CIC
Centro de Investigación del Cáncer

iBMCC
Instituto de Biología Molecular y Celular del Cáncer (USAL - CSIC)

Universidad de Salamanca
Campus de Excelencia Internacional

800 años
1218 - 2018

CSIC
Consejo Superior de Investigaciones Científicas

FONDO EUROPEO DE DESARROLLO REGIONAL
UNIÓN EUROPEA

Junta de Castilla y León
Consejería de Educación

Europa impulsa nuestro crecimiento

PROGRAMA DE FORTALECIMIENTO DE ESTRUCTURAS DE INVESTIGACIÓN DE CASTILLA Y LEÓN "ESCALERA DE EXCELENCIA" COFINANCIADO POR EL P.O. FEDER DE CASTILLA Y LEÓN 14-20 *(Ref. CLC-2017-01)*

El objetivo temático de este tipo de actuaciones es promover el desarrollo tecnológico, la innovación y una investigación de calidad (OT.1)

CIC
Centro de Investigación del Cáncer

IBMCC
INSTITUTO DE BIOLOGÍA MOLECULAR Y CELULAR DEL CÁNCER (USAL - CSIC)

Centro de Investigación del Cáncer - Instituto de Biología Molecular y Celular del Cáncer CIC-IBMCC (USAL-CSIC)
Campus Miguel de Unamuno s/n 37007 Salamanca (Spain)

Phone: +34 923 294 720 • Fax: +34 923 294 743 • E-mail: cicancer@usal.es

https://www.cicancer.org/scireport-2018-2019

Design and layout: a.f. diseño y comunicación / www.afgrafico.com

INDEX

1 FOREWORD 6

2 ORGANIZATION 12

3 RESEARCH UNITS 22

3.1 GTPases and cancer. Ras mediated signaling (Laboratory 1) 24

3.2 Identification of early oncogenic drivers, molecular coadjutants, and pathobiological programs involved in cancer development and progression (Laboratory 2) 30

3.3 Kinases in oncology and neurodegeneration. Signaling by chromatin kinases (Laboratory 4) 38

3.4 Epitranscriptomics and cancer (Laboratory 5) 42

3.5 Tumour-Stroma Signaling (Laboratory 5) 46

3.6 Tumor biophysics (Laboratory 6) 50

3.7 Molecular and genetic determinants of cancer susceptibility, evolution and treatment response (Laboratory 7) 54

3.8 Reversible Processes In Cell Cycle Control (Laboratory 8) 60

3.9 Chromosome segregation and human disease (Laboratory 9) 66

3.10 Immunology and Cancer (Laboratory 11) 70

3.11 Oncohematology (Laboratory 12) 86

3.12 Stem cells, cancer stem cells and cancer biology (Laboratory 13) 114

3.13 Hereditary cancer (Laboratory 14) 118

3.14 Kinases in oncology Signaling by receptor tyrosine kinases (Laboratory 15) 124

3.15 Structural biology of cell adhesion and signaling (Laboratory 17) 130

3.16 Unconventional autophagy in health and disease (Laboratory 18) 134

3.17 Bioinformatics and Functional Genomics of Cancer (Laboratory 19) 138

3.18 Clinical and molecular analysis of solid tumors (Oncology Service) 142

4 SCIENTIFIC SERVICE UNITS 148

4.1 Genomics 150

4.2 Proteomics 152

4.3 Traslational Oncopharmacology 154

4.4 Bioinformatics 156

4.5 Cytometry 158
4.6 Cytogenetics 160
4.7 Molecular Biology 162
4.8 Comparative Molecular Pathology 164
4.9 Structural Biology 166
4.10 Microscopy 168
4.11 Hereditary Cancer & Genetic Counseling 170

5 TECHNICAL SUPPORT UNITS 172
5.1 FICUS Manager 174
5.2 Secretary 174
5.3 Administration 175
5.4 IBMCC-CSIC Manager 175
5.5 Communication & Marketing 176
5.6 Equipment & Building Maintenance 177
5.7 Quality Control & Risk Prevention 178
5.8 Central Warehouse & Radiological Protection 179
5.9 Glassware Cleaning and Sterilization 180
5.10 Information Technologies Service (IT) 181

6 SCIENTIFIC ACTIVITIES 182
6.1 List of journals 184
6.2 CIC-IBMCC Publications by Quartile 2009-2019 190
6.3 National and international collaborations 191
6.4 Oncology Biomedical Research Networking Centre (CIBERONC) 195
6.5 Groups of CIC-IBMCC recognized as "Unidad de Investigación Consolidada" (UIC) for Castilla-León Autonomous Government 196
6.6 Groups of CIC-IBMCC recognized as "Grupos de Investigación Reconocida" (GIR) for the Salamanca University (USAL) 197

7 TRAINING ACTIVITIES 200
7.1 Postgraduate Program: Master degree in "Biology and Clinic of Cancer" 202
7.2 Students Master Program 203
7.3 Master Theses 204
7.4 Postgraduate Program: PhD program entitled "Bioscience: Biology and Clinic of Cancer and Translational Medicine" 207
7.5 Students PHD Program 208
7.6 Doctoral Theses 213
7.7 Conference meetings & scientific courses 216
7.8 Scientific Seminar Program 226

8 SCIENCE OUTREACH 232
8.1 The most relevant activities 2018-2019 234
8.2 Scientific culture and fundraising 238

1

FOREWORD

FOREWORD

This report summarizes the activities of the CIC-IBMCC (Centro de Investigación del Cáncer-Instituto de Biología Molecular y Celular del Cáncer de Salamanca (CSIC-USAL) through the years 2018 and 2019, a biennial period that also encompassed the celebration of the 800th anniversary of our host institution, the University of Salamanca (USAL).

After having successfully achieved most of our foundational strategic goals established in 2000, the CIC IBMCC started in the last quarter of 2017 a renewed, in-depth **SWOT analysis** to identify strengths, weaknesses, opportunities and threats covering the entire chain of the R&D process, with an aim at strengthening our future projection and institutional commitment regarding our mission and vision of conducting first-rate, multidisciplinary cancer research following a comprehensive approach focused on the most efficient translation to the patients and society in general, of the new knowledge generated in the lab.

Based on this SWOT analysis, a new 2018-2023 Strategic Plan (SP) was drafted and submitted to approval by our institutional sponsors including USAL, CSIC and JCyL. Among other aspects, this new SP was geared to realign the CIC-IBMCC research within the framework and strategic objectives of the EU-sponsored, 2014-2020 Regional Strategy for Research and Innovation for a Smart Specialization (RIS3) of Castilla y León (CyL). This Strategy is co-financed by the European Regional Development Fund and involves specific requirements and commitments of our activities with regards to scientific excellence and technological leadership, internationalization and collaboration. After external evaluation of our new SP in a competitive call open to all research centers from CyL, the CIC-IBMCC received accreditation as the first **"Centro de Excelencia"** recognized within the **"Escalera de Excelencia of Castilla y León"** and was awarded a grant of € 2,100,000 for the period 2018-23 to support our SP-related efforts focused on improving our international competitiveness, research excellence and outreach in the field of cancer research.

STRENGTHS

- Top basic and clinical research groups
- High social visibility
- Good managerial and administration practices
- Cutting-edge technological core facilities
- Wide network of international collaborations
- Well-defined strategic goals, research lines, and priorities
- Good funding from competitive regional and national sources
- Good quality of training programs

WEAKNESSES

- Lack of PIs in key strategic research lines
- Dispersion of research activities
- Limited spectrum of tumors studied at the clinical level
- Lack of competitiveness in recruitment of new PIs
- Low ratio of international and female PIs
- Lack of ERC funding
- Limited success in coordination of H2020 projects

OPPORTUNITIES

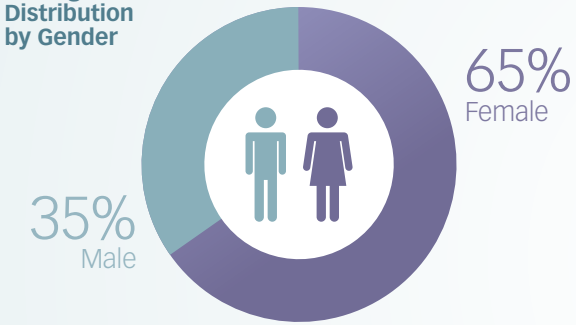
- Incorporation of new internationally competitive research lines
- Capacity to attract funding from EU and other international agencies
- Capacity to attract governmental funding for research centers of excellence (i.e., S. Ochoa program)
- Translational capacity of research outputs of interest for the industrial sector
- New internal and international collaborations
- Creation of a Former Alumni network
- Expansion of our capacity to get phylanthropy-based support

THREATS

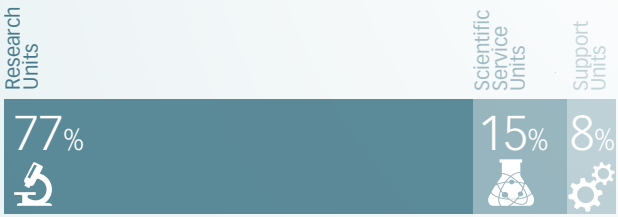
- Poor recycling of faculty due to difficulty in recruit and retain new talent
- Negative international view of the Spanish R&O system, which hampers recruitment of foreign staff
- Loss of productivity of faculty due to excessive administrative, managerial, and fund-rising duties
- Loss of technological advantage due to lack of on-time renovation of equipment and core facilities

We should point out that some of the objectives of the new SP were already implemented during the period. Among them: (i) the reorganization of the research structure of our center into two complementary Research Programs (RP):The Molecular Mechanisms of Cancer (MMC) Program and the Translational and Clinical Research in Cancer (TCRC) Program, and (ii) the renewal of the External Scientific Advisory Board (ESAB) which incorporated three new external international researchers, two of them women. We may also mention that on September 2019 our center received the seal of Excellence in Research Award (HRA) from the European Commission, an accreditation geared at making our center more attractive to European-funded researchers and facilitating the recruitment and incorporation and stabilization of new talent in our center. During 2018-2019 we also renewed or confirmed our ISO 9001and OHSAS 18001 Quality Control certifications covering our socio-sanitary services and activities after evaluation by the corresponding monitoring agencies.

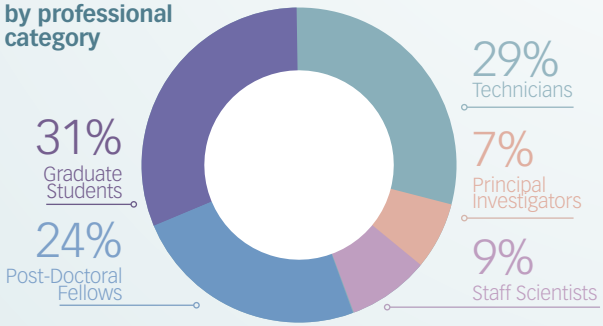
Average Distribution by Gender



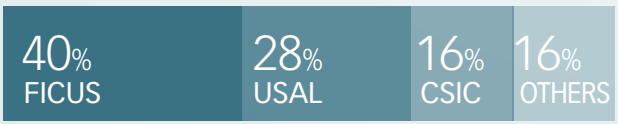
Distribution by Areas



Distribution by professional category



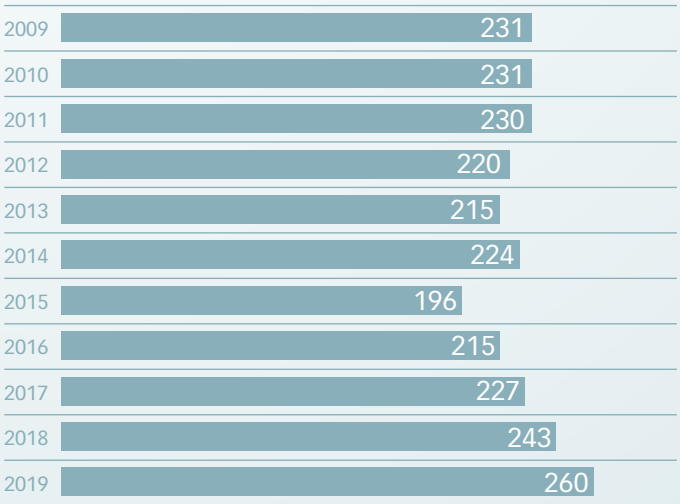
Distribution by institution



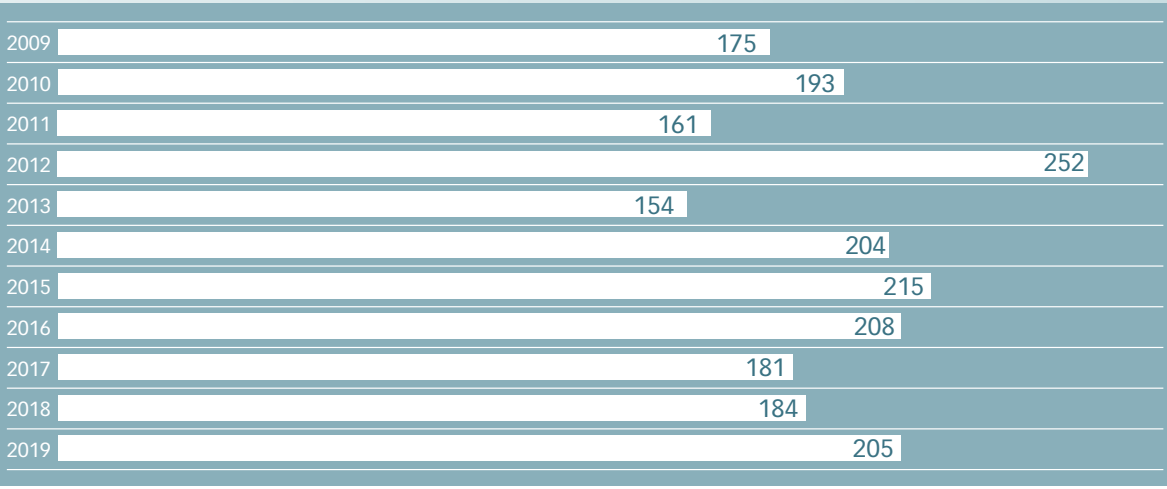
As of Dec 2019, the CIC-IBMCC was composed by 18 independent **Research Units** led by senior PIs, 11 **Research Units** led by junior PIs, 9 **Socio-sanitary Service Units** and 8 **Technical Support Units**. A pleasant highlight for our recruitment efforts during this period has been the incorporation to our roster of two new independent female researchers, **Dr. Sandra Blanco** (Epitranscriptomics and Cancer) and **Dr. Esther Castellano** (Tumor Stroma Signaling), who won competitive calls for permanent CT (Científico Titular) CSIC positions in our Center. On behalf of the rest of our staff, I send a very warm welcome to our new senior researchers and wish them the best of success during their tenure with us.

Consistent with our status as a joint institution (**Instituto Mixto**) of the University of Salamanca (**USAL**) and the Spanish Research Council (**CSIC**), about 44% of our personnel were formally affiliated with either USAL or CSIC, whereas 40% were supported by work contracts underwritten by our supporting **FICUS Foundation**, whose Board of Directors includes members representing USAL, CSIC and the regional Ministries of Health and Education of the **CyL Government**. A small percentage (16%) of the personnel was supported by funds from external institutions dependent from ISCIII, such as CIBERONC or IECSCYL. Notice also the predominant female component (65%) of our scientific staff during this period. The accompanying figures provide further details regarding composition and personnel distribution in our center during this period.

Total Staff 2009-2019



CIC-IBMCC Publications 2009-2019



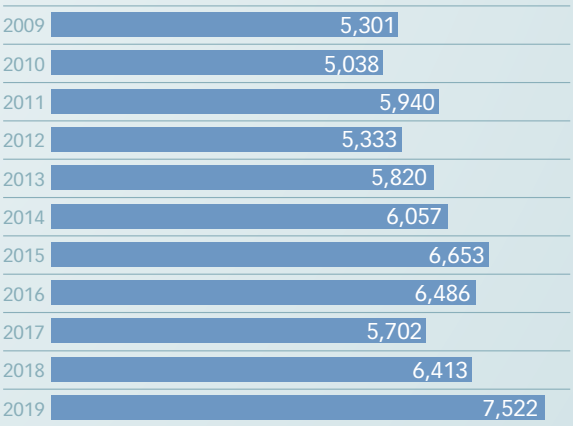
Regarding **scientific productivity,** during 2018-2019, the CIC-IBMCC researchers authored **389 original scientific articles** dealing with various aspects of basic, clinical and applied oncology. Our publications appeared in over 179 indexed journals, most of which **(>73%)** ranked within the first quartile (Q1) of their scientific specialty. The average impact factor (IF) of all our publications during this two-year period reached a remarkable value of 6,997 and we may call special attention to the **55 papers published in journals with IF> 10**. The CIC-IBMCC scientists also kept generating intellectual property during this period by registering **7 different patents** which are currently at different stages of development in the corresponding patent offices.

Concerning competitive projects, the CIC IBMCC scientists worked on 162 different, active scientific projects, 93 of which were won in competitive calls held within this two-year period for a total amount of about 19 M€.

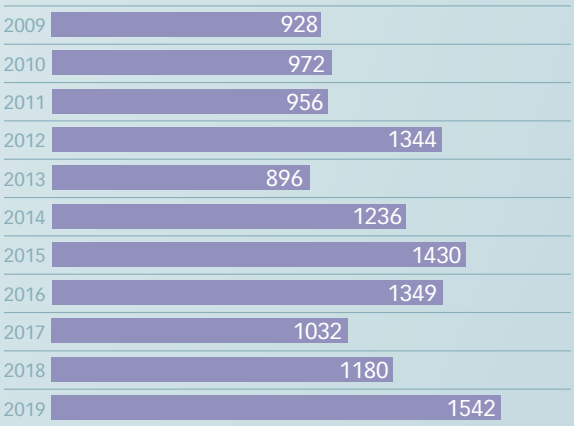
The detailed **list of these publications, patents and projects** can be found in the corresponding section of this report for each individual Research group.

As for **scientific recognition**, during this period, 13 research groups led by PIs from the CIC-IBMCC renewed their accreditation as **«Consolidated Research Units (UIC)»** in CyL on the basis of their excellence and scientific record during recent years, and 9 groups ▸

CIC-IBMCC IF/paper 2009-2019



CIC-IBMCC Impact Factor 2009-2019



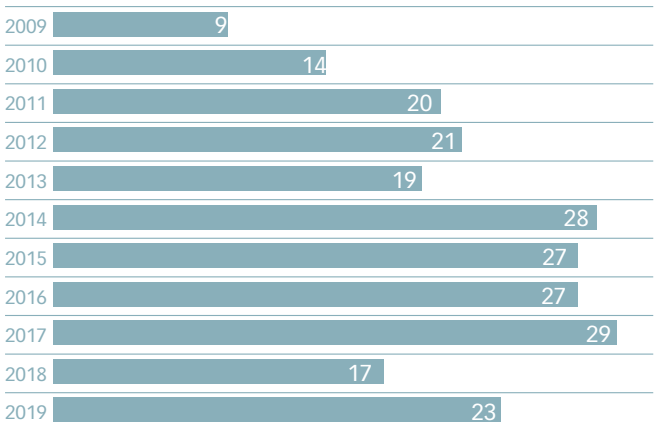
▸ were also accredited as **«Grupos de Investigación Reconocida (GIR)»** in USAL. Of note, on May 2018, the Scientific Foundation of the Spanish Association Against Cancer (AECC) awarded the CIC IBMCC their recognition as an **"FCAECC Accredited Cancer Research Center"**, an accreditation given only to a very short list of research institutions in Spain. The CIC scientists also received significant individual recognitions during this period. In 2019, **Dr A. Orfao** received the Life Achievement Award from the Iberian Cytometry Association as well a Year recognition Award from the CSIC. **Dr X. Bustelo** was also President-Elect of the Spanish Association of Cancer Research (ASEICA) and coordinator of the MM Program of the ISCIII-sponsored CIBERONC during this period.

During this period the CIC-IBMCC scientists have also developed **significant networking and scientific collaborations** with outside scientists and institutions. Special mention should be made to our different groups contributing to cooperative cancer research through the ISCIIII-sponsored **CIBERONC** or through various European and International research consortia. We may cite in this regard the "Early cancer research initiative network on MBL" **(ECRIN)** project, and the "Innovative CAR Therapy Platforms" **(INCAR)** within **Accelerator Award call of CRUK-AIRC-FCAECC** consortium and the participation of research groups of UK, Italy and Spain, as well as the project "Red transfronteriza de innovación en diagnóstico precoz de leucemia para un envejecimiento saludable" **(IDIAL_NET_3_E)**, within the cooperation program **Interreg** V-A Spain-Portugal **(POCTEP)**. Also note the projects "Synthetic Lethality for Personalized Therapy-based Stratification in Acute Leukemia" within **ERA PerMed call** of 1st Joint Call for Proposals (JTC) on Research Projects on Personalised Medicine-Smart Combination of Pre-Clinical and Clinical Research with data and ICT solutions, and the "**NEMHESYS**: NGS Establishment in Multidisciplinary Healthcare System" from Erasmus+-Knowledge Alliances program.

As an accredited University Institute belonging to the USAL academic community, the CIC IBMCC was also responsible for a variety of teaching activities on different cancer areas at the graduate and postgraduate level during 2018-2019. Our activities in this regard included a **Master program on "Biology and Clinic of Cancer"** taught by our PIs, aimed at the basic training of graduates interested in cancer and without prior experimental experience in the fields of molecular and cell biology, from which **49 students** have graduated in the last two academic years. Our **PhD program** fully compliant with the "European Space for Higher Education" entitled **"Bioscience: Biology and Clinic of Cancer and Translational Medicine"** is sponsored by the CIC-IBMCC in collaboration with the USAL departments of Microbiology& Genetics (School of Biology) and Medicine (School of Medicine) with **197 students** enrolled in it.

During 2018-1019, a total **40 Doctoral Theses (PhD)** directed by CIC-IBMC scientists have been presented and successfully defended. Other activities during 2018-2019 included the continuation of our open **Cancer Seminar Series** program, which involved 84 different national and international speakers. In addition, 17 specialized congresses, symposia or curses were also organized in our institution or by researchers of our center that involved the participation of more than 1200 participants. Highlight, the organization in collaboration with the Diz-Pintado Foundation against Cancer, of the **Scientific Symposium** within the framework of the VIII Centennial University of Salamanca on new challenges in cancer research, which was held in Salamanca on November 26-27, 2019 with the participation of the most relevant Spanish researchers in the field of cancer research.

Theses per year
CIC-IBMCC 2009-2019



Communication and outreach activities directed to the outside scientific community as well as to patients, society and the general public are also important goals for an integral, comprehensive cancer research center like ours. To that end, the CIC-IBMCC continued during this period to award the **"Doctores Diz Pintado Award"** that recognizes every year the excellence of the most outstanding Spanish cancer researcher younger than 45. The awardees for 2018 and 2019 were, respectively, **Dr. Raul Rabadán** (Columbia University, New York, USA) and **Dr. Nuria López-Bigas** (IRB, Barcelona), two of the most relevant and recognized young cancer scientists at the current Spanish and international cancer scene.

In addition, during this period our Center has also continued its regular **outreaching activities** to the community receiving visits to our research laboratories of more than 2000 students from various local elementary and high schools located around the Salamanca area.

The **main challenges facing the CIC IBMCC** for the near future with regards to implementing our new SP relate to the maintenance and/or improvement of our past scientific productivity and competitiveness at the national and international levels. In the current situation, it is clearly apparent that we will need a more definite and stable show of economic support from our sponsoring institutions to cover the costs of regular operations (building maintenance, security, administration, etc.) in our Center. It is obvious that our current deficitary situation deeply compromises our competitiveness as well as our ability to keep first-rate scientists in our staff or to attract new, young talented researchers to our cancer center in Salamanca.

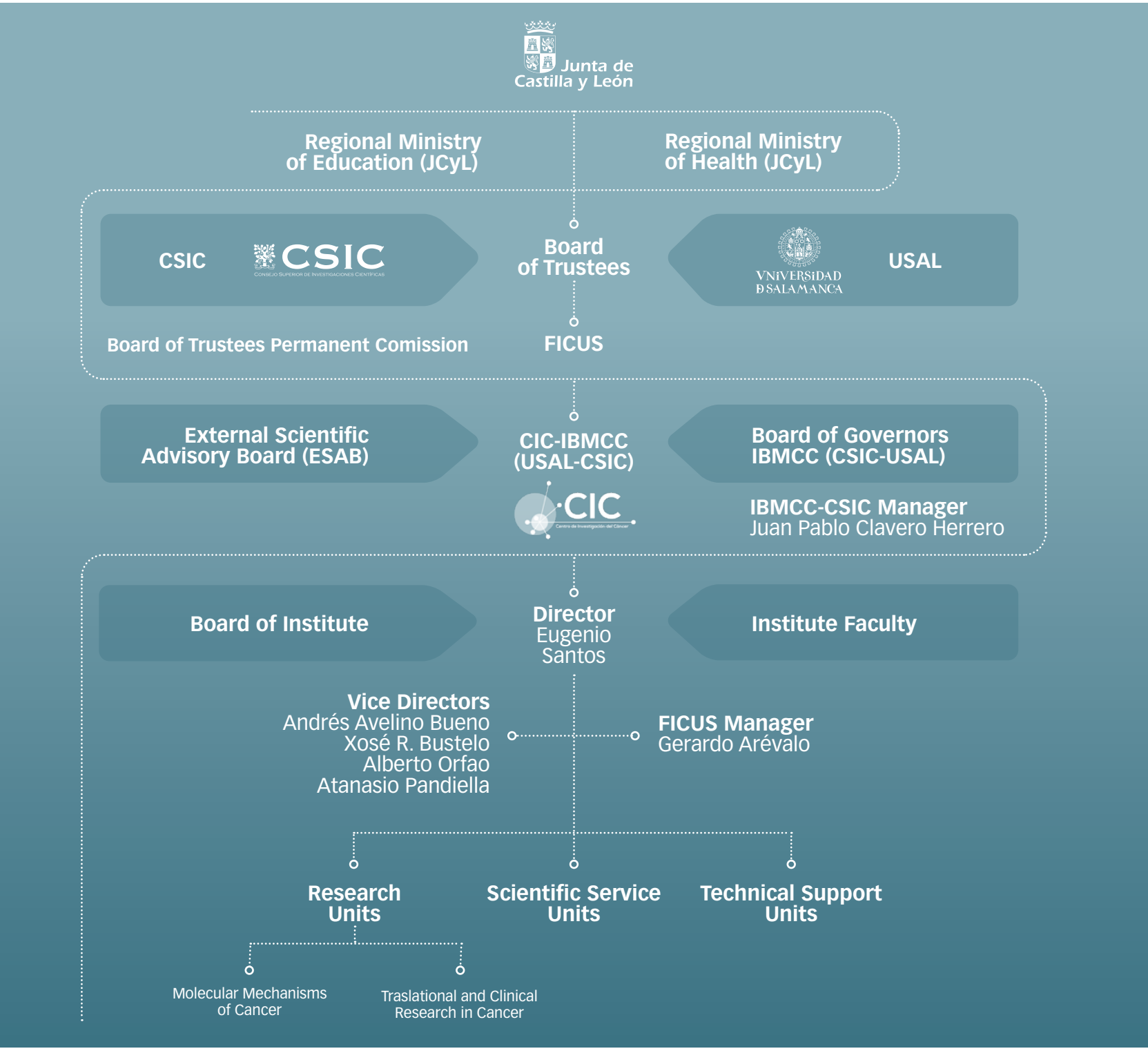
I want to conclude this foreword by expressing the utmost **gratitude and** sincere **recognition to the scientific and technical support staff of our center**, whose commitment and hard work made it possible for the CIC-IBMCC to achieve its scientific goals and reputation at the national and international level during 2018-2019. Our deep gratitude is also due to our External **Scientific Advisory Board** that has always provided scientific guidance and needed steering to proceed adequately with our research work. Thanks also to the **outside sponsors and anonymous donors** who have helped our center during the past two years. I am convinced that adding up all these internal and external contributions will allow the CIC-IBMCC to overcome its present difficulties and to continue producing high quality scientific research in the field of oncology for years to come.

Eugenio Santos
Director, CIC-IBMCC

CENTRO
DE INVESTIGACION
DEL CANCER

2

ORGANIZATION


Junta de Castilla y León
Regional Ministry of Education (JCyL)
Regional Ministry of Health (JCyL)
CSIC
CSIC
Consejo Superior de Investigaciones Científicas
Board of Trustees
USAL
Universidad de Salamanca
Board of Trustees Permanent Comission
FICUS
External Scientific Advisory Board (ESAB)
CIC-IBMCC (USAL-CSIC)
CIC
Centro de Investigación del Cáncer
Board of Governors IBMCC (CSIC-USAL)
IBMCC-CSIC Manager
Juan Pablo Clavero Herrero
Board of Institute
Director
Eugenio Santos
Institute Faculty
Vice Directors
Andrés Avelino Bueno
Xosé R. Bustelo
Alberto Orfao
Atanasio Pandiella
FICUS Manager
Gerardo Arévalo
Research Units
Scientific Service Units
Technical Support Units
Molecular Mechanisms of Cancer
Traslational and Clinical Research in Cancer

ORGANIZATION

SUMMARY

The governing bodies of the CIC-IBMCC are: (i) the Governing Committee composed of two representatives of the CSIC, appointed by the President of CSIC and two representatives of the USAL appointed by the Rector of the Salamanca University, (ii) the Board of the Institute, consisting of the director, Vice-Director, manager, principal investigators of the institute, a representative of the scientific staff, and a representative of the technical and support staff (iii) the Director, appointed by the Presidents of the CSIC and the Rector of the Salamanca University according the proposal of Board of the Institute, (iv) Vice-Director, also appointed by the Presidents of the CSIC and the Rector of the University of Salamanca to proposal director of the center, (v) the center manager, responsible for budget management, economic, and administrative personnel, (vi) the Institute Faculty, an advisory body composed of all staff scientist assigned to the institute and finally (vii) the External Advisory Committee also consultative body appointed by the Governing Committee, after hearing the Board of the Institute, consisting of the least five prestigious international scientists in the lines Institute research.

In addition to this common structure to most research centers, the CIC-IBMCC has the Foundation for Cancer Research at the University of Salamanca (FICUS), which (i) contributes to flow in the center of scientific activity through the recruitment of scientific, technical and administrative, (ii) serves as a bridge between agency activities performed by the CIC-IBMCC and society, channeling funds and sponsorships provided by individuals, private companies and non-governmental organizations to the center, (iii) facilitate the rapid transfer of results obtained by researchers to R+D and finally (iv) promotes research excellence through the promotion of periodic evaluation of the research carried out by an external scientific committee. The FICUS has a Board of Trustees presided by the Rector of the University of Salamanca and the President of CSIC, joined representatives of the University of Salamanca, the CSIC and representatives of the Regional ministries of Education and Health of the Junta de Castilla y León.

BOARD OF TRUSTEES OF THE CANCER RESEARCH FOUNDATION OF THE UNIVERSITY OF SALAMANCA (FICUS)

PRESIDENT

Rector of the Salamanca University (USAL)
Excmo. Sr. D. Ricardo Rivero Ortega

VICEPRESIDENT

President of the Spanish National Research Council (CSIC)
Excma Sra. Dª. Rosa María Menéndez López

MEMBERS

Health Counsellor of Castilla y León Government
Dª. Verónica Casado Vicente (from June 2019)
D. Antonio María Sáez Aguado (until June 2019)

Education Counsellor of Castilla y León Government
Dª María del Rocío Lucas Navas (from June 2019)
D. Fernando Rey Martínez (until June 2019)

Vice-Chancellor of Research and Knowledge Transfer of the Salamanca University
Dª. María Susana Pérez Santos

Vice-Chancellor of Economic Affairs of the Salamanca University
D. Javier González Benito

Director of Institute of Cancer Molecular and Cellular Biology (IBMCC)
D. Eugenio Santos

President of Social Council of the Salamanca University
D. José Ignacio Sánchez Galán.

SECRETARY

Head of Economic Affairs of the Salamanca University
D. Gerardo Arévalo Vicente.

ORGANIZATION

EXTERNAL SCIENTIFIC ADVISORY BOARD (ESAB)

CHAIRMAN

Hospital Clínic /IDIBAPS, Barcelona
Dr. Elías Campo

MEMBERS

University Hospital La Princesa / CNIC, Madrid
Dr. Francisco Sánchez-Madrid

CNRS Research Director, Gif sur Yvette (France)
Dr. Jacqueline Cherfils

Leiden University Medical Center (The Netherlands)
Dr. Jacques van Dongen

Hospital 12 Octubre /CNIO, Madrid
Dr. Luis Paz-Ares

Bristol University (United Kingdom)
Dr. Anne Ridley

Institute of Cancer Molecular and Cellular Biology (IBMCC)
Dr. Eugenio Santos

ORGANIZATION

RESEARCH UNITS

MOLECULAR MECHANISMS OF CANCER PROGRAM

GTPases and cancer. RAS mediated signaling
Eugenio Santos

Identification of early oncogenic drivers, molecular coadjutants, and pathobiological programs involved in cancer development and progression
Xosé R. Bustelo

Kinases in oncology and neurodegeneration. Signaling by chromatin kinases
Pedro Alfonso Lazo-Zbikowski Taracena

Epitranscriptomics and cancer
Sandra Blanco Benavente

Tumour-Stroma Signaling
Esther Castellano Sánchez

Tumor biophysics
Miguel Vicente Manzanares

Molecular and genetic determinants of cancer. Susceptibility, evolution and treatment response
Jesús Pérez Losada

Reversible processes in cell cycle control
Andrés Avelino Bueno Núñez

Chromosome segregation and human disease
Alberto Martín Pendás

Structural biology of cell adhesion and signaling
Jose María de Pereda Vega

Unconventional autophagy in health and disease
Felipe X. Pimentel-Muiños

TRANSLATIONAL AND CLINICAL RESEARCH IN CANCER PROGRAM

Immunology and cancer
José Alberto Orfao de Matos Correia e Vale

Oncohematology
Marcos González Díaz

Stem cells, cancer stem cells and cancer biology
Isidro Sánchez García

Hereditary cancer
Rogelio González Sarmiento

Kinases in oncology. Signaling by receptor tyrosine kinases
Atanasio Pandiella Alonso

Bioinformatics and functional genomics of cancer
Javier De Las Rivas

Clinical and molecular analysis of solid tumors
Juan Jesús Cruz Hernández

SCIENTIFIC SUPPORT UNITS

Genomics. Scientific Coordinator
Xosé R. Bustelo

Proteomics. Scientific Coordinator
Xosé R. Bustelo

Traslational Oncopharmacology. Scientific Coordinator
Atanasio Pandiella Alonso

Bioinformatics. Scientific Coordinator
Javier De las Rivas

Cytometry. Scientific Coordinator
José Alberto Orfao de Matos Correia e Vale

Cytogenetics. Scientific Coordinator
Jesús María Hernández Rivas

Molecular Biology. Scientific Coordinator
Marcos González Díaz

Comparative Molecular Pathology. Scientific Coordinator
Carmen García Macías

Hereditary Cancer & Genetic Counselling. Scientific Coordinators
Rogelio González Sarmiento
Juan Jesús Cruz Hernández

Structural Biology. Scientific Coordinator
José María de Pereda Vega

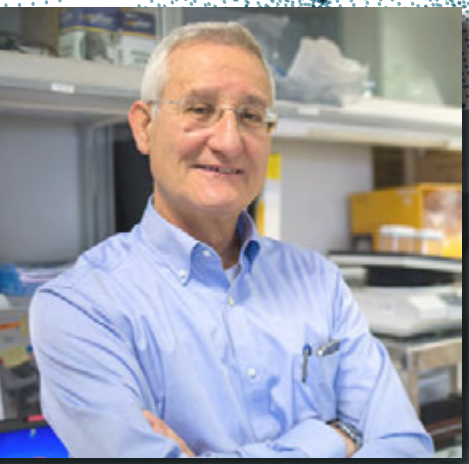
Microscopy. Scientific Coordinators
Alberto Martín Pendás
Miguel Vicente Manzanares

TECHNICAL SUPPORT UNITS

- FICUS Manager
- Secretary
- Administration
- IBMCC-CSIC Manager
- Communication & Marketing
- Equipment & Building Maintenance
- Quality Control & Risk Prevention
- Information Technologies Service
- Central Warehouse & Radiological Protection
- Glassware Cleaning & Sterilizationn

3

RESEARCH UNITS



Team Leader

Eugenio Santos
Phone: +34 923 294 801
E-mail: esantos@usal.es

Research Team

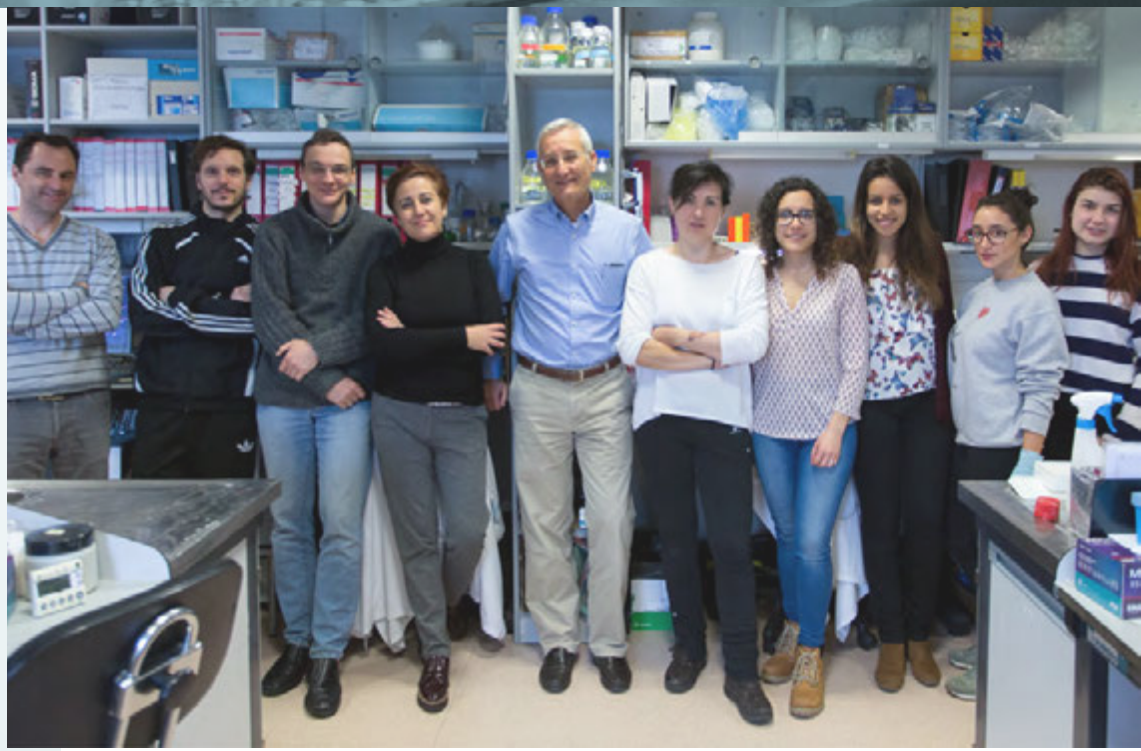
Senior Researcher
Alberto Fernández Medarde

Postdoctorals
Fernando Calvo Baltanás
Carmela Gómez Rodríguez
David Jimeno García
Rósula García Navas

Predoctoral
Rocío Fuentes Mateos

Technician
Nuria Calzada Nieto

Master Students
Marta López Yus
María Carranza Jiménez
Cynthia Mucientes Valdivieso
Juan Carlos Fernández Izquierdo



LABORATORY 1

GTPASES AND CANCER. RAS MEDIATED SIGNALING

During this period, our group focused its activities on analyzing the mechanisms of activation/ of RAS proteins by guanine exchange factors (GEF) and ascertaining the functional specificity/redundancy of various RAS and RasGEF isoforms during physiological and/ or tumoral processes. Our studies, centered on phenotypic and mechanistic characterization (at both the systemic and the cellular level) of various KO mouse models for RAS, SOS and GRF genes and isoforms participating in Ras Signaling Pathways, have been instrumental to identify potential biomarkers and/or therapy targets relevant for RAS-driven tumors. In the recent past years we have analyzed the direct role of Ras GEFs in mouse models of cancer development, and we have also started a new line of work the searching for inhibitors of the GEF activity of SOS proteins and testing their potential usefulness as a therapeutic tools for cancer treatment.

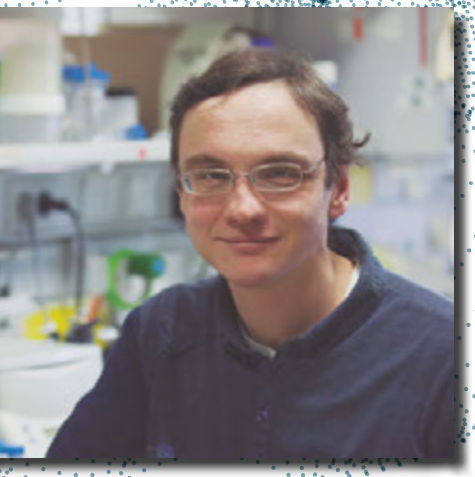
Regarding the functional specificity of RAS family members, our group had previously shown that only KRAS is necessary and sufficient for embryonic development and reaching adult stage homeostasis and had also documented the homo-oligomeric nature of RAS proteins. More recently, our studies have also demonstrated a critical involvement of NRAS in immune modulation/host defense and apoptotic; of KRAS in the control of cell cycle progression; HRAS in the control of systemic vascular pressure; RRas in germinal center formation; and concomitantly both HRAS and NRAS in normal lung maturation during the last stages of embryonic development.

Our latest work with HRAS/NRAS double-KO animals aims to uncover the underlying mechanisms that lead to such delay in lung maturation and the causes of the high postnatal death rates observed in those animals. In addition to defects in pneumocyte differentiation, the combined deletion of HRas and NRas leads to male infertility, but the underlying mechanisms remain unknown and are currently under study.

Our work analyzing RasGRF1 and RasGRF2 KO mice has also demonstrated the differential in vivo functionality of these RasGEFs. Our earlier work identified specific roles of RasGRF1 in pancreatic β-cells and in neurosensory and photoreception processes, and of RasGRF2 in T cell signaling and in alcohol addictive behavior. More recently, we have also uncovered a critical role of RasGRF2 in control of nuclear migration required for proper postnatal development and function of retinal cone photoreceptors as well as in regulation of stem cell density and onset of differentiation during adult neurogenesis in the brain. Our most recent work on this GEF family focuses on analyzing the role of RasGRF2 in olfaction, as well as the regulation of eye lens morphology by RasGRF1.

We have also analyzed the functional role of the SOS1 and SOS2 RasGEFs using KO models in adult mice. In earlier work we showed that SOS1 is essential for mouse embryonic development whereas SOS2 is dispensable in adult mice. More recently, we have used a conditional, tamoxifen-inducible, SOS1-KO model generated in this laboratory to show that SOS1/2-DKO (double-knockout) animals die precipitously whereas individual, adult SOS1-KO and SOS2-KO mice are perfectly viable. These observations demonstrate functional redundancy between SOS1 and SOS2 for homeostasis and survival of the full organism and for development and maturation of T and B-lymphocytes. Furthermore, our functional analysis of SOS1 and SOS2 alleles at the cellular level has uncovered a direct mechanistic link between SOS1 and control of intracellular and mitochondrial oxidative stress and has demonstrated functional prevalence of SOS1 over SOS2 with regards to cellular proliferation and viability. We have also demonstrated recently the critical mechanistic contribution of SOS1 to BCR-ABL-driven leukemogenesis and to skin homeostasis and carcinogenesis in mice.

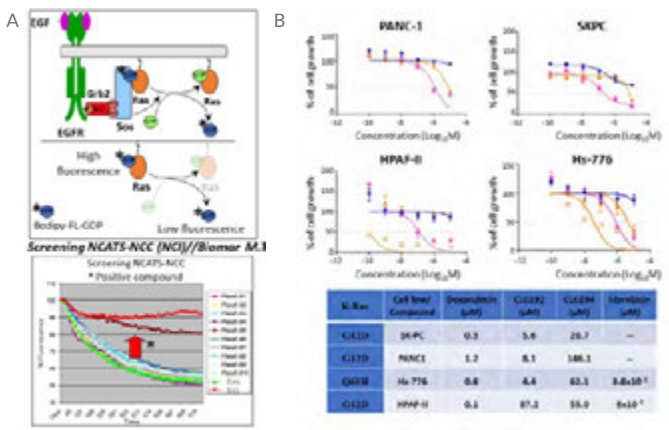
Furthermore, we are currently screening several compound libraries searching for small-molecule inhibitors of Ras activation by SOS, that could be eventually used in cancer treatment.



Alberto Fernández Medarde

Phone.: +34 923 294 801
E-mail: afm@usal.es

Screening of RAS inhibitors in compound libraries from NIH and Biomar Microbial Technologies



A) A fluorescent reaction is used to search for inhibitors of Ras activation. Purifies Ras protein incubate for 1 h with a fluorescent GDP analogue, was added to purified Sos catalytic domain in the presence or absence of the compounds and fluorescence changes were monitored for 700 seconds. B) Results from the first screening of Ras activation inhibitors in compound libraries from NIH and Biomar Microbial Technologies.

SENIOR RESEARCHER

ROLE FOR RAS GUANINE NUCLEOTIDE EXCHANGE FACTORS RASGRF1 AND ASGR2 IN CENTRAL NERVOUS SYSTEM

The latest research goals of Alberto Fernández Medarde lay on the screening of compound libraries to search for inhibitors of Ras activation, analysis of the effect of this inhibition "in vitro" and "in vivo" and their possible application for cancer and developmental disease treatment, through toxicity studies and disease evolution in mice. He is also involved in a second line of research, which focus on RasGRF role in sensory development.

STRATEGIC OBJECTIVES

(I). Screening of Compound libraries and a collection of animal venoms to find Ras-GEF inhibitors.
(II) Analysis of Ras-GEF inhibitors in the inhibition of cell growth and Ras activation in Ras WT and mutant tumoral cell lines.
(III) Toxicity of Ras-GEF inhibitors on adult mice and effects of the compounds on Ras activation "in vivo".
(IV) Effect of Ras-GEF inhibitors on tumor development/growth in mice cancer models.
(V) Role of RasGRF1 in lens morphogenesis.
(VI) Analysis of RasGRF2 physiological role in olfaction.

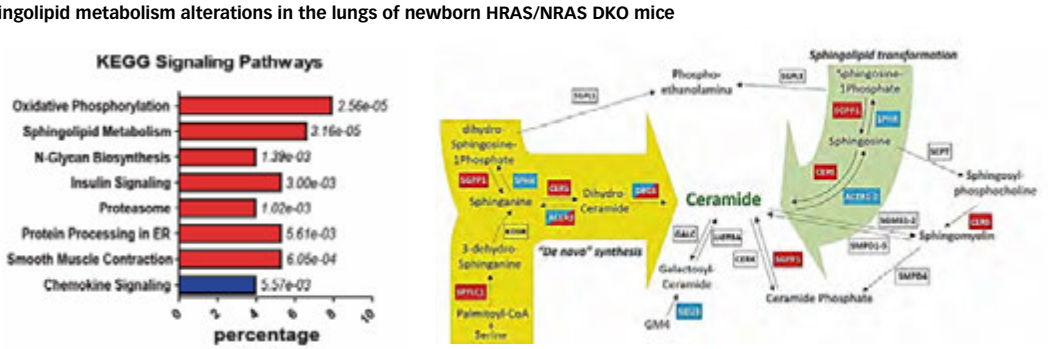
MAIN LINES OF RESEARCH

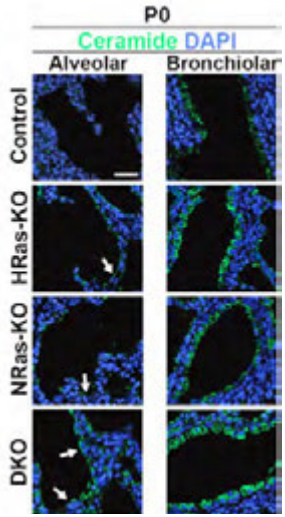
1. Screening of Ras activation inhibitors (major).
2. Analysis of RasGRF2 role in olfaction (minor).
3. Study of RasGRF1 role in lens formation and myopia (minor).

GOALS ACHIEVED

- Finding of the molecular alterations responsible for the defects in memory formation of the RasGRF1 KO mice.
- Discovery of a role for RasGRF1 in two steps of light perception: photoreception and light refraction at the lens.
- Description of the RasGRF1-Pttg1 relationship in pancreatic β-cells.
- Disclosing the role of RasGRF2 in binge drinking and alcohol preference.

Sphingolipid metabolism alterations in the lungs of newborn HRAS/NRAS DKO mice





A) Functional categories enriched in newborn DKO mice. Overexpressed (red bars) or repressed (blue bars) gene probesets identified by GeneCodis as significantly enriched for the indicated KEGG functional categories. B) Enzymatic components of sphingolipid metabolism pathways that showed differential expression in transcriptomic analyses of P0 lungs extracts. In red, genes overexpressed in untreated DKO lungs; in blue, repressed in DKO upon dexamethasone treatment; bi-colored genes showed opposite pattern of differential expression under these conditions. Enzymatic reactions driving either de novo synthesis (yellow arrow) or transformation events (green arrow) lead to ceramide accumulation in the DKO lungs, a trend that was partially corrected by antenatal dexamethasone treatment. C) Representative images of immunostaining for Ceramide (green) and DAPI counterstaining (blue) in lung paraffin sections of newborn P0 mice of the indicated genotypes under basal, untreated conditions. Arrows point to zones with significantly increased ceramide levels observed in alveolar regions of the indicated genotypes.

- Screening of two compound libraries and selection of four Ras-GEF inhibitors.
- Analysis of the effect of the Ras-GEF inhibitors on the growth of cancer cell lines. Three out of four compounds showed activity towards pancreatic cancer cell lines and only two of them against lung cancer cell lines.
- Analysis of the toxicity of the Ras-GEF inhibitors. Two of the compounds are highly toxic and are removed from the study. Only one compound inhibits growth of pancreatic cancer cell lines and is not toxic. We will follow our studies with this compound.

FUTURE GOALS

a) Analysis of RasGRF1 and RasGRF2 in odor detection.
b) Mechanisms underlying the changes in the lens of the RasGRF1 KO animals.
c) New screening of inhibitors of the RasGEF exchanger activity using a new compound library (360 compounds) and a collection of animal venoms.
d) Preclinical studies using mice models of cancer with Ras-GEF inhibitors. Effect on tumor growth and metastasis formation.

PUBLICATIONS

- **Phosphorylation of SOS1 on tyrosine 1196 promotes its RAC GEF activity and contributes to BCR-ABL leukemogenesis.** *Gerboth S, Frittoli E, Palamidessi A, Baltanas FC, Salek M, Rappsilber J, Giuliani C, Troglio F, Rolland Y, Pruneri G, Kreutmair S, Pallavicini I, Zobel M, Cinquanta M, Minucci S, Gómez C, Santos E, Illert AL, Scita G.* **Leukemia. 2018 Mar;32(3):820-827. doi: 10.1038/leu.2017.267.** PMID: 28819285 **IF: 9.944 / D1**

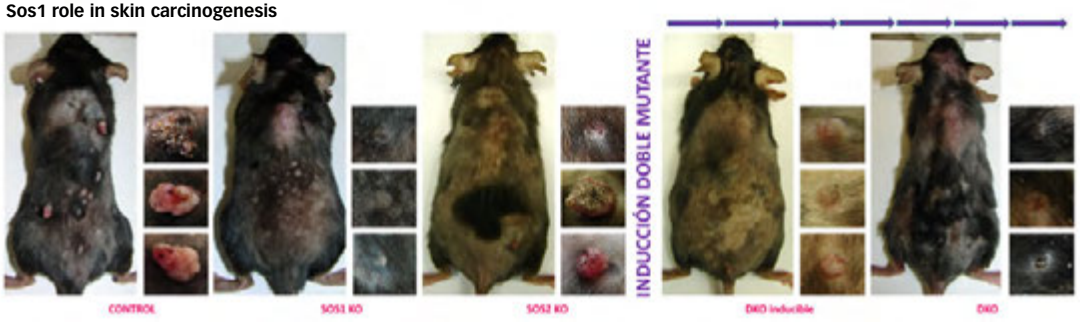
- **R-Ras2 is required for germinal center formation to aid B cells during energetically demanding processes.** *Mendoza P, Martínez-Martín N, Bovolenta ER, Reyes-Garau D, Hernansanz-Agustín P, Delgado P, Díaz-Muñoz MD, Oeste CL, Fernández-Pisonero I, Castellano E, Martínez-Ruiz A, Alonso-Lopez D, Santos E, Bustelo XR, Kurosaki T, Alarcón B.* **Sci Signal. 2018 May 29;11(532). pii: eaal1506. doi: 10.1126/scisignal.aal1506.** PMID: 29844052 **IF: 6.481 / Q3**

- **Differential role of the RasGEFs SOS1 and SOS2 in mouse skin homeostasis and carcinogenesis**. *Liceras-Boillos P, Jimeno D, García-Navas R, Lorenzo-Martín LF, Menacho-Marquez M, Segrelles C, Gómez C, Calzada N, Fuentes-Mateos R, Paramio JM, Bustelo XR, Baltanás FC, Santos E.* **Mol Cell Biol. 2018 May 29. pii: MCB.00049-18. doi: 10.1128/MCB.00049-18.** PMID: 29844066 **IF: 3.735 / Q2**

- **Spatial learning and long-term memory impairments in RasGrf1 KO, Pttg1 KO, and double KO mice.** *Manyes L, Holst S, Lozano M, Santos E, Fernandez-Medarde A.* Brain **Behav. 2018 Sep 26:e01089. doi: 10.1002/brb3.1089.** PMID: 30259712 **IF: 2.072 / Q2**

- **The RAS-ERK pathway: A route for couples.** *Santos E, Crespo P.* **Sci Signal. 2018 Oct 30;11(554). pii: eaav0917. doi: 10.1126/scisignal.aav0917. Review.** PMID: 30377222 **IF: 6.481 / Q3**

Sos1 role in skin carcinogenesis



Sos1 elimination reduces the number and size of papillomas in animal treated with a combination of DMBA and TPA. Sos2 elimination also affects tumor development, as the papillomas in the KO mice grow at slower rate than the WT controls.

