# University Institute of Biomedical Technologies

# Scientific Report 2019

# University of La Laguna

***Editing**: Eladio Frías (Project Manager, Bioavance Foundation) and Diego Álvarez de la Rosa (Director, ITB)*

*The Bioavance Foundation has participated in the drafting of this annual report.*

# INDEX

# PRESENTATION

The University Institute of Biomedical Technologies at the University of La Laguna (ITB, www.institutotecnologiasbiomedicas.com) is an interdisciplinary centre dedicated to basic and applied Biomedical Research. Created in 2006 by The The Canary Islands Government, through the impetus of the University of La Laguna (ULL), it integrates the activity of professors and researchers from different areas and departments at the ULL, as well as researchers at associated university hospitals (University Hospital of The Canary Islands -Hospital Universitario de Canarias-, HUC; and Nª Sª de Candelaria University Hospital -Hospital Universitario Nª Sª de Candelaria-, HUNSC) and at other research centres in The Canary Islands.

# VISION AND MISSION

The vision of the ITB is to promote biomedical research of excellence, with a translational foundation, aimed at addressing the social biomedical needs of our region. The mission of the ITB can be summarised as the use of interdisciplinary approaches in basic medicine, medicinal chemistry and clinical research that will facilitate the transfer of biomedical knowledge and technology to patients and industry.

From the outset, one of ITB's main goals has been to establish synergies between the existing biomedical research entities in the region, in order to consolidate a competitive and sustainable biomedical research space in the Canary Islands. Among other initiatives, the ITB has coordinated and designed strategic pluriannual plans and funding applications to national and European calls. Many of these have been designed in conjunction with other regional institutes and research centres in order to establish common research projects, and to establish significant scientific infrastructures and equipment.

# SPECIFIC OBJETIVES

Contingent on the development of biomedical research of excellence, with a translational outlook and focused on the regional biomedical needs, the specific objectives at the ITB are:

1. To design and execute research projects in the research areas established within the Institute, implementing a management system and a research agenda fully orientated towards producing results.
2. To organise, design and participate in interdisciplinary master's and doctorate programs, staff training courses, seminars, congresses and other training activities at the institute.
3. To establish effective mechanisms aimed at attracting high calibre research, technical and administrative staff, and in retaining and enhancing the institute's human resources.
4. To establish collaborations with other research centres.

5. To collaborate with the manufacturing sector in the development of biotechnological applications to address specific problems, driving innovation, knowledge and technology transfer.
6. To implement healthcare innovations designed from the outcomes of clinical and epidemiological research.
7. To communicate and disseminate biomedical information and advances, helping create a favourable culture for scientific progress.

# HISTORY

From the outset, the ITB has worked to consolidate itself as a centre of excellence, following an objective based strategic plan devised in conjunction with external scientific committees, and with the firm support of the different vice-chancellors at the ULL and of the distinct local institutions (e.g., the Regional Government of Tenerife).

After the initial phases in which the project was drafted and approved by the governing body of the ULL, The Canary Islands Government created the Institute by decree (11/2006, BOC 20th February, 2006). The first Internal Regulations (IR) of the ITB were approved by the Governing Board of the ULL in 2010, with an update being approved on the 21st of December 2018, aimed to adapt the structure and governing bodies more closely to the institute's objectives.

# MILESTONES REACHED

The following milestones were reached by the ITB during 2019:

- The construction of the Institute's facilities has been completed and now, the procurement and installation of the laboratory fittings, and the distribution and furnishing of the management, innovation and transfer facilities, is underway.
- The recruitment of new PhD students, postdoctoral researchers, technicians and technology transfer personnel, is underway through national funding programmes, such as the "Juan de la Cierva" programme and calls for funding associated to the projects funding the activities of the institute's research groups, as well as the "Agustín de Betancourt" programme that is financed by the Regional Government of Tenerife, with a focus on transferability.
- The renewal of the external Scientific Advisory Board, made up of internationally reknown experts, and the visit of this committee to carry out the first evaluation, whose report was delivered in November 2019.
- The dissemination of health knowledge and increased visibility at a regional, national and international level, through the organisation of scientific events in collaboration with associated international centres.
- The organisation of local events and workshops for scientific dissemination: science fairs, meetings with patient associations, etc.

- Active involvement of most of the Institute's groups and research lines in the Biomedicine and Biotechnology Master's degree and Doctorate in Health Sciences programs at the ULL.

# GOVERNING BODIES

The boards that govern and oversee the activities and functioning of the ITB include the Institute's General Council, the Executive Commission and the Management team. The General Council is made up of the Principal Investigators (PIs) at the institute, as well as a balanced representation of the contracted and staff researchers, the researchers in training, administrative and technical personnel.

### Management team

Director:

- Between September 1, 2018 and December 21, 2019, Dr. Tomás González Hernández (Professor of Anatomy, Department of Basic Medical Sciences, ULL) served as the interim director until he was replaced on December 22, 2019 by the new director, Dr. Diego Álvarez de la Rosa (Lecturer of Physiology, Department of Basic Medical Sciences, ULL) following the elections held at the Institute on December 12, 2019.

Vice-Director:

- Dr. Tomás González Hernández (Professor of Anatomy, Department of Basic Medical Sciences, ULL) was replaced by Dr. Carmen María Évora García (Professor in Pharmacy and Pharmaceutical Technology, Department of Chemical Engineering and Pharmaceutical Technology, ULL).

Secretary:

- Dr. Ángel Acebes Vindel (Contracted Lecturer, PhD Physiology, Department of Basic Medical Sciences, ULL).

### Executive committee

The Executive Committee is made up of the Director, who acts as the chairman, the Vice-Director, Secretary and the heads of the different research programmes:

- Head of the Programme of Genetic & Rare Diseases:
  - Carlos Flores Infante (University Hospital Nª Sª de la Candelaria).
- Head of the Programme of Chronic & Age-Related Diseases :
  - Esteban Porrini (Department of Internal Medicine, Dermatology and Psychiatry, ULL).
- Head of the Programme of Drug Development & Target Identification:
  - Carmen María Évora García (Department of Chemical Engineering and Pharmaceutical Technology, ULL).
- Heads of the Neurobiology & Brain-Related Diseases Program:
  - Abraham Acevedo Arozena (University Hospital of The Canary Islands);
  - Niels Janssen (Department of Cognitive, Social and Organisational Psychology, ULL).

# MEMBERS OF THE INSTITUTE

The current investigators at the ITB and the other collaborating researchers belong to different departments of the ULL and associated hospitals:

### ULL Departments

- Biochemistry, Microbiology, Cell Biology and Genetics
- Basic Medical Sciences
- Industrial Engineering
- Chemical Engineering and Pharmaceutical Technology
- Internal Medicine, Dermatology and Psychiatry
- Clinical Psychology, Psychobiology and Methodology
- Cognitive, Social and Organisational Psychology
- Organic Chemistry

### University Hospitals

- University Hospital of The Canary Islands (HUC)
- University Hospital Nª Sª de la Candelaria (HUNSC)

### Principal Investigators and Heads of Research Lines

- Ángel Acebes Vindel, PhD (Programme of Neurobiology & Brain-Related Diseases – Contracted Lecturer, PhD in Physiology, Basic Medical Sciences Department, ULL)
- Abraham Acevedo Arozena, PhD (Programme of Neurobiology & Brain-Related Diseases – "Miguel Servet" Investigator of the SCS/FIISC; HUC Research Unit)
- Diego Álvarez de la Rosa, PhD (Programme of Chronic & Age-Related Diseases – Lecturer of Physiology, Basic Medical Sciences Department, ULL)
- Julio T. Ávila Marrero (Programme of Genetic & Rare Diseases – Professor of Biochemistry and Molecular Biology; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Horacio Barber Friend, PhD (Programme of Neurobiology & Brain-Related Diseases – Lecturer of Basic Psychology, Department of Cognitive, Social and Organisational Psychology, ULL)
- Markus Conrad, PhD (Programme of Neurobiology & Brain-Related Diseases – "Ramón y Cajal" Investigator, Department of Cognitive, Social and Organisational Psychology, ULL)
- Araceli Delgado Hernández, PhD (Programme of Drug Development & Target Identification – Lecturer of Pharmaceutical Technology, Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- José Federico Díaz González, MD, PhD (Programme of Chronic & Age-Related Diseases – Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of the Rheumatology Service, HUC)
- Carmen María Évora García, PhD (Programme of Drug Development & Target Identification – Professor of Pharmaceutical Technology, Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- Carlos Flores Infante, PhD (Programme of Genetic & Rare Diseases – Contracted Investigator SCS/FIISC; HUNSC Research Unit; Genomics Unit at the Technological and Renewable Energy Institute)

- Raimundo Freire Betancor, PhD (Programme of Genetic & Rare Diseases – Contracted Investigator SCS/FUNCANIS, HUC Research Unit)
- Antonio Z. Gimeno García, MD, PhD (Programme of Chronic & Age-Related Diseases – Associate Professor; Department of Internal Medicine, Dermatology and Psychiatry, ULL – Attending Physician in Gastroenterology, HUC)
- Teresa Giráldez Fernández, PhD (Programme of Neurobiology & Brain-Related Diseases – Professor of Physiology, Basic Medical Sciences Department, ULL)
- José Fco. Gómez González, PhD (Programme of Neurobiology & Brain-Related Diseases – Contracted Lecturer, Department of Industrial Engineering, ULL)
- Tomás González Hernández, MD, PhD (Programme of Neurobiology & Brain-Related Diseases – Professor of Human Anatomy, Basic Medical Sciences Department, ULL)
- José Luis González Mora (Programme of Neurobiology & Brain-Related Diseases – Professor of Physiology; Basic Medical Sciences Department, ULL)
- Manuel Hernández-Guerra de Aguilar, MD, PhD (Programme of Chronic & Age-Related Diseases – Lecturer, Department of Internal Medicine, Dermatology and Psychiatry, ULL –Head of the Gastroenterology Service since December 2019, HUC)
- Niels Janssen, PhD (Programme of Neurobiology & Brain-Related Diseases – Contracted Lecturer PhD in Basic Psychology, Department of Cognitive, Social and Organisational Psychology, ULL)
- Félix M. Machín Concepción, PhD (Programme of Genetic & Rare Diseases – Contracted Investigator SCS/FIICS, Research Unit HUNSC)
- Pablo Martín Vasallo (Programme of Genetic & Rare Diseases – Professor of Biochemistry and Molecular Biology, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Juan Francisco Navarro González, MD, PhD (Programme of Chronic & Age-Related Diseases – Head of Service of the Research Unit, HUNSC)
- José Manuel Padrón (Programme of Drug Development & Target Identification – University Lecturer; Department of Organic Chemistry, ULL)
- Ernesto Pereda de Pablo, PhD (Programme of Neurobiology & Brain-Related Diseases – Professor of Electrical Engineering; Department of Industrial Engineering, ULL).
- María del Mar del Pino Yanes, PhD (Programme of Genetic & Rare Diseases – "Ramón y Cajal" Investigator, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Esteban Porrini, MD, PhD (Programme of Chronic & Age-Related Diseases – Investigator "Ramón y Cajal"; Department of Internal Medicine, Dermatology and Psychiatry, ULL)
- Enrique Quintero Carrión, MD, PhD (Programme of Chronic & Age-Related Diseases – Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of the Gastroenterology Service until December 2019, HUC)
- Eduardo Salido Ruiz, MD, PhD (Programme of Genetic & Rare Diseases – Professor of Pathological Anatomy, Basic Medical Sciences Department, ULL; Head of Pathological Anatomy Service HUC)
- Veronique Smits, PhD (Programme of Genetic & Rare Diseases – Contracted Investigator SCS/FIISC, Research Unit, HUC)
- Néstor Torres Darias, PhD (Programme of Drug Development & Target Identification – Professor of Biochemistry and Molecular Biology, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Armando Torres Ramírez, MD, PhD (Programme of Chronic & Age-Related Diseases – Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of the Nephrology Service, HUC)

### Research Staff - doctors, postdoctoral and contract researchers

- Domingo Afonso Oramas, PhD (Programme of Neurobiology & Brain-Related Diseases– Contracted Lecturer Doctor, Basic Medical Sciences Department, ULL)
- Pedro Barroso Chinea, PhD (Programme of Neurobiology & Brain-Related Diseases – Lecturer Doctor, Department of Basic Medical Sciences, ULL)
- David Bartolomé Martín, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, Contracted by ERC project, ULL)
- Alejandro Cerrada de Dueñas, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, contracted by ERC project, ULL; until September 2019)
- Laura Ciuffreda, PhD (Programme of Genetic & Rare Diseases Postdoctoral researcher, SCS/FIISC, Research Unit, HUNSC)
- Julien Dampuré, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- Ignacio de La Cruz Muros, PhD (Programme of Neurobiology & Brain-Related Diseases – Contracted Lecturer, Department of Basic Medical Sciences, ULL)
- Patricia Díaz Rodríguez, PhD (Programme of Drug Development & Target Identification - Lecturer, Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- Miguel X. Fernandes (Programme of Drug Development & Target Identification – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- David Gillespie, PhD (Programme of Genetic & Rare Diseases - Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- Ricardo Gómez García, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, contracted by ERC project, ULL)
- Daniel V. Guebel, PhD (Programme of Drug Development & Target Identification – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- Juan A. Hernández Cabrera, PhD (Programme of Neurobiology & Brain-Related Diseases – Lecturer of Basic Psychology, Department of Clinical Psychology, Psychobiology and Methodology, ULL)
- Guadalberto Hernández Hernández, MD, PhD (Programme of Chronic & Age-Related Diseases – Professor of Physiology; Department of Basic Medical Sciences, ULL)
- Aravind Kshatri, PhD (Programme of Neurobiology & Brain-Related Diseases – "Juan de la Cierva" Postdoctoral researcher, Department of Basic Medical Sciences, ULL)
- Diego Luis-Ravelo Salazar, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- Laura E. Maglio, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, contracted by ERC project, ULL)
- Itahisa Marcelino Rodríguez, PhD (Programme of Genetic & Rare Diseases – Postdoctoral researcher, SCS/FIISC, Research Unit, HUNSC)
- Cristina Martín Higueras, PhD (Programme of Chronic & Age-Related Diseases – "Juan de la Cierva" Postdoctoral researcher since 01/02/2020, Department of Basic Medical Sciences, ULL)

- Cristián D. Modroño Pascual, PhD (Programme of Neurobiology & Brain-Related Diseases – Assistant Lecturer; Department of Basic Medical Sciences, ULL)
- Edgar Pérez Herrero, PhD (Programme of Drug Development & Target Identification – Assistant Lecturer, Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- Elena Quintana, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, contract ACIISI, until July 2019, ULL)
- Ricardo Reyes Rodríguez, PhD Programme of Drug Development & Target Identification – Assistant Lecturer; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Belinda Rivero Pérez, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher; "Agustín de Betancourt" programme, ULL)
- Carmen Laura Sayas Casanova, PhD (Programme of Neurobiology & Brain-Related Diseases – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)
- Silvia Velázquez García, PhD (Programme of Chronic & Age-Related Diseases – Postdoctoral researcher, "Agustín de Betancourt" programme, ULL)

PhD students, collaborating researchers, administrative and technical staff will be listed in their respective research groups.

# SCIENTIFIC ADVISORY BOARD

In accordance with the current Internal Regulations, the Scientific Advisory Board (SAB) is composed of at least three internationally reknown scientists, experts in Biomedicine, with no direct relationship with the ULL or with other higher education or research centres in the Canary Islands. The current composition of the SAB, which was renewed at the end of 2018, is:

- Manuel Carreiras Valiña (Director of the Basque Centre of Cognition, Brain and Language, San Sebastián)
- Brian Harvey (Professor Emeritus of the Department of Molecular Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland)
- Mads Hornum (Professor and Clinical Investigator in Nephrology, Copenhagen University, Denmark)
- Juan Carlos Izpisúa Belmonte (Professor at Salk Institute of Biological Studies, La Jolla, California, USA)
- María Isabel Loza García (Professor of Pharmaceutical Technology, University of Santiago de Compostela)
- Elisa Martí Gorostiza (Research Professor at the Molecular Biology Institute in Barcelona, CSIC, Barcelona)

This committee conducted an evaluation visit between the 29$^{th}$ and 31$^{st}$ October, 2019, during which the SAB attended presentations by the coordinators of each of the ITB programs, and from selected principal investigators. The SAB visited the new ITB building and had the opportunity to meet with PhD students and postdoctoral researchers at the Institute. Finally, the SAB held evaluation sessions

behind closed doors and submitted a final report to the management team with recommendations for the Institute's strategic plan as indicated below. The SAB highlighted the achievements of the ITB in recent years, with a special mention of the new interactions established between basic research and clinical groups, and the Institute's success in attracting funding and international collaborations.

# STRATEGIC PLAN

Between October 29th and 31st, 2019, the ITB was visited by its scientific advisory committee (see above), who made a series of recommendations regarding the institute's strategic plan, which together with the strategic analysis carried out by the management team, resulted in the formulation of the following short- and medium-term objectives:

- Setting up of the new building's facilities (management spaces, common service laboratories and animal facility). It is foreseen that the common management and service areas will be functioning during the first half of 2020. The ITB plans to participate in competitive calls for scientific infrastructure funding at the Regional and National level for the equipment required to set up the animal facility.
- Re-evaluation of the structure of the ITB's research programs to adapt them to the current situation of the Institute and to favour the synergies between research groups.
- Maintenance of the requirements to access or keep the PI category and implement measures to recruit new group leaders.
- Support for funding applications by each group and coordination of applications promoting the Institute's activities and services, including applications to fund infrastructures or for accreditation as a Centre of Excellence.
- Promote translational research based on synergies between basic and clinical research groups, and on relationships established with companies in the relevant technological sectors.
- Strengthen national and international collaborations through the organisation of visits and seminars of researchers from other centres.
- Active participation in the training of researchers by supporting the ULL's Biomedicine and Health Sciences Master's and Doctorate programs, promoting interactions between PhD students and ITB's postdoctoral researchers through joint scientific sessions, and by establishing mechanisms to support the recruitment and scientific development of researchers.
- Dissemination of health and biomedical knowledge through the organisation of local outreach events and interactions with patient associations.
- Strengthen interactions with the Bioavance Foundation of the Regional Government of Tenerife to achieve the aforementioned objectives.

# PROGRAMMES, GROUPS AND RESEARCH LINES

The research groups at the ITB are comprised of teaching and research staff who come together to study specific research lines of interest. It is understood that the members of a group collaborate effectively, participating in common projects, as witnessed by the record of joint publications of sufficient quality and volume to satisfy the demands of the Executive Commission. Every research group must maintain a project that receives significant external funding, led by a researcher with a clear trajectory in the particular area of research, although emerging groups applying for public competitive calls for the first time may be considered as special cases. Following the strategic analyses of the past few years, the activities at the ITB were recently restructured into four research programmes (see below), with a view to applying for status as a "María de Maeztu" Unit of Excellence in the 2019 call.

In addition, the Institute also integrates research groups that work in complementary areas and that have the potential to collaborate in developing research lines, or that provide services to members of the Institute, such as laboratories and associated units from the Biomedical Innovation Platform.

In the description of each group, all the members considered formal members of the Institute are listed, including PIs, Associated Researchers and researchers in trainning. Each group also includes external collaborators and assistant researchers who are not formal members of the Institute.

## 1.- GENETIC & RARE DISEASES

This programme has been designed based on the history and geographical circumstances of the Canary Islands. The current genome of the Canarian population is inherited from the aboriginal people of North Africa and from the European population since the 15th century, making it a unique worldwide genome. In addition, there are a number of pathologies seen in the islands that exhibit a genetic component influenced by the insular concept, due to a founder effect and the lack of infrastructures that in the past favored endogamy. The research groups involved in this programme focus on studying the molecular bases of cancer and rare metabolic diseases. Cancer research is aimed at prevention, diagnosis, the identification of the biological causes and the development of effective treatments, with the ultimate goal that this serious health problem should become a chronic condition as opposed to a fatal one. On the other hand, although individual rare diseases affect only a limited fraction of the population (less than 2,000 people in Europe), the number of different diseases is very high (more than 5,000) and the total number of patients exceeds 30 million in the European Union. This arm of the programme, pursues medium and long-term goals, such as the development of personalised medicines and a reinforcement of the collaborations with industry.

### *Checkpoint response to DNA damage and human diseases*

**Principal Investigator:**

- Veronique Smits, PhD (Contracted investigator SCS/FIISC, HUC Research Unit)

**Postdoctoral Researchers:**

- David Gillespie, PhD (Contracted investigator, Agustín de Betancourt programme, ULL)

**PhD students and trainees:**

- Ignacio Alonso de Vega (Health Sciences Doctoral Programme, The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)
- Yeray Hernández Reyes (Health Sciences Doctoral Programme, The Canary Islands Health Research Foundation, FIISC. Project SAF2016-80626-R)

**Technical and administrative staff:**

- Cristina Paz Cabrera

**Research Lines:**

We study the cellular mechanisms of the response to DNA damage, specifically post-translational modifications like the ubiquitination, SUMOylation and acetylation of proteins in these pathways, and of histones. These modifications seem to be crucial to relax the chromatin structure, and to allow DNA damage to be identified and repaired by DNA damage response proteins. We intend to identify new proteins regulating chromatin modifying enzymes in order to reveal their role in the cellular response to DNA damage.

**Funded projects:**

- Regulation of the cellular response to DNA damage and replicative stress: molecular mechanisms and the role of tumorigeneses (SAF2016-80626-R "Regulación de la respuesta celular al daño del DNA y al estrés replicativo: Mecanismos moleculares e implicaciones en tumorigenesis"). PIs: Raimundo Freire, Veronique Smits. Ministry of Economy and Competitiveness MINECO (2017-2019, 229,900 €).
- Dynamics and chromosome stability (BFU2017-90889-REDT "Networks of Excellence"). PI: Veronique Smits (Network coordinator: Felix Prado). Ministry of Economy and Competitiveness, MINECO (2018-2019, 10,000 €)
- Study of the sensitivity of ovarian cancer cells to chemotherapy by the control of PHF2 (PIFUN 16/18). IP: Veronique Smits. FIISC (2019-2020, 19,314.34 €)
- In vivo screening based on the reversal of cellular phenotypes to find new drugs that inhibit the Chk1 kinase involved in cancer. Project Agustín de Betancourt "Rastreo in vivo basado en la reversión de fenotipo celular para encontrar nuevos fármacos inhibidores contra la quinasa Chk1 implicada en cáncer". PI: David Gillespie; Supervisor: Eduardo Salido Ruiz. Tenerife regional Government (2017-2021, 160,000 €).

**Publications in 2019:**

- Alonso-de Vega I, Paz-Cabrera MC, Wiegant WW, Checa-Rodríguez C, Huertas P, Freire R, van Attikum H, Smits VAJ. PHF2 regulates homology-directed DNA repair by controlling the resection of DNA double strand breaks. BioRxiv, 2019. doi:10.1101/782490
- Sinha D, Nag P, Nanayakkara D, Duijf PHG, Burgess A, Raninga P, Smits VAJ, Bain AL, Subramanian G, Wall M, Finnie JW, Kalimutho M, Khanna KK. Cep55 overexpression promotes genomic instability and tumorigenesis in mice. BioRxiv, 2019. doi: 10.1101/780775
- Smits VAJ, Cabrera E, Freire R, Gillespie DA (2019). Claspin - checkpoint adaptor and DNA replication factor. FEBS J. 2019 Feb;286(3):441-455. doi: 10.1111/febs.14594

**Other selected publications from the last 10 years:**

- Smits VAJ, Gillespie DA. DNA damage control: regulation and functions of checkpoint kinase 1. FEBS J. 2015 Oct;282(19):3681-92. doi: 10.1111/febs.13387
- Delgado-Díaz MR, Martín Y, Berg A, Freire R, Smits VAJ. Dub3 controls DNA damage signalling by direct deubiquitination of H2AX. Mol. Oncol. 2014 Jul;8(5):884-93. doi: 10.1016/j.molonc.2014.03.003
- Alonso de Vega I, Martín Y, Smits VAJ. USP7 controls Chk1 protein stability by direct deubiquitination. Cell Cycle. 2014;13(24):3921-6. doi: 10.4161/15384101.2014.973324
- Warmerdam DO, Brinkman EK, Marteijn JA, Medema RH, Kanaar R, Smits VA. UV-induced G2 checkpoint depends on p38 MAPK and minimal activation of ATR-Chk1 pathway. J Cell Science. 2013 May 1;126(Pt 9):1923-30. doi: 10.1242/jcs.118265
- Smits VAJ. EDD induces cell cycle arrest by increasing p53 levels. Cell Cycle. 2012 Feb 15;11(4):715-20. doi: 10.4161/cc.11.4.19154

### *Replicative stress and tumorigenesis*

**Principal Investigator:**

- Raimundo Freire Betancor, PhD (Contracted investigator SCS/FIISC; HUC Research Unit)

**Postdoctoral Collaborating Researchers:**

- Elisa Cabrera Afonso, PhD (Postdoctoral researcher, Fundación Bioavance contract: Study of genomic instability involving ubiquitin hydrolases – “Estudios de inestabilidad genómica que implican ubiquitin hidrolasas”)
- Juan Ramón Hernández Fernaud, PhD (Postdoctoral researcher, contracted Asociación Española Contra el Cancer/FIISC: Role of UPR in DNA replication control – “Papel de la UPR en el control de la replicación del ADN”)

**PhD students and trainees:**

- Esperanza Hernández Carralero (Role of Ubiquitin hydrolases in DNA replication control – Papel de Ubiquitin hidrolasas en el control de la replicación del ADN. The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)

**Research Lines:**

- Study of new proteins controlling replication in human cells
- Study of the expression of replication proteins in cancer
- Determination of ubiquitin hydrolases involved in genomic instability in human cells

**Funded projects:**

- Regulation of the cellular response to DNA damage and replicative stress: the molecular mechanism and implications for tumorigenesis (SAF2016-80626-R "Regulación de la respuesta celular al daño del DNA y al estrés replicativo: Mecanismos moleculares e implicaciones en tumorigenesis"). PIs: Raimundo Freire, Veronique Smits. Ministry of Economy and Competitiveness, MINECO (2017-2019; extended until October 2020, 229,900 €).

**Publications 2019:**

- Smits VAJ, Cabrera E, Freire R, Gillespie DA. Claspin - checkpoint adaptor and DNA replication factor. FEBS J. 2019 Feb;286(3):441-455. doi: 10.1111/febs.14594
- Herruzo E, Santos B, Freire R, Carballo JA, San-Segundo PA. Characterization of Pch2 localization determinants reveals a nucleolar-independent role in the meiotic recombination checkpoint. Chromosoma. 2019 Sep;128(3):297-316. doi:10.1007/s00412-019-00696-7
- Cabrera E, Raninga P, Khanna K, Freire R. GSK3-β stimulates claspin degradation via β-TrCP ubiquitin ligase and alters cancer cell survival. Cancers (Basel). 2019 Jul 29;11(8). doi: 10.3390/cancers11081073
- Singh AN, Oehler J, Torrecilla I, Kilgas S, Li S, Vaz B, Guérillon C, Fielden J, Hernandez-Carralero E, Cabrera E, Tullis ID, Meerang M, Barber PR, Freire R, Parsons J, Vojnovic B, Kiltie AE, Mailand N, Ramadan K. The p97-Ataxin 3 complex regulates homeostasis of the DNA damage response E3 ubiquitin ligase RNF8. EMBO J. 2019 Oct 4;38(21):e102361. doi: 10.15252/embj.2019102361.

**Other Selected publications from the last 10 years:**

- Cabrera E, Hernández-Pérez S, Koundrioukoff S, Debatisse M, Kim D, Smolka MB, Freire R, Gillespie DA. PERK inhibits DNA replication during the Unfolded Protein Response via Claspin and Chk1. Oncogene. 2017 Feb 2;36(5):678-686. doi:10.1038/onc.2016.239
- Hernandez-Perez S, Cabrera E, Salido E, Lim M, Reid L, Lakhani SR, Khanna KK, Saunus JM, Freire R. DUB3 and USP7 de-ubquitination enzymes control replication inhibitor Geminin: molecular characterization and association with breast cancer. Oncogene. 2017 Aug 17;36(33):4802-4809. doi: 10.1038/onc.2017.21
- Hernandez-Perez S, Cabrera E, Amoedo H, Rodriguez-Acebes S, Koundrioukoff S, Debatisse M, Mendez J, Freire R. USP37 deubiquitinates Cdt1 and contributes to regulate DNA replication. Mol Oncol. 2016 Oct;10(8):1196-206. doi:10.1016/j.molonc.2016.05.008
- Martín Y, Cabrera E, Amoedo H, Hernández-Pérez S, Domínguez-Kelly R, Freire R. USP29 controls the stability of checkpoint adaptor Claspin by deubiquitination. Oncogene. 2015 Feb 19;34(8):1058-63. doi: 10.1038/onc.2014.38
- Domínguez-Kelly R, Martín Y, Koundrioukoff S, Tanenbaum ME, Smits VA, Medema RH, Debatisse M, Freire R. Wee1 controls genomic stability during replication by regulating the Mus81-Eme1 endonuclease. J Cell Biol. 2011 Aug 22;194(4):567-79. doi: 10.1083/jcb.201101047

## *Genomics and Health*

**Principal Investigator:**

- María del Mar del Pino Yanes, PhD ("Ramón y Cajal" Investigator; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)

**Postdoctoral Collaborating Researchers:**

- Luis Fabián Lorenzo Díaz, PhD (Assistant Lecturer; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)

**PhD students and trainees:**

- Natalia Hernández Pacheco (PhD student, contracted PFIS FI16/00136, Institute of Health Carlos III)
- Antonio Espuela Ortiz (PhD student; 2019_10, SAF201783417R, MINECO)
- Esther Herrera Luis (PhD student; FPI PRE2018-083837, Ministry of Science, Innovation and Universities, Project SAF2017-83417-R)
- Javier Pérez García (PhD student; 2019_34, Project SAF201783417R, MINECO)

**Research Lines:**

The Genomics and Health group aims to determine the genetic basis of asthma, focusing on acute complications and the response to available treatments. As such, and in addition to genome wide studies, we analyse genetic ancestry to perform admixture mapping and multiomic data integration. We also carry out asthma microbiome studies using massive sequencing techniques.

**Funded projects:**

- Search for genetic markers of asthma exacerbation: a genome-wide association study and respiratory micobiome analysis (SAF2017-83417-R "Búsqueda de marcadores genéticos relacionados con las exacerbaciones del asma: estudio de asociación genómico y análisis del microbioma respiratorio"). PIs: María del Mar del Pino Yanes and Fabián Lorenzo Díaz. Ministry of Economy, Industry and Competitiveness, MINECO (2018-2020, 171,094 €).
- SysPharmPediA: Systems pharmacology approach to difficult-to-treat paediatric asthma (AC15/00015). PI: María del Mar del Pino Yanes. Institute of Health Carlos III (20162019, 91.113 €).
- National Programme "Ramón y Cajal". Programme for the employment of doctors by Research and Development centres (RYC-2015-17205. "Precision medicine of allergic diseases: genetic susceptibility and treatment response"). PI: María del Mar del Pino Yanes. MINECO (Ramón y Cajal Sub-programme 2016-2021, 268,600 € -salary, 5 years + 40,000 €, research project)

**Publications 2019:**

- Daya M, Rafaels N, Brunetti TM, Chavan S, Levin AM, Shetty A, Gignoux CR, Boorgula MP, Wojcik G, Campbell M, Vergara C, Torgerson DG, Ortega VE, Doumatey A, Johnston HR, Acevedo N, Araujo MI, Avila PC, Belbin G, Bleecker E, Bustamante C, Caraballo L, Cruz A, Dunston GM, Eng C, Faruque MU, Ferguson TS, Figueiredo C, Ford JG, Gan W, Gourraud PA, Hansel NN, Hernandez RD, Herrera-Paz EF, Jiménez S, Kenny EE, Knight-Madden J, Kumar R, Lange LA, Lange EM, Lizee A,

Maul P, Maul T, Mayorga A, Meyers D, Nicolae DL, O'Connor TD, Oliveira RR, Olopade CO, Olopade O, Qin ZS, Rotimi C, Vince N, Watson H, Wilks RJ, Wilson JG, Salzberg S, Ober C, Burchard EG, Williams LK, Beaty TH, Taub MA, Ruczinski I, CAAPA consortium (including Maria Pino-Yanes), Mathias RA, Barnes KC; CAAPA. Association study in African-admixed populations across the Americas recapitulates asthma risk loci in non-African populations. Nat Commun. 2019 Feb 20;10(1):880. doi: 10.1038/s41467-019-08469-7.

