015;17:1030-1035.F.I.:2,077. [doi:10.1007/s12094-015-1450-4]

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Clin Transl Oncol. 2015;17:996-1004.F.I.:2,077. [doi:10.1007/s12094-015-1456-y]

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Cost-utility analysis of nanoparticle albumin-bound paclitaxel (nab-paclitaxel) in combination with gemcitabine in metastatic pancreatic cancer in Spain: results of the PANCOSTABRAX study.
Expert Rev Pharmacoecon Outcomes Res. 2015;15:579-589.F.I.:1,669. [doi:10.1586/14737167.2015.1047349]

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Acta Radiol. 2015;56:1300-1307.F.I.:1,603. [doi:10.1177/0284185114556098]

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Collagen Type XI Alpha 1 Expression in Intraductal Papillomas Predicts Malignant Recurrence.
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Reviews

1 Vera R, Alonso V, Gállego J, González E, Guillén-Ponce C, Pericay C, Rivera F, Safont MJ, Valladares-Ayerbes M.
Current controversies in the management of metastatic colorectal cancer.
Cancer Chemother Pharmacol. 2015;76:659-677.F.I.:2,769. [doi:10.1007/s00280-015-2808-6]

Letters

1 González-López MA, López-Escobar M, Fernández-Llaca H, González-Vela MC, López-Brea M.
Eosinophilic annular erythema in a patient with metastatic prostate adenocarcinoma.
Int J Dermatol. 2015;54:80-82.F.I.:1,312. [doi:10.1111/ijd.12640]

Doctoral Thesis

• Lourdes Calera Urbizu.
Cáncer colorrectal y metástasis exclusivamente hepáticas: nuevo sistema de estadificación. Análisis de factores pronósticos y predictivos. experiencia del Hospital Universitario Marqués de Valdecilla 2004-2011.
Director/es: Jesús González Macías, Fernando Rivera Herrero. UNIVERSIDAD DE CANTABRIA.

New Techniques in Abdominal Surgery

Clinical Group

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Gutiérrez Fernández, Gonzalo (HUMV)
Hernanz de la Fuente, Fernando (HUMV-UC)
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Madrazo Leal, César (HUMV)
Manuel Palazuelos, José Carlos (HUMV)
Martín Parra, José Ignacio (HUMV)
Morales García, Dieter José (HUMV-UC)
Ortega Morales, Carlos (HUMV)
Perea Muñoz, Rodrigo (HUMV)
Rodríguez Sanjuán, Juan Carlos (HUMV-UC)
Seco Olmedo, Isabel (HUMV)
Trugeda Carrera, Mª Soledad (HUMV)

Research lines

1. Liver tumour pathology.

Staging, new diagnosis and therapeutic techniques..

2. Pancreatic tumour pathology.

Staging, new diagnosis and therapeutic techniques.

3. Biliary tumour pathology and non-neoplastic pathology.

Implementing new clinical surgical procedures (Laparoscopic choledocholithotomy).

4. Results in tumour pathology.

Thermal ablation of hepatocellular carcinoma as a bridge to transplantation and Xenotransplantation.

5. Obesity surgery.

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

6. Breast cancer.

Tumour excision using image-guided techniques. Oncoplastic surgical techniques for breast cancer surgery.

7. 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 11,003

Original articles

1 Gómez Ruiz M, Martín Parra I, Manuel Palazuelos C, Alonso Martín J, Cagigas Fernández C, Castillo Diego J, Gómez Fleitas M.

Robotic-Assisted Laparoscopic Transanal Total Mesorectal Excision for Rectal Cancer: A Prospective Pilot Study.

Dis Colon Rectum. 2015;58:145-153.F.I.:3,749. [doi:10.1097/DCR.0000000000000265]

2 Gómez Ruiz M, Martín Parra I, Calleja Iglesias A, Stein H, Sprinkle S, Manuel Palazuelos C, Alonso Martín J, Cagigas Fernández C, Castillo Diego J, Gómez Fleitas M.

Preclinical cadaveric study of transanal robotic proctectomy with total mesorectal excision combined with laparoscopic assistance.

Int J Med Robot. 2015;11:188-193.F.I.:1,526. [doi:10.1002/rcs.1581]

3 Morales-García D, Castanera González R, González Sánchez FJ, González Noriega M, Alonso Martín, J, Gómez Fleitas M.

Appendicitis of stump. An undervalued reality?.

Rev Esp Enferm Dig. 2015;107:461-462.F.I.:1,414.

4 Amado-Diago CA, Gutiérrez-Cuadra M, Armiñanzas C, Arnaíz de Las Revillas F, Gómez Fleitas M, Fariñas MC.

Echinococcosis: A 15-year epidemiological, clinical and outcome overview.

Rev Clin Esp. 2015;215:380-384.F.I.:1,063. [doi:10.1016/j.rce.2015.05.003]

5 Gutiérrez-Baños JL, Ballestero-Diego R, Truan-Cacho D, Aguilera-Tubet C, Villanueva-Peña A, Manuel-Palazuelos JC.

Training of urology residents in laparoscopic surgery preparation of a virtual reality model.

Actas Urol Esp. 2015;39:564-572.F.I.:1,022. [doi:10.1016/j.acuro.2015.04.006]

6 Miguelena Bobadilla JM, Morales García D, Iturburu Belmonte I, Alcázar Montero JA, Serra Aracil X, Docobo Durántez F, López de Cenarruzabeitia I, Sanz Sánchez M, Hernández Hernández JR.

General surgery training in Spain: Core curriculum and specific areas of training.

Cir Esp. 2015;93:147-151.F.I.:0,743. [doi:10.1016/j.ciresp.2014.10.009]

7 Cañón Lara M, Fidalgo García M, Gómez Ruiz M, Gómez Fleitas M.

Hepatic hydatid disease fistulized to the skin surface.

Cir Esp. 2015;93:22-22.F.I.:0,743. [doi:10.1016/j.ciresp.2014.11.006]

8 Trugeda Carrera MS, Fernández Díaz MJ, Rodríguez Sanjuán JC, Manuel Palazuelos JC, de Diego García EM, Gómez Fleitas M.

Initial results of robotic esophagectomy for esophageal cancer.

Cir Esp. 2015;93:396-402.F.I.:0,743. [doi:10.1016/j.ciresp.2015.01.002]

Doctoral Thesis

• Laura Sánchez Moreno, Juan Carlos Rodríguez Sanjuan.

Análisis de supervivencia tras metastasectomía pulmonar y hepática en el carcinoma colorrectal.

Director/a: Manuel Gómez Fleitas. UNIVERSIDAD DE CANTABRIA.

• Carmen María Rodríguez Gómez.

Estenosis mitral reumática. Resultados a muy largo plazo del tratamiento quirúrgico mediante comisurotomía y anuloplastia de Durán.

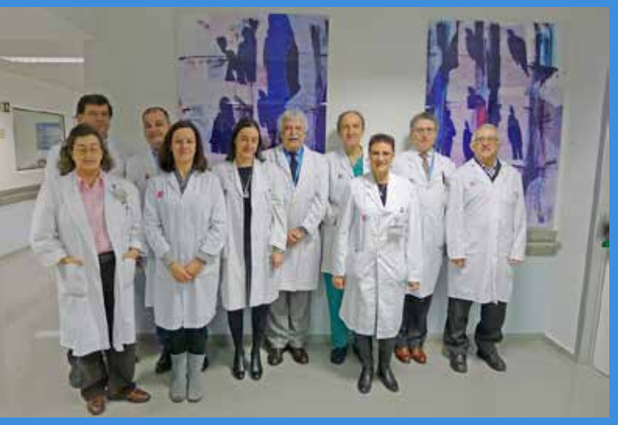
Director/es: José Manuel Bernal Marco, Dieter José Morales García. UNIVERSIDAD DE CANTABRIA.

• Clara Caridad Michel Rollock.

Incidencia de las lesiones traumáticas de la mano y la muñeca de origen laboral: estudio de calidad de vida.

Director/es: Dieter José Morales García, Francisco José Herrero Fernández. UNIVERSIDAD DE CANTABRIA.

Molecular Imaging



Clinical Group

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Martínez Rodríguez, María Isabel

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De Arcocha Torres, Maria
Garcia Martin, Ivan
García Unzueta, María Teresa
Jimenez Bonilla, Julio Francisco
Prada Gómez, Pedro José
Quirce Pisano, Remedios
Revilla García, María Ángeles

Research lines

1. Molecular Imaging od Glucose Metabolism in Oncology.

- Imaging Criteria for measuring the Metabolic Response to treatment in Oncology.
- Assessment of the role of 18F-FDG PET/CT on the effect of biologic therapy in solid tumours.
- Tissue characterization of pulmonary lesions by 18F-FDG PET/CT.
- Assessment of the role of 18F-FDG PET/CT to the nodal staging of lung cancer.

2. Molecular Imaging in the study assessment of the mineralization and inflammation of the carotid atheroma plaque.

- To define an acquisition protocol of 18F-FDG PET/CT to study the carotid plaque metabolism
- To assess the inflammation process of the carotid plaque by 18F-FDG PET/CT
- To assess the calcification process of the carotid plaque by 18FNa PET/CT
- To monitor the response to anti-inflammatory treatment by 18F-FDG PET/CT
- To study the carotid plaque stability and to identify the vulnerable plaque by molecular imaging techniques

3. Assessment and evaluation of the clinical impact of 18F-FNa PET/CT and 18F-FDG PET/CT in the management of atherosclerosis in diabetic patients.

- To establish an acquisition protocol for 18F-FNa PET/CT and 18F-FDG PET/CT for the study of atherosclerosis in diabetic patients
- To identify uptake patterns in different vascular territories of the body in diabetic patients
- To evaluate the correlation between the arterial uptake of 18F-Fna and cardiovascular risk factor of diabetes

4. Molecular Imaging of the protein b-amyloid in the study of the cognitive impairment and assessment of its clinical impact.

- Identification of patients with Alzheimer´s disease
- To establish an acquisition protocol for b-amyloid imaging using 11C-PIB PET/CT
- To determine the 11C-PIB retention patterns in the brain
- To study the contribution of 11C-PIB PET/CT in the study of cognitive impairment
- To identify the patients with b amyloid deposit in the brain
- To assess the role of 11C-PIB in differential diagnose of dementias
- To evaluate quantitatively the contribution of 11C-PIB

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

- To establish an acquisition protocol for 18F-FDG in patients with suspicion of large vessel vasculitis.
- To determine the biokinetics of FDG in the large vessels was, to establish the optimum time for image acquisition
- To identify the normal uptake patterns in different vascular territories
- To quantify the arterial wall activity in relation to the global vascular activity
- To calculate the standard uptake values (SUV) in normal subjects and in patients with arterial wall inflammation

6. Research and Development of new molecular imagen radiotracers.

- To study the application of radiotracers for prostate cancer recurrence
- To assess the role of 11C-methionine in primary hyperparathyroidism
- To evaluate the role of 11C-methionine in the suspicion of brain tumour recurrence
- To carry out the synthesis and clinical and to assess the clinical contribution of 18F-FLT
- To carry out the synthesis and development of new moleculeradiotracers od tau protein

PUBLICATIONS: 16

IMPACT FACTOR 62,650

Original articles

1 Ossenkoppele R, Jansen WJ, Rabinovici GD, Knol DL, van der Flier WM, van Berckel BN, Scheltens P, Visser PJ, Verfaillie SC, Zwan MD, Adriaanse SM, Lammertsma AA, Barkhof F, Jagust WJ, Miller BL, Rosen HJ, Landau SM, Villemagne VL, Rowe CC, Lee DY, Na DL, Seo SW, Sarazin M, Roe CM, Sabri O, Barthel H, Koglin N, Hodges J, Leyton CE, ..., Brooks DJ.

Prevalence of amyloid PET positivity in dementia syndromes: a meta-analysis.

JAMA. 2015;313:1939-1949.F.I.:35,289. [doi:10.1001/jama.2015.4669]

2 Jiménez-Bonilla J, Quirce R, Banzo I, Martínez-Rodríguez I, Carril JM.

11C-Choline and 18F-FDG PET/CT in the Detection of Occult Prostate Cancer in the Context of a Paraneoplastic Syndrome.

Clin Nucl Med. 2015;40:695-696.F.I.:3,931. [doi:10.1097/RLU.0000000000000826]

3 Gómez-Acebo I, Dierssen-Sotos T, Papantoniou K, García-Unzueta MT, Santos-Benito MF, Llorca J.

Association between exposure to rotating night shift versus day shift using levels of 6-sulfatoxymelatonin and cortisol and other sex hormones in women.

CHRONOBIOL INT. 2015;32:128-135.F.I.:3,343. [doi:10.3109/07420528.2014.958494]

4 Pajaron, Marcos, Fernandez-Miera, Manuel F., Allende, Iciar, Arnaiz, Ana M., Gutierrez-Cuadra, Manuel, Cobo-Belaustegui, Manuel, Arminanzas, Carlos, de Berrazueta, Jose R., Farinas, Maria C., Sanroma, Pedro, Hosp Valdecilla Endocarditis Study.

Self-administered outpatient parenteral antimicrobial therapy (S-OPAT) for infective endocarditis: a safe and effective model. Eur J Intern Med.

2015;26:131-136.F.I.:2,891. [doi:10.1016/j.ejim.2015.01.001]

5 Pina T, Armesto S, Lopez-Mejias R, Genre F, Ubilla B, Gonzalez-Lopez MA, Gonzalez-Vela MC, Corrales A, Blanco R, Garcia-Unzueta MT, Hernandez JL, Llorca J, Gonzalez-Gay MA.

Anti-TNF-a therapy improves insulin sensitivity in non-diabetic patients with psoriasis: a 6-month prospective study. J

Eur Acad Dermatol Venereol. 2015;29:1325-1330.F.I.:2,826. [doi:10.1111/jdv.12814]

6 Sayman, Haluk B., Kanmaz, Bedii, Uslu, Ilhami, AL-Nahhas, Adil, Cuocolo, Alberto, Carril, Jose M., Cinaral, Ferahnaz, EL-Refaei, Sherif, Senocak, Mustafa.

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Nanomedicine

Newly Created Group

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Research lines

The IDIVAL Nanomedicine group 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 development of fluorescent probes for in vivo imaging using upconverting particles, without leaving out the exploration of the other possibilities offered by nanomaterials in healthcare, such as the development of nanodrugs (nanovaccines, injectable nanovectors, functional polymeric nanosystems), regenerative medicine as contrast agents for imaging techniques and the detection of tumour-free margins for surgery, nanobiocides, etc.

Our studies show how carbon nanotubes (CNTs) can penetrate cells, interfering with microtubule dynamics and behaving like microtubule stabilising drugs, which act as mitotic spindle disruptors. CNTs interact with microtubules in a biomimetic way, causing aberrant or catastrophic mitosis and triggering cell death. The advantage of CNTs over traditional cytotoxic chemotherapy (taxol and its derivatives, epothilones, colchicine or vinca derivatives) is its large area of interaction with the microtubule, which makes the emergence of resistance highly unlikely.

Our more immediate objectives are to generate a treatment with topical application against CNT-based cancer, for example for use as adjuvant or neoadjuvant therapy in cancers affecting the skin, head and neck cancers or those accessible topically or by injection (or deposit) in the area. This development is already patented. We are currently working on the functionalisation of the CNT surface to preferentially direct them to target cells and develop medium- and long-term parenteral treatment in the future, and the biocompatibility of the CNT so it is more biodegradable through different treatments.

Together with this research we are researching a number of biological applications of luminescent upconverting nanoparticles synthesised by the physicists and chemists of the group, which we will try to adapt (by changing diameters and composition) for use as intracellular nanothermometers and as contrast systems based on the application of infrared light (not harmful to living tissue) for tumour diagnosis and detection.