- **The CSN3 subunit of the COP9 signalosome interacts with the HD region of Sos1 regulating stability of this GEF protein**. *Zarich N, Anta B, Fernández-Medarde A, Ballester A, de Lucas MP, Cámara AB, Anta B, Oliva JL, Rojas-Cabañeros JM, Santos E.* **Oncogenesis. 2019 Jan 4;8(1):2. doi: 10.1038/s41389-018-0111-1.** PMID: 30631038 **IF: 5.995 / Q1**

- **A Nucleotide-Dependent Conformational Switch Controls the Polymerization of Human IMP Dehydrogenases to Modulate their Catalytic Activity.** *Fernández-Justel D, Núñez R, Martín-Benito J, Jimeno D, González-López A, Soriano EM, Revuelta JL, Buey RM.* **J Mol Biol. 2019 Mar 1;431(5):956-969. doi: 10.1016/j.jmb.2019.01.020.** PMID: 30664871 **IF: 5.067 / Q1**

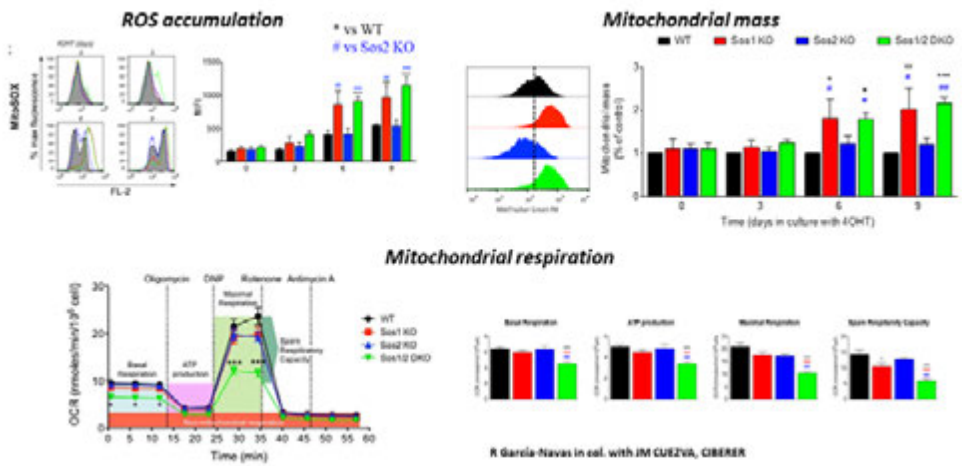
- **Frontline Science: TNF-α and GM-CSF1 priming augments the role of SOS1/2 in driving activation of Ras, PI3K-γ, and neutrophil proinflammatory responses.** *Suire S, Baltanas FC, Segonds-Pichon A, Davidson K, Santos E, Hawkins PT, Stephens LR.* **J Leukoc Biol. 2019 Feb 5. doi: 10.1002/JLB.2HI0918-359RR.** PMID: 30720883 **IF: 4.012 / Q2**

- **Nucleolin reorganization and nucleolar stress in Purkinje cells of mutant PCD mice.** *Baltanás FC, Berciano MT, Tapia O, Narcis JO, Lafarga V, Díaz D, Weruaga E, Santos E, Lafarga M.* **Neurobiol Dis. 2019 Jul;127:312-322. doi: 10.1016/j.nbd.2019.03.017.** PMID: 30905767 **IF: 5.160 / D1**

- **The Inhibition of RasGRF2, But Not RasGRF1, Alters Cocaine Reward in Mice.** *Bernardi RE, Olevska A, Morella I, Fasano S, Santos E, Brambilla R, Spanagel R.* **J Neurosci. 2019 Aug 7;39(32):6325-6338. doi: 10.1523/JNEUROSCI.1120-18.2019.** PMID: 31182637 **IF: 6.074 / D1**

- **Concomitant deletion of HRAS and NRAS leads to pulmonary immaturity, respiratory failure and neonatal death in mice.** *Fuentes-Mateos R, Jimeno D, Gómez C, Calzada N, Fernández-Medarde A, Santos E.* **Cell Death Dis. 2019 Nov 4;10(11):838. doi: 10.1038/s41419-019-2075-2.** PMID: 31685810 **IF: 5.959 / Q1**

Mitochondrial phenotypes in mouse embryonic fibroblasts devoid of Sos1 or Sos1 and Sos2 RAS GEFs

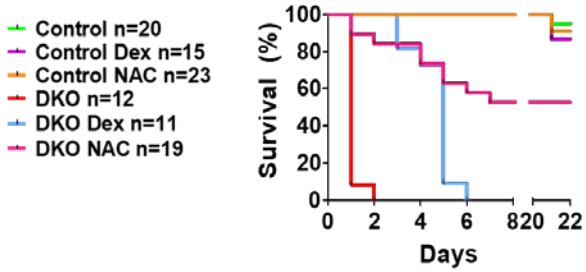


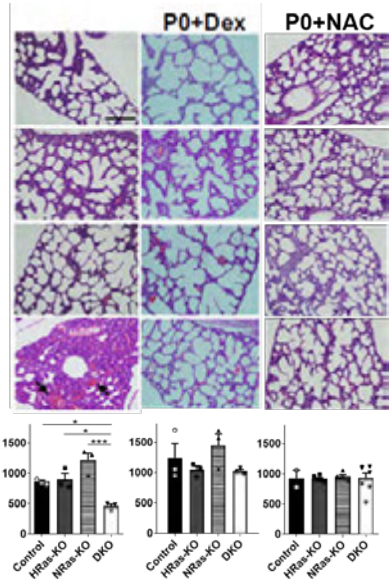
Mitochondrial alterations in Sos1, Sos2 and Sos1/2 knockout Mouse embryonic fibroblasts (MEFs). Sos1 and Sos1/2 DKO MEFs isolated from our knockout mice showed: A) Accumulation of reactive oxygen species (ROS), B) Increase in mitochondrial mass and C) Defects in mitochondrial respiration.

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Identificación y validación de activadores RAS-GEF de las familias SOS y GRF como biomarcadores y dianas terapéuticas en procesos fisiológicos y tumorales mediante el uso de animales modelo y aproximaciones preclínicas (SA043U16)	Eugenio Santos	Regional Government of Castilla and León	2016-2018	120,000.00 €
Programa XI: Programa de financiación de unidades de excelencia de la Universidad de Salamanca (18X0001/463AC01/691)	Eugenio Santos	Salamanca University	2017-2019	175,000.00 €
Caracterización y validación de las proteínas RAS y sus activadores GRF y SOS como drivers oncogénicos, biomarcadores y dianas terapéuticas en procesos tumorales y otras patologías (PI16/02137)	Eugenio Santos	Carlos III Health Institute	2017-2019	147,015.00€
Las proteínas SOS como mediadoras del desarrollo tumoral y posibles dianas terapéuticas (FS/35-2017)	Alberto Fernández Medarde	Solórzano Foundation	2018	3,394.19 €
Subvención directa Consejería Sanidad a la Fundación de Investigación del Cáncer	Eugenio Santos	Regional Government of Castilla and León	2018	254,875.00 €
CIBERONC. Incorporación de nuevas áreas temáticas y nuevos grupos al consorcio CIBER, de la convocatoria 2016 de la Acción Estratégica en Salud 2013 – 2016. ÁREA TEMÁTICA DE CÁNCER (CB16/12/00352)	Eugenio Santos	Carlos III Health Institute	2018-2019	90,000.00 €
Especificidad funcional y caracterización de RAS-GEFS de las familias SOS y GRF como biomarcadores o dianas terapéuticas en cáncer (SA264P18)	Eugenio Santos	Regional Government of Castilla and León	2018-2021	120,000.00 €
Subvención directa Consejería Sanidad a la Fundación de Investigación del Cáncer	Eugenio Santos	Regional Government of Castilla and León	2019	254,875.00 €
Las proteínas SOS como diana terapéutica en el tratamiento del adenocarcinoma de pulmón (FS/20-2018)	Fernando Calvo Baltanás	Solórzano Foundation	2019	1,473.00 €
Medicina de precisión: Los activadores GEF de la familia SOS como dianas terapéuticas en tumores dependientes de RAS	Eugenio Santos	Ramón Areces Foundation	2019-2022	129,357.00 €

Recovery of the respiratory defects of H-RAS/N-RAS double-knockout newborn pups upon antioxidant treatment during pregnancy.





Antioxidant treatment leads to a partial but very significant recovery of the H-Ras/N-Ras newborn mice phenotype. Upon N-acetylcysteine treatment during pregnancy, half of the newborn mice reached adulthood, and showed a complete recovery of lung structure and function.

Team Leader

Xosé R. Bustelo

Phone.: +34 663 195 802 (Office) / +34 923 294 802 (Lab)

E-mail: xbustelo@usal.es

Research Team

Senior Researcher

Mercedes Dosil

Postdoctorals

Jesús Lacal Romero
Javier Conde Aranda
Myriam Cuadrado López
Maribel Fernández Pisonero
Javier Robles Valero

Predoctorals

Laura Clavaín Mateo
Rubén Fernández Caloto
Sonia Gómez Gaspar
Luis Francisco Lorenzo Martín
Blanca Nieto Bernáldez
Sonia Rodríguez Fernández
Lucía Fernández Nevado
Natalia Fernández Parejo

Technicians

Antonio L. Abad de Blas
Maite Blázquez Ramos

Master Students

Elsa N. Astorga Simón
Luis González Moreno
David Bastante Rodríguez

Visiting Researchers

Eva González
Facundo Tonucci
Julia Embacher
Enrique Madriga
Sergio Oterino
Tu Truong Truong
Eva Salas de Diego

LABORATORY 2

IDENTIFICATION OF EARLY ONCOGENIC DRIVERS, MOLECULAR COADJUTANTS, AND PATHOBIOLOGICAL PROGRAMS INVOLVED IN CANCER DEVELOPMENT AND PROGRESSION

Our group aims at characterizing early signaling events and cancer-associated genetic alterations that are linked to cancer origin, progression, metastasis, and/or the pharmacological responsiveness of patients. To achieve this end, we are currently focusing on the following experimental goals:

(1) The development of *in silico* tools to identify, from Pan-Cancer data and other high-throughput genomic studies, new oncogenic drivers, signaling coadjutants, and biological programs that contribute to the origin, progression, and malignant properties of a variety of tumors

(2) The validation of identified pro- and anti-tumorigenic hits using a variety of mouse (knockout, knock-in, CRISPR-Cas9 gene-edited), cellular, organotypic and patient-derived cell models

(3) The dissection of the biochemical activities, signaling pathways, and pathobiological programs regulated by those genes to identify new tumorigenic mechanisms, therapeutic targets, and diagnostic signatures

(4) The understanding of how the identified targets are regulated under normal and oncogenic conditions

(5) The characterization of the specific role of different oncogenic mutant alleles of the same gene in tumorigenesis

(6) The understanding, using *ad hoc*-designed mouse models, of the positive and negative collateral effects that the inhibition of these cancer-associated proteins elicits in the fitness of cancer cells and healthy tissues, respectively

Current molecular pathways under experimental scrutiny include those regulated by small GTPases of the RAS and RHO subfamilies (GTPases, upstream regulators, negative regulators and downstream proximal effectors), metabolic programs associated with primary tumorigenesis and metastasis, the cancer-specific alterations of the ribosome biosynthetic pathway, and the elucidation of crosstalk existing between the foregoing pathways and other signaling routes that favor the fitness of cancer cells.

This work is currently leading to the discovery of new protumorigenic programs, neomorphic mutants, and noncanonical tumor suppressor mechanisms in a number of tumors such as peripheral T cell lymphoma, T cell acute lymphoblastic leukemia, non-small cell lung cancer, ovarian cancer, and head and neck cancer.

SENIOR RESEARCHER

UNDERSTANDING THE REGULATION OF THE RIBOSOME BIOSYNTHETIC PATHWAY IN NORMAL AND CANCER CELLS

Mercedes Dosil

Phone.: +34 923 294 803 (Office)
+34 923 28 4828 (Lab)

E-mail: mdosil@usal.es

Our group is interested on the characterization of the stepwise assembly and regulatory mechanisms that govern the biosynthesis of ribosomes under both normal and pathological conditions, namely in cancer. In this context, our group has the following short-term goals:

(1) To develop new purification, molecular tagging, and proteomic methods to efficiently characterize the structural and regulatory components of the ribosomal biosynthetic machinery in mammalian cells

(2) To study the factors that drive ribosome assembly in normal and transformed cells

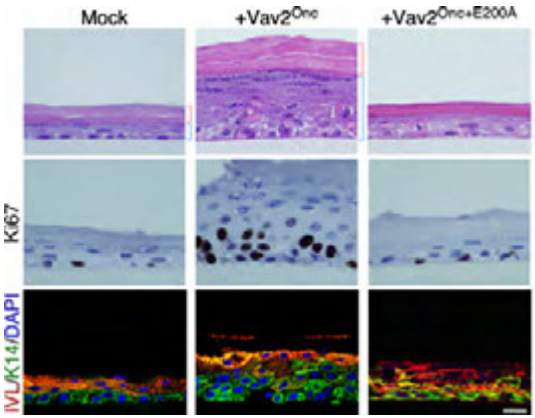
(3) To characterize how the ribosomal biosynthesis machinery crosstalk to other biological processes in cancer cells

(4) To establish how oncogenic pathways impact on the ribosomal biosynthetic pathway

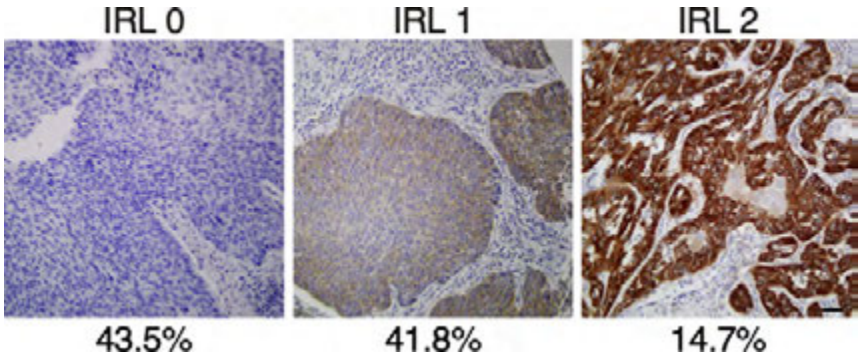
(5) To find genetic alterations that target elements of the ribosomal biosynthetic machinery using Pan-Cancer genomic data and in silico techniques.

(6) To analyze the mechanism of action of anticancer drugs that target this biosynthetic route.

Ongoing work is unveiling new, mammalian-specific steps in the maturation of ribosomal subunits, the nature of multiple preribosomal particles localized in the nucleolus, nucleoplasm and cytosol, and how such stepwise intracellular transit is orchestrated in both normal and cancer cells.



Immunohistochemical analysis of sections from organotypic 3D cultures of primary human keratinocytes expressing the indicated proteins (top).



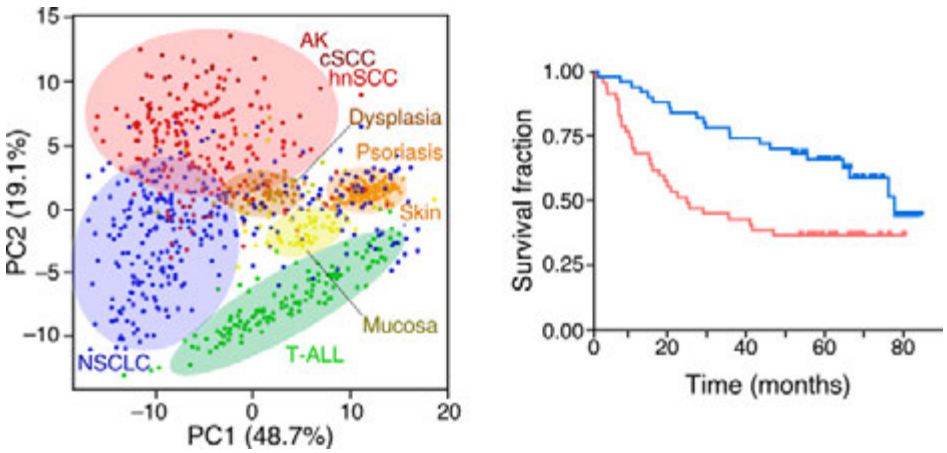
Immunohistochemical analyses of oral squamous carcinome samples using a specific biomarker for poor prognosis.

PUBLICATIONS

- **Ribosome biogenesis and cancer: basic and translational challenges.** *Bustelo XR, Dosil M.* Curr Opin Genet Dev. **2018 Feb;48:22-29. doi: 10.1016/j.gde.2017.10.003. Review.** PMID: 29100209 **IF: 5.288 / Q1**
- **Rho guanosine nucleotide exchange factors are not such bad guys after all in cancer.** *Robles-Valero J, Lorenzo-Martín LF, Fernández-Pisonero I, Bustelo XR.* **Small GTPases. 2018 Jan 24:1-7. doi: 10.1080/21541248.2018.1423851.** PMID: 29313423 **IF: NI**
- **New insights into the Vav1 activation cycle in lymphocytes.** *Barreira M, Rodríguez-Fdez S, Bustelo XR.* **Cell Signal. 2018 May;45:132-144. doi: 10.1016/j.cellsig.2018.01.026. .** PMID: 29410283 **IF: 3.388 / Q2**
- **R-Ras2 is required for germinal center formation to aid B cells during energetically demanding processes**. *Mendoza P, Martínez-Martín N, Bovolenta ER, Reyes-Garau D, Hernansanz-Agustín P, Delgado P, Díaz-Muñoz MD, Oeste CL, Fernández-Pisonero I, Castellano E, Martínez-Ruiz A, Alonso-Lopez D, Santos E, Bustelo XR, Kurosaki T, Alarcón B.* Sci Signal. **2018 May 29;11(532). pii: eaal1506. doi: 10.1126/scisignal.aal1506.** PMID: 29844052 **IF: 6.481 / Q1**
- **Differential role of the RasGEFs SOS1 and SOS2 in mouse skin homeostasis and carcinogenesis.** *Liceras-Boillos P, Jimeno D, García-Navas R, Lorenzo-Martín LF, Menacho-Marquez M, Segrelles C, Gómez C, Calzada N, Fuentes-Mateos R, Paramio JM, Bustelo XR, Baltanás FC, Santos E.* **Mol Cell Biol. 2018 May 29. pii: MCB.00049-18. doi: 10.1128/MCB.00049-18.** PMID: 29844066 **IF: 3.375 / Q2**
- **Vav3-induced cytoskeletal dynamics contribute to heterotypic properties of endothelial barriers.** *Hilfenhaus G, Nguyen DP, Freshman J, Prajapati D, Ma F, Song D, Ziyad S, Cuadrado M, Pellegrini M, Bustelo XR, Iruela-Arispe ML.* **J Cell Biol. 2018 Aug 6;217(8):2813-2830. doi: 10.1083/jcb.201706041.** PMID: 29858212 **F: 8.891 / D1**
- **RHO GTPases in cancer: known facts, open questions, and therapeutic challenges.** *Bustelo XR.* **Biochem Soc Trans. 2018 Jun 19;46(3):741-760. doi: 10.1042/BST20170531. Review.** PMID: 29871878 **IF: 4.291 / Q1**
- **RAS GTPase-dependent pathways in developmental diseases: old guys, new lads, and current challenges.** *Bustelo XR, Crespo P, Fernández-Pisonero I, Rodríguez-Fdez S.* **Curr Opin Cell Biol. 2018 Jul 11;55:42-51. doi: 10.1016/j.ceb.2018.06.007. Review.** PMID: 30007125 **IF: 8.233 / D1**
- **Vav proteins maintain epithelial traits in breast cancer cells using miR-200c-dependent and independent mechanisms.** *Lorenzo-Martín LF, Citterio C, Menacho-Márquez M, Conde J, Larive RM, Rodríguez-Fdez S, García-Escudero R, Robles-Valero J, Cuadrado M, Fernández-Pisonero I, Dosil M, Sevilla MA, Montero MJ, Fernández-Salguero PM, Paramio JM, Bustelo XR.* **Oncogene. 2018 Aug 7. doi: 10.1038/s41388-018-0433-7.** PMID: 30087437 **IF: 6.634 / D1**
- **Protein-Protein Interactions: Emerging Oncotargets in the RAS-ERK Pathway.** *García-Gómez R, Bustelo XR, Crespo P.* **Trends Cancer. 2018 Sep;4(9):616-633. doi: 10.1016/j.trecan.2018.07.002. Review.** PMID: 30149880 **IF: 8.884 / D1**
- **RAS at the Golgi antagonizes malignant transformation through PTPRκ-mediated inhibition of ERK activation**. *Casar B, Badrock AP, Jiménez I, Arozarena I, Colón-Bolea P, Lorenzo-Martín LF, Barinaga-Rementería I, Barriuso J, Cappitelli V, Donoghue DJ, Bustelo XR, Hurlstone A, Crespo P.* **Nat Commun. 2018 Sep 5;9(1):3595. doi: 10.1038/s41467-018-05941-8.** PMID: 30185827 **IF: 11,878 / D1**
- **Cancertool: A Visualization and Representation Interface to Exploit Cancer Datasets.** *Cortazar AR, Torrano V, Martín-Martín N, Caro-Maldonado A, Camacho L, Hermanova I, Guruceaga E,*

Lorenzo-Martín LF, Caloto R, Gomis RR, Apaolaza I, Quesada V, Trka J, Gómez-Muñoz A, Vincent S, Bustelo XR, Planes FJ, Aransay AM, Carracedo A. **Cancer Res. 2018 Nov 1;78(21):6320-6328. doi: 10.1158/0008-5472.CAN-18-1669.** PMID: 30232219
IF: 8.378 / D1

- **An unexpected tumor suppressor role for VAV1.** *Bustelo XR, Lorenzo-Martín LF, Cuadrado M, Fernández-Pisonero I, Robles-Valero J.* **Mol Cell Oncol. 2018 Feb 23;5(3):e1432257. doi: 10.1080/23723556.2018.1432257. eCollection 2018.** PMID: 30250888 IF: NI
- **Editorial overview: New concepts and experimental approaches to understand development, tissue regeneration, and human disease.** *Röper K, Bustelo XR.* **Curr Opin Cell Biol. 2018 Oct 1. pii: S0955-0674(18)30153-4. doi: 10.1016/j.ceb.2018.09.006.** PMID: 30287131
IF: 8.233 / D1
- **Vagal afferents contribute to sympathoexcitation-driven metabolic dysfunctions.** *Lorenzo-Martín LF, Menacho-Márquez M, Fabbiano S, Al-Massadi O, Abad A, Rodríguez-Fdez S, Sevilla MA, Montero MJ, Diéguez C, Nogueiras R, Bustelo XR.* **J Endocrinol. 2019 Mar 1;240(3):483-496. doi: 10.1530/JOE-18-0623.** PMID: 30703063
IF: 4.381 / Q1
- **The Vav GEF Family: An Evolutionary and Functional Perspective.** *Rodríguez-Fdez S, Bustelo XR.* **Cells. 2019 May 16;8(5). pii: E465. doi: 10.3390/cells8050465. Review.** PMID: 31100928 IF: 5.656 / Q1
- **YES1 Drives Lung Cancer Growth and Progression and Predicts Sensitivity to Dasatinib.** *Garmendia I, Pajares MJ, Hermida-Prado F, Ajona D, Bértolo C, Sainz C, Lavín A, Remírez AB, Valencia K, Moreno H, Ferrer I, Behrens C, Cuadrado M, Paz-Ares L, Bustelo XR, Gil-Bazo I, Alameda D, Lecanda F, Calvo A, Felip E, Sánchez-Céspedes M, Wistuba II, Granda-Díaz R, Rodrigo JP, García-Pedrero JM, Pio R, Montuenga LM, Agorreta J.* **Am J Respir Crit Care Med. 2019 Oct 1;200(7):888-899. doi: 10.1164/rccm.201807-1292OC.** PMID: 31166114 IF: 16.494 / D1
- **Pol5 is an essential ribosome biogenesis factor required for 60S ribosomal subunit maturation in** Saccharomyces cerevisiae**.** *Ramos-Saenz A, González-Alvarez D, Rodriguez-Galan O, Rodriguez-Gil A, Gaspar SG, Villalobo E, Dosil M, de la Cruz J.* **RNA. 2019 Aug 14. pii: rna.072116.119. doi: 10.1261/rna.072116.119.** PMID: 31413149 IF: 3.949 / Q2
- **Phosphatidylinositol Monophosphates Regulate Optimal Vav1 Signaling Output.** *Rodríguez-Fdez S, Citterio C, Lorenzo-Martín LF, Baltanás-Copado J, Llorente-González C, Corbalán-García S, Vicente-Manzanares M, Bustelo XR.* **Cells. 2019 Dec 16;8(12). pii: E1649. doi: 10.3390/cells8121649.** PMID: 31888228 IF: 5.656 / Q1



Bioinformatics analyses performed with diagnostic gene expression profiles (left) and a single biomarker (right).

PATENTS

PATENT REFERENCE	TITLE	INVENTORS	PRIORITY DATE
EP 18 382 912.6	Methods and kits for the prognosis of squamous cell carcinomas (SCC)	L.F. Lorenzo Martín & Xosé R. Bustelo	

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Pharmaco-mimetic analysis of the therapeutic role of Vav-dependent metabolic routes in breast cancer	Xosé R. Bustelo	Ramón Areces Foundation	2015-2018	128,000.00 €
Vav family oncoproteins: regulatory layers, pathophysiological functions, and therapeutic potential (SAF2015-64556-R)	Xosé R. Bustelo	Spanish Ministry of Science and Innovation	2016-2018	484,000.00 €
Genetic validation and therapeutic-translational applications of new oncogenic drivers (CSI049U16)	Xosé R. Bustelo	Ministry of Education, Regional Government of Castille and León	2016-2018	120,000.00 €
Function, diagnostic value and pharmacological inhibition of R-Ras2, a new oncogenic driver (GC16173472GARC)	Xosé R. Bustelo	Spanish Association against Cancer (AECC)	2016-2021	1,200,000.00 €
Alterations in the assembly and maturation of ribosomes during cell transformation (FS/36-2017)	Mercedes Dosil	Solórzano Foundation	2018	3,394.19 €
Center of Biomedical Research on Cancer (CIBERONC) (CB16/12/00351)	Xosé R. Bustelo	Carlos III Health Institute	2018-2019	160,000.00 €
Use of cutting-edge techniques to determine the function and therapeutic value of the R-Ras2 oncoprotein-driven signaling pathways (CSI252P18)	Xosé R. Bustelo	Ministry of Education, Regional Government of Castille and León	2018-2020	40,000.00 €
Assembly and maturation of the eurkaryotic small ribosomal subunit (BFU2017-88192-P)	Mercedes Dosil	Spanish Ministry of Science and Innovation	2018-2020	96,800.00 €
Micro/nano-LC-MS/MS equipment for proteomics analyses of high resuluion and sensitivity (EQC2018-004250-P)	Xosé R. Bustelo	Spanish Ministry of Science and Innovation	2018-2019	648.552.00€
Strategic Plan for Center (CLC-2017-01)	Xosé R. Bustelo	Ministry of Education, Regional Government of Castille and León	2018-2023	2,100,000.00 €
RHO guanosine nucleotide exchange factors: friends or foes in cancer? (RTI2018-096481-B-100)	Xosé R. Bustelo	Spanish Ministry of Science and Innovation	2019-2021	310,000.00 €

OTHER ACTIVITIES & RELEVANT FACTS

PROFESIONAL RECOGNITIONS (X. R. BUSTELO)

2017-Present	*Coordinator* Mechanisms of Tumor Progression Program Centro de Investigación Biomédica en Red de Cáncer (CIBERONC) / Center for Biomedical Research in Oncology
2017-Present	*Member of the Executive Committee* (Comité de Dirección) CIBERONC
2017-2018	*President Elect and Vice-President* Spanish Association for Cancer Research / Asociación Española de Investigación sobre el Cáncer
2018	Invited Editor for *Curr. Opin. Cell. Biol.* 2018 issue on Differentiation and Disease
2018-2022	*Director, Strategic Plan* Centro de Investigación del Cáncer/Cancer Research Center, CSIC-University of Salamanca, Salamanca, Spain
2019-2021	President Spanish Association for Cancer Research / Asociación Española de Investigación sobre el Cáncer

EDITORIAL BOARDS (X.R. BUSTELO)

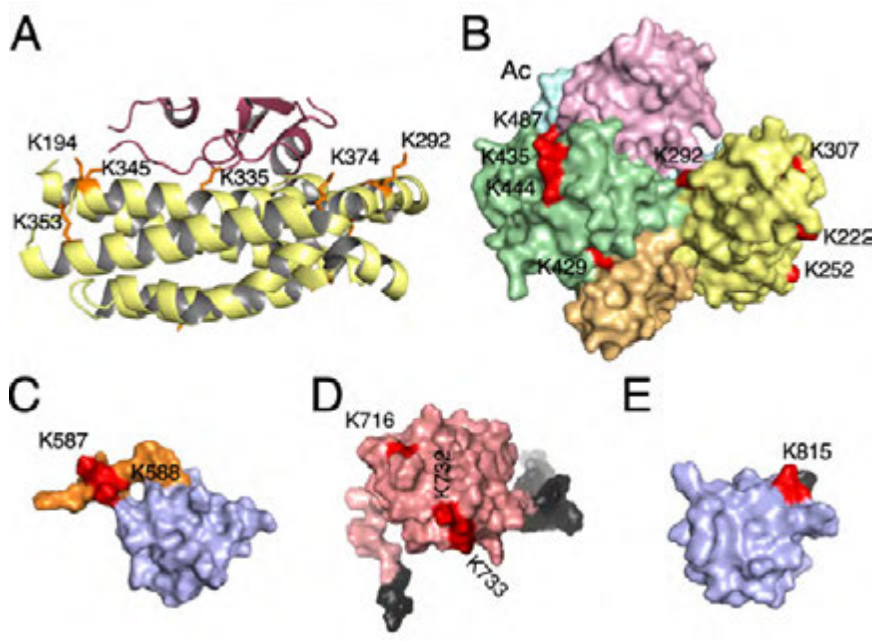
- *Cell Comm Adhes* (2017-2018)
- *Front Immunol* (since 2010)
- *Small GTPases* (since 2011)
- *Encyclopedia of Signaling Molecules* (since 2012)
- *Front Cell Develop Biol* (since 2015)
- *Clin Transl Oncol* (since 2017)

MEMBERSHIP IN SCIENTIFIC COMMITTEES (X.R. BUSTELO)

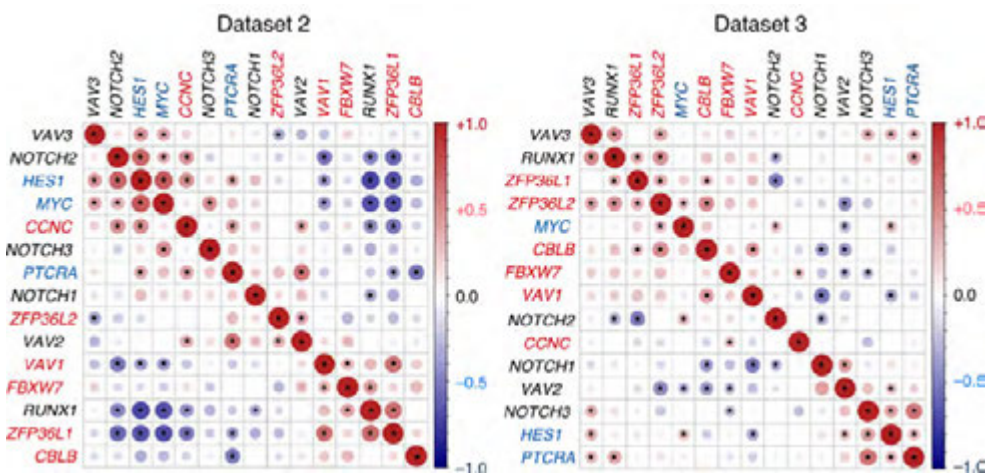
- *External Scientific Committee*
  Oncology Program, Santiago University Hospital (Santiago of Compostela, Spain, 2006-Present)
- *External Scientific Committee*
  Galician Colon Cancer Network (Galicia, Spain, 2012-Present)
- *External Scientific Committee*
  Santiago University Hospital Health Research Institute (Santiago of Compostela, Spain, 2008-Present)
- *External Scientific Committee*
  Marqués de Valdecilla Hospital Research Institute (Santander, Spain, 2009-Present)
- *President and Member of the External Scientific Committee*
  La Princesa Hospital Health Research Institute (Madrid, Spain, 2009-Present)
- Kærtor Foundation Scientific Committee (2017-Present)
  Kærtor Foundation
- *Scientific Committee*
  16th International ASEICA Congress (2018)
- *Scientific Committee*
  18th Congress of the Spanish Society for Cell Biology (Spain, 2019)
- *Scientific Committee*
  II ASEICA Educational Symposium (Spain, 2019)

MAIN TALKS AT SCIENTIFIC MEETINGS AND RESEARCH CENTERS (X.R. BUSTELO)

1. Andalusian Center for Molecular Biology and Regenerative Medicine. Seville, Spain (2018)
2. Chairman, Molecular Mechanisms in Tumor Progression. II Annual Meeting CIBERONC. Madrid, Spain (2018)
3. Hematology Department. Salamanca University Hospital. Salamanca, Spain (2018)
4. Gifu University. Gifu, Japan (2018)
5. Instituto Gulbenkian de Ciência. Lisbon, Portugal (2018)
6. 3rd International Congress of the Portuguese Association for Cancer Research (ASPIC). Lisbon, Portugal (2018)
7. Biochemical Society Meeting on "Small G proteins in cellular signaling and disease". Cambridge, UK (2018)
8. XLI Meeting of the Spanish Society of Biochemistry and Molecular Biology. Session Chairman. Santander, Spain (2018)
9. Instituto de Biocomputación y Física de Sistemas Complejos. Zaragoza, Spain (2018)
10. Chairman of Sesion. 16th ASEICA International Congress. Spanish Association for Cancer Research (ASEICA). Valencia, Spain (2018)
11. Institut of Reserca Biomédica. Barcelona, Spain (2018)
12. 9th Meeting of Galician Young Investigators Working Overseas (Member of discussion table). A Coruña, Galicia, Spain (2018)
13. 4th Meeting of Cancer Researchers of the Valencia Autonomous Region, Alcoi, Spain (2019)
14. *The RAS Superfamily and Related Pathways in Health and Disease.* Ramón Areces Foundation International Symposium, Santander, Spain (2019)
15. Inaugural Lecture. Master of Supramolecular Chemistry. School of Chemistry, University of Salamanca, Salamanca, Spain (2019)
16. Meeting "A Celebration of Molecular Oncology", Madrid, Spain (2019)
17. Innovation Forum. Pfizer Foundation, Madrid, Spain (2019)
18. Chairman of session (Therapeutic approaches of stem cells). XVIII Congress of the Spanish Society of Cell Biology, Badajoz, Spain (2019)
19. Instituto de Salud Carlos III, Majadahonda, Spain (2019)
20. Regional Congress of the Spanish Association Against Cancer of Castilla-León, Salamanca (2019)
21. Joint Meeting Spanish Association for Cancer Research (ASEICA) and Centro de Investigación Biomédica en Red de Cáncer (CIBERONC), Madrid (2019)
22. Meeting of the CIBEROC Work Module on Experimental Models in Cancer, Barcelona (2019)



Top crystal structure of domains of a cancer driver (A-E) indicating specific post-translational modification sites (red).



Co-expression matrix of indicted genes (top,left) in two datasets from the same tumor type.

Team Leader

Pedro Alfonso Lazo-Zbikowski Taracena

Phone.: +34 923 294 804

E-mail: plazozbi@usal.es

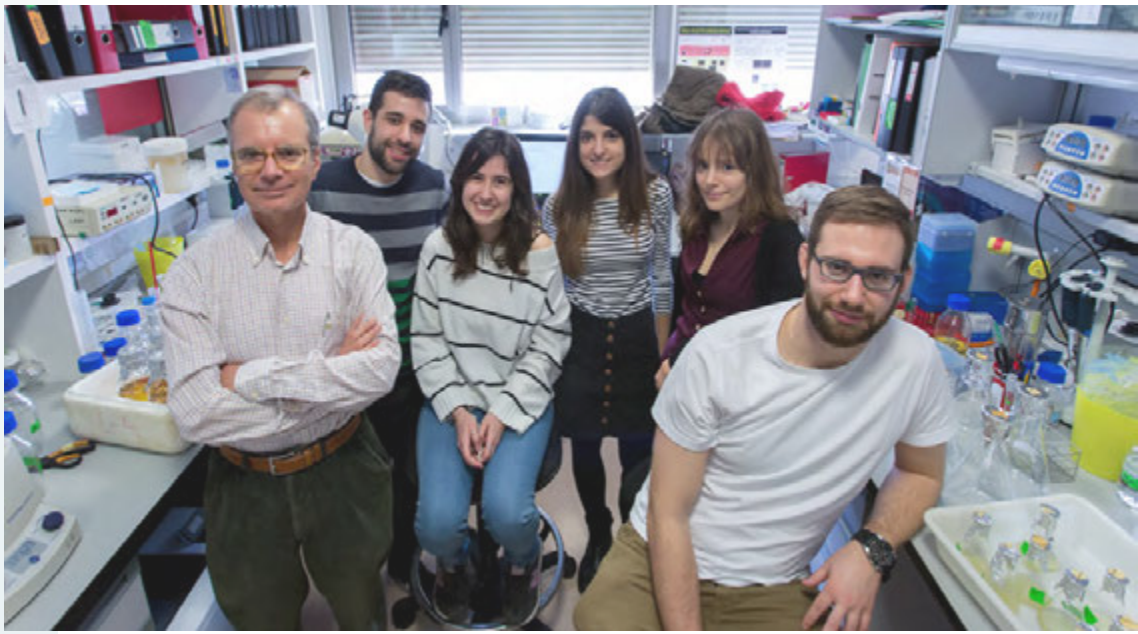
Research Team

Predoctorals

Ignacio Campillo Marcos
Raúl García González
Elena Martín Doncel
Patricia Morejón García
Elena Navarro Carrasco
Eva Monte Serrano

Visiting researchers

Adrivanio Baranoski
Eugenia Pettigiani



LABORATORY 4

KINASES IN ONCOLOGY AND NEURODEGENERATION. SIGNALING BY CHROMATIN KINASES

Ser-Thr kinases regulate and transmit most of the intracellular signals. In the human kinome there is a unique and isolated family of Ser-Thr kinases known as VRK (vaccinia-related kinases), which is formed by three members, appeared very late in evolution and coordinates multiple functions in higher eukaryotes. These kinases affect multiple pathways regulating cell cycle, cell death and responses to many growth factors or cellular stress. Such as DNA damage. The group is focused on the study of the human VRK family signaling pathways and its implications in different phenotypes in relation with oncology in the context of chromatin remodeling and organization, DNA damage responses as well as their pathological implications in tumor biology and in neurological and neurodegenerative diseases. These kinases also regulate asymmetric division of stem cells and the dynamic remodeling of chromatin in different biological processes. In the nervous system, *VRK1* mutations are associated to neuromotor pathology, mainly distal sensorimotor neuropathies that have a variable degree of severity.

MAIN AIM

Identify and characterize the novel signaling pathways where human VRK proteins and determine the steps that form it and its functional interactions with other signaling pathways, particularly in the context of e biological processes associated to cell proliferation, DNA damage responses in the tumor phenotype cancer, and its participation in neurodegenerative syndromes such as Amyotrophic lateral sclerosis (ALS) and ▸ ▸ muscular dystrophies. We have already characterized the rare mutations in the *VRK1* gene alters neuronal migration and cause a defective formation of Cajal bodies that are defective and impair functions associated to spinal muscular atrophy protein.

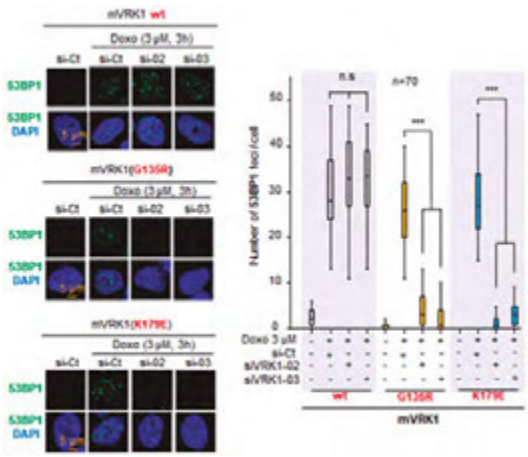
SPECIFIC AIMS

1. Study how VRK proteins are regulated in response to specific stimulation including mitogenic growth factors or DNA damage. This regulation may be mediated by covalent modifications of the protein, or alternatively represent regulation of gene expression.
2. Identify upstream elements for each VRK protein, which are likely to be either a part of the pathway or a regulatory element, and associate them to specific functional responses.
3. Identify downstream elements of VRK proteins. These are likely to be intracellular substrates proteins of the kinases, but may also be interacting proteins. These interactions will be associated to functional responses and to cross-talk mechanisms with other signaling pathways.
4. Study the role of VRK proteins in the context of the cellular response to genetic damage either natural (oxidative stress, UV) or induced (tobacco, radiation, chemotherapy).▸

5. Characterize the role VRK1 in the regulation of alternative epigenetic modifications of histones, acetylation and methylation, which are mediated by four different enzymes whose coordination is unknown in the remodeling of chromatin.
6. Characterize and integrate VRK1 signaling pathways in the context chromatin remodeling and its association to DNA response pathways, neurodegenerative diseases and stem cells.
7. Characterize the mechanism by which human VRK1 mutations contribute to neurological diseases such as spinal muscular atrophy (SMA) or amyotrophic lateral sclerosis (ALS).

In these two years we have demonstrated the role VRK1 plays in the progression of mitotic entry and chromatin condensation by a sequential coordination with AURKB in G2/M phases of cell cycle. Also we have further characterized the different roles that VRK1 has in maintenance of chromosome stability.

In the context of VRK1 role in pediatric neurodevelopmental delays. We have demonstrated that some very rare homozygous mutations in the VRK1 gene cause a defective assembly of Cajal bodies. This Cajal body alteration prevents its interaction and function with proteins associated to spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS).



The VRK1-G135R mutant, detected in distal sensorimotor neuropathy and muscular atrophy, impairs the response to DNA damage caused by doxorubicin and detected by formation of 53BP1 foci that behaves like a kinase-dead VRK1 (K179E).

PUBLICATIONS

- **VRK1 and AURKB form a complex that cross inhibit their kinase activity and the phosphorylation of histone H3 in the progression of mitosis.** *Moura DS, Campillo-Marcos I, Vázquez-Cedeira M, Lazo PA.* **Cell Mol Life Sci. 2018 Jul;75(14):2591-2611. doi: 10.1007/s00018-018-2746-7.** PMID: 29340707. IF: 7.014 / D1

- **Implication of the VRK1 chromatin kinase in the signaling responses to DNA damage: a therapeutic target?** *Campillo-Marcos I, Lazo PA.* **Cell Mol Life Sci. 2018 Jul;75(13):2375-2388. doi: 10.1007/s00018-018-2811-2. . Review.** PMID: 29679095 IF: 7.014 / D1

- **Olaparib and ionizing radiation trigger a cooperative DNA-damage repair response that is impaired by depletion of the VRK1 chromatin kinase.** *Campillo-Marcos I, Lazo PA.* J Exp Clin Cancer Res. 2019 May 17;38(1):203. doi: 10.1186/s13046-019-1204-1. PMID: 31101118 IF: 5.645 / Q1

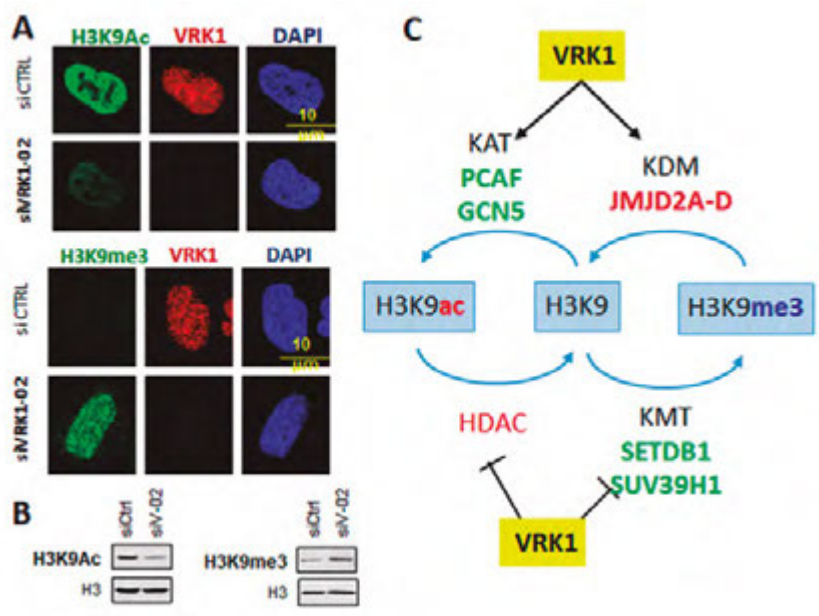
- **VRK1 functional insufficiency due to alterations in protein stability or kinase activity of human VRK1 pathogenic variants implicated in neuromotor syndromes.** *Martín-Doncel E, Rojas AM, Cantarero L, Lazo PA.* **Sci Rep. 2019 Sep 16;9(1):13381. doi: 10.1038/s41598-019-49821-7.** PMID: 31527692 IF: 4.011 / D1

GRANTS FOR RESEARCH IN PROGRESS

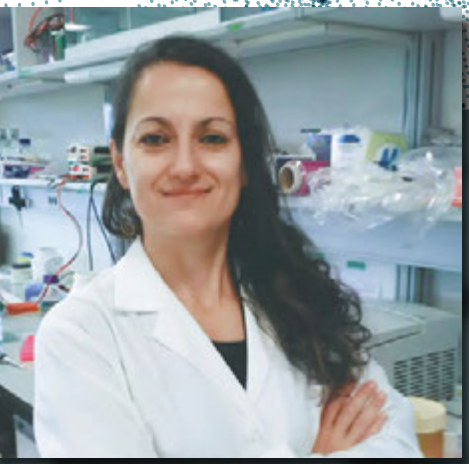
PROJECT	PI	GRANT	TIME	FUNDING
Funciones de la quinasa VRK1 humana en la patogénesis del cáncer y enfermedades neurodegenerativas (SAF2016-75744-R)	Pedro A. Lazo-Zbikowski Taracena	Spanish Ministry of Economy & Competitiveness	2017-2019	314,600.00 €
Spanish network of the International Nucleome Consortium (EU Cost Action CA18127, RED2018-102801-T)	Marc Martí Renom / Pedro A. Lazo-Zbikowski Taracena	Spanish Ministry of Science, Research & Universities	2019-2023	25,000.00 €

OTHER ACTIVITIES & RELEVANT FACTS

- Professor of master course "Mechanisms of Tumor Suppression" 3 (ECTS/annually)
- Member of the DAAD (Deutscher Akademischer Austauschdienst) for academic exchange between Germany and Spain
- Member of the "Latvian Council of Science Commission" for projects funded by European Regional Development Funds
- Editorial board member of Frontiers in Cellular and Developmental Biology journal
- Editorial board member of Clinical and Translational Oncology journal



VRK1 role as epigenetic switch. Depletion of VRK1 alters the epigenetic modifications of Histone H3-Lys9, from acetylation to methylation. This means that VRK1 mediates an epigenetic switch from a transcriptionally active to an inactive chromatin.



Team Leader

Sandra Blanco Benavente

Phone.: +34 923 294 805

E-mail: sandra.blanco@usal.es

Research Team

Postdoctorals

Domenico Rosace

Mª Paz Nombela Blanco

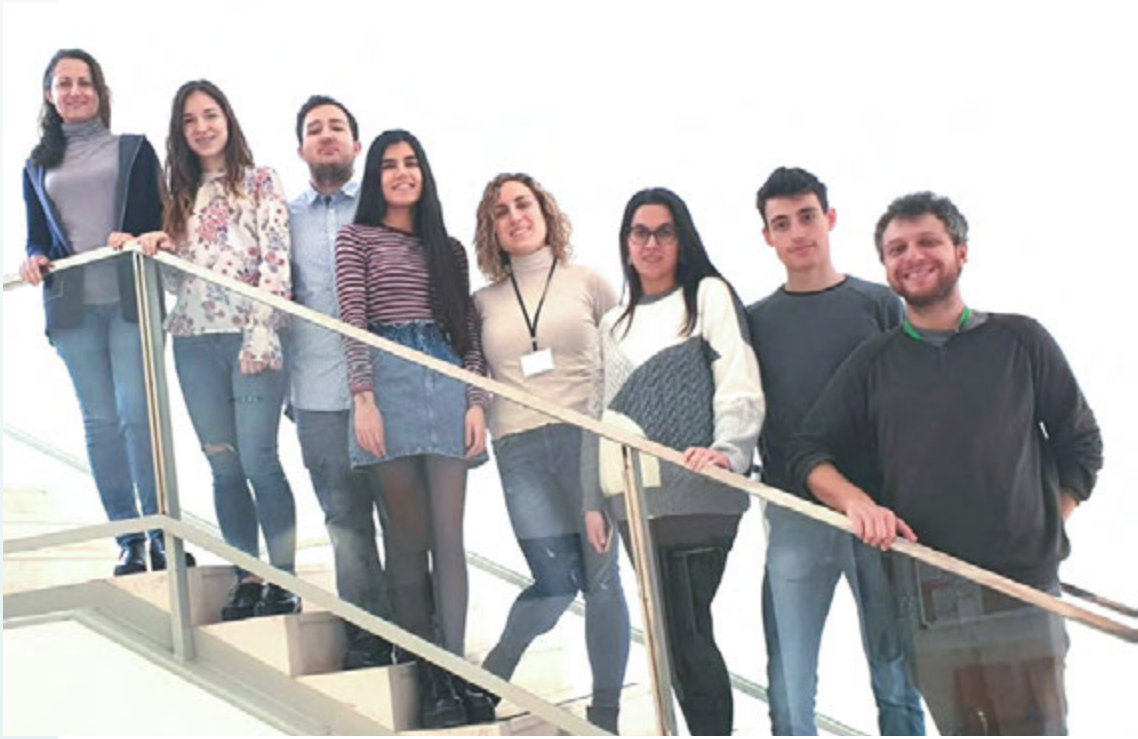
Predoctorals

Raquel García Vilchez

Judith López Luís

Master Student

Ana Macrina Añazco Guenkova



LABORATORY 5

EPITRANSCRIPTOMICS AND CANCER

(from August 2018)

Our research is focused in uncovering the molecular mechanisms regulating tissue homeostasis during normal development and during pathological conditions, in particular in cancer. Using a combination of novel transcriptome-wide analyses, and mouse and human *in vitro* and *in vivo* models, we are focused on studying the role of post-transcriptional modifications such as RNA methylation in normal development and during pathological conditions.

RNA modifications are beginning to define a novel layer of biological complexity that is becoming widely appreciated as the epitranscriptome. To date over 170 chemical modifications are known in RNA. Emerging evidence is revealing that post-transcriptional modifications such as cytosine-5 or adenine-6 methylation mediate regulation of gene expression and protein translation efficiency and accuracy. We have described how cytosine-5 methylation is essential for tissue stem cell differentiation and survival as well as for embryo development. In addition, we have found that aberrant 5-methylcytosine deposition leads to human diseases including cancer and neuro-development disorders. Now, we seek to understand whether and how other covalent RNA modifications regulate self-renewal, differentiation, growth, survival, drug resistance and invasion processes in malignant cells. To this aim, we combine state-of-the-art transcriptome-wide sequencing methods, with biochemical methods, mouse models, human cancer cell lines, stem cell cultures, patient samples and 3D culture models to study the role of post-transcriptional modifications such as RNA methylation in tissue and cancer stem cell functions, development and cancer initiation, progression, metastasis and therapy tolerance development.

Our current research projects are:

1 Identification and characterization of the epitrasncriptome in cancer cells, cancer initiating cells and persister cells in prostate cancer

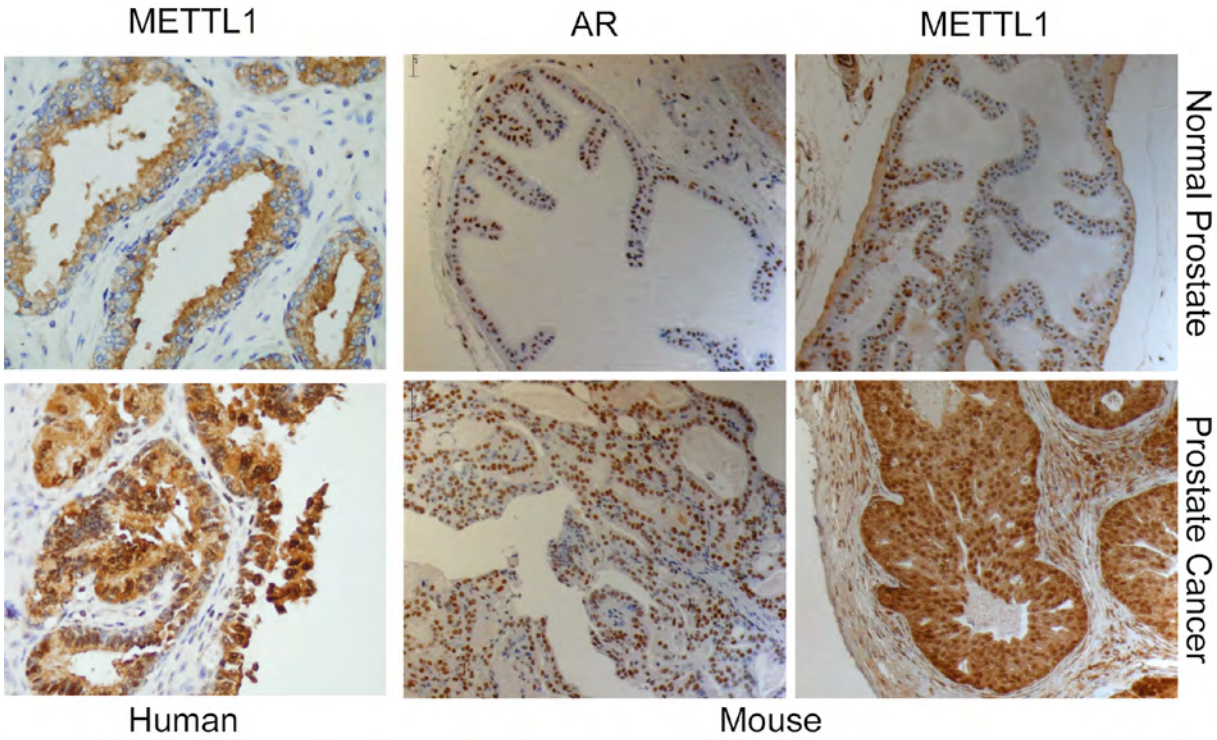
2 Development of new tools to identify novel epitranscriptomic marks relevant in cancer at single nucleotide resolution

3 Identify downstream targets of RNA modifying enzymes altered in cancer and understand the molecular mechanisms underlying the epitranscriptome in cancer

4 Identify upstream elements for those RNA modifying enzymes altered in cancer, and associate them to specific functional responses.