- Spear ML Hu D, Pino-Yanes M, Huntsman S, Eng C, Levin AM, Ortega VE, White MJ, McGarry ME, Thakur N, Galanter J, Mak ACY, Oh SS, Ampleford E, Peters SP, Davis A, Kumar R, Farber HJ, Meade K, Avila PC, Serebrisky D, Lenoir MA, Brigino- Buenaventura E, Cintron WR, Thyne SM, Rodriguez-Santana JR, Ford JG, Chapela R, Estrada AM, Sandoval K, Seibold MA, Winkler CA, Bleecker ER, Myers DA, Williams LK, Hernandez RD, Torgerson DG, Burchard EG. A genome-wide association and admixture mapping study of bronchodilator drug response in African Americans with asthma. Pharmacogenomics J. 2019 Jun;19(3):249-259. doi: 10.1038/s41397-018-0042-4
- Hernandez-Pacheco N, Farzan N, Francis B, Karimi L, Repnik K, Vijverberg SJ, Soares P, Schieck M, Gorenjak M, Forno E, Eng C, Oh SS, Pérez-Méndez L, Berce V, Tavendale R, Samedy LA, Hunstman S, Hu D, Meade K, Farber HJ, Avila PC, Serebrisky D, Thyne SM, Brigino-Buenaventura E, Rodriguez-Cintron W, Sen S, Kumar R, Lenoir M, Rodriguez-Santana JR, Celedón JC, Mukhopadhyay S, Potočnik U, Pirmohamed M, Verhamme KM, Kabesch M, Palmer CNA, Hawcutt DB, Flores C, Maitland-van der Zee AH, Burchard EG, Pino-Yanes M. Genome-wide association study of inhaled corticosteroid response in admixed children with asthma. Clin Exp Allergy. 2019 Jun;49(6):789-798. doi: 10.1111/cea.13354
- Levin AM, Gui H, Hernandez-Pacheco N, Yang M, Xiao S, Yang JJ, Hochstadt S, Barczak AJ, Eckalbar WL, Rynkowski D, Samedy LA, Kwok PY, Pino-Yanes M, Erle DJ, Lanfear DE, Burchard EG, Williams LK. Integrative approach identifies corticosteroid response variant in diverse populations with asthma. J Allergy Clin Immunol. 2019 May;143(5):1791-1802. doi: 10.1016/j.jaci.2018.09.034
- Almoguera B, Vazquez L, Mentch F, March ME, Connolly JJ, Peissig PL, Linneman JG, Plaza-Serón MDC, Pino-Yanes M, Burchard EG, Brilliant M, Sleiman P, Hakonarson H. Novel locus for atopic dermatitis in African Americans and replication in European Americans. J Allergy Clin Immunol. 2019 Mar;143(3):1229-1231. doi: 10.1016/j.jaci.2018.10.038
- Gignoux CR, Torgerson DG, Pino-Yanes M, Uricchio LH, Galanter J, Roth LA, Eng C, Hu D, Nguyen EA, Huntsman S, Mathias RA, Kumar R, Rodriguez-Santana J, Thakur N, Oh SS, McGarry M, Moreno-Estrada A, Sandoval K, Winkler CA, Seibold MA, Padhukasahasram B, Conti DV, Farber HJ, Avila P, Brigino-Buenaventura E, Lenoir M, Meade K, Serebrisky D, Borrell LN, Rodriguez-Cintron W, Thyne S, Joubert BR, Romieu I, Levin AM, Sienra-Monge JJ, Del Rio-Navarro BE, Gan W, Raby BA, Weiss ST, Bleecker E, Meyers DA, Martinez FJ, Gauderman WJ, Gilliland F, London SJ, Bustamante CD, Nicolae DL, Ober C, Sen S, Barnes K, Williams LK, Hernandez RD, Burchard EG. An admixture mapping meta-analysis implicates genetic variation at 18q21 with asthma susceptibility in Latinos. J Allergy Clin Immunol. 2019 Mar;143(3):957-969. doi: 10.1016/j.jaci.2016.08.057
- Hernandez-Pacheco N, Pino-Yanes M, Flores C. Genomic Predictors of Asthma Phenotypes and Treatment Response. Front Pediatr. 2019 Feb 5;7:6. doi: 10.3389/fped.2019.00006
- Herrera-Luis E, Hernandez-Pacheco N, Vijverberg SJ, Flores C, Pino-Yanes M. Role of genomics in asthma exacerbations. 2019 Current Opinion in Pulmonary Medicine 25(1), pp. 101-112. doi: 10.1097/MCP.0000000000000533
- Lona-Durazo F, Hernandez-Pacheco N, Fan S, Zhang T, Choi J, Kovacs MA, Loftus SK, Le P, Edwards M, Fortes-Lima CA, Eng C, Huntsman S, Hu D, Gómez-Cabezas EJ, Marín-Padrón LC, Grauholm J, Mors O, Burchard EG, Norton HL, Pavan WJ, Brown KM, Tishkoff S, Pino-Yanes M, Beleza S,

Marcheco-Teruel B, Parra EJ. Meta-analysis of GWA studies provides new insights on the genetic architecture of skin pigmentation in recently admixed populations. BMC Genet. 2019 Jul 17;20(1):59. doi: 10.1186/s12863-019-0765-5

- Espuela-Ortiz A, Lorenzo-Diaz F, Baez-Ortega A, Eng C, Hernandez-Pacheco N, Oh SS, Lenoir M, Burchard EG, Flores C, Pino-Yanes M. Bacterial salivary microbiome associates with asthma among african american children and young adults. Pediatr Pulmonol. 2019 Dec;54(12):1948-1956. doi: 10.1002/ppul.24504
- Dijk FN, Vijverberg SJ, Hernandez-Pacheco N, Repnik K, Karimi L, Mitratza M, Farzan N, Nawijn MC, Burchard EG, Engelkes M, Verhamme KM, Potočnik U, Pino-Yanes M, Postma DS, Maitland-van der Zee AH, Koppelman GH. IL1RL1 gene variations are associated with asthma exacerbations in children and adolescents using inhaled corticosteroids. Allergy. 2019 Nov 22. doi: 10.1111/all.14125. [Epub ahead of print]
- Samedy-Bates LA, Oh SS, Nuckton TJ, Elhawary JR, White M, Elliot T, Zeiger AM, Eng C, Salazar S, LeNoir MA, Meade K, Farber HJ, Serebrisky D, Brigino-Buenaventura E, Rodriguez-Cintron W, Bibbins-Domingo K, Kumar R, Thyne S, Borrell LN, Rodriguez- Santana JR, Pino-Yanes M, Burchard EG. Racial/ethnic-specific differences in the effects of inhaled corticosteroid use on bronchodilator response in patients with asthma. Clin Pharmacol Ther. 2019 Nov;106(5):1133-1140. doi: 10.1002/cpt.1555

**Other Selected publications from the last 10 years:**

- Hernandez-Pacheco N, Flores C, Alonso S, Eng C, Mak AC, Hunstman S, Hu D, White MJ, Oh SS, Meade K, Farber HJ, Avila PC, Serebrisky D, Thyne SM, Brigino-Buenaventura E, Rodriguez-Cintron W, Sen S, Kumar R, Lenoir M, Rodriguez-Santana JR, Burchard EG, Pino-Yanes M. Identification of a novel locus associated with skin colour in African-admixed populations. Sci Rep 2017;7:44548. doi: 10.1038/srep44548
- Pino-Yanes M, Thakur N, Gignoux CR, Galanter JM, Roth LA, et al. Genetic ancestry influences asthma susceptibility and lung function among Latinos. J Allergy Clin Immunol. 2015 Jan;135(1):228-35. doi: 10.1016/j.jaci.2014.07.053
- Pino-Yanes M, Gignoux CR, Galanter JM, Levin AM, Campbell CD, Eng C, Huntsman S, Nishimura KK, Gourraud PA, Mohajeri K, O'Roak BJ, Hu D, Mathias RA, Nguyen EA, Roth LA, Padhukasahasram B, Moreno-Estrada A, Sandoval K, Winkler CA, Lurmann F, Davis A, Farber HJ, Meade K, Avila PC, Serebrisky D, Chapela R, Ford JG, Lenoir MA, Thyne SM, Brigino-Buenaventura E, Borrell LN, Rodriguez-Cintron W, Sen S, Kumar R, Rodriguez-Santana JR, Bustamante CD, Martinez FD, Raby BA, Weiss ST, Nicolae DL, Ober C, Meyers DA, Bleecker ER, Mack SJ, Hernandez RD, Eichler EE, Barnes KC, Williams LK, Torgerson DG, Burchard EG. Genome-wide association study and admixture mapping reveal new loci associated with total IgE levels in Latinos. J Allergy Clin Immunol. 2015 Jun;135(6):1502-10. doi: 10.1016/j.jaci.2014.10.033
- Igartua C, Myers RA, Mathias RA, Pino-Yanes M, Eng C, Graves PE, Levin AM, Del-Rio-Navarro BE, Jackson DJ, Livne OE, Rafaels N, Edlund CK, Yang JJ, Huntsman S, Salam MT, Romieu I, Mourad R, Gern JE, Lemanske RF, Wyss A, Hoppin JA, Barnes KC, Burchard EG, Gauderman WJ, Martinez FD, Raby BA, Weiss ST, Williams LK, London SJ, Gilliland FD, Nicolae DL, Ober C. Ethnic-specific associations of rare and low-frequency DNA sequence variants with asthma. Nat Commun. 2015 Jan 16;6:5965. doi: 10.1038/ncomms6965
- Pino-Yanes M, Corrales A, Acosta-Herrera M, Pérez-Rodríguez E, Cumplido J, Campo P, Barreto-Luis A, Sánchez-García F, Felipe T, Sánchez-Machín I, Quintela I, García-Robaina JC, Villar J, Blanca

M, Carracedo A, Carrillo T, Flores C. HLA-DRB1*15:01 allele protects from asthma susceptibility. J Allergy Clin Immunol. 2014 Nov;134(5):1201-3. doi: 10.1016/j.jaci.2014.05.031

### *Genomic instability and cancer*

**Principal Investigator:**

- Félix M. Machín Concepción, PhD (Contracted Investigator SCS/FIISC, HUNSC Research Unit)

**PhD students and trainees:**

- Emiliano Matos Perdomo (PhD student, ULL)
- Laura Anaissi Afonso (PhD student, ULL. The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)
- Jessel Ayra Plasencia (PhD student, ULL)
- Silvia Santana Sosa (PhD student, ULL. The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)

**Technical and administrative staff:**

- Isabel Lorenzo Castrillejo (Laboratory technician, FP2, HUNSC)

**Research Lines:**

Genetic instability hinders the ability of cells to pass an accurate copy of their genetic information to their progeny, which leads to cancer and other degenerative diseases. Genetic instability underlies the genetic diversity present in tumours, which accounts for malignancy and resistance to treatment. DNA damage and chromosome mis-segregation during cell division are the most common causes of genetic instability, which are paradoxically also the mechanisms of action of most anti-tumour drugs used to combat cancer cells. Our research focuses on understanding these phenomena and their contribution to the complexity of cancer biology. For these studies we use model organisms like Saccharomyces cerevisiae and occasionally, cell lines like HeLa.

We are also interested in chemical compounds affecting DNA, microtubules, mitochondria, plasma membrane, topoisomerases, protein aggregation, the apoptotic pathway, etc., and their potential use as anti-tumour, antibiotic, anti-fungal and anti-parasitic therapies.

**Funded projects:**

- Characterisation of the signalling and repair of telophase DNA breaks and anaphase bridges. (BFU2017-83954-R – “Caracterización de la señalización y reparación de la rotura del ADN en telofase y en los puentes de anafase”). PI: Félix Machín. Ministry of Economy and Competitiveness, MINECO (018-2021, 170,610 €)
- Screening for natural and synthetic compounds in chemical libraries from The Canary Islands with bio-pharmacological effects combating neurodegenerative disorders (“Identificación de compuestos naturales y sintéticos presentes en las quimiotecas canarias con potencial biofarmacológico contra enfermedades neurodegenerativas”). PI: Félix Machín. The Canary Islands Agency for Research, Innovation and Information Sciences, ACIISI (2018-2020, 70,000 €)

- Screening for anti-apoptotic activities against degenerative diseases in collections of active substances of biomedical interest ("Rastreo de actividades anti-apoptóticas contra enfermedades degenerativas entre colecciones de principios activos de interés biomédico ": PIFIIS19/04). PI: Félix Machín. The Canary Islands Health Research Institute Foundation, FIISC (2020-2022; 28,162.40 €)

**Publications 2019:**


- Ayra-Plasencia J, Machín F. DNA double-strand breaks in telophase lead to coalescence between segregated sister chromatid loci. Nature Communications. 2019 Jun 28;10(1):2862. doi: 10.1038/s41467-019-10742-8
- Matos-Perdomo E, Machín F. Nucleolar and Ribosomal DNA Structure under Stress: Yeast Lessons for Aging and Cancer. Cells. 2019 Jul 26;8(8). pii: E779. doi: 10.3390/cells8080779
- Ayra-Plasencia J, Machín F. Yeast cells can partially revert chromosome segregation to repair late DNA double-strand breaks through homologous recombination. Mol Cell Oncol. 2019 Aug 6;6(5):e1648027. doi: 10.1080/23723556.2019.1648027
- Ramos-Pérez C, Dominska M, Anaissi-Afonso L, Cazorla-Rivero S, Quevedo O, Lorenzo-Castrillejo I, Petes TD, Machín F. Cytological and genetic consequences for the progeny of a mitotic catastrophe provoked by Topoisomerase II deficiency. Aging (Albany NY). 2019 Dec 8;11(23):11686-11721. doi: 10.18632/aging.102573


**Other Selected publications from the last 10 years:**


- Anaissi-Afonso L, Oramas-Royo S, Ayra-Plasencia J, Martín-Rodríguez P, García-Luis J, Lorenzo-Castrillejo I, Fernández-Pérez L, Estévez-Braun A, Machín F. Lawsone, Juglone, and β-Lapachone Derivatives with Enhanced Mitochondrial-Based Toxicity. ACS Chem Biol. 2018 Aug 17;13(8):1950-1957. doi: 10.1021/acschembio.8b00306
- Quevedo O, Ramos-Perez C, Petes TD, Machín F. The transient inactivation of the master cell cycle phosphatase Cdc14 causes genomic inestability in diploid cells of saccharamyces cerevisiae. Genetics. 2015 Jul;200(3):755-69. doi:10.1534/genetics.115.177626
- García-Luis J, Machín F. Mus81-Mms4 and Yen1 resolve a novel anaphase bridge formed by noncanonical Holliday junctions. Nat Commun. 2014 Dec 3;5:5652. doi:10.1038/ncomms6652
- Garcia-Luis J, Clemente-Blanco A, Aragon L, Machín F. Cdc14 targets the Holliday junction solvase Yen1 to the nucleus in early anaphase. Cell Cycle. 2014;13(9):1392-9. doi: 10.4161/cc.28370
- Quevedo O, Garcia-Luis J, Matos-Perdomo E, Aragon L, Machín F. Non-disjunction of a single chromosome leads to breakage and activation of DNA damage checkpoint in G2. PLoS Genet. 2012;8(2):e1002509. doi:10.1371/journal.pgen.1002509


### *Molecular pathology of rare and metabolic diseases*

**Principal Investigator:**

- Eduardo Salido Ruiz, MD, PhD (Professor of Pathological Anatomy, Department of Basic Medical Sciences, ULL; Head of Pathological Anatomy Service HUC)

**Postdoctoral researchers:**

- Cristina Martín Higueras ("Juan de la Cierva" investigator, MICINN)

**PhD students and trainees:**

- Ignacio Alonso de Vega (Studentship programme for training research personnel for PhD thesis, ACIISI)
- Isabel Betancor Fernández (PhD student, ULL)
- Celeste González García (PhD student, ULL)

**Technical and administrative staff:**

- Bárbara Rodríguez Rodríguez (CIBER of rare diseases)

**Research Lines:**

We are interested in the molecular basis of inherited metabolic disorders and orphan diseases, such as Type I Primary Hyperoxaluria. For these studies we design and develop appropriate animal models to test the potential therapeutic effects of active molecules.

**Funded projects:**

- Molecular substrate reduction therapy for primary hyperoxaluria (SAF2015-69796-C2-1-R – "Terapia molecular de reducción de substrato para la hiperoxaluria primaria"). PI: Eduardo Salido Ruiz. Ministry of Science and innovation (2016-2019, 157,300 €)
- In vivo screening based on the reversal of cellular phenotypes to find new drugs inhibiting the Chk1 kinase involved in cancer. Project Agustín de Betancourt – "Rastreo in vivo basado en la reversión de fenotipo celular para encontrar nuevos fármacos inhibidores contra la quinasa Chk1 implicada en cáncer". PI: David Gillespie, Tutor: Eduardo Salido Ruiz Tenerife Regional Government (2017-2021, 160,000 €)
- Gene editing service. "Agustín de Betancourt" Project. PI: Belinda Rivero Pérez; PI-ULL: Eduardo Salido Ruiz. Council of Tenerife (2020-2023, 160,000 €)
- Amendment NO.1 Master Consulting Agreement (Biomarin Pharmaceutical. 2017-2020, 30.000$). PI: Eduardo Salido Ruiz
- Material Transfer Agreement (Uniqure Biopharma. 2018 - present, 28,800 €). PI: Eduardo Salido Ruiz
- Material Transfer Agreement (Biomarin Pharmaceutical. 2015-2020, 55,000 €). PI: Eduardo Salido Ruiz

**Publications 2019:**


- Kukreja A, Lasaro M, Cobaugh C, Forbes C, Tang J-P, Gao X, Martin-Higueras C, Pey AL, Salido E, Sobolov S, Subramanian RR. Systemic Alanine Glyoxylate Aminotransferase mRNA Improves Glyoxylate Metabolism in a Mouse Model of Primary Hyperoxaluria Type 1. Nucleic Acid Ther. 2019 Apr;29(2):104-113. doi: 10.1089/nat.2018.0740
- Medina-Carmona E, Betancor-Fernández I, Santos J, Mesa-Torres N, Grottelli S, Batlle C, Naganathan AN, Oppici E, Cellini B, Ventura S, Salido E, Pey AL. Insight into the specificity and severity of pathogenic mechanisms associated with missense mutations through experimental

and structural perturbation analyses. Hum Mol Genet. 2019 Jan 1;28(1):1-15. doi: 10.1093/hmg/ddy323

- Medina Vega L, Hernández Nieto L, Salido Ruiz E, Álvarez-Argüelles Cabrera H, Raya Sánche JM. Comprehensive clinical, molecular and histopathological analysis of bone marrow in chronic myeloproliferative neoplasia [Análisis integrado clínico, molecular e histopatológico de la médula ósea en las neoplasias mieloproliferativas crónicas]. Rev Clin Esp. 2019 Nov;219(8):440-444. doi: 10.1016/j.rce.2018.11.012
- Garrelfs SF, Rumsby G, Peters-Sengers H, Erger F, Groothoff JW, Beck BB, Oosterveld MJS, Pelle A, Neuhaus T, Adams B, Cochat P, Salido E, Lipkin GW, Hoppe B, Hulton SA; OxalEurope Consortium. Patients with primary hyperoxaluria type 2 have significant morbidity and require careful follow-up. Kidney Int. 2019 Dec;96(6):1389-1399. Kidney Int. 2019 Dec;96(6):1389-1399. doi: 10.1016/j.kint.2019.08.018
- Martinez-Turrillas R, Rodriguez-Diaz S, Rodriguez-Marquez P, Martin-Mallo A, Salido E, Beck BB, Prosper F, Rodriguez-Madoz JR. Generation of an induced pluripotent stem cell line (CIMAi001-A) from a compound heterozygous Primary Hyperoxaluria Type I (PH1) patient carrying p.G170R and p.R122* mutations in the AGXT gene. Stem Cell Res. 2019 Dec;41:101626. doi: 10.1016/j.scr.2019.101626
- Vankova P, Salido E, Timson DJ, Man P, Pey AL. A Dynamic Core in Human NQO1 Controls the Functional and Stability Effects of Ligand Binding and Their Communication across the Enzyme Dimer. Biomolecules. 2019 Nov 12;9(11). pii: E728. doi: 10.3390/biom9110728
- Gonzalez-Sanchez L, Cobos-Fernandez MA, Lopez-Nieva P, Villa-Morales M, Stamatakis K, Cuezva JM, Marin Rubio JL, Vazquez-Dominguez I, Gonzalez-Vasconcellos I, Salido E, Llamas P, Lopez-Lorenzo JL, Santos J, Fernandez-Piqueras J. Exploiting the passenger ACO1-deficiency arising from 9p21 deletions to kill T-cell lymphoblastic neoplasia cells. Carcinogenesis. 2019 Nov 17. pii: bgz185. doi: 10.1093/carcin/bgz185. [Epub ahead of print]
- Martin-Higueras C, Ludwig-Portugall I, Hoppe B, Kurts C. Targeting kidney inflammation as a new therapy for primary hyperoxaluria? Nephrol Dial Transplant. 2019 Jun 1;34(6):908-914. doi: 10.1093/ndt/gfy239

**Other Selected publications from the last 10 years:**

- Martin-Higueras C, Luis-Lima S, Salido E. Glycolate oxidase is a safe and efficient target for substrate reduction therapy in a mouse model of Primary Hyperoxaluria Type I. Mol Ther. 2016 Apr;24(4):719-25. doi: 10.1038/mt.2015.224
- García-Gómez S, Reyes A, Martínez-Jiménez MI, Chocrón ES, Mourón S, Terrados G, Powell C, Salido E, Méndez J, Holt IJ, Blanco L. PrimPol, an archaic primase/polymerase operating in human cells. Mol Cell. 2013 Nov 21;52(4):541-53
- Salido E, Pey AL, Rodriguez R, Lorenzo V. Primary hyperoxalurias: Disorders of glyoxylate detoxification. Biochim Biophys Acta. 2012 Sep;1822(9):1453-64. doi: 10.1016/j.bbadis.2012.03.004
- Salido E, Rodriguez-Pena M, Santana A, Beattie SG, Petry H, Torres A. Phenotypic Correction of a Mouse Model for Primary Hyperoxaluria with Adenoassociated Virus Gene Transfer. Mol Ther. 2011 May;19(5):870-5. doi: 10.1038/mt.2010.270
- Wei C, El Hindi S, Li J, Fornoni A, Goes N, Sageshima J, Maiguel D, Karumanchi SA, Yap HK, Saleem M, Zhang Q, Nikolic B, Chaudhuri A, Daftarian P, Salido E, Torres A, Salifu M, Sarwal MM, Schaefer F, Morath C, Schwenger V, Zeier M, Gupta V, Roth D, Rastaldi MP, Burke G, Ruiz P, Reiser J.

Circulating urokinase receptor as a cause of focal segmental glomerulosclerosis. Nat Med. 2011 Jul 31;17(8):952-60. doi: 10.1038/nm.2411

### *Genetic variation and disease*

**Principal Investigator:**

- Carlos Flores Infante, PhD (Contracted Investigator SCS/FIISC, Research Unit HUNSC and Genomic Unit of the Technological and Renewable Energies Institute)

**Postdoctoral researchers:**

- Itahisa Marcelino Rodríguez, PhD (Postdoctoral investigator, SCS/FIISC, Research Unit HUNSC)
- Laura Ciuffreda, PhD (Postdoctoral investigator, SCS/FIISC, Research Unit HUNSC)

**External postdoctoral collaborators:**

- Rafaela González Montelongo, PhD (Junior Researcher, Genomics Division of the Technological and Renewable Energies Institute)
- Víctor García Olivares, PhD (Postdoctoral Researcher, Genomics Division of the Technological and Renewable Energies Institute)

**PhD students and trainees:**

- Beatriz Guillén Guío (The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI, The Canary Islands Government, TESIS2015010057, 2016-2019)
- Natalia Hernández Pacheco (PFIS FI16/00136, ISCIII, 2017-2020)
- Ana Díaz de Usera (FPU 16/01435, Ministry of Education, Culture and Sport, 2017-2020)
- Tamara Hernández Beeftink (PFIS FI17/00177, ISCIII, 2018-2021)
- Héctor Rodríguez Pérez (PFIS FI18/00230, ISCIII, 2019-2022)
- Alejandro Mendoza Álvarez (CajaSiete ULL, 2018-2021)
- Adrián Muñoz Barrera (Massive Genomics Data Analysis Service, CGIEU0000219140. Regional Goverment of Tenerife, Genomics Division of the Technological and Renewable Energies Institute)
- Luis Alberto Rubio Rodríguez (Massive Genomics Data Analysis Service, CGIEU0000219140. Regional Goverment of Tenerife, Genomics Division of the Technological and Renewable Energies Institute)
- David Jáspez Toledo (UDIGEN project, Spanish Ministry of Science, Innovation and Universities, RTC-2017-6471-1)
- José M. Lorenzo-Salazar (Area coordinator, Genomics Division of the Technological and Renewable Energies Institute)

**Technical and administrative staff:**

- Almudena Corrales Moreno (Technician, SCS/FIISC, Research Unit HUNSC)
- Antonio Íñigo Campos (Technician, Genomics Division of the Technological and Renewable Energies Institute)

**Research Lines:**

- Genetics underlying the development and progression of prevalent (allergies, respiratory, infectious, immunological, etc.) and non-prevalent (mainly respiratory and immunological) diseases ("Genética involucrada en el desarrollo y progresión de enfermedades prevalentes (alérgicas, respiratorias, infecciosas, inmunológicas, etc.) y no prevalentes (principalmente respiratorias e inmunológicas").
- Population dynamics, evolution and disease in The Canary Islands ("Dinámica poblacional, evolución y enfermedad en Canarias").
- Biomarkers of prognosis in critically ill patients (methylome, transcriptome, microbiome, etc.) ("Biomarcadores de pronóstico en enfermos críticos (metiloma, transcriptoma, microbioma, etc.).
- Clinical sequencing: development of bioinformatics tools and applications based on massive sequencing ("Secuenciación clínica, Desarrollo de herramientas bioinformáticas y aplicaciones basadas en secuenciación masiva").

**Funded projects:**

- Generation of a Genomic Diagnostic Unit (UDIGEN, RTC-2017-6471-1 – "Desarrollo de una Unidad de Diagnóstico Genómico"). PI: Carlos Flores. Ministry of Science, Innovation and Universities (2018-2021, 904,828.99 €).
- Multiomics identification of genetic predictors of survival in sepsis patients (PI17/00610 – "Multiómica para la identificación de predictores genéticos de supervivencia en pacientes con sepsis"). PI: Carlos Flores. Institute of Health Carlos III (2018-2020, 99,220 €).
- Pulmonary dysbiosis and early prognosis in patients with sepsis: towards a real- time assessment (PIFUN48/18). PI: Carlos Flores. The Canary Islands Health Research Institute Foundation (2019-2020, 21,863.50 €).
- Genomic ancestry in human populations of the Canary Islands: African mixture, adaptation to the environment and health implications (2018PATRI20 - "Ascendencia genómica en las poblaciones humanas de Canarias: mezcla africana, adaptación al ambiente e implicaciones en salud"). PI: Carlos Flores. CajaCanarias Foundation (2019-2022, 29,475 €).
- Facility for the Massive Analysis of Genomic Data (Tenerife Council, CGIEU0000219140). Contract: 2,700,000 € (2018-2022). PI: Carlos Flores Infante.

**Publications 2019:**


- Hernandez-Pacheco N, Farzan N, Francis B, Karimi L, Repnik K, Vijverberg SJ, Soares P, Schieck M, Gorenjak M, Forno E, Eng C, Oh SS, Pérez-Méndez L, Berce V, Tavendale R, Samedy LA, Hunstman S, Hu D, Meade K, Farber HJ, Avila PC, Serebrisky D, Thyne SM, Brigino-Buenaventura E, Rodriguez-Cintron W, Sen S, Kumar R, Lenoir M, Rodriguez-Santana JR, Celedón JC, Mukhopadhyay S, Potočnik U, Pirmohamed M, Verhamme KM, Kabesch M, Palmer CNA, Hawcutt DB, Flores C, Maitland-van der Zee AH, Burchard EG, Pino-Yanes M. Genome-wide association study of inhaled corticosteroid response in admixed children with asthma. Clin Exp Allergy. 2019 Jun;49(6):789-798. doi: 10.1111/cea.13354
- Hernandez-Pacheco N, Pino-Yanes M, Flores C. Genomic Predictors of Asthma Phenotypes and Treatment Response. Front Pediatr. 2019 Feb 5;7:6. doi: 10.3389/fped.2019.00006

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- Rodríguez-Pérez H, Hernández-Beeftink, Lorenzo-Salazar JM, Roda-García JL, Pérez-González CJ, Colebrook M, Flores C. NanoDJ: a Dockerized Jupyter notebook for interactive Oxford Nanopore MinION sequence manipulation and genome assembly. BMC Bioinformatics. 2019 May 9;20(1):234. doi: 10.1186/s12859-019-2860-z
- Perkins JR, Acosta-Herrera M, Plaza-Serón MC, Jurado-Escobar R, Doña I, García-Martín E, Isidoro-García M, Bartra J, Ribas-Perez D, Mayorga C, Torres MJ, Flores C, Cornejo-García JA. Polymorphisms in CEP68 gene associated with risk of immediate selective reactions to non-steroidal anti-inflammatory drugs. Pharmacogenomics J. 2019 Apr;19(2):191-199. doi: 10.1038/s41397-018-0038-0
- Fregel R, Ordóñez AC, Santana-Cabrera J, Cabrera VM, Velasco-Vázquez J, Alberto V, Moreno-Benítez MA, Delgado-Darias T, Rodríguez-Rodríguez A, Hernández JC, Pais J, González-Montelongo R, Lorenzo-Salazar JM, Flores C, Cruz-de-Mercadal MC, Álvarez-Rodríguez N, Shapiro B, Arnay M, Bustamante CD. Mitogenomes illuminate the origin and migration patterns of the indigenous people of the Canary Islands. PLoS One. 2019 Mar 20;14(3):e0209125. doi: 10.1371/journal.pone.0209125
- Mendoza-Alvarez A, Guillen-Guio B, Baez-Ortega A, Hernandez-Perez C, Lakhwani-Lakhwani S, Maeso MD, Lorenzo-Salazar JM, Morales M, Flores C. Whole-Exome Sequencing Identifies Somatic Mutations Associated With Mortality in Metastatic Clear Cell Kidney Carcinoma. Front Genet. 2019 May 15;10:439. doi: 10.3389/fgene.2019.00439
- Espuela-Ortiz A, Lorenzo-Diaz F, Baez-Ortega A, Eng C, Hernandez-Pacheco N, Oh SS, Lenoir M, Burchard EG, Flores C, Pino-Yanes M. Bacterial salivary microbiome associates with asthma among african american children and young adults. Pediatr Pulmonol. 2019 Dec;54(12):1948-1956. doi: 10.1002/ppul.24504
- Hernández-Beeftink T, Guillen-Guio B, Villar J, Flores C. Genomics and the acute respiratory distress syndrome: Current and future directions. Int J Mol Sci. 2019 Aug 16;20(16). pii: E4004. doi: 10.3390/ijms20164004
- Marcelino-Rodriguez I, Callero A, Mendoza-Alvarez A, Perez-Rodriguez E, Barrios-Recio J, Garcia-Robaina JC, Flores C. Bradykinin-mediated angioedema: An update of the genetic causes and the impact of genomics. Front Genet. 2019 Sep 27;10:900. doi: 10.3389/fgene.2019.00900
- Lorenzo-Salazar JM, Ma SF, Jou J, Hou PC, Guillen-Guio B, Allen RJ, Jenkins RG, Wain LV, Oldham JM, Noth I, Flores C. Novel idiopathic pulmonary fibrosis susceptibility variants revealed by deep sequencing (2019). European Respiratory Journal Open Research ERJ Open Res. 2019 Jun 10;5(2). pii: 00071-2019. doi: 10.1183/23120541.00071-2019
- Serrano-Sánchez JA, Fernández-Rodríguez MJ, Sanchis-Moysi J, Rodríguez-Pérez MDC, Marcelino-Rodríguez I, Cabrera de León A. Domain and intensity of physical activity are associated with metabolic syndrome: A population-based study. PLoS One. 2019 Jul 17;14(7):e0219798. doi: 10.1371/journal.pone.0219798
- Mate Redondo C, Rodríguez-Pérez MC, Domínguez Coello S, Pedrero García AJ, Marcelino Rodríguez I, Cuevas Fernández FJ, Almeida González D, Brito Díaz B, Rodríguez Esteban M, Cabrera de León A. Hospital Mortality in 415 798 AMI Patients: 4 Years Earlier in the Canary Islands Than in the Rest of Spain [Mortalidad hospitalaria de 415.798 pacientes con IAM: 4 años antes en Canarias que en el conjunto de España]. Rev Esp Cardiol (Engl Ed). 2019 Jun;72(6):466-472. doi:10.1016/j.rec.2018.06.023