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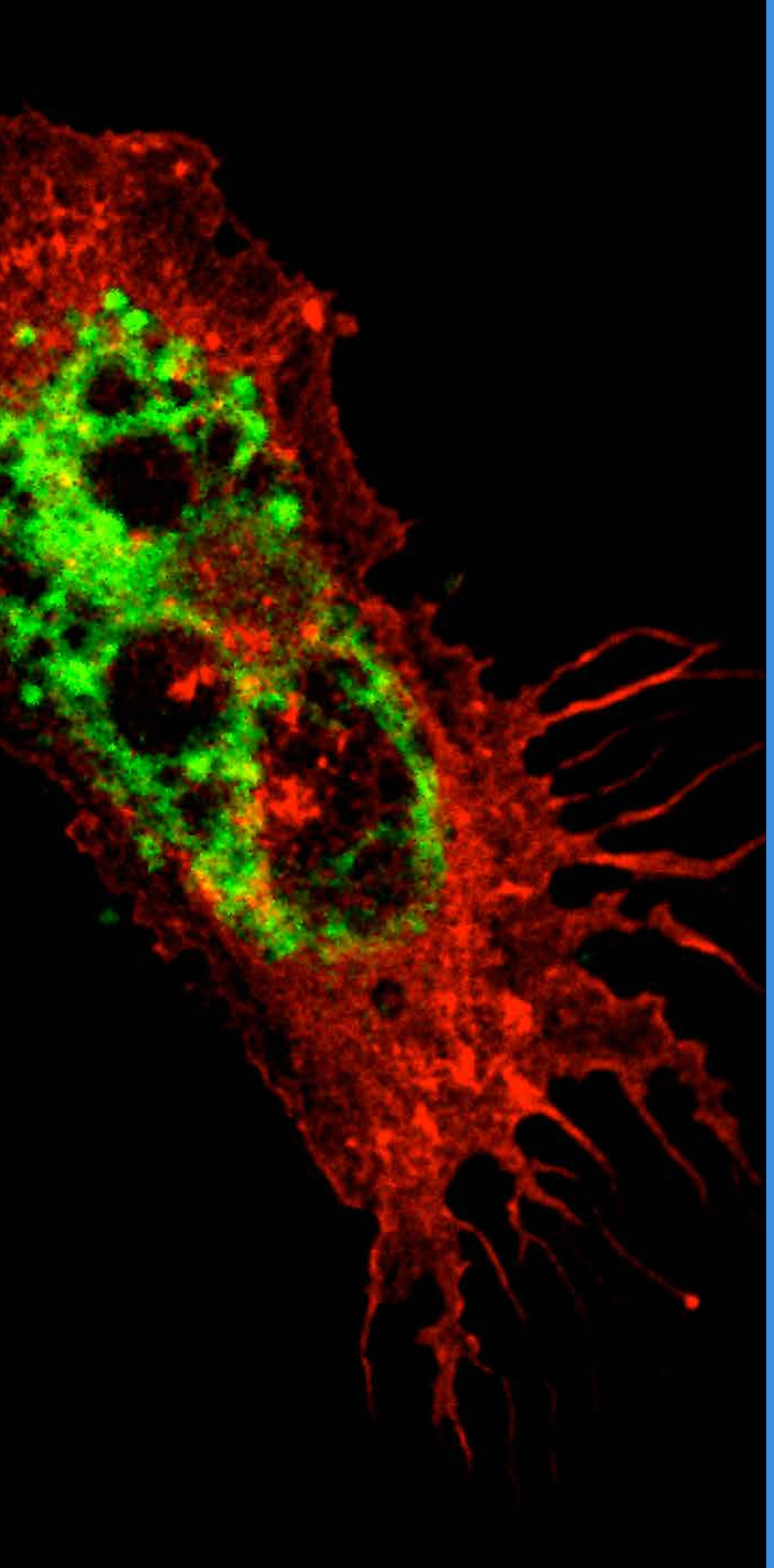

2015
Activity report

Neuroscience Area

Consolidated Groups

- Neurodegenerative diseases
- Psychiatry
- Nuclear Cell Biology

Clinical Groups

- Cephalea Clinic and Genetics
- Neurophysiology in Epilepsy and Neurointensive care

Neurodegenerative diseases

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Vázquez Higuera, José Luis (Fund. Reina Sofía)

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Research lines

1.Peripheral neuropathy.

In a prospective study of six early Guillain-Barré 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) harbouring NEFL mutations, either E397K or Ng8S, 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

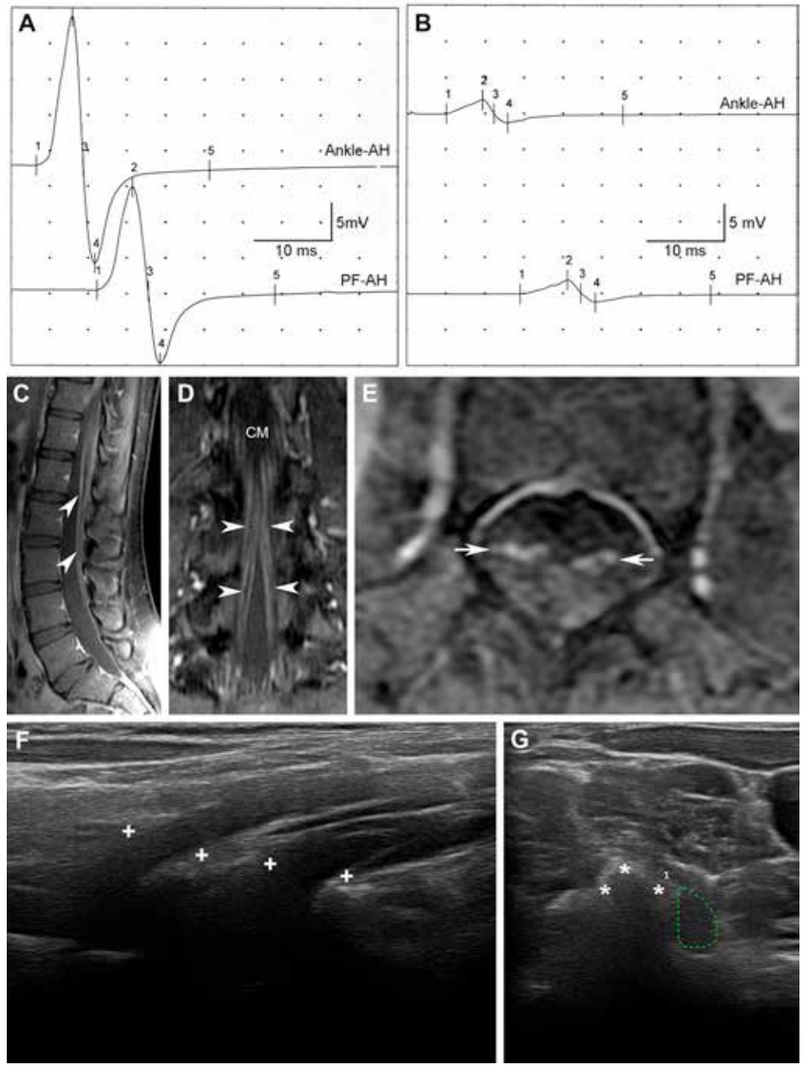

Figure 1. *Picture taken from the paper by Berciano et al (JNNP 2016; 87: 563-5. Epub 2015 May 13) showing electrophysiological and imaging findings in a patient with the paraparetic and axonal form of GBS. (A) Tibial nerve motor conduction velocity (MCV) study on day 4 after onset showing normal compound 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*

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2. Hereditary Ataxias.

We have continued with the SCA Natural 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 LRRK2 G2019S associated Parkinson's disease (PD). Through a blood transcriptomic analysis we have identified 13 candidate genes por 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.

FUNDING

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IMPACT FACTOR 241,745

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Doctoral Thesis

• Javier Riancho Zarrabeitia.

Efecto del bexaroteno en ratones transgénicos con esclerosis lateral amiotrófica (ELA). Estudio histológico y molecular.

Director/es: María Teresa Berciano Blanco, Miguel Ángel Lafarga Coscojuela, José Ángel Berciano Blanco. UNIVERSIDAD DE CANTABRIA.

Psychiatry

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Gaite Pindado, Luis (HUMV)
Gómez del Barrio, Andrés (HUMV)
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Tordesillas Gutiérrez, Diana (IDIVAL)

Nurses:
Martínez García, Mª Obdulia (HUMV)

Predoctorals:
Ruso Julve, Fulgencio (IDIVAL)

Research lines

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

Responsibles: R. ROIZ SANTIÁÑEZ
y D. TORDESILLAS GUTIÉRREZ.
Responsibles: R. Roiz Santiañez and D. Tordesillas Gutierrez.
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 abnomalies) and also study the onset of morphological changes during the course of the disease (neurodegeneration processes). Our work in this area aims to:

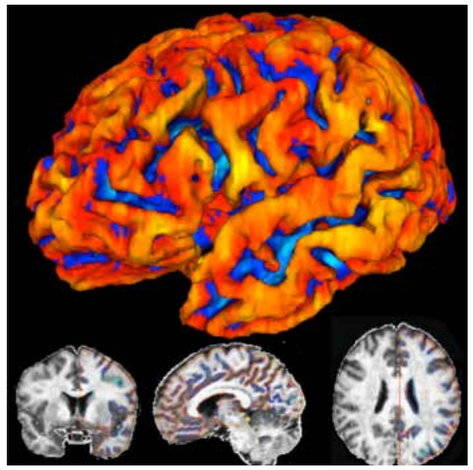
a. To Compare the volume of gray and white matter in the cortex between patients and controls,

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

c. A longitudinal 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.

1. Pharmacogenétics: We aim to study polymorphisms (SNPs) in dopamine and serotonin neurotransmission genes to clarify likely association between genetic variations and clinical characteristics, response phenotypes y outcome.
2. Imaging genetics: We aim to identify and characterize genetic variants that influence measures derived from anatomical brain images (MRI: volumetric, DTI), which are in turn related to brain-related illnesses or fundamental cognitive, emotional and behavioral processes, and are affected by environmental factors.
3. RNA sequencing (gene expression): We aim to compare the gene expression profiles analyzing patients with good and bad clinical response, and those who gain weight.

3. Epidemiology and Clinical characteristics of non-affective psychosis .

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

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

c. To describe predictors of outcome.

d. To advance in the knowledge of biological markers (neuroimage, biochemical, genetic) of Schizophrenia.

e. 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 Hospital Universitario 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.

a. To develop and consolidate a network of health professionals interested in investigating mental health services and needs.

b. To promote the development and dissemination of investigations on instruments of assessment and indicators of outcome (including economic indicators).

8. Molecular basis of non-affective psychosis.

Responsibles: 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, combinated with clinical practice.

b. Determine peripheral differences between patients with an episode of non-affective psychosis and healthy controls, from the onset and over time.

c. Conduct a longitudinal study of the change in biomarkers over time in people with schizophrenia.

d. Study the relationship between changes in peripheral molecules and correlate with longitudinal severity scores.

e. Detect biomarkers to predict treatment response.

9. Classification and assessment of disability in mental health.

Responsibles: Dra. S. HERRERA CASTANEDO
y Dr. L. GAITE PINDADO.

Since 1993, our research group has been involved in the development, publication nad dissemination of the International classification of Fucntionality (ICF) and related instruments of assessment (i.e., World Health Organization Disability Assessment Schedule 11 (WHO-DAS 11)..

FUNDING

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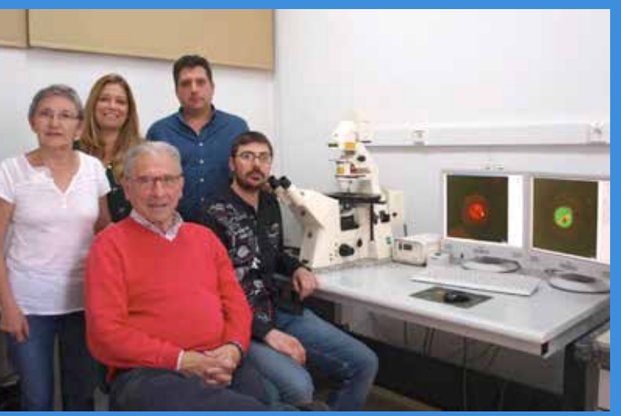
Doctoral Thesis

- Paula Suárez Pinilla.

Cambios morfológicos cerebrales en primeros episodios de psicosis no afectiva: implicación de variaciones de los polimorfismos BDNF, NRG1 Y CNR1.

Director/a: Benedicto Crespo Facorro. UNIVERSIDAD DE CANTABRIA.

Nuclear Cell Biology



Consolidated Group

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Research lines

Research area 1. Regulation of the molecular assembly of nuclear Cajal bodies (CB): importance in the spinal muscular atrophy (SMA).

The Cajal body (CB, Fig. 1) is the nuclear epicenter for the maturation of snRNP ("small nuclear ribonucleoproteins) and snoRNP ("small nucleolar RNP), which are involved in pre-mRNA splicing, specific histone pre-mRNAs processing and pre-rRNA processing. Deletion or mutation in the SMN1 gene, encoding the survival of motor neuron (SMN) protein, an essential component of the CB, is responsible for spinal muscular atrophy (SMA). Severe SMN deficiency in this disease causes a splicing pathology with degeneration and death of motor neurons, muscular atrophy and paralysis. SMA is the most frequent genetic cause of death in infancy.
The main objective of this line is to analyze the molecular mechanisms that regulate the assembly of CBs and the importance of CB depletion in the molecular pathophysiology of the SMA. We have recently shown that the SMN protein is a substrate SUMO1 and SUMOylation of SMN contributes to regulate the formation of CBs. Currently, we are studying the impact of other post-translational modification of SMN, acetylation, on the biogenesis of snRNPs and their assembly into CBs. Our preliminary experiments indicate that SMN is acetylated by the CBP acetyltransferase in the lysine K119. Moreover, mass spectrometry analysis demonstrates that SMN acetylation reduces its interaction with partner proteins involved in snRNP biogenesis and CB assembly.
Finally, in an experimental model of SMA, the transgenic mouse SMAdelta7, we are analyzing the dysfunction of the nucleolus and CBs in spinal motor neurons induced by SMN deficiency.

Research area 2. Neuronal response to DNA damage: importance in neurodegeneration.

There is growing evidence in the literature that the accumulation of DNA damage is involved in the molecular pathophysiology of aging and neurodegenerative processes. Our goal is to analyze the DNA damage response in normal rat neurons exposed to X-ray irradiation (4 Gy) to induce double strand breaks in DNA. In this model, we found that most of the neuronal DNA breaks are repaired within the first 24 hours, but there are a few permanent DNA damage foci of unrepaired DNA that persist for several months. We are characterizing the structural, molecular and transcriptional organization of chromatin compartments in which unrepaired DNA is concentrated and isolated to prevent genomic instability (Fig. 2). At present we are trying to identify DNA sequences of unrepaired DNA by using ChIPseq of persistent DNA damage foci, in order to establish the possible differential vulnerability of neuronal genes to genotoxic agents.

Research area 3. Neuroprotective mechanisms in the murine model of amyotrophic lateral sclerosis (ALS) SOD1-G93A. The sensitive component in ALS.

This line was an initiative of a resident of Neurology, Dr. Javier Riancho, based on an article showing the neuroprotective effect of Bexarotene, a retinoid X receptor agonist, in an animal model of Alzheimer's. Our study shows that oral administration of Bexarotene in SOD1-G93A transgenic mouse, an experimental model of amyotrophic lateral sclerosis (ALS), has a neuroprotective effect on motor neurons: improves motor function and neuronal survival. Particularly, treatment delays the onset of signs of degeneration, preserves axosomatic synapses, minimizes proteostasis disturbances and reduces protein aggregation and reactive astrogliosis. The study opens expectations for the therapeutic application of Bexarotene.
Moreover, in this experimental model we are analyzing the existence of a sensitive component in ALS affects thermal nociception and precedes the motor dysfunction. The target of this disease are the (type B and C) small and medium functional units of the sensory ganglia.

FUNDING

Berciano Blanco, María Teresa; Lafarga Coscojuela, Miguel Ángel. Regulación por acetilación del factor de supervivencia de las neuronas motoras. Su importancia en la biogénesis de snRNPs y en el ensamblaje de los cuerpos nucleares de Cajal. BFU2014-54754-P. MINECO. Duración: 2015-2016.