5 Finding the role of RNA modifications in the regulation of tumour growth, self-renewal and survival to conventional therapies

6 Determination of the therapeutic potential of the manipulation of the epitranscriptome of cancer cells



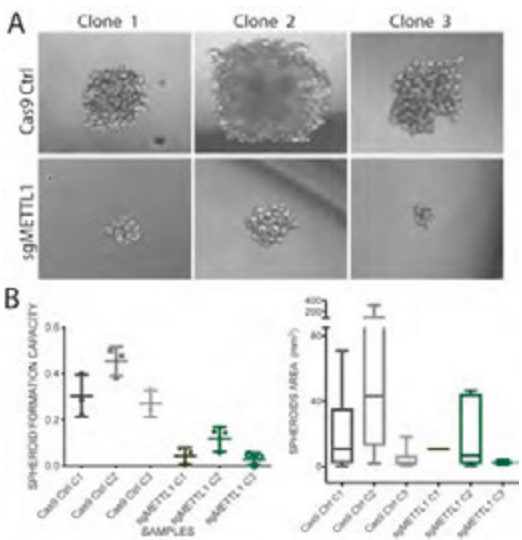
METTL1 is overexpressed in prostate cancer. Images of representative histological sections of mouse and human prostate normal tissue and invasive tumours showing over-expression of the tRNA guanosine methyltransferase METTL1 in mouse prostate tumours. AR (Androgen Receptor) is also over-expressed in prostate cancer.

PUBLICATIONS

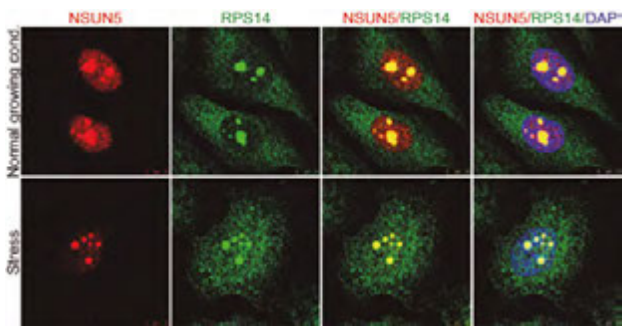
- **Epigenetic loss of RNA-methyltransferase NSUN5 in glioma targets ribosomes to drive a stress adaptive translational program.** *Janin M, Ortiz-Barahona V, de Moura MC, Martínez-Cardús A, Llinàs-Arias P, Soler M, Nachmani D, Pelletier J, Schumann U, Calleja-Cervantes ME, Moran S, Guil S, Bueno-Costa A, Piñeyro D, Perez-Salvia M, Rosselló-Tortella M, Piqué L, Bech-Serra JJ, De La Torre C, Vidal A, Martínez-Iniesta M, Martín-Tejera JF, Villanueva A, Arias A, Cuartas I, Aransay AM, La Madrid AM, Carcaboso AM, Santa-María V, Mora J, Fernandez AF, Fraga MF, Aldecoa I, Pedrosa L, Graus F, Vidal N, Martínez-Soler F, Tortosa A, Carrato C, Balañá C, Boudreau MW, Hergenrother PJ, Kötter P, Entian KD, Hench J, Frank S, Mansouri S, Zadeh G, Dans PD, Orozco M, Thomas G, Blanco S, Seoane J, Preiss T, Pandolfi PP, Esteller M.* **Acta Neuropathol. 2019 Aug 19. doi: 10.1007/s00401-019-02062-4.** PMID: 31428936 **IF: 18,174 / D1**
- **Is hybrid-PBL advancing teaching in biomedicine? A systematic review.** *Jiménez-Saiz R, Rosace D.* **BMC Med Educ. 2019 Jun 24;19(1):226. doi: 10.1186/s12909-019-1673-0.** PMID: 31234856. **IF: 1,870 / Q1**
- **Cytosine-5 RNA methylation links protein synthesis to cell metabolism.** *Gkatza NA, Castro C, Harvey RF, Heiß M, Popis MC, Blanco S, Bornelöv S, Sajini AA, Gleeson JG, Griffin JL, West JA, Kellner S, Willis AE, Dietmann S, Frye M.* **PLoS Biol. 2019 Jun 14;17(6):e3000297. doi: 10.1371/journal.pbio.3000297. eCollection 2019 Jun.** PMID: 31199786 **IF: 8,386 / D1**
- **Post-transcriptional regulation by cytosine-5 methylation of RNA.** *García-Vílchez R, Sevilla A, Blanco S.* **Biochim Biophys Acta Gene Regul Mech. 2019 Mar;1862(3):240-252. doi: 10.1016/j.bbagrm.2018.12.003. Review.** PMID: 30593929 **IF: 4,599 / D1**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Modificaciones post-transcripcionales y procesamiento en ARN en células madre de cáncer (SAF2016-78667-R)	Sandra Blanco Benavente	Spanish Ministry of Economy & Competitiveness	2018-2019	168,190.00 €
Papel de las modificaciones post-transcripcionales de ARN en cáncer (201820I059)	Sandra Blanco Benavente	Spanish National Research Council (CSIC)	2018-2019	5.000,00 €
Alteraciones en los patrones de metilación citosina-5 de ARN en cáncer de próstata (FS/21-2018)	Sandra Blanco Benavente	Solórzano Foundation	2018-2019	1.473,00 €
Con-Ciencia-Con-Arte, una iniciativa de FGCSIC (FGCC-2019-0009)	Sandra Blanco Benavente / Almudena Timón	Fundación General CSIC	2019	3.500,00 €
Post-transcriptionally modified RNAs as survival and growth mediators in cancer cells (LABAE19040BLAN)	Sandra Blanco Benavente	Spanish Association against Cancer (AECC)	2019-2022	300,000.00 €



Single cell-spheroids growing of Cas9 Controls (Cas9 Ctrl) and METTL1 KO (sgMETTL1) prostate cancer cell lines. A) Representative bright field microscope images. B. Quantification of the spheroid formation capacity (number of spheroids obtained normalized to the number of single-cells seeded) (left panel). The right panel indicates the size of spheroids. Area was quantified measuring the width and height of the spheroids.



Localization of the RNA cytosine-5 methyltransferase NSUN5 (red) and the ribosomal protein RPS14 (green) in prostate cancer cells in normal growth conditions (non-treated control) and under stress (post-UV radiation). Nuclei were counterstained with DAPI in blue.

OTHER ACTIVITIES & RELEVANT FACTS

Leader and coordinator together with Almudena Timón of the outreach event: Con-Ciencia-Con-Arte. A Science and Art Exhibition. Prize awarded by Fundación General del CSIC (FGCSIC) to participate in an outreach activity organized by Cuenta la Ciencia programme. With Con-Ciencia-Con-Arte we aim to create a space where both scientists and artists can work together, communicate and learn from each other. We propose this activity in which both researchers and artists will explore the same research question or hypothesis. Their different ways to approach to the same study will be later presented to the general public. We hope that the general public will be able to use the eyes of the artist to understand the work of the researchers. This will engage the audience with an interest towards both science and art and eventually provoke artistic and scientific debates.

Team Leader

Esther Castellano Sánchez

Phone.: +34 663 181 610

E-mail: ecastellano@usal.es

Research Team

Postdoctoral

Cristina Cuesta Apausa

Predoctoral

Cristian Morillo Losada

Master Student

Marta Alcón Pérez

LABORATORY 5

TUMOUR-STROMA SIGNALING

(from March 2019)

The prognosis of lung cancer remains poor, with overall five-year survival figures varying between 5 and 10% worldwide. Unlike other solid tumours where survival rates have improved in the order of 60–90%, the prognosis of lung cancer has changed very little over the past 20 years. KRAS is aberrantly activated by mutations in 30% of Non-Small Cell Lung Carcinoma (NSCLC), the most frequent subtype of lung cancer. Efforts to develop therapies directly targeting mutant RAS have been stymied by several factors, including their complex biology and unique structural and biochemical properties so no treatment is currently available. In this scenario, new research into the biology of this cancer that leads to new therapeutic targets will have a significant impact in the field.

Our lab aims to understand how oncogenic Ras proteins drive cancer development by regulating the interplay between tumour cells and its microenvironment in lung cancer. Interactions between tumoral cells and the surrounding stroma are essential to maintain tumour growth and cancer progression. These interactions provide proliferative and migratory advantages that help tumour development and progression. Ras oncogenes are key players in the initiation and development of cancer. However, little is known about how Ras signaling can modulate the stroma to support tumour progression. Identifying the key molecules required for RAS-dependent tumour-stroma crosstalk is fundamental to better understand the biology of RAS-driven lung cancer. This will lay the foundation for developing new treatments focused on modulating host responses in order to alter the functionality of cancer cells and sensitize them to additional therapies.

Data from our lab shows that disrupting RAS-PI3K signaling in KRAS-driven lung tumours has remarkable and multi-faceted effects in the stroma. We generated a conditional mouse model in which RAS-PI3K binding is disrupted by point mutations in the RAS Binding Domain (RBD) of PI3K subunit p110α Upon crossing RBD mice with a KRAS-driven model of lung cancer (KRAS-LA2), we found that disrupting RAS-PI3K signaling in established tumours:

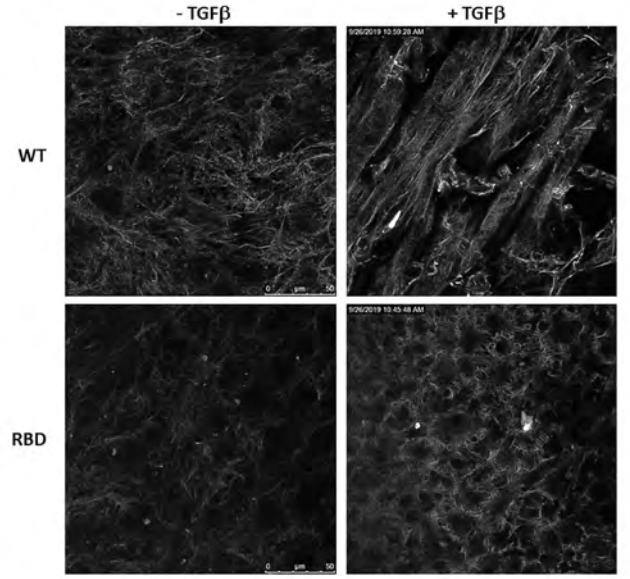
1. induced initial tumour regression followed by long term tumour stasis;
2. decreased tumour angiogenesis;
3. decreased tumour infiltration of macrophages; and
4. impaired CAF activation and function

Based in our preliminary data, the objectives of the lab are:

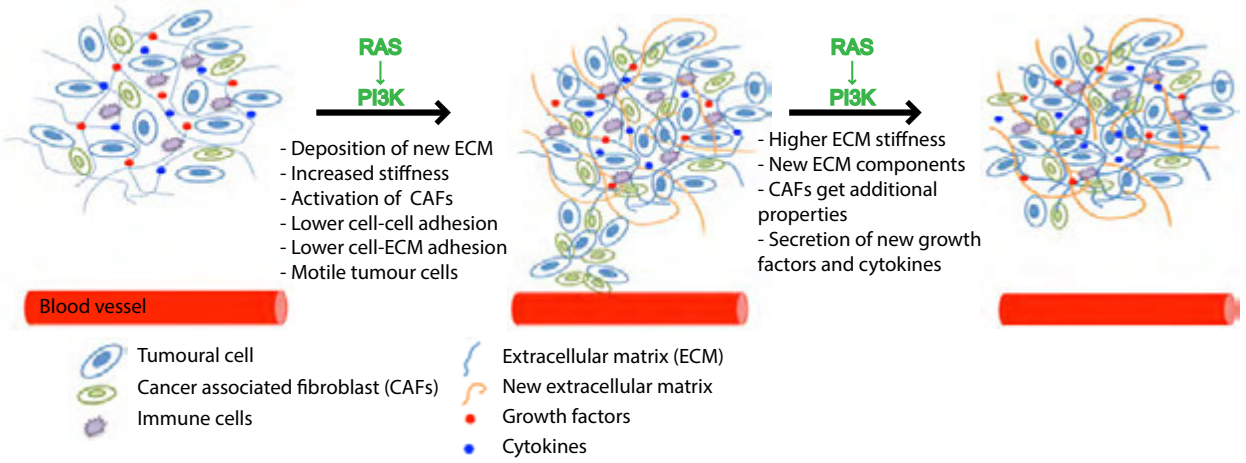
1. Determine the role of RAS-PI3K signaling in the biology of Cancer Associated Fibroblasts (CAFs). RAS signaling has been extensively studied in tumour cells, but little is known about how it affects the function of CAFs and the dynamics of the extracellular matrix (ECM). Using a variety of models and experimental approaches, we are mapping the role of RAS-PI3K signaling in CAFs, aiming to understand the molecular processes regulated by RAS-PI3K in CAF activation and function, how RAS-PI3K signaling in CAFs affects composition and stiffness of the ECM and how differences in ECM composition and stiffness affect behaviour of tumour cells and CAFs. ▸

2. Dissect the role of CAF-specific RAS-PI3K signaling in the recruitment and activity of immune cell populations. The potential of cancer immunotherapy is significant, but there is a concerning lack of mechanistic understanding of the role played by CAFs and the ECM in tumour immune cell infiltration and function. We aim to identify RAS-PI3K signaling-dependent factors essential for tumour recruitment of macrophages and also understand the role that ECM stiffness and composition plays in regulating the function of these immune populations.

3. Define the role of CAF-specific RAS-PI3K signaling during establishment, maintenance and spread of lung tumours. It is important to understand the effect of disrupting RAS-PI3K interaction in CAFs during tumour growth and metastasis formation and understand if and how this approach synergizes with chemotherapy, targeted agents and immune therapies (e.g. checkpoint inhibitors).



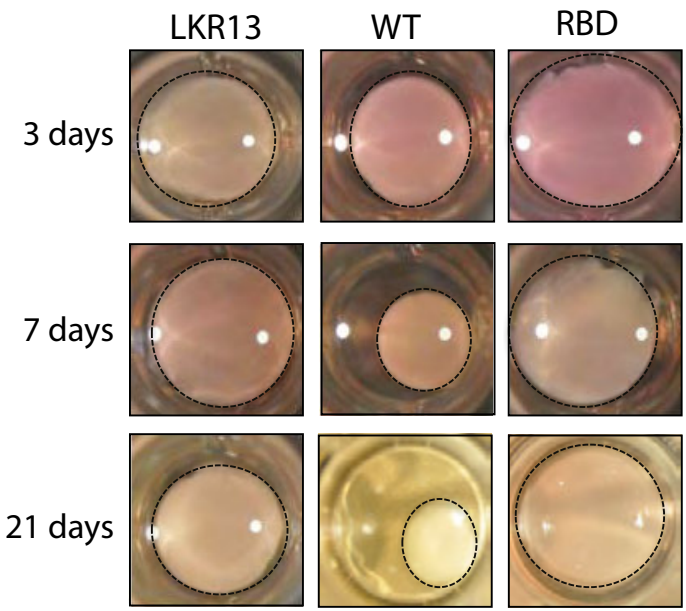
Effect of RAS signaling through PI3K during extracellular matrix (ECM) formation and remodelling. TGF-β induces formation of ECM in WT fibroblasts, increasing the deposition of new fibres, which are aligned. Disruption of RAS-PI3K in TGF-β activated fibroblasts decreases their ability to secrete new fibres, producing thinner ECM and fibres lack orientation.



RAS-PI3K signaling is necessary for the formation of a tumour stroma that sustains tumour growth and progression. Our hypothesis is that during tumour progression RAS-PI3K signaling in CAFs regulates essential molecular networks aimed at controlling their function, secretion of ECM components that increase its stiffness and recruitment of different immune cell populations. All these changes favour the formation of a reactive stroma that promotes tumour growth and spread. Targeting any of these networks has the potential to alter tumour growth and, as such, can be exploited as a new therapeutic option for the treatment of KRAS mutant lung cancer.

PUBLICATIONS

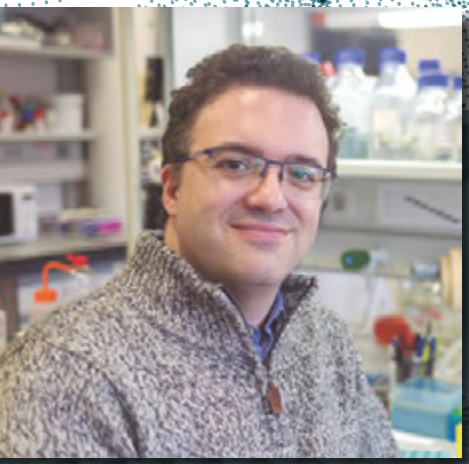
- **R-Ras2 is required for germinal center formation to aid B cells during energetically demanding processes.** *Mendoza P, Martínez-Martín N, Bovolenta ER, Reyes-Garau D, Hernansanz-Agustín P, Delgado P, Díaz-Muñoz MD, Oeste CL, Fernández-Pisonero I, Castellano E, Martínez-Ruiz A, Alonso-Lopez D, Santos E, Bustelo XR, Kurosaki T, Alarcón B.* **Sci Signal. 2018 May 29;11(532). pii: eaal1506. doi: 10.1126/scisignal.aal1506.** PMID: 29844052
  IF: 6.481 / Q1



TGF-β activated fibroblasts rely on RAS-PI3K signaling to contract collagen gels. Disruption of RAS-PI3K signaling impairs the ability of TGF-β activated fibroblasts to shrink collagen gels, as shown by the size of gel within the black dotted circles.

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Efficacy of the BTK inhibitor Acalabrutinib in a preclinical model of lung cancer	Esther Castellano	Acerta Pharma Ltd. Collaborative grant	2017-2021	250,000.00 €
Explore the therapeutic effect of Acalabrutinib (ACP-196) in combination with Stat3 inhibitor (AZD9150) in KRAS-driven lung tumour growth	Esther Castellano	Acerta Pharma Ltd. Collaborative grant	2018-2021	50,000.00 €
Actualización del equipo existente de micro-tomografía por Rayos-X para imagen in-vivo (EQC2019-006712-P)	Esther Castellano	Spanish Ministry of Science, Research & Universities	2019	105,000.00 €
Targeting RAS-PI3K signaling to re-educate the stroma of RAS mutant lung cancers (RTI2018-099161-A-I00)	Esther Castellano	Spanish Ministry of Economy and Competitiveness	2019-2022	157,000.00 €



Team Leader

Miguel Vicente Manzanares

Phone.: +34 923 294 806

E-mail: miguel.vicente@csic.es

Research Team

Predoctorals

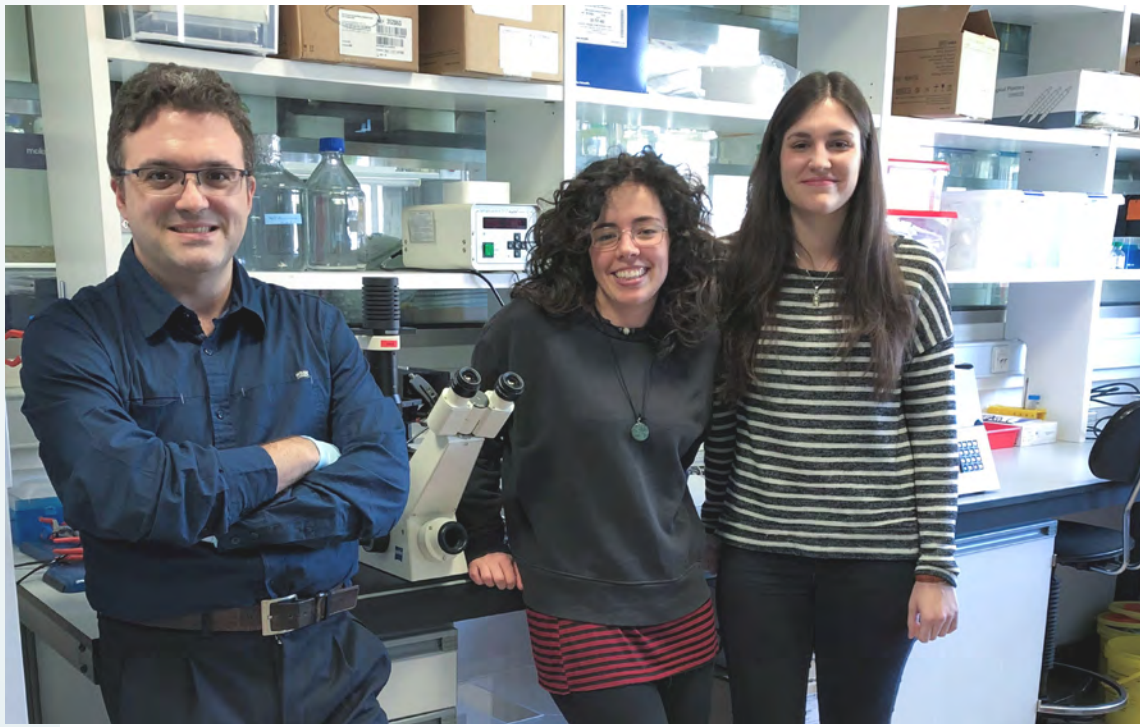
Clara Llorente González

María Millán Salanova

Master Students

Claudia Cifuentes Caballero

Víctor Coca Ruíz



LABORATORY 6

TUMOR BIOPHYSICS

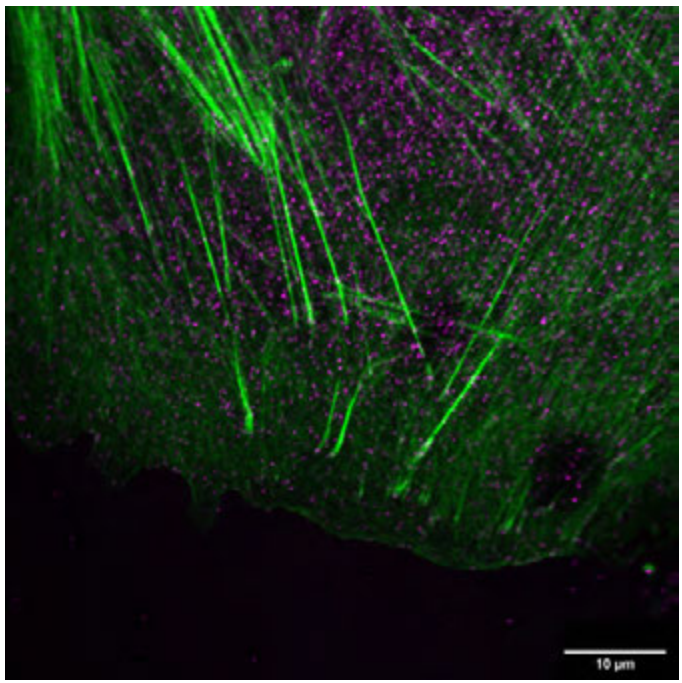
Our research aims at understanding the role of mechanics in metastasis, specifically the ability of individual metastatic cells to migrate and evade the immune response. We are characterizing the correlations between intracellular force generation, tissue mechanics, cell stemness and the ability of metastatic cells to migrate. Part of our research focuses on the identification of novel mechanisms of regulation of the function of molecular motors, which endow cells with increased migrating ability. By revealing novel mechanisms that control the detachment and migration of tumor cells from the primary tumor, we lay the foundation of the development of novel therapeutic approaches aimed at stopping tumor cell dissemination.

We have created and implemented mechanically active nanodevices with the potential to inhibit metastasis by inducing mechanical force around the tumors, a completely novel approach that is yielding valuable basic information on how tumors control their microenvironment, and at the same time allowing us to evaluate the potential of these molecules as “mechanical inhibitors” of cell dissemination.

We are also investigating the relationship between tumor mechanics and immunosuppression. We postulate that mechanical alterations during the development of the tumor niche compromise the ability of resident myeloid cells to perform their immune surveillance function by becoming unable to identify tumor cells and/or migrate to the lymph node. In this regard, we have revealed novel roles for classical molecular motors of the myosin superfamily in the activation of T cells and the establishment of transient contacts between myeloid tumor-resident immune cells and cancer cells. Also, we have identified novel cytoskeletal structures in different myeloid subpopulations and are working towards the characterization of their role in significant myeloid populations in vivo.

Finally, we are collaborating with hematology groups in and out of the CIC to reveal the role of molecular motors of the myosin superfamily in different aspects of leukemic cell biology, particularly their immunosuppressive capability, migration and proliferative abilities.

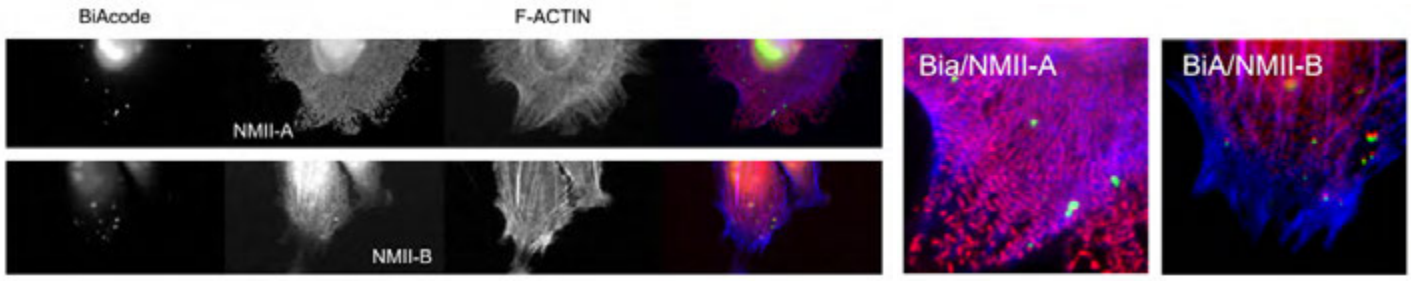
These studies combine traditional approaches, including genetic screenings and biochemistry with omics (proteomics and transcriptomics) and state-of-the-art imaging including different forms of quantitative microscopy, measurements of cell mechanics and in vivo models of tumor metastasis.



Expression of nanoactive devices (purple) in cells in which actin has been illuminated with fluorescent phalloidin (Green).

PUBLICATIONS

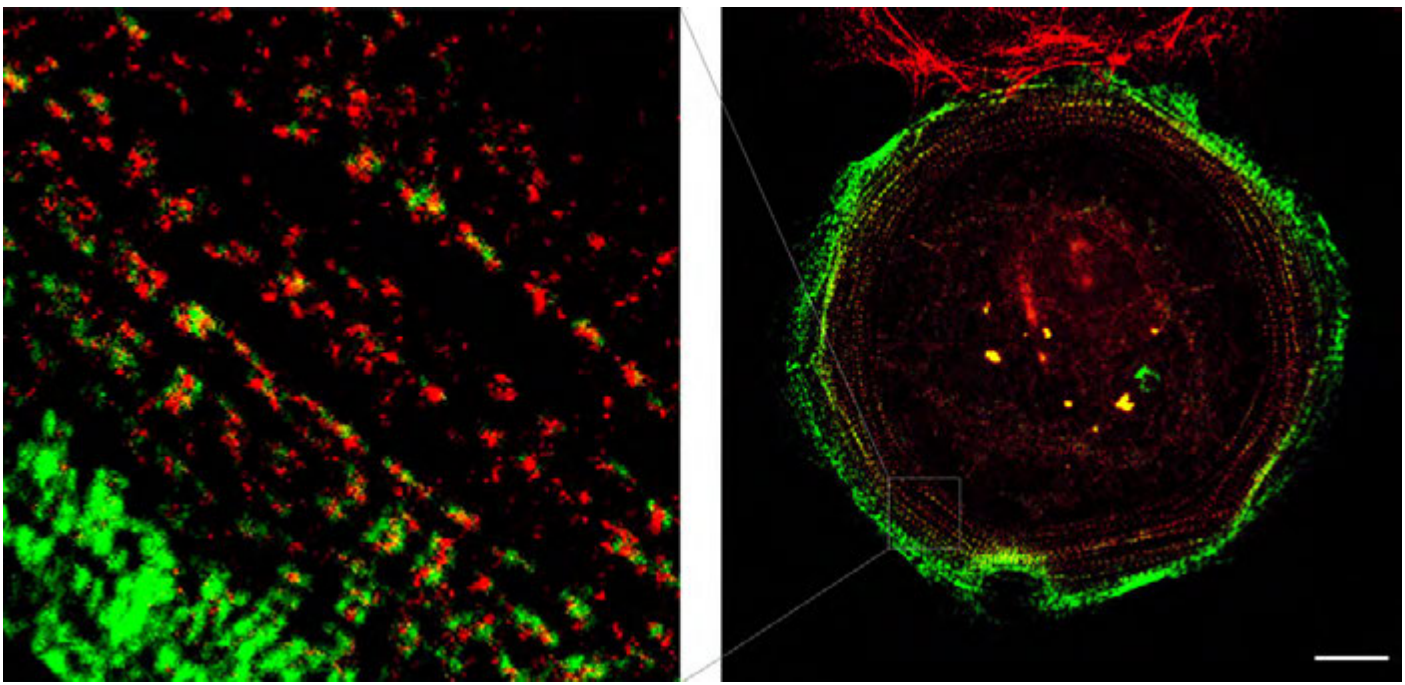
- **Priming of dendritic cells by DNA-containing extracellular vesicles from activated T cells through antigen-driven contacts.** *Torralba D, Baixauli F, Villarroya-Beltri C, Fernández-Delgado I, Latorre-Pellicer A, Acín-Pérez R, Martín-Cófreces NB, Jaso-Tamame ÁL, Iborra S, Jorge I, González-Aseguinolaza G, Garaude J, Vicente-Manzanares M, Enríquez JA, Mittelbrunn M, Sánchez-Madrid F.* **Nat Commun. 2018 Jul 9;9(1):2658. doi: 10.1038/s41467-018-05077-9.** PMID: 29985392 **IF: 11.878 / D1**
- **Targeting the integrin interactome in human disease.** *Vicente-Manzanares M, Sánchez-Madrid F.* Curr Opin Cell Biol. 2018 Jul 10;55:17-23. doi: 10.1016/j.ceb.2018.05.010. Review. PMID: 30006051 **IF: 8.233 / D1**
- **Adhesive Interactions Delineate the Topography of the Immune Synapse.** *Martín-Cófreces NB, Vicente-Manzanares M, Sánchez-Madrid F.* **Front Cell Dev Biol. 2018 Oct 30;6:149. doi: 10.3389/fcell.2018.00149. eCollection 2018. Review.** PMID: 30425987 **IF: 5.206 / Q1**
- **L-selectin expression is regulated by CXCL8-induced reactive oxygen species produced during human neutrophil rolling.** *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.* **Eur J Immunol. 2019 Mar;49(3):386-397. doi: 10.1002/eji.201847710.** PMID: 30443903 **IF: 4.695 / Q1**



Mechanoactive response of tumor cells to nanoactive devices. Nanoactive devices (in green) trigger the juxtaposition of myosin IIB (in red, bottom line and right panel in the colocalization) but not of MIIA (top line and left panel).

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Control de la heterogeneidad y evasión inmune tumoral por la mecánica tisular y la generación de fuerzas intracelulares (SAF172017-87408-R)	Miguel Vicente-Manzanares	Spanish Ministry of Economy and Competitiveness	2018-2020	205,700.00 €
Control de la evasión inmune en melanoma mediante la regulación de la miosina no muscular de clase II (201720I099)	Miguel Vicente-Manzanares	Spanish National Research Council (CSIC)	2017-2018	5,000.00 €
Modeling the role of mechanics in melanoma metastasis using Bioactive, ATP- and actin-dependent, contractile synthetic devices (BiAcode) (IDEAS18018VICE)	Miguel Vicente-Manzanares	Spanish Association against Cancer (AECC)	2018	20,000.00 €



Stimulated emission depletion (STED) nanoscopy of COS7 cells showing the asymmetric assembly of NMII-A (in green, closer to the outer region of the cell) and NMII-B (in red, closer to the most internal regions of the cell). Left panel is a magnification of the boxed region in the image on right, which represents the whole cell. Bar=10 micrometers.

Team Leader

Jesús Pérez Losada

Phone.: +34 923 294 807

E-mail: jPérezlosada@usal.es

Research Team

Postdoctorals

Javier Cañueto Álvarez

Marina Mendiburu-Eliçabe

Predoctorals

Adrián Blanco Gómez

Roberto Corchado Cobos

Julie Milena Galvis Jiménez

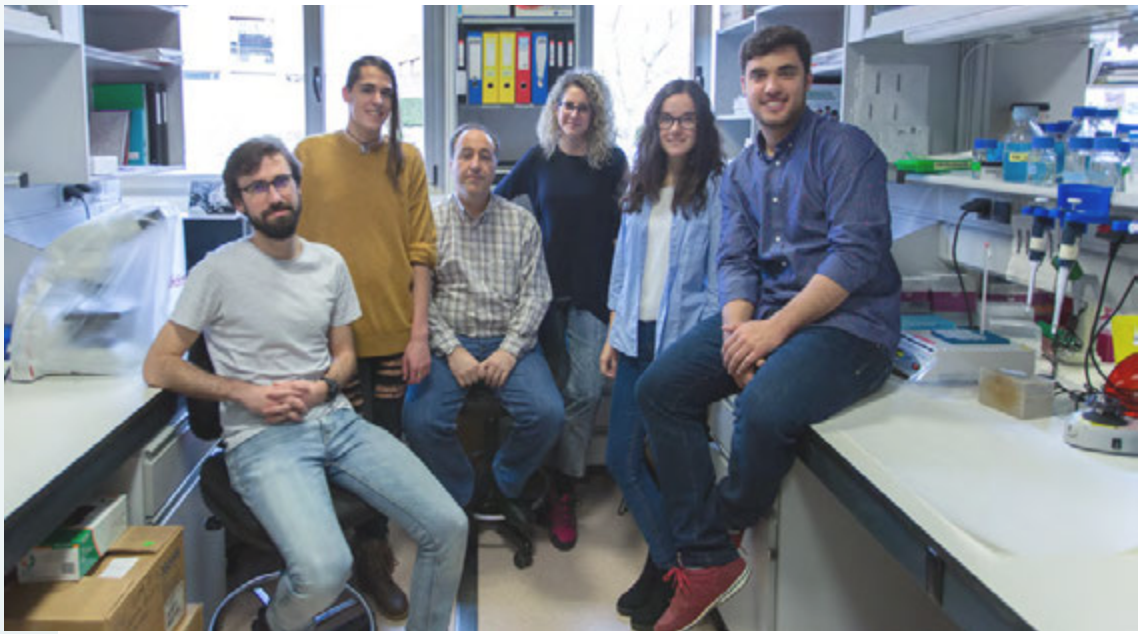
Aurora Gómez Vecino

Natalia García Sancha

Master Students

Alejandro Jiménez Navas

Tatiana Ugalde Catarinella



LABORATORY 7

MOLECULAR AND GENETIC DETERMINANTS OF CANCER SUSCEPTIBILITY, EVOLUTION AND TREATMENT RESPONSE

Cancer is a complex disease or a complex trait, such as other high-prevalence diseases such as type II diabetes, autoimmune diseases, or neurodegenerative diseases, among others. Physiological processes such as height, intelligence or aging are also complex traits. An essential aspect of cancer is the different susceptibility and evolution of the same tumor type among patients; that is, the different phenotypic presentation of the disease in a population., three aspects of cancer as a complex trait must be considered to explain this at the phenotypic, genetic and environmental levels.

(I) At the **phenotypic level**, complex traits are the result of other intermediate phenotypes or subphenotypes (a concept developed by Gottesman and Shields in 1973, in the field of Psychiatry) that are involved in their development. These subphenotypes also may be complex traits, which generates a network of subphenotypes that interact with each other, and are located at different levels: systemic, organ, tissue, cellular niche, and intracellular. The interaction between subphenotypes forms a chaotic system that can be studied from a System Biology or Systems Medicine perspective. For example, breast cancer increases its incidence with age (like many other carcinomas) and, in general, its aggressiveness is higher, the lower the age of the patient. Recently, we studied the relationship between the development of breast cancer and aging, we developed a model to define biological age in terms of oxidative stress by a machine learning strategy; and we studied the relationship between the three complex traits: breast cancer, aging and oxidative stress through a System Biology perspective (Sáez-Freire et al., 2018).

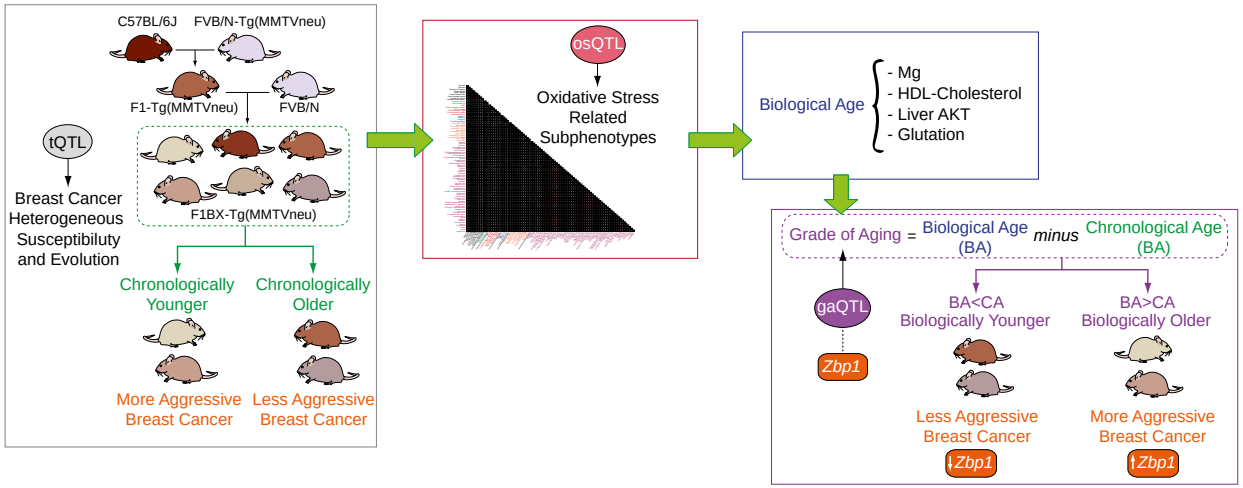
We generated by backcross a cohort of mice with different susceptibility to breast cancer that was treated with anthracyclines and taxanes. Heterogeneous response to treatment was evaluated and subphenotypes were considered at different levels: tumor signaling, metabolomics, epithelial subpopulations of the tumor (epithelial hierarchy), tumor infiltration by subpopulations of leukocytes and study of other components of stroma (fibroblasts and endothelial cells), intratumor levels of miRNAs. Quantitative trait (QTL) regions associated with treatment responses and different subphenotypes have been identified. We are identifying the DNA variants (DSVs) associated with the complex phenotype (treatment response) and associated subphenotypes.

(II) **At the genetic level**, all that subphenotypes are controlled by multiple genes, so quantitative traits are polygenic processes that follow a quantitative Genetics model. Also, it should be noted that Mendelian traits also have a polygenic component that regulates the effect of the primary gene, and that determines that, for example, patients with the same BRCA1 mutation within the same family have different evolutions. When attempting to identify these susceptibility polygenes to a complex genesis disease, such as cancer, the genes identified only account for 30% or less of the phenotypic variability due to Genetics (heritability); this ▸

▸ phenomenon is known as “missing heritability” (that is the expected heritability minus the heritability explained). We postulated that some of the missing heritability would be defined by polygenes associated with intermediate phenotypes that cannot be detected at the level of the complex considering this, we identified new genetic markers of susceptibility to cardiotoxicity due to anthracyclines in breast cancer patients (submitted article); and the response to the treatment of breast cancer by anthracyclines and taxanes (work in preparation).

As a global strategy, we propose that the integration of the heritability of different intermediate phenotypes, whose DSVs have been identified by RNA-Seq, carried out on mice generated by crossovers of non-genic strains (intercross or backcross). Following integration into multivariate statistical models will allow the identification of an essential part of the missing heritability of complex diseases. This, in turn, will allow a better understanding of the pathogenesis of these diseases and the identification of new genetic variants that can influence the risk, prognosis and response to treatment; therefore, moving towards the possibility of more personalized medicine. In this context, we are also interested in deepening the prognostic factors of squamous skin cancer, as a prototype of carcinoma.

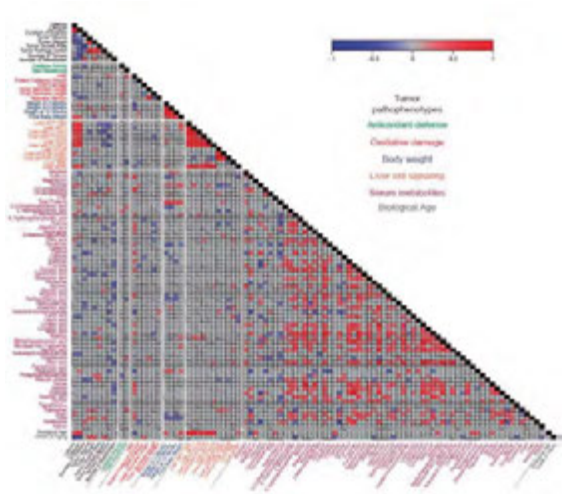
(III) **Environmental influences** in complex traits are significant so if there is some genetic susceptibility to develop a type of cancer, without the environmental influence, do not appear. In the case of cancer, the environment is also essential as a source of mutagens. Also, the environment throughout evolution has been key to modeling the development of the different subphenotypes that control a complex trait and the interaction between them. Thus, the two significant evolutionary pressures have been infections and famines. Therefore, a phenotype can be positive for surviving in early life, but it may not be favorable for surviving in later stages of life (antagonistic pleiotropy). ▸



The incidence of breast cancer increases with age until menopause, and breast cancer is more aggressive in younger women. The existence of epidemiological links between breast cancer and aging indicates that both processes share some common mechanisms of development. Oxidative stress is associated with both cancer susceptibility and aging. Here we observed that ERBB2-positive breast cancer, which developed in genetically heterogeneous ERBB2-positive transgenic mice generated by a backcross, is more aggressive in younger than in older mice, similar to what occurs in humans. In this cohort, we estimated the oxidative biological age using a mathematical model that integrated several subphenotypes directly or indirectly related to oxidative stress. The model selected the serum levels of HDL-cholesterol and magnesium and total AKT1 and glutathione concentrations in the liver. The grade of aging was calculated as the difference between the predicted biological age and the chronological age. This comparison permitted the identification of biologically younger and older mice compared with their chronological age. Interestingly, biologically older mice developed more aggressive breast cancer than the biologically younger mice. Genomic regions on chromosomes 2 and 15 linked to the grade of oxidative aging were identified. The levels of expression of Zbp1 located on chromosome 2, a gene related to necroptosis and inflammation, positively correlated with the grade of aging and tumour aggressiveness. Moreover, the pattern of gene expression of genes linked to the inflammation and the response to infection pathways was enriched in the livers of biologically old mice. This study shows part of the complex interactions between breast cancer and aging (Sáez-Freire et al., FRBM 2018).

So prevalence and the relationship between subphenotypes and diseases that form the diseasome, or between processes such as the high prevalence of breast cancer in humans, should be seen from an Evolutionary Medicine perspective. As Theodosius Dobzhansky said, "Nothing in Biology makes sense except in the light of evolution." Concerning breast cancer, for example, throughout the evolution, the pregnancy was generally early and repeated; only in the Western world in the last 50-70 years pregnancy is often late and unique. This fact, coupled with increased life expectancy, has led to an increase in the incidence of breast cancer.

We think it is possible to use associations between complex phenotypes to try to generate new prevention strategies, in this case, against breast cancer. Previously, we have shown that deficiency in Snai2 produces an effect on postlactational involution and an increase in tumor susceptibility (Castillo-Lluva et al., Oncogene 2015). Also, we have shown that Snai2 deficiency in stromal results in lower aggressiveness of ERBB2+ breast cancer in mice and patients (Blanco-Gómez et al., submitted). One of our current main lines of work is to design breast cancer prevention strategies by modifying post-lactational drug involution (SAF2017 Project). Current prevention strategies have significant side effects and cannot be applied to most of the population; new approaches are needed for fewer side effects of reducing the incidence of breast cancer.



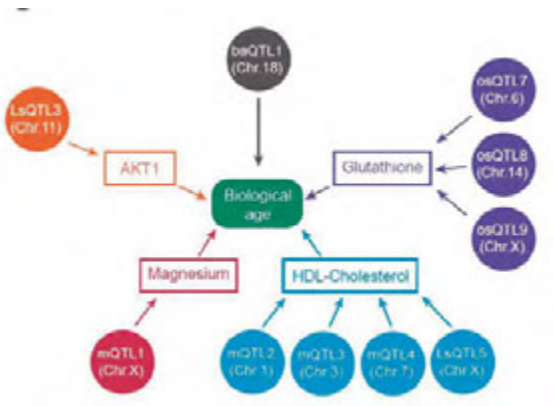
Statistically significant associations between pathophenotypes and different subphenotypes related to oxidative stress. Only statistically significant associations were included. The red colour indicates a positive correlation and the blue colour indicates a negative correlation (Sáez-Freire et al., FRBM 2018).

PUBLICATIONS

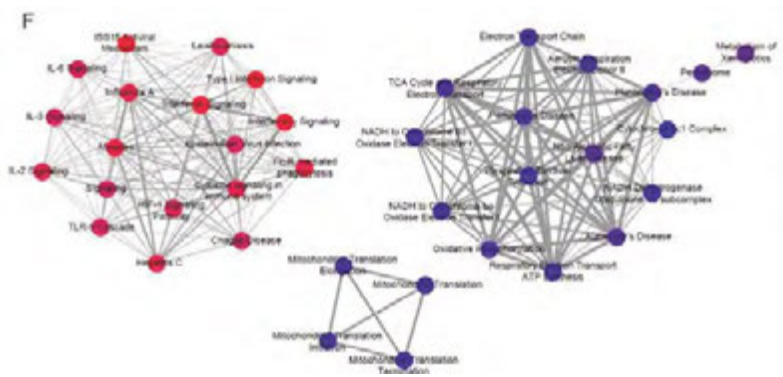
- **FBXW7 deletion contributes to lung tumor development and confers resistance to gefitinib therapy.** *Xiao Y, Yin C, Wang Y, Lv H, Wang W, Huang Y, Perez-Losada J, Snijders AM, Mao JH, Zhang P.* **Mol Oncol. 2018 Jun;12(6):883-895. doi: 10.1002/1878-0261.12200.** PMID: 29633504 **IF: 5.962 / D1**
- **Rapid growth rate is associated with poor prognosis in cutaneous squamous cell carcinoma.** *Cañueto J, Martín-Vallejo J, Cardeñoso-Álvarez E, Fernández-López E, Pérez-Losada J, Román-Curto* **C. Clin Exp Dermatol. 2018 Dec;43(8):876-882. doi: 10.1111/ced.13570.** PMID: 29756221 **IF: 1.771 / Q3**
- **Supplementary data for the biological age linked to oxidative stress modifies breast cancer aggressiveness.** *Sáez-Freire MDM, Blanco-Gómez A, Castillo-Lluva S, Gómez-Vecino A, Galvis-Jiménez JM, Martín-Seisdedos C, Isidoro-García M, Hontecillas-Prieto L, García-Cenador MB, García-Criado FJ, Patino-Alonso MC, Galindo-Villardón P, Mao JH, Prieto C, Castellanos-Martín A, Kaderali L, Pérez-Losada J.* **Data Brief. 2018 Apr 3;18:1172-1184. doi: 10.1016/j.dib.2018.03.132. eCollection 2018 Jun.** PMID: 29900291 **IF: NI**
- **Comparing the eighth and the seventh editions of the ajcc staging system and the brigham and women's hospital alternative staging system for cutaneous squamous cell carcinoma: implications for clinical practice.** *Cañueto J, Burguillo J, Moyano-Bueno D, Viñolas-Cuadros A, Conde-Ferreirós A, Corchete-Sánchez LA, Pérez-Losada J, Román-Curto C.* **J Am Acad Dermatol. 2018 Jul 9. pii: S0190-9622(18)32219-9. doi: 10.1016/j.jaad.2018.06.060.** PMID: 30003984 **IF: 7.102 / D1**
- **Implementation of staging systems in clinical practice for cutaneous squamous cell carcinoma.** *Cañueto J.* **Ann Transl Med. 2019 Mar;7(Suppl 1):S51. doi: 10.21037/atm.2019.03.13.** PMID: 31032330 **IF: 3.689 / Q4**
- **MicroRNA Dysregulation in Cutaneous Squamous Cell Carcinoma.** *García-Sancha N, Corchado-Cobos R, Pérez-Losada J, Cañueto J.* **Int J Mol Sci. 2019 May 2;20(9). pii: E2181. doi: 10.3390/ijms20092181. Review.** PMID: 31052530 **IF: 4.183 / D1**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Estrategias farmacológicas de prevención del cáncer de mama mediante modificación de la involución postlactancia (SAF2017-88854-R)	Jesús Pérez-Losada	Spanish Ministry of Economy & Competitiveness	2018-2020	169,400.00 €
Nuevas aproximaciones terapéuticas para la prevención de la leucemia aguda infantil (CSI234P18)	Isidro Sánchez García (UIC17) (Collaborator: Jesús Pérez Losada)	Ministry of Education. Regional Government of Castilla and León.	2018-2021	120,000.00 €
Identificación de marcadores pronósticos en el carcinoma epidermoide cutáneo y comparación de su expresión en el tumor primario y la metástasis (GRS 1835/A/18)	Javier Cañueto Álvarez.	Regional Health Management. Regional Government of Castilla and León	2019	19,101.00 €



Genetic markers linked to biological age. Scheme showing the oxidative stress subphenotypes that define the biological age and the QTLs linked to them (Sáez-Freire et al., FRBM 2018).



The network shows the enriched pathways in biologically old mice (red nodes) and in biologically young mice (blue nodes). The color intensity of each node is proportional to the mean of the running enrichment score (ES) of the genes of that pathway, reflecting the degree to which the expression of these genes is overrepresented in the liver samples. The thickness of the connections is proportional to the number of enriched genes common among the pathways (Sáez-Freire et al., FRBM 2018).

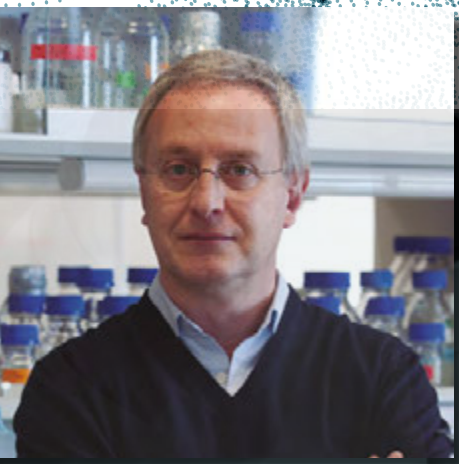
OTHER ACTIVITIES & RELEVANT FACTS

INVITED TALK

- 42nd Congress of the Spanish Society of Biochemistry and Molecular Biology (SEBBM), 16-19th July 2019. Madrid. Working Group Meeting: Computational Molecular Biology and Bioinformatics plus Genomics and Proteomics. Title: "Quantitative Trait Loci and molecular Subphenotypes linked to cardiotoxicity susceptibility due to chemotherapy by anthracyclines".