**Other selected publications from the last 10 years:**


- Botigué LR, Henn BM, Corona E, Gignoux CR, Gravel S, Atzmon G, Burns E, Ostrer H, Flores C, Bertranpetit J, Comas D, Bustamante CD. Gene flow from North Africa contributes to differential human genetic diversity in Southern Europe. Proc Natl Acad Sci USA. 2013 Jul 16;110(29):11791-6. doi: 10.1073/pnas.1306223110
- Noth I, Zhang Y, Ma SF, Flores C, Barber M, Huang Y, Broderick SM, Wade M, Hysi P, Sciurba JD, Richards T, Juan-Guardela BM, Vij R, Han ML, Martinez FJ, Kossen K, Seiwert SD, Christie JD, Nicolae D, Kaminksi N, Garcia JGN. Genetic variants associated with idiopathic pulmonary fibrosis susceptibility and mortality: a genome-wide association study. Lancet Respiratory Medicine. 2013 Jun;1(4):309-317. doi: 10.1016/S2213-2600(13)70045-6
- Baez-Ortega A, Lorenzo-Diaz F, Hernandez M, Gonzalez-Vila CI, Roda-Garcia JL, Colebrook M, Flores C. IonGAP: Integrative bacterial genome analysis for Ion Torrent sequence data. Bioinformatics. 2015 Sep 1;31(17):2870-3. doi: 10.1093/bioinformatics/btv283
- Barreto-Luis A, Pino-Yanes M, Corrales A, Campo P, Callero A, Acosta-Herrera M, Cumplido J, Ma SF, Martinez-Tadeo J, Villar J, Garcia JGN, Carrillo T, Carracedo A, Blanca M, Flores C. Genome-wide association study in Spanish identifies ADAM metallopeptidase with thrombospondin type 1 motif, 9 (ADAMTS9), as a novel asthma susceptibility gene. Journal of Allergy and Clinical Immunology. 2016Mar;137(3):964-6. doi: 10.1016/j.jaci.2015.09.051
- Guillen-Guio B, Lorenzo-Salazar JM, González-Montelongo R, Díaz-de Usera A, Marcelino-Rodríguez I, Corrales A, Cabrera de León A, Alonso S, Flores C. Genomic analyses of human European diversity at the southwestern edge: isolation, African influence and disease associations in the Canary Islands. Molecular Biology and Evolution. Dec 1;35(12):3010-3026. doi: 10.1093/molbev/msy190


### *Developmental biology*

**Principal Investigator:**

- Julio T. Ávila Marrero (Professor of Biochemistry and Molecular Biology, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Pablo Martín Vasallo (Professor of Biochemistry and Molecular Biology, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)

**External collaborators:**

- Manuel José Morales González (Associate Lecturer in Internal Medicine, Head of the Medical Oncology Service, HUNSC)
- Ángela Palumbo (Medical Director, In vitro Fertilization Centre)
- Jairo Hernández Hernández (Laboratory Director, In vitro Fertilization Centre)
- Deborah Rotoli (Visiting Investigator)
- Rebeca González Fernández (SEGAI technician, ULL)

**PhD students and trainees:**

- Rita Marleny Martín Ramírez (PhD student, The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)

- Fabián Leopoldo Poletti Serafini (Traumatology service H. San Juan de Dios, Doctorate Program in Health Sciences)
- María Adela Rodríguez Fuentes (Radiology Service HUC, Doctorate Program in Health Sciences)
- Miriam Dorta Suárez (Medical Oncology-HUNSC)

**Research Lines:**

- Gene expression in granulose and cumulus cells during follicular ovarian cancer development in humans.
- Study of the changes in gene expression associated with the administration of chemotherapy to cancer patients.
- Molecular Biology and the cellular $Na^+/K^+$-ATPase

**Publications 2019:**

- Rotoli D, Morales M, Maeso MD, Ávila J, Pérez-Rodríguez ND, Mobasheri A, van Noorden CJF, Martín-Vasallo P. IQGAP1, AmotL2, and FKBP51 Scaffoldins in the Glioblastoma Microenvironment. J Histochem Cytochem. 2019 Jul;67(7):481-494. doi: 10.1369/0022155419833334
- Mobasheri A, Matta C, Uzielienè I, Budd E, Martín-Vasallo P, Bernotiene E. The chondrocyte "channelome": A narrative review. [Le «channelome» du chondrocyte. Revue narrative]. Revue du Rhumatisme (Edition Francaise). 2019 Mar;86(2):147-154. doi: 10.1016/j.rhum.2018.08.001
- Mobasheri A, Matta C, Uzielienè I, Budd E, Martín-Vasallo P, Bernotiene E. The chondrocyte channelome: A narrative review. Joint Bone Spine. 2019 Jan;86(1):29-35. doi: 10.1016/j.jbspin.2018.01.012

**Other selected publications from the last 10 years:**

- Rotoli D, Morales M, Del Carmen Maeso M, Del Pino Garcia M, Morales A, Avila J, Martin-Vasallo P. Expression and localization of the immunophilin FKBP51 in colorectal carcinomas and primary metastases, and alterations following oxaliplatin chemotherapy. Oncol Lett. 2016 Aug;12(2):1351-1322. doi: 10.3892/ol.2016.4772
- Baker Bechmann M, Rotoli D, Morales M, Maeso M del C, Garcia M, Ávila J, Mobasheri A, Martín-Vasallo P. Na,K-ATPase Isozymes in Colorectal Cancer and Liver Metastases. Front Physiol. 2016 Jan 29;7:9. doi: 10.3389/fphys.2016.00009
- González-Fernández R, Ávila J, Arteaga MF, Canessa CM, Martín-Vasallo P. The neuronal-specific SGK1.1 (SGK1_v2) kinase as a transcriptional modulator of BAG4, Brox, and PPP1CB genes expression. Int J Mol. Sci. 2015 Apr 2;16(4):7462-77. doi:10.3390/ijms16047462
- González-Fernández R, Morales M, Avila J, Martín-Vasallo P. Changes in leukocyte gene expression profiles induced by antineoplastic chemotherapy. Oncol Lett. 2012Jun; 3(6):1341-1349. doi: 10.3892/ol.2012.669
- Mobasheri A, Trujillo E, Arteaga MF, Martín-Vasallo P. Na(+), K(+)-ATPase Subunit Composition in a Human Chondrocyte Cell Line; evidence for the Presence of A1, A3, B1, B2 and B3 Isoforms. Int J Mol Sci. 2012;13(4):5019-34. doi: 10.3390/ijms13045019

## 2.- CHRONIC & AGE-RELATED DISEASES

This programme is dedicated to research into the biological basis of the main human diseases and to finding new therapies for these. Bearing in mind that the severity of most of these conditions increases with age and given the ageing of the population in the EU, the economic impact of these pathologies is clearly very high. The majority of age-related diseases have a complex development and they affect different body systems, requiring a preventive strategy, a global therapeutic approach and a stricter control of lifestyle.

### *Chronic kidney disease, diabetes and kidney transplant complications*

**Principal Investigators:**

- Esteban Porrini, MD, PhD ("Ramón y Cajal" Investigator, Department of Internal Medicine, Dermatology and Psychiatry, ULL)
- Armando Torres Ramírez, MD, PhD (Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of Nephrology Service, HUC)

**Clinical Collaborators:**

- Alejandra Álvarez, MD (HUC)
- Ana González Rinne, MD (HUC)
- Beatriz Escamilla, MD (HUC)
- Domingo Marrero Miranda, MD (HUC)
- Lourdes Pérez Tamajón, MD (HUC)
- Patricia Delgado Mallen, MD (HUC)
- Sara Estupiñán, MD (HUC)

**External postdoctoral collaborators:**

- Sergio Luis Lima, PhD (RedInRen Contracted Investigator, ISCIII)
- Ana Elena Rodríguez Rodríguez, PhD (Contracted Investigator FGULL)
- Javier Donate Correa, PhD (ISCIII "Sara Borrell" Programme, FIISC)
- Marian Cobo Caso, PhD (HUC)
- Rosa Miquel, PhD (HUC)

**PhD students and trainees:**

- Raúl Morales Febles: Exercise and prediabetes after transplantation (PFIS 17/00303)
- Carlos González Alayón: Estimated and measured GFR in cirrhosis
- Pablo Jorge Pérez: Estimated and measured GFR in acute heart failure
- Germán Pérez Suárez: Evolution of bone mineral density and prevalence of renal lithiasis in adult patients diagnosed with idiopathic hypercalciuria in childhood ("Evolución de la densidad mineral ósea y prevalencia de litiasis renal en pacientes adultos diagnosticados de hipercalciuria idiopática en la infancia")

**Technical and administrative staff:**

- Federico González Rinne (Informatician UCICEC-HUC)
- Natalia Negrín Mena (Contracted Research Network RedInRen, ISCIII)

**Research Lines:**

Our aim is to study strategies to prevent the deterioration of kidney function in chronic kidney disease (CKD), and the metabolic and cardiovascular complications associated with kidney transplants. We analyse the impact of diabetes, obesity, metabolic syndrome and insulin resistance on CKD.

Regarding kidney transplantation, we concentrate on the study of post-transplantation diabetes and pre-diabetes. We are interested in epidemiological studies as a proof of concept for randomised clinical trials, and in the use of animal models to study new preventive effects of immunosuppressant drugs with pro-diabetic actions.

**Funded projects:**

- Loss of kidney function in the absence of proteinuria in type 2 diabetic women (PI16/01814 - La pérdida de la función renal en ausencia de proteinuria en mujeres con diabetes tipo 2"). PI: Esteban Porrini. Institute of Health Carlos III (2017-2020, 113,437.50 €).
- Pre-donation kidney reserve: impact on the donor and receptor kidney function in a live donor kidney transplant programme (PIFUN18/17 – "Reserva renal predonación: impacto en la evolución de la función renal del donante y receptor en un programa de trasplante renal de donante vivo"). PIs: Ana González Rinne and Esteban Porrini. The Canary Islands Foundation for Medical Research, FUNCANIS (2018-2020, 30,000 €).
- National "Ramón y Cajal" programme. Postdoctoral contracts for Research and Development centres (RYC-2014-16573. "Diabetic Nephropathy, Post-transplant diabetes"). PI: Esteban Porrini. MINECO (Ramón y Cajal Sub-programme; 2015-2020, 268.600 € -salary, 5 years+ 40,000 €, Research Project).
- REDINREN Kidney research Network: Transplant Program II. (RD16/0009/0031- "Red Temática de Investigación Renal REDINREN: Programa II Trasplante"). PI: Armando Torres. Institute of Health Carlos III (2017-2021, 102,300 €).
- New mechanisms of diabetogenicity for immunosuppressant drugs related to FKBP12 binding, the loss of B-cell identity and changes in insulin secretion (PI16/02151 – "Nuevos mecanismos de diabetogenicidad de los inmunosupresores relacionados con su unión a FKBP12 pérdida de identidad de la célula beta y cambios en la secreción de insulina"). PI: Armando Torres. Institute of Health Carlos III (2017-2021, 121,302.50 €).
- The role of inflammation on prediabetes and diabetes alter renal transplantation; the beneficial effect of moderate exercise. (PI19/01187). PI: Armando Torres. Institute of Health Carlos III (2019-2022, 62,315 €).
- Testing the efficacy of a flavonoid in renal disease. PI: Esteban Porrini. ARAFARMA (2019-2021, 90,000 €).
- Relationship between renal function to endothelial dysfunction in living donors, CONFUCIUS study. PI: Francisco Moreso / Esteban Porrini. TEVA laboratory (2018-2020, 46,000 €).

- Unmasking progressors towards chronic kidney disease in Autosomal Dominant Polycystic Kidney Disease (ADPKD) by measured renal function. Co-PI: Esteban Porrini. OTSUKA laboratory (2017-2020, 25,000 €).
- Efficacy of ENVARSUS in the prevention of PTDM. PI: Armando Torres. Co-PI: Esteban Porrini. Chiesi laboratory (2018-2021, 59.000 €).
- Preclinical development of a new drug for the treatment of hyperuricemia and hyperuremia ("Desarrollo preclínico de un nuevo fármaco para el tratamiento de la hiperuricemia e hiperuremia": Exp. Matriz 19120187). PIs: Araceli Delgado, Esteban Porrini. Arafarma Group S.A., FGULL (2019-2020, 199,870 €).

**Publications 2019:**

- Rodriguez-Rodriguez A, Donate-Correa J, Rovira J, Cuesto G, Luis-Ravelo D, Fernandes MX, Acevedo-Arozena A, Diekmann F, Acebes A, Torres A, Porrini E. Inhibition of the mTOR pathway: A new mechanism of β cell toxicity induced by Tacrolimus. Am J Transplant. 2019 Dec;19(12):3240-3249. doi: 10.1111/ajt.15483
- Fernandez-Fernandez B, Fernandez-Prado R , Górriz JL, Martinez-Castelao A, Navarro-González JF, Porrini E, Soler MJ, Ortiz A. Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation and Study of Diabetic Nephropathy with Atrasentan: What was learned about the treatment of diabetic kidney disease with canagliflozin and atrasentan? Clin Kidney J. 2019 May 31;12(3):313-321. doi: 10.1093/ckj/sfz070
- Porrini E, Ruggenenti P, Luis-Lima S, Carrara F, Jiménez A, de Vries APJ, Torres A, Gaspari F, Remuzzi G. Estimated GFR: time for a critical appraisal. Nat Rev Nephrol. 2019 Mar;15(3):177-190. doi: 10.1038/s41581-018-0080-9
- Sarafidis P, Ferro CJ, Morales E, Ortiz A, Malyszko J, Hojs R, Khazim K, Ekart R, Valdivielso J, Fouque D, London GM, Massy Z, Ruggenenti P, Porrini E, Wiecek A, Zoccali C, Mallamaci F, Hornum M SGLT-2 inhibitors and GLP-1 receptor agonists for nephroprotection and cardioprotection in patients with diabetes mellitus and chronic kidney disease. A consensus statement by the EURECA-m and the DIABESITY working groups of the ERA-EDTA. Nephrol Dial Transplant. 2019 Feb 1;34(2):208-230. doi: 10.1093/ndt/gfy407
- Luis-Lima S, Escamilla-Cabrera B, Negrín-Mena N, Estupiñán S, Delgado-Mallén P, Marrero-Miranda D, González-Rinne A, Miquel-Rodríguez R, Cobo-Caso MÁ, Hernández-Guerra M, Oramas J, Batista N, Aldea-Perona A, Jorge-Pérez P, González-Alayón C, Moreno-Sanfiel M, González-Rodríguez JA, Henríquez L, Alonso-Pescoso R, Díaz-Martín L, González-Rinne F, Lavín-Gómez BA, Galindo-Hernández J, Sánchez-Gallego M, González-Delgado A, Jiménez-Sosa A, Torres A, Porrini E. Chronic kidney disease staging with cystatin C or creatinine-based formulas: Flipping the coin. Nephrol Dial Transplant. 2019 Feb 1;34(2):287-294. doi: 10.1093/ndt/gfy086
- Bettiga A, Fiorio F, Di Marco F, Trevisani F, Romani A, Porrini E, Salonia A, Montorsi F, Vago R. The modern western diet rich in advanced glycation end-products (AGEs): An overview of its impact on obesity and early progression of renal pathology. Nutrients. 2019 Jul 30;11(8). pii: E1748. doi: 10.3390/nu11081748
- González-Rinne A, Luis-Lima S, Escamilla B, Negrín-Mena N, Ramírez A, Morales A, Vega N, García P, Cabello E, Marrero-Miranda D, Aldea-Perona A, Alvarez A, Abad MDC, Pérez-Tamajón L, González-Rinne F, González-Delgado A, Díaz Martín L, Jiménez-Sosa A, Torres A, Porrini E. Impact of errors of creatinine and cystatin C equations in the selection of living kidney donors. Clin Kidney J. 2019 Mar 18;12(5):748-755. doi: 10.1093/ckj/sfz012

- Porrini E, Díaz JM, Moreso F, Lauzurrica R, Ibernon M, Torres IS, Ruiz RB, Rodríguez Rodríguez AE, Mallén PD, Bayés-Genís B, Gainza FJ, Osorio JM, Osuna A, Domínguez R, Ruiz JC, Sosa AJ, Rinne AG, Miranda DM, Macías M, Torres A. Prediabetes is a risk factor for cardiovascular disease following renal transplantation. Kidney Int. 2019 Dec;96(6):1374-1380. doi: 10.1016/j.kint.2019.06.026
- Luis-Lima S, Higueras Linares T, Henríquez-Gómez L, Alonso-Pescoso R, Jimenez A, López-Hijazo AM, Negrín-Mena N, Martín C, Sánchez-Gallego M, Galindo Hernández SJ, Socas Fernández Del Castillo R, Castilla-Marrero M, Domínguez Coello S, Vilchez de León V, Valcárcel-Lopez R, Insausti-Garmendia N, Escamilla B, Estupiñán S, Delgado-Mallén P, Armas-Padrón AM, Marrero-Miranda D, González-Rinne A, Miquel Rodríguez RM, Cobo-Caso MA, Díaz-Martín L, González-Rinne F, González-Delgado A, López-Martínez M, Jiménez-Sosa A, Torres A, Porrini E. The Error of Estimated GFR in Type 2 Diabetes Mellitus. J Clin Med. 2019 Sep 26;8(10). pii: E1543. doi: 10.3390/jcm8101543
- López-Martínez M, Luis-Lima S, Morales E, Navarro-Díaz M, Negrín-Mena N, Folgueras T, Escamilla B, Estupiñán S, Delgado-Mallén P, Marrero-Miranda D, González-Rinne A, Miquel-Rodríguez RM, Cobo-Caso MA, Díaz-Martín L, Jiménez Sosa A, González-Rinne F, Torres A, Porrini E. The estimation of GFR and the adjustment for BSA in overweight and obesity: a dreadful combination of two errors. Int J Obes (Lond). 2019 Oct 22. doi: 10.1038/s41366-019-0476-z. [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Porrini E, Díaz JM, Moreso F, Delgado Mallén PI, Silva Torres I, Ibernon M, Bayés- Genís B, Benitez-Ruiz R, Lampreabe I, Lauzurrica R, Osorio JM, Osuna A, Domínguez-Rollán R, Ruiz JC, Jiménez-Sosa A, González-Rinne A, Marrero-Miranda D, Macía M, García J, Torres A. Clinical evolution of post-transplant diabetes mellitus. Nephrol Dial Transplant. 2016 Mar;31(3):495-505. doi:10.1093/ndt/gfv368
- Luis-Lima S, Rodríguez-Rodríguez AE, Martin-Higueras C, Sierra-Ramos C, Carrara F, Arnau MR, de la Rosa DA, Salido E, Gaspari F, Porrini E. Iohexol plasma clearance, a simple and reliable method to measure renal function in conscious mice. Pflugers Arch. 2016 Sep;468(9):1587-94. doi: 10.1007/s00424-016-1843-4
- D'Agati VD, Chagnac A, de Vries AP, Levi M, Porrini E, Herman-Edelstein M, Praga M. Obesity-related glomerulopathy: clinical and pathologic characteristics and pathogenesis. Nat Rev Nephrol. 2016 Aug;12(8):453-71. doi: 10.1038/nrneph.2016.75
- Porrini E, Ruggenenti P, Mogensen C-E et al., for the ERA-EDTA Working Group Diabesity. A role for non-proteinuric pathways in loss of renal function in patients with type 2 diabetes? Lancet Diabetes Endocrinol. 2015 May;3(5):382-91. doi: 10.1016/S2213-8587(15)00094-7
- Luis-Lima S, Gaspari F, Porrini E, Garcia-Gonzalez M, Batista N, Bosa-Ojeda F, Oramas J, Carrara F, Gonzalez-Posada JM, Marrero D, Salido E, Torres A, Jimenez-Sosa A. Measurement of glomerular filtration rate: Internal and external validations of the iohexol plasma clearance technique by HPLC. Clin Chim Acta. 2014 Mar 20;430:84-5. doi:10.1016/j.cca.2013.12.028
- de Vries AP, Ruggenenti P, Ruan XZ, Praga M, Cruzado JM, Bajema IM, D'Agati VD, Lamb HJ, Pongrac Barlovic D, Hojs R, Abbate M, Rodriquez R, Mogensen CE, Porrini E; ERA-EDTA Working Group Diabesity. Fatty kidney: emerging role of ectopic lipid in obesityrelated renal disease. Lancet Diabetes Endocrinol. 2014 May;2(5):417-26. doi: 10.1016/S2213-8587(14)70065-8

- Rodríguez-Rodríguez AE, Trinanes J, Velázquez-García S, Porrini E, Vega Prieto MJ, Diez Fuentes ML, Arevalo M, Salido Ruiz E, Torres A. The higher diabetogenic risk of tacrolimus depends on pre-existing insulin resistance. A study in obese and lean zucker rats. Am J Transplant. 2013 Jul;13(7):1665-75. doi: 10.1111/ajt.12236
- Triñanes J, Rodriguez-Rodriguez AE, Brito-Casillas Y, Wagner A, De Vries APJ, Cuesto G, Acebes A, Salido E, Torres A, Porrini E. Deciphering Tacrolimus-Induced Toxicity in Pancreatic β Cells. Am J Transplant. 2017 Nov;17(11):2829-2840. doi:10.1111/ajt.14323


### *Inflammatory and neoplastic disease of the gastrointestinal tract, Prevalent Liver Diseases*

**Principal Investigators:**

- Enrique Quintero Carrión, MD, PhD (Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of Gastroenterology Service until December 2019, HUC)
- Manuel Hernández-Guerra de Aguilar, MD, PhD (Associate Lecturer, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of Gastroenterology Service since December 2019, HUC)
- Antonio Z. Gimeno García, MD, PhD (Attending Physician in Gastroenterology, HUC)

**Collaborators and Clinical researchers:**

- David Nicolás Pérez, MD, PhD (Head of the Endoscopy Section, HUC)
- Laura Ramos, MD, PhD (Attending Physician, HUC)
- Marta Carrillo Palau, MD, PhD (Attending Physician, HUC)
- Inmaculada Alonso Abreu, MD, PhD (Attending Physician, HUC)
- Zaida Adrián de Ganzo, MD, PhD (Attending Physician, HUC)
- Yanira González Méndez, MD, PhD (Attending Physician, HUC)
- Goretti Hernández Mesa, MD (HUC)
- Onofre Alarcón Fernández, MD (HUC)
- Noemi Hernández Bouilla, MD (HUC)
- Eduardo Rodríguez Hernández, MD (HUC)
- Dalia Elena Morales Arráez, MD (HUC)
- Carlos González Alayón, MD (HUC)
- Cristina Reygosa (MIR, HUC)
- Alberto Hernández Bustabad (MIR, HUC)
- Francisco Javier Pérez Hernández (MIR, Communityand Family Medicine)
- Natalia González López (D.U.E., HUC)

**PhD students and trainees:**

- Carlos González Alayón, (PhD student, MD, HUC)
- Natalia González López (PhD student, DUE, HUC)
- Cristina Reygosa (Alumna de Doctorado, MIR, HUC)

**Technical and administrative staff:**

- José Luis Baute Dorta (DUE, HUC)

- Beatriz Pérez Abrante (Laboratory technician in Experimental techniques, HUC)
- Eladio Frías Arrocha (Data Manager)

**Research Lines:**

- Gastrointestinal cancer prognostic factors and prevention strategies ("Factores pronósticos y estrategias para la prevención del cáncer gastrointestinal").
- Physiopathology of portal hypertension and new treatments ("Fisiopatología de la hipertensión portal y nuevos tratamientos").
- Immunogenicity and vaccine response of hepatic disease patients ("Inmunogenicidad y respuesta a vacunas en pacientes con enfermedad hepática").
- New functional markers of cirrhosis and ascite physiopathology, and markers of non-alcoholic steatohepatitis ("Nuevos marcadores de función renal en el cirrótico y fisiopatología de la ascitis, así como marcadores de esteatohepatitis no alcohólica").
- Pathogenic factors and new treatments for Chronic Inflammatory Disease ("Factores patogénicos y nuevos tratamientos en la Enfermedad Inflamatoria Crónica").
- Projects for the micro-elimination of hepatitis C virus ("Proyectos de microeliminación del virus de la hepatitis C").

**Funded Projects:**

- Identification of new biomarkers for the prevention of colorectal cancer ("Identificación de nuevos biomarcadores para la prevención del cáncer colorrectal"). PI: Enrique Quintero. Spanish Association against Cancer (2013-2019, 183,896 €).
- Immunological faecal blood test to diagnose iron-deficiency anaemia (PI16/02011- "Evaluación del test inmunológico de sangre oculta en heces en el proceso diagnóstico pacientes con anemia ferropénica"). PI: Enrique Quintero. Heath Institute Carlos III (2017-2019, 57,475 €).
- Improvement of clinical practice management and/or of training within the Foundation, to benefit and improve patient care ("Mejora de la gestión de la práctica clínica y/o, formación dentro de la Fundación, al objeto de beneficiar y mejorar la práctica de la medicina en los pacientes"). PI: Enrique Quintero. ABBVIE (2018, 40,000 €)
- Comparison fecal occult blood test and colonoscopy in familial colorectal cancer screening: adherence, diagnostic yield and cost-effectiveness (PI15/01257). PI: Antonio Z. Gimeno. Institute of Health Carlos III (2016-2019, 110,352 €).

**Publications 2019:**


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- Herreros-Villanueva M, Duran-Sanchon S, Martín AC, Pérez-Palacios R, Vila-Navarro E, Marcuello M, Diaz-Centeno M, Cubiella J, Diez MS, Bujanda L, Lanas A, Jover R, Hernández V, Quintero E, José Lozano J, García-Cougil M, Martínez-Arranz I, Castells A, Gironella M, Arroyo R. Plasma MicroRNA Signature Validation for Early Detection of Colorectal Cancer. Clin Transl Gastroenterol. 2019 Jan;10(1):e00003. doi:10.14309/ctg.0000000000000003

- Gargallo CJ, Lanas Á, Carrera-Lasfuentes P, Ferrandez Á, Quintero E, Carrillo M, Alonso-Abreu I, García-Gonzalez MA. Genetic susceptibility in the development of colorectal adenomas according to family history of colorectal cancer. Int J Cancer. 2019 Feb 1;144(3):489-502. doi: 10.1002/ijc.31858
- Rodríguez-Alcalde D, Carballal S, Moreira L, Hernández L, Rodríguez-Alonso L, Rodríguez-Moranta F, Gonzalo V, Bujanda L, Bessa X, Poves C, Cubiella J, Castro I, González M, Moya E, Oquiñena S, Clofent J, Quintero E, Esteban P, Piñol V, Fernández FJ, Jover R, Cid L, Saperas E, López-Cerón M, Cuatrecasas M, López-Vicente J, Rivero-Sánchez L, Jung G, Vila-Casadesús M, Sánchez A, Castells A, Pellisé M, Balaguer F; Gastrointestinal Oncology Group of the Spanish Gastroenterological Association. High incidence of advanced colorectal neoplasia during endoscopic surveillance in serrated polyposis syndrome. Endoscopy. 2019 Feb;51(2):142-151. doi:10.1055/a-0656-5557
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- Gómez L, Reygosa C, Morales-Arráez DE, Ramos R, Pérez A, Hernández A, Quintero E, Gutiérrez F, Diaz-Flores F, Hernández-Guerra M. Diagnostic test accuracy of the cobas 6800 system for detection of hepatitis c virus viraemia levels from dried blood spots. Enferm Infecc Microbiol Clin. 2019 Dec 4. pii: S0213-005X(19)30300-3. doi: 10.1016/j.eimc.2019.10.009 [Epub ahead of print]
- Morales-Arraez D, Nieto Bujalance Y, Diaz-Flores F, de Vera A, Jiménez A, Garcia Dopico JA, Quintero E, Hernández-Guerra M. Risk of liver fibrosis progression in patients with suboptimal diagnosis of hepatitis C virus infection. Eur J Gastroenterol Hepatol. 2019 Sep 3. doi: 10.1097/MEG.0000000000001534. [Epub ahead of print]
- Morales-Arraez D, Diaz-Flores F, Alonso A, de Vera A, Jimenez A, Garcia Dopico JA, Quintero E, Hernández-Guerra M. Patients with suboptimal hepatitis B virus diagnostic characterization are at risk of liver fibrosis progression. Eur J Gastroenterol Hepatol. 2019 Sep 3. doi: 10.1097/MEG.0000000000001527. [Epub ahead of print]
- Hernández G, Gimeno-García AZ, Quintero E. Strategies to optimise the quality of bowel cleansing [Estrategias para optimizar la calidad de la limpieza colónica]. Gastroenterol Hepatol. 2019 May;42(5):326-338. doi: 10.1016/j.gastrohep.2019.01.010
- Hernández G, Gimeno-García AZ, Quintero E. Strategies to Improve Inadequate Bowel Preparation for Colonoscopy. Front Med (Lausanne). 2019 Nov 8;6:245. doi: 10.3389/fmed.2019.00245
- Gimeno-García AZ, de la Barreda Heuser R, Reygosa C, Hernandez A, Mascareño I, Nicolás-Pérez D, Jiménez A, Lara AJ, Alarcon-Fernández O, Hernandez-Guerra M, Romero R, Alonso I, González Y, Adrian Z, Hernandez G, Hernandez D, Delgado R, Quintero E. Impact of a 1-day versus 3-day low-residue diet on bowel cleansing quality before colonoscopy:A randomized controlled trial. Endoscopy. 2019 Jul;51(7):628-636. doi: 10.1055/a-0864-1942
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Rodríguez JA, Henríquez L, Alonso-Pescoso R, Díaz-Martín L, González-Rinne F, Lavín-Gómez BA, Galindo-Hernández J, Sánchez-Gallego M, González-Delgado A, Jiménez-Sosa A, Torres A, Porrini E. Chronic kidney disease staging with cystatin C or creatinine-based formulas: Flipping the coin. Nephrol Dial Transplant. 2019 Feb 1;34(2):287-294. doi: 10.1093/ndt/gfy086

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- Hernández-Gea V, Procopet B, Giráldez Á, Amitrano L, Villanueva C, Thabut D, Ibañez-Samaniego L, Silva-Junior G, Martinez J, Genescà J, Bureau C, Trebicka J, Llop E, Laleman W, Palazon JM, Castellote J, Rodrigues S, Gluud LL, Noronha Ferreira C, Barcelo R, Cañete N, Rodríguez M, Ferlitsch A, Mundi JL, Gronbaek H, Hernández-Guerra M, Sassatelli R, Dell'Era A, Senzolo M, Abraldes JG, Romero-Gómez M, Zipprich A, Casas M, Masnou H, Primignani M, Krag A, Nevens F, Calleja JL, Jansen C, Robic MA, Conejo I, Catalina MV, Albillos A, Rudler M, Alvarado E, Guardascione MA, Tantau M, Bosch J, Torres F, Garcia-Pagán JC; International Variceal Bleeding Observational Study Group and Baveno Cooperation. Preemptive-TIPS Improves Outcome in High-Risk Variceal Bleeding: An Observational Study. Hepatology. 2019 Jan;69(1):282-293. doi: 10.1002/hep.30182
- Crespo J, Albillos A, Buti M, Calleja JL, García-Samaniego J, Hernández-Guerra M, Serrano T, Turnes J, Acín E, Berenguer J, Berenguer M, Colom J, Fernández I, Fernández Rodríguez C, Forns X, García F, Granados R, Lazarus J, Molero JM, Molina E, Pérez Escanilla F, Pineda JA, Rodríguez M, Romero M, Roncero C, Saiz de la Hoya P, Sánchez Antolín G. Elimination of hepatitis C. Positioning document of the Spanish Association for the Study of the Liver (AEEH). Rev Esp Enferm Dig. 2019 Nov;111(11):862-873. doi: 10.17235/reed.2019.6700/2019
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- Manuel Sousa J, Vergara M, Pulido F, Sánchez Antolín G, Hijona L, Carnicer F, Rincón D, Salmerón J, Mateos-Muñoz B, Jou A, Polo-Lorduy B, Rubín Á, Escarda A, Aguilar P, Aldámiz-Echevarría T,

García-Buey L, Carrión JA, Hernández-Guerra M, Chimeno-Hernández S, Espinosa N, Morillas RM, Andrade RJ, Delgado M, Gallego A, Magaz M, Moreno-Planas JM, Estébanez Á, Rico M, Menéndez F, Sampedro B, Morano L, Izquierdo S, Zozaya JM, Rodríguez M, Morán-Sánchez S, Lorente S, Martín-Granizo I, Von-Wichmann MÁ, Delgado M, Manzanares A. Real-world evidence of the effectiveness of ombitasvir-paritaprevir/r ± dasabuvir ± ribavirin in patients monoinfected with chronic hepatitis C or coinfected with human immunodeficiency virus-1 in Spain. PLoS One. 2019 Nov 12;14(11):e0225061. doi: 10.1371/journal.pone.0225061