PUBLICATIONS

IMPACT FACTOR 18,318

Original articles

1 Aguilera Ó, Gonzalez-Sancho JM, Zazo S, Rincon R, Fernández AF, Tapia O, Canals F, Morte B, Calvanese V, Orgaz JL, Niell N, Aguilar S, Freije JM, Grana O, Pisano DG, Borrero A, Martínez-Useros J, Jiménez B, Fraga MF, García-Foncillas J, López-Otin C, Lafarga M, Rojo F, Muñoz A.
Nuclear DICKKOPF-1 as a biomarker of chemoresistance and poor clinical outcome in colorectal cancer.
Oncotarget. 2015;6:5903-5917.F.I.:6,359. [doi:10.18632/oncotarget.3464]

2 Ferrer-Mayorga G, Álvarez-Díaz S, Valle N, De Las Rivas J, Mendes M, Barderas R, Canals F, Tapia O, Casal JI, Lafarga M, Muñoz A.
Cystatin D Locates in the Nucleus at Sites of Active Transcription and Modulates Gene and Protein Expression.
J Biol Chem. 2015;290:26533-26548.F.I.:4,573. [doi:10.1074/jbc.M115.660175]

3 Riancho J, Ruiz-Soto M, Berciano MT, Berciano J, Lafarga M.
Neuroprotective effect of bexarotene in the SOD1(G93A) mouse model of amyotrophic lateral sclerosis.
FRONT CELL NEUROSCI. 2015;9:250-250.F.I.:4,289. [doi:10.3389/fncel.2015.00250]

4 Gallardo E, Sedano MJ, Orizaola P, Sánchez-Juan P, González-Suárez A, García A, Terán-Villagrá N, Ruiz-Soto M, Alvaro RL, Berciano MT, Lafarga M, Berciano J.
Spinal nerve involvement in early Guillain-Barre syndrome: A clinico-electrophysiological, ultrasonographic and pathological study.
Clin Neurophysiol. 2015;126:810-819.F.I.:3,097. [doi:10.1016/j.clinph.2014.06.051]

Doctoral Thesis

• Javier Riancho Zarrabeitia.
Efecto del bexaroteno en ratones transgénicos con esclerosis lateral amiotrófica (ELA). Estudio histológico y molecular.
Director/es: María Teresa Berciano Blanco, Miguel Ángel Lafarga Coscojuela, José Ángel Berciano Blanco. UNIVERSIDAD DE CANTABRIA

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Research lines

1. Genetics of migraines.

Genetics of migraines. The group has maintained its epidemiological-clinical and basic research activity (mainly in genetic association studies) in the field of cephalalgias. Within this first aspect, we should highlight the demonstration of the dose-dependent association between migraines and tobacco, and studies focusing on proving the usefulness of new neuromodulators (topiramate and zonisamide) in the treatment of refractory chronic migraines. In the field of genetics, the epistatic interaction of genes related to oestrogen metabolism in migraines (oestrogen receptor ESR2) has been described in 594 subjects grouped in 132 families, confirming the existence of a genetic factor in the pathogenesis of migraines as related to sex hormones; we further researched the association of genes of the folate metabolic pathway and migraines, confirming the association of migraines with aura and high homocysteine levels. We have recently demonstrated that there is significant endothelial activation in migraine sufferers and that this activation is more pronounced in chronic migraines. Furthermore, we demonstrated that there are variants of certain subunits of GABA associated with migraines in general.

2. Clinical and Genetic Research in Multiple Sclerosis.

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

a. HLA haplotype study regarding the origin within the region. Influence of HLA on multiple sclerosis.

b. 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.

FUNDING

Oterino Durán, Agustín. Etiopatogenia de la Migraña: Análisis de la expresión de genes diferenciados en migrañosos. Rastreo mutacional y expresión de GABRR1 y prevalencia del gen TRESK en migraña con aura. PI11/01232. Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Duración: 2011-2015.

PUBLICATIONS

IMPACT FACTOR 60,187

Original articles

1 Pascual J.
CGRP antibodies: the Holy Grail for migraine prevention?.
Lancet Neurol. 2015;14:1066-1067.F.I.:21,896. [doi:10.1016/S1474-4422(15)00244-6]

2 Villar LM., Costa-Frossard L, Masterman T, Fernández Ó, Montalban X, Casanova B, Izquierdo G, Coret F, Tumani H, Saiz A, Arroyo R, Fink K, Leyva L, Espejo C, Simo-Castello M, García-Sánchez MI, Lauda F, Llufriú S, Álvarez-Lafuente R, Olascoaga J, Prada A, Oterino A, de Andrés C, Tintoré M, Ramió-Torrenta L, Rodríguez-Martin E, Picón C, Comabella M, Quintana E, Álvarez-Cermeno JC.
Lipid-Specific Immunoglobulin M Bands in Cerebrospinal Fluid Are Associated with a Reduced Risk of Developing Progressive Multifocal Leukoencephalopathy during Treatment with Natalizumab.
Ann Neurol. 2015;77:447-457.F.I.:9,977. [doi:10.1002/ana.24345]

3 Cernuda-Morollón E, Ramón C, Martínez-Camblor P, Serrano-Pertierra E, Larrosa D, Pascual J.
OnabotulinumtoxinA decreases interictal CGRP plasma levels in patients with chronic migraine.
Pain. 2015;156:820-824.F.I.:5,213. [doi:10.1097/j.pain.0000000000000119]

4 Cernuda-Morollón E, Martínez-Camblor P, Álvarez R, Larrosa D, Ramón C, Pascual J.
Increased VIP levels in peripheral blood outside migraine attacks as a potential biomarker of cranial parasympathetic activation in chronic migraine.
Cephalalgia. 2015;35:310-316.F.I.:4,891. [doi:10.1177/0333102414535111]

5 Cernuda-Morollón E, Ramón C, Larrosa D, Álvarez R, Riesco N, Pascual J.
Long-term experience with onabotulinumtoxinA in the treatment of chronic migraine: What happens after one year?.
Cephalalgia. 2015;35:864-868.F.I.:4,891. [doi:10.1177/0333102414561873]

6 Fachal, L, Mosquera-Miguel A, Pastor P, Ortega-Cubero S, Lorenzo E, Oterino-Durán A, Toriello M, Quintans B, Camina-Tato M, Sesar Á, Vega A, Sobrido MJ, Salas A.
No Evidence of Association Between Common European Mitochondrial DNA Variants in Alzheimer, Parkinson, and Migraine in the Spanish Population.
Am J Med Genet. 2015;168:54-65.F.I.:3,416. [doi:10.1002/ajmg.b.32276]

6 Mitsikostas DD, Ashina M, Craven A, Diener HC, Goadsby PJ, Ferrari MD, Lampl C, Paemeleire K, Pascual J, Siva A, Olesen J, Osipova V, Martelletti P, EHF committee.
European headache federation consensus on technical investigation for primary headache disorders.
J Headache Pain. 2015;17:5-5.F.I.:2,801. [doi:10.1186/s10194-016-0596-y]

7 González-Quintanilla V, Toriello-Suárez M, Gutiérrez-González S, Rojo-López A, González-Suárez A, Viadero-Cervera R, Palacio-Portilla EJ, Oterino-Durán A.
Stress at work in migraine patients: Differences in attack frequency.
Neurologia. 2015;30:83-89.F.I.:1,381. [doi:10.1016/j.nrl.2013.10.008]

8 Larrosa-Campo D, Ramón-Carbajo C, Álvarez-Escudero R, Cernuda-Morollón E, García-Cabo C, Pascual J.
Patologia arterial en la migraña: disfuncion endotelial y cambios estructurales en la vasculatura cerebral y sistemica. Rev Neurol. 2015;61:313-322.F.I.:0,830.

Letters

1 Tfelt-Hansen P, Pascual J.
Reporting withdrawals due to adverse events in single-attack acute migraine clinical trials.
Cephalalgia. 2015;35:366-367.F.I.:4,891 [doi:10.1177/0333102414540059]

Doctoral Thesis

• Vicente González Quintanilla.
FUNCIÓN ENDOTELIAL EN ESCLEROSIS MÚLTIPLE Y MIGRAÑA. ESTUDIO TRANSVERSAL CON COMPARADOR ACTIVO.
Director/es: Agustín Oterino Durán, Jesús Castillo Obeso.
UNIVERSIDAD DE CANTABRIA.

Neurophysiology in Epilepsy and Neurointensive care

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Research lines

Durante estos años estamos consolidado la línea de investigación en neurocríticos. Las áreas en las que estamos llevando a cabo nuestras investigaciones incluyen:

1-Refractory nonconvulsive status epilepticus.

2-Super-refractory or malignant nonconvulsive status epilepticus.

3-Multimodal neuromonitoring including intracortical electrodes in acute brain injury patients.

4-EEG patterns and prognosis in hipoxic-ischemic encephalopathy.

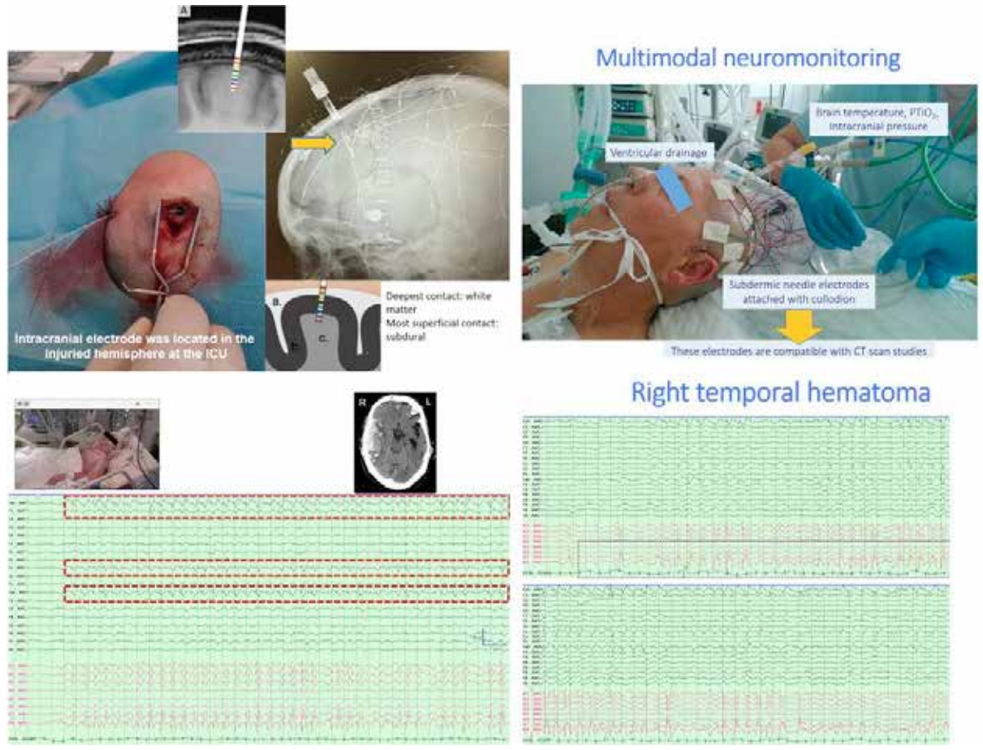
5-Post-anoxic myoclonic status epilepticus. Stimulus-induced postanoxic myoclonus.

6-Utility of EEG in the diagnosis of brain death.

7-Toxic encephalopathy in neurocritical patients.

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

9-Experimental models of status epilepticus. EEG phases of status epilepticus in humans.



PUBLICATIONS

IMPACT FACTOR 10,353

Original articles

1 Cuadrado-Lavín A, Salcines-Caviedes JR, Díaz-Pérez A, Carrascosa MF, Ochagavía M, Fernández-Forcelledo JL, Cobo M, Fernández-Gil P, Ayestarán B, Sánchez B, Campo C, Llorca J, Lorenzo S, Illaro A.

First-line eradication rates comparing two shortened non-bismuth quadruple regimens against Helicobacter pylori: an open-label, randomized, multicentre clinical trial.

J Antimicrob Chemother. 2015;70:2376-2381.F.I.:5,313 [doi:10.1093/jac/dkv089]

2 Fernández-Torre JL, Kaplan PW, Hernández-Hernández MA.

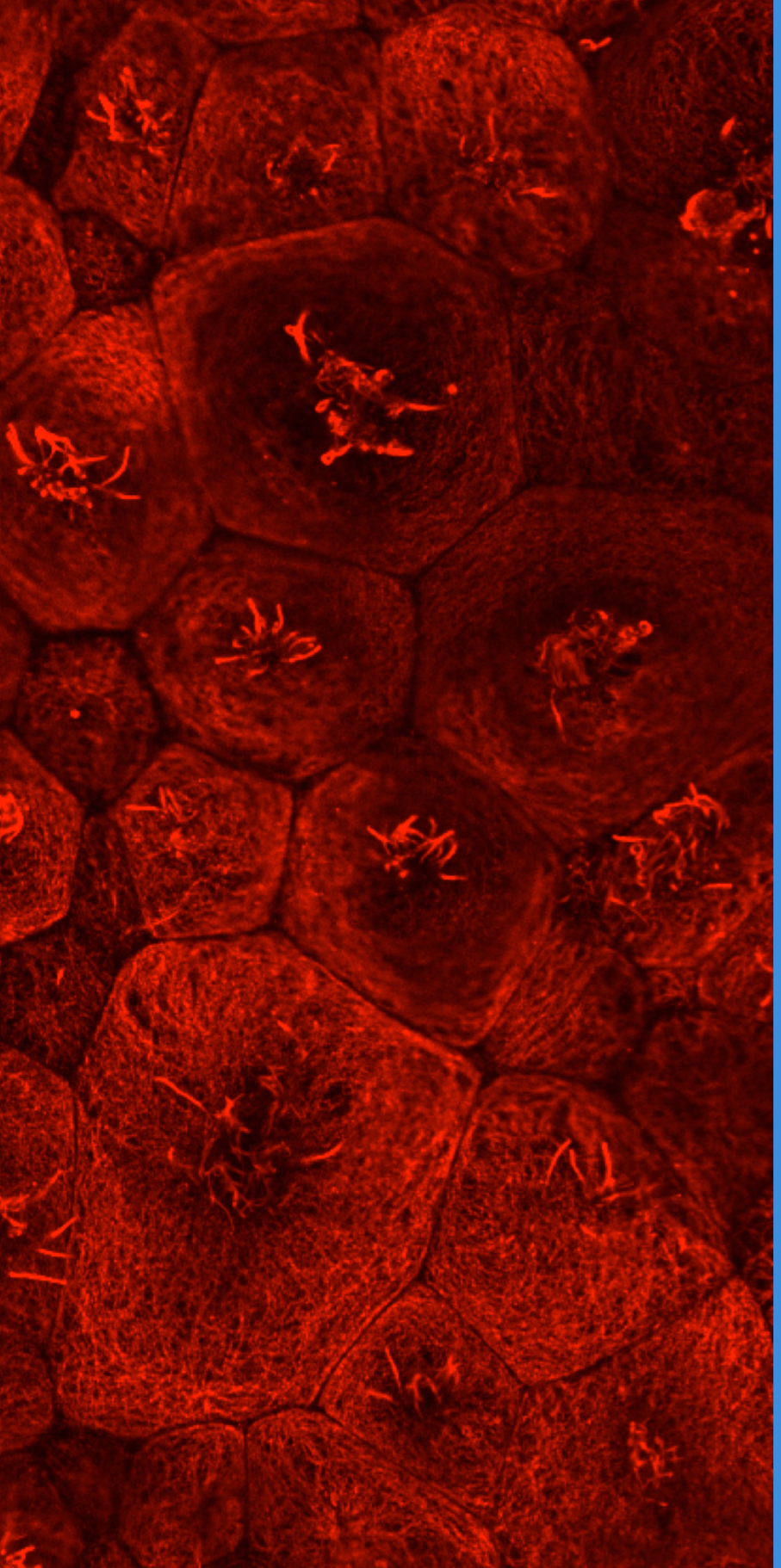
New understanding of nonconvulsive status epilepticus in adults: treatments and challenges.

EXPERT REV NEUROTHER. 2015;15:1455-1473.F.I.:2,783. [doi:10.1586/14737175.2015.1115719]

3 Fernández-Torre JL, Burgueño P, Ballesteros MA, Hernández-Hernández MA, Villagrá-Terán N, de Lucas EM.

Super-refractory nonconvulsive status epilepticus secondary to fat embolism: A clinical, electrophysiological, and pathological study.