CONGRES

- X Simposium Bases Biológicas del Cáncer y Terapias Personalizadas. Universidad de Salamanca. Salamanca, Castilla y León, España. Poster Title: "Studies of the mechanisms mediating the protective effect of pregnancy against breast cancer." Authors: *Adrián Blanco-Gómez; Natalia García-Sancha, Roberto Corchado-Cobos, Aurora Gómez-Vecino, Milena Galvis-Jiménez, Marina Holgado-Madruga, María Begoña García-Cenador, Francisco Javier García-Criado, Isabel Ramos Fernández, Jesús Pérez Losada*.
- X Simposium Bases Biológicas del Cáncer y Terapias Personalizadas. Universidad de Salamanca. Salamanca, Castilla y León, España. Poster Title: "Definition of cardiac damage susceptibility due to anthracyclines and taxanes by intermediate phenotypes". Authors: *Roberto Corchado Cobos; Aurora Gómez Vecino; Adrián Blanco Gómez; Julie Milena Galvis Jiménez; Susana Fraile Martín; Natalia García Sancha; Telmo Rodrigues Teixeira; Carmen García Macías; Pedro Luis Sánchez Fernández; Jesús Pérez Losada.*
- 5th Symposium on Biomedical Research Advances and Perspectives In Pharmacology, Drug Toxicity and Pharmacogenetics. CSIC, Universidad Autónoma de Madrid.Madrid, Comunidad de Madrid, España. Communication Title: "Identification of genetic and molecular determinants associated with cardiotoxicity by anthracyclines and taxanes according to age". Authors: *Roberto Corchado Cobos; Aurora Gómez Vecino; Adrián Blanco Gómez; Julie Milena Galvis Jiménez; Susana Fraile Martín; Natalia García Sancha; Telmo Rodrigues Teixeira; Carmen García Macías; Pedro Luis Sánchez Fernández; Jesús Pérez Losada.*
- XI Simposium Bases Biológicas del Cáncer y Terapias Personalizadas. Universidad de Salamanca. Salamanca, Castilla y León, España. Poster Title: "Pharmacological treatment to potentiate the protective effect of pregnancy against breast cancer". Authors: *Natalia García-Sancha, Roberto Corchado-Cobos, Aurora Gómez-Vecino, María Begoña García-Cenador, Francisco Javier García Criado, Marina Jiménez-Ruiz, Isabel Ramos-Fernández, Marina Holgado-Madruga, Adrián Blanco-Gómez, Jesús Pérez-Losada.*
- XI Simposium Bases Biológicas del Cáncer y Terapias Personalizadas. Universidad de Salamanca. Salamanca, Castilla y León, España. Poster Title: "Estudio del valor pronóstico de los miRNAs en la evolución y respuesta a la quimioterapia del cáncer de mama" Authors: *Julie Milena Galvis-Jiménez, Adrián Blanco-Gómez, Roberto Corchado-Cobos, Natalia García-Sancha, Aurora Gómez-Vecino, Tania Luis-García, Marina Mendiburu-Eliçabe, Diego Alongo López, Carlos Prieto, Javier de las Rivas, Marina Holgado Madruga, Jesús Pérez-Losada.*
- LX Congreso Nacional de la Sociedad Española de Hematología y Hemoterapia (SEHH) y XXXIV Congreso Nacional de la Sociedad Española de Trombosis y Hemostasia (SETH). Granada 8. Communication Title: "Generación de un modelo murino knock-in mediante CRISPR/Cas9 portador de una variante germinal en RUNX1 identificada en pacientes con trastorno plaquetario congénito." Authors: *Marín-Quílez A, García-Tuñón, Hernández-Cano L, Gutiérrez-Herrero S, Méndez-Sánchez L, Herrero-García M, Montaño-Brioso A, Alonso-Pérez V, González S, Rodríguez I, Palma-Barqueros V, Pérez-Losada J, Benito R, Lozano ML, Rivera J, Sánchez-Martín M, Guerrero C, Hernández-Rivas JM, González-Porras JR, Bastida JM*
- 42nd Congress of the Spanish Society of Biochemistry and Molecular Biology (SEBBM).16-19th July 2019. Madrid. Spain. Poster Title: "Definition of cardiotoxicity due to anthracyclines from a systems biology perspective". Authors: *Roberto Corchado-Cobos, Aurora Gómez-Vecino, Adrián Blanco-Gómez, Natalia García-Sancha, Ana Martín-García, Guillermo Macías de Plasencia, Carlos Prieto, Milena Galvis-Jiménez, Asunción García-Sánchez, María Isidoro-García, María Begoña García-Cenador, Francisco Javier García-Criado, Manuel Fuentes, Juan Luis García, Marina Holgado-Madruga, Pedro L Sánchez, Jesús Pérez-Losada*.
- LXI Congreso Nacional de la Sociedad Española de Hematología y Hemoterapia (SEHH) y XXXV Congreso Nacional de la Sociedad Española de Trombosis y Hemostasia (SETH). Valencia Communication Title: "La variante L56S en RUNX1 se relaciona con leve alteración de la función plaquetaria en un modelo de ratón generado por CRISPR/CAS9. Authors: *Marín-Quílez A, Fernández-Infante C, Hernández-Cano L, García-Tuñón I, Méndez-Sánchez L, Herrero-García M, Ordoñez JL, González-Briones S, Palma-Barqueros V, Martín-Izquierdo M, Quijada-Álamo M, Pérez-Losada J, Lozano ML, Rivera J, Sánchez-Martín M, Guerrero C, Benito R·Hernández-Rivas JM, González-Porras JR, Bastida JM.*



Team Leader

Andrés Avelino Bueno Núñez

Phone.: +34 923 294 805

E-mail: abn@usal.es

Research Team

Senior Researcher (Co-PI)

María Sacristán Martín

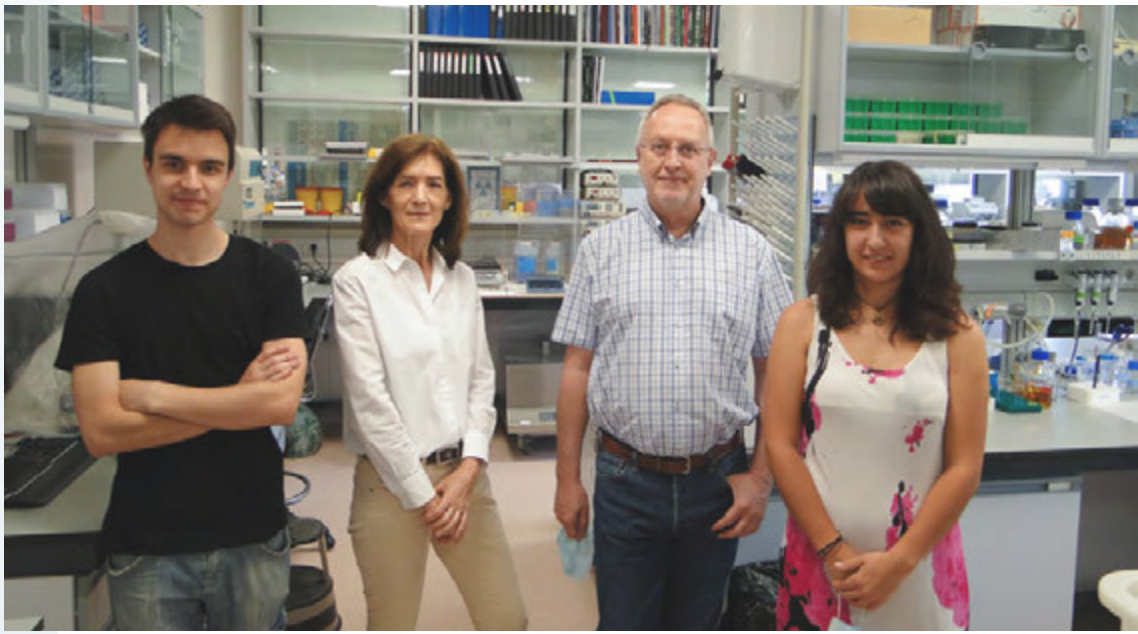
Predoctorals

Vanesa Álvarez Álvarez

Javier Zamarreño Lozano

Master Student

Ana Ordiales Talavero



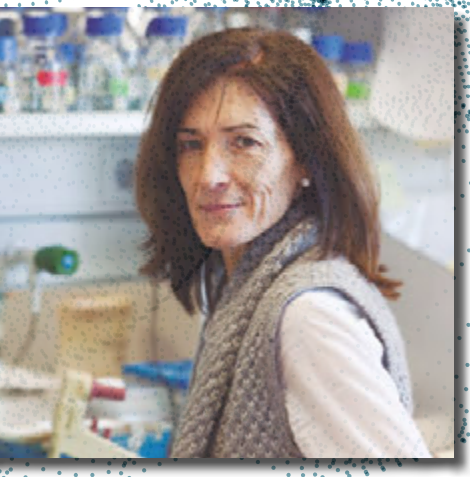
LABORATORY 8

REVERSIBLE PROCESSES IN CELL CYCLE CONTROL

The genome must be completely and faithfully replicated during S-phase before it is segregated into the progeny to ensure genomic stability. Cells are constantly exposed to the threat of endogenous and exogenous DNA damage, a major source of genomic instability and, in multicellular organisms, a driving force for cancer. Cells are particularly sensitive to damage during DNA replication because the stringent nature of replicative DNA polymerases cannot accommodate damaged bases and, consequently, DNA synthesis is blocked with potential deleterious effects. To cope with base damage during DNA replication all three domains of life have evolved damage tolerance mechanisms that allow them to circumvent DNA lesions allegedly to ensure coordinated and timely progression of replication forks. Tolerance to DNA damage is based on translesion DNA synthesis (TLS), a bypass mechanism that allows cells to overcome the potentially lethal effects of confronting DNA base lesions that impede progression of replicative DNA polymerases. DNA Damage Tolerance, or DDT, has been misleadingly known as a post-replication repair mechanism. However, DDT is not a repair tool as DNA lesions are only circumvented as a consequence of using DNA templates containing damaged bases.

The identification of specialized, evolutionary conserved but alternative DNA polymerases with the ability to use damaged templates and effectively bypass lesions, was a landmark discovery indicating the existence of a mechanism to tolerate DNA damage. These enzymes, termed TLS DNA polymerases, are potentially mutagenic as they accommodate templates with bulky lesions, lack proofreading activity, are low-fidelity and, therefore, error-prone. A second mechanism of DDT exists, which is based on template switching (TS), an error-free mechanism that involves sister-strand pairing. TS was first described in prokaryotes as an error-free post-replicative repair mechanism involved in filling-in gaps left behind replication forks. TS plays a not yet fully understood role in replication all throughout the evolutive scale.

The proliferating cell nuclear antigen (PCNA) has a central role in DNA replication. Moreover, it also constitutes a central DNA scaffold for the recruitment of a plethora of components involved in both tolerance and response to DNA damage mechanisms. In eukaryotes, DDT mechanisms are mediated by ubiquitylation of this essential replication factor PCNA, a key processivity factor for polymerases during DNA synthesis. Monoubiquitylation of Lys164 of PCNA (ubPCNA^{K164}) promotes TLS-mediated error-prone translesion synthesis. Further Lys^{63}-linked polyubiquitylation of mono-ubPCNA^{K164} triggers the error-free mechanism based on TS. The prevailing view is that PCNA^{K164} is ubiquitylated in a DNA damage-dependent ▸

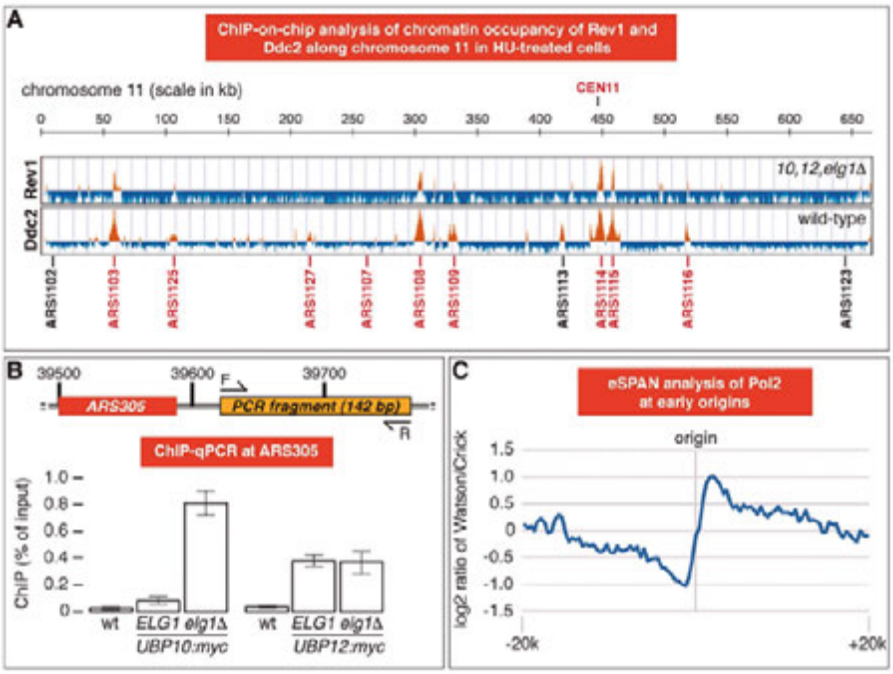


María Sacristán Martín

Phone: +34 923 294 805
E-mail: msacristan@usal.es

manner. Therefore, it is believed that not such modification (ubPCNA^{K164}) occurs in cells during unchallenged S-phase in most organisms except in fission yeast and Xenopus.

Although the evolutionary conserved mechanism of PCNA ubiquitylation is well understood, the deubiquitylation of ubPCNA remains uncharacterized. Our group is interested in understanding the role and, therefore, the biological significance of ubPCNA deubiquitylation in yeast models. Our working hypothesis is that Ubiquitin-specific proteases, or PCNA-DUBs, revert PCNA ubiquitylation to prevent excessive translesion synthesis (TLS) on replicating chromatin. This hypothesis predicts that both branches of the DNA damage tolerance pathway, TLS-DNA polymerases sampling on replicating DNA and template switching during S-phase, would be limited at forks by PCNA deubiquitylation.



Genome-wide analysis by chromatin immunoprecipitation of key components of DNA damage tolerance pathways. (A) ChIP-on-chip analysis of *REV1-myc ubp10Δ ubp12Δ elg1Δ* (*10, 12, elg1Δ*) and *REV1-myc* (wild-type) cells pre-synchronized with α-factor and released for 1 hour in presence of 0.2 M HU. Orange histogram bars in the Y-axis show the average signal ratio of loci significantly enriched in each immunoprecipitated fraction in $\log_2$ scale. The X-axis shows chromosomal coordinated in kilobases along regions in chromosome XI Early-firing (in red) and late/dormant (in black) replication origins are indicated. (B) Deletion of *ELG1* influences Ubp10, but not Ubp12, association to *ARS305*. The indicated cells were cultured as in (A) and processed for ChIP-qPCR. Means and standard deviations of three independent experiments are shown. A schematic of the *ARS305*-proximal DNA fragment amplified is provided. (C) Strand-specific test analysis of the catalytic subunit of DNA polymerase epsilon (*POL2*) made in collaboration with Rodrigo Bermejo group.

RESEARCH AIMS

Given the tremendous impact that PCNA-DUBs ubiquitin-proteases may have in genomic stability, the major aim of our research group is to understand in depth the replication fork-coupled mechanism down-regulating DDT events through PCNA deubiquitylation.

Despite recent progress in the DNA damage tolerance field, a number of important questions remain open. We want to address what we consider the most appealing questions in the field to gain a clear understanding of what is in full the role of PCNA-DUBs at sites of nascent DNA. Particularly, we want to address the following questions:

1. Is the control of DDT at replication forks asymmetric and, consequently, divergent in leading and lagging strands?
2. Is leading strand DNA synthesis at forks permissive for the error-prone branch of DDT?
3. What is the molecular nature of the template switching events at forks prevented by PCNA-DUBs?

GOALS ACHIEVED

1. Smooth and timely progression through S-phase in eukaryotic models requires $PCNA^{K164}$ deubiquitylation.

2. Ubp10 and Ubp12 budding yeast ubiquitin proteases remove ubiquitin from $PCNA^{K164}$ with discrete chain preferences.

3. Replication fork association of Ubp10, but not Ubp12, depends on PCNA binding to lagging strands.

4. PCNA-DUBs Ubp10 and Ubp12 counteract template-switching events and Rev1, a key translesion synthesis adaptor, binding to replication forks.

FUTURE GOALS

I. Analysis of additional ubiquitin-proteases involved in PCNA deubiquitylation.

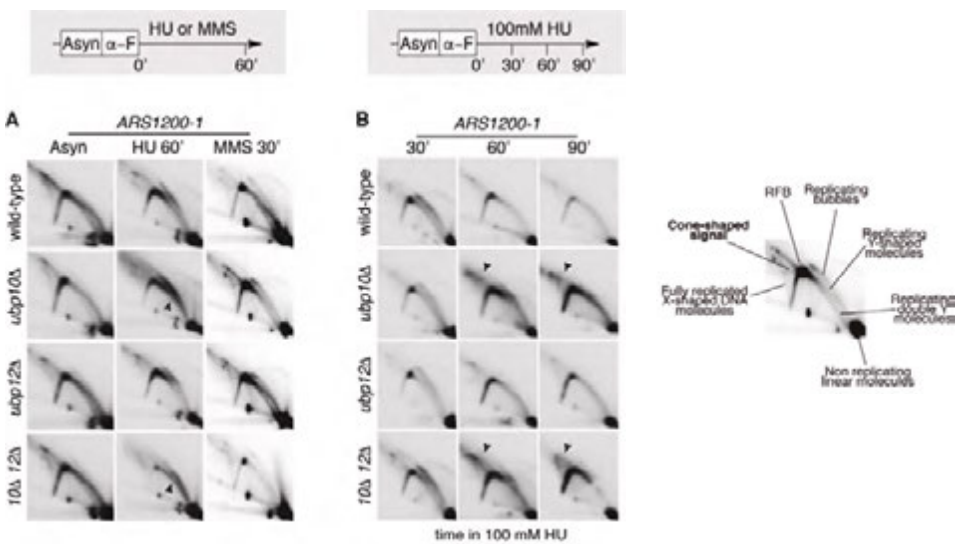
II. Testing asymmetry in DNA Damage Tolerance regulation at replication forks.

III. Analysis of non-canonical small Y-shaped replication intermediates accumulating at stalled forks in *ubp10* and *ubp10 ubp12* mutants.

SPECIFIC OBJECTIVES

a) *Testing interactions in vivo of PCNA-DUBs with replisome components.*

The goal is to identify the interactome of PCNA-DUBs at active replication forks using the isolation of proteins on nascent DNA (iPOND)-method coupled with mass spectrometry. We will validate that PCNA-DUBs are Replisome components during normal and perturbed S-phase. Identifying proteins that interact with PCNA-DUBs and their posttranslational modifications is an additional key element to understanding how the genome is replicated every cell division cycle. ▸



Analysis of replication intermediates by 2D-gel electrophoresis. (A) Wild-type, *ubp10*Δ, *ubp12*Δ and *ubp10*Δ *ubp12*Δ cells were synchronized with α-factor and released in the presence of 200mM HU or 0.033% MMS. Samples were taken after 60 minutes and processed for 2D-gel analysis. Membranes were hybridized to a probe spanning *ARS1200-1* replication origin. (B) Wild-type, *ubp10*Δ, *ubp12*Δ and *ubp10*Δ *ubp12*Δ cells were synchronized with α-factor and released in the presence of 100mM HU. Samples were taken at indicated intervals and processed for 2D-gel analysis. Membranes were hybridized to a probe spanning *ARS1200-1* replication origin. A Schematic of canonical replication intermediates and fully replicated joint molecules detected by 2D-gel analysis at *ARS1200* is shown. Canonical small-Ys (black arrow in A) reflect passive replication by forks emanating outside the probed fragment. Con-shaped non-canonical intermediates in B are pointed by and arrow.

▸ One effective experimental approach to systematically analyse the components, as well as their modifications, of the replisome progression complex is the iPOND method. The purification and identification by mass spectrometry of proteins on newly synthesized DNA using iPOND will allow us to extend the study of the potential temporal association of PCNA-DUBs with replication forks and also to confirm that they are functional components of the replisome as we hypothesized.

b) *eSPAN asymmetry test for PCNA-DUBs and TLS-polymerases.*

eSPAN is a strand-specific analysis based on the enrichment and Sequencing of Protein-Associated to Nascent DNA. eSPAN measures the relative amounts of proteins at nascent leading and lagging strands of DNA replication forks in a step-wise procedure involving chromatin immunoprecipitation of a protein of interest (bait) followed by the enrichment of protein-associated nascent DNA through BrdU immunoprecipitation. The key part is that the isolated ssDNA is then subjected to strand-specific sequencing allowing detection of proteins enriched at leading or lagging strand of nascent DNA. We plan to test asymmetry of PCNA-DUBs and TLS DNA-polymerases at forks by a strand-specific analysis based on eSPAN.

MITOTIC CDC14 PHOSPHATASES IN THE REGULATION OF THE CELL DIVISION CYCLE

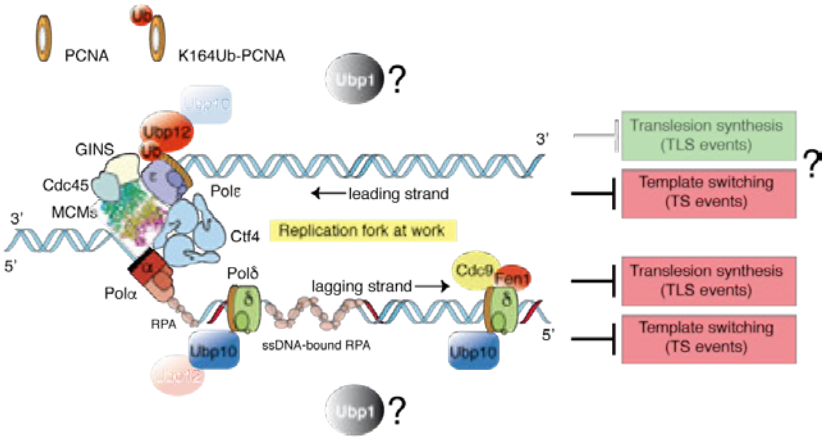
Our group is interested in understanding the mechanisms by which cell division and cell proliferation are regulated to maintaining genomic stability. During the last few years we focused also on the study of the functional relevance of cell cycle regulators in mammalian cells.

Among the different stages of the cell division cycle, mitosis concentrates significant attention. This is because many mitotic proteins have been linked to tumorigenesis and they also constitute the targets of different cancer chemotherapies. Many enzymatic activities are required for mitosis, among which kinases and phosphatases are highlighted.

Cdc14 phosphatase is an essential protein in budding yeast as it removes phosphorylation residues resulting from the activity of the mitotic regulator Cdc28/Cdk1 at the end of mitosis. In the past, our group reported the characterization of the Cdc14 ortholog in fission yeast, Flp1/Clp1, (Cueille et al., J Cell Sci 2001) and its relevance in cellular processes such as the regulation of mitotic progression andcytokinesis (Esteban et al., J Cell Sci 2004; Esteban et al., Cell Cycle 2008) and the checkpoint activation in response to replicative stress (Díaz-Cuervo et al., Mol Biol Cell. 2008). Moreover, data from our work on mitotic regulators led to contribute to the characterization of human Cdc14 orthologs, Cdc14A and Cdc14B (Vázquez-Novelle et al., J Biol Chem. 2005) and to the identification of human Cdc14A as a new cell cycle gene in controlling Cdk1 activity at the entry into mitosis (Sacristán et al., Cell Cycle 2011). We reported that depletion of Cdc14A leads to a premature G2/M transition with potential consequences in chromosome segregation and genomic instability. Cdc14A phosphatase regulates Cdk1/CyclinB1 complexes through direct dephosphorylation of their both positive and negative regulators, the Cdc25A and Cdc25B phosphatases, and the Wee1 kinase, respectively (Esteban et al., Cell Cycle 2006; Vázquez-Novelle et al., J Biol Chem. 2010; Ovejero et al., Mol Biol Cell. 2012).

Our recent work has characterized some of the mechanisms that regulate Cdc14A activity at the entry into mitosis. Our experimental data point out differences in the regulatory mechanisms of these proteins in the different orthologs. Thus, we have demonstrated that, unlike in yeast, Cdc14A is phosphorylated by Cdk1/CyclinB1 complexes at specific residues not to regulate its catalytic activity, but to modulate the binding with specific substrates in early mitosis (Ovejero et al., Sci Rep. 2018).

Our interest in deciphering the mechanisms regulating the cell division cycle, leads us to collaborate with research groups that share the same objective. MASTL/Greatwall is an essential mitotic kinase recently identified. Its activity, together with that of Cdk1, is required to properly progress through mitosis. MASTL/Greatwall indirectly controls PP2A-B55, a phosphatase that counterbalances Cdk1/Cyclin B1 activity during mitosis, through direct phosphorylation of ARP19 and ENSA, turning them into potent PP2AB55 inhibitors. Recent work identified the relevance of ARP19 in the regulation of mitosis and early embryonic development, while ENSA is more involved in S-phase progression (Hached et al., J Cell Biol 2019).



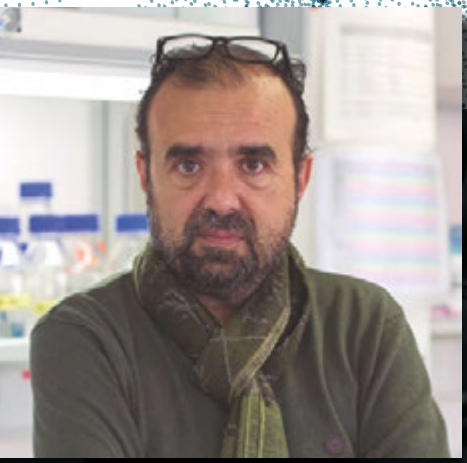
Working model for DNA Damage Tolerance suppression at replication forks through PCNA deubiquitylation. Budding yeast ubiquitin proteases (Ubp) differentially cooperate in PCNA deubiquitylation when associated to replication forks likely as functional components of the replisome. These ubiquitin proteases downregulate in situ translesion DNA polymerases recruitment and template switch events engaging nascent strands, revealing that PCNA deubiquitylation is a key mechanism for modulation of lesion bypass during replication at forks, thus, to facilitate a processive replication of chromosomal DNA (Álvarez et al., 2019 Cell Reports). The leading strand may be permissive for the errorprone (TLS) branch of DDT. Ubp10 interacts with Fen1 and Cdc9, key components of the maturation of Okazaki fragments. The relative contribution of Ubp1 to DDT regulation and interaction with replication forks is currently under study.

PUBLICATIONS

- **Biochemical analyses reveal amino acid residues critical for cell cycle-dependent phosphorylation of human Cdc14A phosphatase by cyclin-dependent kinase 1**. *Ovejero S, Ayala P, Malumbres M, Pimentel-Muiños FX, Bueno, A, Sacristán, MP*. **Sci. Rep. 2018 Aug 8;8(1):11871. doi: 10.1038/s41598-018-30253-8.** PMID: 30089874 **IF: 4,011 / Q1**
- **ENSA and ARPP19 differentially control cell cycle progression and development.** *Hached K, Goguet P, Charrasse S, Vigneron S, Sacristan MP, Lorca T, Castro A.* **J Cell Biol. 2019 Feb 4;218(2):541-558. doi: 10.1083/jcb.201708105.** PMID: 30626720 **IF: 8.891 / D1**
- **Disruption of the Caenorhabditis elegans Integrator complex triggers a non-conventional transcriptional mechanism beyond snRNA genes.** *Gómez-Orte E, Sáenz-Narciso B, Zheleva A, Ezcurra B, de Toro M, López R, Gastaca I, Nilsen H, Sacristán MP, Schnabel R, Cabello J.* **PLoS Genet. 2019 Feb 26;15(2):e1007981. doi: 10.1371/journal.pgen.1007981. eCollection 2019 Feb.** PMID: 30807579 **IF: 5.224 / D1**
- **PCNA Deubiquitylases Control DNA Damage Bypass at Replication Forks.** Álvarez, V., *Frattini, C., Sacristán, M., Gallego-Sánchez, A., Bermejo, R. and Bueno, A.* **Cell Reports 2019 29: 1323-1335. doi: 10.1016/j.celrep.2019.09.054** PMID: 31665643 **IF: 7.815 / D1**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Reversible processes in cell cycle control: PCNA ubiquitylation and protein phosphorylation in response to DNA damage (BFU2015-69709-P)	Avelino Bueno / María Sacristán	Spanish Ministry of Economy & Competitiveness	2016-2019	142,296.00 €
Autofagia en cáncer y en enfermedades inflamatorias (SA042P17)	Avelino Bueno	Regional Government of Castilla and León	2017-2019	120,000.00 €



Team Leader

Alberto Martín Pendás

Phone.: +34 923 294 809

E-mail: amp@usal.es

Research Team

Senior Researcher

Elena Llano Cuadra

Postdoctoral

Paloma Duque Álvarez

Predoctorals

Laura Gómez Hernández

Yazmine Bejarano Condezo

Raquel Sainz Urruela

Fernando Sánchez Sáez

LABORATORY 9

CHROMOSOME SEGREGATION AND HUMAN DISEASE

The gametogenesis is among the most complex and highly regulated differentiation programmes that make use of a unique reductional division or meiosis to give rise to highly specialized cells: the gametes. The oocytes and spermatozoa thus generated are the most genetically (meiotic haploid products), epigenetically (epigenetic erasure and histone replacement), and morphologically (oocytes and sperm) distinctive cells of an adult organism and are essential for the continuity of life. At present, we are far from understanding the genetic basis of mammalian gametogenesis and the molecular mechanisms underlying its pathological condition, infertility. Our main objective is to expand our current knowledge of the "fertility loci kit" (coding and non-coding) and the mechanism by which these molecules are essential to carry out gametogenesis/reproduction. We are also interested to understand the causative role of the miss-expression of these proteins in several human tumors and the involvement of the meiotic DNA repair machinery in the genome diploidization process that occur after transformation of tumor cells. To do that we make use of a combination of forward and reverse genetic approaches using the mouse as a model via genome edition.

We had dissected in vivo the consequence of the lack of one protein, named Shugoshin-2, involved in the protection of the integrity of the Cohesin Complex. This protective system is essential for the faithful separation of homologous chromosomes during mitosis and meiosis which is the physical basis of Mendelian inheritance. More recently, we identified and characterized biochemically, cytologically, and functionally a new subunit of the α-kleisin of the Cohesin Complex which is evolutionary conserved from fish to mammals. Through the development of a KO mouse of RAD21L1 we showed that whereas female mice deficient for RAD21L1 were fertile mutant males showed a severe meiotic arrest at late zygotene that ultimately led to azoospermia. Based on these results, we postulated that non obstructive azoospermia and POF can be due to genetic mutations in the cohesin pathway. To test this hypothesis, we undertook the genetic study of meiotic cohesins in human infertility by NGS of families affected of premature ovarian failure. In this respect, we identified in collaboration with the group of Dr. Vilain and Dr. Veitia a large consanguineous family with inherited premature ovarian failure. Using whole-exome sequence analysis we identified a homozygous 1-bp deletion inducing a frameshift mutation in the gene encoding the cohesin subunit STAG3. The pathogenicity of the STAG3 mutations was functionally validated with a loss-of-function mouse model for STAG3 in oogenesis. Female mice devoid of Stag3 were sterile, and their fetal oocytes were arrested at early prophase I, leading to oocyte depletion as early as at 1 week of age. However, and since none of the male members of this family was homozygous for the mutant allele, we made use of the mouse model to show that male mice devoid of Stag3 display a severe meiotic phenotype that includes a meiotic arrest at zygonema-like, demonstrating that STAG3 is a crucial cohesin subunit in mammalian gametogenesis and supporting our proposal that STAG3 is a strong candidate gene for human male infertility. Based on these results we postulate that the meiotic cohesins are responsible for a fraction of idiopathic human infertility syndromes and that meiotic genes are not haploinsuficient in humans as they are not also in mouse mutants.

Based in a large GWAS studies of human fertility we have functionally characterized a non-synonimous SNP rs1254319 and showed that this anonymous cSNP within the ORF named SIX6OS1, encodes a novel central element protein of the SC (2) that specifically interacts with the central element protein 1 (SYCE1). By using genomic editing techniques, we showed that mice lacking SIX6OS1 are defective in chromosome synapsis ▸

Elena Llano Cuadra

Phone: +34 923 294 809
E-mail: ellano@usal.es

at meiotic prophase I, which provokes an arrest at the pachytene-like stage and results in infertility. In accordance with its role as a modifier of the human recombination rate, SIX6OS1 is essential for the appropriate processing of intermediate recombination nodules before crossover formation.

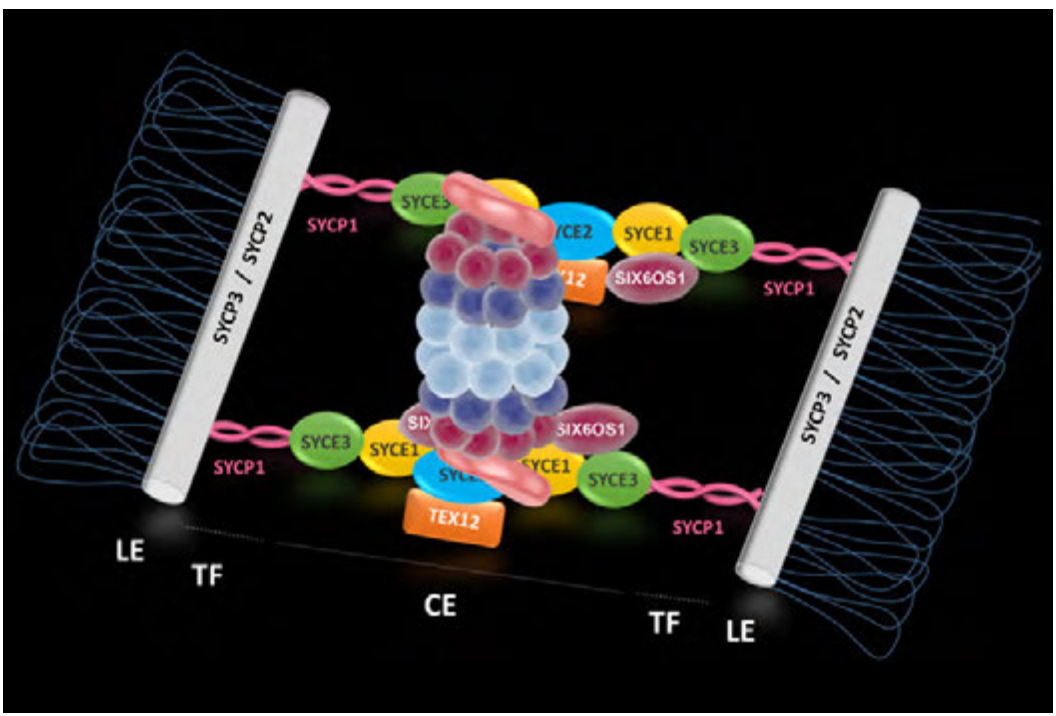
More recently, we have described the role that separase plays during DNA repair, a previously unknown function of separase in mammalian cells and moved forward to the ubiquitin proteasome system (UPS) which plays important roles in meiotic recombination. To this respect, we have dissected the function of the Ubiquitin system in fertility through the involvement of USP26 in male infertility and the functional relevance of the spermatoproteasome, through its Psma8 subunit, in the proteostasis of meiosis and human disease. PSMA8 was localized to and dependent on the central region of the synaptonemal complex. Accordingly, synapsis-deficient mice show delocalization of PSMA8. Moreover, though Psma8-deficient mice are proficient in meiotic homologous recombination, there are alterations in the proteostasis of several key meiotic players that, in addition to the known substrate acetylated histones, have been shown by a proteomic approach to interact with PSMA8, such as SYCP3, SYCP1, CDK1 and TRIP13. These alterations lead to an accumulation of spermatocytes in metaphase I and II which either enter massively into apoptosis or give rise to a low number of aberrant round spermatids that apoptose before histone replacement takes place.

PUBLICATIONS

- **The Post-anaphase SUMO Pathway Ensures the Maintenance of Centromeric Cohesion through Meiosis I-II Transition in Mammalian Oocytes.** Ding Y, Kaido M, Llano E, **Pendas AM**, Kitajima TS. Curr Biol. 2018 May 21;28(10):1661-1669.e4. doi: 10.1016/j.cub.2018.04.019. PMID: 29754905 IF: 9.193 / D1
- **Local activation of mammalian separase in interphase promotes double-strand break repair and prevents oncogenic transformation.** Hellmuth S, Gutiérrez-Caballero C, Llano E, **Pendás AM***, Stemmann O*. EMBO J. 2018 Oct 10. pii: e99184. doi: 10.15252/embj.201899184. PMID: 30305303 IF: 9.944 / D1. *corresponding author
- **Ubiquitin-specific protease 26 (USP26) is not essential for mouse gametogenesis and fertility.** Felipe-Medina N, Gómez-H L, Condezo YB, Sánchez-Martín M, Barbero JL, Ramos I, Llano E, **Pendás AM**. Chromosoma. 2019 Mar 18. doi: 10.1007/s00412-019-00697-6. PMID: 30887115 IF: 3.530 / Q2
- **Shugoshin protects centromere pairing and promotes segregation of nonexchange partner chromosomes in meiosis.** Previato de Almeida L, Evatt JM, Chuong HH, Kurdzo EL, Eyster CA, Gladstone MN, Gómez-H L, Llano E, Meyer R, **Pendas AM**, Pezza RJ, Dawson DS. Proc Natl Acad Sci U S A. 2019 Apr 24. pii: 201902526. doi: 10.1073/pnas.1902526116. PMID: 31019073 IF: 9.580 / D1
- **Three-Dimensional Genomic Structure and Cohesin Occupancy Correlate with Transcriptional Activity during Spermatogenesis.** Vara C, Paytuví-Gallart A, Cuartero Y, Le Dily F, García F, Salvà-Castro J, Gómez-H L, Julià E, Moutinho C, Aiese Cigliano R, Sanseverino W, Fornas O, **Pendás AM,** Heyn H, Waters PD, Marti-Renom MA, Ruiz-Herrera A. Cell Rep. 2019 Jul 9;28(2):352-367.e9. doi: 10.1016/j.celrep.2019.06.037. PMID: 31291573. IF: 7.815 / D1
- **The PSMA8 subunit of the spermatoproteasome is essential for proper meiotic exit and mouse fertility.** Gómez-H L, Felipe-Medina N, Condezo YB, García-Valiente R, Ramos I, Suja JA, Barbero JL, Roig I, Sánchez-Martín M, de Rooij DG, Llano E, **Pendas AM**. PLoS Genet. 2019 Aug 22;15(8):e1008316. doi: 10.1371/journal.pgen.1008316. eCollection 2019 Aug. PMID: 31437213 IF: 5.224 / D1

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Análisis funcional de la gametogénesis en mamíferos (BFU2017-89408-R)	Alberto Martín Pendás	Spanish Ministry of Economy & Competitiveness	2018-2020	250,000.00 €
Análisis funcional de dos nuevos genes esenciales para la gametogénesis de mamíferos (CSI239P18)	Alberto Martín Pendás	Regional Government of Castilla and León	2018-2021	120,000.00 €
Actualización de la unidad de Microscopía del IBMCC (EQC2018-004699-P)	Alberto Martín Pendás	Spanish Ministry of Economy & Competitiveness	2018-2019	249,819.05 €
Sistema de microscopía de campo ancho para experimentos in vivo con iluminación evanescente, capacidad opto-genética, FRAP y de ablación, súper-resolución PALM/STORM y aclaramiento computacional instantáneo	Alberto Martin Pendas	Spanish Ministry of Economy & Competitiveness	2019-2020	590,000.00 €



PSMA8, a subunit of the spermatoproteasome.

Team Leader

José Alberto Orfao de Matos Correia e Vale

Phone.: +34 923 294 811
+34 923 295 811
E-mail: orfao@usal.es

Research Team

Senior Researchers

Julia Almeida Parra
Manuel Fuentes García
Andrés Celestino García Montero
José María Sayagués Manzano
María Dolores Tabernero Redondo

Postdoctorals

Martín Pérez de Andrés
María Aránzazu Rodríguez Caballero
Sergio Matarraz Sudón
Andrea Mayado Colino
Juan Alejandro Flores Montero
Quentin Lecrevisse
Paula Díez García

José Ignacio Sánchez Gallego
María Lourdes Martín Martín
Rafael Góngora Fernández
Sara Gutiérrez Herrero
María González González
Ignacio Criado García
Ana Isabel Rasillo Martín
Elena Blanco Álvarez

Predoctorals

Daniela Pinto Damasceno
Noelia Dasilva Freire
Pilar Leoz
Javier Ignacio Muñoz González
Noemí Muñoz García
Luzalba Sanoja Flores
Guillermo Oliva Ariza
Blanca Fuentes Herrero
Alicia Landeira Viñuela Francisco
Javier Morán Plata
Pablo Juanes Velasco
Alba Pérez Pons

Technicians

Alba Torres Valle
Bárbara Mª Gomulka
Guillermo Tabernero Redondo
Mª Luz Sánchez García

Master Students

Sara Armenteros González
Judith Jeniffer Azaña Yupanqui
Marina Belver Jiménez
Jimena Alvarez Freile
Lydia De La Torre Quintana
Rosa Ayala Bueno
Vanessa Acebes Fernández
Sandra Álvarez Marnina
Ángela Patricia Hernández García
Andrea Otazo Pérez

Visiting Researchers

Carlos E. Pedreira
Elaine Sobral da Costa

LABORATORY 11

IMMUNOLOGY AND CANCER

The research activity of this area focuses on the relationship between the immune response and cancer, as well as on the study of malignancies derived from cells of the immune system, such as leukemias and lymphomas. Among other areas, it relates with improved diagnosis and classification of leukemias and lymphomas, as well evaluation of treatment effectiveness during follow-up via detection of low numbers of therapy-resistant malignant cells, i.e. detection of «minimal residual disease» (MRD).

As the various types of hematological malignancies resemble their normal counterparts, combined studies of normal hematopoietic cells and their malignant counterparts are essential to support the unraveling of oncogenic events that induce deregulation of cellular processes and malignant transformation, including the potential role of immune responses and the immune system in controlling and/or promoting malignant transformation and expansion of neoplastic cells. Therefore, this research field combines cellular, genetic and molecular studies on normal and malignant hematopoiesis, including the immune responses associated with cancer development and control. Translation of the obtained information into novel diagnostics has high priority for this group.

Immunophenotyping is one of the primary bases for the diagnosis, classification and treatment monitoring of hematological malignancies. In the last years, large technological improvements have been achieved in this field, which have allowed a more rational panel design (i.e. more sensitive and specific) for the study of leukemias and lymphomas; however, in parallel, they have led to an increased complexity of flow immunophenotypic data, since no new tools have been developed to ease data interpretation. In order to address the complexity and subjectivity of analysis of flow cytometry data, it is also an essential research activity of our group to **design, develop and validate high throughput systems and tools for the automated and standardized flow cytometry data analysis**, for the diagnostic (screening), classification, prognostic evaluation and treatment monitoring of hematological malignancies, and **to translate** these new automated tools **to clinical settings**.

A more recent research activity of our group -closely related with the one referred above, focused on studying normal hematological/immune cells- is to develop and implement sensitive and specific approaches by multiparametric flow cytometry, to measure and **monitor immune responses after immunotherapy** (i.e. after antitumor immunotherapy).

OBJECTIVES:

The general aim of this program is based on the fact that the oncogenic events that induce deregulation of cellular processes in hematological malignancies may translate into aberrant protein patterns displayed by malignant cells, which could be useful from the clinical point of view, for diagnosis, classification, prognosis evaluation and treatment monitoring in patients suffering from hematological malignancies. In the same line, understanding of the role of the (normal) immune system on different malignancies/clonal disorders, through the analysis of the interactions between tumor cells and the immune microenvironment, could constitute the basis for novel immunotherapeutic strategies in the near future, and can help design strategies for monitoring the immune system after (antitumor) immunotherapy.

Andrés Celestino García Montero
Phone.: +34 923 294 400 ext. 5475
E-mail: angarmon@usal.es

SENIOR RESEARCHER

PHENOTYPIC AND MOLECULAR CHARACTERIZATION OF SYSTEMIC MASTOCYTOSIS: CORRELATION BETWEEN DISEASE PROGRESSION, IMMUOPHENOTYPE AND THE SPECIFIC GENETIC BACKGROUND

Systemic mastocytosis (SM) are orphan diseases, indolent in most patients (ISM) that can progress to aggressive forms (ASM). Pathologic mast cells (MC) displayed particular immunophenotypes and functions with a potential immunomodulatory role over other cell types of the innate and/or adaptive immune responses of the SM patients. Objective: to clarify whether such immune interactions could have any role on the clinic-biological features and progression of the disease and to identify the potential molecular patterns associated to the severity and evolution of SM. Lines of research and challenges: 1) Transcriptomics and genomics of purified MC to identify molecular pathways altered in ASM vs ISM. 2) Detailed immune characterization of the different cell compartments of the innate and adaptive immune responses to know their potential role on the clinic-biological features of SM. 3) Identification of somatic and/or germinal genetic variants responsible for the malignant transformation associated to the D816V *KIT* mutation in myeloid neoplasia, using as a model the transformation from ISM to ASM, and to evaluate the potential clinical utility of the genetic markers detected in the prognostic stratification of the SM patients; and 4) Analysis of the potential correlation between immunophenotype, molecular events, functional profiles, clinical data and environmental features in order to define their utility as diagnostic/prognostic biomarkers and/or as potential therapeutic targets.

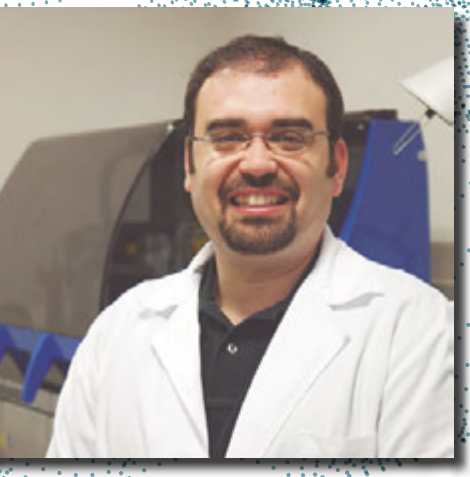
Julia Almeida Parra
Phone.: +34 923 294 811
E-mail: jalmeida@usal.es

SENIOR RESEARCHER

CHRONIC LYMPHOID NEOPLASMS: FACTORS INVOLVED IN ONTO-PATHOGENESIS AND TRANSFORMATION OF PRELEUKEMIC CONDITIONS INTO CLONAL/MALIGNANT DISEASES

Her research is focused on "Immunology and Cancer" applied to hematological malignancies (leukemias and lymphomas) derived from mature T/NK and B cells (*chronic lymphoproliferative disorders, from the onto-pathogenesis to clinical settings,* these latter including their potential application in diagnosis –particularly early diagnosis-, classification and treatment monitoring of these neoplasms). **Major research activities**: i) the identification of mechanisms involved in the transformation/evolution of reactive to clonal and malignant conditions (i.e. the early stages of cancer, both prior to the onset of the disease and before recurrence after therapy), ii) phenotypic, genetic/molecular and functional characterization of these cells and iii) its translation to diagnosis, classification and treatment monitoring of these neoplasms; iv) biological characterization of their normal (T/NK- and B-) cell counterparts; and v) role of the immune system in the control and progression of the disease, with special focus on hematological malignancies. As a consequence of its scientific activity, the team led by Almeida has published 20 international scientific papers in the last 6 years, from which 85% are Q1, with a mean impact factor of 6.7, and registered 2 licensed patents, for a total production of 133 articles in international indexed scientific journals (PI H-index of 41 with >5,000 citations). Almeida is a member of the EuroFlow Consortium (European collaborative group) since its creation in 2006, which aims at standardization and automation in flow cytometry, to improve current flow cytometry strategies applied to the diagnosis, classification and monitoring after treatment of patients with hematological malignancies; specifically, she is the responsible person for the design and development of the T- and NK-cell CLPD panels. More recently (2018-19), she has contributed to an in depth characterization of distinct compartments of normal blood immune cells, such as monocytes (J Allergy Clin Immunol 2019), CD4+ T cells (Frontiers in Immunology 2020) and their alterations in tumor-associated (secondary) immune deficiencies (Haematologica 2018 and Leukemia 2018), and has contributed to the feasibility of applying automated strategies for reproducible analysis by flow-cytometry (J. Immunol Methods 2019); also, she has shown for the first time the potential role of an activated (though defective) immune system in promoting progression to leukemic stages from earlier pre-tumor conditions (Haematologica 2018 and Leukemia 2018), and the finding that monoclonal B lymphocytosis (a pre-tumor condition) is also very frequent in non-Western populations (Haematologica 2019).

In the near future, her activities will focus on in-depth analyses of the onto-pathogenic factors involved in chronic B-cell leukemia, and early detection and (potential) intervention (at monoclonal B lymphocytosis stages).



Manuel Fuentes García
Phone.: +34 923 294 811
E-mail: mfuentes@usal.es

SENIOR RESEARCHER

IMMUNOTECHNOLOGY, NANOTECHNOLGY, AND PROTEOMICS APPROACHES FOR BIOMARKER AND DRUG DISCOVERY IN CANCER AND IMMUNOPATHOLOGIES

Immunotherapies that train or stimulate the inherent immunological systems to recognize, attack & erradicate tumor cells with minimal damages to healthy cells have demonstrated promising clinical responses. Recently, a huge progress has been experienced in two main Immuno-Onco-Therapy (IO) areas: Chimeric Antigen Receptor (CAR-T cells) & Immune modulation by blocking suppressive Immune Check-points (IC). Although IO has demonstrated exciting clinical responses, they are some limitations: high cost, efficacy restricted to certain patients subsets, biomarkers for patient stratification, resistant to IO, dose-limiting-auto-immune effects like cytokine release syndrome... Despite that Immune Checkpoint Inhibitors (ICI) has revolutionize the management of cancer, by increasing the immune response towards tumors, already in the clinical setting; however, it is still required active investigation because the low responses and some patients are primary unresponsive to develop ulterior resistance to these drugs (primary & acquire resistance). Nowadays, there are several clinical trials which promotes the combination of ICIs with other onco-therapeutic strategies: ablative cancer treatments (radiotherapy, chemotherapy,...) that cause tumoral cell death in an immunogenic way. The Immunogenic Cell Death (ICD) enhances immune stimulatory or subvert immune suppressive effects for the activation, proliferation, T cells tumor infiltration to synergize with current ICI therapies. Hence, it is necessary to decipher molecular basis of anti-tumor immune response to design the optimal IO combination[x]. The anti-tumor immune response consists of key steps: i.-Antigen released from tumoral cells are captured by antigen-presentation cells (APCs). ii.-Danger Associated Molecular Patterns (DAMPs) such as pro-inflammatory cytokines and factors released by dying tumoral cells signal APCs maturation. iii.-Activated APCs present Tumor Associated Antigens (TAAs) on MHC-I & MHC-II to T cells, resulting in the activation of effector T cells against tumor-specific-antigens. iv.-Activated effector T cells traffic to and infiltrate tumor bed where they specifically recognized tumoral cells through integration between T-cell receptor (TCR) and MHC-I bound cognate antigen and kill tumor cells. v.-Tumor death cells release TAAs to increase the breadth and depth to the immune response in subsequent revolutions of cycle.

Thus, there is a potential mechanism of combined benefits of TOT based on Nanomedicines and Immunotherapy based on ICIs. Because Nanomedicines allow learning from biology and nanotechnology to design approaches that can address some of the challenges in IO: (i) Enabling the combination of molecular targeted therapies with immunotherapies which could be pharma- and biologically compatible; (ii) Early monitoring of efficacy of immunotherapies; (iii) Personalizing an immune response to a patient´s tumor.

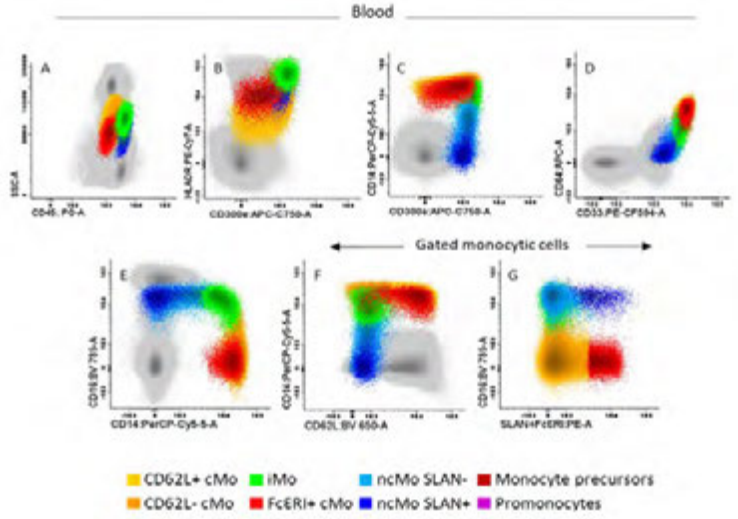
Then, the main goal of our group to design and validate a immunoproteogenomics strategy, in order to perform ortogonal verification of the panel of biomarkers useful in combination of targeted onco-therapy and immune-checkpoint inhibitors to improve the therapeutic scheme.

This immunoproteogenomic methodology is based on the systematic integration of next generation genomic, transcriptomic, proteomics and immune monitoring (in array format) that allows ortogonal validation of biomarkers (in haematological and solid tumors) in order to promote a rapid translation into the clinic. In particular, we are focused on:

1. Establish correlation between somatic mutations and cell signaling pathways by proteogenomics.
2. Inter-relationship of Characterization of TCR sequences and HLA immunopeptidomes.
3. Design and development of methods for the proteomic quantification of proteins and their encoded proteoforms according to genomic alterations and immunpeptidomes.
4. Identify differential tumor associated antigen (TAAs) profiles according to altered protein profiles and immunopeptidomes.
5. Immune monitoring in high-density array for the rapid and simultaneous determination soluble components of immune response and immunogenic cell death.

PUBLICATIONS

- **Automated database-guided expert-supervised orientation for immunophenotypic diagnosis and classification of acute leukemia.** *Lhermitte L, Mejstrikova E, van der Sluijs-Gelling AJ, Grigore GE, Sedek L, Bras AE, Gaipa G, Sobral da Costa E, Novakova M, Sonneveld E, Buracchi C, de Sá Bacelar T, Te Marvelde JG, Trinquand A, Asnafi V, Szczepanski T, Matarraz S, Lopez A, Vidriales B, Bulsa J, Hrusak O, Kalina T, Lecrevisse Q, Martin Ayuso M, Brüggemann M, Verde J, Fernandez P, Burgos L, Paiva B, Pedreira CE, van Dongen JJM, Orfao A, van der Velden VHJ.* **Leukemia. 2018 Apr;32(4):874-881. doi: 10.1038/leu.2017.313.** PMID: 29089646 **IF: 9.944 / D1**
- **Prognostic value of antigen expression in multiple myeloma: a PETHEMA/GEM study on 1265 patients enrolled in four consecutive clinical trials.** *Arana P, Paiva B, Cedena MT, Puig N, Cordon L, Vidriales MB, Gutiérrez NC, Chiodi F, Burgos L, Anglada LL, Martínez-Lopez J, Hernandez MT, Teruel AI, Gironella M, Echeveste MA, Rosiñol L, Martínez R, Oriol A, De la Rubia J, Orfao A, Blade J, Lahuerta JJ, Mateos MV, San Miguel JF.* **Leukemia. 2018 Apr;32(4):971-978. doi: 10.1038/leu.2017.320.** PMID: 29099494 **IF: 9.944 / D1**
- **Screening Phage-Display Antibody Libraries Using Protein Arrays.** *Jara-Acevedo R, Díez P, González-González M, Dégano RM, Ibarrola N, Góngora R, Orfao A, Fuentes M.* **Methods Mol Biol. 2018;1701:365-380. doi: 10.1007/978-1-4939-7447-4_20.** PMID: 29116516 **IF: NI**
- **Clinical and biochemical correlates of male hypogonadism in type 2 diabetes.** *Herrero A, Marcos M, Galindo P, Miralles JM, Corrales JJ.* **Andrology. 2018 Jan;6(1):58-63. doi: 10.1111/andr.12433.** PMID: 29145714 **IF: 3.259 / Q1**
- **Efficacy and safety of native versus pegylated Escherichia coli asparaginase for treatment of adults with high-risk, Philadelphia chromosome-negative acute lymphoblastic leukemia.** *Ribera JM, Morgades M, Montesinos P, Martino R, Barba P, Soria B, Bermúdez A, Moreno MJ, González-Campos J, Vives S, Gil C, Abella E, Guàrdia R, Martínez-Carballeira D, Martínez-Sánchez P, Amigo ML, Mercadal S, Serrano A, López-Martínez A, Vall-Llovera F, Sánchez-Sánchez MJ, Peñarrubia MJ, Calbacho M, Méndez JA, Bergua J, Cladera A, Tormo M, García-Belmonte D, Feliu E, Ciudad J, Orfao A; PETHEMA Group, Spanish Society of Hematology.* **Leuk Lymphoma. 2018 Jul;59(7):1634-1643. doi: 10.1080/10428194.2017.1397661.** PMID: 29165013 **IF: 2.674 / Q2**
- **Molecular detection of minimal residual disease in multiple myeloma.** *Bai Y, Orfao A* **Chim CS. Br J Haematol. 2018 Apr;181(1):11-26. doi: 10.1111/bjh.15075. Review.** PMID: 29265356 **IF: 5.206 / Q1**
- **A Perspective on Proteomics of Infectious Diseases.** *Venkatesh A, Gil C, Fuentes M, LaBaer J, Srivastava S.* **Proteomics Clin Appl. 2018 Jul;12(4):e1700139. doi: 10.1002/prca.201700139.** PMID: 29282898 **IF: 2.324 / Q2**
- **Characterization of CD34+ hematopoietic cells in systemic mastocytosis: Potential role in disease dissemination.** *Mayado A, Teodosio C, Dasilva-Freire N, Jara-Acevedo M, García-Montero AC, Álvarez-Twose I, Sánchez-Muñoz L, Matito A, Caldas C, Muñoz-González JI, Henriques A, Sánchez-Gallego JI, Escribano L, Orfao A.* **Allergy. 2018 Jun;73(6):1294-1304. doi: 10.1111/all.13413.** PMID: 29331029 **IF: 6.771 / Q1**
- **In-Depth Proteomic Characterization of Classical and Non-Classical Monocyte Subsets.** *Segura V, Valero ML, Cantero L, Muñoz J, Zarzuela E, García F, Aloria K, Beaskoetxea J, Arizmendi JM, Navajas R,*



Identification of different subsets of circulating monocytes in representative peripheral blood samples from a healthy donor (Damasceno et al, JACI 2019).