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- Téllez T, Abitei C, Padilla-Ruiz MDC, Rivas-Ruiz F, Fúnez R, Pereda T, Rodrigo I, Alcaide J, Baré ML, Morales Suárez-Varela MM, Zabalza I, Sánchez Del Charco M, Borrero Martín JJ, García Del Moral R, Escobar A, Quintana JM, Aguirre U, Redondo M; REDISSEC-CARESS/CCR group (Gimeno-Garcia AZ). Biological and prognostic differences between symptomatic colorectal carcinomas and those detected by screening. Eur J Surg Oncol. 2019 Oct;45(10):1876-1881. doi: 10.1016/j.ejso.2019.05.027
- Martin-Cardona A, Fernandez-Esparrach G, Subtil JC, Iglesias-Garcia J, Garcia-Guix M, Barturen Barroso A, Gimeno-Garcia AZ, Esteban JM, Pardo Balteiro A, Velasco-Guardado A, Vazquez-Sequeiros E, Loras C, Martinez-Moreno B, Castellot A, Huertas C, Martinez-Lapiedra M, Sanchez-Yague A, Teran A, Morales-Alvarado VJ, Betes M, de la Iglesia D, Sánchez-Montes C, Lozano MD, Lariño-Noia J, Gines A, Tebe C, Gornals JB; On belhaf of Spanish Group for EUS-Guided TA in the adrenal gland. EUS-guided tissue acquisition in the study of the adrenal glands: Results of a nationwide multicenter study. PLoS One. 2019 Jun 6;14(6):e0216658. doi: 10.1371/journal.pone.0216658
- Puig I, López-Cerón M, Arnau A, Rosiñol Ò, Cuatrecasas M, Herreros-de-Tejada A, Ferrández Á, Serra-Burriel M, Nogales Ó, Vida F, de Castro L, López-Vicente J, Vega P, Álvarez-González MA, González-Santiago J, Hernández-Conde M, Díez-Redondo P, Rivero-Sánchez L, Gimeno-García AZ, Burgos A, García-Alonso FJ, Bustamante-Balén M, Martínez-Bauer E, Peñas B, Pellise M; EndoCAR group, Spanish Gastroenterological Association and the Spanish Digestive Endoscopy Society. Accuracy of the Narrow-Band Imaging International Colorectal Endoscopic Classification System in Identification of DeepInvasion in Colorectal Polyps. Gastroenterology. 2019 Jan;156(1):75-87. doi: 10.1053/j.gastro.2018.10.004
- Albéniz E, Gimeno-García AZ, Fraile M, Ibáñez B, Guarner-Argente C, Alonso-Aguirre P, Álvarez MA, Gargallo CJ, Pellisé M, Ramos Zabala F, Herreros de Tejada A, Nogales Ó, Martínez-Ares D, Múgica F, de la Peña J, Espinós J, Huerta A, Álvarez A, Gonzalez-Santiago JM, Navajas F, Martínez-Cara JG, Redondo-Cerezo E, Merlo Mas J, Sábado F, Rivero L, Saperas E, Soto S, Rodríguez-Sánchez J, López-Roses L, Rodríguez-Téllez M, Rullán Iriarte M, Elosua González A, Pardeiro R, Valdivielso Cortázar E, Concepción-Martín M, Huelin Álvarez P, Colán Hernández J, Cobian J, Santiago J, Jiménez A, Remedios D, López-Viedma B, García O, Martínez-Alcalá F, Pérez-Roldán F, Carbó J, Enguita M. Clinical validation of risk scoring systems to predict risk of delayed bleeding after EMR of large colorectal lesions. Gastrointest Endosc. 2019 Oct 23. pii: S0016-5107(19)32382-X. doi: 10.1016/j.gie.2019.10.013 [Epub ahead of print]

**Other selected publications from the last 10 years:**


- Quintero E, Castells A, Bujanda L. et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. N Engl J Med. 2012 Feb 23;366(8):697-706. doi:10.1056/NEJMoa1108895
- Quintero E, Carrillo M, Leoz ML, Cubiella J, Gargallo C, Lanas A, Bujanda L, Gimeno-García AZ, Hernández-Guerra M, Nicolas-Perez D, Alonso-Abreu I, Morillas JD, Balaguer F, Muriel A; Oncology Group of the Asociacion Española de Gastroenterología (AEG). Risk of Advanced Neoplasia in First-Degree Relatives with Colorectal Cancer: A Large Multicenter Cross-Sectional Study. PLoS Medicine 2016 May 3;13(5):e1002008. doi: 10.1371/journal.pmed.1002008
- Jover R, Zapater P, Bujanda L, Hernandez V, Cubiella J, Pellise M, Ponce M,Ono A, Lanas A, Seoane A, Marin-Gabriel JC, Chaparro M, Cacho G, Herreros-de-Tejada A, Fernandez-Diez S, Peris A, Nicolas-Perez D, Murcia O, Castells A, Quintero E; COLONPREV Study Investigators. Endoscopist characteristics that influence the quality of colonoscopy. Endoscopy 2016 Mar;48(3):241-7. doi: 10.1055/s-0042-100185
- Castells A, Bessa X, Quintero E, et al. Risk of Advanced Proximal Neoplasms According to Distal Colorectal Findings: Comparison of Sigmoidoscopy-Based Strategies. J Natl Cancer Inst. 2013 Jun 19;105(12):878-886
- Quintero E, Carrillo M, Gimeno-García AZ, Hernández-Guerra M, Nicolás-Pérez D, Alonso-Abreu I, Díez-Fuentes ML, Abraira V. Equivalency of Fecal Immunochemical Tests and Colonoscopy in Familial Colorectal Cancer Screening. Gastroenterology. 2014 Nov;147(5):1021-30.e1; quiz e16-7. doi: 10.1053/j.gastro.2014.08.004
- Abraldes JG, Villanueva C, Aracil C, Turnes J, Hernandez-Guerra M, Genesca J, Rodriguez M, Castellote J, García-Pagán JC, Torres F, Calleja JL, Albillos A, BoschJ; BLEPS Study Group. Addition of Simvastatin to Standard Therapy for the Prevention of Variceal Rebleeding Does Not Reduce Rebleeding but Increases Survival in Patients with Cirrhosis. Gastroenterology. 2016 May; 150(5): 1160-1170. doi: 10.1053/j.gastro.2016.01.004
- Hernández-Guerra M, de Ganzo ZA, Gonzalez-Mendez Y, Salido E, Abreu P, Moreno M, Felipe V, Abrante B, Quintero E. Chronic intermittent hypoxia aggravates intrahepatic endothelial dysfunction in cirrhotic rats. Hepatology. 2013 Apr;57(4):1564-74. doi: 10.1002/hep.26152


### *Physiopathology of mineralocorticoids*

**Principal Investigator:**

- Diego Álvarez de la Rosa, PhD (Lecturer of Physiology, Department of Basic Medical Sciences Department, ULL)

**Postdoctoral Researchers:**

- Guadalberto Hernández Hernández, MD, PhD (Professor of Physiology, Department of Basic Medical Sciences, ULL)
- Silvia Velázquez García, PhD (Agustín de Betancourt Researcher, ULL)

**PhD students and trainees:**

- Brian Almeida Prieto (FPI, MINECO, BES-2017-082939, associated to project BFU2016-78374-R)

- Arianna Vastola Mascolo (MICINN, BFU2016-78374-R)

**Research Lines:**

In the laboratory we study the mechanisms of action of adrenal mineralocorticoids and glucocorticoids through the following research lines:

- Identification and analysis of the physiological target genes of aldosterone and glucocorticoid. The main objective of this research is to improve our understanding of cellular and molecular glucocorticoid hormone signalling under physiological conditions, and in association with different pathologies: hypertension, kidney and vascular damage, metabolic syndrome. To this end, we aim to develop relevant animal models for these pathologies and identify new therapeutic targets.
- The study of the cellular biology and molecular mechanisms involved in mineralocorticoid receptor activation, with a view to identify the cellular processes and structural features involved in aldosterone and glucocorticoid signal transduction.

**Funded Projects:**

- Altered mineralocorticoid receptor activation: mechanisms and physiopathology (INMIR, BFU2016-78374-R – "Activación inapropiada del receptor de mineralocorticoides: fisiopatología y Mecanismos"). PI: Diego Álvarez de la Rosa. Ministry of Economy and Competitiveness, MINECO (2017-2019, 200,000 €)
- MetSPLAT: An in vivo platform for metabolic syndrome preclinical drug tests. Agustín de Betancourt Project. PI: Silvia Velázquez García; Tutor: Diego Álvarez de la Rosa. Regional Government of Tenerife (2017-2021, 160,000 €)

**Publications 2019:**

- Knoepp F, Ashley Z, Barth D, Baldin JP, Jennings M, Kazantseva M, Saw EL, Katare R, Alvarez de la Rosa D, Weissmann N, Fronius M. Shear force sensing of epithelial Na+ channel (ENaC) relies on N-glycosylated asparagines in the palm and knuckle domains of αENaC. Proc Natl Acad Sci USA. 2020 Jan 7;117(1):717-726. doi: 10.1073/pnas.1911243117. Epub 2019 Dec 23
- Armas-Capote N, Maglio LE, Pérez-Atencio L, Martin-Batista E, Reboreda A, Barios JA, Hernandez G, Alvarez de la Rosa D, Lamas JA, Barrio LC, Giraldez T. SGK1.1 Reduces Kainic Acid-Induced Seizure Severity and Leads to Rapid Termination of Seizures. Cereb Cortex. 2019 Dec 9. pii: bhz302. doi: 10.1093/cercor/bhz302
- Butterworth MB, Alvarez de la Rosa D. Regulation of Aldosterone Signaling by MicroRNAs. Vitam Horm. 2019;109:69-103. doi: 10.1016/bs.vh.2018.09.002
- Herrera JL, Ordoñez-Gutierrez L, Fabrias G, Casas J, Morales A, Hernandez G, Acosta NG, Rodriguez C, Prieto-Valiente L, Garcia-Segura LM, Wandosell FG, Alonso R. Ovarian Hormone-Dependent Effects of Dietary Lipids on APP/PS1 Mouse Brain. Front Aging Neurosci. 2019 Dec 19;11:346. doi: 10.3389/fnagi.2019.00346

**Other selected publications from the last 10 years:**

- Jiménez-Canino R, Lorenzo-Díaz F, Odermatt A, Bailey MA, Livingstone DE, Jaisser F, Farman N, Alvarez de la Rosa D. 11β-HSD2 SUMOylation Modulates Cortisol-induced Mineralocorticoid

Receptor Nuclear Translocation Independently of Effects on Transactivation. Endocrinology. 2017 Nov 1;158(11):4047-4063. doi: 10.1210/en.2017-00440

- Jiménez-Canino R, Fernandes MX, Alvarez de la Rosa D. Phosphorylation of mineralocorticoid receptor ligand binding domain impairs receptor activation and has a dominant negative effect over non-phosphorylated receptors. J Biol Chem. 2016 Sep 2;291(36):19068-78. doi: 10.1074/jbc.M116.718395
- Jiménez-Canino R, Lorenzo-Diaz F, Jaisser F, Farman N, Giráldez T, Álvarez de la Rosa D. Histone deacetylase 6-controlled Hsp90 acetylation significantly alters mineralocorticoid receptor subcellular dynamics but not its transcriptional activity. Endocrinology. 2016 Jun;157(6):2515-32. doi: 10.1210/en.2015-2055
- Hernandez-Diaz I, Giráldez T, Morales S, Hernández G, Salido E, Canessa CM, Álvarez de la Rosa D. Heterogeneous nuclear ribonucleoprotein A2/B1 is a tissue-specific aldosterone target gene with prominent induction in the rat distal colon. Am J Physiol Gastrointest Liver Physiol. 2013 Jan 15;304(2):G122-31. doi: 10.1152/ajpgi.00130.2012
- Urbanet R, Nguyen Dinh Cat A, Feraco A, Gravez B, El Mograhbi S, Sierra-Ramos C, Alvarez de la Rosa D, Quilliot D, Rossignol P, Venteclef N, Clement K, Fallo F, Touyz RM, Jaisser F. Adipocyte mineralocorticoid receptor activation leads to metabolic syndrome and induction of Prostaglandin D2 Synthase. Hypertension. 2015 Jul;66(1):149-57. doi: 10.1161/HYPERTENSIONAHA.114.04981

### *Kidney and cardiovascular disease research*

**Principal Investigator:**

- Juan Francisco Navarro González, MD, PhD (Head of Service Research Unit, HUNSC)

**External postdoctoral collaborators:**

- Javier Donate Correa. PhD in Biology. Postdoctoral Researcher. FIISC
- Víctor García Tagua. PhD in Molecular Biology and Biomedicine. Postdoctoral Researcher. FIISC

**Collaborators and Clinical Researchers:**

- Nayra Pérez Delgado (Clinical Analysis Service)
- Carolina Hernández Carballo (Internal Medicine)
- Sergio Rodríguez Ramos (Trasplant Coordination)
- Purificación Cerro (Trasplant Coordination)
- Ángel López Castillo (Vascular Surgery)
- Alejandro Delgado Molinos (Vascular Surgery)
- Victoria Castro (Pathological Anatomy)
- Carol Prieto Morín (Clinical Analysis)
- Orlando Siverio Morales (Nephrology)
- Desirée Luis Rodríguez (Nephrology)

**PhD students and trainees:**

- Ernesto Martín Núñez (PFIS, Institute of Health Carlos III, FI14/00033)

- Carla María Ferri (The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI, TESIS2018010110)
- Víctor García Tagua (Stop Fuga de Cerebros ("Stop Brain Drain") Fellowship. Roche Pharma - FIISC, C16/004)

**Research Lines:**

- Diabetic kidney disease.
- Chronic kidney disease and complications.
- Role of inflammation in high prevalence diseases.
- System FGF23/Klotho.

**Funded projects:**

- The FGF23/Klotho system as a predictor of cardiovascular morbidity and mortality (PI16/00024 – "Sistema FGF23/Klotho como predictor de morbi-mortalidad cardiovascular"). PI: Juan Francisco Navarro. Institute of Health Carlos III (2017-2019, 50,215 €).
- Kidney research Network (REDINREN, RD16/0009/0022 – "Red de Investigación Renal"). PI: Juan Francisco Navarro. Institute of Health Carlos III (2017-2021, 118,673.50 €).
- The FGF23/Klotho system in subclinical atherosclerotic vascular disease. Pathophysiological implications and therapeutic approach (PI19/00035 – "Sistema FGF23/Klotho en la enfermedad vascular aterosclerótica subclínica. Implicaciones fisiopatológicas y aproximación terapéutica). PI: Juan F. Navarro. Institute of Health Carlos III (2020-2022, 56,870 €).

**Publications 2019:**

- Fernandez-Fernandez B, Fernandez-Prado R, Górriz JL, Martinez-Castelao A, Navarro-González JF, Porrini E, Soler MJ, Ortiz A. Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation and Study of Diabetic Nephropathy with Atrasentan: What was learned about the treatment of diabetic kidney disease with canagliflozin and atrasentan? Clin Kidney J. 2019 May 31;12(3):313-321. doi: 10.1093/ckj/sfz070
- Heerspink HJL, Parving HH, Andress DL, Bakris G, Correa-Rotter R, Hou FF, Kitzman DW, Kohan D, Makino H, McMurray JJV, Melnick JZ, Miller MG, Pergola PE, Perkovic V, Tobe S, Yi T, Wigderson M, de Zeeuw D; SONAR Committees and Investigators (Navarro JF). Atrasentan and renal events in patients with type 2 diabetes and chronic kidney disease (SONAR): a double-blind, randomised, placebo-controlled trial. Lancet. 2019 May 11;393(10184):1937-1947. doi: 10.1016/S0140-6736(19)30772-X
- Donate-Correa J, Martín-Núñez E, Hernández-Carballo C, Ferri C, Tagua VG, Delgado-Molinos A, López-Castillo Á, Rodríguez-Ramos S, Cerro-López P, López-Tarruella VC, Felipe-García R, Arévalo-Gomez MA, Pérez-Delgado N, Mora-Fernández C, Navarro-González JF. Fibroblast growth factor 23 expression in human calcified vascular tissues. Aging (Albany NY). 2019 Sep 22;11(18):7899-7913. doi: 10.18632/aging.102297
- Valls J, Cambray S, Pérez-Guallar C, Bozic M, Bermúdez-López M, Fernández E, Betriu À, Rodríguez I, Valdivielso JM, NEFRONA cohort (Navarro González JF). Association of candidate gene polymorphisms with chronic kidney disease: Results of a case-control analysis in the NEFRONA cohort. Front Genet. 2019 Feb 26;10:118. doi: 10.3389/fgene.2019.00118
- Pérez-Morales RE, Del Pino MD, Valdivielso JM, Ortiz A, Mora-Fernández C, Navarro-González JF. Inflammation in Diabetic Kidney Disease. Nephron. 2019;143(1):12-16. doi: 10.1159/000493278

- Donate-Correa J, García-Tagua V, Ferri CM, Martín-Núñez, E, Hernández-Carballo C, Ureña-Torres P, Ruiz-Ortega M, Ortiz A, Mora-Fernández C, Navarro-González JF. Pentoxifylline for renal protection in diabetic kidney disease. A model of old drugs for new horizons. J Clin Med. 2019 Feb 27;8(3). pii: E287. doi: 10.3390/jcm8030287
- Donate-Correa J, Martín-Núñez E, Ferri C, Hernández-Carballo C, García-Tagua V, Delgado-Molinos A, López-Castillo A, Rodríguez-Ramos S, Cerro-López P, Castro López-Tarruella V, Arévalo-González MA, Pérez-Delgado N, Mora-Fernández C, Navarro-González JF. FGF23 and Klotho levels are independently associated with diabetic foot síndrome in type 2 diabetes mellitus. J Clin Med. 2019 Apr 3;8(4). pii: E448. doi: 10.3390/jcm8040448
- Martín-Núñez E, Donate-Correa J, Kannengiesser C, De Brauwere DP, Leroy C, Oudin C, Friedlander G, Prieto-Morín C, Tagua VG, Ureña-Torres PA, Navarro- González JF. A novel heterozygous deletion variant in KLOTHO gene leading to haploinsufficiency and impairment of fibroblast growth factor 23 signaling pathway. J Clin Med. 2019 Apr 12;8(4). pii: E500. doi: 10.3390/jcm8040500
- Valdivielso JM, Bozic M, Galimudi RK, Bermúdez-López M, Navarro-González JF, Fernández E, Betriu A, on behalf of the NEFRONA investigators. Association of the rs495392 Klotho polymorphism with atheromatosis progression in chronic kidney disease patients. Nephrol Dial Transplant. 2019 Dec 1;34(12):2079-2088. doi: 10.1093/ndt/gfy207

**Selected publications from the last 10 years:**

- Navarro-González JF, Sánchez-Niño MD, Donate-Correa J, Martín-Núñez E, Ferri C, Pérez-Delgado N, Górriz JL, Martínez-Castelao A, Ortiz A, Mora-Fernández C. Effects of pentoxifylline on soluble Klotho concentrations and renal tubular cell expression in diabetic kidney disease. Diabetes Care. 2018 Aug;41(8):1817-1820. doi:10.2337/dc18-0078
- Donate-Correa J, Henriquez-Palop F, Martín-Núñez E, Pérez-Delgado N, Muros-de-Fuentes M, Mora-Fernandez C, Navarro-González JF. Effect of Paricalcitol on FGF-23 and Klotho in kidney transplant recipients. Transplantation. 2016;100(11):2432-2438. doi: 10.1097/TP.0000000000001339
- Donate-Correa J, Martín-Núñez E, Perez Delgado N, Muros de Fuentes M, Ortiz Arduan A, Mora-Fernandez C, Navarro-Gonzalez JF. Implications of fibroblast growth factor/Klotho system in glucose metabolism and diabetes. Cytokine Growth Factor Rev. 2016 Apr;28:71-7. doi: 10.1016/j.cytogfr.2015.12.003
- Donate-Correa J, Martín-Núñez E, Martinez-Sanz R, Muros de Fuentes M, Mora-Fernandez C, Pérez-Delgado N, Navarro-González JF. Influence of Klotho gene polymorphisms on vascular gene expression and its relationship to cardiovascular disease. J Cell Mol Med. 2016 Jan;20(1):128-33. doi: 10.1111/jcmm.12710
- Navarro-González JF, Mora-Fernández C, Muros de Fuentes M, Chahin J, Méndez ML, Gallego E, Macía M, del Castillo N, Rivero A, Getino MA, García P, Jarque A, García J. Effect of pentoxifylline on renal function and urinary albumin excretion in patients with diabetic kidney disease: the PREDIAN trial. J Am Soc Nephrol. 2015 Jan;26(1):220-9. doi: 10.1681/ASN.2014010012

### *Inflammatory response and tissue damage in rheumatoid arthritis*

**Principal Investigator:**

- José Federico Díaz González, MD, PhD (Professor of Medicine, Department of Internal Medicine, Dermatology and Psychiatry, ULL – Head of Rheumatology Service, HUC)

**Postdoctoral clinical collaborators:**

- Judith Mª López Fernández, MD, PhD (Attending Physician, Endocrinology Service, HUC)
- Iván Ferraz Amaro, MD, PhD (Attending Physician, Rheumatology Service, HUC)

**External postdoctoral collaborators:**

- Javier Rafael Castro Hernández, PhD (PI Project: Role of autophagy in the regulation of intercellular junctions mediated by alpha 2 adrenergic receptors in endothelial cells. – "Papel de la autofagia en la regulación de las uniones intercelulares mediadas por los receptores alpha2 adrenérgicos en células endoteliales" FUNCANIS 24,500 €. 2018-2020)

**PhD students and trainees:**

- María Teresa Arce Franco (Predoctoral Researcher, The Canary Islands Health Research Institute Foundation, FIISC. Role of Alpha 2 adrenergic receptor subtypes in the acute and joint inflammatory response *in vivo* – "Papel de los subtipos de receptores alpha2 adrenérgicos en la regulación de la respuesta inflamatoria aguda y articular *in vivo*").
- Sergio Ivan Santos Concepción (Predoctoral Researcher, The Canary Islands Health Research Institute Foundation, FIISC. Role of Alpha 2 adrenergic receptor subtypes in the acute and joint inflammatory response in vivo – "Papel de los subtipos de receptores alpha2 adrenérgicos en la regulación de la respuesta inflamatoria aguda y articular in vivo").

**Technical and administrative staff:**

- Elsa González Oramas (Administrative, Project Manager, Predoctoral Researcher, FIISC)

**Research Lines:**

- Role of free oxygen radicals in regulating first phase inflammatory responses.
- In vivo effect of anti-L-selectin substances in neutrophil migration.
- Modulation of the acute inflammatory response by the Alpha 2 adrenergic receptor.
- Role of B cell secreted soluble factors, cytokines and chemokines in the pathogenesis of rheumatoid arthritis.
- The capacity of resident pancreatic tissue stem cells to differentiate into adult endocrine pancreatic cells.
- Modulation of the acute and chronic inflammatory response by LXR receptors.
- Physical activity in patients with chronic joint diseases: a link between clinical activity and the capacity for movement.

**Funded projects:**

- Role of Alpha 2 adrenergic receptor subtypes in the acute and joint inflammatory response in vivo ("Papel de los subtipos de receptores alpha2 adrenérgicos en la regulación de la respuesta inflamatoria aguda y articular in vivo"). PI: Federico Díaz. Institute of Health Carlos III (2016-2019, 90,000 €).

**Publications 2019:**

- Sanchez-Piedra C, Hernández Miguel MV, Manero J, Roselló R, Sánchez-Costa JT, Rodríguez-Lozano C, Campos C, Cuende E, Fernández-Lopez JC, Bustabad S, Martín Domenech R, Pérez-Pampín E, Del Pino-Montes J, Millan-Arciniegas AM, Díaz-González F, Gómez-Reino JJ; On behalf of the BIOBADASER Study Group. Objectives and methodology of BIOBADASER phase III [Objetivos y metodología de la fase III de BIOBADASER]. Reumatol Clin. 2019 Jul Aug;15(4):229-236. doi: 10.1016/j.reuma.2017.08.001
- Ferraz-Amaro I, Hernández-Hernández MV, Tejera-Segura B, Delgado-Frías E, Macía-Díaz M, Machado JD, Diaz-González F. Effect of IL-6 Receptor Blockade on Proprotein Convertase Subtilisin/Kexin Type-9 and Cholesterol Efflux Capacity in Rheumatoid Arthritis Patients. Horm Metab Res. 2019 Mar;51(3):200-209. doi: 10.1055/a-0833-4627
- Hernandez MV, Sanchez-Piedra C, Garcia-Magallon B, Cuende E, Manero J, Campos-Fernandez C, Martin-Domenech R, Del Pino-Montes J, Manrique S, Castro-Villegas MC, Ruiz-Montesinos D, Sanchez-Alonso F, Diaz-Gonzalez F, Cea-Calvo L, Gómez-Reino JJ; BIOBADASER Study Group. Factors associated with long- term retention of treatment with golimumab in a real-world setting: an analysis of the Spanish BIOBADASER registry. Rheumatol Int. 2019 Mar;39(3):509-515. doi: 10.1007/s00296-018-4177-z
- Domínguez-Luis MJ, Armas-González E, Herrera-García A, Arce-Franco M, Feria M, Vicente-Manzanares M, Martínez-Ruiz A, Sánchez-Madrid F, Díaz-González F. L-selectin expression is regulated by CXCL8-induced reactive oxygen species produced during human neutrophil rolling. Eur J Immunol. 2019 Mar;49(3):386-397. doi: 10.1002/eji.201847710
- López-Isac E, Acosta-Herrera M, Kerick M, Assassi S, Satpathy AT, Granja J, Mumbach MR, Beretta L, Simeón CP, Carreira P, Ortego-Centeno N, Castellvi I, Bossini-Castillo L, Carmona FD, Orozco G, Hunzelmann N, Distler JHW, Franke A, Lunardi C, Moroncini G, Gabrielli A, de Vries-Bouwstra J, Wijmenga C, Koeleman BPC, Nordin A, Padyukov L, Hoffmann-Vold AM, Lie B; European Scleroderma Group (Diaz-Gonzalez F). GWAS for systemic sclerosis identifies multiple risk loci and highlights fibrotic and vasculopathy pathways. Nat Commun. 2019 Oct 31;10(1):4955. doi: 10.1038/s41467-019-12760-y
- Seoane-Mato D, Sánchez-Piedra C, Silva-Fernández L, Sivera F, Blanco FJ, Pérez Ruiz F, Juan-Mas A, Pego-Reigosa JM, Narváez J, Quilis Martí N, Cortés Verdú R, Antón-Pagés F, Quevedo Vila V, Garrido Courel L, Del Amo NDV, Paniagua Zudaire I, Añez Sturchio G, Medina Varo F, Ruiz Tudela MDM, Romero Pérez A, Ballina J, Brandy García A, Fábregas Canales D, Font Gayá T, Bordoy Ferrer C, González Álvarez B, Casas Hernández L, Álvarez Reyes F, Delgado Sánchez M, Martínez Dubois C, Sánchez-Fernández SÁ, Rojas Vargas LM, García Morales PV, Olivé A, Rubio Muñoz P, Larrosa M, Navarro Ricos N, Graell Martín E, Chamizo E, Chaves Chaparro L, Rojas Herrera S, Pons Dolset J, Polo Ostariz MÁ, Ruiz-Alejos Garrido S, Macía Villa C, Cruz Valenciano A, González Gómez ML, Morcillo Valle M, Palma Sánchez D, Moreno Martínez MJ, Mayor González M, Atxotegi Sáenz de Buruaga J, Urionagüena Onaindia I, Blanco Cáceres BA, Díaz-González F, Bustabad S. Prevalence of rheumatic diseases in adult population in Spain (EPISER 2016 study): Aims and methodology

[Prevalencia de enfermedades reumáticas en población adulta en España (estudio EPISER 2016). Objetivos y metodología]. Reumatol Clin. 2019 Mar - Apr;15(2):90-96. doi: 10.1016/j.reuma.2017.06.009

- Rodríguez-Lozano B, González-Febles J, Garnier-Rodríguez JL, Dadlani S, Bustabad-Reyes S, Sanz M, Sánchez-Alonso F, Sánchez-Piedra C, González-Dávila E, Díaz-González F. Association between severity of periodontitis and clinical activity in rheumatoid arthritis patients: A case-control study. Arthritis Res Ther. 2019 Jan18;21(1):27. doi: 10.1186/s13075-019-1808-z
- Rovin BH, Solomons N, Pendergraft WF 3rd, Dooley MA, Tumlin J, Romero-Diaz J, Lysenko L, Navarra SV, Huizinga RB; AURA-LV Study Group (Diaz-Gonzalez F). A randomized, controlled double-blind study comparing the efficacy and safety of dose-ranging voclosporin with placebo in achieving remission in patients with active lupus nephritis. Kidney Int. 2019 Jan;95(1):219-231. doi: 10.1016/j.kint.2018.08.025
- Urruticoechea-Arana A, Cobo-Ibáñez T, Villaverde-García V, Santos Gómez M, Loza E, Vargas-Osorio K, Fariñas Padrón L, Diaz-Gonzalez F, Calvo-Río V, Blanco R. Efficacy and safety of biological therapy compared to synthetic immunomodulatory drugs or placebo in the treatment of Behçet's disease associated uveitis: a systematic review. Rheumatol Int. 2019 Jan;39(1):47-58. doi: 10.1007/s00296-018-4193-z
- Abad Hernández MÁ, Andreu JL, Balsa Criado A, Díaz-González F, Moreno Muelas JV, Queiro Silva R, Gómez-Reino JJ. Update of the Position Paper of the Spanish Society of Rheumatology on Biosimilar Drugs. Reumatol Clin. 2019 May 1. pii: S1699-258X(19)30059-2. doi: 10.1016/j.reuma.2019.03.007. [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Álvaro-Gracia JM, Jover JA, García-Vicuña R, Carreño L, Alonso A, Marsal S, Blanco F, Martínez-Taboada VM, Taylor P, Martín-Martín C, DelaRosa O, Tagarro I, Díaz-González F. Intravenous administration of expanded allogeneic adipose-derived mesenchymal stem cells in refractory rheumatoid arthritis (Cx611): results of a multicentre, dose escalation, randomised, single-blind, placebo-controlled phase Ib/IIa clinical trial. Ann Rheum Dis. 2017 Jan;76(1):196-202. doi:10.1136/annrheumdis-2015-208918
- Cutolo M, Myerson GE, Fleischmann RM, Liote F, Díaz-González F, Van den Bosch F, Mazo-Ortega H, Feist E, Shan K, Hu C, Stevens RM, Poder A. A phase III, randomized, controlled trial of Apremilast in patients with psoriatic arthritis: resilys of the PALACE 2 trial. JRheumatol. 2016 Sep;43(9):1724-34. doi:10.3899/jrheum.151376
- Armas-González E, Diaz-Martin A, Dominguez-Luis MJ, Arce Franco MT, Herrero Garcia A, Hernandez-Hernandez MV, Bustabad S, Usategui A, Pablos JL, Canete JD, Díaz-González F. Differential antigen-presenting B cell phenotypes from synovial microenvironment of patients with rheumatoid and psoriatic arthritis. J Rheumatol. 2015 Oct;42(10):1825-34. doi: 10.3899/jrheum.141577
- Delgado-Frias E, Lopez-Mejias R, Genre F, Ubilla B, Gomez Rodriguez-Bethencourt MA, González-Díaz A, de Vera-Gonzalez AM, Gonzalez-Rivero AF, Diaz-Gonzalez F, Gonzalez-Gay MA, Ferraz-Amato I. Relatioship between endothelial dysfunction and osteoprotegerin, vitamin D, and bone mineral density in patients with rheumatoid arthritis. Clin Exp Rheumatol. 2015 Mar-Apr;33(2):241-9

- Ferraz-Amaro I, Gonzalez-Gay MA, Diaz-González F. Retinol-binding Protein 4 in Rheumatoid Arthritis-related Insulin Resistance and β-cell Function. J Rheumatol. 2014 Apr;41(4):658-65. doi: 10.3899/jrheum.130834
- Herrera-García AM, Domínguez-Luis MJ, Arce-Franco M, Armas-González E, Álvarez de La Rosa D, Machado JD, Pec MK, Feria M, Barreiro O, Sánchez-Madrid F, Díaz-González F. Prevention of neutrophil extravasation by α2-adrenoceptor-mediated endothelial stabilization. J Immunol. 2014 Sep 15;193(6):3023-35. doi:10.4049/jimmunol.1400255

## 3.- DRUG DEVELOPMENT & TARGET IDENTIFICATION

This programme has recently been created to promote the development of projects focused on the search for new compounds with therapeutic potential, new drug delivery systems and the identification of pharmacological targets. This programme brings together three research teams that use complementary approaches and numerous collaborations with groups from the other three programmes of the Institute.