Epilepsy Behav. 2015;49:184-188.F.I.:2,257. [doi:10.1016/j.yebeh.2015.04.045]



2015
Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Transplantation Area

Consolidated Groups

- Haematologic Neoplasms And Haematopoietic Stem Cells Transplantation
- Transplantation and Autoimmunity
- Cytokines and Growth Factors in Pathological Tissue Plasticity Phenomena

Clinical Groups

- Cardiovascular research Group

Emerging Groups

- Infection, Immunity and Digestive Diseases

Haematologic Neoplasms and Haematopoietic Stem Cells Transplantation

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Colorado Araujo, Mercedes (HUMV)
Cuesta García, Amalia (HUMV)
Gonzalez-Mesones Galan, Belen (HUMV)
González Villambrosia, Sonia (HUMV)
Insunza Gamide, Andrés (HUMV)
López Duarte, Mónica (HUMV)
Lopez Pereira, Brenda (HUMV)
Montes Gaisán, Carmen (HUMV)
Núñez Céspedes, Javier (HUMV)
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Pérez Vázquez, Germán (HUMV)
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Romón Alonso, Íñigo (HUMV)
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Red Temática de Investigación Cooperativa en Cáncer

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Research lines

1. Cell biology of blood diseases.

1.1. Prognostic significance of BCL6 and MYC expression in lymphomas. MYC and BCL6 expression seems to have a prognostic and therapeutic importance in NHL. A collaboration has started with Dr. Piris' group.

1.2. FANC genes/proteins in cancer and development. Fanconi Aplasia is a chromosomal instability, caused by mutations in at least 13 genes and characterised by malformations, bone marrow failure and cancer susceptibility.

1.3. Molecular biology and genetics of MDS. The biological and genetic variables of MDS are being collected in a multicentre clinical study. We are also studying the role of MYC in MDS.

1.4. Molecular biology and genetics of chronic myeloid leukaemia (CML). Investigates the action of certain drugs, including imatinib, on genes involved in cell proliferation, such as MYC and SPI.

1.5. Cooperative research on the biology of lymphoid neoplasms. Studies biological and genetic factors in lymphoid tumour banks.

2. Diagnostic and therapeutic innovation.

2.1. Clinical research on new drugs. Active participation in research aimed at treating patients with neoplasms using new drugs or new onco-haematological treatment regimens.

3. Stem cell transplantation.

3.1. Clinical results of alloHSCT in patients with AML conditioned with busulfan and fludarabine.

PUBLICATIONS

IMPACT FACTOR 39,631

Original articles

1 Batlle-López A, Cortiguera MG, Rosa-Garrido M, Blanco R, Del Cerro E, Torrano V, Wagner SD, Delgado MD.

Novel CTCF binding at a site in exon1A of BCL6 is associated with active histone marks and a transcriptionally active locus.

Oncogene. 2015;34:246-256.F.I.:8,459. [doi:10.1038/onc.2013.535]

2 Purroy N, Bergua J, Gallur L, Prieto J, López LA, Sancho JM, García-Marco JA, Castellví J, Montes-Moreno S, Batlle A, de Villambrosia SG, Carnicero F, Ferrando-Lamana L, Piris MA, López A.

Long-term follow-up of dose-adjusted EPOCH plus rituximab (DA-EPOCH-R) in untreated patients with poor prognosis large B-cell lymphoma. A phase II study conducted by the Spanish PETHEMA Group.

Br J Haematol. 2015;169:188-198.F.I.:4,711. [doi:10.1111/bjh.13273]

3 Poiré X, Labopin M, Cornelissen JJ, Volin L, Richard Espiga C, Veelken JH, Milpied N, Cahn JY, Yacoub-Agha I, van Imhoff GW, Michallet M, Michaux L, Nagler A, Mohty M.

Outcome of conditioning intensity in acute myeloid leukemia with monosomal karyotype in patients over 45 year-old: A study from the acute leukemia working party (ALWP) of the European group of blood and marrow transplantation (EBMT).

Am J Hematol. 2015;90:719-724.F.I.:3,798. [doi:10.1002/ajh.24069]

4 Onaindia A, Montes-Moreno S, Rodríguez-Pinilla SM, Batlle A, González de Villambrosía S, Rodríguez AM, Alegre V, Bermúdez GM, González-Vela C, Piris MA.

Primary cutaneous anaplastic large cell lymphomas with 6p25.3 rearrangement exhibit particular histological features.

Histopathology. 2015;66:846-855.F.I.:3,453. [doi:10.1111/his.12529]

5 Sánchez-Castro J, Marco-Betés V, Gómez-Arbonés X, García-Cerecedo T, López R, Talavera E, Fernández-Ruiz S, Ademà V, Marugan I, Luño E, Sanzo C, Vallespí T, Arenillas L, Marco Buades J, Batlle A, Buño I, Martín Ramos ML, Blázquez Rios B, Collado Nieto R, Vargas MT, González Martínez T, Sanz G, Solé F, Spanish Group for MDS Study (GESMD) and the Spanish Group for Clinical Cytogenet.

Fluorescence in situ hybridization of TP53 for the detection of chromosome 17 abnormalities in myelodysplastic syndromes.

Leuk Lymphoma. 2015;56:3183-3188.F.I.:2,891. [doi:10.3109/10428194.2015.1028053]

6 Sánchez-Carrera D, García-Puga M, Yáñez L, Romón Í, Pipaón C.

Delta Np73 is capable of inducing apoptosis by co-ordinately activating several BH3-only proteins.

Biosci Rep. 2015;35:F.I.:2,637. [doi:10.1042/BSR20150039]

7 Kharfan-Dabaja MA, Labopin M, Bazarbachi A, Socie G, Kroeger N, Blaise D, Veelken H, Bermudez A, Or R, Lioure B, Beelen D, Fegueux N, Hamladji RM, Nagler A, Mohty M.

Higher busulfan dose intensity appears to improve leukemia-free and overall survival in AML allografted in CR2: An analysis from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation.

Leuk Res. 2015;39:933-937.F.I.:2,351. [doi:10.1016/j.leukres.2015.04.009]

8 Yáñez L, Insunza A, Ibarrondo P, de Miguel C, Bermúdez A, Colorado M, López-Duarte M, Richard C, Conde E.

Experience with anidulafungin in patients with allogeneic hematopoietic stem cell transplantation and graft-versus-host disease.

Transpl Infect Dis. 2015;17:761-767.F.I.:2,064. [doi:10.1111/tid.12429]

9 Raya JM, Martín-Santos T, Luño E, Sanzo C, Perez-Sirvent ML, Such E, Navarro JT, Millá F, Alonso E, Domingo A, Rozman M, Díaz-Beya M, Batlle A, González-de-Villambrosia S, Tuset E, Vallespí T, Ortega M, Bermejo A, Martín-Ramos M, Peri V, Solé F, Florensa L, On behalf of the Grupo Español de Citología Hematológica (GECH), Working Group i.

Acute myeloid leukemia with inv(3)(q21q26.2) or t(3;3)(q21;q26.2): clinical and biological features and comparison with other acute myeloid leukemias with cytogenetic aberrations involving long arm of chromosome 3.

HEMATOLOGY. 1;F.I.:0,000. [doi:10.1179/1607845415Y.0000000003]

Letters

1 Onaindia A, Gómez S, Piris-Villaespesa M, Martínez-Laperch C, Cereceda L, Montes-Moreno S, Batlle A, González de Villambrosia S, Pollán M, Martín-Acosta P, González-Rincón J, Menarguez J, Alvés J, Rodríguez-Pinilla SM, García JF, Mollejo M, Fraga M, García-Marco JA, Piris MA, Sánchez-Beato M.

Chronic lymphocytic leukemia cells in lymph nodes show frequent NOTCH1 activation.

Haematologica. 2015;100:F.I.:5,814. [doi:10.3324/haematol.2014.117705]

2 Montes Moreno S, Climent F, González de Villambrosía S, González Barca EM, Batlle A, Insunza A, Pané Foix M, Colorado M, Martín Sánchez G, Richard Espiga C, Conde E, Piris MA.

CD 30-positive transformed follicular lymphoma: two case reports and literature review.

Histopathology. 2015;67:918-922.F.I.:3,453. [doi:10.1111/his.12733]

Doctoral Thesis

• Lucrecia Yáñez San Segundo.

Impacto de los cambios en el procedimiento del trasplante alogénico de células progenitoras hematopoyéticas sobre la evolución y morbi-mortalidad de las complicaciones.

• Carmen Montes Gaisán.

Supervivencia a largo plazo de los pacientes trasplantados por leucemia mieloblástica aguda. Análisis de los factores de riesgo.

Director/a: Eulogio Conde García. UNIVERSIDAD DE CANTABRIA.

Transplantation and Autoimmunity

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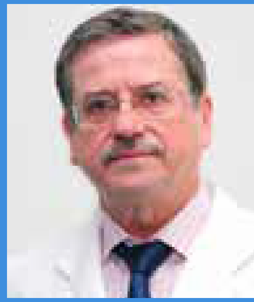

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Research lines

1. Solid organ transplantation.

1. Non-invasive peripheral blood and urine biomarkers (solubles and cellular) for clinical events in transplantation (rejection, infection, immunosuppression changes, short- and long-term survival). We are specially focused in antibody-mediated rejection in renal, lung and liver transplantation. Our group coordinates the multicenter study ImmuForum (financed by Astellas Pharma) and developed in the context of REDINREN (Red de Investigación en Enfermedades Renales: Ref 12/0021). Clinical translation of this area of research has been our commitment in the Spanish National Programme of Donor Paired Exchange and the Hypersensitized Programme (PATHI).

2. Immunoregulation in renal and lung transplantation. We analyze the possible role of regulatory T cells in both renal and lung transplantation as biomarkers. These T cell subsets are analyzed together with other effector cells since we have demonstrated that the balance between regulatory and effector cells has more diagnostic/prognostic value than any of them alone.

3. Cardiovascular disease in renal transplantation and hemodiálisis. This goal is undertaken within the Inpacto Programme from MINECO in collaboration with the Gerona University and Gendiag S.L. As deliverable we have developed a patent with a gene profile associated with electrocardiogram changes in these patient populations.

4. Intensive treatment donors to increase the number of suitable lung grafts for transplantation. Intensive treatment of multiorgan donors ventilatory based on a specific therapy, haemodynamic targets guided by extrapulmonary water and hormone increases the number of lung grafts suitable for transplantation. This increase in the number of lung grafts available due to improvement in oxygenation of the lungs in the period between death and removal of organs.

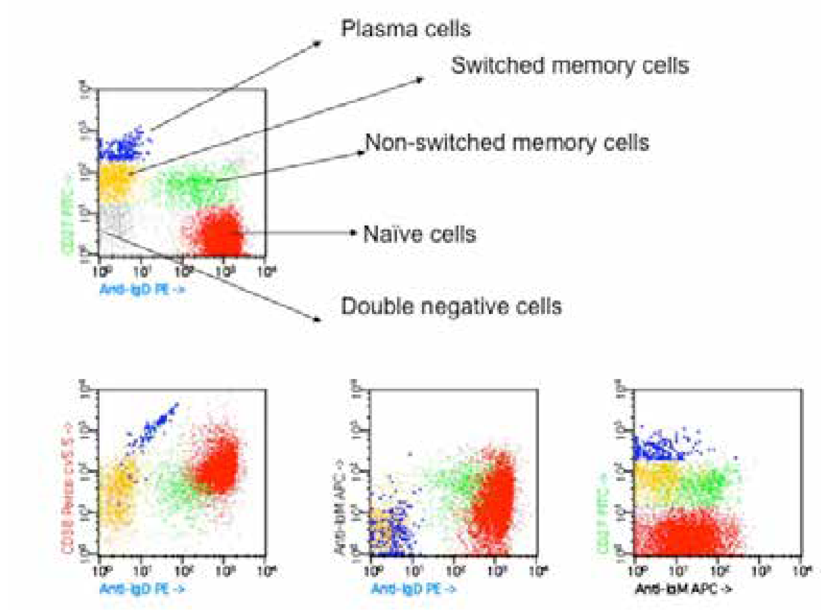

Figure. Definition of B cell maturation stages by flow cytometry according to the expression of different cell surface molecules.

2. Autoimmune diseases.

1. Antiphospholipid syndrome. We are specially focused in the role of the innate immune response (i.e., TLRs) and its influence in the induction of regulatory cell subsets in the pathogeny of this syndrome.

2. Autoinmune Pancreatitis. The group has contributed to the development of serological diagnostic markers and researches in triggering the pathogenic mechanisms involved seem to share elements with glandular diseases such as Sjögren's syndrome. Immunology laboratory is a national reference for the study of anti-type II anhydrous carbonic in diagnosing the disease.

3. Biomarkers. The group has a wide serum bank associated with clinical data and collected since 1997 (registered in the ISCIII investigator collections). This allows the validation of new markers involved in the diagnosis, prognosis and response to treatment of autoimmune disease. In addition, we have all type of methods required for setting up and carrying out serologic studies of autoimmunity. As a result of the exploitation of this seroteca we have defined new diagnostic utilities hitherto unexplored antibodies (anti-PR3) in diseases such as inflammatory bowel disease, together with gastrointestinal pathology group IDIVAL.

3. Inflammation

1. Inflammatory diseases of the elderly (Giant Cell Arteritis, Polymialgia Rheumatica, elderly-onset rheumatoid artritis). Our 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 use cell markers (phenotypic and functional), serologic and genetic (expression and genetic polymorphisms). This line has been strong so far in productivity in the form of doctoral theses and articles.

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IMPACT FACTOR 122,285

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Letters

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Doctoral Thesis

• Sara Díaz Angulo.

Estudio de la prevalencia de disfunción y autoinmuniad tiroidea en pacientes con urticaria crónica, vitíligo y alopecia areata en la comunidad autónoma de Cantabria.

Director/es: Marcos Antonio González López, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.

• Elisabeth Coll Torres.

Protocolo de tratamiento del donante multiorgánico para el incremento de la donación pulmonar. Estudio multicentrico nacional.

Director/es: Gil Rodriguez Carvaca, Eduardo Miñambres García. UNIVERSIDAD REY JUAN CARLOS I.

Cytokines and Growth Factors in Pathological Tissue Plasticity Phenomena

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Lantigua Romero, Sara (HUMV)

Research lines

1. Pathological plasticity of myocardium.

We are analysing the involvement of transforming growth factors beta (TGF-βs, activin and BMPs) in the molecular pathophysiology of myocardial remodelling secondary to haemodynamic stress and in altered development.

1.1. Pathological plasticity of myocardium subjected to pressure overload. Aortic stenosis is the most frequent valvular cause for surgery in our area and is associated with a left ventricular hypertrophy which is a response of pathological significance in these patients. We are studying the molecular mechanisms of myocardial remodelling in this context using samples of myocardium of patients with aortic stenosis, a murine experimental model of this pathology and cell cultures.

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

FUNDING

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PUBLICATIONS

IMPACT FACTOR 29,135

Original articles

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Barriers to HCV treatment in the era of triple therapy: a prospective multi-centred study in clinical practice.

Liver Int. 2015;35:401-408.F.I.:4,850. [doi:10.1111/liv.12536]

5 Savignac HM, Tramullas M, Kiely B, Dinan TG, Cryan JF.

Bifidobacteria modulate cognitive processes in an anxious mouse strain.

Behav Brain Res. 2015;287:59-72.F.I.:3,028. [doi:10.1016/j.bbr.2015.02.044]

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Self-administered outpatient parenteral antimicrobial therapy (S-OPAT) for infective endocarditis: A safe and effective model.

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Reviews

1 Expósito V, Seras M, Fernández-Fresnedo G.

Oral anticoagulation in chronic kidney disease with atrial fibrillation.

Med Clin (Barc). 2015;144:452-456.F.I.:1,417. [doi:10.1016/j.medcli.2014.03.029]

Doctoral Thesis

• Susana García Cerro.

Estudio del efecto de la reducción del número de copias del gen DYRK1A sobre distintos fenotipos funcionales y neuromorfológicos encontrados en un modelo murino de síndrome de Down y en ratones euploides.