Paradela A, Diez P, Dégano RM, Fuentes M, Orfao A, Montero AG, Garin-Muga A, Corrales FJ, Pino MMSD. **Proteomes. 2018 Feb 5;6(1). pii: E8. doi: 10.3390/proteomes6010008.** PMID: 29401756 **IF: NI**

- **Richter transformation driven by Epstein-Barr virus reactivation during therapy-related immunosuppression in chronic lymphocytic leukaemia.** *García-Barchino MJ, Sarasquete ME, Panizo C, Morscio J, Martínez A, Alcoceba M, Fresquet V, González-Farre B, Paiva B, Young KH, Robles EF, Roa S, Celay J, Larrayoz M, Rossi D, Gaidano G, Montes-Moreno S, Piris MA, Balanzategui A, Jiménez C, Rodriguez I, Calasanz MJ, Larrayoz MJ, Segura V, García-Muñoz R, Rabasa MP, Yi S, Li J, Zhang M, Xu-Monette ZY, Puig-Moron N, Orfao A, Böttcher S, Hernandez-Rivas JM, Miguel JS, Prosper F, Tousseyn T, Sagaert X, González M, Martínez-Climent JA.* **J Pathol. 2018 May;245(1):61-73. doi: 10.1002/path.5060.** PMID: 29464716 **IF: 5.942 / Q1**
- **Loss of Pax5 Exploits Sca1-BCR-ABLp190 Susceptibility to Confer the Metabolic Shift Essential for pB-ALL.** *Martín-Lorenzo A, Auer F, Chan LN, García-Ramírez I, González-Herrero I, Rodríguez-Hernández G, Bartenhagen C, Dugas M, Gombert M, Ginzel S, Blanco O, Orfao A, Alonso-López D, Rivas JL, García-Cenador MB, García-Criado FJ, Müschen M, Sánchez-García I, Borkhardt A, Vicente-Dueñas C, Hauer J.* **Cancer Res. 2018 May 15;78(10):2669-2679. doi: 10.1158/0008-5472.CAN-17-3262.** PMID: 29490943 **IF: 8.378 / Q1**
- **Age-associated distribution of normal B-cell and plasma cell subsets in peripheral blood.** *Blanco E, Pérez-Andrés M, Arriba-Méndez S, Contreras-Sanfeliciano T, Criado I, Pelak O, Serra-Caetano A, Romero A, Puig N, Remesal A, Torres Canizales J, López-Granados E, Kalina T, Sousa AE, van Zelm M, van der Burg M, van Dongen JJM, Orfao A; EuroFlow PID group.* **J Allergy Clin Immunol. 2018 Jun;141(6):2208-2219.e16. doi: 10.1016/j.jaci.2018.02.017.** PMID: 29505809 **IF: 14.110 / D1**
- **Differential expression of CD73, CD86 and CD304 in normal vs. leukemic B-cell precursors and their utility as stable minimal residual disease markers in childhood B-cell precursor acute lymphoblastic leukemia.** *Sędek Ł, Theunissen P, Sobral da Costa E, van der Sluijs-Gelling A, Mejstrikova E, Gaipa G, Sonsala A, Twardoch M, Oliveira E, Novakova M, Buracchi C, van Dongen JJM, Orfao A, van der Velden VHJ, Szczepański T; EuroFlow Consortium.* **J Immunol Methods. 2018 Mar 9. pii: S0022-1759(17)30126-6. doi: 10.1016/j.jim.2018.03.005.** PMID: 29530508 **IF: 1.913 / Q3**
- **Low-count monoclonal B-cell lymphocytosis persists after seven years of follow up and is associated with a poorer outcome.** *Criado I, Rodríguez-Caballero A, Gutiérrez ML, Pedreira CE, Alcoceba M, Nieto W, Teodosio C, Bárcena P, Romero A, Fernández-Navarro P, González M, Almeida J, Orfao A; Primary Health Care Group of Salamanca for the Study of MBL.* **Haematologica. 2018 Jul;103(7):1198-1208. doi: 10.3324/haematol.2017.183954.** PMID: 29567775 **IF: 7.570 / D1**
- **Basophil-lineage commitment in acute promyelocytic leukemia predicts for severe bleeding after starting therapy.** *Matarraz S, Leoz P, Fernández C, Colado E, Chillón MC, Vidriales MB, González M, Rivera D, Osuna CS, Caballero-Velázquez T, Van Der Velden V, Jongen-Lavrencic M, Gutiérrez O, Bermejo AY, Alonso LG, García MB, De Ramón Sánchez C, García-Donas G, Mateo AG, Recio I, Sánchez-Real J, Mayado A, Gutiérrez ML, Bárcena P, Barrena S, López A, Van Dongen J, Orfao A.* **Mod Pathol. 2018 Aug;31(8):1318-1331. doi: 10.1038/s41379-018-0038-2.** PMID: 29572500 **IF: 6.365 / D1**
- **New Hybrids Derived from Podophyllic Aldehyde and Diterpenylhydroquinones with Selectivity toward Osteosarcoma Cells.** *Hernández ÁP, Díez P, García PA, Miguel Del Corral JM, Pérez-Andrés M, Díez D, San Feliciano A, Fuentes M, Castro MÁ.* **ACS Med Chem Lett. 2018 Mar 8;9(4):328-333. doi: 10.1021/acsmedchemlett.7b00493. eCollection 2018 Apr 12.** PMID: 29670695 **IF: 3.737 / Q1**
- **KIT D816V Positive Acute Mast Cell Leukemia Associated with Normal**

Karyotype Acute Myeloid Leukemia. *Lopes M, Teixeira MDA, Casais C, Mesquita V, Seabra P, Cabral R, Palla-García J, Lau C, Rodrigues J, Jara-Acevedo M, Freitas I, Vizcaíno JR, Coutinho J, Escribano L, Orfao A, Lima M.* **Case Rep Hematol. 2018 Feb 18;2018:3890361. doi: 10.1155/2018/3890361. eCollection 2018.** PMID: 29670776 **IF: NI**

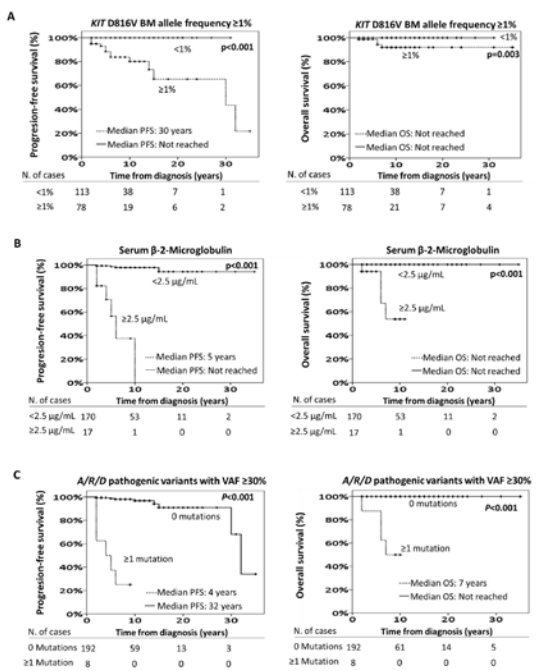
- **Combined assessment of the TNM stage and BRAF mutational status at diagnosis in sporadic colorectal cancer patients.** *Sayagués JM, Del Carmen S, Del Mar Abad M, Corchete LA, Bengoechea O, Anduaga MF, Baldeón MJ, Cruz JJ, Alcazar JA, Angoso M, González M, García J, Muñoz-Bellvis L, Orfao A, Sarasquete ME.* **Oncotarget. 2018 May 8;9(35):24081-24096. doi: 10.18632/oncotarget.25300. eCollection 2018 May 8.** PMID: 29844874 **IF: NI**
- **Lmo2 expression defines tumor cell identity during T-cell leukemogenesis.** *García-Ramírez I, Bhatia S, Rodríguez-Hernández G, González-Herrero I, Walter C, González de Tena-Dávila S, Parvin S, Haas O, Woessmann W, Stanulla M, Schrappe M, Dugas M, Natkunam Y, Orfao A, Domínguez V, Pintado B, Blanco O, Alonso-López D, De Las Rivas J, Martín-Lorenzo A, Jiménez R, García Criado FJ, García Cenador MB, Lossos IS, Vicente-Dueñas C, Borkhardt A, Hauer J, Sánchez-García I.* **EMBO J. 2018 Jul 13;37(14). pii: e98783. doi: 10.15252/embj.201798783.** PMID: 29880602 **IF: 11.227 / Q1**
- **Residual normal B-cell profiles in monoclonal B-cell lymphocytosis versus chronic lymphocytic leukemia.** *Criado I, Blanco E, Rodríguez-Caballero A, Alcoceba M, Contreras T, Gutiérrez ML, Romero A, Fernández-Navarro P, González M, Solano F, Gómez C, Pérez-Andrés M, van Dongen JJM, Almeida J, Orfao A; EuroFlow PID Group and The Primary Health Care Group of Salamanca for the Study of MBL.* **Leukemia. 2018 Jun 21. doi: 10.1038/s41375-018-0164-3.** PMID: 29930299 **IF: 9.944 / D1**
- **Prognostic stratification of adult primary glioblastoma multiforme patients based on their tumor gene amplification profiles.** *González-Tablas M, Crespo I, Vital AL, Otero Á, Nieto AB, Sousa P, Patino-Alonso MC, Corchete LA, Tão H, Rebelo O, Barbosa M, Almeida MR, Guedes AF, Lopes MC, French PJ, Orfao A, Tabernero MD.* **Oncotarget. 2018 Jun 15;9(46):28083-28102. doi: 10.18632/oncotarget.25562. eCollection 2018 Jun 15.** PMID: 29963263 **IF: NI**
- **Self-assembling functional programmable protein array for studying protein-protein interactions in malaria parasites.** *Arévalo-Pinzón G, González-González M, Suárez CF, Curtidor H, Carabias-Sánchez J, Muro A, LaBaer J, Patarroyo MA, Fuentes M.* **Malar J. 2018 Jul 17;17(1):270. doi: 10.1186/s12936-018-2414-2.** PMID: 30016987 **IF: 2.798 / Q1**
- **Frequency and clinical impact of CDKN2A/ARF/CDKN2B gene deletions as assessed by in-depth genetic analyses in adult T cell acute lymphoblastic leukemia.** *Genescà E, Lazarenkov A, Morgades M, Berbis G, Ruíz-Xivillé N, Gómez-Marzo P, Ribera J, Juncà J, González-Pérez A, Mercadal S, Guardia R, Artola MT, Moreno MJ, Martínez-López J, Zamora L, Barba P, Gil C, Tormo M, Cladera A, Novo A, Pratcorona M, Nomdedeu J, González-Campos J, Almeida M, Cervera J, Montesinos P, Batlle M, Vives S, Esteve J, Feliu E, Solé F, Orfao A, Ribera JM.* **J Hematol Oncol. 2018 Jul 24;11(1):96. doi: 10.1186/s13045-018-0639-8.** PMID: 30041662 **IF: 8.731 / D1**
- **Frequent issues and lessons learned from EuroFlow QA.** *Kalina T, Brdickova N, Glier H, Fernandez P, Bitter M, Flores-Montero J, van Dongen JJM, Orfao A.* **J Immunol Methods. 2018 Sep 17. pii: S0022-1759(17)30140-0. doi: 10.1016/j.jim.2018.09.008.** PMID: 30237053 **IF: 1.913 / Q3**
- **A multiple myeloma classification system that associates normal B-cell subset phenotypes with prognosis.** *Bødker JS, Brøndum RF, Schmitz A, Schönherz AA, Jespersen DS, Sønderkær M, Vesteghem C, Due H, Nørgaard CH, Perez-Andres M, Samur MK, Davies F, Walker B, Pawlyn C, Kaiser M, Johnson D, Bertsch U, Broyl A, van Duin M, Shah R, Johansen P, Nørgaard MA, Samworth RJ, Sonneveld P, Goldschmidt H, Morgan GJ, Orfao A, Munshi N, Johnson HE, El-Galaly T, Dybkær K, Bøgsted M.* **Blood Adv. 2018 Sep 25;2(18):2400-2411. doi: 10.1182/bloodadvances.2018018564.** PMID: 30254104 **IF: NI**
- **Increased Survival due to Lower Toxicity for High Risk T-cell Acute Lymphoblastic Leukemia Patients in 2 consecutive Pediatric-Inspired PETHEMA Trials.** *Barba P, Morgades M, Montesinos P, Gil C, Fox ML, Ciudad J, Moreno MJ, González-Campos J, Genescà E, Martínez-Carballeira D, Martino R, Vives S, Guardia R, Mercadal S, Artola MT, Cladera A, Tormo M, Esteve J, Bergua J, Vall-Llovera F, Ribera J, Martínez-Sánchez P, Amigo ML, Bermúdez A, Calbacho M, Hernández-Rivas JM, Feliu E, Orfao A, Ribera JM; PETHEMA Group.* **Eur J Haematol. 2018 Sep 29. doi: 10.1111/ejh.13178.** PMID: 30267597 **IF: 2.217 / Q2**
- **A Systematic Analysis Workflow for High-Density Customized Protein Microarrays in Biomarker Screening.** *García-Valiente R, Fernández-García J, Carabias-Sánchez J, Landeira-Viñuela A, Góngora R, González-González M, Fuentes M.* **Methods Mol Biol. 2019;1871:107-122. doi: 10.1007/978-1-4939-8814-3_7.** PMID: 30276735 **IF: NI**
- **Flow cytometric assessment of leukocyte kinetics for the monitoring of tissue damage.** *van den Bossche WBL, Rykov K, Teodosio C, Ten Have BLEF, Knobben BAS, Sietsma MS, Josiassen K, de Bruin-Versteeg S, Orfao A, van Dongen JJM, van Raay JJAM.* **Clin Immunol. 2018 Oct 2;197:224-230. doi: 10.1016/j.clim.2018.09.014.** PMID: 30290225 **IF: 3.548 / Q2**
- **Spatio-temporal tumor heterogeneity in metastatic CRC tumors: a mutational-based approach.** *Del Carmen S, Sayagués JM, Bengoechea O, Anduaga MF, Alcazar JA, Gervas R, García J, Orfao A, Bellvis LM, Sarasquete ME, Del Mar Abad M.* **Oncotarget. 2018 Sep 28;9(76):34279-34288. doi: 10.18632/oncotarget.26081. eCollection 2018 Sep 28.** PMID: 30344942 **IF: NI**
- **Impact of somatic and germline mutations on the outcome of systemic mastocytosis.** *Muñoz-González JI, Jara-Acevedo M, Alvarez-Twose I, Merker JD, Teodosio C, Hou Y, Henriques A, Roskin KM, Sánchez-Muñoz L, Tsai AG, Caldas C, Matito A, Sánchez-Gallego JI, Mayado A, Dasilva-Freire N, Gotlib JR, Escribano L, Orfao A, García-Montero AC.* **Blood Adv. 2018 Nov 13;2(21):2814-2828. doi: 10.1182/bloodadvances.2018020628.** PMID: 30373888 **IF: NI**
- **Next generation flow for minimally-invasive blood characterization of MGUS and multiple myeloma at diagnosis based on circulating tumor plasma cells (CTPC).** *Sanoja-Flores L, Flores-Montero J, Garcés JJ, Paiva B, Puig N, García-Mateo A, García-Sánchez O, Corral-Mateos A, Burgos L, Blanco E, Hernández-Martín J, Pontes R, Díez-Campelo M, Millacoy P, Rodríguez-Otero P, Prosper F, Merino J, Vidriales MB, García-Sanz R, Romero A, Palomera L, Ríos-Tamayo R, Pérez-Andrés M, Blanco JF, González M, van Dongen JJM, Durie B, Mateos MV, San-Miguel J, Orfao A; EuroFlow consortium.* **Blood Cancer J. 2018 Nov 19;8(12):117. doi: 10.1038/s41408-018-0153-9.** PMID: 30455467 **IF: 7.895 / Q1**
- **Flow cytometry for fast screening and automated risk assessment in systemic light-chain amyloidosis.** *Puig N, Paiva B, Lasa M, Burgos L, Perez JJ, Merino J, Moreno C, Vidriales MB, Toboso DG, Cedena MT, Ocio EM, Lecumberri R, García de Coca A, Labrador J, González ME, Palomera L, Gironella M,*

Cabañas V, Casanova M, Oriol A, Krsnik I, Pérez-Montaña A, de la Rubia J, de la Puerta JE, de Arriba F, Prosper F, Martínez-Lopez J, Lecrevisse Q, Verde J, Mateos MV, Lahuerta JJ, Orfao A, San Miguel JF. Leukemia. **2018 Dec 12. doi: 10.1038/s41375-018-0308-5.** PMID: 30542145 **IF: 9.944 / D1**

- **PERISCOPE: road towards effective control of pertussis.** *PERISCOPE Consortium.* **Lancet Infect Dis. 2019 May;19(5):e179-e186. doi: 10.1016/S1473-3099(18)30646-7. Review.** PMID: 30503084 **IF: 27.516 / D1**
- **Adverse reactions to drugs and biologics in patients with clonal mast cell disorders: A Work Group Report of the Mast Cells Disorder Committee, American Academy of Allergy, Asthma & Immunology.** *Carter MC, Metcalfe DD, Matito A, Escribano L, Butterfield JH, Schwartz LB, Bonadonna P, Zanotti R, Triggiani M, Castells M, Brockow K.* **J Allergy Clin Immunol. 2019 Mar;143(3):880-893. doi: 10.1016/j.jaci.2018.10.063.** PMID: 30528617 **IF: 14.110 / D1**
- **Flow cytometry for fast screening and automated risk assessment in systemic light-chain amyloidosis.** *Puig N, Paiva B, Lasa M, Burgos L, Perez JJ, Merino J, Moreno C, Vidriales MB, Toboso DG, Cedena MT, Ocio EM, Lecumberri R, García de Coca A, Labrador J, González ME, Palomera L, Gironella M, Cabañas V, Casanova M, Oriol A, Krsnik I, Pérez-Montaña A, de la Rubia J, de la Puerta JE, de Arriba F, Prosper F, Martínez-Lopez J, Lecrevisse Q, Verde J, Mateos MV, Lahuerta JJ, Orfao A, San Miguel JF.* **Leukemia. 2019 May;33(5):1256-1267. doi: 10.1038/s41375-018-0308-5.** PMID: 30542145 **IF: 9.944 / D1**
- **Genetic variation at the glycosaminoglycan metabolism pathway contributes to the risk of psoriatic arthritis but not psoriasis.** *Ateriido A, Cañete JD, Tornero J, Ferrándiz C, Pinto JA, Gratacós J, Queiró R, Montilla C, Torre-Alonso JC, Pérez-Venegas JJ, Fernández Nebro A, Muñoz-Fernández S, González CM, Roig D, Zarco P, Erra A, Rodríguez J, Castañeda S, Rubio E, Salvador G, Díaz-Torné C, Blanco R, Willisch Domínguez A, Mosquera JA, Vela P, Sánchez-Fernández SA, Corominas H, Ramírez J, de la Cueva P, Fonseca E, Fernández E, Puig L, Dauden E, Sánchez-Carazo JL, López-Estebaranz JL, Moreno D, Vanaclocha F, Herrera E, Blanco F, Fernández-Gutiérrez B, González A, Pérez-García C, Alperi-López M, Olivé Marques A, Martínez-Taboada V, González-Álvaro I, Sanmartí R, Tomás Roura C, García-Montero AC, Bonàs-Guarch S, Mercader JM, Torrents D, Codó L, Gelpí JL, López-Corbeto M, Pluma A, López-Lasanta M, Tortosa R, Palau N, Absher D, Myers R, Marsal S, Julià A.* **Ann Rheum Dis. 2019 Mar;78(3). pii: e214158. doi: 10.1136/annrheumdis-2018-214158X.** PMID: 30552173 **IF: 14.299 / D1**
- **A decade of Nucleic Acid Programmable Protein Arrays (NAPPA) availability: News, actors, progress, prospects and access.** *Manzano-Román R, Fuentes M.* J Proteomics. **2019 Apr 30;198:27-35. doi: 10.1016/j.jprot.2018.12.007.** PMID: 30553075 **IF: 3.537 / Q1**
- **Exosome beads array for multiplexed phenotyping in cancer.** *Jara-Acevedo R, Campos-Silva C, Valés-Gómez M, Yáñez-Mó M, Suárez H, Fuentes M.* **J Proteomics. 2019 Apr 30;198:87-97. doi: 10.1016/j.jprot.2018.12.023.** PMID: 30594577 **IF: 3.537 / Q1**
- **Bone Marrow Mast Cell Antibody-Targetable Cell Surface Protein Expression Profiles in Systemic Mastocytosis.** *Dasilva-Freire N, Mayado A, Teodosio C, Jara-Acevedo M, Álvarez-Twose I, Matito A, Sánchez-Muñoz L, Caldas C, Henriques A, Muñoz-González JI, García-Montero AC, Sánchez-Gallego JI, Escribano L, Orfao A.* **Int J Mol Sci. 2019 Jan 28;20(3). pii: E552. doi: 10.3390/ijms20030552.** PMID: 30696068 **IF: 4.183 / D1**
- **Proposed Diagnostic Algorithm for Patients with Suspected Mast Cell Activation Syndrome**. *Valent P, Akin C, Bonadonna P, Hartmann K, Brockow K, Niedoszytko M, Nedoszytko B, Siebenhaar F, Sperr WR, Oude Elberink JNG, Butterfield JH, Alvarez-Twose I, Sotlar K, Reiter A, Kluin-Nelemans HC, Hermine O, Gotlib J, Broesby-Olsen S, Orfao A, Horny HP, Triggiani M, Arock M, Schwartz LB, Metcalfe DD.* **J Allergy Clin Immunol Pract. 2019 Apr;7(4):1125-1133.e1. doi: 10.1016/j.jaip.2019.01.006.. Review.** PMID: 30737190 **IF: 7.550 / Q2**
- **Defects in memory B-cell and plasma cell subsets expressing different immunoglobulin-subclasses in patients with CVID and immunoglobulin subclass deficiencies.** *Blanco E, Pérez-Andrés M, Arriba-Méndez S, Serrano C, Criado I, Del Pino-Molina L, Silva S, Madruga I, Bakardjieva M, Martins C, Serra-Caetano A, Romero A, Contreras-Sanfeliciano T, Bonroy C, Sala F, Martín A, Bastida JM, Lorente F, Prieto C, Dávila I, Marcos M, Kalina T, Vlkova M, Chovancova Z, Cordeiro AI, Philippé J, Haerynck F, López-Granados E, Sousa AE, van der Burg M, van Dongen JJM, Orfao A; EuroFlow PID group.* **J Allergy Clin Immunol. 2019 Sep;144(3):809-824. doi: 10.1016/j.jaci.2019.02.017.** PMID: 30826363 **IF: 14.110 / D1**
- **Maturation-associated gene expression profiles during normal human bone marrow erythropoiesis.** *Mello FV, Land MGP, Costa ES, Teodósio C, Sánchez ML, Bárcena P, Peres RT, Pedreira CE, Alves LR, Orfao A.* Cell Death Discov. 2019 Feb 28;5:69. doi:. eCollection 2019. PMID: 30854228 **IF: 7.501 / Q1**
- **The EuroFlow PID Orientation Tube for Flow Cytometric Diagnostic Screening of Primary Immunodeficiencies of the Lymphoid System.** *van der Burg M, Kalina T, Perez-Andres M, Vlkova M, Lopez-Granados E, Blanco E, Bonroy C, Sousa AE, Kienzler AK, Wentink M, Mejstríková E, Šinkorova V, Stuchly J, van Zelm MC, Orfao A, van Dongen JJM.* **Front Immunol. 2019 Mar 4;10:246. doi: 10.3389/fimmu.2019.00246. eCollection 2019.** PMID: 30886612 **IF: 4.716 / Q1**
- **Distribution of subsets of blood monocytic cells throughout life.** *Damasceno D, Teodosio C, van den Bossche WBL, Perez-Andres M, Arriba-Méndez S, Muñoz-Bellvis L, Romero A, Blanco JF, Remesal A, Puig N, Matarraz S, Vicente-Villardón JL, van Dongen JJM, Almeida J, Orfao A; TiMaScan Study Group.* **J Allergy Clin Immunol. 2019 Jul;144(1):320-323.e6. doi: 10.1016/j.jaci.2019.02.030.** PMID: 30890326 **IF: 14.110 / D1**
- **The poor prognosis of low hypodiploidy in adults with B-cell precursor acute lymphoblastic leukaemia is restricted to older adults and elderly patients.** *Ribera J, Granada I, Morgades M, Vives S, Genescà E, González C, Nomdedeu J, Escoda L, Montesinos P, Mercadal S, Coll R, González-Campos J, Abella E, Barba P, Bermúdez A, Gil C, Tormo M, Pedreño M, Martínez-Carballeira D, Hernández-Rivas JM, Orfao A, Martínez-López J, Esteve J, Bravo P, García-Guiñon A, Debén G, Moraleda JM, Queizán JA, Ortín X, Moreno MJ, Feliu E, Solé F, Ribera JM; PETHEMA Group, Spanish Society of Haematology.* **Br J Haematol. 2019 Jul;186(2):263-268. doi: 10.1111/bjh.15887.** PMID: 30916384 **IF: 5.206 / Q1**
- **Genetic association between CD96 locus and immunogenicity to anti-TNF therapy in Crohn's disease.** *Ateriido A, Palau N, Domènech E, Nos Mateu P, Gutiérrez A, Gomollón F, Mendoza JL, García-Planella E, Barreiro-de Acosta M, Muñoz F, Vera M, Saro C, Esteve M, Andreu M, Chaparro M, Panés J, García-Sánchez V, López-Lasanta M, Pluma A, Codó L, García-Montero A, Manyé J, Gisbert JP, Marsal S, Julià A.* **Pharmacogenomics J. 2019**

Dec;19(6):547-555. doi: 10.1038/s41397-019-0090-4. PMID: 31043678 IF: 2.265 / Q2

- **Proposed diagnostic criteria for classical chronic myelomonocytic leukemia (CMML), CMML variants and pre-CMML conditions.** *Valent P, Orazi A, Savona MR, Patnaik MM, Onida F, van de Loosdrecht AA, Haase D, Haferlach T, Elena C, Pleyer L, Kern W, Pemovska T, Vladimer GI, Schanz J, Keller A, Lübbert M, Lion T, Sotlar K, Reiter A, De Witte T, Pfeilstöcker M, Geissler K, Padron E, Deininger M, Orfao A, Horny HP, Greenberg PL, Arber DA, Malcovati L, Bennett JM.* Haematologica. 2019 Oct;104(10):1935-1949. doi: 10.3324/haematol.2019.222059. PMID: 31048353 IF: 7.570 / D1
- **Issue Highlights - May 2019.** *Orfao A.* Cytometry B Clin Cytom. 2019 May;96(3):177-180. doi: 10.1002/cyto.b.21786. PMID: 31091004 IF: 2.938 / Q1
- **Identification of Alzheimer's Disease Autoantibodies and Their Target Biomarkers by Phage Microarrays.** *San Segundo-Acosta P, Montero-Calle A, Fuentes M, Rábano A, Villalba M, Barderas R.* J Proteome Res. 2019 Jul 5;18(7):2940-2953. doi: 10.1021/acs.jproteome.9b00258. PMID: 31136180 IF: 3.780 / Q1
- **Frequency of clonal mast cell diseases among patients presenting with anaphylaxis: A prospective study in 178 patients from 5 tertiary centers in Spain.** *González-de-Olano D, Esteban-López MI, Alonso-Díaz-de-Durana MD, González-Mancebo E, Prieto-García A, Gandolfo-Cano M, Mohedano-Vicente E, Balugo-López V, Fiandor A, Mielgo-Ballesteros R, Vega-Castro A, García-Montero A, Orfao A, Escribano L, Álvarez-Twose I.* J Allergy Clin Immunol Pract. 2019 May 28. pii: S2213-2198(19)30484-2. doi: 10.1016/j.jaip.2019.05.027. PMID: 31146019 IF: 7.550 / Q2
- **Frequency and prognostic impact of KIT and other genetic variants in indolent systemic mastocytosis**. *Muñoz-González JI, Álvarez-Twose I, Jara-Acevedo M, Henriques A, Viñas E, Prieto C, Sánchez-Muñoz L, Caldas C, Mayado A, Matito A, Dasilva-Freire N, Orfao A, García-Montero AC.* Blood. 2019 Aug 1;134(5):456-468. doi: 10.1182/blood.2018886507. PMID: 31151985 IF: 16.562 / D1
- **Fluorochrome choices for multi-color flow cytometry.** *Flores-Montero J, Kalina T, Corral-Mateos A, Sanoja-Flores L, Pérez-Andrés M, Martin-Ayuso M, Sedek L, Rejlova K, Mayado A, Fernández P, van der Velden V, Bottcher S, van Dongen JJM, Orfao A.* J Immunol Methods. 2019 Jun 7. pii: S0022-1759(19)30132-2. doi: 10.1016/j.jim.2019.06.009. PMID: 31181212 IF: 1.913 / Q3
- **Impact of blood storage and sample handling on quality of high dimensional flow cytometric data in multicenter clinical research.** *Diks AM, Bonroy C, Teodosio C, Groenland RJ, de Mooij B, de Maertelaere E, Neirynck J, Philippé J, Orfao A, van Dongen JJM, Berkowska MA.* J Immunol Methods. 2019 Jun 7. pii: S0022-1759(19)30114-0. doi: 10.1016/j.jim.2019.06.007. PMID: 31181213 IF: 1.913 / Q3
- **Standardized Minimal Residual Disease Detection by Next-Generation Sequencing in Multiple Myeloma.** *Yao Q, Bai Y, Orfao A* Chim CS. Front Oncol. 2019 Jun 6;9:449. doi: 10.3389/fonc.2019.00449. eCollection 2019. PMID: 31245284 IF: 4.137 / Q1
- **EuroFlow-Based Flowcytometric Diagnostic Screening and Classification of Primary Immunodeficiencies of the Lymphoid System.** *van Dongen JJM, van der Burg M, Kalina T, Perez-Andres M, Mejstrikova E, Vlkova M, Lopez-Granados E, Wentink M, Kienzler AK, Philippé J, Sousa AE, van Zelm MC, Blanco E, Orfao A.* Front Immunol. 2019 Jun 13;10:1271. doi: 10.3389/fimmu.2019.01271. eCollection 2019. PMID: 31263462 IF: 4.716 / Q1
- **From big flow cytometry datasets to smart diagnostic strategies: The EuroFlow approach.** *Pedreira CE, Costa ESD, Lecrevise Q, Grigore G, Fluxa R, Verde J, Hernandez J, van Dongen JJM, Orfao A; EuroFlow.* J Immunol Methods. 2019 Jul 12:112631. doi: 10.1016/j.jim.2019.07.003. Review. PMID: 31306640 IF: 1.913 / Q3
- **Molecular profiling refines minimal residual disease-based prognostic assessment in adults with Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia.** *Ribera J, Zamora L, Morgades M, Vives S, Granada I, Montesinos P, Gómez-Seguí I, Mercadal S, Guàrdia R, Nomdedeu J, Pratcorona M, Tormo M, Martínez-Lopez J, Hernández-Rivas JM, Ciudad J, Orfao A, González-Campos J, Barba P, Escoda L, Esteve J, Genescà E, Solé F, Feliu E, Ribera JM; Spanish PETHEMA Group; Spanish Society of Hematology.* Genes Chromosomes Cancer. 2019 Nov;58(11):815-819. doi: 10.1002/gcc.22788. PMID: 31340073 IF: 2.940 / Q2



PFS and OS curves of the variables with independent prognostic value in the multivariate analysis. PFS (left panels) and OS (right panels) curves of ISM patients grouped according to the KIT D816V allele frequency in the BM (A), sb2M levels (B), and the presence vs absence of pathogenic variants in the A/R/D gene panel with VAFs $ 30% (C).

- **A decision-tree approach for the differential diagnosis of chronic lymphoid leukemias and peripheral B-cell lymphomas.** *Moraes LO, Pedreira CE, Barrena S, Lopez A, Orfao A.* **Comput Methods Programs Biomed. 2019 Sep;178:85-90. doi: 10.1016/j.cmpb.2019.06.014.** PMID: 31416565 **IF: 3.424 / Q1**

- **EuroFlow Lymphoid Screening Tube (LST) data base for automated identification of blood lymphocyte subsets.** *Flores-Montero J, Grigore G, Fluxá R, Hernández J, Fernandez P, Almeida J, Muñoz N, Böttcher S, Sedek L, van der Velden V, Barrena S, Hernández A, Paiva B, Lecrevisse Q, Lima M, Santos AH, van Dongen JJM, Orfao A.* **J Immunol Methods. 2019 Aug 24:112662. doi: 10.1016/j.jim.2019.112662.** PMID: 31454495 **IF: 1.913 / Q3**

- **Discovery of an autoantibody signature for the early diagnosis of knee osteoarthritis: data from the Osteoarthritis Initiative.** *Camacho-Encina M, Balboa-Barreiro V, Rego-Perez I, Picchi F, VanDuin J, Qiu J, Fuentes M, Oreiro N, LaBaer J, Ruiz-Romero C, Blanco FJ.* **Ann Rheum Dis. 2019 Aug 30. pii: annrheumdis-2019-215325. doi: 10.1136/annrheumdis-2019-215325.** PMID: 31471297 **IF: 14.299 / D1**

- **MARS: Mutation-Adjusted Risk Score for Advanced Systemic Mastocytosis.** *Jawhar M, Schwaab J, Álvarez-Twose I, Shoumariyeh K, Naumann N, Lübke J, Perkins C, Muñoz-González JI, Meggendorfer M, Kennedy V, Metzgeroth G, Fabarius A, Pfeifer D, Sotlar K, Horny HP, von Bubnoff N, Haferlach T, Cross NCP, Hofmann WK, Sperr WR, García-Montero AC, Valent P, Gotlib J, Orfao A, Reiter A.* **J Clin Oncol. 2019 Sep 11:JCO1900640. doi: 10.1200/JCO.19.00640.** PMID: 31509472 **IF: 28.245 / D1**

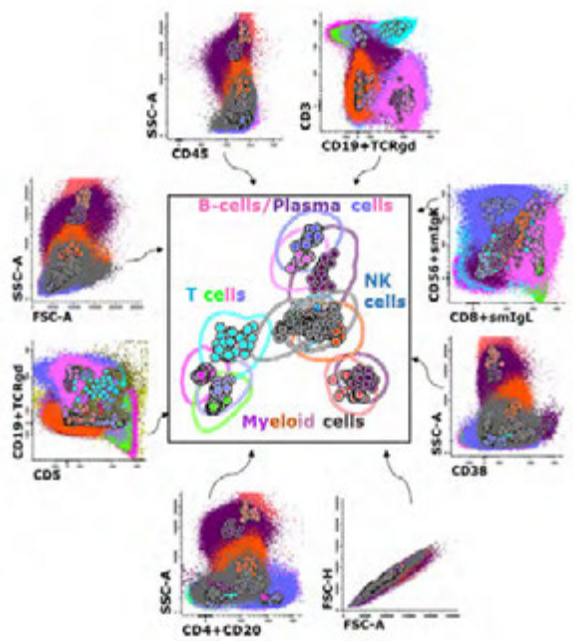
- **Systemic mastocytosis associated with myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis: report of three cases.** *Mimiola E, Bomben R, De Matteis G, Perbellini O, Guglielmelli P, Bonifacio M, Parisi A, Gattei V, Zamò A, Mannelli F, García Montero AC, Zanotti R.* **Hematol Oncol. 2019 Sep 16. doi: 10.1002/hon.2680.** PMID: 31523839 **IF: 3.493 / Q3**

- **Unique clinico-biological, genetic and prognostic features of adult early T cell precursor acute lymphoblastic leukemia.** *Genescà E, Morgades M, Montesinos P, Barba P, Gil C, Guàrdia R, Moreno MJ, Martínez-Carballeira D, García-Cadenas I, Vives S, Ribera J, González-Campos J, González-Gil C, Zamora L, Ramírez JL, Díaz-Beya M, Mercadal S, Artola MT, Cladera A, Tormo M, Bermúdez A, Vall-Llovera F, Martínez P, Amigo ML, Monsalvo S, Novo A, Cervera M, García-Guiñon A, Juncà J, Ciudad J, Orfao A, Ribera JM.* **Haematologica. 2019 Sep 19. pii: haematol.2019.225078. doi: 10.3324/haematol.2019.225078.** PMID: 31537688 **IF: 7.570 / D1**

- **Interactions of Nanoparticles and Biosystems: Microenvironment of Nanoparticles and Biomolecules in Nanomedicine.** *Auría-Soro C, Nesma T, Juanes-Velasco P, Landeira-Viñuela A, Fidalgo-Gómez H, Acebes-Fernandez V, Gongora R, Almendral Parra MJ, Manzano-Roman R, Fuentes M.* **Nanomaterials (Basel). 2019 Sep 24;9(10). pii: E1365. doi: 10.3390/nano9101365. Review.** PMID: 31554176 **IF: 4.034 / Q1**

- **Transcriptional profiling of circulating tumor cells in multiple myeloma: a new model to understand disease dissemination.** *Garcés JJ, Simicek M, Vicari M, Brozova L, Burgos L, Bezdekova R, Alignani D, Calasanz MJ, Growkova K, Goicoechea I, Agirre X, Pour L, Prosper F, Rios R, Martínez-Lopez J, Millacoy P, Palomera L, Del Orbe R, Perez-Montaña A, Garate S, Blanco L, Lasa M, Maiso P, Flores-Montero J, Sanoja-Flores L, Chyra Z, Vdovin A, Sevcikova T, Jelinek T, Botta C, El Omri H, Keats J, Orfao A, Hajek R, San-Miguel JF, Paiva B.* **Leukemia. 2020 Feb;34(2):589-603. doi: 10.1038/s41375-019-0588-4.** PMID: 31595039 **IF: 9.944 / D1**

- **Guidelines for the use of flow cytometry and cell sorting in immunological studies (second edition).** *Cossarizza A, Chang HD, Radbruch A, Acs A, Adam D, Adam-Klages S, Agace WW, Aghaeepour N, Akdis M, Allez M, Almeida LN, Alvisi G, Anderson G, Andrä I, Annunziato F, Anselmo A, Bacher P, Baldari CT, Bari S, Barnaba V, Barros-Martins J, Battistini L, Bauer W, Baumgart S, Baumgarth N, Baumjohann D, Baying B, Bebawy M, Becher B, Beisker W, Benes V, Beyaert R, Blanco A, Boardman DA, Bogdan C, Borger JG, Borsellino G, Boulais PE, Bradford JA, Brenner D, Brinkman RR, Brooks AES, Busch DH, Büscher M, Bushnell TP, Calzetti F, Cameron G, Cammarata I, Cao X, Cardell SL, Casola S, Cassatella MA, Cavani A, Celada A, Chatenoud L, Chattopadhyay PK, Chow S, Christakou E, Čičin-Šain L, Clerici M, Colombo FS, Cook L, Cooke A, Cooper AM, Corbett AJ, Cosma A, Cosmi L, Coulie PG, Cumano A, Cvetkovic L, Dang VD, Dang-Heine C, Davey MS, Davies D, De Biasi S, Del Zotto G, Dela Cruz GV, Delacher M, Della Bella S, Dellabona P, Deniz G, Dessing M, Di Santo JP,*



Schematic representation of merged reference data files included in the LST-PB (Lymphocyte Screening Tube – Peripheral Blood) data base for advanced flow cytometry analyses. Every color represents a different cell population of lymphoid and myeloid cells as color coded in the text inside the central plot (Flores-Montero et al, JIM 2019).

Diefenbach A, Dieli F, Dolf A, Dörner T, Dress RJ, Dudziak D, Dustin M, Dutertre CA, Ebner F, Eckle SBG, Edinger M, Eede P, Ehrhardt GRA, Eich M, Engel P, Engelhardt B, Erdei A, Esser C, Everts B, Evrard M, Falk CS, Fehniger TA, Felipo-Benavent M, Ferry H, Feuerer M, Filby A, Filkor K, Fillatreau S, Follo M, Förster I, Foster J, Foulds GA, Frehse B, Frenette PS, Frischbutter S, Fritzsche W, Galbraith DW, Gangaev A, Garbi N, Gaudilliere B, Gazzinelli RT, Geginat J, Gerner W, Gherardin NA, Ghoreschi K, Gibellini L, Ginhoux F, Goda K, Godfrey DI, Goettlinger C, González-Navajas JM, Goodyear CS, Gori A, Grogan JL, Grummitt D, Grützkau A, Haftmann C, Hahn J, Hammad H, Hämmerling G, Hansmann L, Hansson G, Harpur CM, Hartmann S, Hauser A, Hauser AE, Haviland DL, Hedley D, Hernández DC, Herrera G, Herrmann M, Hess C, Höfer T, Hoffmann P, Hogquist K, Holland T, Höllt T, Holmdahl R, Hombrink P, Houston JP, Hoyer BF, Huang B, Huang FP, Huber JE, Huehn J, Hundemer M, Hunter CA, Hwang WYK, Iannone A, Ingelfinger F, Ivison SM, Jäck HM, Jani PK, Jávega B, Jonjic S, Kaiser T, Kalina T, Kamradt T, Kaufmann SHE, Keller B, Ketelaars SLC, Khalilnezhad A, Khan S, Kisielow J, Klenerman P, Knopf J, Koay HF, Kobow K, Kolls JK, Kong WT, Kopf M, Korn T, Kriegsmann K, Kristyanto H, Kroneis T, Krueger A, Kühne J, Kukat C, Kunkel D, Kunze-Schumacher H, Kurosaki T, Kurts C, Kvistborg P, Kwok I, Landry J, Lantz O, Lanuti P, LaRosa F, Lehuen A, LeibundGut-Landmann S, Leipold MD, Leung LYT, Levings MK, Lino AC, Liotta F, Litwin V, Liu Y, Ljunggren HG, Lohoff M, Lombardi G, Lopez L, López-Botet M, Lovett-Racke AE, Lubberts E, Luche H, Ludewig B, Lugli E, Lunemann S, Maecker HT, Maggi L, Maguire O, Mair F, Mair KH, Mantovani A, Manz RA, Marshall AJ, Martínez-Romero A, Martrus G, Marventano I, Maslinski W, Matarese G, Mattioli AV, Maueröder C, Mazzoni A, McCluskey J, McGrath M, McGuire HM, McInnes IB, Mei HE, Melchers F, Melzer S, Mielenz D, Miller SD, Mills KHG, Minderman H, Mjösberg J, Moore J, Moran B, Moretta L, Mosmann TR, Müller S, Multhoff G, Muñoz LE, Münz C, Nakayama T, Nasi M, Neumann K, Ng LG, Niedobitek A, Nourshargh S, Núñez G, O'Connor JE, Ochel A, Oja A, Ordonez D, Orfao A, Orlowski-Oliver E, Ouyang W, Oxenius A, Palankar R, Panse I, Pattanapanyasat K, Paulsen M, Pavlinic D, Penter L, Peterson P, Peth C, Petriz J, Piancone F, Pickl WF, Piconese S, Pinti M, Pockley AG, Podolska MJ, Poon Z, Pracht K, Prinz I, Pucillo CEM, Quataert SA, Quatrini L, Quinn KM, Radbruch H, Radstake TRDJ, Rahmig S, Rahn HP, Rajwa B, Ravichandran G, Raz Y, Rebhahn JA, Recktenwald D, Reimer D, Reis E Sousa C, Remmerswaal EBM, Richter L, Rico LG, Riddell A, Rieger AM, Robinson JP, Romagnani C, Rubartelli A, Ruland J, Saalmüller A, Saeys Y, Saito T, Sakaguchi S, Sala-de-Oyanguren F, Samstag Y, Sanderson S, Sandrock I, Santoni A, Sanz RB, Saresella M, Sautes-Fridman C, Sawitzki B, Schadt L, Scheffold A, Scherer HU, Schiemann M, Schildberg FA, Schimisky E, Schlitzer A, Schlosser J, Schmid S, Schmitt S, Schober K, Schraivogel D, Schuh W, Schüler T, Schulte R, Schulz AR, Schulz SR, Scottá C, Scott-Algara D, Sester DP, Shankey TV, Silva-Santos B, Simon AK, Sitnik KM, Sozzani S, Speiser DE, Spidlen J, Stahlberg A, Stall AM, Stanley N, Stark R, Stehle C, Steinmetz T, Stockinger H, Takahama Y, Takeda K, Tan L, Tárnok A, Tiegs G, Toldi G, Tornack J, Traggiai E, Trebak M, Tree TIM, Trotter J, Trowsdale J, Tsoumakidou M, Ulrich H, Urbanczyk S, van de Veen W, van den Broek M, van der Pol E, Van Gassen S, Van Isterdael G, van Lier RAW, Veldhoen M, Vento-Asturias S, Vieira P, Voehringer D, Volk HD, von Borstel A, von Volkmann K, Waisman A, Walker RV, Wallace PK, Wang SA, Wang XM, Ward MD, Ward-Hartstonge KA, Warnatz K, Warnes G, Warth S, Waskow C, Watson JV, Watzl C, Wegener L, Weisenburger T, Wiedemann A, Wienands J, Wilharm A, Wilkinson RJ, Willimsky G, Wing JB, Winkelmann R, Winkler TH, Wirz OF, Wong A, Wurst P, Yang JHM, Yang J, Yazdanbakhsh M, Yu L, Yue A, Zhang H, Zhao Y, Ziegler SM, Zielinski C, Zimmermann J, Zychlinsky A. **Eur J Immunol. 2019 Oct;49(10):1457-1973. doi: 10.1002/eji.201970107.** PMID: 31633216 **IF: 4.695 / Q1**

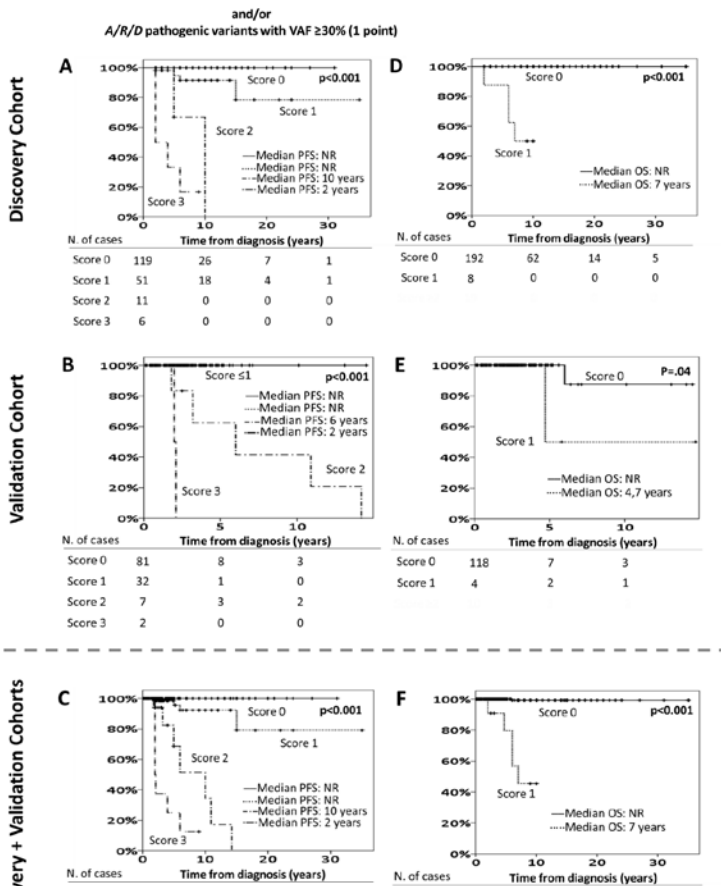
- **Comments on EuroFlow standard operating procedures for instrument setup and compensation for BD FACS Canto II, Navios and BD FACS Lyric instruments.** *Glier H, Novakova M, Te Marvelde J, Bijkerk A, Morf D, Thurner D, Rejlova K, Lange S, Finke J, van der Sluijs-Gelling A, Sedek L, Flores-Montero J, Böttcher S, Fernandez P, Ritgen M, van Dongen JJM, Orfao A, van der Velden VHJ, Kalina T.* **J Immunol Methods. 2019 Dec;475:112680. doi: 10.1016/j.jim.2019.112680.** PMID: 31655051 **IF: 1.913 / Q3**
- **International prognostic scoring system for mastocytosis (IPSM): a retrospective cohort study.** *Sperr WR, Kundi M, Alvarez-Twose I, van Anrooij B, Oude Elberink JNG, Gorska A, Niedoszytko M, Gleixner KV, Hadzijusufovic E, Zanotti R, Bonadonna P, Bonifacio M, Perkins C, Illerhaus A, Elena C, Merante S, Shoumariyeh K, von Bubnoff N, Parente R, Jawhar M, Belloni Fortina A, Caroppo F, Brockow K, Zink A, Fuchs D, Kilbertus AJ, Yavuz AS, Doubek M, Hägglund H, Panse J, Sabato V, Bretterklieber A, Niederwieser D, Breynaert C, Hartmann K, Triggiani M, Nedoszytko B, Reiter A, Orfao A, Hermine O, Gotlib J, Arock M, Kluin-Nelemans HC, Valent P.* **Lancet Haematol. 2019 Dec; 6(12):e638-e649. doi: 10.1016/S2352-3026(19)30166-8.** PMID: 31676322 **IF: 11.990 / Q1**
- **Immunophenotypic dissection of normal hematopoiesis.** *Orfao A, Matarraz S, Pérez-Andrés M, Almeida J, Teodosio C, Berkowska MA, van Dongen JJM; EuroFlow.* **J Immunol Methods. 2019 Dec;475:112684. doi: 10.1016/j.jim.2019.112684.** PMID: 31676343 **IF: 1.913 / Q3**
- **Blood monitoring of circulating tumor plasma cells by next generation flow in multiple myeloma after therapy.** *Sanoja-Flores L, Flores-Montero J, Puig N, Contreras-Sanfeliciano T, Pontes R, Corral-Mateos A, García-Sánchez O, Díez-Campelo M, Pessoa de Magalhães RJ, García-Martín L, Alonso-Alonso JM, García-Mateo A, Aguilar-Franco C, Labrador J, Barez-García A, Maiolino A, Paiva B, San Miguel J, Sobral da Costa E, González M, Mateos MV, Durie B, van Dongen JJM, Orfao A.* **Blood. 2019 Dec 12; 134(24):2218-2222. doi: 10.1182/blood.2019002610.** PMID: 31697808 **IF: 16.562 / D1**
- **CD Maps-Dynamic Profiling of CD1-CD100 Surface Expression on Human Leukocyte and Lymphocyte Subsets.** *Kalina T, Fišer K, Pérez-Andrés M, Kuzílková D, Cuenca M, Bartol SJW, Blanco E, Engel P, van Zelm MC.* **Front Immunol. 2019 Oct 23;10:2434. doi: 10.3389/fimmu.2019.02434. eCollection 2019.** PMID: 31708916 **IF: 4.716 / Q1**
- **High frequency of chronic lymphocytic leukemia-like low-count monoclonal B-cell lymphocytosis in Japanese descendants living in Brazil.** *de Faria-Moss M, Yamamoto M, Arrais-Rodrigues C, Criado I, Perez-Gómez C, Chauffaille ML, Gonçalves MV, Kimura E, Koulieris E, Borges F, Dighiero G, Bosco-Pesquero J, Almeida J, Orfao A.* **Haematologica. 2019 Nov 14. pii: haematol.2019.230813. doi: 10.3324/haematol.2019.230813.** PMID: 31727770 **IF: 7.570 / D1**
- **EuroFlow and its activities: Introduction to the special EuroFlow issue of The Journal of Immunological Methods.** *van Dongen JJM, O'Gorman MRG, Orfao A.* **J Immunol Methods. 2019 Dec;475:112704. doi: 10.1016/j.jim.2019.112704.** PMID: 31758969 **IF: 1.913 / Q3**
- **Measurable Residual Disease by Next-Generation Flow Cytometry in Multiple Myeloma.** *Paiva B, Puig N, Cedena MT, Rosiñol L, Cordón L, Vidriales MB, Burgos L, Flores-*

Montero J, Sanoja-Flores L, Lopez-Anglada L, Maldonado R, de la Cruz J, Gutiérrez NC, Calasanz MJ, Martin-Ramos ML, García-Sanz R, Martínez-Lopez J, Oriol A, Blanchard MJ, Rios R, Martin J, Martínez-Martínez R, Sureda A, Hernandez MT, de la Rubia J, Krsnik I, Moraleda JM, Palomera L, Bargay J, Van Dongen JJM, Orfao A, Mateos MV, Blade J, San-Miguel JF, Lahuerta JJ; GEM (Grupo Español de Mieloma)/PETHEMA (Programa Para el Estudio de la Terapéutica en Hemopatías Malignas) Cooperative Study Group. **J Clin Oncol. 2019 Nov 26:JCO1901231. doi: 10.1200/JCO.19.01231.** PMID: 31770060 **IF: 28.245 / D1**

- **Complete Multilineage CD4 Expression Defect Associated With Warts Due to an Inherited Homozygous CD4 Gene Mutation.** *Fernandes RA, Perez-Andres M, Blanco E, Jara-Acevedo M, Criado I, Almeida J, Botafogo V, Coutinho I, Paiva A, van Dongen JJM, Orfao A, Faria E.* **Front Immunol. 2019 Nov 8;10:2502. doi: 10.3389/fimmu.2019.02502. eCollection 2019.** PMID: 31781092 **IF: 4.716 / Q1**
- **Infectious stimuli promote malignant B-cell acute lymphoblastic leukemia in the absence of AID.** *Rodríguez-Hernández G, Opitz FV, Delgado P, Walter C, Álvarez-Prado ÁF, González-Herrero I, Auer F, Fischer U, Janssen S, Bartenhagen C, Raboso-Gallego J, Casado-García A, Orfao A, Blanco O, Alonso-López D, Rivas JL, Tena-Dávila SG, Müschen M, Dugas M, Criado FJG, Cenador MBG, Vicente-Dueñas C, Hauer J, Ramiro AR, Sánchez-García I, Borkhardt A.* **Nat Commun. 2019 Dec 5;10(1):5563. doi: 10.1038/s41467-019-13570-y.** PMID: 31804490 **IF: 11.878 / Q1**
- **Monozygotic Twins Concordant for Common Variable Immunodeficiency: Strikingly Similar Clinical and Immune.** *Silva SL, Fonseca M, Pereira MLM, Silva SP, Barbosa RR, Serra-Caetano A, Blanco E, Rosmaninho P, Pérez-Andrés M, Sousa AB, Raposo AASF, Gama-Carvalho M, Victorino RMM, Hammarstrom L, Sousa AE.* **Front Immunol. 2019 Nov 22;10:2503. doi: 10.3389/fimmu.2019.02503. eCollection 2019.** PMID: 31824477 **IF: 4.716 / Q1**
- **Delineating Human B Cell Precursor Development With Genetically Identified PID Cases as a Model.** *Wentink MWJ, Kalina T, Perez-Andres M, Del Pino Molina L, IJspeert H, Kavelaars FG, Lankester AC, Lecrevisse Q, van Dongen JJM, Orfao A, van der Burg M.* **Front Immunol. 2019 Nov 26;10:2680. doi: 10.3389/fimmu.2019.02680. eCollection 2019.** PMID: 31849931 **IF: 4.716 / Q1**

OTHER PUBLICATIONS & BOOK CHAPTERS

- **Disección inmunofenotípica de la hematopoyesis normal.** **En: "Diagnóstico y monitorización inmunofenotípica de las neoplasias leucocitarias"** *Orfao A, Matarraz S, Perez-Andres M, Almeida J*:. Muñoz Calleja C y Minguela Puras A (eds). Elsevier, Barcelona (España); 1-14, 2018.