### *Drug release systems*

**Principal Investigators:**

- Carmen María Évora García, PhD (Professor of Pharmaceutical Technology, Department of Clinical Engineering and Pharmaceutical Technology, ULL)
- Araceli Delgado Hernández, PhD (Professor of Pharmaceutical Technology, Department of Clinical Engineering and Pharmaceutical Technology, ULL)

**Postdoctoral Researchers:**

- Edgar Pérez Herrero, PhD (Assistant Lecturer; Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- Ricardo Reyes Rodríguez, PhD (Assistant Lecturer, Department of Chemical Engineering and Pharmaceutical Technology, ULL)
- Patricia Díaz Rodríguez, PhD (Assistant Lecturer, Department of Chemical Engineering and Pharmaceutical Technology, ULL)

**PhD students and trainees:**

- Patricia García García (PhD student)

**Research Lines:**

- Systems of release for cartilage and bone regeneration, and for the resection of leiomyomas
- Biodistribution of nanoparticle systems

**Funded projects:**

- Injectable systems for bone regeneration in Osteoporosis (MAT2014-55657-R – "Sistemas inyectables para regeneración ósea en Osteoporosis"). PI: Carmen M. Évora. Ministry of Economy and Competitiveness, MINECO (2014-2018, extended until September 2019, 60,500 €)
- Oligonucleotide-hybrid-nanosystems for local and systemic targeted therapies (RTI2018-097324-B-I00). PI: Carmen Évora, Araceli Delgado. Ministry of Science, Innovation and Universities (2019-2021, 181,500 €)
- Preclinical development of a new drug for the treatment of hyperuricemia and hyperuremia (Exp. Matriz 19120187 – "Desarrollo preclínico de un nuevo fármaco para el tratamiento de la hiperuricemia e hiperuremia"). PIs: Araceli Delgado, Esteban Porrini. Arafarma Group S.A., FGULL (2019-2020, 199,870 €)

**Publications 2019:**

- García-García P, Reyes R, Segredo-Morales E, Pérez-Herrero E, Delgado A, Évora C. PLGA-BMP-2 and PLA-17β-Estradiol Microspheres Reinforcing a Composite Hydrogel for Bone Regeneration in Osteoporosis. Pharmaceutics. 2019 Dec 3;11(12). pii: E648. doi: 10.3390/pharmaceutics11120648
- Goimil L, Santos-Rosales V, Delgado A, Évora C, Reyes R, Lozano-Pérez A, Aznar-Cervantes S, Cenis JL, Gómez-Amoza JL, Concheiro A, Alvarez-Lorenzo C, García-González CA. ScCO2-foamed silk fibroin aerogel/poly (ϵ-caprolactone) scaffolds containing dexamethasone for bone regeneration. Journal of $CO_2$ Utilization. 2019; 31, pp. 51-64. doi: 10.1016/j.jcou.2019.02.016
- Vayas R, Reyes R, Arnau MR, Évora C, Delgado A. Injectable Scaffold for Bone Marrow Stem Cells and Bone Morphogenetic Protein-2 to Repair Cartilage. Cartilage. 2019 Apr. doi: 10.1177/1947603519841682 [Epub ahead of print]
- Pérez-Herrero E, García-García P, Gómez-Morales J, Llabrés M, Delgado A, Évora C. New injectable two-step forming hydrogel for delivery of bioactive substances in tissue regeneration. Regenerative Biomaterials. 2019 Jun;6(3):149-162. doi: 10.1093/rb/rbz018
- García-García P, Ruiz M, Reyes R, Delgado A, Évora C, Riancho JA, Rodríguez-Rey JC, Pérez-Campo FM. Smurf1 Silencing Using a LNA-ASOs/Lipid Nanoparticle System to Promote Bone Regeneration. Stem Cells Transl Med. 2019 Dec;8(12):1306-1317. doi: 10.1002/sctm.19-0145
- de Moraes Lenz T, Escanéz Pérez A, Tur R, Delgado A, Évora C, Almansa E. First attempts of the use of intake tracers in encapsulated diets with chitosan for octopus paralarvae. Aquaculture Research. 2019 Oct;50(10):3070-3073. doi: 10.1111/are.14234
- Garcia-Orue I, Gainza G, Garcia-Garcia P, Gutierrez FB, Aguirre JJ, Hernandez RM, Delgado A, Igartua M. Composite nanofibrous membranes of PLGA/Aloe vera containing lipid nanoparticles for wound dressing applications. Int J Pharm. 2019 Feb 10;556:320-329. doi: 10.1016/j.ijpharm.2018.12.010
- Selected publications from the last 10 years:
- Segredo-Morales E, Reyes R, Arnau MR, Delgado A, Évora C. In situ gel-forming system for dual BMP-2 and 17β-estradiol controlled release for bone regeneration in osteoporotic rats. Drug Deliv Transl Res. 2018 Oct;8(5):1103-1113. doi: 10.1007/s13346-018-0574-9
- Del Rosario C, Rodriguez-Evora M, Reyes R, Évora C. BMP-2, PDGF-BB and bone marrow mesenchymal cells in a macroporous d-TCP scaffold for critical-size bone defect repair in rats. Biomed Mater. 2015 Jul 23;10(4):045008. doi: 10.1088/1748-6041/10/4/045008
- Del Rosario C, Rodriguez-Evora M, Reyes R, Gonzalez-Orive A, Hernandez-Creus A, Shakesheff KM, White LJ, Delgado A, Évora C. Evaluation of nanostructure and microstructure of bone

regenerated by BMP-2-porous scaffolds. J Biomed Mater Res A. 2015 Sep;103(9):2998-3011. doi: 10.1002/jbm.a.35436
- Rodríguez-Evora M, Reyes R, Alvarez-Lorenzo C, Concheiro A, Delgado A, Evora C. Bone regeneration induced by an in situ gel-forming poloxamine, bone morphogenetic protein-2 system. J Biomed Nanotechnol. 2014 Jun;10(6):959-69. doi: 10.1166/jbn.2014.1801 Modelización matemática de sistemas biológicos y enfermedades humanas

### *Mathematical modelling of biological systems and human diseases*

**Principal Investigator:**

- Néstor Torres Darias, PhD (Professor of Biochemistry and Molecular Biology, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)

**Postdoctoral Researchers:**

- Daniel V. Guebel, PhD ("Agustín de Betancourt" Researcher, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)
- Carmen Laura Sayas Casanova "Agustín de Betancourt" Researcher, Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL)

**Research lines:**

We use a combination of mathematical modelling, computational biology and machine learning techniques to tackle biomedical and biotechnological problems. So far, we have concentrated our efforts on identifying molecular targets for the treatment of infectious diseases (malaria, leishmania, AIDS), bioprocess optimisation and improvement (carnitine, terpenes), and more recently, in analysing the molecular basis in Alzheimer's disease. In this latter field, we are currently developing a technological transfer project to set up a reliable non-invasive method for early Alzheimer's diagnosis.

**Funded projects:**

- Identification of therapeutic targets and generation of neuroprotective peptides in Alzheimer's disease and related taupathies. Agustín de Betancourt Project ("Identificación de nuevas dianas terapéuticas y generación de nuevos péptidos neuroprotectores en la enfermedad de Alzheimer y tauopatías relacionadas"). PI: Laura Sayas Casanova; Supervisor: Néstor Torres. Regional Government of Tenerife (2017-2021, 160,000 €.)
- Proof of concept for a non-invasive technology for early diagnosis of Sporadic Alzheimer's Disease based on circulating exosomes in peripheral blood. Agustín de Betancourt Project ("Prueba de concepto para una tecnología no-invasiva de diagnóstico temprano de Enfermedad de Alzheimer Esporádica basada en exosomas circulantes en sangre periférica") PI: Daniel V. Guebel; IP-ULL: Néstor Torres. Regional Government of Tenerife (granted in 2018, implementation 2019-2023, 160,000 €)

**Publications 2019:**

- Dorta-Guerra R, Marrero I, Abdul-Jalbar B, Trujillo-González R, Torres NV. A new academic performance indicator for the first term of first-year science degrees students at La Laguna University: a predictive model. FEBS Open Bio. 2019 Sep;9(9):1493-1502. doi: 10.1002/2211-5463.12707
- Sayas CL, Medina M, Cuadros R, Ollá I, García E, Pérez M, Ferrer I, Hernández F, Avila J. Role of tau N-terminal motif in the secretion of human tau by End Binding proteins. PLoS One. 2019 Jan 22;14(1): e0210864. doi: 10.1371/journal.pone.0210864
- Sayas CL, Basu S, van der Reijden M, Bustos-Morán E, Liz M, Sousa M, van IJcken WFJ, Avila J, Galjart N. Distinct Functions for Mammalian CLASP1 and -2 During Neurite and Axon Elongation. Front Cell Neurosci. 2019 Jan 29;13:5. doi: 10.3389/fncel.2019.00005
- Gozes I, Ivashko-Pachima Y, Kapitansky O, Sayas CL, Iram T. Single-cell analysis of cytoskeleton dynamics: From isoelectric focusing to live cell imaging and RNA-seq. J Neurosci Methods. 2019 Jul 15;323: 119-124. doi: 10.1016/j.jneumeth.2019.05.014
- Ivashko-Pachima Y, Hadar A, Grigg I, Korenková V, Kapitansky O, Karmon G, Gershovits M, Sayas CL, Kooy RF, Attems J, Gurwitz D, Gozes I. Discovery of autism/intellectual disability somatic mutations in Alzheimer's brains: mutated ADNP cytoskeletal impairments and repair as a case study. Mol Psychiatry. 2019 Oct 30. doi: 10.1038/s41380-019-0563-5. [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Guebel DV, Torres NV. Sexual dimorphism and aging in the human hippocampus: Identification, validation and impact of differentially expressed genes by factorial microarray and network analysis. Front Aging Neurosci. 2016 Oct 5;8:229. doi: 10.3389/fnagi.2016.00229
- Santos G, Díaz M, Torres NV. Lipid Raft Size and Lipid Mobility in Non-raft Domains Increase during Aging and Are Exacerbated in APP/PS1 Mice Model of. Predictions from an Agent-Based Mathematical Model. Front Physiol. 2016 Mar 15;7:90. doi: 10.3389/fphys.2016.00090
- Guebel DV, Perera-Aberto M, Torres NV. Q-GDEMAR: a general method for the identification of differentially expressed genes in microarrays with unbalanced groups. Mol Biosyst. 2016 Jan;12(1):120-32. doi: 10.1039/c5mb00541h
- Santos G, Torres NV. New Targets for Drug Discovery against Malaria. PLoS ONE. 2013;8(3):e59968. doi: 10371/journal.pone.00599968
- Santos G, Hormiga JA, Arense P, Canovas M, Torres NV. Modelling and analysis of central metabolism operating regulatory interactions in salt stress conditions in a L-carnitine overproducing E. coli strain. PLoS ONE. 2012;7(4):e34533. doi: 10.1371/journal.pone.0034533

### *BioLab ("Phenotypic drug discovery")*

**Principal Investigator:**

- José Manuel Padrón (University Lecturer; Department of Organic Chemistry, ULL)

**Postdoctoral Researchers:**

- Miguel X. Fernandes ("Agustín de Betancourt" Researcher, ULL)

**PhD students and trainees:**

- Adrián Puerta Arocha (Doctorate Program in Health Sciences, PGC2018-094503-B-C22, MCIU/AEI/FEDER, UE)
- Alexis Galán Rodríguez (Doctorate Program in Chemistry, PGC2018-094503-B-C22, MCIU/AEI/FEDER, UE)
- Amina Moutayakine (Doctorate Program in Chemistry, PGC2018-094503-B-C22, MCIU/AEI/FEDER, UE)
- Alicia Hernández Pérez (Doctorate Program in Health Sciences, Doctorado Industrial, Orfan Biotech SL)

**Research lines:**

- Drug discovery: Early identification of the therapeutic targets of biologically active molecules. The identification of the biological targets with which the small molecules interact is determined based on phenotypic and in silico experimental data. Once the biological target has been predicted, the process to validate it goes through the confirmation of the activity of the compound on the proposed target. The next step involves studying the effect in live models, when the compound gains added value and the viability of its technology transfer is evaluated.
- Bioprospecting of marine and terrestrial resources. The search for new bioactive compounds from natural sources has been motivated by the increase in the worldwide incidence of various types of cancer and the emergence of pathogens resistant to the available antibiotics. Our institute participates in the bioprospecting of marine and terrestrial resources in our region, Latin America, Africa and Asia in order to access substances of interest to the pharmaceutical, cosmetic, food or veterinary industries.
- Design and synthesis of molecular probes. The fluorescent probes used in immunofluorescence techniques are usually antibodies. However, anchoring a fluorescent group to a small molecule by derivatisation facilitates cell localization studies. Based on the results of structure-function studies, we can define the site in the reference molecule where a fluorescent fragment can be introduced.

**Funded projects:**

- Preparation of the MSC-ITN action “Multitargeted therapies against pancreatic ductal adenocarcinoma (PANCNET, EIN2019-102928) PI: José M. Padrón (01/06/2019 to 31/05/2021, 16,200 €).
- Inhibition of glutamine metabolism as therapy against pancreatic ductal adenocarcinoma ("Inhibición del metabolismo de la glutamina como terapia contra el adenocarcinoma ductal pancreático. "Agustín de Betancourt") project. PI: Miguel X. Fernandes; IP-ULL: José M. Padrón. Regional Government of Tenerife (2018-2022, 160,000 €).

**Publicactions 2019:**

- Filipović NR, Ristić P, Janjić G, Klisuric O, Padron JM, Donnard M, Gulea M, Todorović TR. Silver-based monomer and coordination polymer with organic thiocyanate ligand: Structural, computational and antiproliferative activity study. 2019 Polyhedron 173,114132 doi: 10.1016/j.poly.2019.114132

- Sánchez-Fernández EM, García-Moreno MI, Arroba AI, Aguilar-Diosdado M, Padrón JM, García-Hernández R, Gamarro F, Fustero S, Sánchez-Aparicio J-E, Masgrau L, García Fernández JM, Ortiz Mellet C. Synthesis of polyfluoroalkyl SP2-iminosugar glycolipids and evaluation of their immunomodulatory properties towards anti-tumor, anti-leishmanial and anti-inflammatory therapies. 2019 European Journal of Medicinal Chemistry 182,111604. doi: 10.1016/j.ejmech.2019.111604
- Roldán-Peña JM, Romero-Real V, Hicke J, Maya I, Franconetti A, Lagunes I, Padrón JM, Petralla S, Poeta E, Naldi M, Bartolini M, Monti B, Bolognesi ML, López Ó, Fernández-Bolaños JG. Tacrine-O-protected phenolics heterodimers as multitarget-directed ligands against Alzheimer's disease: Selective subnanomolar BuChE inhibitors. 2019 Eur J Med Chem. 2019 Nov 1;181:111550. doi: 10.1016/j.ejmech.2019.07.053
- Cortés-Percino A, Vega-Báez JL, Romero-López A, Puerta A, Merino-Montiel P, Meza-Reyes S, Padrón JM, Montiel-Smith S. Synthesis and evaluation of pyrimidine steroids as antiproliferative agents. Molecules. 2019 Oct 12;24(20). pii: E3676. doi: 10.3390/molecules24203676
- Ingold M, Colella L, Hernández P, Batthyány C, Tejedor D, Puerta A, García-Tellado F, Padrón JM, Porcal W, López GV. A Focused Library of NO-Donor Compounds with Potent Antiproliferative Activity Based on Green Multicomponent Reactions. ChemMedChem. 2019 Sep 18;14(18):1669-1683. doi: 10.1002/cmdc.201900385
- Sánchez-Fernández EM, García-Moreno MI, García-Hernández R, Padrón JM, García Fernández JM, Gamarro F, Ortiz Mellet C. Thiol-ene "click" synthesis and pharmacological evaluation of C-glycoside SP2-iminosugar glycolipids. Molecules. 2019 Aug 8;24(16). pii: E2882. doi: 10.3390/molecules24162882
- Sánchez-Tafolla L, Padrón JM, Mendoza G, Luna-Rodríguez M, Fernández JJ, Norte M, Trigos Á. Antiproliferative activity of biomass extract from Pseudomonas cedrina. 2019 Electronic Journal of Biotechnology 40, pp. 40-44. doi: 10.1016/j.ejbt.2019.03.010
- Castillo QA, Padrón JM, Wojtas L, Keramane M, Germosén EA. Koanolide A, antiproliferative germacrane-type sesquiterpene lactone from Koanophyllon gibbosum. 2019 Tetrahedron Letters 60(25), pp. 1640-1642. doi: 10.1016/j.tetlet.2019.05.036
- Luque-Agudo V, Albarrán-Velo J, Light ME, Padrón JM, Román E, Serrano JA, Gil MV. Synthesis and antiproliferative activity of new 2-glyco-3-nitro-2H-chromenes. Bioorg Chem. 2019 Jun;87:112-116. doi: 10.1016/j.bioorg.2019.03.016
- Castro SJ, Casero CN, Padrón JM, Nicotra VE. Selective Antiproliferative Withanolides from Species in the Genera Eriolarynx and Deprea. J Nat Prod. 2019 May 24;82(5):1338-1344. doi: 10.1021/acs.jnatprod.9b00117
- Patel DM, Sharma MG, Vala RM, Lagunes I, Puerta A, Padrón JM, Rajani DP, Patel HM. Hydroxyl alkyl ammonium ionic liquid assisted green and one-pot regioselective access to functionalized pyrazolodihydropyridine core and their pharmacological evaluation. Bioorg Chem. 2019 May;86:137-150. doi: 10.1016/j.bioorg.2019.01.029
- Hamulić D, Stadler M, Hering S, Padrón JM, Bassett R, Rivas F, Loza-Mejía MA, Dea-Ayuela MA, González-Cardenete MA. Synthesis and Biological Studies of (+)-Liquiditerpenoic Acid A (Abietopinoic Acid) and Representative Analogues: SAR Studies. J Nat Prod. 2019 Apr 26;82(4):823-831. doi: 10.1021/acs.jnatprod.8b00884
- Beer MF, Bivona AE, Sánchez Alberti A, Cerny N, Reta GF, Martín VS, Padrón JM, Malchiodi EL, Sülsen VP, Donadel OJ. Preparation of sesquiterpene lactone derivatives: Cytotoxic activity and selectivity of action. Molecules. 2019 Mar 20;24(6). pii: E1113. doi: 10.3390/molecules24061113

- Padrón JM, Emiliano A, Castillo QA. Secondary Metabolites from Pterocaulon alopecuroides and their Antiproliferative Activities. 2019 Pharmacognosy Journal 11(3), pp. 493-495. doi: 10.5530/pj.2019.11.78
- Franceschy C, Espinoza C, Padrón JM, Landa-Cadena G, Norte M, Fernández JJ, Shnyreva A, Trigos Á. Antiproliferative potential of 3β,5α,6β,7α- tetrahydroxyergosta-8(14),22-diene produced by Acremonium persicinum isolated from an alkaline crater lake in Puebla, Mexico. Nat Prod Res. 2019 Sep 26:1-4. doi: 10.1080/14786419.2019.1669032. [Epub ahead of print]
- Brahmbhatt GC, Sutariya TR, Atara HD, Parmar NJ, Gupta VK, Lagunes I, Padrón JM, Murumkar PR, Yadav MR. New pyrazolyl-dibenzo[b,e][1,4]diazepinones: room temperature one-pot synthesis and biological evaluation. Mol Divers. 2019 May 24. doi: 10.1007/s11030-019-09958-z. [Epub ahead of print]
- Lagunes I, Begines P, Silva A, Galán AR, Puerta A, Fernandes MX, Maya I, Fernández-Bolaños JG, López Ó, Padrón JM. Selenocoumarins as new multitarget antiproliferative agents: Synthesis, biological evaluation and in silico calculations. Eur J Med Chem. 2019 Oct 1;179:493-501. doi: 10.1016/j.ejmech.2019.06.073
- Dinić J, Ríos-Luci C, Karpaviciene I, Cikotiene I, Fernandes MX, Pešić M, Padrón JM. CKT0353, a novel microtubule targeting agent, overcomes paclitaxel induced resistance in cancer cells. Invest New Drugs. 2019 Jun 8. doi: 10.1007/s10637-019- 00803-6. [Epub ahead of print]
- Rodriguez-Rodriguez AE, Donate-Correa J, Rovira J, Cuesto G, Luis-Ravelo D, Fernandes MX, Acevedo-Arozena A, Diekmann F, Acebes A, Torres A, Porrini E. Inhibition of the mTOR pathway: A new mechanism of β cell toxicity induced by Tacrolimus. Am J Transplant. 2019 Dec;19(12):3240-3249. doi: 10.1111/ajt.15483
- Serina J, Fernandes MX, Castilho PC. Effects of hydroxycinnamic acids on the glycolysis pathway. 2019 South African Journal of Botany 120, pp. 219-229. doi: 10.1016/j.sajb.2018.06.016
- Other selected publications from the last 10 years:
- Podolski-Renić A, Banković J, Dinić J, Ríos-Luci C, Fernandes MX, Ortega N, Kovačević-Grujičić N, Martín VS, Padrón JM, Pešić M. DTA0100, dual topoisomerase II and microtubule inhibitor, evades paclitaxel resistance in P- glycoprotein overexpressing cancer cells. Eur J Pharm Sci. 2017 Jul 15;105:159-168. doi: 10.1016/j.ejps.2017.05.011
- Silveira-Dorta G, Sousa IJ, Fernandes MX, Martín VS, Padrón JM. Synthesis and identification of unprecedented selective inhibitors of CK1ε. Eur J Med Chem. 2015;96:308-17. doi: 10.1016/j.ejmech.2015.03.046
- Silveira-Dorta G, Martín VS, Padrón JM. Synthesis and antiproliferative activity of glutamic acid-based dipeptides. Amino Acids. 2015 Aug;47(8):1527-32. doi: 10.1007/s00726-015-1987-0

## 4.- NEUROBIOLOGY & BRAIN-RELATED DISEASES

This programme integrates groups working on the biology and pathology of the Nervous System, specifically: neurodegenerative diseases, the molecular and cellular basis of neuronal vulnerability, the development of animal models to study the genetic basis of neurodegeneration, and the analysis of global brain function and the biological basis of cognition. The role of specific membrane proteins (ion channels and transporters) and signalling molecules in different excitable cells is studied at the cellular and molecular level using electrophysiological, molecular and morphological techniques. An emerging platform within this programme is dedicated to developing novel animal models for neurodegenerative diseases. Several research lines centre on the analysis of the human brain as a

whole, using electrophysiological and neuroimaging techniques. Together, these studies provide a holistic approach to the human nervous system, which will contribute to the search for new therapies to combat neurodegenerative diseases.

## Molecular and Cellular Neurobiology

### *Molecular basis of human channelopathies (MOLCAN)*

**Principal Investigator:**

- Teresa Giráldez Fernández, PhD (Lecturer in Physiology, Department of Basic Medical Sciences, ULL)

**Postdoctoral Researchers:**

- Alejandro Cerrada de Dueñas, PhD (Postdoctoral researcher, contracted by ERC project until September 2019, ULL)
- Aravind Kshatri, PhD ("Juan de la Cierva" researcher, Department of Basic Medical Sciences, ULL)
- David Bartolomé Martín, PhD (Postdoctoral researcher, contracted by ERC project, ULL)
- Ricardo Gómez García, PhD (Postdoctoral researcher, contracted by ERC project, ULL)
- Laura E. Maglio, PhD (Postdoctoral researcher, contracted by ERC Project, ULL)
- Belinda Rivero, PhD (Postdoctoral researcher, "Agustín de Betencourt" programme, Department of Basic Medical Sciences, ULL)

**PhD students and trainees:**

- Alberto J. González Hernández (funded by FPU, ULL)
- Elva Martín Batista (funded by FPU, ULL)
- Rebeca Martínez Lázaro (Master's project and PhD student)

**Technical and administrative staff:**

- Nair Mesejo Nores (Project manager, contracted by ERC Project, ULL)

**Research Lines:**

Teresa Giráldez's group is interested in the structure-function of ion channels involved in controlling neuronal excitability, and on their role in different neurological and psychiatric diseases (epilepsy, fragile X syndrome, autism, etc.). They employ cellular and molecular biology, and biochemical techniques, as well as advanced microscopy and fluorescence methods (confocal and super-resolution microscopy). These methods are combined with conventional and novel electrophysiological approaches, such as patch-clamp, two electrode voltage clamp and patch-clamp fluorimetry. In the mid-term, the group's objectives are: (i) to reveal novel regulatory mechanisms of calcium nanodomains using different sources of $Ca^{2+}$ (presynaptic voltage-gated calcium channels and postsynaptic NMDAR receptors); (ii) to understand the role of NMDAR-BK complexes in neuronal plasticity and the development of seizures; (iii) to establish new animal models bearing endogenous calcium sensor nanodomains based on "big" potassium channels (BK) previously developed in our laboratory.

**Funded projects:**

- Optoelectrical dynamics of ion channel activation and calcium nanodomains (NANOPDICS; ERC-CoG-2014). PI: Teresa Giráldez. European Research Council (ERC Consolidator Grant; 2015-2020, 1,999,742 €).
- Pathophysiological roles of NMDAR-BK complexes in the brain (NeuroGluNBK, RTI2018-098768-B-C21). IPI: Teresa Giráldez. National I+D+i (R+D+I) programme directed at challenges in society. MINECO (2019-2021, 190,000 € + 1 PhD studentship FPI)
- Molecular mechanisms underlying the neuroprotective and anti-seizure activity of the neuronal SGK1.1 kinase through Kv7 ion channels (SGK-EPIK; BFU2015-66490-R – "Mecanismos moleculares subyacentes al papel neuroprotector y anticonvulsionante de la quinasa neuronal SGK1.1 mediante regulación de canales iónicos Kv7"). PI: Teresa Giráldez. MINECO (National I+D+i (R+D+I) programme directed at challenges in society; 2016-2019 157,300 €+ 1 PhD studentship FPI).
- National "Ramón y Cajal" Programme. Postdoctoral contracts for Research and Development centres (RYC-2012-11349). PI: Teresa Giráldez. MINECO (Ramón y Cajal Sub-programme; 2014-2019, 268,600 € 5 year salary + 40,000 € Research Project).

**Publications 2019:**

- Armas-Capote N, Maglio LE, Pérez-Atencio L, Martin-Batista E, Reboreda A, Barios JA, Hernandez G, Alvarez de la Rosa D, Lamas JA, Barrio LC, Giraldez T. SGK1.1 Reduces Kainic Acid-Induced Seizure Severity and Leads to Rapid Termination of Seizures. Cereb Cortex. 2019 Dec 9. pii: bhz302. doi: 10.1093/cercor/bhz302
- Noriega-Prieto JA, Maglio LE, Gallero-Salas Y, Fernández de Sevilla D. Nitric Oxide-Dependent LTD at Infralimbic Cortex. Neuroscience. 2019 Oct 15;418:149-156. doi: 10.1016/j.neuroscience.2019.08.029
- Bartolomé-Martín D, Ibáñez I, Piniella D, Martínez-Blanco E, Pelaz SG, Zafra F. Identification of potassium channel proteins Kv7.2/7.3 as common partners of the dopamine and glutamate transporters DAT and GLT-1. Neuropharmacology. 2019 Dec 15;161:107568. doi: 10.1016/j.neuropharm.2019.03.011
- Ibáñez I, Bartolomé-Martín D, Piniella D, Giménez C, Zafra F. Activity dependent internalization of the glutamate transporter GLT-1 requires calcium entry through the NCX sodium/calcium exchanger. Neurochem Int. 2019 Feb;123:125-132. doi: 10.1016/j.neuint.2018.03.012
- Rampérez A, Bartolomé-Martín D, García-Pascual A, Sánchez-Prieto J, Torres M. Photoconversion of FM1-43 Reveals Differences in Synaptic Vesicle Recycling and Sensitivity to Pharmacological Disruption of Actin Dynamics in Individual Synapses. ACS Chem Neurosci. 2019 Apr 17;10(4):2045-2059. doi: 10.1021/acschemneuro.8b00712

**Other selected publications from the last 10 years:**

- Miranda P, Holmgren M, Giráldez T. Voltage-dependent dynamics of the BK channel cytosolic gating ring are coupled to the membrane-embedded voltage sensor. Elife. 2018. 11;7. pi: e40664. doi: 10.7554/eLife.40664
- Miranda P, Giráldez T, Holmgren M. Interactions of divalent cations with calcium binding sites of BK channels reveal independent motions within the gating ring. Proc Natl Acad Sci U. S. A. 2016 Dec 6;113(49):14055-14060. doi: 10.1073/pnas.1611415113

- Gonzalez-Montelongo R, Barros F, Álvarez de la Rosa D, Giráldez T. Plasma membrane insertion of epithelial sodium channels occurs with dual kinetics. Pflugers Arch. 2016 May;468(5):859-70. doi: 10.1007/s00424-016-1799-4.
- Miranda P, Contreras JE, Plested AJ, Sigworth FJ, Holmgren M, Giráldez T. State-dependent FRET reports calcium-and voltage-dependent gatingring motions in BK channels. Proc Natl Acad Sci U.S.A. 2013 Mar 26;110(13):5217-22. doi: 10.1073/pnas.1219611110
- Miranda P, Cadaveira-Mosquera A, Gonzalez-Montelongo R, Villaroel A, González-Hernández T, Lamas JA, Álvarez de la Rosa D, Giráldez T. The neuronal serum and glucocorticoid regulated kinase 1.1 reduces neuronal excitability and protects against seizures through upregulation of the M-current. J Neurosci. 2013 Feb 6;33(6):2684-96. doi: 10.1523/JNEUROSCI.3442-12.2013


### *Molecular mechanisms in neurodegeneration*

**Principal Investigator:**

- Ángel Acebes Vindel, PhD (Contracted Lecturer, Doctor in Physiology, Department of Basic Medical Sciences, ULL)

**Postdoctoral researchers:**

- Elena Quintana, PhD ACIISI (Postdoctoral Researcher, The Canary Islands Agency for Research, Innovation and Information Sciences, ACIISI, ProID2017010101, ULL)
- Carlos Cairós, PhD ("Agustín de Betancourt" Researcher; Department of Basic Medical Sciences, ULL, ULL, since January 2020).

**PhD students and trainees:**

- Ninovska Romero Luis (Health Sciences Doctoral Programme, contracted by Project ProID2017010101, until July 2019)

**Research Lines:**

Using genetic and molecular tools in Drosophila melanogaster and transgenic mouse models, we analyse the effect of increasing the number of synapses in vivo in animal models during the early onset of Alzheimer's disease (AD), characterized by the extensive loss of Synaptic Connections. In both animal models, overexpression of the phosphoinositide-3-kinase (PI3K) synaptogenic tool will take place early in the development to increase the number of synapses, and to restore sensory and neuronal deficits generated after genetically and pharmacologically induced neurodegeneration. Our main goal is to identify and validate pro-synaptic tools with the potential to be used as therapies in human neurodegenerative diseases.

**Funded projects:**

- A novel genetic, molecular and cellular approach to combat Alzheimer's disease. (ProID2017010101 - "Enfermedad de Alzheimer: hacia un nuevo abordaje genético, molecular y celular"). PI: Ángel Acebes. The Canary Islands Agency of Research, Innovation and Information Sciences (2017-2020, 70,000 €).

- Laboratory intership abroad during the practical education of biological-technical Assistants (2019-1-DE02-KA102-005946). Spanish Coordinator: Ángel Acebes. Erasmus + European Union Programme (2019-2021, 212,999 €).
- Spanish Olfactory Network ("Red olfativa española" – RED2018-102662-T). Aid to promote dynamization actions "Research networks" ("Ayudas para las acciones de dinamización "Redes de investigación"). Co-PI: Ángel Acebes; MICINN (2020-2021, 17,000 €).
- MICROFAVAR: Development of a high-resolution, high-speed quantitative phase-contrast microscope for 3D imaging of biological samples ("Desarrollo de un microscopio de contraste de fase cuantitativa de alta resolución y alta velocidad para la obtención de imágenes en 3D de muestras biológicas"). "Agustín de Betancourt" project. PI: Carlos Cairós; PI-ULL: Ángel Acebes. Regional Government of Tenerife (2020-2024, 160,000 €).

**Publications 2019:**

- Rodriguez-Rodriguez AE, Donate-Correa J, Rovira J, Cuesto G, Luis-Ravelo D, Fernandes MX, Acevedo-Arozena A, Diekmann F, Acebes A, Torres A, Porrini E. Inhibition of the mTOR pathway: A new mechanism of β cell toxicity induced by Tacrolimus. Am J Transplant. 2019 Dec;19(12):3240-3249. doi: 10.1111/ajt.15483
- Lahoz F, Acebes A, González-Hernández T, de Armas-Rillo S, Soler-Carracedo K, Cuesto G, Mesa-Infante V. Random lasing in brain tissues. Organic Electronics. 2019 Dec;75, Article number 105389. doi: 10.1016/j.orgel.2019.105389

**Other selected publications from the last 10 years:**

- Jordán-Álvarez S, Santana E, Casas-Tintó S, Acebes A, Ferrús A. The equilibrium between antagonistic signaling pathways determines the number of synapses in Drosophila. PLoS One. 2017 Sep 11;12(9):e0184238. doi:10.1371/journal.pone.0184238
- Triñanes J, Rodriguez-Rodriguez A, Brito-Casillas Y, Wagner A, De Vries APJ, Cuesto G, Acebes A, Salido E, Torres A, Porrini E. Deciphering tacrolimus-induced toxicity in pancreatic β-cells. Am J Transplant. 2017 Nov;17(11):2829-2840. doi:10.1111/ajt.14323
- Acebes A. Brain mapping and synapse quantification in vivo: It's time to imaging. Front Neuroanat. 2017 Mar 7;11:17. doi: 10.3389/fnana.2017.00017
- Cuesto G, Jordán-Álvarez S, Enriquez-Barreto L, Ferrus A, Morales M, Acebes A. GSK3β inhibition promotes synaptogenesis in Drosophila and mammalian neurons. PLoS One. 2015 Mar 12;10(3):e0118475. doi: 10.1371/journal.pone.0118475
- Acebes A, Devaud JM, Arnes M, Ferrus A. Central adaptation to odorants depends on PI3K levels in local interneurons of the antennal lobe. J Neurosci. 2012 Jan 11;32(2):417-22. doi: 10.1523/JNEUROSCI.2921-11.2012
- Cuesto G, Enriquez-Barreto L, Caramés C, Cantarero M, Gasull X, Sandi C, Ferrús A, Acebes A, Morales M. PI3K activation controls synaptogenesis and spinogenesis in hippocampal neurons. J Neurosci. 2011 Feb 23;31(8):2721-33. doi: 10.1523/JNEUROSCI.4477-10.2011

### *Neurodegenerative animal models*

**Principal Investigator:**

- Abraham Acevedo Arozena, PhD ("Miguel Servet" Investigator, SCS/FIISC, Research Unit, HUC)

**Postdoctoral Research Collaborators:**

- José Miguel Brito Armas (CIBERNED Researcher)
- Judith Noda Mayor (FIISC Investigator)

**PhD students and trainees:**

- Alessandro Marrero Gagliardi (PhD student ACIISI, 2018-2021)

**Research Lines:**

The research lines in this laboratory focus on the genetic pathways involved in neurodegenerative disorders, particularly Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD). We are developing mouse models that will allow us to study the molecular mechanisms underlying these diseases, particularly looking at TDP-43, a key protein in the pathophysiology of both ALS and FTD. We are building worldwide collaborations with experts in genetics, biochemistry and cell biology interested in our research studies.