Director/es: Carmen Martínez-Cue Pesini, Noemí Rueda Revilla. UNIVERSIDAD DE CANTABRIA.

• Sara Velategui Camus.

Papel del microrna-30C en la percepción dolorosa.

Director/es: María Amor Hurlé González, Mónica Tramullas Fernández. UNIVERSIDAD DE CANTABRIA.

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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.

c. Percutaneous Structural Heart Disease Interventions

-Atrial septal defects closure

-Transcatheter aortic valve implantations (TAVI)

-Prosthetic leaks closure

-Left arial appendage closure

d. Preconditioning in acute coronary syndromes.

2. Cardiovascular Diagnosis

a. Genetics in mitral valve prolapse

b. Prevalence and clinical significance of Coronary aneurysms.

2. Multimodality Cardiac Imaging.

a. Diagnosis and charcterizaction of Cardiac Allograft Vasculopathy with intravascular ultrasonography (IVUS), optical coherence and virtual histology.

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

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

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

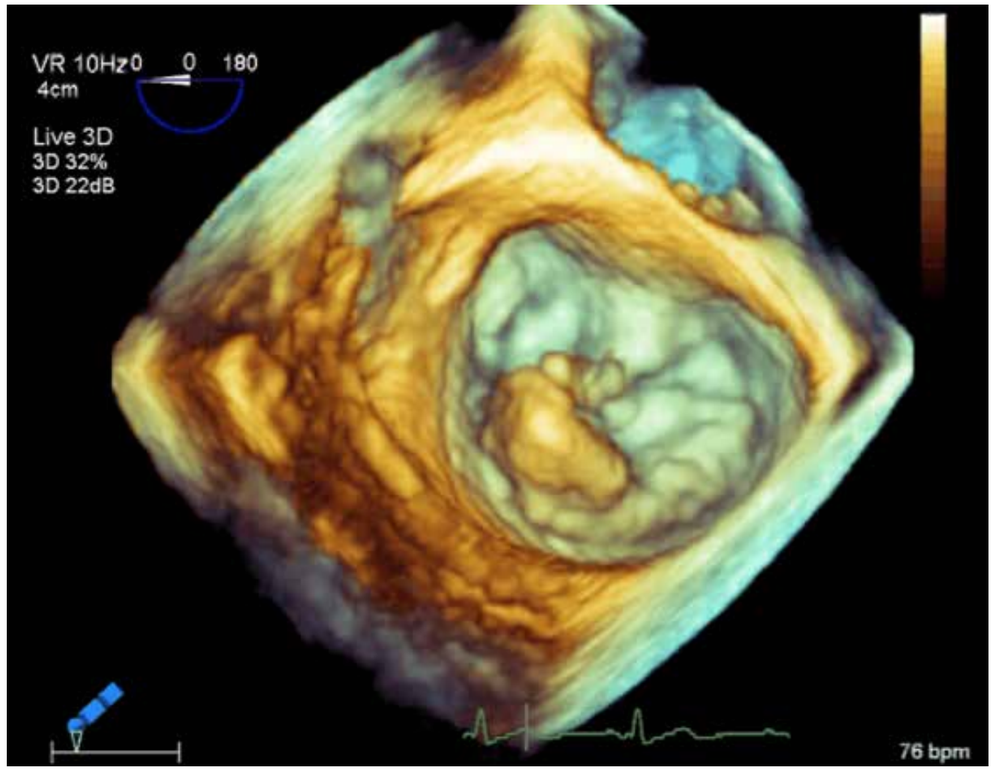

Figura. *Ecocardiograma tridimiensional demostrativo de un prolapso de la válvula mitral*

PUBLICATIONS

IMPACT FACTOR 87,036

Original articles

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A Prospective Randomized Trial of Drug-Eluting Balloons Versus Everolimus-Eluting Stents in Patients With In-Stent Restenosis of Drug-Eluting Stents The RIBS IV Randomized Clinical Trial.

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J Am Coll Cardiol. 2015;66:1414-1414.F.I.:16,503. [doi:10.1016/j.jacc.2015.07.044]

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2014 Update on Interventional Cardiology.

Rev Esp Cardiol (Engl Ed). 2015;68:324-330.F.I.:3,792. [doi:10.1016/j.rec.2014.12.009]

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Comments on the 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation.

Rev Esp Cardiol (Engl Ed). 2015;68:1061-1067.F.I.:3,792. [doi:10.1016/j.rec.2015.11.001]

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Dual Antiplatelet Therapy for 6 Months vs 12 Months After New-generation Drug-eluting Stent Implantation: Matched Analysis of ESTROFA-DAPT and ESTROFA-2.

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Donor/recipient sex mismatch and survival after heart transplantation: only an issue in male recipients? An analysis of the Spanish Heart Transplantation Registry.

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Health-related quality of life, social support, and caregiver burden between six and 120 months after heart transplantation: a Spanish multicenter cross-sectional study.

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Outcomes of Patients Undergoing Balloon Aortic Valvuloplasty in the TAVI Era: A Multicenter Registry.

J Invasive Cardiol. 2015;27:547-553.F.I.:0,949.

Editoriales

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Letters

1 de la Torre Hernández JM, Hernández F, Alfonso F.

The Optimal Cutoff Value for Left Main Minimal Lumen Area of 4.5 mm(2): A Word of Caution.

JACC Cardiovasc Interv. 2015;8:122-123.F.I.:7,345. [doi:10.1016/j.jcin.2014.09.011]

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Evaluation of the preoperative vasoactive-inotropic score as a predictor of postoperative outcomes in patients undergoing heart transplantation.

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Use of the New Antiplatelet Agents in Acute Coronary Syndromes: Limitations Related to Patient Characteristics.

Rev Esp Cardiol (Engl Ed). 2015;68:448-450.F.I.:3,792. [doi:10.1016/j.rec.2014.12.019]

Doctoral Thesis

• Cristina Ruisánchez Villar.

Impacto de nuevas técnicas ecocardiográficas para la detección de disfunción miocárdica en la diabetes mellitus tipo 1 asintomática. Papel de la deformación miocárdica y la ecocardiografía tridimensional.

Director/es: José Antonio Amado Señaris, Francisco Jesús González Vílchez. UNIVERSIDAD DE CANTABRIA.

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Research lines

1. Hepatitis C virus (HCV).

To determine the epidemiology of HCV infection in our region. To define the role of the innate immune system in the spontaneous clearance and chronification of HCV infection and in the response to new direct-acting antiviral agents (DAA). To describe resistance HCV variants to DAA. To characterize whether HCV causes endothelial dysfunction, subclinical atheromatosis or neurocognitive manifestations and their potential reversibility after HCV erradication with new DAA.

2. Obesity and insulin resistance are associated with a chronic inflammatory state NAFLD2.

Current evidence indicates that the activation of the innate immune system through receptors such as TLRs and NLRs plays a central role in the initiation of the inflammatory signaling. These two families of receptors, together with RLRs, constitute the pattern recognition receptors (PRRs). However, their role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) is largely unknown. In patients with obesity it is posible that differences in gene and protein expression of PPRs in tissues (e.g. liver or adipose tissue) could lead to a different susceptibility to develop .

3. Hepatocarcinoma (HCC).

From a genomic perspective HCC is a very heterogeneous disease possibly reflecting the multiple etiologies causing this type of cancer. Taking advantage of the Whole Genome/Exome Sequencing data already generated for HCC, we have designed a targeted approach based on the mutational analysis of a specific selection of 112 genes (HepatoExoma). This technology will enable us to characterize the mutational profile of each HCC and thus perform targeted and individualized therapies in a time compatible with clinical practice. Using this approach it is estimated that we might be able to guide therapies in around 45.5 % of the patients with HCC. We have already performed a functional analysis of the effect of different targeted therapies (alone and in combination) on HepG2, Huh7 and SNU 449 cells. We are in the process of generating the mutational profile of paired clinical samples (tumor and non-tumor DNA) by applying the HepatoExoma.

4. Liver transplantation.

To study whether anti-HLA antibodies against donor-specific determinants might be involved in the development of complications after liver transplantation such as rejection (both humoral and cellular), biliary disease, and hepatic artery complications. In order to achieve this goal we will determine their levels in serum and in the liver graft whenever a liver biopsy is performed.

5. Transitional elastography and organ donation.

To assess the role of transitional elastography in the evaluation of the deceased donor liver quality.

6. Hepatopulmonary syndrome.

To study the prevalence of this syndrome in patients with liver cirrhosis and to develop screening strategies for its early diagnosis.

7. Liver cirrhosis and anticoagulation.

Cirrhosis is no longer considered a bleeding disorder, but rather a disease in which a delicate equilibrium between pro-thrombotic and pro-hemorrhagic profiles is frequently unbalanced towards the former. Importantly, pro-thrombotic states are also thought to contribute to liver fibrosis by generating thrombi in the hepatic microcirculation responsible for parenchymal extinction and by activating hepatic stellate cells via protease-activated receptors. The lines of research in this area include: 1) to determine if the administration of ribaroxaban, a direct factor Xa inhibitor, to patients with liver cirrhosis will increase transplant free survival without developing portal hypertension decompensations; 2) to determine the efficacy and safety of low-molecular-weight heparins in preventing deep vein thrombosis in hospitalised patients with liver cirrhosis; 3) To analyze the relationship between the presence of thrombophilic disorders and development of significant fibrosis.

FUNDING

Antonio Cuadrado Lavín. Terapia erradicadora de primera línea de la infección por Helicobacter Pylori: Ensayo clínico abierto, randomizado, multicéntrico de tres brazos comparando la triple terapia clásica frente a una terapia secuencial modificada y una terapia concomitante. EC11-528. Ministerio de Sanidad y Consumo. Duración: 2012-2014.

Javier Crespo García. Implicación de diferentes factores de la inmunidad innata y adaptativa en la etiopatogenia de la enfermedad hepática por depósito graso en pacientes con obesidad mórbida. PI12/02026. Instituto De Salud Carlos III. Ministerio De Economía Y Competitividad. Duración: 2012-2015

María Teresa Arias Loste. Implicación de diferentes factores de la inmunidad innata y adaptativa en la etiopatogenia de la enfermedad hepática por depósito graso en pacientes con obesidad mórbida. FEAD12/08. Fundacion Española del Aparato Digestivo "FEAD".

PUBLICATIONS

IMPACT FACTOR 127,863

Original articles

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The addition of a protease inhibitor increases the risk of infections in patients with hepatitis C-related cirrhosis.

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Percutaneous passage of an extraction balloon to assist recanalization of the common bile duct after surgical transection.

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Barriers to HCV treatment in the era of triple therapy: a prospective multi-centred study in clinical practice.

Liver Int. 2015;35:401-408.F.I.:4,850. [doi:10.1111/liv.12536]

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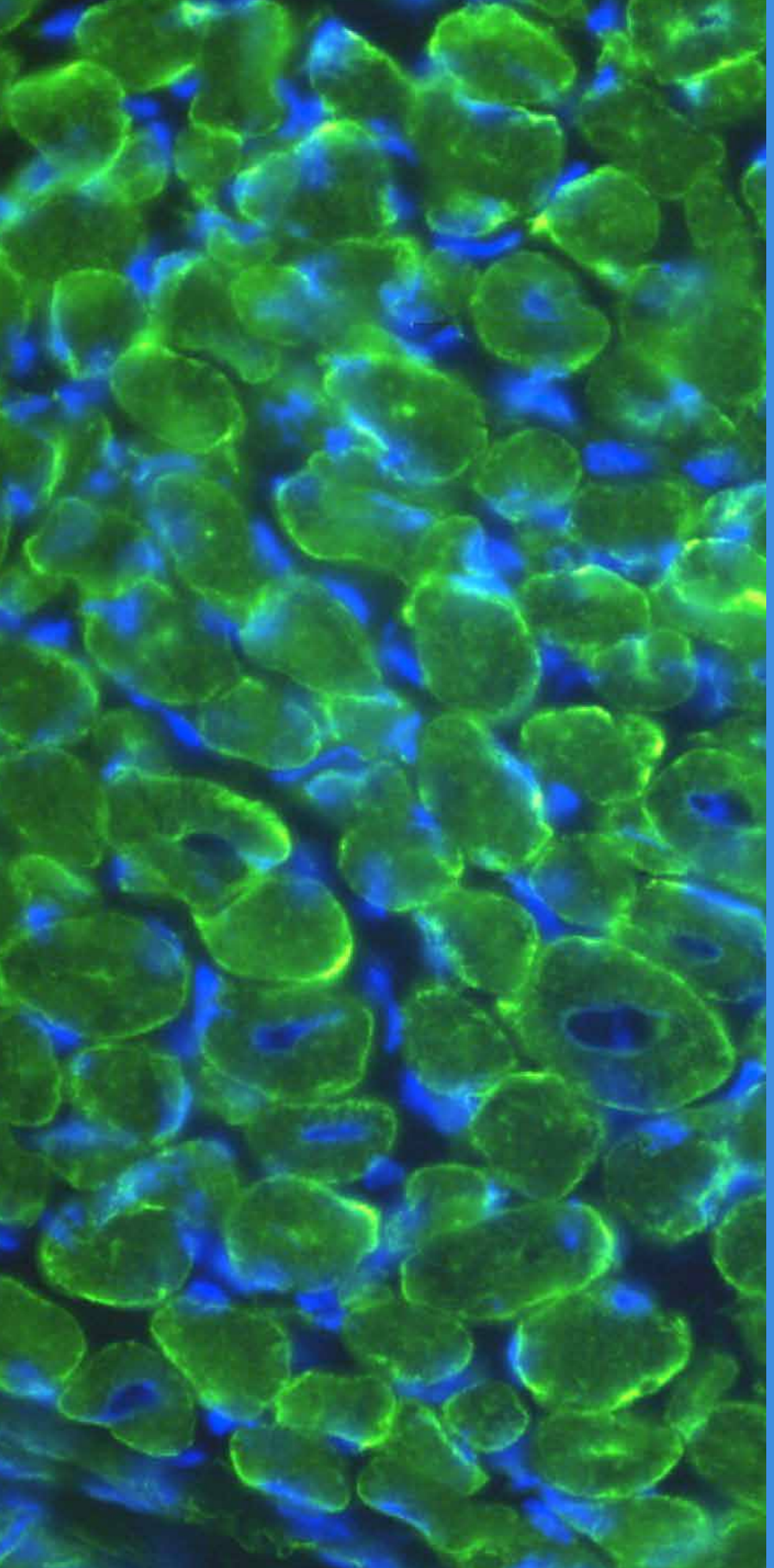

2015

Activity report

Valdecilla Instituto de Investigación Sanitaria IDIVAL

Metabolism Area

Consolidated Groups

- Mineral and Lipid Metabolism.
- Diagnosis and Treatment Using Imaging (Radiology).

Mineral and Lipid Metabolism

Consolidated Group

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red envejecimiento y fragilidad

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, Univesidad de la Laguna) and Dr. Gomez-Cimiano (Servicio de Traumatología del HUMV) it is developing an experimental model consisting of using mesenchymal stem cells modified in the treatment of fractures of critical size.

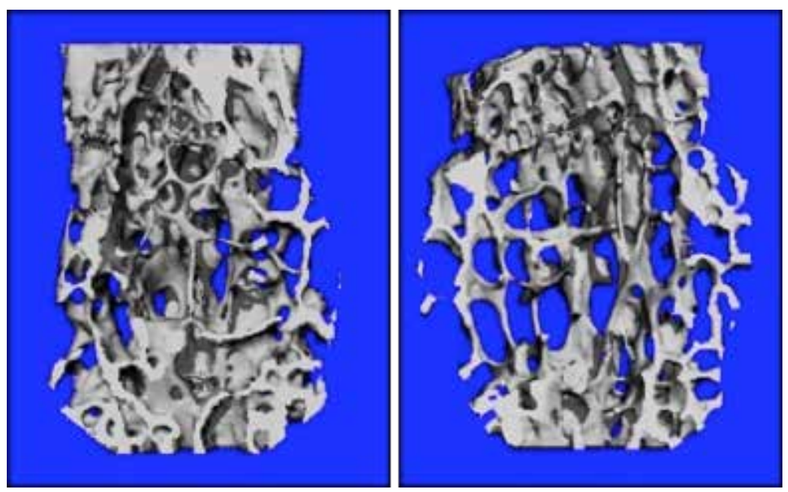

Figura. Imagenes de hueso por micro TC de animales OVX y control

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Use of positron emission tomography (PET) for the diagnosis of large-vessel vasculitis.
Rev Esp Med Nucl Imagen Mol. 2015;34:372-377.F.I.:1,054. [doi:10.1016/j.remn.2015.07.002]

Reviews

1 Loricera J, Blanco R, Hernández JL, Carril JM, Martínez-Rodríguez I, Canga A, Peiró E, Alonso-Gutiérrez J, Calvo-Río V, Ortiz-Sanjuán F, Mata C, Pina T, González-Vela MC, Martínez-Amador N, González-Gay MA.
Non-infectious aortitis: a report of 32 cases from a single tertiary centre in a 4-year period and literature review.
Clin Exp Rheumatol. 2015;33:19-31.F.I.:2,724.