PFS and OS curves of ISM patients, grouped according to the proposed scoring systems, for the discovery and/or the validation patient cohorts. Scoring systems for PFS (A,C,E) and OS (B,D,F) are based on (1) the combination of sb2M levels at diagnosis (score 1 when $ 2.5 mg/mL), and/or the KIT D816V VAF in BM (score 1 when $1%), and/or pathogenic variants in the A/R/D gene panel with VAF$30% (score 1 when$1 mutation with VAF$30% in any of these 3 genes) (A,C,E) and (2) pathogenic variants in the A/R/D gene panel with VAF $ 30% (score 1 if there was a mutation in any of these 3 genes with VAF $ 30%) (B,D,F). Please note that all patients who scored 1 in (A) had multilineage involvement of BM hematopoiesis by the KIT mutation with sb2M levels , 2.5 mg/mL. NR, not reached.

PATENTS

PATENT REFERENCE	TITLE	INVENTORS	PRIORITY DATE
15/849,233	Methods, Reagents and Kits for Flow Cytometric Immunophenotyping	Jacobus Johannes, María van Dongen, José Alberto Orfao de Matos Correia e Vale, Juan Alejandro Flores Montero, Julia María Almeida Parra, Vincent Henricus Johannes van der Velden, Sebastian Böttcher, Andrew Craig Rawstron, Ruth Mary de Tute, Ludovic Bernard Simon Lhermitte, Vahid Asnafi, Ester Mejstríková, Tomasz Szczepanski, Paulo Jorge Monteiro Da Silva Lucio, Marta Martin Ayuso, Carlos Eduardo Pedreira.	28/06/2018
15/618,437	Method of Digital Information Classification	Rafael Fluxá Rodríguez, José Alberto Orfao de Matos Correia E Vale, Juan Bernardo Hernández Herrero.	28/06/2018
15/812,384	Methods, Reagents and Kits for Detecting Minimal Residual Disease	Jacobus Johannes María van Dongen, José Alberto Orfao de Matos Correia e Vale,Juan Alejandro Flores Montero,Julia María Almeida Parra, Vincent Henricus Johannes van der Velden, Sebastian Böttcher, Anthonie Willem Langerak, Ester Mejstríková, Tomasz Szczepanski, Paulo Jorge Monteiro Da Silva Lucio, Matthias Ritgen.	24/05/2018
EP 1367.84	One Step Phagocytosis-cell activation-cell death assay (PAD-Assay)	Manuel Fuentes García, Paula Díez García, Cristina Isabel Gonzalvez Ghruno Teodosio, Jose Alberto Orfao de Matos, Ricardo Jara Acevedo	05/07/2018
201930619	Dispositivo y procedimiento para la liofilización simultánea de una pluralidad de muestras biológicas	Andrés García- Montero, Alberto Orfao de Matos Correia e Vale, Francisco Javier García Palomo, Catia Daniela Quintas Faria, Roberto José García Martin, María Pérez-Caro.	04/07/2019
119646NL00	Means and methods for multiparameter cytometry-based leukocyte subsetting	Jacques J.M. van Dongen, Alberto Orfao de Matos Correia e Vale, Cristina Isabel Gonçalves Grunho Teodosio, Martin Perez-Andres, Julia María Almeida Parra, Wouter Bernard Louis Van den Bossche, Vitor Dessanti Botafogo Gonçalves, Magdalena Agnieska Berkowska, Kyra van der Pan, Elena Blanco Alvarez, Annieck Margo Dicks, Daniela Pinto Damasceno, Alejandro Hernández Delgado	18/11/2019

GRANTS FOR RESEARCH IN PROGRESS

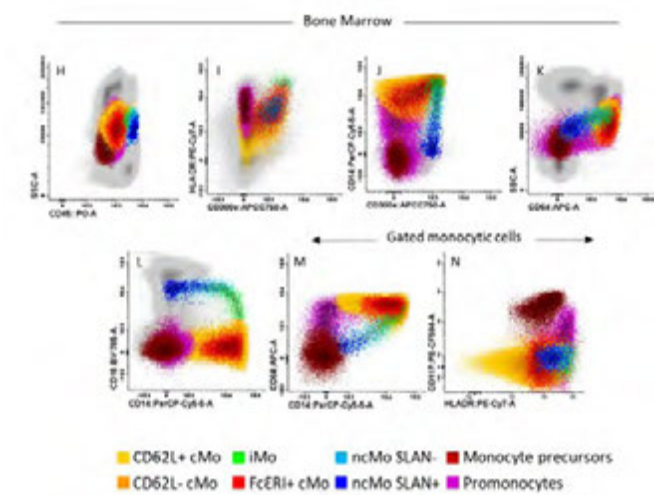
PROJECT	PI	GRANT	TIME	FUNDING
Recursos Biomoleculares y Bioinformáticos (PRB2-ISCIII; PT13/0001/0003)	Manuel Fuentes García	Carlos III Health Institute	2014-2018	184,481.00 €
Automated multidimensional flow cytometry for high-sensitive screening and to monitor response in AL amyloidosis	Alberto Orfao	International Myeloma Foundation USA	2015-2018	40,800.00 €
Automated, highly sensitive flow cytometry method for standardized detection of minimal residual disease in multiple myeloma	Alberto Orfao	International Myeloma Foundation USA	2015-2018	40,000.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Diseño y validación de un algoritmo genético para predecir la transformación maligna de mastocitosis indolentes a formas agresivas y otras hemopatías malignas (SA013U16)	Alberto Orfao	Regional Government of Castilla and León	2016-2018	120,000.00 €
AUTOMATISMO: automatización de fases pre-analíticas, analíticas y post-analíticas en citometría de flujo para ayuda en la toma de decisiones del experto en citometría (AEESD-IT de la Acción Estratégica de Economía y Sociedad Digital-Impulso Tecnológico. Cytognos / USAL)	Alberto Orfao	Spanish Ministry of Economy and Competitiveness	2016-2019	609,433.00 €
Desarrollo de una plataforma de software para gestión análisis y representación de datos provenientes de diferentes fuentes con aplicación a datos relevantes para el diagnóstico de enfermedades-MIDAS (Massive Information Data Analysis Software (RTC-2016-4865-1 RETOS de la Sociedad de la Acción Estratégica de Economía y Sociedad Digital-Impulso Tecnológico Cytognos/USAL)	Alberto Orfao	Spanish Ministry of Economy and Competitiveness	2016-2019	114,350.00 €
Identification of circulating tumor plasma cells in peripheral blood of multiple myeloma vs MGUS: clinical impact and implications in disease behavior	Alberto Orfao	International Myeloma Foundation USA	2016-2019	105,600.00 €
CYTOPREP: Metodología innovadora para el procesamiento de muestras en estudios multiparamétricos por citometría de flujo en el laboratorio clínico (RTC-2016-4707-1 RETOS de la Sociedad de la Acción Estratégica de Economía y Sociedad Digital-Impulso Tecnológico Inmunostep SL/USAL)	Alberto Orfao	Spanish Ministry of Economy and Competitiveness	2016-2019	111,393.00 €
PERISCOPE: PERtussIS Correlates of Protection Europe" (Innovative Medicines Initiative, de la Unión Europea en colaboración con la Fundación Bill y Melinda Gates)	Alberto Orfao	European Union	2016-2021	547,500.00 €
Diseño, evaluación técnica y validación clínica de un método de nueva generación para monitorización de enfermedad mínima residual en médula ósea y sangre en leucemias agudas (PI16/00787)	Alberto Orfao	Carlos III Health Institute	2017-2019	212,052.00 €
Identificación de las alteraciones genéticas asociadas a la actividad oncogénica de la mutación D816V de KIT en neoplasias mieloides: la mastocitosis sistémica como modelo de estudio de la transformación maligna" (PI16/00642)	Andrés C. García Montero	Carlos III Health Institute	2017-2020	122,815.00 €
Diseño y desarrollo de novedosas estrategias proteómicas de base nanotecnológica para la evaluación del inmuno tumoral (FS/38-2017)	Manuel Fuentes García	Solórzano Foundation	2018	2,715,35 €
Análisis del transcriptoma y variabilidad genética de pacientes con LLC-B con distinto estado mutacional IGVH y diferente hidrofobicidad de la cadena peptídica de la región CDR3 del receptor BCR: implicaciones en la ontopatogenia y el pronóstico de la enfermedad (FS/37-2018)	Aránzazu Rodríguez Caballero	Solórzano Foundation	2018	3,394.19 €
Center of Biomedical Research on Cancer (CIBERONC) (CB16/12/00400)	Alberto Orfao	Carlos III Health Institute	2018-2019	127,300.00 €
Plataforma de recursos biomoleculares, PRB3 (PT17/0019/0023)	Manuel Fuentes García	Carlos III Health Institute	2018-2020	123,750.00 €
Identificación de factores involucrados en la ontopatogenia de la leucemia linfática crónica y de parámetros asociados a riesgo de transformación maligna en fases preleucémicas (PI17/00399)	Julia Mª Almeida Parra	Carlos III Health Institute	2018-2020	112,530.00 €

PROJECT	PI	GRANT	TIME	FUNDING
INCAR: Innovative CAR Therapy Platforms (AECC-Accelerator Award call)	Alberto Orfao	Spanish Association against Cancer Foundation (FCAECC)	2018-2023	963,418.97 €
Early Cancer Research Initiative Network on MBL (ECRIN-M3) (AECC-Accelerator Award call)	Alberto Orfao	Spanish Association against Cancer Foundation (FCAECC)	2018-2023	1,565,659.00 €
Identificación de los cambios en los perfiles de la respuesta inmune en pacientes con adenocarcinoma ductal de páncreas y sus implicaciones en el tratamiento de la enfermedad (FS/22-2018)	María Laura Gutiérrez Troncoso	Solórzano Foundation	2019	2,000.00 €
Caracterización inmunofenotípica y molecular de los síndromes de actividad mastocitaria: identificación de marcadores que mejoren el diagnóstico y la estratificación pronóstica de los pacientes	Alberto Orfao	Spanish Association of Mastocitosis	2019-2020	10,000.00 €
Red Transfronteriza de Innovación en Diagnóstico Precoz de Leucemia para un envejecimiento saludable (IDIAL_NET) (0639_ IDIAL_NET_3_E)	Alberto Orfao	POCTEP Program –Interreg (European Union)	2019-2021	559,545.00 €
Monitorización simultánea de células leucémicas y del sistema inmune circulantes en leucemia aguda linfoblástica de precursores B del adulto mediante NGF de >25 colores: impacto pronóstico (PI19/01183)	Alberto Orfao	Carlos III Health Institute	2020-2022	309,457.50 €
Modulación de la respuesta del sistema inmune en mastocitosis sistémica: papel del micro-medioambiente celular y potencial asociación a la progresión clínica de la enfermedad (PI19/01166)	Andrés C. García Montero	Carlos III Health Institute	2020-2022	98,010.00 €
Desarrollo de un prototipo de sistema multiplex por citometría de flujo para un novedoso diagnóstico etiopatogénico multiparamétrico del daño renal agudo (DTS 15/000166)	Manuel Fuentes García	Carlos III Health Institute		96,918.00 €

OTHER ACTIVITIES & RELEVANT FACTS

- Evaluación "Outstanding" de la actividad investigadora desarrollada en el periodo 2014-2018 como Investigador Principal de uno de los grupos de investigación adscritos al Centro de Investigación del Cáncer de la Universidad de Salamanca/Consejo Superior de Investigaciones Científicas (CIC), por parte del Comité Científico Externo del CIC.
- Pereira da Silva JA, Reis F, Pereira A, Matos S, Caseiro Alves F, Gonçalves L, Barbosa de Melo J, Mota Pinto A, **Orfao A**, da Silva Martins AP, Madama D, Carvalho A: Planeamento estratégico 19/24. Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal, 2018.
- "Internacionalización". Programa de Alta Dirección de Instituciones de Investigación, Innovación y Transferencia (PADIIT). IESE Business School con la colaboración de la Fundación Gadea para la Ciencia. Madrid, Junio de 2019.
- **ORFAO A,** BENITEZ J, CORRALES F, MARTIN-SUBERO JI, ORDOVAS JM: Ciencias Ómicas. Informes Anticipando, Observatorio de Medicina Personalizada de Precisión, Instituto Roche, Madrid, diciembre de 2019; pp:1-30.



Identification of different subsets of circulating monocytes in representative bone marrow samples from a healthy donor (Damasceno et al, JACI 2019).

Team leader

Marcos González Díaz

Phone: +34 923 294 812
+34 923 291 100 Ext: 55384 / 55942
E-mail: margondi@usal.es

Research team

Senior Researchers

Jesús María Hernández Rivas
Mercedes Garayoa Berrueta
Ramón García Sanz
Mª Dolores Caballero Barrigón
Mª Victoria Mateos Manteca
Fermín M. Sánchez-Guijo
Norma C. Gutiérrez Gutiérrez
Enrique M Ocio San Miguel
Juan Luis García Hernández
María Belén Vidríales Vicente
María Díez Campelo
Jose M. Bastida Bermejo
Jose Ramón González Porras
Lucía López Corral

Postdoctorals

Teresa Paíno Gómez
Noemí Puig Morón
Miguel Alcoceba Sánchez
Mª Eugenia Alonso Sarasquete
Mª Rocío Benito Sánchez
Verónica González de la Calle
Francisco Boix Giner
Mª Carmen Chillón Santos
Ignacio García Tuñón Llanio
Mª Teresa González Martínez
María Hernández Sánchez
Cristina Jiménez Sánchez
Patryk Krzeminski
Irena Misiewicz-Krzeminska
Sandra Muntión Olave
Lika Osugui
Silvia Preciado Pérez
José Luis Ordóñez García
Ana Eugenia Rodríguez Vicente
Mª Isabel Prieto Conde
Miriam Vilches Moreno
Mónica Del Rey González
María García Álvarez
Susana Hernández García
Kamila Janusz
Mª Isabel Prieto Conde
Luis Antonio Corchete Sánchez
Eva María Díez Baeza

Predoctorals

Macarena Algarín Pachón
Andrea Díaz Tejedor
Pedro Mogollón Arroyo
Eva Lumbreras González
Ana Marín Quilez
Marta Martín Izquierdo
Alejandro Medina Herrera
Adrián Montaño Brioso
Miguel Quijada Álamo
Dalia Salim Quwaider
Ana Rico Sorlí
Elizabeta Rojas Ricardo
Cristina de Ramón Sánchez
Ignacio Jesús Cardona Benavides
Gerardo Javier Martí Chillón
Claudia Pérez Carretero
Sofía María Toribio Castelló
Tamara Jiménez Solas

Office manager

María José Rodrigo Egido

Technicians

Laura San Segundo Payo
Alicia Antón Gómez
Estrella Arnés Moreta
Ana Balanzategui Echevarría
Ana Belén Díaz Martín
Leticia Gallo Melchor
Teresa García Montes
Lorena González Méndez
Montserrat Martín Sánchez
Sara González Briones
Vanesa Gutiérrez Moreta
Mª Ángeles Hernández García
Montserrat Hernández Ruano
Isabel María Isidro Hernández
Isabel Jiménez Hernaz
Rubén López Blanco
Sandra Lucas Sánchez
Rebeca Maldonado Sánchez
María Almudena Martín Martín
María José del Pozo Hernández
Mª Teresa Prieto Martín
Sandra Pujante Fernández
Mª Ángeles Ramos Rodríguez
Concepción Rodríguez Serrano
Irene Rodríguez Iglesias
Ana Isabel Sánchez
Ana Simón Muñoz
M. Pilar Terradillos Sánchez
Inmaculada Villares
Jhonatan Matias Martin
Cristina Casquero Hernández
Ana Gómez de la Torre
Armenteros

Master Students

Beatriz Benayas López
Darnel Marchena Mendoza
Alonso Rodríguez Pescador
Rocío Anahi Martínez
Sandra Santos Mínguez
Alejandro Crespo Carazo
Mauro Lorenzo Mohamed
María Matorra Miguel
Verónica Salgado Pacheco

Visiting Researchers

Silvia Martín
Irene Dogliotti
Paula Di Stilio
Barbara Strojny-Cieslak
Sharlene S. Santiago Díaz
Ruth Maribel Forero
Jayoung Lee

LABORATORY 12

ONCOHEMATOLOGY

The main characteristic of Prof González's group is the translational research, resulting from the interaction between laboratory 12 at the Cancer Research Center and Hematology Department of the University Hospital of Salamanca. This interaction has been very fruitful, not only because of the number of scientific publications, but also, because of the diagnostic and therapeutic advances for patients. Although the interest of the group involves all haematological malignancies, a special focus has been put on multiple myeloma (MM), acute myeloid leukemia (AML) / myelodisplastic syndromes (MDS) and chronic lymphoproliferative disorders (CLL) / lymphomas.

STRATEGIC OBJECTIVES

1. To deepen into the knowledge of the tumor clone through multiparametric studies (phenotypic, cytogenetic, molecular and functional) with the final goal of identifying novel prognostic markers.
2. Development of diagnostic tools applicable to clinical practice. Standardization and validation of Next Generation Sequencing and Next Generation Flow techniques to be implemented in routine therapeutic monitoring. Development of new-generation Multiplarameter Flow Cytometry and NGS, applicability for diagnosis and Minimal Residual Disease.
3. To evaluate potential antitumoral targets in order to design novel therapeutic strategies in the preclinical setting that could be quickly translated into the clinic.

MAIN LINES OF RESEARCH

The lines, based on the strategic objectives, are divided into four main research areas:

1. OncoHaematologic Molecular Cytogenetics.

- Molecular cytogenetics and genomic arrays in haematological malignancies.
- Analysis of the tumor transcriptome and exome.
- Study of the functional status of p53 in multiple myeloma and its impact on therapeutic response and patient survival.
- Investigation of RNA splicing and its regulation in multiple myeloma.
- Protein biomarker discovery and validation using capillary electrophoresis with immunoassay (ProteinSimple).

2. Molecular Biology and Immunopathology.

- Study of genomic expression and mutations in genes associated with cancer: clinico-biological correlations.
- Immunophenotypic and molecular markers for the detection of minimal residual disease.
- Analysis of genetic polymorphisms: role on etiopathogenesis and prognosis.
- Study of antigenic receptors for B & T lymphocytes: applications in the diagnosis and etiopathogenesis of lymphoproliferative disorders.

3. Cell Therapy and Transplantation.

- Study of hematopoiesis and bone marrow microenvironment in hematological disorders.
- Clinical investigation in haematopoietic transplantation. Novel procedures and complications.
- Analysis of extracellular Vesicles in haematological diseases and GVHD.

4. Novel Therapies in hematological malignancies.

- Preclinical development of targeted antitumor drugs and immunotherapies.
- Intrinsic and bone marrow microenvironment-mediated mechanisms of drug resistance.
- Phase I/II/III clinical trials with experimental agents.

ACHIEVED GOALS

Among the main achieved goals in the last years we can highlight: a) Our group has described the prognostic value of several cytogenetic and molecular abnormalities in MM, NHL, MDS or CLL, and we have also significantly contributed to the whole sequencing of the genome of CLL. b) Establishment of the prognostic impact of MRD by flow cytometry (International Reference). c) In the field of novel antitumoral drugs, our group has identified novel agents and combinations, which has allowed the leadership of our group in several clinical trials (phase I/II and phase III for registration), including participation in intenational clinical trials on CAR T-cells in both DLBCL and MM.

FUTURE CHALLENGES

- To deepen into the genomic mechanisms responsible for the development of haematological neoplasms and mechanisms of tansformation into a more aggressive disease. Evaluation of clonal heterogeneity and identification of the ancestor clonogenic cell.
- To identify and characterize the tumor stem cells and to gain further insights into the role of the tumour microenvironment.
- To analyze the mechanisms responsible for the development of drug-resistance.
- Analysis of new immunotherapeutic approaches: check-point inhibitors, *CAR (Chimeric Antigenic Receptor) T-cells and NK-cells, BAR (B-cell Antigenic Receptor) T-cells*.
- Identification of synthetic lethal vulnerabilities in multiple myeloma: construction of isogenic cell lines for *MMSET, c-MAF, MAFB* or *c-MYC* and genome-scale CRISPR-Cas9 knockout screening.

Jesús María Hernández Rivas
Phone.: +34 923 294 812
E-mail: jmhr@usal.es

SENIOR RESEARCHER

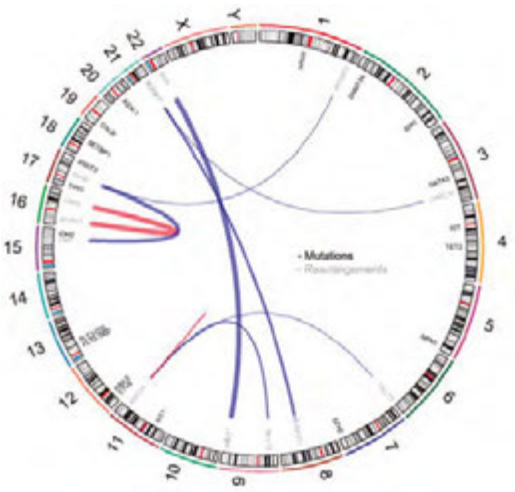
GENETICS IN ONCOHEMATOLOGY

This group is focused in the cytogenetic and molecular characterization of cancer. The scientific contribution of this line of research is competitive and internationally recognized. The **main lines of research** being develop are the following:

A) The comprehensive genomic analysis by integrating copy number variations, expression profiling by high-density microarrays and next generation sequencing of hematological malignancies.
B) The genomic and epigenomic studies on solid tumors.
C) Pharmacogenomics of new drugs used in cancer therapy.
D) Functional analysis by using CRISPR approaches.

The **future challenges** of the group will be the integration of data obtained on the differen research lines in order to provide a personalized medicine in cancer therapy. In addition, implementation of the new tools, including Next Generation Sequencing, and the translation to the clinical setting is a main goal of the group. More specifically, the future challenges are the following:

- To analyze the mechanisms responsible for the development of drug-resistance using high-throughput CRISPR/Cas9 technology
- Generation of new leukemia-derived cell lines and animal models harboring specific mutations and reproducing the genomic heterogeneity seen in hemotological malignancies, by using the CRISPR/Cas9 technology
- *In vitro* and *In vivo* assessment of CRISPR/Cas9 to the targeted cancer cells translating this tool for novel therapeutic approaches
- *To use Big Data* to deliver information that will help improve the care of patients with hematologic malignancies. This will be achieved by gathering, integrating and analyzing patient data from several high quality sources, thereby defining clinical endpoints and outcomes that will be assessed by all key stakeholders. This will facilitate and improve decision making for policy makers and physicians alike to help them choose the right treatment for the right patient at the right time.



Circos plot depicting the rearrangements and mutations found with the targeted-DNA capture next-generation sequencing (NGS) strategy [from Prieto-Conde MI *et al*. J Mol Diagn 2020 Jan;22(1):60-71. doi: 10.1016/j.jmoldx.2019.08.002.

Mercedes Garayoa Berrueta
Phone.: +34 923 295 812
E-mail: mgarayoa@usal.es

SENIOR RESEARCHER

BONE MARROW MICROENVIRONMENT IN MULTIPLE MYELOMA AND BONE LESIONS

Our group has focused on the study of the role of the bone marrow microenvironment in the pathogenesis of multiple myeloma (MM) and in the development of bone lesions associated to this disease. We have also been involved in preclinical studies of targeted agents with an anti-myeloma effect and/or being beneficial on osteolytic lesions. More recently, we are engaged in evaluating the mechanism of action of monoclonal antibodies against MM, identifying mechanisms of resistance to current therapies and exploring the role of exosomes (50-100 nm vesicles) in the biology of the disease.

LINES OF RESEARCH AND STRATEGIC OBJECTIVES

1) To study the interactions of myeloma cells and bone marrow stromal cells (MSCs), and to determine the gene expression/epigenetic/functional changes in both types of cells after those interactions and their role in myeloma pathophysiology.
2) To elucidate the role of exosomes as paracrine signaling mediators in myeloma bone marrow microenvironment.
3) To characterize the efficacy and mechanism of action *(in vitro* and *in vivo* models) of targeted and immunotherapeutic agents with anti-myeloma and/or bone anabolic/anti-resorptive effects.
4) To decipher intrinsic and bone marrow microenvironment-mediated mechanisms of resistance to anti-myeloma agents.

FUTURE CHALLENGES

- To characterize the effects and mechanism of action of new immunotherapeutic agents alone and in combination with standard agents in multiple myeloma, using appropriate *in vitro* and *in vivo* models.
- To identify mechanisms by which the bone marrow microenvironment mediates therapeutic resistance and survival to myeloma cells.
- To implement genome-wide screenings for the search of MM intrinsic mechanisms of resistance to therapeutic agents.
- To explore the potential biomarker value of circulating exosomes from myeloma patients.

PUBLICATIONS

- **Wilms Tumor 1 gene expression levels improve risk stratification in AML patients. Results of a multicentre study within the Spanish Group for Molecular Biology in Haematology.** *Martínez-Laperche C, Kwon M, Franco-Villegas AC, Chillón MC, Castro N, Anguita E, Dolz S, Rodríguez-Medina C, Hermosín L, Bellón JM, Prieto-Conde MI, Barragán E, Gómez-Casares M, Ayala R, Martínez-López J, González-Díaz M, Díez-Martin JL, Buño I; Cooperative Group for Molecular Biology in Haematology (GBMH).* **Br J Haematol. 2018 May;181(4):542-546. doi: 10.1111/bjh.14635.** PMID: 28369773 **IF: 5.206 / Q1**
- **Frequency and prognostic significance of additional cytogenetic abnormalities to the Philadelphia chromosome in young and older adults with acute lymphoblastic leukemia**. *Motlló C, Ribera JM, Morgades M, Granada I, Montesinos P, Mercadal S, González-Campos J, Moreno MJ, Barba P, Cervera M, Barrios M, Novo A, Bernal T, Hernández-Rivas JM, Abella E, Amigo ML, Tormo M, Martino R, Lavilla E, Bergua J, Serrano A, García-Belmonte D, Guàrdia R, Grau J, Feliu E; PETHEMA Group, Spanish Society of Hematology.* **Leuk Lymphoma. 2018 Jan;59(1):146-154. doi: 10.1080/10428194.2017.1326596.** PMID: 28554259 **IF: 2.674 / Q2**
- **Characterizing patients with multiple chromosomal aberrations detected by FISH in chronic lymphocytic leukemia.** *González-Gascón Y Marín I, Hernández-Sánchez M, Rodríguez-Vicente AE, Puiggros A, Collado R, Luño E, González T, Ruiz-Xivillé N, Ortega M, Gimeno E, Muñoz C, Infante MS, Delgado J, Vargas MT, González M, Bosch F, Espinet B, Hernández-Rivas JM, Hernández JÁ; Grupo Español de Leucemia Linfática Crónica (GELLC) and Grupo Cooperativo Español de Citogenética Hematológica (GCECGH).* **Leuk Lymphoma. 2018 Mar;59(3):633-642. doi: 10.1080/10428194.2017.1349901.** PMID: 28728469 **IF: 2.674 / Q2**
- **Identification of two novel mutations in RASGRP2 affecting platelet CalDAG-GEFI expression and function in patients with bleeding diathesis**. *Sevivas T, Bastida JM, Paul DS, Caparros E, Palma-Barqueros V, Coucelo M, Marques D, Ferrer-Marín F, González-Porras JR, Vicente V, Hernández-Rivas JM, Watson SP, Lozano ML, Bergmeier W, Rivera J.* **Platelets. 2018 Mar;29(2):192-195. doi: 10.1080/09537104.2017.1336214.** PMID: 28762304; PMCID: PMC5942149 **IF: 3.106 / Q2**
- **Integrating genomic alterations in diffuse large B-cell lymphoma identifies new relevant pathways and potential therapeutic targets**. *Karube K, Enjuanes A, Dlouhy I, Jares P, Martin-García D, Nadeu F, Ordóñez GR, Rovira J, Clot G, Royo C, Navarro A, González-Farre B, Vaghefi A, Castellano G, Rubio-Perez C, Tamborero D, Briones J, Salar A, Sancho JM, Mercadal S, González-Barca E, Escoda L, Miyoshi H, Ohshima K, Miyawaki K, Kato K, Akashi K, Mozos A, Colomo L, Alcoceba M, Valera A, Carrió A, Costa D, Lopez-Bigas N, Schmitz R, Staudt LM, Salaverria I, López-Guillermo A, Campo E.* **Leukemia. 2018 Mar;32(3):675-684. doi: 10.1038/leu.2017.251.** PMID: 28804123; PMCID: PMC5843901 **IF: 9.944 / D1**
- **Prospective randomized trial of 5 days azacitidine versus supportive care in patients with lower-risk myelodysplastic syndromes without 5q deletion and transfusion-dependent anemia.** *Sánchez-García J, Falantes J, Medina Perez A, Hernandez-Mohedo F, Hermosin L, Torres-Sabariego A, Bailen A, Hernandez-Sánchez JM, Solé Rodriguez M, Casaño FJ, Calderon C, Labrador M, Vahí M, Serrano J, Lumbreras E, Hernández-Rivas JM; Grupo Andaluz SMD.* Leuk Lymphoma. **2018 May;59(5):1095-1104. doi: 10.1080/10428194.2017.1366998.** PMID: 28836866 **IF: 2.674 / Q2**
- **Biocompatibility of two model elastin-like recombinamer-based hydrogels formed through physical or chemical cross-linking for various applications in tissue engineering and regenerative medicine.** *Ibáñez-Fonseca A, Ramos TL, González de Torre I, Sánchez-Abarca LI, Muntión S, Arias FJ, Del Cañizo MC, Alonso M, Sánchez-Guijo F, Rodríguez-Cabello JC.* **J Tissue Eng Regen Med. 2018 Mar;12(3):e1450-e1460. doi: 10.1002/term.2562.** PMID: 28865091 **IF: 3.319 / Q2**
- **Clinical impact of the subclonal architecture and mutational complexity in chronic lymphocytic leukemia**. *Nadeu F, Clot G, Delgado J, Martín-García D, Baumann T, Salaverria I, Beà S, Pinyol M, Jares P, Navarro A, Suárez-Cisneros H, Aymerich M, Rozman M, Villamor N, Colomer D, González M, Alcoceba M, Terol MJ, Navarro B, Colado E, Payer ÁR, Puente XS, López-Otín C, López-Guillermo A, Enjuanes A, Campo E.* **Leukemia. 2018 Mar;32(3):645-653. doi: 10.1038/leu.2017.291.** PMID: 28924241 **IF: 9.944 / D1**
- **Selection and validation of antibody clones against IgG and IgA subclasses in switched memory B-cells and plasma cells.** *Blanco E, Perez-Andres M, Sanoja-Flores L, Wentink M, Pelak O, Martín-Ayuso M, Grigore G, Torres-Canizales J, López-Granados E, Kalina T, van der Burg M, Arriba-Méndez S, Santa Cruz S, Puig N, van Dongen JJM, Orfao A.* **J Immunol Methods. 2019 Dec;475:112372. doi: 10.1016/j.jim.2017.09.008.** PMID: 28965920 **IF: 1.913 / Q3**
- **Introducing high-throughput sequencing into mainstream genetic diagnosis practice in inherited platelet disorders.** *Bastida JM, Lozano ML, Benito R, Janusz K, Palma-Barqueros V, Del Rey M, Hernández-Sánchez JM, Riesco S, Bermejo N, González-García H, Rodriguez-Alén A, Aguilar C, Sevivas T, López-Fernández MF, Marneth AE, van der Reijden BA, Morgan NV, Watson SP, Vicente V, Hernández-Rivas JM, Rivera J, González-Porras JR.* **Haematologica. 2018 Jan;103(1):148-162. doi: 10.3324/haematol.2017.171132.** PMID: 28983057 **IF: 7.570 / D1**
- **Prognostic value of antigen expression in multiple myeloma: a PETHEMA/GEM study on 1265 patients enrolled in four consecutive clinical trials.** *Arana P, Paiva B, Cedena MT, Puig N, Cordon L, Vidriales MB, Gutiérrez NC, Chiodi F, Burgos L, Anglada LL, Martínez-Lopez J, Hernandez MT, Teruel AI, Gironella M, Echeveste MA, Rosiñol L, Martínez R, Oriol A, De la Rubia J, Orfao A, Blade J, Lahuerta JJ, Mateos MV, San Miguel JF.* **Leukemia. 2018 Apr;32(4):971-978. doi: 10.1038/leu.2017.320.** PMID: 29099494 **IF: 9.944 / D1**
- **The mutational landscape of small lymphocytic lymphoma compared to non-early stage chronic lymphocytic**

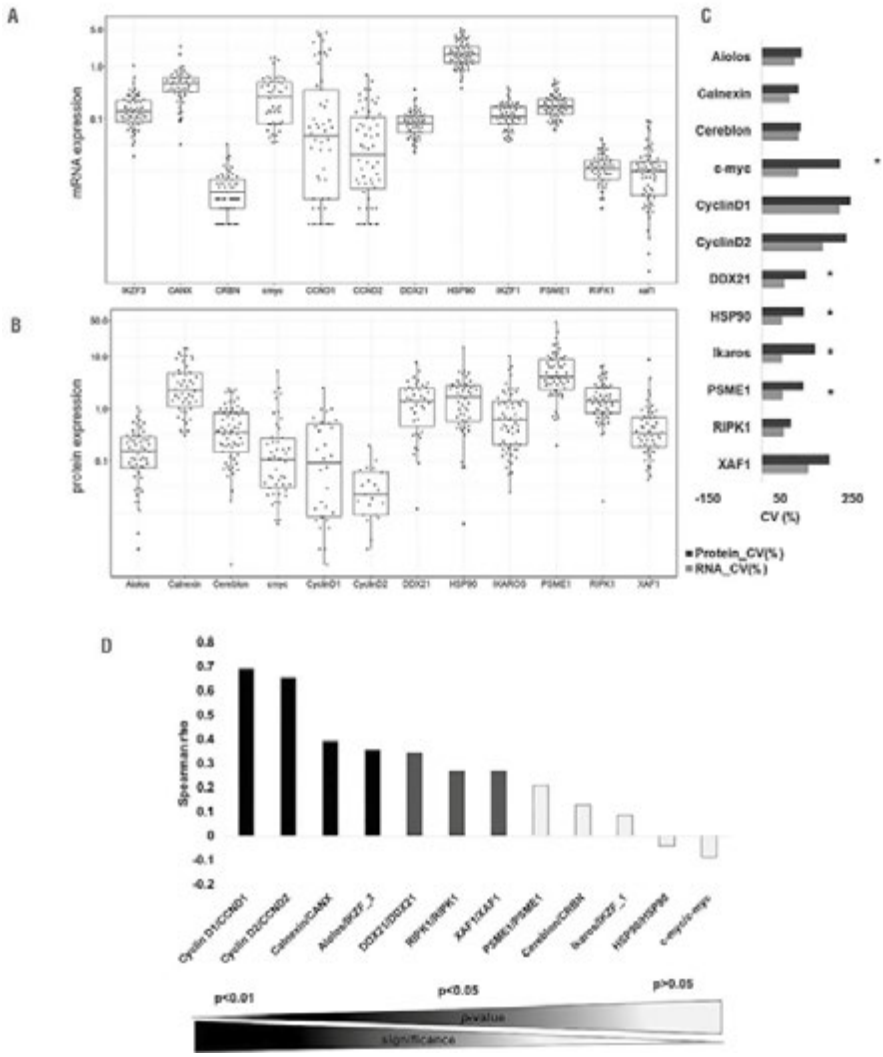
leukemia. *Martínez-Trillos A, Pinyol M, Delgado J, Aymerich M, Rozman M, Baumann T, González-Díaz M, Hernández JM, Alcoceba M, Muntañola A, Terol MJ, Navarro B, Giné E, Jares P, Beà S, Navarro A, Colomer D, Nadeu F, Colado E, Payer AR, García-Cerecedo T, Puente XS, López-Otin C, Campo E, López-Guillermo A, Villamor N.* **Leuk Lymphoma. 2018 Oct;59(10):2318-2326. doi: 10.1080/10428194.2017.1397660.** PMID: 29115891 h **IF: 2.674 / Q2**

- **Mesenchymal Stromal Cell Irradiation Interferes with the Adipogenic/ Osteogenic Differentiation Balance and Improves Their Hematopoietic-Supporting Ability.** *Preciado S, Muntión S, Rico A, Pérez-Romasanta LA, Ramos TL, Ortega R, Borrajo J, Corchete LA, Rodríguez C, Díez-Campelo M, Sánchez-Abarca LI, Del Cañizo MC, Sánchez-Guijo F.* **Biol Blood Marrow Transplant. 2018 Mar;24(3):443-451. doi: 10.1016/j.bbmt.2017.11.007.** PMID: 29155314 **IF: 3.599 / Q1**
- **Different tools for the diagnosis and molecular follow-up of leukemias and lymphomas.** *Sayagués JM, Sarasquete ME.* **Med Clin (Barc). 2018 Mar 9;150(5):202-203. doi: 10.1016/j.medcli.2017.10.012. Review. English, Spanish.** PMID: 29162275 **IF: 1.277 / Q3**
- **Current Status of Cardio-Oncology in Spain: A National Multidisciplinary Survey.** *Martín-García A, Mitroi C, García Sanz R, Santaballa Bertrán A, Arenas M, López-Fernández T; Spanish National Cardio-Oncology Working Group.* **Rev Esp Cardiol (Engl Ed). 2019 Jan;72(1):84-86. doi: 10.1016/j.rec.2017.11.002.** PMID: 29203166 **IF: 5.078 / Q3**
- **Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma.** *Mateos MV, Dimopoulos MA, Cavo M, Suzuki K, Jakubowiak A, Knop S, Doyen C, Lucio P, Nagy Z, Kaplan P, Pour L, Cook M, Grosicki S, Crepaldi A, Liberati AM, Campbell P, Shelekhova T, Yoon SS, Iosava G, Fujisaki T, Garg M, Chiu C, Wang J, Carson R, Crist W, Deraedt W, Nguyen H, Qi M, San-Miguel J; ALCYONE Trial Investigators.* **N Engl J Med. 2018 Feb 8;378(6):518-528. doi: 10.1056/NEJMoa1714678.** PMID: 29231133 **IF: 70.670 / D1**
- **Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond.** *Chim CS, Kumar SK, Orlowski RZ, Cook G, Richardson PG, Gertz MA, Giralt S, Mateos MV, Leleu X, Anderson KC.* **Leukemia. 2018 Feb;32(2):252-262. doi: 10.1038/leu.2017.329. Review. Erratum in: Leukemia. 2019 Apr;33(4):1058-1059.** PMID: 29257139 **IF: 9.944 / D1**
- **A question of class: Treatment options for patients with relapsed and/or refractory multiple myeloma.** *Cook G, Zweegman S, Mateos MV, Suzan F, Moreau P.* **Crit Rev Oncol Hematol. 2018 Jan;121:74-89. doi: 10.1016/j.critrevonc.2017.11.016. Review.** PMID: 29279102 **IF: NI**
- **CD34+ Cell Selection versus Reduced-Intensity Conditioning and Unmodified Grafts for Allogeneic Hematopoietic Cell Transplantation in Patients Age >50 Years with Acute Myelogenous Leukemia and Myelodysplastic Syndrome.** *Barba P, Martino R, Zhou Q, Cho C, Castro-Malaspina H, Devlin S, Esquirol A, Giralt S, Jakubowski AA, Caballero D, Maloy M, Papadopoulos EB, Piñana JL, Fox ML, Márquez-Malaver FJ, Valcárcel D, Solano C, López-Corral L, Sierra J, Perales MA.* **Biol Blood Marrow Transplant. 2018 May;24(5):964-972. doi: 10.1016/j.bbmt.2017.12.804.** PMID: 29305194; PMCID: PMC6800017 **IF: 3.599 / Q1**
- **Diagnosis, treatment, and response assessment in solitary plasmacytoma: updated recommendations from a European Expert Panel.** *Caers J, Paiva B, Zamagni E, Leleu X, Bladé J, Kristinsson SY, Touzeau C, Abildgaard N, Terpos E, Heusschen R, Ocio E, Delforge M, Sezer O, Beksac M, Ludwig H, Merlini G, Moreau P, Zweegman S, Engelhardt M, Rosiñol L.* **J Hematol Oncol. 2018 Jan 16;11(1):10. doi: 10.1186/s13045-017-0549-1.** PMID: 29338789; PMCID: PMC5771205 **IF: 8.731 / D1**
- **Unraveling the heterogeneity of IgM monoclonal gammopathies: a gene mutational and gene expression study.** *Jiménez C, Prieto-Conde MI, García-Álvarez M, Alcoceba M, Escalante F, Chillón MDC, García de Coca A, Balanzategui A, Cantalapiedra A, Aguilar C, Corral R, González-López T, Marín LA, Bárez A, Puig N, García-Mateo A, Gutiérrez NC, Sarasquete ME, González M, García-Sanz R.* **Ann Hematol. 2018 Mar;97(3):475-484. doi: 10.1007/s00277-017-3207-3.** PMID: 29353304 **IF: 2.850 / Q2**
- **Secondary malignancies and survival outcomes after autologous stem cell transplantation for follicular lymphoma in the pre-rituximab and rituximab eras: a long-term follow-up analysis from the Spanish GELTAMO registry.** *Jiménez-Ubieto A, Grande C, Caballero D, Yáñez L, Hernández-García MT, Novelli S, Arranz R, Ferreiro JJ, Bobillo S, Mercadal S, Galeo A, Jiménez JL, Moraleda JM, Vallejo C, Albo C, Pérez E, Marrero C, Magnano L, Palomera L, Jarque I, Martínez-Sánchez P, Martín A, Coria E, López-Guillermo A, Salar A, Lahuerta JJ; GELTAMO (Grupo Español de Linfomas y Trasplantes de Médula Ósea) Cooperative Study Group.* **Bone Marrow Transplant. 2018 Jun;53(6):780-783. doi: 10.1038/s41409-018-0096-6.** PMID: 29362504 **IF: 4.674 / Q2**
- **Pomalidomide Plus Low-Dose Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma and Renal Impairment: Results From a Phase II Trial.** *Dimopoulos M, Weisel K, van de Donk NWCJ, Ramasamy K, Gamberi B, Streetly M, Offidani M, Bridoux F, de la Rubia J, Mateos MV, Ardizzoia A, Kueenburg E, Collins S, Di Micco A, Rosettani B, Li Y, Bacon P, Sonneveld P.* **J Clin Oncol. 2018 Jul 10;36(20):2035-2043. doi: 10.1200/JCO.2017.76.1742.** PMID: 29394124 **IF: 28.245 / D1**
- **Denosumab versus zoledronic acid in bone disease treatment of newly diagnosed multiple myeloma: an international, double-blind, double-dummy, randomised, controlled, phase 3 study.** *Raje N, Terpos E, Willenbacher W, Shimizu K, García-Sanz R, Durie B, Legieć W, Krejčí M, Laribi K, Zhu L, Cheng P, Warner D, Roodman GD.* **Lancet Oncol. 2018 Mar;19(3):370-381. doi: 10.1016/S1470-2045(18)30072-X.** PMID: 29429912 **IF: 35.386 / D1**
- **Carfilzomib in relapsed or refractory multiple myeloma patients with early or late relapse following prior therapy: A subgroup analysis of the randomized phase 3 ASPIRE and ENDEAVOR trials.** *Mateos MV, Goldschmidt H, San-Miguel J, Mikhael J, DeCosta L, Zhou L, Obreja M, Blaedel J, Szabo Z, Leleu X.* **Hematol Oncol. 2018 Apr;36(2):463-470. doi: 10.1002/hon.2499.** PMID: 29446103 **IF: 3.439 / Q3**
- **Richter transformation driven by Epstein-Barr virus reactivation during therapy-related immunosuppression in chronic lymphocytic leukaemia.** *García-Barchino MJ, Sarasquete ME, Panizo C, Morscio J, Martínez A, Alcoceba M, Fresquet V, González-Farre B, Paiva B, Young KH,*

Robles EF, Roa S, Celay J, Larrayoz M, Rossi D, Gaidano G, Montes-Moreno S, Piris MA, Balanzategui A, Jiménez C, Rodriguez I, Calasanz MJ, Larrayoz MJ, Segura V, García-Muñoz R, Rabasa MP, Yi S, Li J, Zhang M, Xu-Monette ZY, Puig-Moron N, Orfao A, Böttcher S, Hernandez-Rivas JM, Miguel JS, Prosper F, Tousseyn T, Sagaert X, González M, Martínez-Climent JA. **J Pathol. 2018 May;245(1):61-73. doi: 10.1002/path.5060.** PMID: 29464716 **IF: 5.942 / D1**

- **ERIC recommendations for TP53 mutation analysis in chronic lymphocytic leukemia-update on methodological approaches and results interpretation**. *Malcikova J, Tausch E, Rossi D, Sutton LA, Soussi T, Zenz T, Kater AP, Niemann CU, González D, Davi F, González Díaz M, Moreno C, Gaidano G, Stamatopoulos K, Rosenquist R, Stilgenbauer S, Ghia P, Pospisilova S; European Research Initiative on Chronic Lymphocytic Leukemia (ERIC) — TP53 network.* Leukemia. **2018 May;32(5):1070-1080. doi: 10.1038/s41375-017-0007-7. . Review.** PMID: 29467486 **IF: 9.944 / D1**
- **Correction to: A phase I-II study of plerixafor in combination with fludarabine, idarubicin, cytarabine, and G-CSF (PLERIFLAG regimen) for the treatment of patients with the first early-relapsed or refractory acute myeloid leukemia**. *Martínez-Cuadrón D, Boluda B, Martínez P, Bergua J, Rodríguez-Veiga R, Esteve J, Vives S, Serrano J, Vidriales B, Salamero O, Cordón L, Sempere A, Jiménez-Ubieto A, Prieto-Delgado J, Díaz-Beyá M, Garrido A, Benavente C, Pérez-Simón JA, Moscardó F, Sanz MA, Montesinos P; CETLAM and PETHEMA groups.* **Ann Hematol. 2018 May;97(5):923. doi: 10.1007/s00277-018-3277-x. Erratum for: Ann Hematol. 2018 May;97(5):763-772.** PMID: 29473097 **IF: 2.850 / Q2**
- **A cost-effectiveness analysis of denosumab for the prevention of skeletal-related events in patients with multiple myeloma in the United States of America.** *Raje N, Roodman GD, Willenbacher W, Shimizu K, García-Sanz R, Terpos E, Kennedy L, Sabatelli L, Intorcia M, Hechmati G.* **J Med Econ. 2018 May;21(5):525-536. doi: 10.1080/13696998.2018.1445634.** PMID: 29480139 **IF: 1.885 / Q1**
- **Age-associated distribution of normal B-cell and plasma cell subsets in peripheral blood.** *Blanco E, Pérez-Andrés M, Arriba-Méndez S, Contreras-Sanfeliciano T, Criado I, Pelak O, Serra-Caetano A, Romero A, Puig N, Remesal A, Torres Canizales J, López-Granados E, Kalina T, Sousa AE, van Zelm M, van der Burg M, van Dongen JJM, Orfao A; EuroFlow PID group.* **J Allergy Clin Immunol. 2018 Jun;141(6):2208-2219.e16. doi: 10.1016/j.jaci.2018.02.017.** PMID: 29505809 **IF: 14.110 / D1**
- **Early myeloma-related death in elderly patients: development of a clinical prognostic score and evaluation of response sustainability role.** *Rodríguez-Otero P, Mateos MV, Martínez-López J, Martín-Calvo N, Hernández MT, Ocio EM, Rosiñol L, Martínez R, Teruel AI, Gutiérrez NC, Bargay J, Bengoechea E, González Y, de Oteyza JP, Gironella M, Encinas C, Martín J, Cabrera C, Palomera L, de Arriba F, Cedena MT, Paiva B, Puig N, Oriol A, Bladé J, Lahuerta JJ, San Miguel JF.* **Leukemia. 2018 Nov;32(11):2427-2434. doi: 10.1038/s41375-018-0072-6. Erratum in: Leukemia. 2019 Mar 8.** PMID: 29515235 **IF: 9.944 / D1**
- **A novel nano-immunoassay method for quantification of proteins from CD138-purified myeloma cells: biological and clinical utility.** *Misiewicz-Krzeminska I, Corchete LA, Rojas EA, Martínez-López J, García-Sanz R, Oriol A, Bladé J, Lahuerta JJ, Miguel JS, Mateos MV, Gutiérrez NC.* **Haematologica. 2018 May;103(5):880-889. doi: 10.3324/haematol.2017.181628.** PMID: 29545347; PMCID: PMC5927993 **IF: 7.570 / D1**
- **Low-count monoclonal B-cell lymphocytosis persists after seven years of follow up and is associated with a poorer outcome.** *Criado I, Rodríguez-Caballero A, Gutiérrez ML, Pedreira CE, Alcoceba M, Nieto W, Teodosio C, Bárcena P, Romero A, Fernández-Navarro P, González M, Almeida J, Orfao A; Primary Health Care Group of Salamanca for the Study of MBL.* **Haematologica. 2018 Jul;103(7):1198-1208. doi: 10.3324/haematol.2017.183954.**PMID: 29567775 **IF: 7.570 / D1**
- **Association between response kinetics and outcomes in relapsed/refractory multiple myeloma: analysis from TOURMALINE-MM1.** *Garderet L, Laubach JP, Stoppa AM, Hari P, Cavo M, Ludwig H, Mateos MV, Luptakova K, Lin J, Yung G, van de Velde H, Berg D, Moreau P, Richardson PG.* **Leukemia. 2018 Sep;32(9):2032-2036. doi: 10.1038/s41375-018-0091-3.** PMID: 29568098 **IF: 9.944 / D1**
- **Basophil-lineage commitment in acute promyelocytic leukemia predicts for severe bleeding after starting therapy.** *Matarraz S, Leoz P, Fernández C, Colado E, Chillón MC, Vidriales MB, González M, Rivera D, Osuna CS, Caballero-Velázquez T, Van Der Velden V, Jongen-Lavrencic M, Gutiérrez O, Bermejo AY, Alonso LG, García MB, De Ramón Sánchez C, García-Donas G, Mateo AG, Recio I, Sánchez-Real J, Mayado A, Gutiérrez ML, Bárcena P, Barrena S, López A, Van Dongen J, Orfao A.* **Mod Pathol. 2018 Aug;31(8):1318-1331. doi: 10.1038/s41379-018-0038-2.** PMID: 29572500 **IF: 6.365 / D1**
- **Ibrutinib versus temsirolimus: 3-year follow-up of patients with previously treated mantle cell lymphoma from the phase 3, international, randomized, open-label RAY study.** *Rule S, Jurczak W, Jerkeman M, Rusconi C, Trneny M, Offner F, Caballero D, Joao C, Witzens-Harig M, Hess G, Bence-Bruckler I, Cho SG, Thieblemont C, Zhou W, Henninger T, Goldberg J, Vermeulen J, Dreyling M.* **Leukemia. 2018 Aug;32(8):1799-1803. doi: 10.1038/s41375-018-0023-2.** PMID: 29572505; PMCID: PMC6087720 **IF: 9.944 / D1**
- **Azacitidine improves outcome in higher-risk MDS patients with chromosome 7 abnormalities: a retrospective comparison of GESMD and GFM registries.** *Díez-Campelo M, Lorenzo JI, Itzykson R, Rojas SM, Berthon C, Luño E, Beyne-Rauzy O, Perez-Oteyza J, Vey N, Bargay J, Park S, Cedena T, Bordessoule D, Muñoz JA, Gyan E, Such E, Visanica S, López-Cadenas F, de Botton S, Hernández-Rivas JM, Ame S, Stamatoullas A, Delaunay J, Salanoubat C, Isnard F, Guieze R, Pérez Guallar J, Badiella L, Sanz G, Cañizo C, Fenaux P.* **Br J Haematol. 2018 May;181(3):350-359. doi: 10.1111/bjh.15190.** PMID: 29611196 **IF: 5.206 / Q1**
- **Response and progression-free survival according to planned treatment duration in patients with relapsed multiple myeloma treated with carfilzomib, lenalidomide, and dexamethasone (KRd) versus lenalidomide and dexamethasone (Rd) in the phase III ASPIRE study.** *Dimopoulos M, Wang M, Maisnar V, Minarik J, Bensinger W, Mateos MV, Obreja M, Blaedel J, Moreau P.* **J Hematol Oncol. 2018 Apr 4;11(1):49. doi: 10.1186/s13045-018-0583-7**. PMID: 29615082 **IF: 3.439 / Q3**

- **New Challenges in Targeting Signaling Pathways in Acute Lymphoblastic Leukemia by NGS Approaches: An Update.** *Montaño A, Forero-Castro M, Marchena-Mendoza D, Benito R, Hernández-Rivas JM.* **Cancers (Basel). 2018 Apr 7;10(4). pii: E110. doi: 10.3390/cancers10040110. Review.** PMID: 29642462 IF: 6.162 / D1
- **A new prognostic model identifies patients aged 80 years and older with diffuse large B-cell lymphoma who may benefit from curative treatment: A multicenter, retrospective analysis by the Spanish GELTAMO group.** *Pardal E, Díez Baeza E, Salas Q, García T, Sancho JM, Monzón E, Moraleda JM, Córdoba R, de la Cruz F, Queizán JA, Rodríguez MJ, Navarro B, Hernández JA, Díez R, Vahi M, Viguria MC, Canales M, Peñarrubia MJ, González-López TJ, Montes-Moreno S, González-Barca E, Caballero D, Martín A; GELTAMO Spanish Collaborative Group.* **Am J Hematol. 2018 Jul;93(7):867-873. doi: 10.1002/ajh.25107.** PMID: 29658143 IF: 6.137 / Q1
- **Efficacy of bendamustine and rituximab as first salvage treatment in chronic lymphocytic leukemia and indirect comparison with ibrutinib: a GIMEMA, ERIC and UK CLL FORUM study.** *Cuneo A, Follows G, Rigolin GM, Piciocchi A, Tedeschi A, Trentin L, Perez AM, Coscia M, Laurenti L, Musuraca G, Farina L, Delgado AR, Orlandi EM, Galieni P, Mauro FR, Visco C, Amendola A, Billio A, Marasca R, Chiarenza A, Meneghini V, Ilariucci F, Marchetti M, Molica S, Re F, Gaidano G, González M, Forconi F, Ciolli S, Cortelezzi A, Montillo M, Smolej L, Schuh A, Eyre TA, Kennedy B, Bowles KM, Vignetti M, de la Serna J, Moreno C, Foà R, Ghia P; GIMEMA, European Research Initiative on CLL (ERIC) and UK CLL forum.* **Haematologica. 2018 Jul;103(7):1209-1217. doi: 10.3324/haematol.2018.189837.** PMID: 29674504 IF: 7.570 / D1
- **Reduced intensity conditioning increases risk of severe cGVHD: identification of risk factors for cGVHD in a multicenter setting.** *Afram G, Simón JAP, Remberger M, Caballero-Velázquez T, Martino R, Piñana JL, Ringden O, Esquirol A, Lopez-Corral L, García I, López-Godino O, Sierra J, Caballero D, Ljungman P, Vazquez L, Hägglund H.* **Med Oncol. 2018 Apr 25;35(6):79. doi: 10.1007/s12032-018-1127-2.** PMID: 29696461; PMCID: PMC5918523 IF: 3.252 / Q1

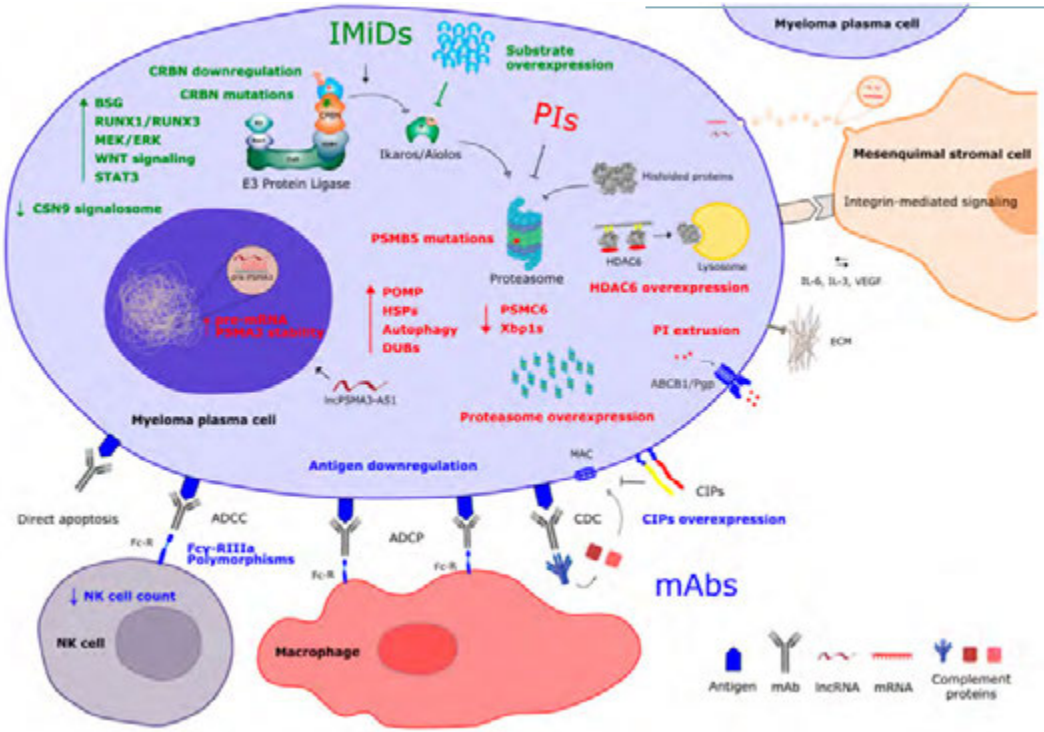


Two levels of analysis of each gene RNA and protein from CD138-purified myeloma cells. mRNA expression of each gene was assessed by qRT-PCR and normalized relative to GAPDH and expressed as 2−ΔCt. Protein levels were analyzed by Capillary nanoimmunoassay and the signal of each protein was normalized to GAPDH protein level [from Misiewicz-Krzeminska I et al. Haematologica 2018;103:880-889].