**Funded projects:**

- Neuronal function of TDP-43 and the potential role of USP10 in its regulation (PI17/00244 – "Investigando la función neuronal de TDP-43 y el posible papel de USP10 en su regulación"). PI: Abraham Acevedo. Institute of Health Carlos III (2018-2020, 146,712.50 €).
- Screening of chemical libraries from The Canary Islands for natural and synthetic compounds with bio-pharmacological effects against neurodegenerative disorders (ProID2017010167 – "Identificación de compuestos naturales y sintéticos presentes en las quimiotecas Canarias con potencial biofarmacológico contra enfermedades neurodegenerativas"). PIs: Abraham Acevedo and Félix Machín. The Canary Islands Agency of Research, Innovation and Information Sciences (2018-2020, 70,000 €).
- Incorporation of new groups into the CIBERNED consortium (CB18/05/0000). PI: Abraham Acevedo Arozena. Institute of Health Carlos III, ISCIII (2019-2020, 70,000 €).
- Role of TDP-43, the key protein in ALS and FTD on the stress response (PIFUN13/18). PI: Abraham Acevedo Arozena. Canary Islands Foundation of Health Research, FUNCANIS (2019-2020, 21,900 €).

**Publications 2019:**


- Rodriguez-Rodriguez AE, Donate-Correa J, Rovira J, Cuesto G, Luis-Ravelo D, Fernandes MX, Acevedo-Arozena A, Diekmann F, Acebes A, Torres A, Porrini E. Inhibition of the mTOR pathway: A new mechanism of β cell toxicity induced by Tacrolimus. Am J Transplant. 2019 Dec;19(12):3240-3249. doi: 10.1111/ajt.15483
- Stewart M, Lau P, Banks G, Bains RS, Castroflorio E, Oliver PL, Dixon CL, Kruer MC, Kullmann DM, Acevedo-Arozena A, Wells SE, Corrochano S, Nolan PM. Loss of Frrs1 disrupts synaptic AMPA

receptor function, and results in neurodevelopmental, motor, cognitive and electrographical abnormalities. Dis Model Mech. 2019 Feb 22;12(2). doi: 10.1242/dmm.036806

- Tan S, Kermasson L, Hoslin A, Jaako P, Faille A, Acevedo-Arozena A, Lengline E, Ranta D, Poirée M, Fenneteau O, Ducou le Pointe H, Fumagalli S, Beaupain B, Nitschké P, Bôle-Feysot C, de Villartay JP, Bellanné-Chantelot C, Donadieu J, Kannengiesser C, Warren AJ, Revy P. EFL1 mutations impair eIF6 release to cause Shwachman-Diamond syndrome. Blood. 2019 Jul 18;134(3):277-290. doi: 10.1182/blood.2018893404
- Nair RR, Corrochano S, Gasco S, Tibbit C, Thompson D, Maduro C, Ali Z, Fratta P, Arozena AA, Cunningham TJ, Fisher EMC. Uses for humanised mouse models in precision medicine for neurodegenerative disease. Mamm Genome. 2019 Aug;30(7-8):173-191. doi: 10.1007/s00335-019-09807-2
- De Giorgio F, Maduro C, Fisher EMC, Acevedo-Arozena A. Transgenic and physiological mouse models give insights into different aspects of amyotrophic lateral sclerosis. Dis Model Mech. 2019 Jan 2;12(1). pii: dmm037424. doi: 10.1242/dmm.037424

**Other selected publications from the last 10 years:**

- Fratta P, Sivakumar P, Humphrey J, Lo K, Ricketts T, Oliveira H, Brito-Armas JM, Kalmar B, Ule A, Yu Y, Birsa N, Bodo C, Collins T, Conicella AE, Mejia Maza A, Marrero-Gagliardi A, Stewart M, Mianne J, Corrochano S, Emmett W, Codner G, Groves M, Fukumura R, Gondo Y, Lythgoe M, Pauws E, Peskett E, Stanier P, Teboul L, Hallegger M, Calvo A, Chiò A, Isaacs AM, Fawzi NL, Wang E, Housman DE, Baralle F, Greensmith L, Buratti E, Plagnol V, Fisher EM, Acevedo-Arozena A. Mice with endogenous TDP-43 mutations exhibit gain of splicing function and characteristics of amyotrophic lateral sclerosis. EMBO Journal. 2018 Jun 1;37(11). doi: 10.15252/embj.201798684
- Corrochano S, Blanco G, Williams D, Wettstein J, Simon M, Kumar S, Moir L, Agnew T, Stewart M, Landman A, Kotiadis VN, Duchen MR, Wackerhage H, Rubinsztein DC, Brown SDM, Acevedo-Arozena A. A genetic modifier suggests that endurance exercise exacerbates Huntington's disease. Human Molecular Genetics. 2018 May 15;27(10):1723-1731. doi: 10.1093/hmg/ddy077
- Joyce PI, Fratta P, Landman AS, McGoldrick P, Wackerhage H, Groves M, Busam BS, Galino J, Corrochano S, Beskina OA, Esapa C, Ryder E, Carter S, Stewart M, Codner G, Hilton H, Teboul L, Tucker J, Lionikas A, Estabel J, Ramirez-Solis R, White JK, Brandner S, Plagnol, V, Bennet DL, Abramov AY, Greensmith L, Fisher EM, Acevedo-Arozena A. Deficiency of the zinc finger protein ZFP106 causes motor and sensory neurodegeneration. Hum Mol Genet. 2016 Jan 15;25(2):291-307. doi: 10.1093/hmg/ddv471
- Joyce PI, McGoldrick P, Saccon RA, Weber W, Fratta P, West SJ, Zhu N, Carter S, Phatak V, Stewart M, Simon M, Kumar S, Heise I, Bros-Facer V, Dick J, Corrochano S, Stanford MJ, Luong TV, Nolan PM, Meyer T, Brandner S, Bennett DL, Ozdinler PH, Greensmith L, Fisher EM, Acevedo-Arozena A. A novel SOD1-ALS mutation separates central and peripheral effects of mutant SOD1 toxicity. Hum Mol Genet. 2015 Apr 1;24(7):1883-97. doi: 10.1093/hmg/ddu605
- Corrochano S, Mannikko R, Joyce PI, McGoldrick P, Wettstein J, Lassi G, Raja Rayan DL, Blanco G, Quinn C, Liavas A, Lionikas A, Amior N, Dick J, Healy EG, Stewart M, Carter S, Hutchinson M, Bentley L, Fratta P, Cortese A, Cox R, Brown SDM, Tucci V, Wackerhage H, Amato AA, Greensmith L, Koltzenburg M, Hanna MG, Acevedo-Arozena A. Novel mutations in human and mouse SCN4A implicate AMPK in myotonia and periodic paralysis. Brain. 2014 Dec;137(Pt 12):3171-85. doi: 10.1093/brain/awu292

### *Vulnerability and neuronal plasticity*

**Principal Investigator:**

- Tomás González Hernández, MD, PhD (Professor of Human Anatomy, Department of Basic Medical Sciences, ULL)

**Postdoctoral Researchers:**

- Domingo Afonso Oramas, PhD (Contracted Lecturer Doctor, Department of Basic Medical Sciences, ULL)
- Pedro Barroso Chinea, PhD (Assistant Lecturer, Department of Basic Medical Sciences, ULL)
- Ignacio de La Cruz Muros, PhD (Assistant Lecturer, Department of Basic Medical Sciences, ULL)
- Diego Luis-Ravelo Salazar, PhD (Postdoctoral researcher, Agustín de Betancourt programme, Department of Basic Medical Sciences, ULL)

**PhD students and trainees:**

- Felipe Fumagallo Reading (Doctorate Program in Health Sciences. MINECO, BES2014-067781)
- Alejandro Febles Casquero (Doctorate Program in Health Sciences. MINECO, BES-2017-079923)
- Virginia Mesa Infante (Doctorate Program in Health Sciences. The Canary Islands Government, TESIS2018010044)

**Technical and administrative staff:**

- Josmar Salas Hernández (Laboratory technician FP2 contract, ULL)
- Julia Rodríguez Núñez (Laboratory technician FP2 contract, ULL)

**Research Lines:**

We study the biological mechanisms of neurodegeneration, and the molecular and cellular basis of neuronal vulnerability. Using animal and cellular models we investigate the role of membrane and intracellular proteins in the onset and progression of neurodegenerative diseases, particularly in Parkinson's and Huntington's disease. In the intermediate and long term, our objective is to find new therapeutic targets for the treatment of these diseases, and to search for new molecules that can block or reduce early neuronal changes in order to prevent or delay neurodegeneration.

**Funded projects:**

- Autophagy, dopaminergic receptors and neuroprotection (ProID2017010091 - "Autofagia, receptores dopaminérgicos y neuroprotección"). PI: Tomás González. The Canary Islands Agency of Research, Innovation and Information Sciences (2018-2020, 69,834 €).
- The regulation of autophagy by dopaminergic agonists D2R/D3R: induction and inhibition, D2R or D3R selectivity and neuroprotection (BFU2016-77363-R – "Regulación de autofagia a través de agonistas dopaminérgicos D2R/D3R: Inducción o inhibición. Selectividad por D2R o D3R y neuroprotección"). PI: Tomás González. MINECO (2017-2019, 200,000 €).
- Autophagy induction through D2R/D3R receptors in Parkinson's and Huntington's disease. Agustín de Betancourt Programme ("Inducción de autofagia a través de receptores D2R/D3R en la enfermedad de Parkinson y la de Huntington"). PI: Diego Luis Ravelo; Supervisor: Tomás González. Regional Government of Tenerife (2017-2021, 160,000 €).

- Collaboration agreement between the The Canary Islands Foundation for Advances in Biomedicine and Biotechnology and the Orfan Biotech SL company to generate an in vitro model of Huntington's disease and validation analysis of the proposed approach ("Convenio de colaboración entre la Fundación Canaria para el Avance de la Biomedicina y de la Biotecnología y la empresa Orfan Biotech SL para la realización de un modelo in vitro de la enfermedad de Huntington y ensayos de validación del abordaje propuesto"). PI: Tomás González (2019, 15,000 €).

**Publications 2019:**

- Lahoz F, Acebes A, González-Hernández T, de Armas-Rillo S, Soler-Carracedo K, Cuesto G, Mesa-Infante V. Random lasing in brain tissues. Organic Electronics. 2019 Dec; 75, Article number 105389. doi: 10.1016/j.orgel.2019.105389
- Barroso-Chinea P, Luis-Ravelo D, Fumagallo-Reading F, Castro-Hernandez J, Salas-Hernandez J, Rodriguez-Nuñez J, Febles-Casquero A, Cruz-Muros I, Afonso-Oramas D, Abreu-Gonzalez P, Moratalla R, Millan M, Gonzalez-Hernandez T. DRD3 (dopamine receptor D3) but not DRD2 activates autophagy through MTORC1 inhibition preserving protein synthesis. Autophagy. 2019 Oct 2:1-17. doi: 10.1080/15548627.2019.1668606 [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Barroso-Chinea P, Cruz-Muros I, Afonso-Oramas D, Castro-Hernández J, Salas-Hernández J, Chtarto A, Luis-Ravelo D, Humbert-Claude M, Tenenbaum L, González-Hernández T. Long-term controlled GDNF over-expression reduces dopamine transporter activity without affecting tyrosine hydroxylase expression in the rat mesostriatal system. Neurobiol Dis. 2016 Apr;88:44-54. doi: 10.1016/j.nbd.2016.01.002
- Castro-Hernandez J, Afonso-Oramas D, Cruz-Muros I, Salas-Hernandez J, Barroso-Chinea P, Moratalla R, Millan MJ, Gonzalez-Hernandez T. Prolonged treatment with pramipexole promotes physical interaction of striatal dopamine D3 Authoreceptor with dopamine transporters to reduce dopamine uptake. Neurobiol Dis. 2015 Feb;74:325-35. doi: 10.1016/j.nbd.2014.12.007
- Afonso-Oramas D, Cruz-Muros I, Castro-Hernandez J, Salas-Hernandez J, Barroso-Chinea P, Garcia-Hernandez S, Lanciego JL, Gonzalez-Hernandez T. Striatal vessels receive phosphorylated tyrosine hydroxylase-rich innervation from midbrain dopaminergic neurons. Front Neuroanat. 2014 Aug 26;8:84. doi: 10.3389/fnana.2014.00084. eCollection 2014
- Gonzalez-Hernandez T, Cruz-Muros I, Afonso-Oramas D, Salas-Hernandez J, Castro-Hernandez J. Vulnerability of mesostriatal dopaminergic neurons in Parkinson’s disease. Front euroanat. 2010 Oct 20;4:140. doi: 10.3389/fnana.2010.00140
- Afonso-Oramas D, Cruz-Muros I, Barroso-Chinea P, Alvarez de la Rosa D, Castro-Hernandez J, Salas-Hernandez J, Giraldez T, Gonzalez-Hernandez T. The dopamine transporter is differentially regulated after dopaminergic lesion. Neurobiol Dis. 2010 Dec;40(3):518-30. doi: 10.1016/j.nbd.2010.07.012

## Clinical and cognitive neuroscience

### *Bilingualism and emotion-cognition coupling*

**Principal Investigator:**

- Markus Conrad, PhD ("Ramón y Cajal" Investigator, Department of Cognitive, Social and Organisational Psychology, ULL)

**Postdoctoral Research Collaborators:**

- Enrique Meseguer Felip (Lecturer, Department of Cognitive, Social and Organisational Psychology

**External collaborators:**

- Prof. Christian von Scheve (Freie Universität Berlin, Germany)
- Prof. Tobias Schröder (Fachhochschule Potsdam, Germany)
- Dr Margaret Gillon Dowens (University of Nottingham, Ningbo, China)

**Research Lines:**

This group focuses on studying the differences in affection and sociability between individuals with different linguistic and/or cultural backgrounds, or from distinct socio-economic environments. We study the emotional connotation of words from different languages in bilingual populations, or from two semantic categories, corresponding to basic dimensions of sociability, authorship, authority and community, assuming that the emotional content is the result of subjective experiences in social and trans-cultural interactions.

We use computer simulations based on the Affect Control to examine the link between emotional connotation and social interactions, with the aim of assessing emotional effects of prototypic social interaction sequences. In addition, we look at the neuronal and psychological correlates of emotion resulting from linguistic representation of social interactions or cultural experiences.

Another research interest of this group is the study of possible non-arbitrary relationships between sounds and meaning in language (sound symbolism).

**Funded projects:**

- National "Ramón y Cajal" programme. Postdoctoral contracts for Research and Development centres (RYC-2015-18955). PI: Markus Conrad. MINECO (Sub-programme Ramón y Cajal; 2017-2022, 268,600 € 5 year salary + 40,000 €, Research project).

**Publications 2019:**


- Schauenburg G, Conrad M, von Scheve C, Barber HA, Ambrasat J, Aryani A, Schröder T. Making sense of social interaction: Emotional coherence drives semantic integration as assessed by event-related potentials. Neuropsychologia. 2019 Mar;125:1-13. doi: 10.1016/j.neuropsychologia.2019.01.002
- Rabovsky M, Conrad M, Álvarez CJ, Paschke-Goldt J, Sommer W. Attentional modulation of orthographic neighborhood effects during reading: Evidence from event-related brain potentials

in a psychological refractory period paradigm. PLoS One. 2019 Jan 25;14(1):e0199084. doi: 10.1371/journal.pone.0199084

**Other selected publications from the last 10 years:**

- Hsu CT, Jacobs AM, Conrad M. Can Harry Potter still put a spell on us in a second language? An fMRI study on reading emotion-laden literature in late bilinguals. Cortex. 2015 Feb;63:282-95. doi: 10.1016/j.cortex.2014.09.002
- Ambrasat J, von Scheve C, Conrad M, Schauenburg G, Schröder T. Consensus and stratification in the affective meaning of human sociality. Proc Natl Acad Sci U S A. 2014 Jun 3;111(22):8001-6. doi: 10.1073/pnas.1313321111
- Conrad M, Recio G, Jacobs AM. The time course of emotion effects in first and second language processing: a cross cultural ERP study with German–Spanish bilinguals. Front Psychol. 2011 Dec 6;2:351. doi: 10.3389/fpsyg.2011.00351
- Oganian Y, Conrad M, Aryani A, Spalek K, Heekeren HR. Activation patterns throughout the word processing network of l1-dominant bilinguals reflect language similarity and language decisions. J Cogn Neurosci. 2015 Nov;27(11):2197-214. doi: 10.1162/jocn_a_00853
- Aryani A, Conrad M, Schmidtke D, Jacobs A. Why 'piss' is ruder than 'pee'? The role of sound in affective meaning making. PLoS One. 2018 Jun 6;13(6):e0198430. doi: 10.1371/journal.pone.0198430

### *Brain imaging laboratory*

**Principal Investigator:**

- Niels Janssen, PhD (Contracted Lecturer, Doctor of Basic Psychology, Department of Cognitive, Social and Organisational Psychology, ULL)

**PhD students and trainees:**

- Laura María Ezama Foronda (Doctorate Program in Health Sciences, ULL. FPI Agencia The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)
- Sara Lozano Seoane (Doctorate Program in Health Sciences, ULL. FPI The Canary Islands Agency of Research, Innovation and Information Sciences, ACIISI)
- Judith Dominguez Pérez (Collaboration Scholarship, MECD programme)

**Research Lines:**

We work on developing new neuroscience data analysis tools and their applications in brain research, both in healthy states and pathological conditions. We use computational and experimental approaches to analyse Brain Magnetic Resonance Imaging (MRI) and Electroencephalography (EEG) data.

**Funded projects:**

- Dynamics of whole-brain fMRI activity: A new analytic technique (PSI2017-91955-EXP). PI: Niels Janssen. MINECO (2018-2019, 36,300 €).

- Hippocampal substructures in aging and pathology: a high resolution MRI study (PSI2017-84933). PI: Niels Janssen. MINECO (2018-2021, 96,800 €).

**Publications 2019:**

- Janssen N, Mendieta CCR. The Dynamics of Speech Motor Control Revealed with Time-Resolved fMRI. Cereb Cortex. 2019 May 9. pii: bhz084. doi: 10.1093/cercor/bhz084. [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Kho KH, Janssen N. Intermanual transfer in an artist with Parkinson's disease. Neurocase. 2016;22(1):119-21. doi: 10.1080/13554794.2015.1053492
- Janssen N, Hernandez JA, van der Meij M, Barber HA. Tracking the time course of competition during word production: Evidence for a post-retrieval mechanism of conflict resolution. Cereb Cortex. 2015 Sep;25(9):2960-9. doi: 10.1093/cercor/bhu092
- Janssen N, Pajtas PE, Caramazza A. Task influences on the production and comprehension of compounds words. Mem Cognit. 2014;42(5):780-93. doi: 10.3758/s13421-014-0396-z
- Janssen N, Hernández-Cabrera JA, Foronda LE. Improving the signal detection accuracy of functional Magnetic Resonance Imaging. Neuroimage. 2018 Aug 1;176:92-109. doi: 10.1016/j.neuroimage.2018.01.076
- Caffarra S, Janssen N, Barber HA. Two sides of gender: ERP evidence for the presence of two routes during gender agreement processing. Neuropsychologia. 2014;63:124-34. doi: 10.1016/j.neuropsychologia.2014.08.016
- Ries S, Janssen N, Burle B, Alario FX. Response-locked brain dynamics of word production. PloS One. 2013;8(3):e58197. doi: 10.1371/journal. pone.0058197

### *Electrical engineering and bioengineering*

**Principal Investigators:**

- Ernesto Pereda de Pablo, PhD (Professor of Electrical Engineering, Department of Industrial Engineering, ULL)
- José Fco. Gómez González, PhD (Contracted Lecturer, Department of Industrial Engineering, ULL)

**PhD students and trainees:**

- Juan García-Prieto Cuesta (Contracted Researcher, Department of Industrial Engineering, ULL)

**Research Lines:**

In this laboratory we use bioengineering techniques to develop experimental techniques and software programmes for biological simulation, and to measure brain activity from multivariate neurological data. These tools aim to determine functional connectivity patterns and to implement new analysis tools for the study of complex systems.

**Funded projects:**

- Improving optic data decoding in fibre networks using neuromorphic photonic devices (TEC2016-80063-C3-2-R "Mejorando la descodificación de datos de forma óptica en redes de

comunicaciones por fibra utilizando dispositivos fotónicos neuro-inspirados"). PI: Alex Arenas (Ernesto Pereda de Pablo, ULL). Ministry of Economy and Competitiveness, MINECO (2016-2019, 35,000 €).

- Extraction and classification of brain activity information via portable electroencephalographs: application to brain-machine interface systems for patients with restricted mobility. (ProID2017010100 - Extracción y clasificación de la información de la actividad cerebral detectada con electroencefalógrafo portátil. Aplicación a sistemas de interface cerebromáquina para pacientes con movilidad reducida"). PI: José F. Gómez González. The Canary Islands Agency of Research, Innovation and Information Sciences (2017-2020, 69,996.33 €).

**Publications 2019:**

- Hughes LE, Henson RN, Pereda E, Bruña R, López-Sanz D, Quinn AJ, Woolrich MW, Nobre AC, Rowe JB, Maestú F; BioFIND Working Group. Biomagnetic biomarkers for dementia: A pilot multicentre study with a recommended methodological framework for magnetoencephalography. Alzheimers Dement (Amst). 2019 Jun 14;11:450-462. doi: 10.1016/j.dadm.2019.04.009
- Camara C, Warwick K, Bruña R, Aziz T, Pereda E. Closed-loop deep brain stimulation based on a stream-clustering system. Expert Systems with Applications. 2019 Jul;126:187-199. doi: 10.1016/j.eswa.2019.02.024
- Camara C, Warwick K, Aziz T, Pereda E. Non-linear dynamical analysis of resting tremor for demand-driven deep brain stimulation. Sensors (Basel). 2019 May 31;19(11). pii: E2507. doi: 10.3390/s19112507
- López ME, Pusil S, Pereda E, Maestú F, Barceló F. Dynamic low frequency EEG phase synchronization patterns during proactive control of task switching. Neuroimage. 2019 Feb 1;186:70-82. doi: 10.1016/j.neuroimage.2018.10.068
- Dimitriadis SI, López ME, Maestu F, Pereda E. Modeling the switching behavior of functional connectivity microstates(fcμstates) as a novel biomarker for mild cognitive impairment. Front Neurosci. 2019 Jun 11;13:542. doi: 10.3389/fnins.2019.00542
- Pusil S, Dimitriadis SI, López ME, Pereda E, Maestú F. Aberrant MEG multi- frequency phase temporal synchronization predicts conversion from mild cognitive impairment-to-Alzheimer's disease. Neuroimage Clin. 2019;24:101972. doi: 10.1016/j.nicl.2019.101972

**Other selected publications from the last 10 years:**

- Garcés P, Pereda E, Hernández-Tamames JA, Del-Pozo F, Maestú F, Pineda-Pardo JÁ. Multimodal description of whole brain connectivity: A comparison of resting state MEG, fMRI, and DWI. Hum Brain Mapp. 2016 Jan;37(1):20-34. doi: 10.1002/hbm.22995
- Niso G, Carrasco S, Gudin M, Maestu F, Del-Pozo F, Pereda E. What graph theory tells about resting state interictal MEG epileptic activity. Neuroimage Clin. 2015 May 23;8:503-15. doi: 10.1016/j.nicl.2015.05.008
- Niso G, Bruna R, Pereda E, Gutierrez R, Bajo R, Maestu F, del-Pozo F, HERMES: towards an integrated toolbox to characterize functional and effective brain connectivity. Neuroinformatics. 2013 Oct;11(4):405-34. doi: 10.1007/s12021-013-9186-1
- Gonzalez JJ, Manas S, De Vera L, Mendez LD, Lopez S, Garrido JM, Pereda E. Assessmentof electroencephalographic functional connectivity in term and preterm neonates. Clin Neurophysiol. 2011 Apr;122(4):696-702. doi: 10.1016/j.clinph.2010.08.025

- Martín-Mateos I, Méndez Pérez JA, Reboso Morales JA, Gómez-González JF. Adaptive pharmacokinetic and pharmacodynamic modelling to predict propofol effect using BIS-guided anesthesia. Comput Biol Med. 2016 Aug 1;75:173-80. doi: 10.1016/j.compbiomed.2016.06.007
- Gómez González JF, Mel BW, Poirazi P. Distinguishing Linear vs. Non-Linear Integration in CA1 Radial Oblique Dendrites: It's about Time. Front Comput Neurosci. 2011 Nov 14;5:44. doi: 10.3389/fncom.2011.00044


### *Cognitive and psycholinguistic neuroscience*

**Principal Investigator:**

- Horacio A. Barber Friend, PhD (Lecturer in Basic Psychology, Department of Cognitive, Social and Organisational Psychology, ULL)

**Postdoctoral Researchers:**

- Julien Dampuré, PhD (Agustín de Betancourt Researcher, Department of Cognitive, Social and Organisational Psychology, ULL)
- Juan A. Hernández Cabrera, PhD (Lecturer in Basic Psychology, Department of Clinical Psychology, Psychobiology and Methodology, ULL)

**PhD students and trainees:**

- Martín Antúnez García (FPI. MINECO. BES-2017-081797)
- Laura Hernández Ramos (Doctorate in Psychology program, ULL)
- Benjamín Vega Peñate (Doctorate in Psychology program, ULL)

**Research Lines:**

Our research group works on a number of consolidated basic research lines regarding language processing and visual perception, and it is currently starting to explore some clinical applications. We intend to extend our research to executive functions in addictive behaviour in which inhibitory processes are involved, and into the study of neurological disorders related to pain perception like fibromyalgia and neuropathic pain. We are also working on the development of therapeutic strategies based on neuromodulation, with new techniques such as neurofeedback and non-invasive brain stimulation (TMS and TDSs). Our group works primarily with electroencephalogram (EGG) electrophysiological recordings but also, we incorporate neuroimaging techniques like Functional Magnetic Resonance (fMRI) in combination with transcranial stimulation, ocular movement recording or behavioural response analysis.

**Funded projects:**

- Parafoveal reading and perception: the role of visual depth (PSI2016-79624-P – "Lectura y percepción parafoveal: el papel de la amplitud visual"). PI: Horacio Barber. MINECO (2017-2019, 60,000 €.)
- Neuromodulation techniques as new therapeutic approaches for addictive behaviour. Agustín de Betancourt Project ("Técnicas neuromodulatorias como nuevas aproximaciones terapéuticas

frente a las conductas adictivas"). PI: Julien Dampuré; Tutor: Horacio Barber. Regional Government of Tenerife (2017-2021, 160,000 €).

**Publications 2019:**

- Schauenburg G, Conrad M, von Scheve C, Barber HA, Ambrasat J, Aryani A, Schröder T. Making sense of social interaction: Emotional coherence drives semantic integration as assessed by event-related potentials. Neuropsychologia. 2019 Mar;125:1-13. doi: 10.1016/j.neuropsychologia.2019.01.002
- Dampuré J, López-Pérez PJ, Barber HA. Meaning-based attentional guidance as a function of foveal and task-related cognitive loads. Language, Cognition and Neuroscience. 2019 Jan;34(1):1-12. doi: 10.1080/23273798.2018.1484149
- Morera Y, van der Meij M, de Vega M, Barber HA. Are sensory-motor relationships encoded ad hoc or by default?: An ERP study. Front Psychol. 2019 May 3;10:966. doi: 10.3389/fpsyg.2019.00966
- Dampuré J, Benraiss A, Vibert N. Modulation of parafoveal word processing by cognitive load during modified visual search tasks. Q J Exp Psychol (Hove). 2019 Jul;72(7):1805-1826. doi: 10.1177/1747021818811123
- León I, Rodrigo MJ, El-Deredy W, Modroño C, Hernández-Cabrera JA, Quiñones I. Limbic-visual attenuation to crying faces underlies neglectful mothering. Sci Rep. 2019 Apr 23;9(1):6373. doi: 10.1038/s41598-019-42908-1
- Soares AP, Oliveira H, Ferreira M, Comesaña M, Macedo AF, Ferré P, Acuña-Fariña C, Hernández-Cabrera J, Fraga I. Lexico-syntactic interactions during the processing of temporally ambiguous L2 relative clauses: An eye-tracking study with intermediate and advanced Portuguese-English bilinguals. PLoS One. 2019 May 29;14(5):e0216779. doi: 10.1371/journal.pone.0216779
- Soares AP, Macedo J, Oliveira HM, Lages A, Hernández-Cabrera J, Pinheiro AP. Self-reference is a fast-acting automatic mechanism on emotional word processing: evidence from a masked priming affective categorisation task. Journal of Cognitive Psychology. 2019 Apr;31(3):317-325. doi: 10.1080/20445911.2019.1599003
- Cedres N, Machado A, Molina Y, Diaz-Galvan P, Hernández-Cabrera JA, Barroso J, Westman E, Ferreira D. Subjective cognitive decline below and above the age of 60: a multivariate study on neuroimaging, cognitive, clinical, and demographic measures. J Alzheimers Dis. 2019;68(1):295-309. doi: 10.3233/JAD-180720
- Gonzalez-Burgos L, Hernández-Cabrera JA, Westman E, Barroso J, Ferreira D. Cognitive compensatory mechanisms in normal aging: A study on verbal fluency and the contribution of other cognitive functions. Aging. 2019 Jun 22;11(12):4090-4106. doi: 10.18632/aging.102040
- Marrero-Quevedo RJ, Blanco-Hernández PJ, Hernández-Cabrera JA. Adult Attachment and Psychological Well-Being: The Mediating Role of Personality. Journal of Adult Development. 2019 Mar;26(1)41-56. doi: 10.1007/s10804-018-9297-x
- Marrero RJ, Carballeira M, Hernández-Cabrera JA. Does Humor Mediate the Relationship Between Positive Personality and Well-Being? The Moderating Role of Gender and Health. 2019 Journal of Happiness Studies. doi: 10.1007/s10902-019-00121-x [Epub ahead of print]

**Other selected publications from the last 10 years:**

- Carreiras M, Quiñones I, Mancini S, Hernández-Cabrera JA, Barber HA. Verbal and nominal agreement: an fMRI study. Neuroimage. 2015 Oct 15; 120:88-103. doi: 10.1016/j.neuroimage.2015.06.075
- Janssen N, Hernández JA, Van der Meij M, Barber HA. Tracking the time course of competition during word production: Evidence for a post-retrieval mechanism of conflict resolution. Cereb Cortex. 2015 Sep;25(9):2960-9. doi: 10.1093/cercor/bhu092
- Caffarra S, Janssen N, Barber HA. Two sides of gender: ERP evidence for the presence of two routes during gender agreement processing. Neuropsychologia. 2014 Oct;63:124-34. doi: 10.1016/j.neuropsychologia.2014.08.016
- Barber HA, Van der Meij M, Kutas M. An electrophysiological analysis of contextual and temporal constraints on parafoveal word processing. Psychophysiology. 2013 Jan;50(1):48-59. doi: 10.1111/j.1469-8986.2012.01489.x
- Vigliocco G, Vinson DP, Druks J, Barber HA, Cappa SF. Nouns and Verbs in the Brain: A Review of Behavioural, Electrophysiological, Neuropsychological and Imaging Studies. Neurosci Biobehav Rev. 2011 Jan;35(3):407-26. doi: 10.1016/j.neubiorev.2010.04.007

### *Neurochemistry and Neuroimagen*

**Principal investigator:**

- José Luis González Mora (Professor of Physiology; Department of Basic Medical Sciences, ULL)

**Postdoctoral Researchers:**

- Cristián D. Modroño Pascual (Assistant Lecturer, Department of Basic Medical Sciences, ULL)

**Postdoctoral collaborating researchers:**

- Francisco Marcano Serrano (Agustín de Betancourt programme Investigator; Department of Basic Medical Sciences, ULL)
- David Díaz Hernández (Contracted by MACBIOIDI project)
- Marcial Galván Sosa (Researcher contracted by MACBIOIDI, ULL)
- Iñigo Fernández Bats (Agustín de Betancourt programme Investigator; Department of Basic Medical Sciences, ULL)
- Estefanía Hernández Martín (Postdoctoral Researcher, University of Southern California, Los Angeles CA, USA)
- Carmen Jiménez Espinoza (Postdoctoral Researcher in Karolinska Institutet, Suecia)
- Pedro Salazar Carballo (Assistant Lecturer, ULL)
- Julio Plata Bello (Assistant lecturer ULL, Physician HUC)

**PhD students and trainees:**

- Tania Pacheco Ramos (Doctorate program, TEA Project)
- Carolina Romero González (Peripheral Neuropathy Project)

**Technical and administrative staff:**

- Idaira Hueso Falcón (SRMIB-SEGAI technician, ULL)
- José Maria Pérez González (SRMIB-SEGAI technician, ULL e IMETISA)

**Research Lines:**

- Development of biomedical technologies for rehabilitation and sensory restoration.
- Development of immuno sensors and biosensors for application in medical diagnosis.
- Development of techniques and methods in Biomedical Engineering.
- Diagnostic methods for autism spectrum disorders (ASD).