Letters

1 Pérez-Campo FM, Sañudo C, Riancho JA.
Avoiding introduction of bias in the analysis of the methylation of free circulating DNA.
Clin Chim Acta. 2015;444:206-207.F.I.:2,824. [doi:10.1016/j.cca.2015.02.020]

Doctoral Thesis

• Marta García Hoyos.
Estudio de masa ósea y marcadores de remodelación en personas con síndrome de Down.
Director/es: José Antonio Riancho Moral, Carmen Valero Díaz De Lamadrid. UNIVERSIDAD DE CANTABRIA.

• José Luis González Fernández.
Validación del modelo predictivo de fractura osteoporótica frax en mujeres postmenopaúsicas y varones mayores de 50 años.
Director/es: José Luís Hernández Hernández, José Manuel Olmos Martínez. UNIVERSIDAD DE CANTABRIA.

• Lucrecia Yáñez San Segundo.
Impacto de los cambios en el procedimiento del trasplante alogénico de células progenitoras hematopoyéticas sobre la evolución y morbi-mortalidad de las complicaciones infecciosas.
Director/es: Eulogio Conde García, José Luís Hernández Hernández. UNIVERSIDAD DE CANTABRIA.

• Lourdes Calera Urbizu.
Cáncer colorrectal y metástasis exclusivamente hepáticas: nuevo sistema de estadificación. análisis de factores pronósticos y predictivos. experiencia del Hospital Universitario Marqués De Valdecilla 2004-2011.
Director/es: Jesús González Macías, Fernando Rivera Herrero. UNIVERSIDAD DE CANTABRIA.

• Magdalena Fernández García.
Tendencia secular de la incidencia de la fractura de cadera en Cantabria (1988-2010).
Director/es: José Luís Hernández Hernández, José Manuel Olmos Martínez. UNIVERSIDAD DE CANTABRIA.

Diagnosis and Treatment Using Imaging (Radiology).

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Villaespesa Diaz, Cristina (HUMV)
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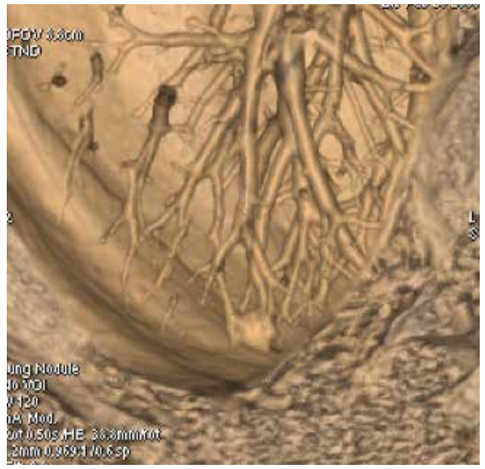
Lines of Research



1. Studies evaluating new percutaneous breast biopsy devices with image monitoring.
2. Evaluation of tomosynthesis techniques applied to digital mammography.
3. Studies on arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia (HHT). This study is being carried out in collaboration with the Hereditary Hemorrhagic Telangiectasia unit of Sierrallana Hospital.
4. Quantification of coronary calcium as a predictor of cardiovascular risk.
5. Study on complications in aortic stents.
6. Development of hybrid techniques: surgical-radiological techniques in the treatment of vascular disease.
7. Contribution of imaging methods (ultrasound, MRI) to the study of diffuse liver disease.
8. Evaluation of the usefulness and complications of thermal ablation treatments applied to patients with neoplastic disease.
9. Contribution of contrast-enhanced ultrasounds to the study of patients with abdominal disease, with special interest in liver, kidney and intestinal disease.
10. Value of the intima-media thickness of the carotid artery as a cardiovascular risk factor.
11. Evaluation of multidetector CT scans in the study of the stroke code.
12. Study on cerebral connectivity with MRI diffusion tensor.
13. Anatomical-radiological (ultrasound) correlation studies in cutaneous pathology.
14. Ultrasound in the diagnosis and monitoring of hidradenitis suppurativa.
15. Optimising the radiation dose in CT scans in the study of musculoskeletal pathology.
16. Evaluation of the CT scan for tibiofibular syndesmosis and the

long-term results of treatment of Maisonneuve fractures.

17. Anatomical-radiological (MRI) correlation studies in joint pathology.

18. Anatomical-radiological correlation studies in soft tissue sarcomas.

19. Anatomical-radiological correlation studies in bone sarcomas.

20. Biomechanics of the calcaneus joint.

21. Contribution of the multi-slice CT scan in the assessment of perforating arteries prior to reconstructive plastic surgery.

22. CT scan assessment of treatment response in cancer patients.

PUBLICATIONS

IMPACT FACTOR 33,366

Original articles

1 Roiz-Santiañez R, Ortiz-García de la Foz V, Ayesa-Arriola R, Tordesillas-Gutiérrez D, Jorge R, Varela-Gómez N, Suárez-Pinilla P, Córdova-Palomera A, Navasa-Melado JM, Crespo-Facorro B.

No progression of the alterations in the cortical thickness of individuals with schizophrenia-spectrum disorder: a three-year longitudinal magnetic resonance imaging study of first-episode patients.

Psychol Med. 2015;45:2861-2871.F.I.:5,938. [doi:10.1017/S0033291715000811]

2 Tordesillas-Gutiérrez D, Koutsouleris N, Roiz-Santiañez R, Meisenzahl E, Ayesa-Arriola R, Marco de Lucas E, Soriano-Mas C, Suárez-Pinilla P, Crespo-Facorro B.

Greymatter volume differences in non-affective psychosis and the effects of age of onset on grey matter volumes: A voxelwise study.

Schizophr Res. 2015;164:74-82.F.I.:3,923. [doi:10.1016/j.schres.2015.01.032]

3 Martino J, Mato D, de Lucas EM, García-Porrero JA, Gabarrós A, Fernández-Coello A, Vázquez-Barquero A.

Subcortical anatomy as an anatomical and functional landmark in insulo-opercular gliomas: implications for surgical approach to the insular region.

J Neurosurg. 2015;123:1081-1092.F.I.:3,737. [doi:10.3171/2014.11.JNS141992]

4 Gallardo E, Sedano MJ, Orizaola P, Sánchez-Juan P, González-Suárez A, García A, Terán-Villagrá N, Ruiz-Soto M, Alvaro RL, Berciano MT, Lafarga M, Berciano J

Spinal nerve involvement in early Guillain-Barré syndrome: a clinico-electrophysiological, ultrasonographic and pathological study.

Clin Neurophysiol. 2015;126:810-819.F.I.:3,097 [doi:10.1016/j.clinph.2014.06.051]

5 Loewe C, Arnaiz J, Krause D, Marti-Bonmati L, Haneder S, Kramer U, DDALIA Study Group.

MR Angiography at 3 T of Peripheral Arterial Disease: A Randomized Prospective Comparison of Gadoterate Meglumine and Gadobutrol.

AJR Am J Roentgenol. 2015;204:1311-1321.F.I.:2,731. [doi:10.2214/AJR.14.12604]

6 Fernández-Torre JL, Burgueño P, Ballesteros MA, Hernández-Hernández MA, Villagrá-Terán N, de Lucas EM.

Super-refractory nonconvulsive status epilepticus secondary to fat embolism: A clinical, electrophysiological, and pathological study.

Epilepsy Behav. 2015;49:184-188.F.I.:2,257. [doi:10.1016/j.yebeh.2015.04.045]

7 Alonso-Peña D, Arnaiz-García ME, Valero-Gasalla JL, Arnaiz-García AM, Campillo-Campaña R, Alonso-Peña J, González-Santos JM, Fernández-Díaz AL, Arnaiz J.

Feet sunk in molten aluminium: The burn and its prevention.

BURNS. 2015;41:1122-1125.F.I.:1,880. [doi:10.1016/j.burns.2014.12.003]

8 Freire J, García-Berbel L, García-Berbel P, Pereda S, Azueta A, García-Arranz P, De Juan A, Vega A, Hens Á, Enguita A, Muñoz-Cacho P, Gómez-Román J.

Collagen Type XI Alpha 1 Expression in Intraductal Papillomas Predicts Malignant Recurrence.

Biomed Res Int. 2015;2015:812027-812027.F.I.:1,579. [doi:10.1155/2015/812027]

9 Hernando MF, Cerezal L, Pérez-Carro L, Abascal F, Canga A.

Deep gluteal syndrome: anatomy, imaging, and management of sciatic nerve entrapments in the subgluteal space.

Skeletal Radiol. 2015;44:919-934.F.I.:1,510. [doi:10.1007/s00256-015-2124-6]

10 Cerezal L, Carro LP, Llorca J, Fernández-Hernando M, Llopis E, Montero JA, Canga A.

Usefulness of MR arthrography of the hip with leg traction in the evaluation of ligamentum teres injuries.

Skeletal Radiol. 2015;44:1585-1595.F.I.:1,510. [doi:10.1007/s00256-015-2210-9]

11 Riancho J, Jiménez-LópezY, Marco-de Lucas E, Berciano J.

Sudden onset of facial diplegia and aphagia.

Rev Clin Esp. 2015;215:540-541.F.I.:1,063. [doi:10.1016/j.rce.2015.04.010]

Reviews

1 Loricera J, Blanco R, Hernández JL, Carril JM, Martínez-Rodríguez I, Canga A, Peiró E, Alonso-Gutiérrez J, Calvo-Río V, Ortiz-Sanjuán F, Mata C, Pina T, González-Vela MC, Martínez-Amador N, González-Gay MA.

Non-infectious aortitis: a report of 32 cases from a single tertiary centre in a 4-year period and literature review.

Clin Exp Rheumatol. 2015;33:19-31.F.I.:2,724.

2 Arnaiz-García AM, Arnaiz-García ME, Arnaiz J.

Management of furuncle, furunculosis and anthrax.

Med Clin (Barc). 2015;144:376-378.F.I.:1,417. [doi:10.1016/j.medcli.2014.10.023]

Letters

1 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. 1;F.I.:0,000. [doi:10.1136/jnnp-2015-310601]

Doctoral Thesis

• Ana Canga Villegas.

Ligamento redondo de la cadera: estudio anatómico, radiológico, funcional y molecular.

Director/es: Juan Antonio García-Porrero Pérez, Juan Antonio Montero Simón. UNIVERSIDAD DE CANTABRIA.

• Juan Crespo Del Pozo.

Diagnóstico y estadiaje del cáncer rectal: influencia de los cambios posteriores a quimio y radioterapia en la valoración mediante RM de la fascia mesorrectal.

Director/a: Daniel Casanova Rituerto. UNIVERSIDAD DE CANTABRIA.

• Alfonso Fernando Corrales Martínez.

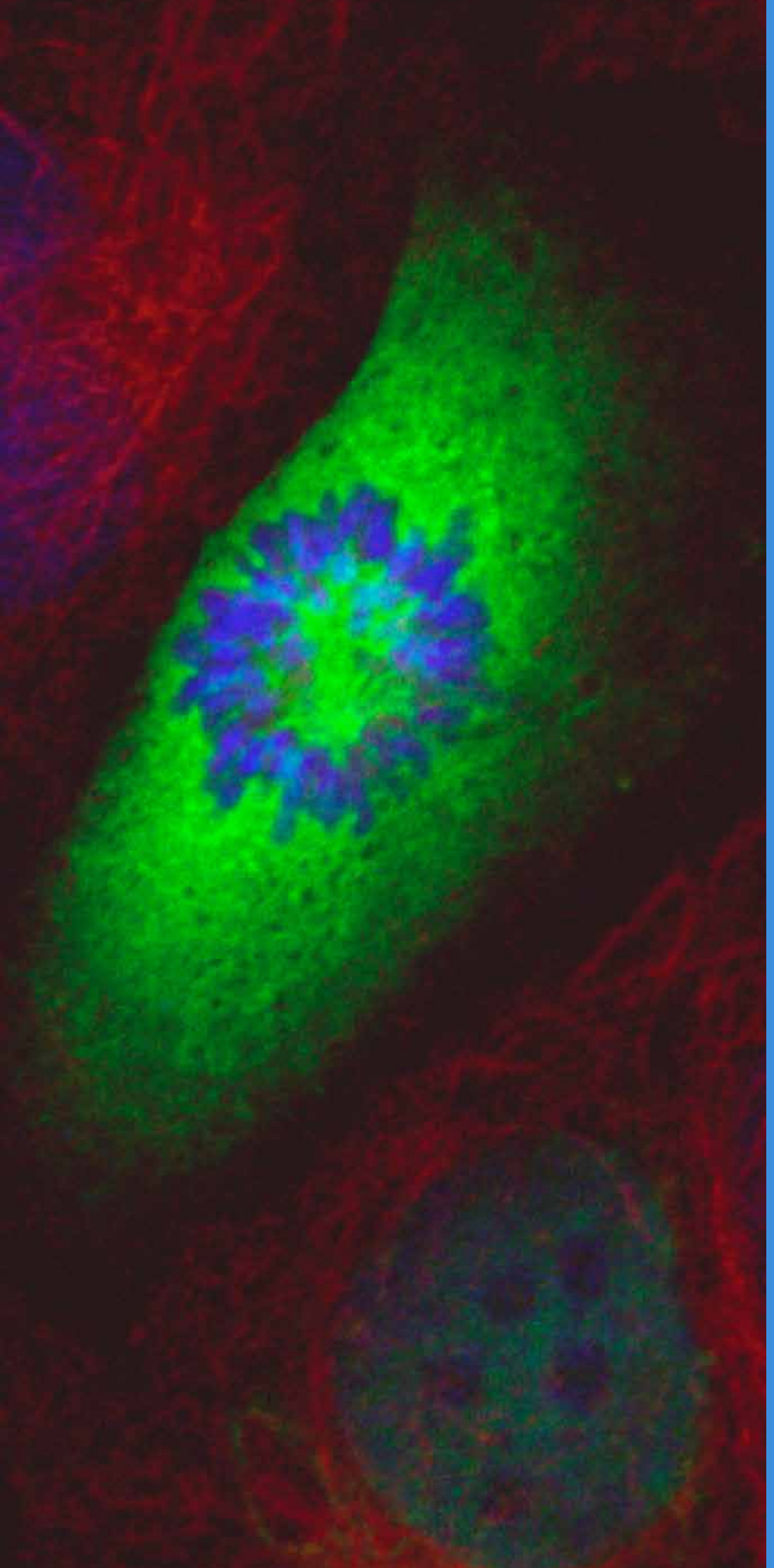
Evaluación del riesgo cardiovascular en pacientes con artritis reumatoide.

Director/es: Javier Llorca Díaz, José Antonio Parra Blanco, Miguel Ángel González-Gay Mantecón. UNIVERSIDAD DE CANTABRIA.

• Roberto Zarrabeitia Puente.

Epidemiología de la telangiectasia hemorrágica hereditaria en España: experiencia de la unidad especializada del Hospital Sierrallana (2003-2013).

Director/es: José Antonio Parra Blanco, María Del Carmen Fariñas Álvarez. UNIVERSIDAD DE CANTABRIA.