- **Prevention and management of adverse events of novel agents in multiple myeloma: a consensus of the European Myeloma Network.** *Ludwig H, Delforge M, Facon T, Einsele H, Gay F, Moreau P, Avet-Loiseau H, Boccadoro M, Hajek R, Mohty M, Cavo M, Dimopoulos MA, San-Miguel JF, Terpos E, Zweegman S, Garderet L, Mateos MV, Cook G, Leleu X, Goldschmidt H, Jackson G, Kaiser M, Weisel K, van de Donk NWCJ, Waage A, Beksac M, Mellqvist UH, Engelhardt M, Caers J, Driessen C, Bladé J, Sonneveld P.* **Leukemia. 2018 Jul;32(7):1542-1560. doi: 10.1038/s41375-018-0040-1. Review.** PMID: 29720735 **IF: 9.944 / D1**
- **The International Prognostic Index for Patients with Chronic Lymphocytic Leukemia Has the Higher Value in Predicting Overall Outcome Compared with the Barcelona-Brno Biomarkers Only Prognostic Model and the MD Anderson Cancer Center Prognostic Index.** *Muñoz-Novas C, Poza-Santaella M, González-Gascón Y Marín I, Hernández-Sánchez M, Rodríguez-Vicente AE, Infante MS, Heras C, Foncillas MÁ, Marín K, Hernández-Rivas JM, Hernández JÁ.* **Biomed Res Int. 2018 Mar 15;2018:9506979. doi: 10.1155/2018/9506979. eCollection 2018.** PMID: 29736400 **IF: 2.197 / Q2**
- **A safety profile of medications used to treat Waldenström's macroglobulinemia.** *García-Sanz R, Jiménez C, González De La Calle V, Sarasquete ME.* **Expert Opin Drug Saf. 2018 Jun;17(6):609-621. doi: 10.1080/14740338.2018.1477936. .** PMID: 29768934 **IF: 3.220 / Q1**
- **Transcriptomic rationale for synthetic lethality-targeting ERCC1 and CDKN1A in chronic myelomonocytic leukaemia.** *Hurtado AM, Luengo-Gil G, Chen-Liang TH, Amaral F, Batta K, Palomo L, Lumbreras E, Przychodzen B, Caparros E, Amigo ML, Diez-Campelo M, Zamora L, Salido Fierrez EJ, Maciejewski JP, Ortuño FJ, Vicente V, Del Canizo M, Sole F, Ferrer-Marin F, Wiseman DH, Jerez A.* **Br J Haematol. 2018 Aug;182(3):373-383. doi: 10.1111/bjh.15408.** PMID: 29797327 **IF: 5.206 / Q1**
- **Sequential intravenous allogeneic mesenchymal stromal cells as a potential treatment for thromboangiitis obliterans (Buerger's disease).** *Martin-Rufino JD, Lozano FS, Redondo AM, Villaron EM, Rueda R, Fernandez-Samos R, Sánchez-Guijo F.* **Stem Cell Res Ther. 2018 May 30;9(1):150. doi: 10.1186/s13287-018-0901-6.** PMID: 29848379; PMCID: PMC5977545 **IF: 4.627 / D1**
- **Ibrutinib as Treatment for Patients With Relapsed/Refractory Follicular Lymphoma: Results From the Open-Label, Multicenter, Phase II DAWN Study.** *Gopal AK, Schuster SJ, Fowler NH, Trotman J, Hess G, Hou JZ, Yacoub A, Lill M, Martin P, Vitolo U, Spencer A, Radford J, Jurczak W, Morton J, Caballero D, Deshpande S, Gartenberg GJ, Wang SS, Damle RN, Schaffer M, Balasubramanian S, Vermeulen J, Cheson BD, Salles G.* **J Clin Oncol. 2018 Aug 10;36(23):2405-2412. doi: 10.1200/JCO.2017.76.8853.** PMID: 29851546 **IF: 28.245 / D1**
- **Phase 3 Trial of Ibrutinib plus Rituximab in Waldenström's Macroglobulinemia.** *Dimopoulos MA, Tedeschi A, Trotman J, García-Sanz R, Macdonald D, Leblond V, Mahe B, Herbaux C, Tam C, Orsucci L, Palomba ML, Matous JV, Shustik C, Kastritis E, Treon SP, Li J, Salman Z, Graef T, Buske C; iNNOVATE Study Group and the European Consortium for Waldenström's Macroglobulinemia.* **N Engl J Med. 2018 Jun 21;378(25):2399-2410. doi: 10.1056/NEJMoa1802917.** PMID: 29856685 **IF: 70.670 / D1**
- **Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of a randomised, phase 3 study.** *Moreau P, Mateos MV, Berenson JR, Weisel K, Lazzaro A, Song K, Dimopoulos MA, Huang M, Zahlten-Kumeli A, Stewart AK.* **Lancet Oncol. 2018 Jul;19(7):953-964. doi: 10.1016/S1470-2045(18)30354-1. Erratum in: Lancet Oncol. 2018 Aug;19(8):e382.** PMID: 29866475 **IF: 35.386 / D1**
- **A novel ex vivo high-throughput assay reveals antiproliferative effects of idelalisib and ibrutinib in chronic lymphocytic leukemia.** *Primo D, Scarfò L, Xochelli A, Mattsson M, Ranghetti P, Espinosa AB, Robles A, Gorrochategui J, Martínez-López J, de la Serna J, González M, Gil AC, Anguita E, Iraheta S, Munugalavadla V, Quéva C, Tannheimer S, Rosenquist R, Stamatopoulos K, Ballesteros J, Ghia P.* **Oncotarget. 2018 May 25;9(40):26019-26031. doi: 10.18632/oncotarget.25419. eCollection 2018 May 25.** PMID: 29899839 **IF: NI**
- **Monoclonal gammopathies of unknown significance and smoldering myeloma: Assessment and management of the elderly patients.** *González-Calle V, Mateos MV.* **Eur J Intern Med. 2018 Dec;58:57-63. doi: 10.1016/j.ejim.2018.05.029.** PMID: 29907380 **IF: 3.660 / Q2**
- **Beyond maximum grade: modernising the assessment and reporting of adverse events in haematological malignancies.** *Thanarajasingam G, Minasian LM, Baron F, Cavalli F, De Claro RA, Dueck AC, El-Galaly TC, Everest N, Geissler J, Gisselbrecht C, Gribben J, Horowitz M, Ivy SP, Jacobson CA, Keating A, Kluetz PG, Krauss A, Kwong YL, Little RF, Mahon FX, Matasar MJ, Mateos MV, McCullough K, Miller RS, Mohty M, Moreau P, Morton LM, Nagai S, Rule S, Sloan J, Sonneveld P, Thompson CA, Tzogani K, van Leeuwen FE, Velikova G, Villa D, Wingard JR, Wintrich S, Seymour JF, Habermann TM.* **Lancet Haematol. 2018 Nov;5(11):e563-e598. doi: 10.1016/S2352-3026(18)30051-6. . Review. Erratum in: Lancet Haematol. 2019 Mar;6(3):e121.** PMID: 29907552 **IF: 11.990 / D1**
- **CXCR7 expression in diffuse large B-cell lymphoma identifies a subgroup of CXCR4+ patients with good prognosis.** *Moreno MJ, Gallardo A, Novelli S, Mozos A, Aragó M, Pavón MÁ, Céspedes MV, Pallarès V, Falgàs A, Alcoceba M, Blanco O, González-Díaz M, Sierra J, Mangues R, Casanova I.* **PLoS One. 2018 Jun 19;13(6):e0198789. doi: 10.1371/journal.pone.0198789. eCollection 2018.** PMID: 29920526 **IF: 2.776 / D1**
- **Residual normal B-cell profiles in monoclonal B-cell lymphocytosis versus chronic lymphocytic leukemia.** *Criado I, Blanco E, Rodríguez-Caballero A, Alcoceba M, Contreras T, Gutiérrez ML, Romero A, Fernández-Navarro P, González M, Solano F, Gómez C, Pérez-Andrés M, van Dongen JJM, Almeida J, Orfao A; EuroFlow PID Group and The Primary Health Care Group of Salamanca for the Study of MBL.* **Leukemia. 2018 Jun 21. doi: 10.1038/s41375-018-0164-3.** PMID: 29930299 **IF: 9.944 / D1**
- **A phase I/II dose-escalation study investigating all-oral ixazomib-melphalan-prednisone induction followed by single-agent ixazomib maintenance in transplant-ineligible newly diagnosed multiple myeloma.** *San-Miguel JF, Echeveste Gutiérrez MA, Špicka I, Mateos MV, Song K, Craig MD, Bladé J, Hájek R, Chen C, Di Bacco A,*

Estevam J, Gupta N, Byrne C, Lu V, van de Velde H, Lonial S. **Haematologica. 2018 Sep;103(9):1518-1526. doi: 10.3324/haematol.2017.185991.**PMID: 29954932 IF: 7.570 / D1

- **Mutational screening of newly diagnosed multiple myeloma patients by deep targeted sequencing.** *Ruiz-Heredia Y, Sánchez-Vega B, Onecha E, Barrio S, Alonso R, Martínez-Ávila JC, Cuenca I, Agirre X, Braggio E, Hernández MT, Martínez R, Rosiñol L, Gutiérrez N, Martin-Ramos M, Ocio EM, Echeveste MA, de Oteyza JP, Oriol A, Bargay J, Gironella M, Ayala R, Bladé J, Mateos MV, Kortum KM, Stewart K, García-Sanz R, Miguel JS, Lahuerta JJ, Martínez-Lopez J.* **Haematologica. 2018 Nov;103(11):e544-e548. doi: 10.3324/haematol.2018.188839.** PMID: 29954938 IF: 7.570 / D1
- **Drug-to-drug interactions of tyrosine kinase inhibitors in chronic myeloid leukemia patients. Is it a real problem?.** *Osorio S, Escudero-Vilaplana V, Gómez-Centurión I, Pérez-López R, Ayala R, Vall-Llovera F, García-Gutiérrez V, Gómez Casares MT, González San Miguel JD, Hernández-Rivas JÁ, Sánchez-Guijo F, Martínez-García AB, Villalón L, Conesa-García V, Rodriguez A, Casado F, García-González X, Sáez Perdomo MN, Baños Ú, Steegmann JL; CML Spanish Group (GELMC).* **Ann Hematol. 2018 Nov;97(11):2089-2098. doi: 10.1007/s00277-018-3413-7.** PMID: 29955943 IF: 2.850 / Q2
- **Treatment and outcome patterns in European patients with Waldenström's macroglobulinaemia: a large, observational, retrospective chart review.** *Buske C, Sadullah S, Kastritis E, Tedeschi A, García-Sanz R, Bolkun L, Leleu X, Willenbacher W, Hájek R, Minnema MC, Cheng M, Bilotti E, Graef T, Dimopoulos MA; European Consortium for Waldenström's Macroglobulinemia.* **Lancet Haematol. 2018 Jul;5(7):e299-e309. doi: 10.1016/S2352-3026(18)30087-5.** PMID: 29958569 IF: 11.990 / D1
- **Sitosterolemia: diagnosis, metabolic and hematological abnormalities, cardiovascular disease and management.** *Bastida JM, Giros ML, Benito R, Janusz K, Hernandez-Rivas JM, González-Porras JR.* **Curr Med Chem. 2018 Jul 5. doi: 10.2174/0929867325666180705145900.** PMID: 29984642 IF: NI
- **Targeted genome editing in acute lymphoblastic leukemia: a review.** *Montaño A, Forero-Castro M, Hernández-Rivas JM, García-Tuñón I, Benito R.* **BMC Biotechnol. 2018 Jul 17;18(1):45. doi: 10.1186/s12896-018-0455-9. Review.** PMID: 30016959 IF: 2.303 / Q2
- **PD-1 genotype of the donor is associated with acute graft-versus-host disease after HLA-identical sibling donor stem cell transplantation.** *Santos N, Rodríguez-Romanos R, de la Cámara R, Brunet S, Nieto JB, Buño I, Martínez C, Jiménez-Velasco A, Vallejo C, González M, Solano C, Ferrá C, Sampol A, Pérez-Simón JA, López-Jiménez J, Díez JL, Gallardo D; GvHD/Immunotherapy Working Party of the Spanish Group of Hematopoietic Transplant (GETH).* **Ann Hematol. 2018 Nov;97(11):2217-2224. doi: 10.1007/s00277-018-3438-y. .** PMID: 30019128 IF: 2.850 / Q2
- **Multiple Myeloma Treatment in Real-world Clinical Practice: Results of a Prospective, Multinational, Noninterventional Study.** *Mohty M, Terpos E, Mateos MV, Cavo M, Lejniece S, Beksac M, Bekadja MA, Legiec W, Dimopoulos M, Stankovic S, Durán MS, De Stefano V, Corso A, Kochkareva Y, Laane E, Berthou C, Salwender H, Masliak Z, Pečeliūnas V, Willenbacher W, Silva J, Louw V, Nemet D, Borbényi Z, Abadi U, Pedersen RS, černelč P, Potamianou A, Couturier C, Feys C, Thoret-Bauchet F, Boccadoro M; EMMOS Investigators.* **Clin Lymphoma Myeloma Leuk. 2018 Oct;18(10):e401-e419. doi: 10.1016/j.clml.2018.06.018.** PMID: 30030033 IF: 2.274 / Q2
- **A novel predictive approach for GVHD after allogeneic SCT based on clinical variables and cytokine gene polymorphisms.** *Martínez-Laperche C, Buces E, Aguilera-Morillo MC, Picornell A, González-Rivera M, Lillo R, Santos N, Martín-Antonio B, Guillem V, Nieto JB, González M, de la Cámara R, Brunet S, Jiménez-Velasco A, Espigado I, Vallejo C, Sampol A, Bellón JM, Serrano D, Kwon M, Gayoso J, Balsalobre P, Urbano-Izpizua Á, Solano C, Gallardo D, Díez-Martín JL, Romo J, Buño I; GVHD/Immunotherapy Committee of the Spanish Group for Hematopoietic Transplantation.* **Blood Adv. 2018 Jul 24;2(14):1719-1737. doi: 10.1182/bloodadvances.2017011502.** PMID: 30030270 IF: NI
- **Outcomes of Advanced Hodgkin Lymphoma after Umbilical Cord Blood Transplantation: A Eurocord and EBMT Lymphoma and Cellular Therapy & Immunobiology Working Party Study.** *Paviglianiti A, Tozatto Maio K, Rocha V, Gehlkopf E, Milpied N, Esquirol A, Chevallier P, Blaise D, Gac AC, Leblond V, Cahn JY, Abecasis M, Zuckerman T, Schouten H, Gurman G, Rubio MT, Beguin Y, Corral LL, Nagler A, Snowden JA, Koc Y, Mordini N, Bonifazi F, Volt F, Kenzey C, Robinson SP, Montoto S, Gluckman E, Ruggeri A.* **Biol Blood Marrow Transplant. 2018 Nov;24(11):2265-2270. doi: 10.1016/j.bbmt.2018.07.019.** PMID: 30031070 IF: 3.599 / Q1
- **Manufacturing Mesenchymal Stromal Cells for the Treatment of Graft-versus-Host Disease: A Survey among Centers Affiliated with the European Society for Blood and Marrow Transplantation.** *Trento C, Bernardo ME, Nagler A, Kuçi S, Bornhäuser M, Köhl U, Strunk D, Galleu A, Sánchez-Guijo F, Gaipa G, Introna M, Bukauskas A, Le Blanc K, Apperley J, Roelofs H, Van Campenhout A, Beguin Y, Kuball J, Lazzari L, Avanzini MA, Fibbe W, Chabannon C, Bonini C, Dazzi F.* **Biol Blood Marrow Transplant. 2018 Nov;24(11):2365-2370. doi: 10.1016/j.bbmt.2018.07.015.** PMID: 30031938 IF: 3.599 / Q1
- **Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: long-term follow up of a multicenter randomized controlled clinical trial (phase I/II).** *Lamo-Espinosa JM, Mora G, Blanco JF, Granero-Moltó F, Núñez-Córdoba JM, López-Elío S, Andreu E, Sánchez-Guijo F, Aquerreta JD, Bondía JM, Valentí-Azcárate A, Del Consuelo Del Cañizo M, Villarón EM, Valentí-Nin JR, Prósper F.* **J Transl Med. 2018 Jul 31;16(1):213. doi: 10.1186/s12967-018-1591-7.** PMID: 30064455; PMCID: PMC6069715 IF: 4.098 / Q1
- **Cereblon gene expression and correlation with clinical outcomes in patients with relapsed/refractory multiple myeloma treated with pomalidomide: an analysis of STRATUS.** *Qian X, Dimopoulos MA, Amatangelo M, Bjorklund C, Towfic F, Flynt E, Weisel KC, Ocio EM, Yu X, Peluso T, Sternas L, Zaki M, Moreau P, Thakurta A.* **Leuk Lymphoma. 2019 Feb;60(2):462-470. doi: 10.1080/10428194.2018.1485915.** PMID: 30068263 IF: 2.674 / Q2
- **Rituximab and the risk of transformation of follicular lymphoma: a retrospective**



Schematic representation of main resistance mechanisms described to the present backbones in multiple myeloma (MM) treatment: proteasome inhibitors (PIs), immunomodulatory agents (IMiDs), and the more recently incorporated monoclonal antibodies (mAbs) [from Mogollón P et al. Cells (2019); 8 (11) doi: 10.3390/cells8111432. Review. pii: E1432].

pooled analysis. *Federico M, Caballero Barrigón MD, Marcheselli L, Tarantino V, Manni M, Sarkozy C, Alonso-Álvarez S, Wondergem M, Cartron G, Lopez-Guillermo A, Issa D, Morschhauser F, Alcoceba M, Kimby E, Rusconi C, Chamuleau M, Holte H, Lockmer S, Montoto S, Gomes da Silva M, Aurer I, Zucca E, Paszkiewicz-Kozik E, Minoia C, Skrypets T, Blaker YN, Salles G, Coiffier B; Aristotle Consortium.* **Lancet Haematol. 2018 Aug;5(8):e359-e367. doi: 10.1016/S2352-3026(18)30090-5.** PMID: 30078408 **IF: 11.990 / D1**

- **Second-line treatment for acute graft-versus-host disease with mesenchymal stromal cells: A decision model.** *Thielen FW, Blommestein HM, Oosten LEM, Calkoen FG, Lankester AC, Zwaginga JJ, Le Blanc K, Redondo A, Sánchez-Guijo F, Algeri M, Locatelli F, Fibbe WE, Uyl-de Groot CA.* **Eur J Haematol. 2018 Aug 6. doi: 10.1111/ejh.13158.** PMID: 30084111 **IF: 2.217 / Q2**

- **Maintenance Treatment and Survival in Patients with Myeloma: A Systematic Review and Network Meta-analysis.** *Gay F, Jackson G, Rosiñol L, Holstein SA, Moreau P, Spada S, Davies F, Lahuerta JJ, Leleu X, Bringhen S, Evangelista A, Hulin C, Panzani U, Cairns DA, Di Raimondo F, Macro M, Liberati AM, Pawlyn C, Offidani M, Spencer A, Hájek R, Terpos E, Morgan GJ, Bladé J, Sonneveld P, San-Miguel J, McCarthy PL, Ludwig H, Boccadoro M, Mateos MV, Attal M.* **JAMA Oncol. 2018 Oct 1;4(10):1389-1397. doi: 10.1001/jamaoncol.2018.2961.** PMID: 30098165 **IF: 22.416 / D1**

- **Correction: Mutations in the DNA methylation pathway and number of driver mutations predict response to azacitidine in myelodysplastic syndromes.** *Cedena MT, Rapado I, Santos-Lozano A, Ayala R, Onecha E, Abaigar M, Such E, Ramos F, Cervera J, Díez-Campelo M, Sanz G, Rivas JH, Lucía A, Martínez-López J.* **Oncotarget. 2018 Jul 20;9(56):30936. doi: 10.18632/oncotarget.25856. Erratum for: Oncotarget. 2017 Oct 27;8(63):106948-106961. PMID: 30112119;** PMCID: PMC6089387 **IF: NI**

- **Posttransplant monomorphic Burkitt's lymphoma: clinical characteristics and outcome of a multicenter series.** *Bobillo S, Abrisqueta P, Sánchez-González B, Giné E, Romero S, Alcoceba M, González-Barca E, González de Villambrosía S, Sancho JM, Gómez P, Bento L, Montoro J, Montes S, López A, Bosch F; Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea (GEL/TAMO cooperative group).* **Ann Hematol. 2018 Dec;97(12):2417-2424. doi: 10.1007/s00277-018-3473-8.** PMID: 30116871 **IF: 2.850 / Q2**

- **Human Bone Marrow Mesenchymal Stromal Cells Promote Bone Regeneration in a Xenogeneic Rabbit Model: A Preclinical Study.** *Blanco JF, García-Briñon J, Benito-Garzón L, Pescador D, Muntión S, Sánchez-Guijo F.* **Stem Cells Int. 2018 Jul 5;2018:7089484. doi:**

10.1155/2018/7089484. PMID: 30123292; PMCID: PMC6079361 IF: NI

- **Autologous stem cell transplantation may be curative for patients with follicular lymphoma with early therapy failure who reach complete response after rescue treatment.** *Jiménez-Ubieto A, Grande C, Caballero D, Yáñez L, Novelli S, Hernández-García MT, Manzanares M, Arranz R, Ferreiro JJ, Bobillo S, Mercadal S, Galeo A, Jiménez JL, Moraleda JM, Vallejo C, Albo C, Pérez E, Marrero C, Magnano L, Palomera L, Jarque I, Martínez-Sánchez P, Martín A, Coria E, López-Guillermo A, Salar A, Lahuerta JJ; GELTAMO (Grupo Español de Linfomas y Trasplantes de Médula Ósea) Cooperative Study Group.* Hematol Oncol. 2018 Dec;36(5):765-772. doi: 10.1002/hon.2553. PMID: 30129233 IF: 3.439 / Q3
- **Redefining synchronous colorectal cancers based on tumor clonality.** *Perea J, García JL, Corchete L, Lumbreras E, Arriba M, Rueda D, Tapial S, Pérez J, Vieiro V, Rodríguez Y, Brandáriz L, García-Arranz M, García-Olmo D, Goel A, Urioste M, Sarmiento RG.* Int J Cancer. 2019 Apr 1;144(7):1596-1608. doi: 10.1002/ijc.31761. PMID: 30151896 IF: 3.982 / D1
- **Aggressive primary cutaneous CD30+ lymphoproliferative disorder in an organ transplant recipient in sustained complete remission with brentuximab vedotin.** *Cañueto J, Ocio EM, Román-Curto C.* Int J Dermatol. 2018 Dec;57(12):e153-e155. doi: 10.1111/ijd.14214. PMID: 30191555 IF: 1.794 / Q2
- **Prognostic utility of serum free light chain ratios and heavy-light chain ratios in multiple myeloma in three PETHEMA/GEM phase III clinical trials.** *Lopez-Anglada L, Cueto-Felgueroso C, Rosiñol L, Oriol A, Teruel AI, Lopez de la Guia A, Bengoechea E, Palomera L, de Arriba F, Hernandez JM, Granell M, Peñalver FJ, García-Sanz R, Besalduch J, González Y, Martínez RB, Hernandez MT, Gutiérrez NC, Puerta P, Valeri A, Paiva B, Blade J, Mateos MV, San Miguel J, Lahuerta JJ, Martínez-Lopez J; GEM (Grupo Español de MM)/PETHEMA (Programa para el Estudio de la Terapéutica en Hemopatías Malignas) Cooperative Study Group.* PLoS One. 2018 Sep 7;13(9):e0203392. doi: 10.1371/journal.pone.0203392. eCollection 2018. PMID: 30192814 IF: 2.776 / D1
- **CLL cells cumulate genetic aberrations prior to the first therapy even in outwardly inactive disease phase.** *Hernández-Sánchez M, Kotaskova J, Rodríguez AE, Radova L, Tamborero D, Abáigar M, Plevova K, Benito R, Tom N, Quijada-Álamo M, Bikos V, Martín AÁ, Pal K, García de Coca A, Doubek M, López-Bigas N, Hernández-Rivas JM, Pospisilova S.* Leukemia. 2018 Sep 12. doi: 10.1038/s41375-018-0255-1. PMID: 30209402 IF: 9.944 / D1
- **Daratumumab plus bortezomib and dexamethasone versus bortezomib and dexamethasone in relapsed or refractory multiple myeloma: updated analysis of CASTOR.** *Spencer A, Lentzsch S, Weisel K, Avet-Loiseau H, Mark TM, Spicka I, Masszi T, Lauri B, Levin MD, Bosi A, Hungria V, Cavo M, Lee JJ, Nooka AK, Quach H, Lee C, Barreto W, Corradini P, Min CK, Scott EC, Chanan-Khan AA, Horvath N, Capra M, Beksac M, Ovilla R, Jo JC, Shin HJ, Sonneveld P, Soong D, Casneuf T, Chiu C, Amin H, Qi M, Thiyagarajah P, Sasser AK, Schecter JM, Mateos MV.* Haematologica. 2018 Dec;103(12):2079-2087. doi: 10.3324/haematol.2018.194118. PMID: 30237264 IF: 7.570 / D1
- **Mutations in RAS-BRAF-MAPK-ERK pathway define a specific subgroup of patients with adverse clinical features and provide new therapeutic options in chronic lymphocytic leukemia.** *Giménez N, Martínez-Trillos A, Montraveta A, Lopez-Guerra M, Rosich L, Nadeu F, Valero JG, Aymerich M, Magnano L, Rozman M, Matutes E, Delgado J, Bauman T, Gine E, González M, Alcoceba M, Terol MJ, Navarro B, Colado E, Payer AR, Puente XS, López-Otín C, Lopez-Guillermo A, Campo E, Colomer D, Villamor N.* Haematologica. 2018 Sep 27. pii: haematol.2018.196931. doi: 10.3324/haematol.2018.196931. PMID: 30262568 IF: 7.570 / D1
- **Increased Survival due to Lower Toxicity for High Risk T-cell Acute Lymphoblastic Leukemia Patients in 2 consecutive Pediatric-Inspired PETHEMA Trials.** *Barba P, Morgades M, Montesinos P, Gil C, Fox ML, Ciudad J, Moreno MJ, González-Campos J, Genescà E, Martínez-Carballeira D, Martino R, Vives S, Guardia R, Mercadal S, Artola MT, Cladera A, Tormo M, Esteve J, Bergua J, Vall-Llovera F, Ribera J, Martínez-Sánchez P, Amigo ML, Bermúdez A, Calbacho M, Hernández-Rivas JM, Feliu E, Orfao A, Ribera JM; PETHEMA Group.* Eur J Haematol. 2018 Sep 29. doi: 10.1111/ejh.13178. PMID: 30267597 IF: 2.217 / Q2
- **Polymorphisms in Receptors Involved in Opsonic and Nonopsonic Phagocytosis, and Correlation with Risk of Infection in Oncohematology Patients.** *Herrero-Sánchez MC, Angomás EB, de Ramón C, Tellería JJ, Corchete LA, Alonso S, Ramos MDC, Peñarrubia MJ, Márquez S, Fernández N, García Frade LJ, Sánchez Crespo M.* Infect Immun. 2018 Nov 20;86(12). pii: e00709-18. doi: 10.1128/IAI.00709-18. Print 2018 Dec. PMID: 30275011 IF: 3.160 / Q1
- **Hidden myelodysplastic syndrome (MDS): A prospective study to confirm or exclude MDS in patients with anemia of uncertain etiology.** *Bastida JM, López-Godino O, Vicente-Sánchez A, Bonanad-Boix S, Xicoy-Cirici B, Hernández-Sánchez JM, Such E, Cervera J, Caballero-Berrocal JC, López-Cadenas F, Arnao-Herráiz M, Rodríguez I, Llopis-Calatayud I, Jiménez MJ, Del Cañizo-Roldán MC, Díez-Campelo M.* Int J Lab Hematol. 2019 Feb;41(1):109-117. doi: 10.1111/ijlh.12933. PMID: 30290085 IF: 2.073 / Q2
- **Multirefractory primary immune thrombocytopenia; targeting the decreased sialic acid content.** *Revilla N, Corral J, Miñano A, Mingot-Castellano ME, Campos RM, Velasco F, González N, Galvez E, Berrueco R, Fuentes I, González-Lopez TJ, de la Morena-Barrio ME, González-Porras JR, Vicente V, Lozano ML.* Platelets. 2019;30(6):743-751. doi: 10.1080/09537104.2018.1513476. PMID: 30296193 IF: 3.106 / Q2
- **Using the Lymph2Cx assay for assessing cell-of-origin subtypes of HIV-related diffuse large B-cell lymphoma.** *Baptista MJ, Tapia G, Morgades M, Muncunill J, Muñoz-Marmol AM, Montoto S, Gribben JG, Calaminici M, Martínez A, González-Farre B, Dlouhy I, González-Barca E, Terol MJ, Miralles P, Alcoceba M, Vall-Llovera F, Briones J, Abrisqueta P, Abella E, Provencio M, García-Ballesteros C, Moraleda JM, Sancho JM, Ribera JM, Mate JL, Navarro JT.* Leuk Lymphoma. 2019 Apr;60(4):1087-1091. doi: 10.1080/10428194.2018.1512711. . PMID: 30322315 IF: 2.674 / Q2
- **Usefulness of eltrombopag for treating thrombocytopenia after allogeneic stem cell transplantation.** *Rivera D, Bastida JM, Lopez-Corral L, Sánchez-Guijo F, Cabrero M, Martin A, Perez E, Lopez-Parra M, Avendaño A, Veiga A, Baile M, Arratibel N, Carrillo J, Vazquez L, Caballero MD, González-Porras JR.* Bone Marrow Transplant. 2019

May;54(5):757-761. doi: 10.1038/s41409-018-0368-1. PMID: 30356164 IF: 4.674 / Q2

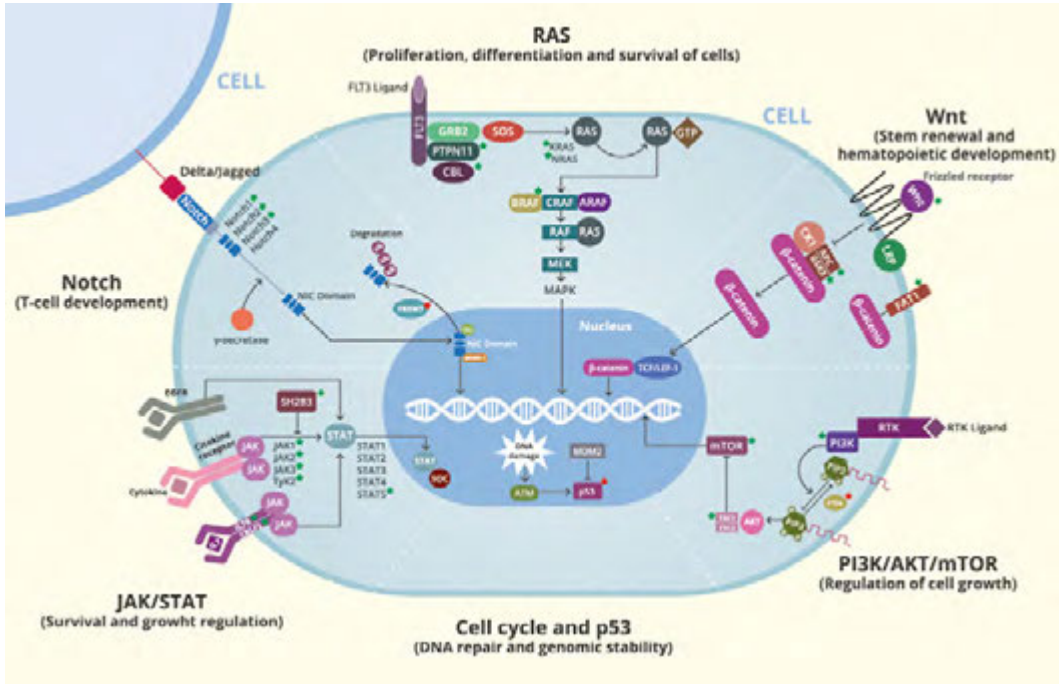
- **No Differences in Levels of Circulating Progenitor Endothelial Cells or Circulating Endothelial Cells Among Patients Treated With Ticagrelor Compared With Clopidogrel During Non- ST -Segment-Elevation Myocardial Infarction.** *Diego-Nieto A, Vidriales MB, Alonso-Orcajo N, Moreno-Samos JC, Martin-Herrero F, Carbonell R, Cid B, Cruz-González I, Martin-Moreiras JC, Cuellas C, Pascual C, Lopez-Benito M, Sánchez PL, Fernandez-Vazquez F, de Prado AP.* J Am Heart Assoc. 2018 Oct 2;7(19):e009444. doi: 10.1161/JAHA.118.009444. PMID: 30371302; PMCID: PMC6404906 IF: 4.660 / D1
- **Personalized medicine into health national services: barriers and potentialities.** *Rodríguez Vicente AE, Herrero Cervera MJ, Bernal ML, Rojas L, Peiró AM.* Drug Metab Pers Ther. 2018 Dec 19;33(4):159-163. doi: 10.1515/dmpt-2018-0017. PMID: 30391933 IF: NI
- **Summary of the Second Annual BMT CTN Myeloma Intergroup Workshop on Minimal Residual Disease and Immune Profiling.** *Holstein SA, Ye JC, Howard A, Bhutani M, Gormley N, Hahn T, Hillengass J, Krishnan A, Landgren CO, Munshi NC, Oliva S, Owen RG, Pasquini MC, Puig N, Weinhold N, Weisel K, McCarthy PL.* Biol Blood Marrow Transplant. 2019 Mar;25(3):e89-e97. doi: 10.1016/j.bbmt.2018.11.001. PMID: 30408566; PMCID: PMC6445685 IF: 3.599 / Q1
- **Timing of treatment of smoldering myeloma: early treatment.** *Mateos MV, González-Calle V.* Blood Adv. 2018 Nov 13;2(21):3045-3049. doi: 10.1182/bloodadvances.2018021220. PMID: 30425068 IF: NI
- **Focal Adhesion Genes Refine the Intermediate-Risk Cytogenetic Classification of Acute Myeloid Leukemia**. *Pallarès V, Hoyos M, Chillón MC, Barragán E, Prieto Conde MI, Llop M, Falgàs A, Céspedes MV, Montesinos P, Nomdedeu JF, Brunet S, Sanz MÁ, González-Díaz M, Sierra J, Mangues R, Casanova I.* Cancers (Basel). 2018 Nov 13;10(11). pii: E436. doi: 10.3390/cancers10110436. PMID: 30428571 IF: 6.162 / D1
- **Ring chromosome 15 - cytogenetics and mapping arrays: a case report and review of the literature.** *Paz-Y-Miño C, Guevara-Aguirre J, Paz-Y-Miño A, Velarde F, Armendáriz-Castillo I, Yumiceba V, Hernández JM, García JL, Leóne PE.* J Med Case Rep. 2018 Nov 16;12(1):340. doi: 10.1186/s13256-018-1879-5. Review. PMID: 30442194 IF: NI
- **Next generation flow for minimally-invasive blood characterization of MGUS and multiple myeloma at diagnosis based on circulating tumor plasma cells (CTPC).** *Sanoja-Flores L, Flores-Montero J, Garcés JJ, Paiva B, Puig N, García-Mateo A, García-Sánchez O, Corral-Mateos A, Burgos L, Blanco E, Hernández-Martín J, Pontes R, Díez-Campelo M, Millacoy P, Rodríguez-Otero P, Prosper F, Merino J, Vidriales MB, García-Sanz R, Romero A, Palomera L, Ríos-Tamayo R, Pérez-Andrés M, Blanco JF, González M, van Dongen JJM, Durie B, Mateos MV, San-Miguel J, Orfao A; EuroFlow consortium.* Blood Cancer J. 2018 Nov 19;8(12):117. doi: 10.1038/s41408-018-0153-9. PMID: 30455467 IF: 7.895 / Q1
- **Evolution of multiple myeloma treatment practices in Europe from 2014 to 2016.** *Raab MS, Fink L, Schoen P, González-McQuire S, Flinois A, Cavo M, Mateos MV, Yong K.* Br J Haematol. 2019 Jun;185(5):981-984. doi: 10.1111/bjh.15680. PMID: 30467828 IF: 5.206 / Q1
- **A precision medicine test predicts clinical response after idarubicin and cytarabine induction therapy in AML patients.** *Martínez-Cuadrón D, Gil C, Serrano J, Rodríguez G, Pérez-Oteyza J, García-Boyero R, Jiménez-Bravo S, Vives S, Vidriales MB, Lavilla E, Pérez-Simón JA, Tormo M, Colorado M, Bergua J, López JA, Herrera P, Hernández-Campo P, Gorrochategui J, Primo D, Rojas JL, Villoria J, Moscardó F, Troconiz I, Linares Gómez M, Martínez-López J, Ballesteros J, Sanz M, Montesinos P;* Spanish PETHEMA group. Leuk Res. 2019 Jan;76:1-10. doi: 10.1016/j.leukres.2018.11.006. PMID: 30468991 IF: 2.036 / Q2
- **Aneuploid acute myeloid leukemia exhibits a signature of genomic alterations in the cell cycle and protein degradation machinery.** *Simonetti G, Padella A, do Valle IF, Fontana MC, Fonzi E, Bruno S, Baldazzi C, Guadagnuolo V, Manfrini M, Ferrari A, Paolini S, Papayannidis C, Marconi G, Franchini E, Zuffa E, Laginestra MA, Zanotti F, Astolfi A, Iacobucci I, Bernardi S, Sazzini M, Ficarra E, Hernandez JM, Vandenberghe P, Cools J, Bullinger L, Ottaviani E, Testoni N, Cavo M, Haferlach T, Castellani G, Remondini D, Martinelli G.* Cancer. 2019 Mar 1;125(5):712-725. doi: 10.1002/cncr.31837. PMID: 30480765; PMCID: PMC6587451 IF: 6.102 / Q1
- **Subcutaneous bortezomib in newly diagnosed patients with multiple myeloma nontransplant eligible: Retrospective evaluation.** *de Arriba de la Fuente F, Durán MS, Álvarez MÁ, Sanromán IL, Dios AM, Ríos Tamayo R, García R, González MS, Prieto E, Bárez A, Escalante F, Tejedor A, Ballesteros M, Cabañas V, Capote FJ, Couto C, Garzón S, González-Pardo M, Mateos Manteca MV.* Semin Hematol. 2018 Oct;55(4):189-196. doi: 10.1053/j.seminhematol.2017.09.002. Review. PMID: 30502846 IF: 3.738 / Q1
- **Feasibility of treatment discontinuation in chronic myeloid leukemia in clinical practice: results from a nationwide series of 236 patients.** *Hernández-Boluda JC, Pereira A, Pastor-Galán I, Alvarez-Larrán A, Savchuk A, Puerta JM, Sánchez-Pina JM, Collado R, Díaz-González A, Angona A, Sagüés M, García-Gutiérrez V, Boqué C, Osorio S, Vallansot R, Palomera L, Mendizábal A, Casado LF, Pérez-Encinas M, Pérez-López R, Ferrer-Marín F, Sánchez-Guijo F, García C, Heras NL, López-Lorenzo JL, Cervantes F, Steegmann JL; Grupo Español de Leucemia Mieloide Crónica (GELMC).* Blood Cancer J. 2018 Dec 2;8(10):91. doi: 10.1038/s41408-018-0125-0. PMID: 30504932; PMCID: PMC6275158 IF: 7.895 / Q1
- **Clinical significance of complex karyotype at diagnosis in pediatric and adult patients with de novo acute promyelocytic leukemia treated with ATRA and chemotherapy.** *Labrador J, Luño E, Vellenga E, Brunet S, González-Campos J, Chillón MC, Holowiecka A, Esteve J, Bergua J, González-Sanmiguel JD, Gil C, Tormo M, Salamero O, Manso F, Fernández I, de laSerna J, Moreno MJ, Pérez-Encinas M, Krsnik I, Ribera JM, Cervera J, Calasanz MJ, Boluda B, Sobas M, Lowenberg B, Sanz MA, Montesinos P.* Leuk Lymphoma. 2019 May;60(5):1146-1155. doi: 10.1080/10428194.2018.1522438. PMID: 30526152 IF: 2.674 / Q2
- **Flow cytometry for fast screening and automated risk assessment in systemic light-chain amyloidosis.** *Puig N, Paiva B, Lasa M, Burgos L, Perez JJ, Merino J, Moreno C, Vidriales MB, Toboso DG, Cedena MT, Ocio EM, Lecumberri R, García de Coca A, Labrador J, González ME, Palomera L, Gironella M, Cabañas V, Casanova M, Oriol A, Krsnik I, Pérez-Montaña A, de la Rubia*

J, de la Puerta JE, de Arriba F, Prosper F, Martínez-Lopez J, Lecrevisse Q, Verde J, Mateos MV, Lahuerta JJ, Orfao A, San Miguel JF. **Leukemia. 2018 Dec 12. doi: 10.1038/s41375-018-0308-5.** PMID: 30542145 **IF: 9.944 / D1**

- **Oral ixazomib maintenance following autologous stem cell transplantation (TOURMALINE-MM3): a double-blind, randomised, placebo-controlled phase 3 trial.** *Dimopoulos MA, Gay F, Schjesvold F, Beksac M, Hajek R, Weisel KC, Goldschmidt H, Maisnar V, Moreau P, Min CK, Pluta A, Chng WJ, Kaiser M, Zweegman S, Mateos MV, Spencer A, Iida S, Morgan G, Suryanarayan K, Teng Z, Skacel T, Palumbo A, Dash AB, Gupta N, Labotka R, Rajkumar SV; TOURMALINE-MM3 study group.* **Lancet. 2019 Jan 19;393(10168):253-264. doi: 10.1016/S0140-6736(18)33003-4.** PMID: 30545780 **IF: 59.102 / D1**
- **Donor lymphocyte infusions for B-cell malignancies relapse after T-cell replete allogeneic hematopoietic cell transplantation.** *Ortí G, García-Cadenas I, López-Corral L, Pérez A, Jiménez MJ, Sánchez-Ortega I, Alonso L, Sisinni L, Fox L, Villacampa G, Badell I, de Heredia CD, Parody R, Ferrà C, Solano C, Caballero D, Martino R, Querol S, Valcárcel D.* **Bone Marrow Transplant. 2019 Jul;54(7):1133-1137. doi: 10.1038/s41409-018-0422-z. Erratum in: Bone Marrow Transplant. 2019 Feb 7;:** PMID: 30546069 **IF: 4.674 / Q2**
- **Bendamustine as part of conditioning of autologous stem cell transplantation in patients with aggressive lymphoma: a phase 2 study from the GELTAMO group.** *Redondo AM, Valcárcel D, González-Rodríguez AP, Suárez-Lledó M, Bello JL, Canales M, Gayoso J, Colorado M, Jarque I, Del Campo R, Arranz R, Terol MJ, Rifón JJ, Rodríguez MJ, Ramírez MJ, Castro N, Sánchez A, López-Jiménez J, Montes-Moreno S, Briones J, López A, Palomera L, López-Guillermo A, Caballero D, Martín A; Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO).* **Br J Haematol. 2019 Mar;184(5):797-807. doi: 10.1111/bjh.15713.** PMID: 30548583 **IF: 5.206 / Q1**
- **Exportin-1 E571K mutation is a common finding in patients with classical Hodgkin lymphoma.** *Navarro-Bailón A, Jiménez C, Alonso-Álvarez S, Alcoceba M, González-Calle V, Chillón MC, García-Álvarez M, Prieto I, Medina A, González M, Caballero MD, Blanco Ó, Díaz LG, García-Sanz R, Sarasquete ME.* **Hematol Oncol. 2019 Apr;37(2):215-218. doi: 10.1002/hon.2570.** PMID: 30548996 **IF: 3.439 / Q3**
- **Lenalidomide as maintenance for every newly diagnosed patient with multiple myeloma.** *Mateos MV, de la Calle VG.* **Lancet Oncol. 2019 Jan;20(1):5-6. doi: 10.1016/S1470-2045(18)30764-2.** PMID: 30559052 **IF: 35.386 / D1**
- **Comparative genomic hybridization analysis of basal cell carcinoma.** *Palacios-Álvarez I, Bueno E, Fernández-López E, García JL, González-Sarmiento R.* **J Dtsch Dermatol Ges. 2019 Feb;17(2):197-200. doi: 10.1111/ddg.13740.** PMID: 30629797 **IF: 3.924 / Q3**
- **Subconjunctival injection of mesenchymal stromal cells protects the cornea in an experimental model of GVHD.** *Martínez-Carrasco R, Sánchez-Abarca LI, Nieto-Gómez C, Martín García E, Sánchez-Guijo F, Argüeso P, Aijón J, Hernández-Galilea E, Velasco A.* **Ocul Surf. 2019 Apr;17(2):285-294. doi: 10.1016/j.jtos.2019.01.001.** PMID: 30630121 **IF: 9.108 / D1**
- **Genetic polymorphisms in genes of class switch recombination and multiple myeloma risk and survival: an IMMEnSE study.** *Campa D, Martino A, Macauda A, Dudziński M, Suska A, Druzd-Sitek A, Raab MS, Moreno V, Huhn S, Butrym A, Sainz J, Szombath G, Rymko M, Marques H, Lesueur F, Vangsted AJ, Vogel U, Kruszewski M, Subocz E, Buda G, Iskierka-Jażdżewska E, Ríos R, Merz M, Schöttker B, Mazur G, Perrial E, Martínez-Lopez J, Butterbach K, García Sanz R, Goldschmidt H, Brenner H, Jamroziak K, Reis RM, Kadar K, Dumontet C, Wątek M, Haastrup EK, Helbig G, Jurczyszyn A, Jerez A, Varkonyi J, Barington T, Grzasko N, Zaucha JM, Andersen V, Zawirska D, Canzian F.* **Leuk Lymphoma. 2019 Jul;60(7):1803-1811. doi: 10.1080/10428194.2018.1551536.** PMID: 30633655 **IF: 2.674 / Q2**
- **Safety and activity of ibrutinib in combination with nivolumab in patients with relapsed non-Hodgkin lymphoma or chronic lymphocytic leukaemia: a phase 1/2a study.** *Younes A, Brody J, Carpio C, Lopez-Guillermo A, Ben-Yehuda D, Ferhanoglu B, Nagler A, Ozcan M, Avivi I, Bosch F, Caballero Barrigón MD, Hellmann A, Kuss B, Ma DDF, Demirkan F, Yağci M, Horowitz NA, Marlton P, Cordoba R, Wrobel T, Buglio D, Streit M, Hodkinson BP, Schaffer M, Alvarez J, Ceulemans R, Balasubramanian S, de Jong J, Wang SS, Fourneau N, Jurczak W.* **Lancet Haematol. 2019 Feb;6(2):e67-e78. doi: 10.1016/S2352-3026(18)30217-5.** PMID: 30642819 **IF: 11.990 / D1**
- **Factors regulating microRNA Expression and Function in Multiple Myeloma.** *Misiewicz-Krzeminska I, Krzeminski P, Corchete LA, Quwaider D, Rojas EA, Herrero AB, Gutiérrez NC.* **Noncoding RNA. 2019 Jan 16;5(1). pii: E9. doi: 10.3390/ncrna5010009. Review.** PMID: 30654527 **IF: NI**
- **Brentuximab vedotin and ESHAP is highly effective as second-line therapy for Hodgkin lymphoma patients (long-term results of a trial by the Spanish GELTAMO Group).** *García-Sanz R, Sureda A, de la Cruz F, Canales M, González AP, Pinana JL, Rodriguez A, Gutiérrez A, Domingo-Domenech E, Sánchez-González B, Rodriguez G, Lopez J, Moreno M, Rodriguez-Salazar MJ, Jiménez-Cabrera S, Caballero MD, Martínez C.* **Ann Oncol. 2019 Apr 1;30(4):612-620. doi: 10.1093/annonc/mdz009.** PMID: 30657848 **IF: 14.196 / D1**
- **High subclonal fraction of 17p deletion is associated with poor prognosis in multiple myeloma.** *Thakurta A, Ortiz M, Blecua P, Towfic F, Corre J, Serbina NV, Flynt E, Yu Z, Yang Z, Palumbo A, Dimopoulos MA, Gutiérrez NC, Goldschmidt H, Sonneveld P, Avet-Loiseau H.* **Blood. 2019 Mar 14;133(11):1217-1221. doi: 10.1182/blood-2018-10-880831.** PMID: 30692124 **IF: 16.562 / D1**
- **Randomized Phase III Study of Alisertib or Investigator's Choice (Selected Single Agent) in Patients With Relapsed or Refractory Peripheral T-Cell Lymphoma.** *O'Connor OA, Özcan M, Jacobsen ED, Roncero JM, Trotman J, Demeter J, Masszi T, Pereira J, Ramchandren R, Beaven A, Caballero D, Horwitz SM, Lennard A, Turgut M, Hamerschlak N, d'Amore FA, Foss F, Kim WS, Leonard JP, Zinzani PL, Chiattone CS, Hsi ED, Trümper L, Liu H, Sheldon-Waniga E, Ullmann CD, Venkatakrishnan K, Leonard EJ, Shustov AR; Lumiere Study Investigators.* **J Clin Oncol. 2019 Mar 10;37(8):613-623. doi: 10.1200/JCO.18.00899.** PMID: 30707661; PMCID: PMC6494247 **IF: 28.245 / D1**
- **Author Correction: Donor lymphocyte infusions for B-cell malignancies relapse after T-cell replete allogeneic hematopoietic cell transplantation.** *Ortí G, García-Cadenas I, López-Corral L,*

Pérez A, Jiménez MJ, Sánchez-Ortega I, Alonso L, Sisinni L, Fox L, Villacampa G, Badell I, de Heredia CD, Parody R, Ferrà C, Solano C, Caballero D, Martino R, Querol S, Valcárcel D. **Bone Marrow Transplant. 2019 Jul;54(7):1176. doi: 10.1038/s41409-019-0471-y. Erratum for: Bone Marrow Transplant. 2019 Jul;54(7):1133-1137.** PMID: 30733543 IF: 4.674 / Q2

- **SHP1 and SHP2 inhibition enhances the pro-differentiative effect of phorbol esters: an alternative approach against acute myeloid leukemia.** *Pérez-Fernández A, López-Ruano G, Prieto-Bermejo R, Ijurko C, Díez-Campelo M, Sánchez-Guijo F, Hernández-Hernández Á.* **J Exp Clin Cancer Res. 2019 Feb 14;38(1):80. doi: 10.1186/s13046-019-1097-z.** PMID: 30764849; PMCID: PMC6376690 IF: 5.645 / Q1
- **Life expectancy of follicular lymphoma patients in complete response at 30 months is similar to that of the Spanish general population**. *Magnano L, Alonso-Alvarez S, Alcoceba M, Rivas-Delgado A, Muntañola A, Nadeu F, Setoain X, Rodríguez S, Andrade-Campos M, Espinosa-Lara N, Rodríguez G, Sancho JM, Moreno M, Mercadal S, Carro I, Salar A, García-Pallarols F, Arranz R, Cannata J, Terol MJ, Teruel AI, Jiménez-Ubieto A, Rodriguez A, González de Villambrosía S, Bello JL, López L, Novelli S, de Cabo E, Infante ME, Pardal E, Monsalvo S, González M, Martín A, Caballero MD, López-Guillermo A; Grupo Español de Linfomas y Trasplante Autólogo de Médula Ósea (GELTAMO).* **Br J Haematol. 2019 May;185(3):480-491. doi: 10.1111/bjh.15805.** PMID: 30793290 IF: 5.206 / Q1
- **Autologous mesenchymal stromal cells embedded in tricalcium phosphate for posterolateral spinal fusion: results of a prospective phase I/II clinical trial with long-term follow-up.** *Blanco JF, Villarón EM, Pescador D, da Casa C, Gómez V, Redondo AM, López-Villar O, López-Parra M, Muntión S, Sánchez-Guijo F.* **Stem Cell Res Ther. 2019 Feb 22;10(1):63. doi: 10.1186/s13287-019-1166-4.** PMID: 30795797; PMCID: PMC6387529 IF: 4.627 / D1
- **Health-related quality of life in the ENDEAVOR study: carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed/refractory multiple myeloma.** *Ludwig H, Moreau P, Dimopoulos MA, Mateos MV, Kaiser M, Hajek R, Feng S, Cocks K, Buchanan J, Weisel K.* **Blood Cancer J. 2019 Feb 22;9(3):23. doi: 10.1038/s41408-019-0181-0.** PMID: 30796199 IF: 7.895 / Q1
- **DNA damage response-related alterations define the genetic background of patients with chronic lymphocytic leukemia and chromosomal gains.** *Hernández-Sánchez M, Rodríguez-Vicente AE, González-Gascón Y Marín I, Quijada-Álamo M, Hernández-Sánchez JM, Martín-Izquierdo M, Hernández-Rivas JÁ, Benito R, Hernández-Rivas JM.* **Exp Hematol. 2019 Apr;72:9-13. doi: 10.1016/j.exphem.2019.02.003.** PMID: 30807786 IF: 2.462 / Q2



Cellular pathways affected by genes significantly mutated in ALL. Asterisks show the genes that are mutated in each cellular program and the biological effect of these mutations on the pathway (Green: activation mutation; Red: inactivating mutation) [from Montaño A et al., Cancers (2018);10(4). pii: E110. doi: 10.3390/cancers10040110].