**Funded projects:**

- Magnetic resonance imaging of active neuronal tracts (SAF2017-91824- EXP – "Imagen de resonancia magnética de tractos neuronales activos"). PI: José Luis González Mora. Ministry of Science, Innovation and Universities (2018-2019, 40,000 €).
- Boosting the cohesion of the Macaronesian ORs through a common ICT platform for the management of scientific data (MacBioIDi – "Impulsando la cohesión de las RUPs macaronésicas mediante una plataforma TIC común para el manejo de datos científicos"). PI (sub-proyect ULL): José Luis González Mora. European Community - FEDER (2017-2020, total amount: 2,900,000 €; sub-project ULL: 350,000 €).
- Upgrade of the 3.0T Magnetic Resonance Equipment for Biomedical Research (EQC2018-004106-P – "Actualización del Equipo de Resonancia Magnética de 3.0T para Investigación Biomédica"). Research Infrastructures and Scientific-Technical Equipment (State Plan I+D+i 2017-2020) PI: José Luis Gonzalez Mora (2020, 996,019.42 €).
- Desarrollo de un prototipo avanzado de alta calidad científica y tecnológica para aplicaciones biomédicas basado en reconstrucción de imágenes de infrarrojo cercano DOT-NIR ("Development of an advanced high-quality scientific-technological prototype for biomedical applications based on DOT near-infrared (NIR) image reconstruction"). Agustín de Betancourt programme. PI: Francisco J. Marcano Serrano; PI-ULL: Justo Roberto Pérez Cruz. Regional Government of Tenerife (2017-2021, 160,000 €).
- Development and application of nanostructured magnetic platforms in the detection of pathogens: environmental applications in the agri-food industry and in water intended for human consumption ("Desarrollo y aplicación de plataformas magnéticas nanoestructuradas en la detección de agentes patógenos: aplicaciones medioambientales, en la industria agroalimentaria y en aguas de consumo humano"). Agustín de Betancourt programme. PI: Íñigo Fernández Bats; PI-ULL: José Luis González Mora. Government of Tenerife (2019-2023, 160,000 €).

**Publications 2019:**


- Modroño C, Navarrete G, Nicolle A, González-Mora JL, Smith KW, Marling M, Goel V. Developmental grey matter changes in superior parietal cortex accompany improved transitive reasoning. Think Reason. 2018 Oct 3;25(2):151-170. doi: 10.1080/13546783.2018.1481144
- Salazar P, Martín M, González-Mora JL. In situ electrodeposition of cholesterol oxidase-modified polydopamine thin film on nanostructured screen printed electrodes for free cholesterol determination. Journal of Electroanalytical Chemistry. March 2019; 837:191-199. doi: 10.1016/j.jelechem.2019.02.032

- Plata Bello J, García-Peña C, Modroño C, Hernández-Martín E, Pérez-Martín Y, Marcano F, González-Mora JL. Visual inputs decrease brain activity in frontal areas during silent lipreading. PLoS One. 2019 Oct 10;14(10):e0223782. doi: 10.1371/journal.pone.022378
- Hernandez-Martin E, Marcano F, Modroño-Pascual C, Casanova-González O, Plata-Bello J, González-Mora JL. Is it possible to measure hemodynamic changes in the prefrontal cortex through the frontal sinus using continuous wave DOT systems. Biomedical Optics Express. 2019 Jan 24;10(2):817-837. doi: 10.1364/BOE.10.000817
- Vartanian O, Navarrete G, Chatterjee A, Fich LB, Leder H, Modroño C, Rostrup N, Skov M, Corradi G, Nadal M. Preference for curvilinear contour in interior architectural spaces: Evidence from experts and nonexperts. Psychology of Aesthetics, Creativity, and the Arts. 2019 Feb;13(1):110-116. doi: 10.1037/aca0000150
- León I, Rodrigo MJ, El-Deredy W, Modroño C, Hernández-Cabrera JA, Quiñones I. Limbic-visual attenuation to crying faces underlies neglectful mothering. Sci Rep. 2019 Apr 23;9(1):6373. doi: 10.1038/s41598-019-42908-1
- Modroño C, Bermúdez S, Cameirão M, Pereira F, Paulino T, Marcano F, Hernández- Martín E, Plata-Bello J, Palenzuela N, Núñez-Pádron D, Pérez-González JM, González-Mora JL. Is it necessary to show virtual limbs in action observation neurorehabilitation systems? J Rehabil Assist Technol Eng. 2019 Jul 16;6:2055668319859140. doi: 10.1177/2055668319859140

**Other selected publications from the last 10 years:**

- Limongi R, Pérez FJ, Modroño C, González-Mora JL. Temporal Uncertainty and Temporal Estimation Errors Affect Insular Activity and the Frontostriatal Indirect Pathway during Action Update: A Predictive Coding Study. Front Hum Neurosci. 2016 Jun 27;10:276. doi: 10.3389/fnhum.2016.00276
- Modroño C, Plata-Bello J, Zelaya F, García S, Galván I, Marcano F, Navarrete G, Casanova Ó, Mas M, González-Mora JL. Enhancing Sensorimotor Activity by Controlling Virtual Objects with Gaze. PLoS One. 2015 Mar 23;10(3):e0121562. doi: 10.1371/journal.pone.0121562
- Vartanian O, Navarrete G, Chatterjee A, Fich LB, Gonzalez-Mora JL, Leder H, Modroño C, Nadal M, Rostrup N, Skov M: Architectural Design and the Brain: Effects of Ceiling Height and Perceived Enclosure on Beauty Judgments and Approach-avoidance Decisions. Journal of Environmental Psychology 2014 Nov; 41. doi: 10.1016/j.jenvp.2014.11.006
- Plata Bello J, Modroño C, Marcano F, González-Mora JL: The Mirror Neuron System and Motor Dexterity: What happens? Neuroscience. 2014 Sep 5;275:285-95. doi: 10.1016/j.neuroscience.2014.06.010
- Salazar P, Martín M, González-Mora JL, González-Elipe AR: Application of Prussian Blue electrodes for amperometric detection of free chlorine in water samples using Flow Injection Analysis. Talanta. 2016;146:410-6. doi: 10.1016/j.talanta.2015.08.072

# BIOMEDICAL INNOVATION PLATFORM: Laboratories and Associated Units

This section refers to the associated research groups, laboratories and services that collaborate with the ITB in emerging areas and programmes, or that carry out specific innovation and biomedical technology transfer activities, particularly those at the ULL or that are part of the Canary Islands Health Service but also, other those at institutions.

### *AQUACULTURE NUTRITION RESEARCH GROUP (ULL)*

Despite its focus on aquaculture nutrition, this group has been collaborating closely with groups at the ITB for a long time, studying physiological aspects of nutrition and particularly, the role of lipids in human biology and pathology. Its role in this platform is to establish lines of collaboration with other programmes, analysing the role of human nutrition in health and disease, as well as assisting in lipidomics studies.

**Principal Investigator:**

- Covadonga Rodríguez González, PhD (Lecturer in Zoology, Department of Animal Biology, Soil Science and Ecology, ULL)

**Postdoctoral Researchers:**

- Ana Bolaños Martín, PhD (Lecturer in Zoology, Department of Animal Biology, Soil Science and Ecology, ULL)
- José Antonio Pérez Pérez, PhD (Postdoctoral researcher, Department of Animal Biology, Soil Science and Ecology, ULL)
- Diego Garrido Lorenzo, PhD (Postdoctoral researcher, Department of Animal Biology, Soil Science and Ecology, ULL)

**Technical and administrative staff:**

- Nieves Guadalupe Acosta González (Laboratory technician)

**PhD students and trainees:**

- Sara García Ravelo (Contracted predoctoral researcher, La Caixa Foundation and Caja-Canarias Foundation)

**Research Lines:**

Contribution to the development of technology for the sustainable culture of marine species, gaining an in-depth knowledge of their nutritional needs and nutritional physiology. The analytic technology developed for lipidomics can be applied to any area of nutrition, including human nutrition.

**Funded projects:**

- Demonstrative and technology transfer project to help business develop new products and processes in the context of Macaronesian blue biotechnology (Macbioblue. MAC/1.1.b/086, Interreg – "Proyecto demostrativo y de transferencia tecnológica para ayudar a las empresas a desarrollar nuevos productos y procesos en el ámbito de la biotecnología azul de la Macaronesia"). PI: Covadonga Rodríguez. European regional development fund, FEDER (2017-2019, sub-project ULL: 137,234.69 €; total amount: 1,499,699.96 €).

**Selected publications from the last 10 years:**


- Diaz M, Dopido R, Gomez T, Rodriguez C. Membrane lipid microenviroment modulates thermodynamic properties of the $Na^+$-$K^+$-ATPase in branchial and intestinal epithelia in euryhaline fish in vivo. Frontiers in Physiology. 2016 Dec 15;7:589. doi: 10.3389/fphys.2016.00589
- Reis DB, Acosta NG, Almansa E, Tocher DR, Andrade JP, Sykes AV, Rodriguez C. Composition and metabolism of phospholipids in Octopus vulgaries and Sepia officinalis hatchings. Comp Biochem Physiol B Biochem Mol Biol. 2016 Oct;200:62- 8. doi: 10.1016/j.cbpb.2016.06.001
- Zarate R, Cequier-Sanchez E, Rodriguez C, Dorta-Guerra R, El Jaber-Vazdekis N, Ravelo AG. Improvement of polyunsaturated fatty acid production in Echium acanthocarpum transformed hairy root cultures by application of different abiotic stress conditions. ISRN Biotechnol. 2013 Nov 13;2013:169510. doi: 10.5402/2013/169510


### *HEALTH TECHNOLOGIES ASSESMENT UNIT (SCS)*

Research carried out by this group is integrated within The Canary Islands Health Assessment Service, which focuses particularly on safety and cost-benefit assessment of new health technologies, telemedicine applications and shared decision making, as well as their economic, organisational, ethical and social impact.

**Principal Investigators:**

- Pedro Serrano Aguilar, MD, PhD (Head of SCS Assessment and Planning Service, and Head of the Health Technologies Assessment Unit)
- Lilisbeth Perestelo Pérez, PhD (Assessment and Planning Service, SCS)

**Collaborating Researchers:**

- Iván Castilla Rodríguez, PhD (RedETS contract)
- María del Mar Trujillo Martín, PhD (RedETS contract)
- Amado Rivero Santana, PhD (RedETS contract)
- Ana Toledo Chávarri, PhD (RedETS contract)
- Tasmania del Pino Sedeño, PhD (RedETS contract)
- Néstor Benítez, PhD (RedETS contract)
- Beatriz León Salas, PhD (RedETS contract)
- Lidia García Pérez (RedETS contract)
- Yolanda Ramallo Fariña (RedETS contract)
- Renata Linertova (RedETS contract)
- Cristina Valcárcel Nazco (RedETS contract)

- Yolanda Álvarez (RedETS contract)
- Vanesa Ramos (RedETS contract)
- Leticia Rodríguez (RedETS contract)

**Research Lines:**

- Health Assessment Services focusing on telemedicine, health technologies viability assessments and the economic impact of diseases.
- Health Technologies Assessment, and studies of the effectiveness and efficacy of health technologies through systematic review and cost-effectiveness analysis.
- Shared decision making through the development, assessment and implementation of techniques and tools that aid shared decision-making.

**Funded projects:**

- Effectiveness and cost-effectiveness over 5 years for complex ITC knowledge transfer interventions designed for health improvement in DM2 (INDICA-DOS, PI16/00769 – "Efectividad y coste-efectividad de intervenciones complejas de transferencia de conocimiento basadas en TICs a 5 años, para mejorar la salud en pacientes con DM2"). PI: Pedro Serrano. Institute of Health Carlos III (2017-2019, 50,215 €).
- EUnetHTA Joint Action 3. PI: Pedro Serrano. EU Executive Agency for Health and Consumers (2016-2020, 88,000 €).
- Health Service Research Network on Chronic Diseases (REDISSEC – "Red de Investigación en Servicios de Salud en Enfermedades Crónicas"). PI: Pedro Serrano. Institute of Health Carlos III 2017-2020, 240,000 €).
- Improving digital health literacy in Europe. European Commission. PI: Lilisbeth Perestelo. FUNCANIS (2016-2018, 149,875 €).
- Clinical and economic impact of ozone-therapy on patients waiting for herniated disc surgery (PI17/00120 – "Impacto clínico y económico de la ozonoterapia intradiscal en pacientes en lista de espera para cirugía por hernia de disco"). PI: Renata Linertova. Institute of Health Carlos III (2018-2020, 32,065 €).

**Selected publications from the last 10 years:**


- Vallejo-Torres L, Garcia-Lorenzo B, Castilla I, Valcárcel-Nazco C, Garcia-Perez L, Linertova R, Polentinos-Castro E, Serrano-Aguilar P. On the estimation of the cost- effectiveness threshold: why, what, how? Value in Health. 2016 Jul-Aug;19(5):558-66. doi: 10.1016/j.jval.2016.02.020
- Lopez-Bastida J, Oliva-Moreno J, Linertová R, Serrano-Aguilar P. Social/economic costs and health-related quality of life in patients with rare diseases in Europe. Eur J Health Econ. 2016;Suppl 1:1-5. doi: 10.1007/s10198-016-0780-7
- Abt Sacks A, Perestelo-Pérez L, Rodriguez-Martin B, Cuellar-Pompa L, Algara Lopez M, Gonzalez Hernandez N, Serrano-Aguilar P. Breast cancer patients'narrative experiences about communication during the oncology care process: a qualitative study. Eur J Cancer Care (Engl.). 2016 Sep;25(5):719-33. doi: 10.1111/ecc.12384
- Perestelo-Pérez L, Rivero Santana A, Boronat M, Sanchez-Afonso JA, Perez-Ramos JM, Montori VM, Serrano-Aguilar P. Effect of the statin choice encounter decision aid in Spanish patients with type 2 diabetes: A randomized trial. Patient Educ Couns. 2016 Feb;99(2):295-9. doi: 10.1016/j.pec.2015.08.032

- Del Pino-Sedeño T, Trujillo-Martin MM, Ruiz-Irastorza G, Cuellar-Pompa L, de Pascual-Medina AM, Serrano-Aguilar P. Spanish Systemic Lupus Erythematosus CPG Development Group. Effectiveness of nonpharmacologic interventions for decreasing fatigue in adults with systemic lupus erythematosus: a systematic review. Arthritis Care Res (Hoboken). 2016 Jan;68(1):141-8. doi:10.1002/acr.22675
- Vallejo-Torres L, Castilla I, Couce ML, Perez-Cerda C, Martin-Hernandez E, Pineda M, Campistol J, Arrospide A, Morris S, Serrano-Aguilar P. Cost-efectiveness analysis of a national newborn screening program for biotinidase deficiency. Pediatrics. 2015 Aug;136(2):e424-32. doi: 10.1542/peds.2014-3399
- Serrano-Aguilar P, Trujillo-Martin MM, Perez de la Rosa A, Cuellar-Pompa L, Saavedra-Medina H, Linertova R, Perestelo-Perez L, Perez-Ramos J, Rivero-Santana A. Patient participation in a Clinical Guideline Development for Systemic Lupus Erythematosus. Patient Education and Counseling. 2015 Sep;98(9):1156-63. doi: 10.1016/j.pec.2015.05.022
- Vallejo-Torres L, Castilla I, Gonzalez N, Hunter R, Serrano-Perez P, Perestelo-Pérez L. Cost-effectiveness of electroconvulsive therapy compared to repetitive transcranial magnetic stimulation for treatment-resistant severe depression: a decision model. Psychol Med. 2015 May;45(7):1459-70. doi: 10.1017/S0033291714002554


## *THE CANARY ISLANDS FOUNDATION FOR ADVANCES IN BIOMEDICINE AND BIOTECHNOLOGY (BIOAVANCE FOUNDATION, REGIONAL GOVERNMENT OF TENERIFE-ULL)*

Setting up Bioavance in 2006 was the result of a collaboration between the ULL and the Regional Government of Tenerife to promote biomedical and biotechnological research. At that time, the ITB Institute at the ULL and Bioavance Foundation by the Regional Government of Tenerife were created simultaneously to explicitly support the establishment of Institute. The foundation is governed by a board presided by the head of the Regional Government of Tenerife and its vice-president is the vice-chancellor of the ULL. The other members of the board currently include the president of the ULL's Social Council and representatives of other ULL research institutes. From the outset, the role of this Foundation, funded by the Regional Government of Tenerife, has been to leverage the development of biomedical and biotechnological research in Tenerife and The Canary Islands, promoting partnerships between different research entities (institutes and teaching hospitals, among others). In this context, the Foundation helps manage privately funded biomedical research projects, it offers support to applications for public funding from both national and international calls, and to assist in the management of these projects. It promotes biomedical and biotechnology innovation and transfer, it helps disseminate the groups' research activities, as well as assisting in the organisation of events related to these activities. An example of the Foundation's involvement in the ITB's include the successful application and management of projects ADE-210/00046 (Construction and development of the Research Centre of The Canary Islands: Institute of Health Carlos III, 2011–2018, 8,030,000 €) and FP7-REGPOT-2012-2013-1 (Improving Biomedical Research and Innovation in the Canary Islands, IMBRAIN; European Commission, 2012-2016, 4,158,874 €).

**Scientific Director:**

• Rafael Alonso Solís, MD, PhD (Professor of Physiology ULL, former director ITB)

**Project Director:**

• Randolph Revoredo Chocano

**Technical and administrative staff:**

• Irene López Jiménez (Administrative management)

• Eladio Frías Arrocha (Project manager)

**Innovation and Technology Transfer Advisory Committee:**

Among the most relevant actions carried out by the Foundation was establishing an advisory committee, a panel of national and international advisors to provide the research groups with expert advice on the valorisation of any technology developed in the field of biomedicine and biotechnology. Aside from its advisory role, the committee in itself offers added value by providing access to an international network of contacts and expert level consultancy. The current members of the committee are:

- Javier García Cogorro (Columbus Venture Capital, Madrid)
-Frank Heemskerk (Research Innovation Management Services, Brussels)
-Michael Johnson (LifeArch, London)
-Manuel López Figueroa (Bay City Capital, San Francisco)
-David Pardoe (LifeArch, London)
-Christian Stein (Ascenion, Munich)
-Christian J. Suojanen (TTS Global Initiative, Miami)

# INSTALLATIONS AND SCIENTIFIC INFRASTRUCTURES

The first phase of the construction of the ITB main building and facilities was recently completed. At present, the procurement and installation of the furnishings is underway, finishing the data transfer and telephone systems, and programming the relocation of the large equipment initially situated in the laboratories of the different departments. The new building, located on the Health Sciences Campus and near the HUC, has an extension of about 4,000 $m^2$ distributed on three floors: (i) 1st floor - a state-of-the-art animal house for rodents and other small animals, especially designed for the generation and maintenance of genetically modified animals; (ii) 2nd floor – will include a space for the transfer activities organised through the Bioavance Foundation, along with laboratories to house the institute's common large equipment, and a large space for experimental laboratories that will accommodate the researchers; and (iii) a technical plant, located between these two floors to monitor the maintenance of the building's general facilities.

During the construction of the new building, the ITB research groups have participated in a coordinated manner in competitive calls for infrastructure funding at the National and European

level. This effort has allowed the necessary equipment to be acquired and renovated progressively but at an appropriate pace. At present, the institute's common infrastructures consist of the following units, platforms and services:

- Advanced cell studies unit, including: (i) cutting-edge equipment for confocal microscopy, fluorescence microscopy and electron microscopy; (ii) a system for microdissection and the creation of optical sections at a cellular level; (iii) flow cytometry; (iv) electrophysiology for cellular and sub-cellular studies.
- Instrumentation and sample preparation service, including: (i) spectrometry, spectrofluorometry and microplate readers; (ii) bench top centrifuges and ultracentrifuges; (iii) advanced systems for protein and DNA quantification in different preparations; (iv) cell and particle counters.
- Cell and tissue culture rooms, including P2 facilities.
- Brain and tissue bank.
- Omics unit (prepared for genomics, lipidomics, metabolomics and proteomics).
- Phenotyping, genotyping and behavioural studies in rodents (in the animal facility).
- Cognitive neuroscience.

In addition, the groups at the institute have access to the General Research Support Services (SEGAI) at the ULL, at the Anchieta Campus, which include common equipment, as well as scientific and technical support for both in-house and external groups. In the case of the specific infrastructure for biomedical and biotechnological experimentation, this service includes: a general animal facility, microscopy, genomics, magnetic nuclear resonance (MNR) for chemical analysis and structural biology, and MNR for brain function studies. Moreover, the groups at the institute that are involved in translational research have access to and usually collaborate with the Clinical Trials Unit at the HUC - which is part of the Spanish Clinical Trials Center (CAIBER) and the Biobank service accredited by the Institute of Health Carlos III. In addition, through the collaboration between the ITB and the Institute of Technology and Renewable Energies (ITER), the researchers at the institute have access to the TEIDE supercomputer and the genomics laboratory at this institution.

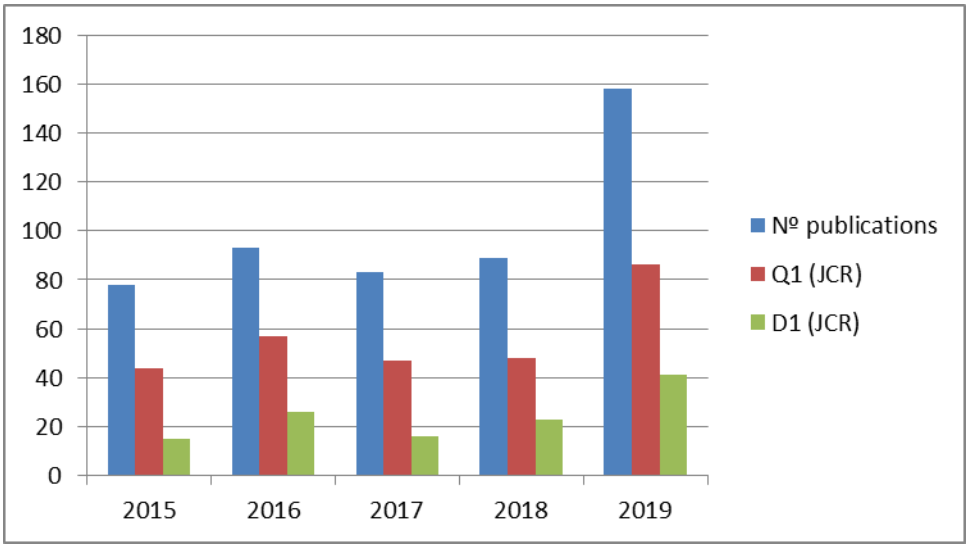
# SCIENTIFIC PRODUCTION 2019

The publications of each research group can be consulted in the section corresponding to each of them. The following table shows data regarding the Institute’s scientific production in 2019 (only articles and reviews):

| **No. publications** | **159** |
|---|---|
| Q1 JCR | 87 (54.7%) |
| D1 JCR | 41 (25.8%) |
| Q1 SJR | 116 (73.0%) |
| D1 SJR | 61 (38.4%) |

In addition, the following table shows the evolution of the Institute's scientific production in the last 5 years (2015-2019), taking as reference both the Journal Citation Reports (JCR-WoS) and the Scimago Journal & Country Rank (SJR-Scopus):

| | 2015 | 2016 | 2017 | 2018 | 2019 | TOTAL |
|---|---|---|---|---|---|---|
| **No. publications** | **78** | **93** | **83** | **89** | **159** | **502** |
| **Q1 (JCR)** | 44 (56.4%) | 57 (61.3%) | 47 (56.6%) | 48 (53.9%) | 87 (54.7%) | 283 (56.4%) |
| **D1 (JCR)** | 15 (19.2%) | 26 (28%) | 16 (19.3%) | 23 (25.8) | 41 (25.8%) | 121 (24.1%) |
| **Accumulated IF (JCR)** | 295,09 | 456,33 | 333,93 | 521,33 | 787,6 | 2.394,28 |
| **Q1 (SJR)** | 62 (79.5%) | 74 (79.6%) | 58 (69.9%) | 67 (75.3%) | 116 (73%) | 377 (75.1%) |
| **D1 (SJR)** | 37 (47.4%) | 43 (46.2%) | 41 (49.4%) | 44 (49.4%) | 61 (38.4%) | 226 (45%) |
| **Accumulated IF (SJR)** | 154.88 | 231.95 | 149.14 | 235.05 | 301.13 | 1,072.15 |



# TRAINING PROGRAMME FOR RESEARCHERS

The ITB professors and researchers participate extensively in the post-graduate programmes at the ULL related to biomedicine, biotechnology and health sciences. To complement this, the institute organizes a programme of weekly research seminars, with the participation of national and international researchers in scientific areas of interest. Most of the ITB researchers participate as professors and/or tutors in these post-graduate programmes, whose academic direction is the responsibility of Dr Guadalberto Hernández (PhD in Health Sciences) and Dr Ángel Acebes (Master's in Biomedicine), who are members of the institute. In addition, there is a strong participation of ITB professors and researchers in the Academic Committee of both programmes, and all the research groups at the institute are ascribed as official research lines for both programmes, acting as recipient laboratories for the corresponding students.

### *Organisation of Courses and Seminars*

The ITB works together with the Medical School on the Health Sciences Campus to organize a programme of courses and scientific seminars, co-funded by other public and private entities (Bioavance Foundation, Spanish Ministry of Economy and Competiveness -MINECO, Institute of Health Carlos III, ULL, EU, etc.). The Institute has organized 14 of these seminars and courses that were included in the programme for 2019, as listed below:

1. *Deciphering the brain: From its anatomy and activity to pathologies.* Scientific Conferences at the Institute of Biomedical Technologies (ITB). University of La Laguna, School of Medicine (17/05/2019). Dr Francisco Gómez Scholl (Department of Medical Physiology and Biophysics, Institute for Biomedicine in Seville (IBiS), Dr Javier De Felipe (Cajal Cortical Circuit Laboratory, Centre for Biomedical Technolgy, Technical University of Madrid).

2. *Advanced Systems for a better future*. Simposium en honor al Dr Nicholas A. Peppas (University of Texas, Austin, USA). Faculty of Pharmacy, University of La Laguna (15-16/05/2019).

3. *Seminars on neurodegeneration*. Scientific Conferences at the Institute of Biomedical Technologies (ITB). University of La Laguna, Medical School (24/05/2019). Dr Adolfo López de Munaín (University Hospital of Donostia, Biodonostia), Dr José J. Lucas (Centre for Molecular Biology "Severo Ochoa", CSIC).

4. *Nuevas perspectivas en el tratamiento de las enfermedades neurodegenerativas* (New perspectives for the treatment of neurodegenerative diseases). Scientific Conferences at the ITB. ULL, School of Medicine (10/05/2019). Dr José Luis Lanciego Pérez (Applied Medical Research Centre (CIMA, University of Navarre), Dr Jordi Alberch Vié, Institute of Neurocience, University of Barcelona).

5. *Update in digestive disease for general practitioners internal residents*. University Hospital of the Canary Islands, San Cristóbal de La Laguna (06-08 and 13-15 May 2019). Dr Manuel Hernández-Guerra.

6. *Update in gastroenterology and liver diseases*. University Hospital of the Canary Islands, San Cristóbal de La Laguna (June-November 2019). Dr Manuel Hernández-Guerra, Dr Enrique Quintero.

7. *Orfan Biotech SL: Primeros pasos de una empresa farmacéutica en Tenerife* (First steps of a pharmaceutical company in Tenerife). End-of Master's project, "Communication Skills" Seminar. Health Sciences Campus, School of Medicine, University of La Laguna (05/11/2019). Dr Miguel X. Fernandes.

8. *Perspectiva genómica del aislamiento y adaptación en las poblaciones humanas contemporáneas de Canarias* (Genomic perspective on isolation and adaptation in the contemporary human population of the Canary Islands). University of La Laguna (06/11/2019). Dr José Miguel Lorenzo (Genomics Unit at the Technological and Renewable Energy Institute).

9. *De la Universidad a la empresa privada y vice versa* (From the University to the private sector and back). School of Medicine, University of La Laguna (07/11/2019). Dr J.C. Luis Jorge (Applications of Plant Biology group, ULL).

10. *Análisis de los factores genéticos asociados con la enfermedad de Chagas mediante un estudio amplio del genoma - GWAS* (Analysis of genetic factors associated with Chagas disease through a genome-wide association study -GWAS). Biology Section, Faculty of Sciences, University of La Laguna (08/11/2019). Dr Marialbert Acosta Herrera ("López Neira"Parasitology and Biomedicine Institute, CSIC, Granada).

11. *Descifrando un genoma milenario: la historia de un cáncer transmisible* (Deciphering a millennial genome: the story of a transmissible cancer) School of Medicine, ULL (09/11/2019). Dr Adrián Báez Ortega (University of Cambridge).

12. *DNA-protein crosslink proteolysis repair: from molecular insight to cancer therapy*. School of Medicine, University of La Laguna (11/12/2019). Dr Kristijan Ramadan, Oxford Institute for Radiation Oncology, University of Oxford, UK).

13. *Co-translational association of mRNAs encoding components of the action potential* (Gail A Robertson, School of Medicine and Public Health, University of Wisconsin - Madison). School of Medicine, University of La Laguna (16/12/2019). Dr Guadalberto Hernández.

14. *The K+ homeostasis machinery in a bacterium* (Joao Cabral, Instituto de Investigaçao a Inovaçao em Saúde and Instituto de Biologia Celular e Molecular, Porto, Portugal). School of Medicine, University of La Laguna (17/12/2019). Dr Guadalberto Hernández.

### *PhD Theses Directed or co-directed by Members of the Institute*

1. Title: *Behavioral consequences of electrical versus chemical synapse restoration in a Drosophila model of neurodegeneration*. Author: Ana Ninovska Romero Luis. Supervisor: Ángel Acebes

Vindel. Host Institution: University of La Laguna. Date of thesis defence: 12/07/2019. Qualification: Summa Cum Laude

2. Title: *Aldosterone-induced morphological and functional remodeling of colon epithelium in health and disease*. Author: Natalia Serrano Morillas. Supervisors: Diego Álvarez de la Rosa and Teresa Giráldez. Host Institution: University of La Laguna. Date of thesis defence: 12/04/2019. Qualification: Summa Cum Laude

3. Title: *Optoelectrical Dynamics of Ion Channels and Subcellular Calcium Nanodomains*. Author: Roger Gimeno Llobet. Supervisors: Teresa Giráldez and Diego Álvarez de la Rosa. Host Institution: University of La Laguna. Date of thesis defence: 01/02/2019. Qualification: Summa Cum Laude

4. Title: *Hidrogeles bioactivos para la regeneración ósea en osteoporosis* ("*Bioactive hydrogels for bone regeneration in osteoporosis*"). Author: Elisabet Segredo Morales. Supervisors: Araceli Delgado and Carmen M. Évora. Host Institution: University of La Laguna. Date of thesis defence: 21/05/2019. Qualification: Summa Cum Laude

5. Title: *Investigating TDP-43 mutations in mouse and developing a knockin humanised TDP-43 mouse model of Amyotrophic Lateral Sclerosis*. Author: Francesca De Giorgio. Supervisor: Abraham Acevedo. Host Institution: University College London. Date of thesis defence: 28/08/2019.

6. Title: *Post-translational modifications in the DNA damage response*. Author: Ignacio Alonso de Vega. Supervisor: Veronique Smits. Host Institution: University of La Laguna. Date of thesis defence: 12/12/2019. Qualification: Summa Cum Laude.

# COMMUNICATION, DISSEMINATION AND OUTREACH ACTIVITIES

ITB researchers have assumed the responsibility of communicating their results to society and of disseminating their scientific activities through different media. This section lists some of the activities undertaken during 2019 in collaboration with different entities.

### *Organisation of events*

1. Young investigators building Neuroscience and Rita Levi-Montalcini Award. XVIII Congress of the Spanish Society of Neuroscience, SENC (Santiago de Compostela, 04/09/2019). Dr Ángel Acebes.

2. 3rd International Conference in Engineering Applications (ICEA2019). University of Azores, Portugal (8-11/07/2019). Dr Carlos Flores, member of the Advisory Committee and the Scientific Committee.

3. XXXVI Annual Meeting of the Canary Islands Society of Nephrology. La Laguna (24-25/05/2019). Dr Armando Torres, President of the Organization Committee.

4. IV Multidisciplinary Meeting of Biological Therapy and Small Molecules. New indications, special situations and new drugs. Santa Cruz de Tenerife. (08-09/02/2019). Dr Federico Díaz, Organization Committee Member.

5. 21st Conference of the European Society for Cognitive Psychology - ESCoP-2019, Adeje, Tenerife (25-28/09/2019). Dr Horacio Barber, Dr Markus Conrad and Dr Niels Janssen.

6. XXIX GEENDIAB Meeting and II Training Workshop for Nephrologists experts in Diabetic Kidney Disease. Madrid (17-18/05/2019). Dr Juan F. Navarro, National Coordinator of the Spanish Group for the Study of Diabetic Nephropathy (GEENDIAB), Spanish Society of Nephrology.

7. Advances in Precision Medicine. International Workshop, as part of Campus América ULL 2019. Faculty of Sciences, ULL, San Cristóbal de La Laguna (10-11/07/2019). Dr Mª Mar del Pino Yanes.

8. IV Meeting of the SysPharmPediA consortium. Vice-Rectorate of Internationalisation, ULL, San Cristóbal de La Laguna (11-12/07/2019). Dr Mª Mar del Pino Yanes.

9. 22nd Meeting of the Spanish Association of Gastroenterology. Madrid (20- 22/30/2019). Dr Antonio Z. Gimeno, member of the Scientific Committee.