2015
Activity report

Valdecilla
Instituto de Investigación Sanitaria
IDIVAL

Infection and Immunity Area

Consolidated Groups

- Immunopathology of Rheumatic Diseases.
- Clinical and Molecular Microbiology.
- Genetic epidemiology and atherosclerosis in systemic inflammatory diseases

Clinical Groups

- Pathogenic Epidemiology and Mechanisms of Infectious Diseases

Emerging Groups

- Genomics, Proteomics and Vaccines

Immunopathology of Rheumatic Diseases

Consolidated Group

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Iglesias Lozano, Marcos (UC)
Postigo Fernández, Jorge (UC)
Ruiz Jimeno, Teresa (H. Sierrallana)
Villa Blanco, Ignacio (H. Sierrallana)

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Cobo Rosado, Natalia (UC)
Vega Miranda, Yordana (UC)

Predoctoral
Álvarez Sáiz De La Maza, Pilar (UC)
Augustín Rodríguez, Juan Jesús (UC)

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.

-Jaime Calvo coordinates the following clinical research lines:

- Impact of gender on prognosis of rheumatoid arthritis, with particular emphasis on quality of life.
- Influence of treatment with TNF inhibitors in the oxidative phenotype of HDL cholesterol and its influence on their anti-atherogenic capacity in patients with rheumatoid arthritis.
- Lipoprotein profiles and HDL phenotypes in patients with systemic lupus 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.

FUNDING

Merino Pérez, Jesús. Estudio del papel antiinflamatorio de la apolipoproteina E (APOE) en autoinmunidad. SAF2012/34059. Ministerio de Ciencia e Innovación.Duración: 2013-2015.

PUBLICATIONS

IMPACT FACTOR 34,272

Original articles

1 Iglesias-Ara A, Zenarruzabeitia O, Buelta L, Merino J, Zubiaga AM.
E2F1 and E2F2 prevent replicative stress and subsequent p53-dependent organ involution.
Cell Death Differ. 2015;22:1577-1589.F.I.:8,184. [doi:10.1038/cdd.2015.4]

2 Fernández-Nebro A, Rúa-Figueroa Í, López-Longo FJ, Galindo-Izquierdo M, Calvo-Alén J, Olivé-Marqués A, Ordóñez-Cañizares C, Martín-Martínez MA, Blanco R, Melero-González R, Ibáñez-Rúan J, Bernal-Vidal JA, Tomero-Muriel E, Uriarte-Isacelaya E, Horcada-Rubio L, Freire-González M, Narváez J, Boteanu AL, Santos-Soler G, Andreu JL, Pego-Reigosa JM.
Cardiovascular Events in Systemic Lupus Erythematosus A Nationwide Study in Spain From the RELESSER Registry.
Medicine (Baltimore). 2015;94:F.I.:5,723. [doi:10.1097/MD.0000000000001183]

3 Rúa-Figueroa Í, Richi P, López-Longo FJ, Galindo M, Calvo-Alén J, Olivé-Marqués A, Loza-Santamaría E, Vicente SP, Erausquin C, Tomero E, Horcada L, Uriarte E, Sánchez-Atrio A, Rosas J, Montilla C, Fernández-Nebro A, Rodríguez-Gómez M, Vela P, Blanco R, Freire M, Silva L, Díez-Álvarez E, Ibáñez-Barceló M, Zea A, Narváez J, Martínez-Taboada V, Marenco JL, de Castro MF, Fernández-Berrizbeitia O, ..., Pego-Reigosa JM.
Comprehensive Description of Clinical Characteristics of a Large Systemic Lupus Erythematosus Cohort from the Spanish Rheumatology Society Lupus Registry (RELESSER) With Emphasis on Complete Versus Incomplete Lupus Differences.
Medicine (Baltimore). 2015;94:F.I.:5,723. [doi:10.1097/MD.0000000000000267]

4 Inês L, Silva C, Galindo M, López-Longo FJ, Terroso G, Romão VC, Rúa-Figueroa I, Santos MJ, Pego-Reigosa JM, Nero P, Cerqueira M, Duarte C, Miranda LC, Bernardes M, Gonçalves MJ, Mouriño-Rodriguez C, Araújo F, Raposo A, Barcelos A, Couto M, Abreu P, Otón-Sanchez T, Macieira C, Ramos F, Branco JC, Silva JA, Canhão H, Calvo-Alén J.
Classification of Systemic Lupus Erythematosus: Systemic Lupus International Collaborating Clinics Versus American College of Rheumatology Criteria. A Comparative Study of 2,055 Patients From a Real-Life, International Systemic Lupus Erythematosus Cohort.
Arthritis Care Res (Hoboken). 2015;67:1180-1185.F.I.:4,713. [doi:10.1002/acr.22539]

5 Loricera J, Blanco R, Hernández JL, Castañeda S, Mera A, Pérez-Pampín E, Peiró E, Humbría A, Calvo-Alén J, Aurrecoechea E, Narváez J, Sánchez-Andrade A, Vela P, Díez E, Mata C, Lluch P, Moll C, Hernández I, Calvo-Río V, Ortiz-Sanjuán F, González-Vela C, Pina T, González-Gay MÁ.
Tocilizumab in giant cell arteritis: Multicenter open-label study of 22 patients.
Semin Arthritis Rheum. 2015;44:717-723.F.I.:3,925. [doi:10.1016/j.semarthrit.2014.12.005]

6 Rosal-Vela A, García-Rodríguez S, Postigo J, Iglesias M, Longobardo V, Lario A, Merino J, Merino R, Zubiaur M, Sancho J.
Distinct serum proteome profiles associated with collagen-induced arthritis and complete Freund's adjuvant-induced inflammation in CD38(-/-) mice: The discriminative power of protein species or proteoforms.
Proteomics. 2015;15:3382-3393.F.I.:3,807. [doi:10.1002/pmic.201400536]

7 Pego-Reigosa JM, Rúa-Figueroa Í, López-Longo FJ, Galindo-Izquierdo M, Calvo-Alén J, Olivé-Marqués A, Del Campo V, García-Yébenes MJ, Loza-Santamaría E, Blanco R, Melero-González R, Vela-Casasempere P, Otón-Sánchez T, Tomero-Muriel E, Uriarte-Isacelaya E, Fito-Manteca MC, Freire-González M, Narváez J, Fernández-Nebro A, Zea-Mendoza A, Carlos Rosas J.
Analysis of disease activity and response to treatment in a large Spanish cohort of patients with systemic lupus erythematosus.
Lupus. 2015;24:720-729.F.I.:2,197. [doi:10.1177/0961203314563818]

Clinical and Molecular Microbiology

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Ramos Vivas, José (IDIVAL)

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Fernández Torres, Marina (HUMV)
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Lázaro Díez, María (IDIVAL)
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Roiz Mesones, M. Pía (HUMV)
Ruiz de Alegría Puig, Carlos (HUMV)
Ruiz del Castillo, Belén (IDIVAL)
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González Gutiérrez, Sheila (IDIVAL)
Lecea Cuello, Mª Jesús (IDIVAL)

Research lines

1. Antimicrobial resistance in gram-negative bacteria of medical interest.

Antimicrobial resistance is a current major health problem. A large proportion of the research activities in our group is related to the study of genetic and biochemical aspects of the mechanisms of resistance to antimicrobial agents (with emphasis on beta-lactams, quinolones and aminoglycosides) in gram-negative bacteria of medical importance. We consider both Enterobacteria (Escherichia coli, Klebsiella pneumoniae, Enterobacter spp., etc.) and non-fermenters (Pseudomonas aeruginosa, Actinetobacter baumannii, Stenotromophomonas maltophilia, Burkholderia cepacia complex, among others). Within this problem, we are particularly focused on multiresistance and low-level resistance. The clinical importance of multiresistant bacteria is capital, as there are quite few new agents under development aimed to fight against these pathogens.

Our group is contributing to the "Resistance Program" of the Spanish network for research on infection diseases (Red Española de Investigación en Patología Infecciosa, REIPI, http://reipi.org/) supported by the Institute of Health Carlos III (ISCIII). This network has developed and is developing different multicenter studies on clinical and microbiological aspects of infections caused by resistant bacteria of clinical relevance, a major problem in many Spanish hospitals. Our collaboration on the study of the molecular bases of resistance has allowed obtaining new information on infections caused by Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii. Our group is also participating in another REIPI research program related to infections in transplanted patients.

Our objectives include characterization of genes and mobile elements (plasmids, transposons, integrons, gene cassettes, etc.) involved in antimicrobial resistance. Our studies have contributed to the discovery of new beta-lactamases (i.e., the new oxacillinase OXA-207 in Acinetobacter pittii -a microorganism related to A. baumannii, which is also important as a nosocomial pathogen).

Beta-lactams continue to be very frequently prescribed antibacterials. Among them, carbapenems (very broad-spectrum beta-lactams) are often considered the preferred therapeutic option against infections caused by different resistant gram-negative pathogens. Unfortunately, acquired resistance to carbapenems has been well documented, and is increasingly recognized among different gram-negative species. This is due very frequently to the production of enzymes (carbapenemases) hydrolyzing these agents. We are applying phenotypic and genotypic methods for study and characterization of carbapenem-resistance caused by metallo-beta-lactamases (MBL; including IMP-, VIM-, SPM- and NDM-types), or serine beta-lactamases of Ambler classes A and D. We are also interested in the characterization of these enzymes in environmental organisms, such as Pseudomonas putida and other taxonomically-related species such as P. monteilii, which represent reservoirs of multiresistance genes (including genes coding for MBL). We have reported nosocomial infections caused by strains of the later organisms producing the VIM-2 MBL in severely ill/immunocompromised patients.

Fluoroquinolones are broad-spectrum antimicrobial agents. They are clinically useful for treating infections caused by (among others) gram-positive and gram-negative organisms. Because they are synthetic compounds, it was thought that transferable resistance was extremely unlike, as there are (presumably) not environmental producer organisms, which could represent a source of resistance genes. However, multiple variants of qnr (quinolone resistance) genes have been identified worldwide in a great variety of bacteria (particularly in gram-negative organisms). We were involved in the discovery of qnr genes, and the group is still active in the analysis of these genes and others causing plasmid-mediated quinolone resistance.

The study of aminoglycoside-resistance in gram-negative bacteria (both Enterobacteria and non-fermenters) is another objective of our group. We are particularly interested in (1) aminoglycoside-modifying enzymes [N-acetyltransferases (AAC), O-phosphotransferases (APH) and O-nucleotidyltransferases (ANT)] which interferes with the ability of the corresponding substrate to interact with the ribosome, impairing its activity, and (2) ARN 16S methyl-transferases, which cause methylation at certain positions of the ribosome and cause high-level resistance to many clinically used aminoglycosides. Genes coding for these enzymes are frequently included in plasmid, which favors their dissemination among different bacterial hosts.

An additional objective for us is the evaluation of the role of active efflux pumps in the intrinsic resistance of gram-negative bacteria to clinically relevant antimicrobial agents (including beta-lactams, quinolones, aminoglycosides and other families). Similarly, the group has great experience on the study of the importance of porins of enterobacteria (mainly K. pneumoniae, E. coli, Enterobacter spp.) in low-level resistance and in the evaluation of the regulation of the gene coding for the OprD porin of P. aeruginosa, involved in carbapenem resistance.

Finally, in the context of the previously detailed information on mechanisms of antimicrobial resistance, we are also considering:

* Analysis of the relationship between antimicrobial resistance and virulence.

* Study of the molecular epidemiology of resistant bacteria, in particular on the problem of multiresistance in nosocomial infections.

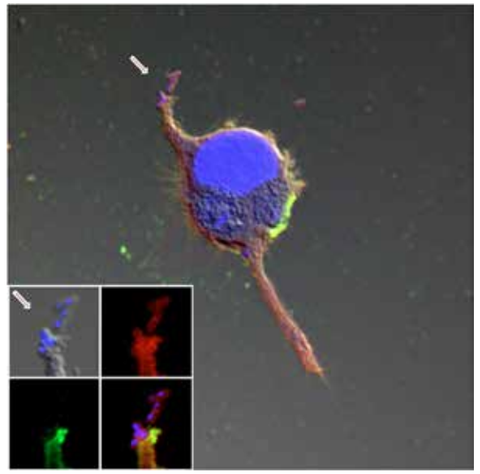
* Implementation of massive sequencing technology for a better understanding of both resistance and virulence.

2. Mechanisms of pathogenicity in gram-negative bacteria of medical interest.

We are interested in deciphering the molecular mechanisms implicated in the infections caused by Pseudomonas aeruginosa and Burkholderia cepacia. These bacteria are able to release huge quantities of hydrolytic enzymes inside host cells by means of complex secretion systems (TSS) partially inserted into the bacterial membrane.
One of these systems is the type VI secretion system (T6SS), first identified in 2006. The T6SS is a one step mechanism that is used widely throughout gram-negative bacterial species in injecting effector proteins and virulence factors from across the cytoplasm of a bacterial cell into a target cell (both bacterial and eukaryotic cells).
Protein secretion is a key issue in bacterial pathogenesis and many of the proteins secreted by the currently known T6SS are also implicated in bacterial adherence and invasion, as well as growth and intracellular survival inside macrophages.
We focus on new T6SS effector proteins of P. aeruginosa and several species of the B. cepacia complex. On the other hand, it is well known that the T6SS of P. aeruginosa is also implicated in biofilm formation and antimicrobial resistance. A biofilm can be defined as a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface. Growth in biofilms enhances the survival of bacterial populations in hospital environments and during host infections (i.e., in the presence of antibiotics), increasing the probability of causing nosocomial infections. Our group is also implicated in the discovery and characterization of quorum sensing regulators that may play a role in biofilm formation and dispersion. We use genomic and transcriptomic tools to understand the molecular determinants that contribute to the virulence and antimicrobial resistance in these pathogens.

3. Host-Pathogen Interactions.

Acinetobacter spp. have become major pathogens in hospital-associated infections, especially in critical care settings such as intensive care units (ICUs). They can survive in the hospital environment for long periods and have a remarkable propensity to develop resistance to multiple classes of antibiotics. This antibiotic resistance trend is a serious concern given the prospect of a further reduction in therapeutic options for infections by these multi-drug-resistant bacteria. While the epidemiology and antibiotic resistance of the species A. baumannii have been extensively studied, the molecular and genetic basis of A. baumannii, A. nosocomialis and A. pittii virulence remains poorly understood, and there is still lack of knowledge in host cell response to these bacteria. Answering the need for studies of the mechanisms involved in the antimicrobials and host-pathogen (H-P) relationship, we seek to develop a multi-disciplinary research on host-pathogen interactions in these clinically relevant Acinetobacter species by using cell sorting, advanced microscopy, qPCR arrays, and, more recently, next generation sequencing.



Our main objectives are:

1) To develop new tools for the study of host-pathogen interactions in Acinetobacter.

2) To study the impact of different antibiotics at subMICs on Acinetobacter species, biofilms, and on relevant host-pathogen interactions in vitro.

3) To unravel the dynamics and roles of vesicle-like droplets produced by Acinetobacter species on biofilms and during host-pathogen interactions.

4) To perform a detailed analysis of the immune responses of human immune and non-immune cells against Acinetobacter strains with different phenotypes.

4. Antimicrobial Resistance mechanisms in gran-positive bacteria.

We currently face multiresistant infectious disease organisms that are difficult and, sometimes, impossible to treat successfully. Multiresistance or multiple drug resistance (MDR) is often associated with mobile genetic elements implicated in horizontal gene transfer. This occurs both in gram-negative and gram-positive bacteria.
For gram-positive bacteria, we focus our activity on basic plasmid biology as well as in factors that allow the appearance and spread of multidrug resistant bacteria. Our model is Enterococcus, mainly E. faecalis and E. faecium. The most common nosocomial infections produced by these organisms are urinary tract infections, endocarditis and bacteriemia. We study horizontal gene transfer (conjugation) of diverse mobile genetic elements such as the sex pheromone plasmids (present in 95% of clinical isolates of E. faecalis associated with hospital outbreaks with a transference rate near 100%). Also, we are studying the mechanisms of gene expression regulation (activation or repression) in these sex pheromone plasmids, as the mechanisms that coordinately regulate basic plasmid processes (replication, partition, conjugation).
We also perform the identification and characterization of plasmids present in multirresistant E. faecium clinical isolates carrying vancomycin resistant genes (and also resistance to aminoglycosides and macrolides).

5. Infections caused by coryneform bacteria.

We focus on antimicrobial resistance in several species of corynebacteria. These bacteria are widely distributed in nature, and are found in the soil, water and on the skin of humans and animals.
Several species cause disease in humans. The most important is C. diphteriae, but C. amycolatum, C. urealyticum, C. jeikeium and C. striatum are also occasionally cultured from clinical samples. In the last years, we have studied several aspects related to coryneform bacteria: antimicrobial resistance mechanisms, their spread and their interactions with the host.

6. Diagnostic Methodology and Epidemiology

Our team is also implicated in the development and application of new diagnostic methods in clinical microbiology, using genomic and proteomic techniques and nanotechnology.
Molecular infectious disease testing has become an outstanding arm of our Service of Microbiology, including sequencing or direct detection of genes related to microbial identification and resistance mechanisms.
For over 100 years, infectious diseases agents have been identified after they were growth in culture and their phenotypic traits were considered. In the molecular era, there is an opportunity to detect pathogens more rapidly and accurately based on their genetic signatures. Molecular methods, essentially those based upon the polymerase chain reaction (PCR), have become an indispensable tool in the diagnosis of infectious diseases. Over the past decade, there has been an explosion in the use of molecular tests to diagnose and manage infectious diseases. As a result, the Clinical Microbiology laboratory of the HUMV offers a growing and consolidated number of nucleic acid amplification tests (NAATs) for detection and identification of bacterial, viral and fungal pathogens. A good example is the expertise we have acquired in gene amplification and sequencing of the 16S rDNA gene and of genes related with antibiotic resistance.
We understand that, given the complexity of the microbial world and the increasing sophistication of NAATs, the expertise is required not only for assay development and performance, but also for consultation. This rational improves patient care, reduces antibiotic usage, enhances test utilization, and increases laboratory and hospital efficiency.
Recently, we have also incorporated an automated mass spectrometry microbial identification system that uses Matrix Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF) technology and a comprehensive database of clinically relevant species for results in minutes.
On the other side, it is sometimes important to analyze multiple isolates within a given species to determine whether they represent a single strain or multiple strains. The process of differentiating strains based on their phenotypic and genotypic differences is known as 'typing'. Genotyping methods involve the study of the microbial DNA. The develo-

pment of molecular genotyping methods has revolutionized the possibility for classification of microorganisms at the sub-species level, which is crucial for deciding the molecular relatedness of isolates for epidemiological studies. In this aim, new PCR-based typing methods in the last years have supposed an important advance in determining the molecular epidemiology of microorganisms. Major advantages of these methods are flexibility, technical simplicity and high discriminatory power. Although most of these PCR-based typing methods are less time-consuming and easy to perform and of interpretation, other approaches, however, depending on the species studied, are required to the study of the clonal relationship among microbial isolates. These include the pulsed-field gel electrophoresis (PFGE, the current gold standard method for typing most bacterium and fungi), multilocus sequence typing (MLST), and variable number tandem repeat typing (VNRT).
These typing methods are also performed in different specific areas of our Clinical laboratory, and are useful in hospital infection control, epidemiological studies, and understanding the pathogenesis of infection.

7. in vitro activity of new antimicrobials

Different organizations, including the WHO, have alerted that antimicrobial resistance is one of the main health problems in the world. One of the high-priority strategies to confront this menace is the development of new antimicrobial agents. Our group participates in multicenter studies pursuing the evaluation of new antimicrobials, challenging a wide collection of bacterial clinical isolates.
Also, we participate in the evaluation of reference automated methods that incorporate new antimicrobial agents. In the last years, we have studied the activity of daptomycin, linezolid, chelocardin and ceftaroline, collaborating to establish MIC breakpoints and the interpretation of in vitro susceptibility tests to define clinical categories.
Our group has also collaborated in the study of the variables that influence the in vitro activity of ceftaroline, a new broad-spectrum cephalosporin with activity against methicillin resistant Staphylococcus aureus (MRSA).
We have also contributed to the in vitro study of a new antimicrobial, chelocardin, whose synthesis has been improved by genetic engineering and with promising in vitro activity against several species of multidrug resistant bacteria. These studies have been developed in collaboration with members of the University of Cantabria and the University of Lubljana (Slovenia).

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Genetic epidemiology and atherosclerosis in systemic inflammatory diseases

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Research lines

1. Epidemiology of autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis, giant cell arteritis, systemic sclerosis and systemic lupus erythematosus).

Study on the incidence, clinical spectrum and outcome of these conditions in Spanish individuals.

2. Cardiovascular disease risk and cardiovascular events in autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, psoriasis, ankylosing spondylitis, giant cell arteritis, systemic sclerosis, systemic lupus erythematosus).

Study on the implication of genetic factors, mediators of inflammation and biomarkers of endothelial cell activation in the risk of cardiovascular disease and cardiovascular events in inflammatory arthritis and connective-tissue diseases. This study encompasses the assessment of genetic polymorphism and laboratory, clinical and imaging data associated to inflammation, which could be involved in the development of cardiovascular disease and premature mortality in patients with these conditions.

3. Genetics of autoimmune diseases (rheumatoid arthritis, psoriatic arthritis, spondyloarthropathies and vasculitis [giant cell arteritis and Henoch-Schönlein purpura]) in Spanish individuals.

This study is focused on the study of the pattern of genetic susceptibility to chronic inflammatory rheumatic diseases and systemic vascultides..

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Doctoral Thesis

• Alfonso Fernando Corrales Martínez.
Evaluación del riesgo cardiovascular en pacientes con artritis reumatoide.
Director/es: Javier Llorca Díaz, José Antonio Parra Blanco, Miguel Ángel González-Gay Mantecón. UNIVERSIDAD DE CANTABRIA.

• Trinitario Pina Murcia.
Modificación de marcadores de riesgo cardiovascular en psoriasis tras terapia anti-tnf.
Director/es: Javier Llorca Díaz, Miguel Ángel González-Gay Mantecón. UNIVERSIDAD DE CANTABRIA.

• Javier Loricera García.
Caracterización clínica de las vasculitis cutáneas.
Director/es: Miguel Ángel González-Gay Mantecón, María Del Carmen González Vela, Ricardo Blanco Alonso. UNIVERSIDAD DE CANTABRIA.

• Vanesa Calvo Del Río.
Caracterización clínica de la púrpura de Schoenlein-Henoch.
Director/es: Miguel Ángel González-Gay Mantecón, María Del Carmen González Vela, Ricardo Blanco Alonso. UNIVERSIDAD DE CANTABRIA.

• Natalia Palmou Fontana.
Efecto de los farmacos inhibidores del factor de necrosis tumoral alfa sobre la calidad de vida en pacientes con espondilitis anquilosante y artritis psoriasica.
Director/es: Joaquín Jordán Bueso, Julián Eloy Solís García del Pozo. UNIVERSIDAD DE CASTILLA-LA MANCHA.

• Sara Díaz Angulo.
Estudio de la prevalencia de disfunción y autoinmuniad tiroidea en pacientes con urticaria crónica, vitíligo y alopecia areata en la comunidad autónoma de Cantabria.
Director/es: Marcos Antonio González López, Marcos López Hoyos. UNIVERSIDAD DE CANTABRIA.

• Vicente González Quintanilla.
Función endotelial en esclerosis múltiple y migraña. Estudio transversal con comparador activo.
Director/es: Agustín Oterino Durán, Jesús Castillo Obeso. UNIVERSIDAD DE CANTABRIA.

Genomics, Proteomics and Vaccines

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Emerging Group

Research lines

1.1. 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 adyuvants 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 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.

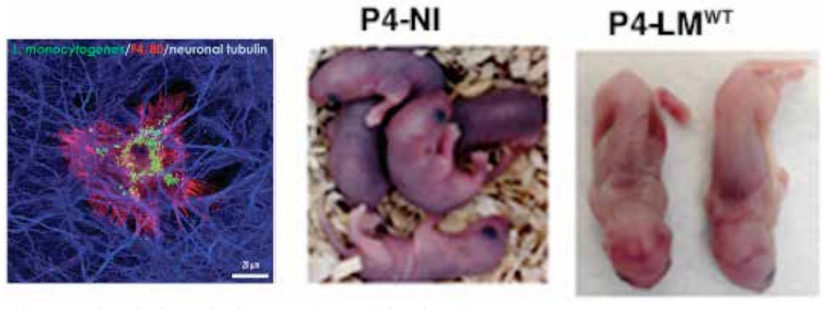

Figura 1.- Listeriosis cerebral neonatal y papel de microglía

3. Listeria based dendritic vaccines loaded with peptides against melanoma

(PI: Dr. C. Alvarez Dominguez and Co-PI: Dra. S. Yañez Diaz/Grants: SAF2009-08695 y SAF2012-34203 and Approved Clinical Study: CEIC-Acta 30/2012). A Listeria based dendritic vaccine loaded with LLO91-99 peptide as anti-adhesive therapy for melanoma using murine models (col. Dr. J. Gomez-Roman, Pathologic Anatomy Dpt-HUMV) and prepare an anti-melanoma vaccine in collaboration with Oncology and Dermatology Departments at HUMV (cols. Dr. H. Fernandez-Llaca and Dra. A. Garcia) and Human Melanoma Group at Basque Country University-UPV (col. Dr. D. Boyano Lopez).

4. Listeria based Nanovaccines and their applications

(PI: Dr. C. Alvarez Dominguez, Dr. S. Gomez Salces and Dr. S. Yañez Diaz/Grants: SAF2012-34203, and Approved Clinical Study: CEIC-Acta 1/2016-2015.177). In this study we used as vaccine vectors gold glyconanoparticles (AuGNP) of 2 nm size conjugated to Listeria peptides, LLO91-99 and GAPDH1-22. The group of CIC-biomaGUNE collaborates with our group preparing AuGNP (cols. Dr. M. Marradi, Dr. I. Garcia and Dr. S. Penades). We have performed studies with a prophylactic experimental nanovaccine against listeriosis and a non-pathogenic tuberculosis model. The efficiency of nanovaccine is based in their targeting to dendritic cells, lack of toxicity, biocompatibility and induction of a cytotoxic cellular immune response. Other applications with these Nanovaccines and their modifications are tumor therapies.

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

FUNDING

Álvarez Domínguez, Carmen. Estudio de diferentes vectores vacuna basados en Listeria monocytogenes frente a distintos procesos inflamatorios, infecciosos y cancerosos. SAF2012-34203. Ministerio de Ciencia e Innovación. Duración: 2013-2015.

PUBLICATIONS

IMPACT FACTOR 11,044

Original articles

1 Rodríguez-Del Río E, Marradi M, Calderón-González R, Frande-Cabanes E, Penadés S, Petrovsky N, Álvarez-Domínguez C.
A gold glyco-nanoparticle carrying a listeriolysin O peptide and formulated with Advax (TM) delta inulin adjuvant induces robust T-cell protection against listeria infection.
Vaccine. 2015;33:1465-1473.F.I.:3,624. [doi:10.1016/j.vaccine.2015.01.062]

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A Novel Therapy for Melanoma Developed in Mice: Transformation of Melanoma into Dendritic Cells with Listeria monocytogenes.
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Novel nanoparticle vaccines for Listeriosis.
Hum Vaccin Immunother. 2015;11:2501-2503.F.I.:2,366. [doi:10.1080/21645515.2015.1063756]

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Pathogenic Epidemiology and Mechanisms of Infectious Diseases

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Puente de Mateo, Elena (IDIVAL)

Clinical Group

Research lines

1. Infections in Solid Organ transplants.

Our group is consolidating this line of research initiated in 2012 by participating in projects from the Network for Pathology Research in Infectious Diseases (REIPI); and by obtaining a multicentre FIS Project in 2013 in which our centre is the main researcher on the Colonisation and Infection by multiresistant enterobacteria in Liver and Kidney transplantation.

In addition, regarding lung transplantation, we are conducting a study on biomarkers in the immediate postoperative period. This research also began in 2012 in order to evaluate the usefulness of different biological markers in the early detection of infectious complications in patients undergoing lung transplantation. The result was an international publication in 2012 and several conference papers. Currently, we are heading a multicentre national study which has been funded by the Mutua Madrileña Foundation.

2. The study of Prosthetic Joint Infections.

This line was started in 2009 by introducing the study of the role of sonication in the diagnosis of prosthetic joint infections. The positive results have led to incorporating the technique into the routine of the Microbiology laboratory. A study is currently being conducted on Systemic Markers in the diagnosis of infection in a Prosthetic Knee or Hip such as IL-6, Procalcitonin, VEGF (Vascular Endothelial Growth Factor) or NETs (Neutrophils extracellular traps) prior to removal of the implant is currently.

3. Optimisation of an antimicrobial treatment and the impact of antibiotic consumption in cost savings and bacterial resistance.

The excessive and inappropriate use of antimicrobials is currently a major 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 standardised use of antimicrobials by an individual with experience in this area, the result of a multidisciplinary collaboration.
At present, the accumulated experience of the Marqués de Valdecilla Hospital is being transferred to other hospitals by training professionals from other hospitals working in Infectious Diseases.

4. Epidemiology of Infective Endocarditis.

With the creation of the Group for Assistance in Managing Endocarditis in Spain (GAMES) in 2007 which is made up of 35 hospitals, a better understanding of this disease is being achieved that is affecting both a better diagnostic and therapeutic approach. Our unit heads one of the seven nodes that have been divided up among the participating Hospitals and has contributed to the formation of the HUMV multidisciplinary endocarditis group in which the Cardiology, Cardiovascular Surgery, Home Hospitalisation and Microbiology Departments also participate. It has currently published various articles and also has many under review.

5. Research in the area of sepsis.

Focused on the global study of sepsis, both from the viewpoint of predisposing factors to its development, and the optimisation of its treatment and the identification of prognostic factors. This line of research began in 2005 and remains active, with its results including a FIS grant, PUBLICATIONS in national and international first quartile journals and papers at national and international conferences.

6. Genetic variations linked to increased susceptibility to Tuberculosis Infection/Disease.

Studies on alleles and haplotypes of the main histocompatibility complex among healthy controls, individuals with latent tuberculosis and individuals with active pulmonary tuberculosis among the population of Cantabria is one of the lines started in 2008 and which continues to be active.

7. Study of new molecular and imaging techniques for estimating cardiovascular risk in patients with HIV infection.

A research project evaluating the importance of new diagnostic techniques for subclinical cardiovascular disease in patients with HIV infection for the early detection of atherosclerosis.

FUNDING

Fariñas Álvarez, Carmen. Colonización intestinal por enterobacterias multirresistentes en pacientes con trasplante renal y hepático: estudio multicéntrico de cohortes y ensayo clínico aleatorizado, controlado y abierto. PI13/01191. Ministerio de Ciencia e Innovación. Duración: 2014-2017.

PUBLICATIONS

IMPACT FACTOR 70,380

Original articles

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Tuberculosis Prophylaxis With Levofloxacin in Liver Transplant Patients Is Associated With a High Incidence of Tenosynovitis: Safety Analysis of a Multicenter Randomized Trial.

Clin Infect Dis. 2015;60:1642-1649.F.I.:8,886. [doi:10.1093/cid/civ156]

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Clin Microbiol Infect. 2015;21:F.I.:5,768. [doi:10.1016/j.cmi.2015.07.014]

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Current Epidemiology and Outcome of Infective Endocarditis A Multicenter, Prospective, Cohort Study. Medicine (Baltimore). 2015;94:F.I.:5,723.

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Factors Related to the Development of CMV-Specific CD8+T cell Response in CMV-Seropositive Solid Organ Transplant Candidates.

Am J Transplant. 2015;15:715-722.F.I.:5,683. [doi:10.1111/ajt.13012]

5 Ruiz-Morales J, Ivanova-Georgieva R, Fernández-Hidalgo N, García-Cabrera E, Miró JM, Muñoz P, Almirante B, Plata-Ciézar A, González-Ramallo V, Gálvez-Acebal J, Fariñas MC, Bravo-Ferrer JM, Goenaga-Sánchez MA, Hidalgo-Tenorio C, Goikoetxea-Agirre J, de Alarcón-González A, Spanish Collaboration on Endocarditis Group-Grupo de Apoyo al Manejo de la Endoc.

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J Infect. 2015;71:627-641.F.I.:4,441. [doi:10.1016/j.jinf.2015.09.005]

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