### *Outreach activities involving members of the ITB*

1. VI Canary Islands Fair of Scientific Vocations and Careers 2019 (FGULL). San Cristóbal de La Laguna (Marzo 2019). Dr Ángel Acebes, Dr Tomás González, Dr Veronique Smits, Dr Raimundo Freire, Dr Teresa Giráldez.

2. Introductory workshop on genomics and bioinformatics. University of La Laguna (25/06/2019). Dr Carlos Flores.

3. TeleTraining Next Generation Sequencing with HoloLens. Vocational Training Centre “Los Gladiolos”, Santa Cruz de Tenerife (23/05/2019). Dr Carlos Flores.

4. Training webinar Genome Assembly Using a NanoDJ Notebook in CyVerse. CyVerse, University of Arizona, USA (13/09/2019). Dr Carlos Flores.

5. Training webinar Metagenomic Analysis Using NanoDJ Notebooks. CyVerse, University of Arizona, USA (27/09/2019). Dr. Carlos Flores.

6. Workshop on method to measure GFR in animal models (rodents), 2019. Dr Esteban Porrini

7. Visit of Seconday Schools: British School of Tenerife, annual visit 2019. Dr Abraham Acevedo.

8. ADEXSOM Project: A machine-learning platform to enable early stage AD diagnosis via blood exosome analysis. European Alliance for personalised Medicine Meeting, Brussels, Belgium (2019). Dr Néstor Torres.

9. Sporadic Alzheimer's disease: searching its pathogenic mechanisms by exhaustive deconstruction of the distinct levels of information in a microarray. 41st Meeting of the Spanish Society of Biochemist and Molecular Biology, Madrid, Spain (2019). Dr Néstor Torres.

10. Article: Lo que vemos cuando leemos: flexibilidad y plasticidad cerebra. HIPÓTESIS (What we see when we read: flexibility and brain plasticity. HYPOTHESIS). Digital magazine, No. 5, University of La Laguna, (2019). Dr Horacio Barber.

11. Visit of students from the "Hogar Escuela" College (Tenerife) to the MOLCAN laboratory (17/01/2019). Dr Teresa Giráldez.

12. International Women's Day Awards, Santa Cruz de Tenerife City Council (29/01/2019). Dr Teresa Giráldez.

13. Informative session for secondary school students, San Andrés Secondary School, León (23/02/2019). Dr Teresa Giráldez

14. Open Day Science and Technology Campus, University of La Laguna. Training programme for Secondary School students in the MOLCAN laboratory (July 2019). Dr Teresa Giráldez.

15. Macaronight. Researchers' Night, student visits, La Laguna. (27/09/2019). Dr Teresa Giráldez.

16. Open Day of the Genetics Laboratory for students from "Las Galletas" Secondary School (29/11/2019). Dr Mª Mar del Pino Yanes.

17. Human microbiome: implication for health. Invited speaker at the VI Fair of Scientific Vocations and Careers of the Canary Islands, La Laguna (27/03/2019). Dr Mª Mar del Pino Yanes.

18. "Nosotras hacemos ciencia" (Women do science), 2nd Edition. Documentary about the role of women in science. ULL Media (https://www.youtube.com/watch?v=UkjChlcIVaA), University of La Laguna (11/02/2019). Dr Mª Mar del Pino Yanes.

19. Invited speaker: Pursue your research vocation. "Nosotras hacemos ciencia" (Women do sicience), 2nd Edition. University of La Laguna (11/02/2019). Dr Mª Mar del Pino Yanes.

20. Participation in the VII Edition of the Scientific Dissemination Contest – Dissemination of scientific projects with the video "Jamás una gota dio para tanto" (A drop never served for so much: https://youtu.be/VXlWJ0KAV6o). Dr Manuel Hernández-Guerra.

21. Talento, transferencia del conocimiento e infraestructura: factores claves del ecosistema de innovación (Talent, knowledge transfer and infrastructure: key factors of the innovation ecosystem). 1st INtech Tenerife Innovation Observatory (25/10/2019). Dr Carmen Laura Sayas.

22. "Rutas de la Ciencia" (Scientific Routes), Macaronesian Researchers' Night 2019. Tenerife (27/09/2019). Dr David Bartolomé Martín.

23. Biology Workshop, VI Night of Stars. La Salle La Laguna School, San Cristóbal de La Laguna, Tenerife (02/30/2019). Dr Belinda Rivero.

24. Rutas Científicas a la Universidad de La Laguna (Scientific Routes around the University of La Laguna). Practical training for secondary school students to promote scientific vocations. La Laguna, Tenerife (14/03/2019). Dra. Belinda Rivero

25. El genoma entre costuras (The genome between seams). Charlitas con cienític@s (Chats with scientists). European Researchers' Night - Macaronight. La Laguna, Tenerife (27/09/2019). Dr Belinda Rivero

### *Seminars and invited speakers*

1. Tecnologías genómicas de alto rendimiento e impacto en salud (High-throughput and high-impact genomics technologies in health – Sessions of the Continuous Training Committee). Nª Sª de Candelaria University Hospital, Santa Cruz de Tenerife (02/10/2019). Dr Carlos Flores.

2. Modifiers of Steroid Receptor Action. Signal Transduction Laboratory, National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH), Research Triangle Park, NC, USA. Host: Dr. J.A. Cidlowski (11/02/2019). Dr Diego Álvarez de la Rosa.

3. The quaternary structure of the mineralocorticoid receptor depends on ligand and DNA binding. Laboratory of Receptor Biology and Gene Expression (LRBGE). National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD, USA. Host: Dr G.L. Hager (17/06/2019). Dr Diego Álvarez de la Rosa.

4. Mineralocorticoid receptor quaternary structure dynamics. Structural Biophysics interest group. National Institute of Neurological Diseases and Stroke (NINDS), National Institutes of Health (NIH). Bethesda, MD, USA. Host: Dr K.J. Swartz (10/07/2019). Dr Diego Álvarez de la Rosa.

5. Nuevos usos de antagonistas del receptor de mineralocorticoides (Novel uses of mineralocorticoid receptor antagonists). Pharmaceutical Conferences University of La Laguna – CSIC. Faculty of Pharmacy, ULL. Host: Dr Alicia Boto (24/09/2019). Dr Diego álvarez de la Rosa.

6. Pathogenesis of post-transplant diabetes: the role of immunosuppression. First Mayo Clinic-Granada Nephrology Meeting, Granada (29-30/03/2019). Dr Armando Torres.

7. Overview of the error of creatinine and cystatin-c-based formulas in clinical practice. ERA-EDTA Annual Meeting, Budapest (15/06/2019). Dr Esteban Porrini.

8. Post-transplant diabetes mellitus: from man to mice and from mice to man. CEDOC “Centre for chronic diseases”, Lisboa. Host: Dr Paula Macedo (07/02/2019). Dr Esteban Porrini.

9. Post-transplant diebetes mellitus. Catalan Society for Organ Transplant Trasplante, Barcelona (14/03/2019). Dr Esteban Porrini.

10. Visual Attention in Reading. University College London (UCL), Faculty of Brain Sciences, Londres, United Kingdom (11/12/2019). Dr Horacio Barber.

11. Parafoveal word processing: What can we learn from “unnatural reading paradigms”? 20th European Conference on Eye Movements, Alicante, Spain (18/08/2019). Dr Horacio Barber.

12. Klotho: ¿un nuevo protagonista en la enfermedad cardiovascular? (Klotho: A new player in cardiovascular disease?). Health Research Institute INCLIVA, Valencia (25/01/2019). Dr Juan F. Navarro.

13. Fármacos antidiabéticos y ERC (Anti-diabetic drugs and CKD). 14th Course on Arterial Hypertension and Cardiovascular Risk Course for Resident Physicians in Nephrology, Madrid (07-09/02/2019). Dr Juan F. Navarro.

14. Factores de progresión de Enfermedad Renal Diabética (Predictive factors in Diabetic Kidney Disease progression – PROGRESER study). Preliminary results. XXIX GEENDIAB Meeting and II Training Workshop for nephrologists specialised in Diabetic Kidney Disease, Madrid (17-18/05/2019). Dr Juan F. Navarro.

15. Mecanismos de acción de los iSGLT2: nuevos conceptos y datos recientes (Mechanisms of Action of iSGLT2: New Concepts and Recent Evidence). XXIX GEENDIAB Meeting and II Training Workshop for nephrologists specialised in Diabetic Kidney Disease, Madrid (17-18/05/2019). Dr Juan F. Navarro.

16. Presentación del registro agonistas GLP1 e inhibidores SGLT2 (Presentation of the GLP1 agonist and SGLT2 inhibitor registry). XXIX GEENDIAB Meeting and II Training Workshop for nephrologists specialised in Diabetic Kidney Disease, Madrid (17-18/05/2019). Dr Juan F. Navarro.

17. Importancia de la evaluación global y del riesgo cardiovascular en el paciente con DM y ERC (Importance of global assessment and cardiovascular risk in patients with DM and CKD). I Training workshop on Diabetic Kidney Disease in the Canary Islands, Las Palmas de Gran Canaria (15/11/2019). Dr Juan F. Navarro.

18. Inhibidores SGLT2: mecanismo de acción, efectos vasculares y renales y resultados de estudios recientes (SGLT2 inhibitors: mechanism of action, vascular and kidney effects and results of recent studies). I Training workshop on Diabetic Kidney Disease in the Canary Islands, Las Palmas de Gran Canaria (15/11/2019). Dr Juan F. Navarro.

19. Nuevas oportunidades terapéuticas en la Enfermedad Renal Diabética (New therapeutic opportunities in Diabetic Kidney Disease). 6th Congress of the Galician Society of Nephrology, Ferrol (15-16/11/2019). Dr Juan F. Navarro.

20. Dislipemia en la enfermedad renal crónica (Dyslipidemia in chronic kidney disease). XVI Update Meeting in Nephrology, Sevilla (22-23/11/2019). Dr Juan F. Navarro.

21. Elucidating novel disease mechanisms through the generation of new ALS mouse models. Ciien Congress 2019, Valencia (18-20/09/2019). Dr Abraham Acevedo.

22. Murine models of ELA: Metabolismo, Sistemas Modelo y Terapias para la ELA (Murine models of ALS: metabolism, model systems and therapies for ALS). Third International Meeting of ELA Research in Spain, Ramón Areces Foundation, Madrid (02/07/2019). Dr Abraham Acevedo.

23. Resonancia Magnetica funcional (Functional Magnetic Resonance). National University of Medellín, Colombia (16/12/2019). Dr Niels Janssen.

24. Functional organization of the medial temporal lobe during an object naming task: A task-fMRI data-driven approach. University of California, Irvine, USA (18/04/2019). Dr Niels Janssen.

25. Measuring dynamic brain activity with fMRI: insights from speech production. University of Albuquerque, New Mexico, USA (12/04/2019). Dr Niels Janssen.

26. Measuring dynamic brain activity with fMRI: insights from speech production. La Laguna, Tenerife (08/02/2019). Dr Niels Janssen.

27. Understanding BK function with patch-clamp fluorometry. Georgetown University, Washington DC. EEUU (29/04/2019). Host Tina Brelidze (10/07/2019). Dr Teresa Giráldez.

28. Development and optimization of calcium fluorescent sensors based on ion channels. Congress of the Spanish Society of Neuroscience (SENC), Santiago de Compostela (0406/09/2019). Dr Teresa Giráldez.

29. Optoelectrical dynamics of BK channel activation. EBSA meeting, Madrid (20-24/07/2019). Dr Teresa Giráldez.

30. Role of the neuronal BK4 subunit in the formation of calcium nanodomains constituted by BK and voltage-gated calcium channels. Meeting of the Spanish Network of Ionic Channels (RECI), Cáceres (15-17/05/2019). Dr Teresa Giráldez.

31. El aula invertida (The inside-out classroom). Invited speaker at the XIII Medical Education Annual Meeting 2019. El Escorial (15/07/2019). Dr Enrique Quintero.

32. Situacion actual CCE & “Práctica Diaria”: Colonoscopia Incompleta, Screening & IBD (Present situation of CCE & "Daily Practice": Incomplete colonoscopy, Screening & IBD. Capsule Endoscopy Training Course. Pamplona (22/02/2019). Dr Enrique Quintero.

33. Screening del Cáncer Colorectal: Colonoscopía vs. Test de Sangre Oculta en Heces (Screening of colorectal cancer: Colonoscopy vs. Faecal Occult Blood Test). Refresher Course 2019, 75 years of the Gastroenterology Clinic, in recognition of Prof. Henry Cohen. Montevideo, Uruguay (07/11/2019). Dr Enrique Quintero.

34. Flipped learning and peer instruction as teaching innovation in the grade of medicine. Santander (29/03/2019). Dr Manuel Hernández-Guerra.

35. Eliminating barriers to eliminate hepatitis C virus infection in drug addiction centers. Congreso PsicoDrogoAlcohol, Malaga (08/30/2019). Dr Manuel Hernández-Guerra.

36. Manejo del enfermo cirrótico (Managing the cirrhotic patient). Congress of the Spanish Society of Digestive Pathology, Santander (June 2019). Dr Manuel Hernández-Guerra.

37. Familial and hereditary colorectal cancer, update of the diagnosis and prevention of the Spanish guideline. 22nd Meeting of the Spanish Association of Gastroenterology, Madrid (20-22/03/2019). Dr Antonio Z. Gimeno.

38. Strategies of colon cleansing in hard to prepare patients. XII Training Course in Colonoscopy Quality, Tenerife (14/02/2019). Dr Antonio Z. Gimeno.

39. Comparison of Two Intensive Bowel Cleansing Regimens in Patients with Previous Poor Bowel Preparation: A Randomized Controlled Study. Awards by the Royal Academy of Medicine of Tenerife. (26/02/2019). Dr Antonio Z. Gimeno.

40. DNA double strand breaks in telophase creates de novo anaphase bridges and coalescence between sister loci. Plenary talk at the conference: From cancer to developmental defects: the control of DNA segregation and human disease. Baeza, Andalusia, Spain (14/10/2019). Dr Félix Machín.

41. The Fate of the Progeny of Yeast Topoisomerase II Mutants: Senescence, Death and Genome Instability. Short Talk at the EMBO Workshop: DNA topology and topoisomerases in genome dynamics. Les Diablerets, Switzerland (18/09/2019). Dr Félix Machín.

42. Seeking new therapies against neurodegenerative diseases in present and past drugs. Seminar given at Nª Sª de Candelaria University Hospital, Tenerife (06/11/2019). Dr Félix Machín.

43. Yeast cells partly regress chromosome segregation after DNA double strand breaks in telophase. Seminar given at Nª Sª de Candelaria University Hospital, Tenerife (24/10/2019). Dr Félix Machín.

44. Development and optimization of calcium fluorescent sensors based on BK ion channels. 18$^{th}$ Annual Meeting of the Spanish Society of Neuroscience (04-06/09/2019). Dr David Bartolomé Martín.

45. Cerrando el círculo..., ¿o no? (Closing the circle..., or not?). Fourth Young Scientists Meeting - Christmas Meeting, Faculty of Health Sciences, University of La Laguna (19/12/2019). Dr Carmen Laura Sayas.

# KNOWLEDGE AND TECHNOLOGY TRANSFER

### *Emerging lines associated with technology transfer: "Agustín de Betancourt" Programme*

The "Agustín de Betancourt" programme is an initiative of the Council of Tenerife, first established in 2016, to provide support to the research groups and institutes at the ULL, in order to maintain research activity with high potential for technology transfer. It is also committed to the recruitment of human resources with skills for the development of advanced technological products and services that could have an impact on the market, driving their commercial exploitation in priority sectors for the economy of The Canary Islands. After being selected through a public tendering process, the research personnel recruited through this program are brought together with consolidated research groups to carry out their own research projects under the supervision of the group leader.

The active ITB research projects that represent emerging lines related to technology transfer are:

1. **Identification of new therapeutic targets and the generation of neuroactive peptides in Alzheimer's disease and other related taupathies** ("Identificación de nuevas dianas terapéuticas y generación de péptidos neuroactivos en la enfermedad de Alzheimer y otras taupatías relacionadas". Principal investigator: Carmen Laura Sayas Casanova, PhD; PI-ULL: Néstor Torres Darias; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL). Programme of "Drug Development & Target Identification".

2. **Proof of concept for a non-invasive technology for the early diagnosis in Sporadic Alzheimer's Disease based on circulating exosomes** ("Prueba de concepto para una tecnología no-invasiva de diagnóstico temprano de Enfermedad de Alzheimer Esporádica basada en exosomas circulantes. Principal investigator: Daniel V. Guebel, PhD; PI-ULL: Néstor Torres Darias; Department of Biochemistry, Microbiology, Cellular Biology and Genetics, ULL). Programme of "Drug Development & Target Identification".

3. **Neuromodulatory techniques as new therapeutic approaches against addictive behaviours** ("Técnicas neuromodulatorias como nuevas aproximaciones terapéuticas frente a las conductas adictivas"). Principal investigator: Julien Dampuré, PhD; PI-ULL: Horacio Barber Friend; Department of Cognitive, Social and Organisational Psychology, ULL). Programme of "Neurobiology & Brain-Related Diseases".

4. **The induction of autophagy through D2R/D3R receptors in Parkinson's and Huntington's disease.** ("Inducción de autofagia a través de receptores D2R/D3R en la enfermedad de Parkinson y la de Huntington". Principal investigator: Diego Luis-Ravelo, PhD; PI-ULL: Tomás González Hernández; Department of Basic Medical Sciences, ULL). Programme of "Neurobiology & Brain-Related Diseases".

5. **MetSPLAT: An in vivo platform for preclinical drug trials against metabolic syndrome.** Agustín de Betancourt project (Principal investigator: Silvia Velázquez García, PhD; PI-ULL: Diego Álvarez de la Rosa; Department of Basic Medical Sciences, ULL). "Chronic & Age-Related Diseases" Programme.

6. **In vivo screening based on the reversal of cellular phenotypes to find new drugs that inhibit the Chk1 kinase involved in cancer** ("Rastreo in vivo basado en la reversión de fenotipo celular para encontrar nuevos fármacos inhibidores contra la quinasa Chk1 implicada en cáncer". Principal investigator: David Gillespie, PhD; PI-ULL: Eduardo Salido Ruiz; Department of Basic Medical Sciences, ULL). "Genetic & Rare Diseases" Programme.

7. **Development and application of nanostructured magnetic platforms in the detection of pathogens: environmental applications in the agri-food industry and in water intended for human consumption** ("Desarrollo y aplicación de plataformas magnéticas nanoestructuradas en la detección de agentes patógenos: aplicaciones medioambientales, en la industria agroalimentaria y en aguas de consumo humano". Principal investigator: Íñigo Fernández Bats, PhD; PI-ULL: José Luis González Mora; Department of Basic Medical Sciences, ULL). Programme of "Neurobiology & Brain-Related Diseases".

8. **Gene Editing Service** ("Servicio de edición génica". Principal investigator: Belinda Rivero Pérez, PhD; PI-ULL: Eduardo Salido Ruiz; Department of Basic Medical Sciences). "Chronic & Age-Related Diseases" Programme

9. METAPANC: Inhibition of glutamine metabolism as therapy for pancreatic ductal adenocarcinoma ("Inhibición del metabolismo de la glutamina como terapia contra el adenocarcinoma ductal pancreático". Principal investigator: Miguel X. Fernandes, PhD; PI-ULL: José M. Padrón; Department ofOrganic Chemistry, ULL). "Drug Development & Target Identification" Programme.

10. MICROFAVAR: Development of a high-resolution, high-speed quantitative phase-contrast microscope for 3D imaging of biological samples ("Desarrollo de un microscopio de contraste de fase cuantitativa de alta resolución y alta velocidad para la obtención de imágenes en 3D de muestras

biológicas". Principal investigator: Carlos Cairós; PI-ULL: Ángel Acebes, Department of Basic Medical Sciences, ULL). Programme of "Neurobiology & Brain-Related Diseases".

### *Technology transfer*

1. Facility for the Massive Analysis of Genomic Data (Regional Government of Tenerife, CGIEU0000219140). Contract: 2,700,000 € (2018-2022). Dr Carlos Flores.

2. Agreement between the Institute of Technology and Renewable Energies, HUNSC and The Canary Islands Health Research Institute Foundation to contribute to strengthening education, training, research, development and scientific and technological innovation in genomics, precision medicine and biotechnology (OA17/008). Contract: 320,000 € (2017-2020). Dr Carlos Flores.

3. Collaboration agreement between the The Canary Islands Foundation for Advances in Biomedicine and Biotechnology (Bioavance) and the company Orfan Biotech SL to generate an in vitro model of Huntington's disease and to validation the proposed approach ("Convenio de colaboración entre la Fundación Canaria para el Avance de la Biomedicina y de la Biotecnología (Bioavance) y la empresa Orfan Biotech SL para la realización de un modelo in vitro de la enfermedad de Huntington y ensayos de validación del abordaje propuesto"). Contract: 15,000 € (22/02/2019 - 01/10/2019). Dr Tomás González Hernández.

# FUNDING

### *Construction and development of the ITB building and of its general research support services (2010-2019)*

A fundamental part of the activities carried out in the past years were aimed at obtaining competitive funding for the design and construction of the ITB building on the Health Sciences Campus, and the acquisition of its scientific equipment, in close cooperation with the HUC. In this regard, a key advance was the execution of the ADE-210/00046 project, aimed at the construction of the ITB building, including the animal house facility of the General Research Support Services (SEGAI). This was achieved thanks to funding in the form of a loan from the Institute of Health Carlos III, with the commitment to return the money through a collaboration and funding agreement with the Tenerife City Council, Tenerife Area 2030.

Most of the budget assigned to this project was allocated to the construction of the first phase of the building that will host the ITB facilities - including units for large common equipment, administration and management, general laboratories and the animal house, with the added function of hosting the main offices of the Canary Islands Foundation for Advances in Biomedicine and Biotechnology (see Biomedical Innovation Platform). The building, as shown below, occupies about 4,000 $m^2$ in its first phase and it includes a basement, a ground floor and a semi-basement for the control of technical installations/building systems, the work on which has already been completed. At present, the installation of the furnishings and the adaptation of the building are underway. In addition, the project included a strategic analysis aimed at defining the organization of the institute into groups

and thematic programmes, designing the road-map for the subsequent years that has been under development to date.

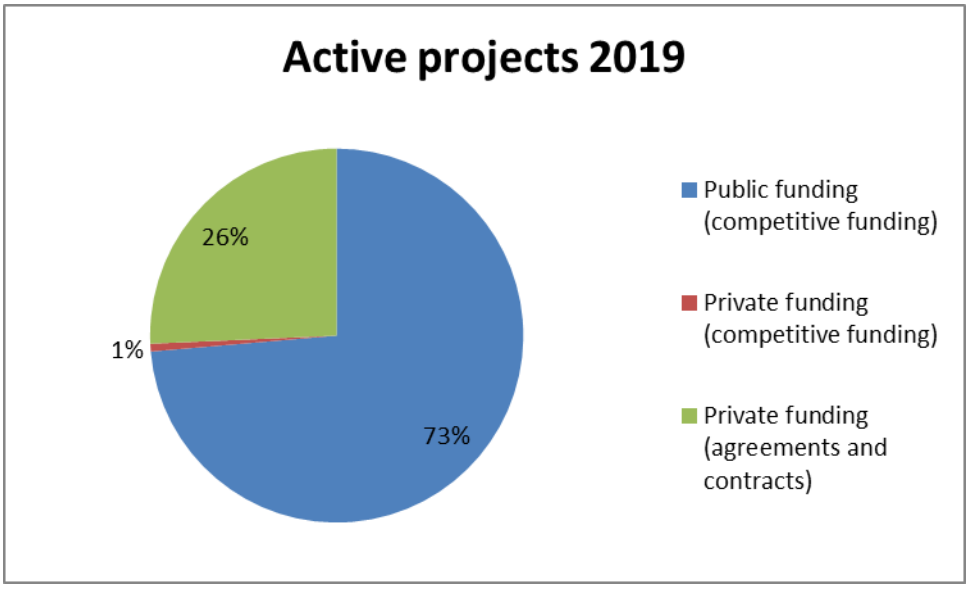

*View of the ITB building in the first phase of construction on the Health Sciences Campus, located next to the School of Medicine and the University Hospital of the Canary Islands.*

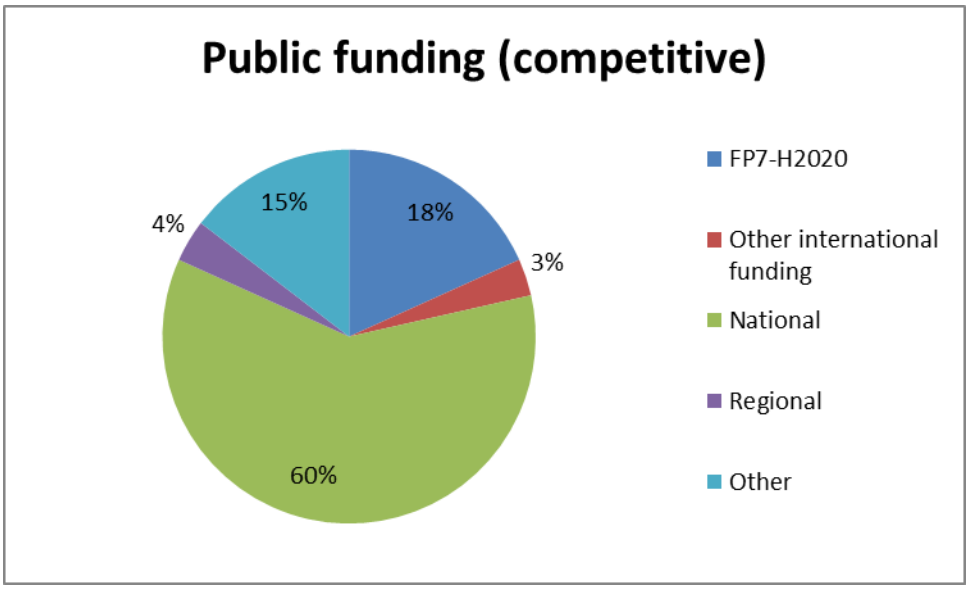
| CONSTRUCTION AND DEVELOPMENT OF THE CANARY ISLANDS CENTRE FOR BIOMEDICAL RESEARCH | |
|---|---|
| Project information | Reference: ADE-210/00046. Programa de dinamización del entorno investigador del Sistema Nacional de Salud: Apoyo a la creación de Institutos de Investigación Sanitaria (Programme to Stimulate Research activities in the NHS: Support for the creation of Health Research Institutes). Principal Investigator: Rafael Alonso Solís. |
| Implementation period | Requested in October 2010 and awarded by The Spanish Ministry of Science, Innovation and Universities (MICINN) on November 29th, 2010, to be executed between 2011 and 2018 (extended). |
| Funding Body | Institute of Health Carlos III - Spanish Ministry of Economy and Competitivity/Council of Tenerife (Instituto de Salud Carlos III-MINECO/Cabildo Insular de Tenerife). |
| Beneficiary institution | University of La Laguna (Universidad de La Laguna) |
| Collaborating institutions | University Hospital of the Canary Islands (Hospital Universitario de Canarias), University Hospital Nª Sª de la Candelaria (Hospital Universitario Nª Sª de la Candelaria), Council of Tenerife (Cabildo Insular de Tenerife). |
| Budget | 8,030,000 € |

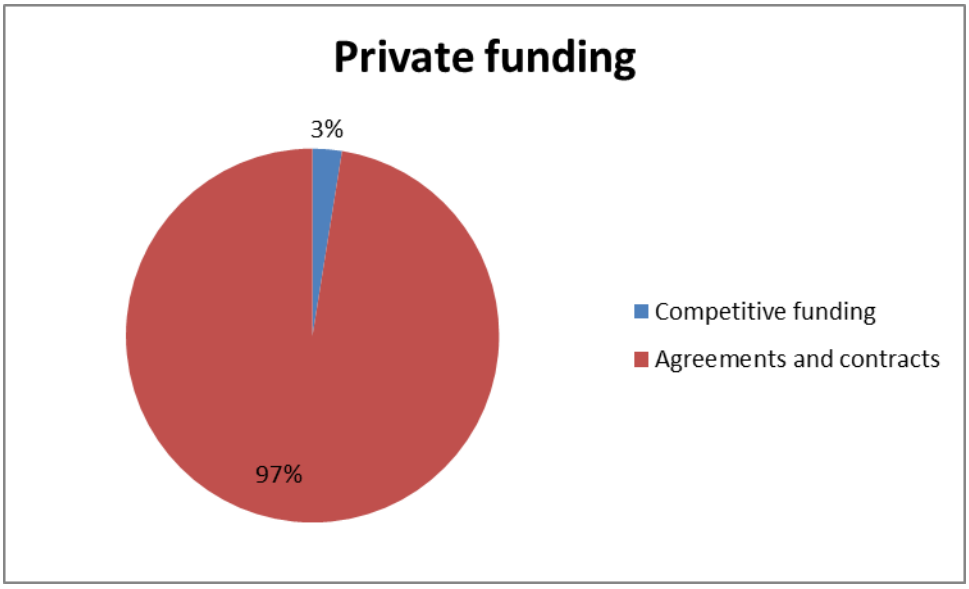
### *Ongoing projects held by ITB research groups in 2019*

The projects of each of the institute's research groups can be found in the information corresponding to each of these groups. The following table and graphs show the aggregated data of the active projects held by ITB research groups during 2019, and the source of the funding:

| **TOTAL FUNDING FOR ACTIVE RESEARCH PROJECTS IN 2019** | |
|---|---|
| **Public funding (A)** | **10,954,045.24 €** |
| ***Competitive funding*** | **10,954,045.24 €** |
| FP7-H2020 | 1,999,742.00 € |
| Other international funding | 350,000.00 € |
| National funding | 6,603,634.41 € |
| Regional funding | 400,668.83 € |
| Other | 1,600,000.00 € |
| | |
| **Private funding (B)** | **3,921,045.74 €** |
| ***Competitive funding*** | **99,376.74 €** |
| ***Agreements and Contracts*** | **3,821,669.00 €** |
| International | 469,799.00 € |
| National | 3,324,870.00 € |
| **TOTAL (A + B)** | **14,875,090.98 €** |






# Implementation of the ITB's budget for the 2019 financial year

### *Annual Budget of the University of La Laguna*

The amount allocated in the annual budget of the University of La Laguna for the Institute of Biomedical Technologies in 2019 was 2,850 €, which was used as follows:

- **Printing expenses: 150 €** –Printing of 6 copies of the Institute's 2018 annual report;

- **Translation expenses: 1,615.40 €** – To cover the translation and adaptation into English of the ITB 2018 Report for the planned evaluation of our accreditation as a "María de Maeztu Unit of Excellence";
- **Web services expenses: 1,084.60 €** - Expenses to cover the design, development, hosting, maintenance and adaptation into English of the new ITB website (www.institutotecnologiasbiomedicas.com).

| **Implementation of the ITB institutional budget for the financial year 2019** | | | |
|---|---|---|---|
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| **Account Key: 180317AA** | | | |
| **Budget: 2,850 €** | | | |
| | | | |
| ***Company*** | ***Invoice No.*** | ***Amount (w/o IGIC)**** | ***Description and details*** |
| Gráficas Sabater | 20194623 | 150 € | Hard copies of the ITB's Annual Report 2018 |
| BiomedRed | B132/19-11 | 1,615.40 € | Translation into English of the ITB's Annual Report 2018 |
| Web Empresas | 80/2019 | 1,084.60 € | ITB website |
| **TOTAL EXPENSES** | | **2,850 €** | |

### *Aid to promote excellence in research activities*

In connection with the application for accreditation as a "María de Maeztu Unit of Excellence", the ITB was granted 10,000 € by the Vice-Chancellor of Research at the University of La Laguna under the "Aid to promote excellence in research activities" programme, the details of which are indicated below:

- **Printing expenses: 348 €** –to print 14 copies of the Institute's 2018 annual report, as the Institute's baseline funding was not enough to print sufficient copies;
- **Translation expenses: 284.60 €** – These expenses correspond to the translation and adaptation into English of the ITB website for the planned evaluation of our for accreditation as a "María de Maeztu Unit of Excellence;
- **MdM proposal drafting expenses: 9,367.40 €** corresponding to the technical advice, preparation and submission of the application for accreditation of the Institute as a "María de Maeztu Unit of Excellence", drafted by the Bioavance Foundation.

| **Aid to promote excellence in research activities** | | | |
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| ***Company*** | ***Invoice No.*** | ***Amount (w/o IGIC)**** | ***Description and details*** |
| Gráficas Sabater | 20194622 | 348 € | Hard copies of the ITB's Annual Report 2018 |

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|---|---|---|---|
| BiomedRed | B133/19-11 | 284.60 € | Translation into English of the ITB's website |
| Fundación Bioavance | 15.2019 | 9,367.40 € | MdM proposal drafting 2019 |
| **TOTAL EXPENSES** | | **10,000 €** | |

### *Application for accreditation as a "María de Maeztu Unit of Excellence"*

In 2019, after confirming that the requirements were met, the ITB presented a proposal to the Vice-Chancellor of Research to prepare an application to become a "María de Maeztu Unit of Excellence" in the call opened by the Ministry of Science, Innovation and Universities, Once the pre-proposal had been approved and internal funding was obtained to draft the proposal, the application was correctly submitted on time. At present, the proposal submitted is under evaluation.