- **Management of cardiovascular risk in patients with multiple myeloma.** *Plummer C, Driessen C, Szabo Z, Mateos MV.* **Blood Cancer J. 2019 Feb 26;9(3):26. doi: 10.1038/s41408-019-0183-y. Review.** PMID: 30808934 IF: 7.895 / Q1
- **Clinical and Molecular Comparative Study of Colorectal Cancer Based on Age-of-onset and Tumor Location: Two Main Criteria for Subclassifying Colorectal Cancer.** *Álvaro E, Cano JM, García JL, Brandáriz L, Olmedillas-López S, Arriba M, Rueda D, Rodríguez Y, Cañete Á, Arribas J, Inglada-Pérez L, Pérez J, Gómez C, García-Arranz M, García-Olmo D, Goel A, Urioste M, González-Sarmiento R, Perea J.* **Int J Mol Sci. 2019 Feb 22;20(4). pii: E968. doi: 10.3390/ijms20040968.** PMID: 30813366 IF: 4.183 / D1
- **INSIGHT MM: a large, global, prospective, non-interventional, real-world study of patients with multiple myeloma.** *Costello C, Davies FE, Cook G, Vela-Ojeda J, Omel J, Rifkin RM, Berdeja J, Puig N, Usmani SZ, Weisel K, Zonder JA, Terpos E, Spencer A, Leleu X, Boccadoro M, Thompson MA, Romanus D, Stull DM, Hungria V.* **Future Oncol. 2019 May;15(13):1411-1428. doi: 10.2217/fon-2019-0013.** PMID: 30816809; PMCID: PMC6854441 IF: 2.279 / Q3
- **Correction: Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond.** *Chim CS, Kumar SK, Orlowski RZ, Cook G, Richardson PG, Gertz MA, Giralt S, Mateos MV, Leleu X, Anderson KC.* **Leukemia. 2019 Apr;33(4):1058-1059. doi: 10.1038/s41375-019-0410-3.** PMID: 30842604 IF: 9.944 / D1
- **Correction: Early myeloma-related death in elderly patients: development of a clinical prognostic score and evaluation of response sustainability role**. *Rodríguez-Otero P, Mateos MV, Martínez-López J, Martín-Calvo N, Hernández MT, Ocio EM, Rosiñol L, Martínez R, Teruel AI, Gutiérrez NC, Bargay J, Bengoechea E, González Y, de Oteyza JP, Gironella M, Encinas C, Martín J, Cabrera C, Palomera L, de Arriba F, Cedena MT, Paiva B, Puig N, Oriol A, Bladé J, Lahuerta JJ, Miguel JFS.* **Leukemia. 2019 Apr;33(4):1056. doi: 10.1038/s41375-019-0408-x.** PMID: 30846864 IF: 9.944 / D1
- **Standardisation and consensus guidelines for minimal residual disease assessment in Philadelphia-positive acute lymphoblastic leukemia (Ph+ALL) by real-time quantitative reverse transcriptase PCR of e1a2 BCR-ABL1.** *Pfeifer H, Cazzaniga G, van der Velden VHJ, Cayuela JM, Schäfer B, Spinelli O, Akiki S, Avigad S, Bendit I, Borg K, Cavé H, Elia L, Reshmi SC, Gerrard G, Hayette S, Hermanson M, Juh A, Jurcek T, Chillón MC, Homburg C, Martinelli G, Kairisto V, Lange T, Lion T, Mueller MC, Pane F, Rai L, Damm-Welk C, Sacha T, Schnittger S, Touloumenidou T, Valerhaugen H, Vandenberghe P, Zuna J, Serve H, Herrmann E, Markovic S, Dongen JJMV, Ottmann OG.* **Leukemia. 2019 Aug;33(8):1910-1922. doi: 10.1038/s41375-019-0413-0.** PMID: 30858550 IF: 9.944 / D1
- **1q23.1 homozygous deletion and downregulation of Fc receptor-like family genes confer poor prognosis in chronic lymphocytic leukemia.** *Daniele G, L'Abbate A, Turchiano A, Palumbo O, Carella M, Lo Cunsolo C, Iuzzolino P, Lonoce A, Hernández-Sánchez M, Minoia C, Leone P, Hernandez-Rivas JM, Storlazzi CT.* **Clin Exp Med. 2019 May;19(2):261-267. doi: 10.1007/s10238-019-00551-0.** PMID: 30877410 IF: 2.642 / Q2
- **Predicting long-term disease control in transplant-ineligible patients with multiple myeloma: impact of an MGUS-like signature.** *Rodríguez-Otero P, Mateos MV, Martínez-López J, Hernández MT, Ocio EM, Rosiñol L, Martínez R, Teruel AI, Gutiérrez NC, Bargay J, Bengoechea E, González Y, de Oteyza JP, Gironella M, Nuñez-Córdoba JM, Encinas C, Martín J, Cabrera C, Palomera L, de Arriba F, Cedena MT, Puig N, Oriol A, Paiva B, Bladé J, Lahuerta JJ, San Miguel JF.* **Blood Cancer J. 2019 Mar 18;9(4):36. doi: 10.1038/s41408-019-0176-x.** PMID: 3088613**9** IF: 7.895 / Q1
- **Distribution of subsets of blood monocytic cells throughout life.** *Damasceno D, Teodosio C, van den Bossche WBL, Perez-Andres M, Arriba-Méndez S, Muñoz-Bellvis L, Romero A, Blanco JF, Remesal A, Puig N, Matarraz S, Vicente-Villardón JL, van Dongen JJM, Almeida J, Orfao A; TiMaScan Study Group.* **J Allergy Clin Immunol. 2019 Jul;144(1):320-323.e6. doi: 10.1016/j.jaci.2019.02.030.** PMID: 30890326 IF: 14.110 / D1
- **High prognostic value of measurable residual disease detection by flow cytometry in chronic lymphocytic leukemia patients treated with front-line fludarabine, cyclophosphamide, and rituximab, followed by three years of rituximab maintenance.** *García-Marco JA, Jiménez JL, Recasens V, Zarzoso MF, González-Barca E, De Marcos NS, Ramírez MJ, Parraga FJP, Yañez L, De La Serna Torroba J, Malo MDG, Ariznavarreta GD, Persona EP, Guinaldo MAR, De Paz Arias R, Llanos EB, Jarque I, Valle MDCF, Tatay AC, De Oteyza JP, Martin EMD, Fernández IP, Martínez RM, Costa MAA, Champ D, Suarez JG, Díaz MG, Ferrer S, Carbonell F, García-Vela JA; GELLC Study Group.* **Haematologica. 2019 Nov;104(11):2249-2257. doi: 10.3324/haematol.2018.204891.** PMID: 30890600; PMCID: PMC6821631 IF: 7.570 / D1
- **Treatment of patients with multiple myeloma progressing on frontline-therapy with lenalidomide.** *Moreau P, Zamagni E, Mateos MV.* **Blood Cancer J. 2019 Mar 20;9(4):38. doi: 10.1038/s41408-019-0200-1.** PMID: 30894516 IF: 7.895 / Q1
- **Improving the conditioning regimen in multiple myeloma.** *Mateos MV, González-Calle V.* **Lancet Haematol. 2019 May;6(5):e234-e235. doi: 10.1016/S2352-3026(19)30028-6.** PMID: 30910540 IF: 11.990 / D1
- **The poor prognosis of low hypodiploidy in adults with B-cell precursor acute lymphoblastic leukaemia is restricted to older adults and elderly patients.** *Ribera J, Granada I, Morgades M, Vives S, Genescà E, González C, Nomdedeu J, Escoda L, Montesinos P, Mercadal S, Coll R, González-Campos J, Abella E, Barba P, Bermúdez A, Gil C, Tormo M, Pedreño M, Martínez-Carballeira D, Hernández-Rivas JM, Orfao A, Martínez-López J, Esteve J, Bravo P, García-Guiñon A, Debén G, Moraleda JM, Queizán JA, Ortín X, Moreno MJ, Feliu E, Solé F, Ribera JM; PETHEMA Group, Spanish Society of Haematology.* **Br J Haematol. 2019 Jul;186(2):263-268. doi: 10.1111/bjh.15887.** PMID: 30916384 IF: 5.206 / Q1
- **Identification of the first large intronic deletion responsible of type I antithrombin deficiency not detected by routine molecular diagnostic methods.** *De la Morena-Barrio B, Borràs N, Rodríguez-Alén A, de la Morena-Barrio ME, García-Hernández JL, Padilla J, Bravo-Pérez C, Miñano A, Rollón N, Corral J, Vidal F, Vicente V.* **Br J Haematol. 2019 Aug;186(4):e82-e86. doi: 10.1111/bjh.15913.** PMID: 30941754 IF: 5.206 / Q1
- **Exome sequencing identifies germline variants in DIS3 in familial multiple**

myeloma. *Pertesi M, Vallée M, Wei X, Revuelta MV, Galia P, Demangel D, Oliver J, Foll M, Chen S, Perrial E, Garderet L, Corre J, Leleu X, Boyle EM, Decaux O, Rodon P, Kolb B, Slama B, Mineur P, Voog E, Le Bris C, Fontan J, Maigre M, Beaumont M, Azais I, Sobol H, Vignon M, Royer B, Perrot A, Fuzibet JG, Dorvaux V, Anglaret B, Cony-Makhoul P, Berthou C, Desquesnes F, Pegourie B, Leyvraz S, Mosser L, Frenkiel N, Augeul-Meunier K, Leduc I, Leyronnas C, Voillat L, Casassus P, Mathiot C, Cheron N, Paubelle E, Moreau P, Bignon YJ, Joly B, Bourquard P, Caillot D, Naman H, Rigaudeau S, Marit G, Macro M, Lambrecht I, Cliquennois M, Vincent L, Helias P, Avet-Loiseau H, Moreno V, Reis RM, Varkonyi J, Kruszewski M, Vangsted AJ, Jurczyszyn A, Zaucha JM, Sainz J, Krawczyk-Kulis M, Wątek M, Pelosini M, Iskierka-Jażdżewska E, Grząśko N, Martínez-Lopez J, Jerez A, Campa D, Buda G, Lesueur F, Dudziński M, García-Sanz R, Nagler A, Rymko M, Jamroziak K, Butrym A, Canzian F, Obazee O, Nilsson B, Klein RJ, Lipkin SM, McKay JD, Dumontet C.* **Leukemia. 2019 Sep;33(9):2324-2330. doi: 10.1038/s41375-019-0452-6.** PMID: 30967618; PMCID: PMC6756025 **IF: 9.944 / D1**

- **Daratumumab is a safe and effective rescue therapy for multiple myeloma patients who relapse after allo-HSCT.** *González-Rodriguez AP, Lopez-Corral L, Fajardo DFM, González-Huerta AJ, Palomo P, Bermudez A, Ripa TZ, Santos-Díaz P, González-Muñiz S, Zanabilli J, Ubieto AJ, de Arriba F, Arnao-Herraiz M, Sordo-Bahamonde C, López-Soto A, González S, Rosiñol L, Mateos MV.* **Bone Marrow Transplant. 2019 Apr 15. doi: 10.1038/s41409-019-0525-1.** PMID: 30988379 **IF: 4.674 / Q2**
- **Identification of novel variants in ten patients with Hermansky-Pudlak syndrome by high-throughput sequencing.** *Bastida JM, Morais S, Palma-Barqueros V, Benito R, Bermejo N, Karkucak M, Trapero-Marugan M, Bohdan N, Pereira M, Marin-Quilez A, Oliveira J, Yucel Y, Santos R, Padilla J, Janusz K, Lau C, Martin-Izquierdo M, Couto E, Francisco Ruiz-Pividal J, Vicente V, Hernández-Rivas JM, González-Porras JR, Luisa Lozano M, Lima M, Rivera J.* **Ann Med. 2019 Mar;51(2):141-148. doi: 10.1080/07853890.2019.1587498.** PMID: 30990103 **IF: 3.049 / D1**
- **Role of urine immunofixation in the complete response assessment of MM patients other than light-chain-only disease.** *Lahuerta JJ, Jiménez-Ubieto A, Paiva B, Martínez-López J, González-Medina J, López-Anglada L, Cedena MT, Puig N, Oriol A, Blanchard MJ, Ríos R, Martin J, Martínez R, Sureda A, Hernández MT, de la Rubia J, Krsnik I, Cabañas V, Palomera L, Bargay J, Mateos MV, Rosiñol L, San Miguel JF, Blade J.* **Blood. 2019 Jun 20;133(25):2664-2668. doi: 10.1182/blood.2019000671.** PMID: 31010846 **IF: 16.562 / D1**
- **Incidence and outcome after first molecular versus overt recurrence in patients with Philadelphia chromosome-positive acute lymphoblastic leukemia included in the ALL Ph08 trial from the Spanish PETHEMA Group.** *Ribera JM, García O, Moreno MJ, Barba P, García-Cadenas I, Mercadal S, Montesinos P, Barrios M, González-Campos J, Martínez-Carballeira D, Gil C, Ribera J, Vives S, Novo A, Cervera M, Serrano J, Lavilla E, Abella E, Tormo M, Amigo ML, Artola MT, Genescà E, Bravo P, García-Belmonte D, García-Guiñón A, Hernández-Rivas JM, Feliu E; PETHEMA Group of the Spanish Society of Hematology.* **Cancer. 2019 Aug 15;125(16):2810-2817. doi: 10.1002/cncr.32156.** PMID: 31012967 **IF: 6.102 / Q1**
- **Molecular Diagnosis of Inherited Coagulation and Bleeding Disorders.** *Bastida JM, Benito R, Lozano ML, Marín-Quilez A, Janusz K, Martín-Izquierdo M, Hernández-Sánchez J, Palma-Barqueros V, Hernández-Rivas JM, Rivera J, González-Porras JR.* **Semin Thromb Hemost. 2019 Oct;45(7):695-707. doi: 10.1055/s-0039-1687889.** PMID: 31041795 **IF: 3.401 / D1**
- **Vitamin D Modifies the Incidence of Graft-versus-Host Disease after Allogeneic Stem Cell Transplantation Depending on the Vitamin D Receptor (VDR) Polymorphisms.** *Carrillo-Cruz E, García-Lozano JR, Márquez-Malaver FJ, Sánchez-Guijo FM, Montero Cuadrado I, Ferra I Coll C, Valcárcel D, López-Godino O, Cuesta M, Parody R, López-Corral L, Alcoceba M, Caballero-Velázquez T, Rodríguez-Gil A, Bejarano-García JA, Ramos TL, Pérez-Simón JA.* **Clin Cancer Res. 2019 Aug 1;25(15):4616-4623. doi: 10.1158/1078-0432.CCR-18-3875.** PMID: 31043390 **IF: 8.911 / D1**
- **Response to Novel Drugs before and after Allogeneic Stem Cell Transplantation in Patients with Relapsed Multiple Myeloma.** *López-Corral L, Caballero-Velázquez T, López-Godino O, Rosiñol L, Pérez-Vicente S, Fernandez-Avilés F, Krsnik I, Morillo D, Heras I, Morgades M, Rifon JJ, Sampol A, Iniesta F, Ocio EM, Martin J, Rovira M, Cabero M, Castilla-Llorente C, Ribera JM, Torres-Juan M, Moraleda JM, Martínez C, Vázquez A, Gutiérrez G, Caballero D, San Miguel JF, Mateos MV, Pérez-Simón JA.* **Biol Blood Marrow Transplant. 2019 Sep;25(9):1703-1712. doi: 10.1016/j.bbmt.2019.04.026.** PMID: 31054983 **IF: 3.599 / Q1**
- **Splice donor site sgRNAs enhance CRISPR/Cas9-mediated knockout efficiency.** *García-Tuñón I, Alonso-Pérez V, Vuelta E, Pérez-Ramos S, Herrero M, Méndez L, Hernández-Sánchez JM, Martín-Izquierdo M, Saldaña R, Sevilla J, Sánchez-Guijo F, Hernández-Rivas JM, Sánchez-Martín M.* **PLoS One. 2019 May 9;14(5):e0216674. doi: 10.1371/journal.pone.0216674. eCollection 2019.** PMID: 31071190 **IF: 2.776 / Q1**
- **Pembrolizumab combined with lenalidomide and low-dose dexamethasone for relapsed or refractory multiple myeloma: phase I KEYNOTE-023 study.** *Mateos MV, Orlowski RZ, Ocio EM, Rodríguez-Otero P, Reece D, Moreau P, Munshi N, Avigan DE, Siegel DS, Ghori R, Farooqui MZH, Marinello P, San-Miguel J.* **Br J Haematol. 2019 Sep;186(5):e117-e121. doi: 10.1111/bjh.15946.** PMID: 31090915 **IF: 5.206 / Q1**
- **Intermediate-onset colorectal cancer: A clinical and familial boundary between both early and late-onset colorectal cancer.** *Arriba M, Sánchez C, Vivas A, Nutu OA, Rueda D, Tapial S, Rodríguez Y, Brandáriz L, García JL, García-Olmo D, Goel A, González-Sarmiento R, Urioste M, Perea J.* **PLoS One. 2019 May 16;14(5):e0216472. doi: 10.1371/journal.pone.0216472. eCollection 2019.** PMID: 31095598 **IF: 2.776 / D1**
- **Understanding mortality in multiple myeloma: Findings of a European retrospective chart review.** *Mohty M, Cavo M, Fink L, González-McQuire S, Leleu H, Mateos MV, Raab MS, Schoen P, Yong K.* **Eur J Haematol. 2019 Aug;103(2):107-115. doi: 10.1111/ejh.13264. PMID: 31112311;** PMCID: PMC6851592 **IF: 2.217 / Q2**
- **Daratumumab plus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma.** *Chari A, Martínez-Lopez J, Mateos MV, Bladé J, Benboubker L, Oriol A, Arnulf B, Rodriguez-Otero P, Pineiro L, Jakubowiak*

A, de Boer C, Wang J, Clemens PL, Ukropec J, Schecter J, Lonial S, Moreau P. **Blood. 2019 Aug 1;134(5):421-431. doi: 10.1182/blood.2019000722.** PMID: 31113777
IF: 16.562 / D1

- **International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders.** *Hillengass J, Usmani S, Rajkumar SV, Durie BGM, Mateos MV, Lonial S, Joao C, Anderson KC, García-Sanz R, Riva E, Du J, van de Donk N, Berdeja JG, Terpos E, Zamagni E, Kyle RA, San Miguel J, Goldschmidt H, Giralt S, Kumar S, Raje N, Ludwig H, Ocio E, Schots R, Einsele H, Schjesvold F, Chen WM, Abildgaard N, Lipe BC, Dytfeld D, Wirk BM, Drake M, Cavo M, Lahuerta JJ, Lentzsch S.* **Lancet Oncol. 2019 Jun;20(6):e302-e312. doi: 10.1016/S1470-2045(19)30309-2. Review. Erratum in: Lancet Oncol. 2019 Jul;20(7):e346.** PMID: 31162104 IF: 35.386 / D1
- **Deferasirox reduces oxidative DNA damage in bone marrow cells from myelodysplastic patients and improves their differentiation capacity.** *Jiménez-Solas T, López-Cadenas F, Aires-Mejía I, Caballero-Berrocal JC, Ortega R, Redondo AM, Sánchez-Guijo F, Muntión S, García-Martín L, Albarrán B, Alonso JM, Del Cañizo C, Hernández-Hernández Á, Díez-Campelo M.* **Br J Haematol. 2019 Oct;187(1):93-104. doi: 10.1111/bjh.16013.** PMID: 31172513 IF: 5.206 / Q1
- **The Incorporation of Extracellular Vesicles from Mesenchymal Stromal Cells Into CD34+ Cells Increases Their Clonogenic Capacity and Bone Marrow Lodging Ability.** *Preciado S, Muntión S, Corchete LA, Ramos TL, de la Torre AG, Osugui L, Rico A, Espinosa-Lara N, Gastaca I, Díez-Campelo M, Del Cañizo C, Sánchez-Guijo F.* Stem Cells. **2019 Oct;37(10):1357-1368. doi: 10.1002/stem.3032.** PMID: 31184411 IF: 5.614 / Q1
- **Immunoglobulin gene rearrangement IGHV3-48 is a predictive marker of histological transformation into aggressive lymphoma in follicular lymphomas.** *García-Álvarez M, Alonso-Álvarez S, Prieto-Conde I, Jiménez C, Sarasquete ME, Chillón MC, Medina A, Balanzategui A, Maldonado R, Antón A, Puig N, Rodríguez M, Blanco O, Tamayo P, González-Calle V, Martín A, García-Sanz R, González M, Caballero MD, Alcoceba M.* **Blood Cancer J. 2019 Jun 17;9(7):52. doi: 10.1038/s41408-019-0213-9.** PMID: 31209206 IF: 7.895 / Q1
- **Daratumumab-based regimens are highly effective and well tolerated in relapsed or refractory multiple myeloma regardless of patient age: subgroup analysis of the phase 3 CASTOR and POLLUX studies.** *Mateos MV, Spencer A, Nooka AK, Pour L, Weisel K, Cavo M, Laubach JP, Cook G, Iida S, Benboubker L, Usmani SZ, Yoon SS, Bahlis NJ, Chiu C, Ukropec J, Schecter JM, Qin X, O' Rourke L, Dimopoulos MA.* **Haematologica. 2019 Jun 20. pii: haematol.2019.217448. doi: 10.3324/haematol.2019.217448.** PMID: 31221782 IF: 7.570 / D1
- **Quality control and quantification in IG/TR next-generation sequencing marker identification: protocols and bioinformatic functionalities by EuroClonality-NGS.** *Knecht H, Reigl T, Kotrová M, Appelt F, Stewart P, Bystry V, Krejci A, Grioni A, Pal K, Stranska K, Plevova K, Rijntjes J, Songia S, Svatoň M, Froňková E, Bartram J, Scheijen B, Herrmann D, García-Sanz R, Hancock J, Moppett J, van Dongen JJM, Cazzaniga G, Davi F, Groenen PJTA, Hummel M, Macintyre EA, Stamatopoulos K, Trka J, Langerak AW, González D, Pott C, Brüggemann M, Darzentas N; EuroClonality-NGS Working Group.* **Leukemia. 2019 Sep;33(9):2254-2265. doi: 10.1038/s41375-019-0499-4.** PMID: 31227779
IF: 9.944 / D1
- **Cost-Effective, Safe, and Personalized Cell Therapy for Critical Limb Ischemia in Type 2 Diabetes Mellitus.** *Soria-Juan B, Escacena N, Capilla-González V, Aguilera Y, Llanos L, Tejedo JR, Bedoya FJ, Juan V, De la Cuesta A, Ruiz-Salmerón R, Andreu E, Grochowicz L, Prósper F, Sánchez-Guijo F, Lozano FS, Miralles M, Del Río-Solá L, Castellanos G, Moraleda JM, Sackstein R, García-Arranz M, García-Olmo D, Martín F, Hmadcha A, Soria B; Collaborative Working Group "Noma Project Team".* **Front Immunol. 2019 Jun 4;10:1151. doi: 10.3389/fimmu.2019.01151.** PMID: 31231366; PMCID: PMC6558400
IF: 4.716 / Q1
- **Randomized phase III study (ADMYRE) of plitidepsin in combination with dexamethasone vs. dexamethasone alone in patients with relapsed/refractory multiple myeloma.** *Spicka I, Ocio EM, Oakervee HE, Greil R, Banh RH, Huang SY, D'Rozario JM, Dimopoulos MA, Martínez S, Extremera S, Kahatt C, Alfaro V, Carella AM, Meuleman N, Hájek R, Symeonidis A, Min CK, Cannell P, Ludwig H, Sonneveld P, Mateos MV.* **Ann Hematol. 2019 Sep;98(9):2139-2150. doi: 10.1007/s00277-019-03739-2.** PMID: 31240472
IF: 2.850 / Q2
- **Standardized next-generation sequencing of immunoglobulin and T-cell receptor gene recombinations for MRD marker identification in acute lymphoblastic leukaemia; a EuroClonality-NGS validation study.** *Brüggemann M, Kotrová M, Knecht H, Bartram J, Boudjogrha M, Bystry V, Fazio G, Froňková E, Giraud M, Grioni A, Hancock J, Herrmann D, Jiménez C, Krejci A, Moppett J, Reigl T, Salson M, Scheijen B, Schwarz M, Songia S, Svaton M, van Dongen JJM, Villarese P, Wakeman S, Wright G, Cazzaniga G, Davi F, García-Sanz R, González D, Groenen PJTA, Hummel M, Macintyre EA, Stamatopoulos K, Pott C, Trka J, Darzentas N, Langerak AW; EuroClonality-NGS working group.* **Leukemia. 2019 Sep;33(9):2241-2253. doi: 10.1038/s41375-019-0496-7.** PMID: 31243313; PMCID: PMC6756028
IF: 9.944 / D1
- **Subcutaneous delivery of daratumumab in relapsed or refractory multiple myeloma.** *Usmani SZ, Nahi H, Mateos MV, van de Donk NWCJ, Chari A, Kaufman JL, Moreau P, Oriol A, Plesner T, Benboubker L, Hellemans P, Masterson T, Clemens PL, Luo M, Liu K, San-Miguel J.* **Blood. 2019 Aug 22;134(8):668-677. doi: 10.1182/blood.2019000667.** PMID: 31270103
IF: 16.562 / D1
- **Chronic graft-versus-host disease could ameliorate the impact of adverse somatic mutations in patients with myelodysplastic syndromes and hematopoietic stem cell transplantation.** *Caballero JC, Sánchez Barba M, Hernández Sánchez JM, Such E, Janusz K, Sanz G, Cabrero M, Chillón C, Cervera J, Hurtado AM, Jerez A, Calderón Cabrera C, Valcárcel D, Lumbreras E, Abáigar M, López Cadenas F, Hernández Rivas JM, Del Cañizo MC, Díez Campelo M.* **Ann Hematol. 2019 Sep;98(9):2151-2162. doi: 10.1007/s00277-019-03751-6.** PMID: 31312927
IF: 2.850 / Q2
- **Autologous stem cell transplantation may be curative for patients with follicular lymphoma with early therapy failure without the need for immunotherapy.** *Jiménez-Ubieto A, Grande C, Caballero D, Yáñez L, Novelli S, Hernández-García MT, Manzanares M, Arranz R, Ferreiro JJ, Bobillo S, Mercadal S,*

Galeo A, Jiménez JL, Moraleda JM, Vallejo C, Albo C, Pérez E, Marrero C, Magnano L, Palomera L, Jarque I, Rodriguez A, Lorza L, Martín A, Coria E, López-Guillermo A, Salar A, José Lahuerta J; GELTAMO (Grupo Español de Linfomas y Trasplantes de Médula Ósea) Cooperative Study Group. **Hematol Oncol Stem Cell Ther. 2019 Dec;12(4):194-203. doi: 10.1016/j.hemonc.2019.06.001.** PMID: 31319058 **IF: NI**

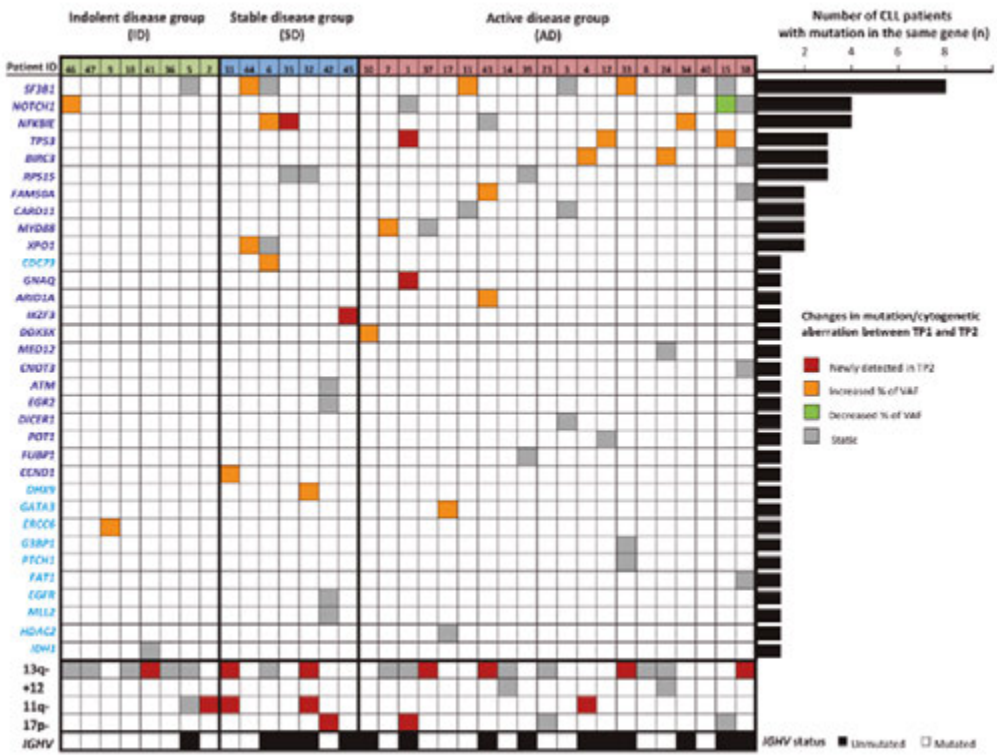
- **Preclinical evaluation of the simultaneous inhibition of MCL-1 and BCL-2 with the combination of S63845 and venetoclax in multiple myeloma.** *Algarín EM, Díaz-Tejedor A, Mogollón P, Hernández-García S, Corchete LA, San-Segundo L, Martín-Sánchez M, González-Méndez L, Schoumacher M, Banquet S, Kraus-Berthier L, Kloos I, Derreal A, Halilovic E, Maacke H, Gutiérrez NC, Mateos MV, Paíno T, Garayoa M, Ocio EM.* **Haematologica. 2019 Jul 18. pii: haematol.2018.212308. doi: 10.3324/haematol.2018.212308.** PMID: 31320555 **IF: 7.570 / D1**
- **Cimp-Positive Status is More Representative in Multiple Colorectal Cancers than in Unique Primary Colorectal Cancers.** *Tapial S, Olmedillas-López S, Rueda D, Arriba M, García JL, Vivas A, Pérez J, Pena-Couso L, Olivera R, Rodríguez Y, García-Arranz M, García-Olmo D, González-Sarmiento R, Urioste M, Goel A, Perea J.* **Sci Rep. 2019 Jul 19;9(1):10516. doi: 10.1038/s41598-019-47014-w.** PMID: 31324877 **IF: 4.011 / D1**
- **Pembrolizumab plus pomalidomide and dexamethasone for patients with relapsed or refractory multiple myeloma (KEYNOTE-183): a randomised, open-label, phase 3 trial.** *Mateos MV, Blacklock H, Schjesvold F, Oriol A, Simpson D, George A, Goldschmidt H, Larocca A, Chanan-Khan A, Sherbenou D, Avivi I, Benyamini N, Iida S, Matsumoto M, Suzuki K, Ribrag V, Usmani SZ, Jagannath S, Ocio EM, Rodriguez-Otero P, San Miguel J, Kher U, Farooqui M, Liao J, Marinello P, Lonial S; KEYNOTE-183 Investigators.* **Lancet Haematol. 2019 Sep;6(9):e459-e469. doi: 10.1016/S2352-3026(19)30110-3.** PMID: 31327687 **IF: 11.990 / D1**
- **Molecular profiling refines minimal residual disease-based prognostic assessment in adults with Philadelphia chromosome-negative B-cell precursor acute lymphoblastic leukemia.** *Ribera J, Zamora L, Morgades M, Vives S, Granada I, Montesinos P, Gómez-Seguí I, Mercadal S, Guàrdia R, Nomdedeu J, Pratcorona M, Tormo M, Martínez-Lopez J, Hernández-Rivas JM, Ciudad J, Orfao A, González-Campos J, Barba P, Escoda L, Esteve J, Genescà E, Solé F, Feliu E, Ribera JM; Spanish PETHEMA Group; Spanish Society of Hematology.* **Genes Chromosomes Cancer. 2019 Nov;58(11):815-819. doi: 10.1002/gcc.22788.** PMID: 31340073 **IF: 2.940 / Q2**
- **Genomic analysis of a familial myelodysplasia/acute myeloid leukemia and inherited RUNX1 mutations without a pre-existing platelet disorder.** *Prieto-Conde MI, Labrador J, Hermida G, Alonso S, Jiménez C, García-Álvarez M, Medina A, Balanzategui A, Alcoceba M, Sarasquete ME, Puig N, González V, Gutiérrez NC, García-Sanz R, González-Díaz M, Chillón MDC.* **Leuk Lymphoma. 2019 Aug 6:1-4. doi: 10.1080/10428194.2019.1648801.** PMID: 31385734 **IF: 2.674 / Q2**
- **Atrial Fibrillation in Active Cancer Patients: Expert Position Paper and Recommendations.** *López-Fernández T, Martín-García A, Roldán Rabadán I, Mitroi C, Mazón Ramos P, Díez-Villanueva P, Escobar Cervantes C, Alonso Martín C, Alonso Salinas GL, Arenas M, Arrarte Esteban VI, Ayala de La Peña F, Castro Fernández A, García Pardo H, García-Sanz R, González Porras JR, López de Sá E, Lozano T, Marco Vera P, Martínez Marín V, Mesa Rubio D, Montero Á, Oristrell G, Pérez de Prado A, Velasco Del Castillo S, Virizuela Echaburu JA, Zatarain-Nicolás E, Anguita Sánchez M, Tamargo Menéndez J;* **Expert reviewers. Rev Esp Cardiol (Engl Ed). 2019 Sep;72(9):749-759. English, Spanish. doi: 10.1016/j.rec.2019.03.019.** PMID: 31405794 **IF: 5.078 / Q3**
- **Chimeric Antigen Receptor T-cell therapy for multiple myeloma: a consensus statement from The European Myeloma Network.** *Moreau P, Sonneveld P, Boccadoro M, Cook G, Mateos MV, Nahi H, Goldschmidt H, Dimopoulos MA, Lucio P, Bladé J, Delforge M, Hajek R, Ludwig H, Facon T, San Miguel JF, Einsele H.* Haematologica. 2019 Aug 22. pii: haematol.2019.224204. doi: 10.3324/haematol.2019.224204. PMID: 31439675 **IF: 7.570 / D1**
- **Bortezomib, lenalidomide, and dexamethasone as induction therapy prior to autologous transplantation in multiple myeloma.** *Rosiñol L, Oriol A, Rios R, Sureda A, Blanchard MJ, Hernández MT, Martínez-Martínez R, Moraleda JM, Jarque I, Bargay J, Gironella M, de Arriba F, Palomera L, González-Montes Y, Marti J, Krsnik I, Arguiñano JM, González ME, González AP, Casado LF, Lopez-Anglada L, Paiva B, Mateos MV, San Miguel J, Lahuerta JJ, Bladé J.* **Blood. 2019 Sep 4. pii: blood.2019000241. doi: 10.1182/blood.2019000241.** PMID: 31484647 **IF: 16.562 / D1**
- **Management of Adult Patients with Primary Immune Thrombocytopenia (ITP) in Clinical Practice: A Consensus Approach of the Spanish ITP Expert Group.** *Mingot-Castellano ME, Román MTÁ, Fernández Fuertes LF, González-López TJ, Guinea de Castro JM, Jarque I, López-Fernández MF, Lozano ML, Sánchez González B, Ferreiras DV, González Porras JR.* **Adv Hematol. 2019 Aug 22;2019:4621416. doi: 10.1155/2019/4621416.** PMID: 31534457; PMCID: PMC6724426 **IF: NI**
- **Safety and efficacy of oral panobinostat plus chemotherapy in patients aged 65 years or younger with high-risk acute myeloid leukemia.** *DeAngelo DJ, Walker AR, Schlenk RF, Sierra J, Medeiros BC, Ocio EM, Röllig C, Strickland SA, Thol F, Valera SZ, Dasgupta K, Berkowitz N, Stuart RK.* **Leuk Res. 2019 Oct;85:106197. doi: 10.1016/j.leukres.2019.106197.** PMID: 31541945 **IF: 2.036 / Q2**
- **Mitochondrial Reprogramming Underlies Resistance to BCL-2 Inhibition in Lymphoid Malignancies.** *Guièze R, Liu VM, Rosebrock D, Jourdain AA, Hernández-Sánchez M, Martínez Zurita A, Sun J, Ten Hacken E, Baranowski K, Thompson PA, Heo JM, Cartun Z, Aygün O, Iorgulescu JB, Zhang W, Notarangelo G, Livitz D, Li S, Davids MS, Biran A, Fernandes SM, Brown JR, Lako A, Ciantra ZB, Lawlor MA, Keskin DB, Udeshi ND, Wierda WG, Livak KJ, Letai AG, Neuberg D, Harper JW, Carr SA, Piccioni F, Ott CJ, Leshchiner I, Johannessen CM, Doench J, Mootha VK, Getz G, Wu CJ.* **Cancer Cell. 2019 Oct 14;36(4):369-384.e13. doi: 10.1016/j.ccell.2019.08.005.** PMID: 31543463 **IF: 23.916 / D1**
- **Efficacy of bortezomib to intensify the conditioning regimen and the graft-versus-host disease prophylaxis for high-risk myeloma patients undergoing transplantation.** *Caballero-Velázquez T, Calderón-Cabrera C, López-Corral L, Puig N, Marquez-Malaver F, Pérez-López E, García-Calderón C, Rosso-Fernández CM, Caballero Barrigón D, Martín J, Mateos MV, San Miguel*

J, Pérez-Simón JA; European Myeloma Network. **Bone Marrow Transplant. 2019 Sep 24. doi: 10.1038/s41409-019-0670-6.** PMID: 31551517 **IF: 4.674 / D1**

- **Response-adapted treatment with rituximab, bendamustine, mitoxantrone, and dexamethasone followed by rituximab maintenance in patients with relapsed or refractory follicular lymphoma after first-line immunochemotherapy: Results of the RBMDGELTAMO08 phase II trial.** *Peñalver FJ, Márquez JA, Durán S, Giraldo P, Martín A, Montalbán C, Sancho JM, Ramírez MJ, Terol MJ, Capote FJ, Gutiérrez A, Sánchez B, López A, Salar A, Rodríguez-Caravaca G, Canales M, Caballero MD; GELTAMO (The Spanish Lymphoma Cooperative Group).* **Cancer Med. 2019 Nov;8(16):6955-6966. doi: 10.1002/cam4.2555.** PMID: 31573746; PMCID: PMC6853826 **IF: 3.357 / D1**

- **Pembrolizumab in Relapsed or Refractory Primary Mediastinal Large B-Cell Lymphoma.** *Armand P, Rodig S, Melnichenko V, Thieblemont C, Bouabdallah K, Tumyan G, Özcan M, Portino S, Fogliatto L, Caballero MD, Walewski J, Gulbas Z, Ribrag V, Christian B, Perini GF, Salles G, Svoboda J, Zain J, Patel S, Chen PH, Ligon AH, Ouyang J, Neuberg D, Redd R, Chatterjee A, Balakumaran A, Orlowski R, Shipp M, Zinzani PL.* **J Clin Oncol. 2019 Dec 1;37(34):3291-3299. doi: 10.1200/JCO.19.01389.** PMID: 31609651; PMCID: PMC6881098 **IF: 28.245 / D1**

- **Benchmarking of survival outcomes following haematopoietic stem cell transplantation: A review of existing processes and the introduction of an international system from the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE).** *Snowden JA, Saccardi R, Orchard K, Ljungman P, Duarte RF, Labopin M, McGrath E, Brook N, de Elvira CR, Gordon D, Poirel HA, Ayuk F, Beguin Y, Bonifazi F, Gratwohl A, Milpied N, Moore J, Passweg J, Rizzo JD, Spellman SR, Sierra J, Solano C, Sánchez-Guijo F, Worel N, Gusi A, Adams G, Balan T, Baldomero H, Macq G, Marry E, Mesnil F, Oldani E, Pearce R, Perry J, Raus N, Schanz U, Tran S, Wilcox L, Basak GW, Chabannon C, Corbacioglu S, Dolstra H, Kuball J, Mohty M, Lankester A, Montoto S, Nagler A, Styczynski J, Yakoub-Agha I, de Latour RP, Kroeger N, Brand R, de Wreede LC, van Zwet E, Putter H.* **Bone Marrow Transplant. 2019 Oct 21. doi: 10.1038/s41409-019-0718-7. Erratum in: Bone**



Overview of the mutational landscape in chronic lymphocytic leukaemia during disease course before CLL-related therapy. List of genes with driver mutations validated using deep targeted sequencing and their changes in variant allele frequency (VAF) between time-points. Mutations were considered to be changed if they were significantly different between samples (evolution p-value < 0.05) and their ratio of VAF between Time point TP2 (prior to CLL-related therapy) and Time-point 1 TP1 (inactive stage of the disease close to the diagnosis) was higher than 1.5 (for "increased" mutations) or lower than 0.375 (for "decreased" mutations). Genes with dark blue labels (on the left axis) were CLL drivers previously identified and, where those in light blue were unknown as CLL drivers to date. Three groups of patients were then characterized based on disease activity in the TP2: (i) Active disease (AD) group - patients with TP2 in disease's active phase; (ii) Stable disease (SD) group - patients with TP2 in disease's inactive phase followed by active phase and therapy need; (iii) Indolent disease (ID) group - patients with TP2 taken in inactive phase, no disease activity or therapy need was reached during follow-up of 3 years. [from Hernández-Sánchez M et al., Leukemia. 2019 Feb;33(2):518-558. doi: 10.1038/s41375-018-0255-1].

Marrow Transplant. 2019 Nov 21;:
PMID: 31636397 IF: 4.674 / Q2

- **Blood monitoring of circulating tumor plasma cells by next generation flow in multiple myeloma after therapy.** *Sanoja-Flores L, Flores-Montero J, Puig N, Contreras-Sanfeliciano T, Pontes R, Corral-Mateos A, García-Sánchez O, Díez-Campelo M, Pessoa de Magalhães RJ, García-Martín L, Alonso-Alonso JM, García-Mateo A, Aguilar-Franco C, Labrador J, Barez-García A, Maiolino A, Paiva B, San Miguel J, Sobral da Costa E, González M, Mateos MV, Durie B, van Dongen JJM, Orfao A.* **Blood. 2019 Dec 12; 134(24):2218-2222. doi: 10.1182/blood.2019002610.** PMID: 31697808 IF: 16.562 / D1

- **Lenalidomide maintenance for diffuse large B-cell lymphoma patients responding to R-CHOP: quality of life, dosing, and safety results from the randomised controlled REMARC study.** *Thieblemont C, Howlett S, Casasnovas RO, Mounier N, Perrot A, Morschhauser F, Fruchart C, Daguindau N, van Eygen K, Obéric L, Bouabdallah R, Pica GM, Nicolas-Virezelier E, Abraham J, Fitoussi O, Snauwaert S, Eisenmann JC, Lionne-Huyghe P, Bron D, Tricot S, Deeren D, González H, Costello R, Le Du K, da Silva MG, Grosicki S, Trotman J, Catalano J, Caballero D, Greil R, Cohen AM, Gaulard P, Roulin L, Takeshita K, Casadebaig ML, Tilly H, Coiffier B.* **Br J Haematol. 2019 Nov 8. doi: 10.1111/bjh.16300.** PMID: 31702836 IF: 5.206 / Q1

- **Drug-induced Thrombotic Microangiopathy During Maintenance Treatment in a Patient With Multiple Myeloma.** *Higuero Saavedra V, González-Calle V, Sobejano E, Sebastiá J, Cabrero M, Bastida JM, Puig N, Ocio EM, Mateos MV.* Hemasphere. **2019 Jun 4;3(3):e192. doi: 10.1097/HS9.0000000000000192.** PMID: 31723829; PMCID: PMC6746023 IF: NI

- **Transcriptome analysis reveals significant differences between primary plasma cell leukemia and multiple myeloma even when sharing a similar genetic background.** *Rojas EA, Corchete LA, Mateos MV, García-Sanz R, Misiewicz-Krzeminska I, Gutiérrez NC.* **Blood Cancer J. 2019 Nov 20;9(12):90. doi: 10.1038/s41408-019-0253-1.** PMID: 31748515; PMCID: PMC6868169 IF: 7.895 / Q1

- **Correction: Benchmarking of survival outcomes following haematopoietic stem cell transplantation: A review of existing processes and the introduction of an international system from the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE).** *Snowden JA, Saccardi R, Orchard K, Ljungman P, Duarte RF, Labopin M, McGrath E, Brook N, de Elvira CR, Gordon D, Poirel HA, Ayuk F, Beguin Y, Bonifazi F, Gratwohl A, Milpied N, Moore J, Passweg J, Rizzo JD, Spellman SR, Sierra J, Solano C, Sánchez-Guijo F, Worel N, Gusi A, Adams G, Balan T, Baldomero H, Macq G, Marry E, Mesnil F, Oldani E, Pearce R, Perry J, Raus N, Schanz U, Tran S, Wilcox L, Basak GW, Chabannon C, Corbacioglu S, Dolstra H, Kuball J, Mohty M, Lankester A, Montoto S, Nagler A, Styczynski J, Yakoub-Agha I, de Latour RP, Kroeger N, Brand R, de Wreede LC, van Zwet E, Putter H.* **Bone Marrow Transplant. 2019 Nov 21. doi: 10.1038/s41409-019-0740-9. Erratum for: Bone Marrow Transplant. 2019 Oct 21;**
PMID: 31754251 IF: 4.674 / Q2

- **Biological Background of Resistance to Current Standards of Care in Multiple Myeloma.** *Mogollón P, Díaz-Tejedor A, Algarín EM, Paíno T, Garayoa M, Ocio EM.* **Cells. 2019 Nov 13;8(11):1432. doi: 10.3390/cells8111432.** PMID: 31766279; PMCID: PMC6912619 IF: 5.656 / Q1

- **Measurable Residual Disease by Next-Generation Flow Cytometry in Multiple Myeloma.** *Paiva B, Puig N, Cedena MT, Rosiñol L, Cordón L, Vidriales MB, Burgos L, Flores-Montero J, Sanoja-Flores L, Lopez-Anglada L, Maldonado R, de la Cruz J, Gutiérrez NC, Calasanz MJ, Martin-Ramos ML, García-Sanz R, Martínez-Lopez J, Oriol A, Blanchard MJ, Rios R, Martin J, Martínez-Martínez R, Sureda A, Hernandez MT, de la Rubia J, Krsnik I, Moraleda JM, Palomera L, Bargay J, Van Dongen JJM, Orfao A, Mateos MV, Blade J, San-Miguel JF, Lahuerta JJ; GEM (Grupo Español de Mieloma)/PETHEMA (Programa Para el Estudio de la Terapéutica en Hemopatías Malignas) Cooperative Study Group.* **J Clin Oncol. 2019 Nov 26:JCO1901231. doi: 10.1200/JCO.19.01231.** PMID: 31770060 IF: 28.245 / D1

- **Targeting the Immune System With Mesenchymal Stromal Cell-Derived Extracellular Vesicles: What Is the Cargo's Mechanism of Action?** *Martin-Rufino JD, Espinosa-Lara N, Osugui L, Sánchez-Guijo F.* **Front Bioeng Biotechnol. 2019 Nov 5;7:308. doi: 10.3389/fbioe.2019.00308.** PMID: 31781552; PMCID: PMC6856662 IF: 5.122 / Q1

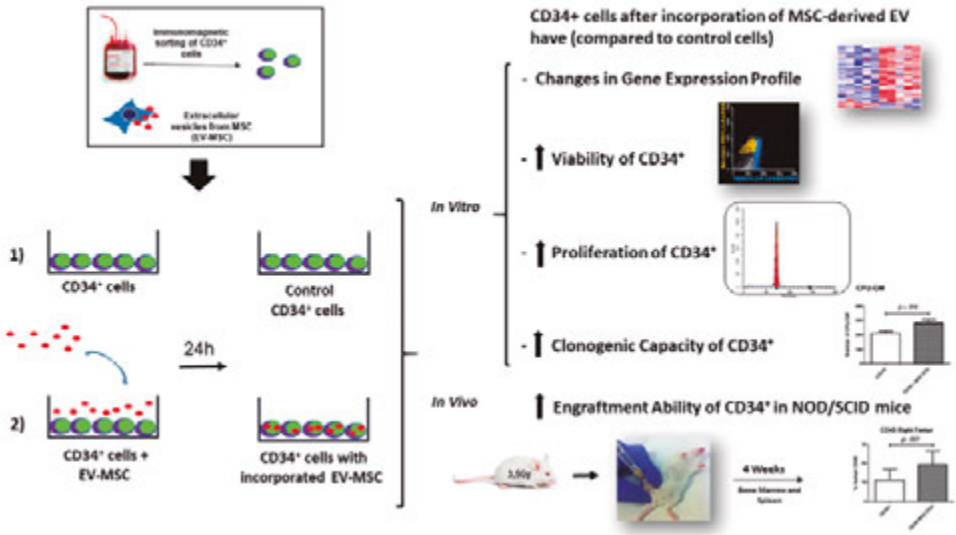
- **Association of Polyps with Early-Onset Colorectal Cancer and Throughout Surveillance: Novel Clinical and Molecular Implications.** *Perea García J, Arribas J, Cañete Á, García JL, Álvaro E, Tapial S, Narváez C, Vivas A, Brandáriz L, Hernández-Villafranca S, Rueda D, Rodríguez Y, Pérez-García J, Olmedillas-López S, García-Olmo D, Cavestro GM, Urioste M, Goel A, González-Sarmiento R.* **Cancers (Basel). 2019 Nov 29;11(12). pii: E1900. doi: 10.3390/cancers11121900.**
PMID: 31795313 IF: 6.162 / D1

- Immediate Effects of Dasatinib on the Migration and Redistribution of Naïve and Memory Lymphocytes Associated With Lymphocytosis in Chronic Myeloid Leukemia Patients. *Colom-Fernández B, Kreutzman A, Marcos-Jiménez A, García-Gutiérrez V, Cuesta-Mateos C, Portero-Sainz I, Pérez-García Y, Casado LF, Sánchez-Guijo F, Martínez-López J, Ayala RM, Boqué C, Xicoy B, Montero I, Soto C, Paz R, Silva G, Vega-Piris L, Steegmann JL, Muñoz-Calleja C.* **Front Pharmacol. 2019 Nov 25;10:1340. doi: 10.3389/fphar.2019.01340.** PMID: 31824308; PMCID: PMC6886582 IF: 3.845 / Q1

- **Transcriptomic analysis of patients with immune thrombocytopenia treated with eltrombopag.** *Hernández-Sánchez JM, Bastida JM, Alonso-López D, Benito R, González-Porras JR, De Las Rivas J, Hernández Rivas JM, Rodríguez-Vicente AE.* **Platelets. 2019 Dec 14:1-8. doi: 10.1080/09537104.2019.1702156.** PMID: 31838946 IF: 3.106 / Q2

- **Current functioning of cardio-oncology units in Spain.** *Mitroi C, Martín-García A, Mazón Ramos P, Virizuela Echaburu JA, Arenas-Prat M, García-Sanz R, Arrarte Esteban V, García-Pinilla JM, Cosín-Sales J, López-Fernández T.* **Clin Transl Oncol. 2019 Dec 20. doi: 10.1007/s12094-019-02250-4.**PMID: 31863353 IF: 2.441 / Q2

- **A phase 2 study of ibrutinib in combination with bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma.** *Hajek R, Pour L, Ozcan M, Martin Sánchez J, García Sanz R, Anagnostopoulos A, Oriol A, Cascavilla N, Terjung A, Lee Y, Briso EM, Dobkowska E, Hauns B, Špička I. Eur J Haematol.* **2019 Dec 28. doi: 10.1111/ejh.13377.** PMID: 31883396 IF: 2.217 / Q2



Experimental workflow for the incorporation of extracellular vesicles from mesenchymal stromal cells (MSC-Evs) into CD34+ cells. CD34+ cells isolated from leukapheresis (for *in vitro* experiments) or from cord blood (for *in vivo* experiments) were co-cultured with MSC-VEs for 24 hours. After that, gene expression profile, viability, proliferation capacity and colony forming capacity of CD34+ cells was assessed in both CD34+ cells co-cultivated alone or with MSC-VEs. Finally, their bone marrow engraftment ability was analyzed in NOD/SCID mice: the percentage of human CD45+ cells (donor chimerism) in total bone marrow samples from the right femur (injected site) [from Preciado S *et al.* Stem Cells (2019) 37(10): 1357-1368. doi: 10.1002/stem.3032]

OTHER PUBLICATIONS & BOOK CHAPTERS

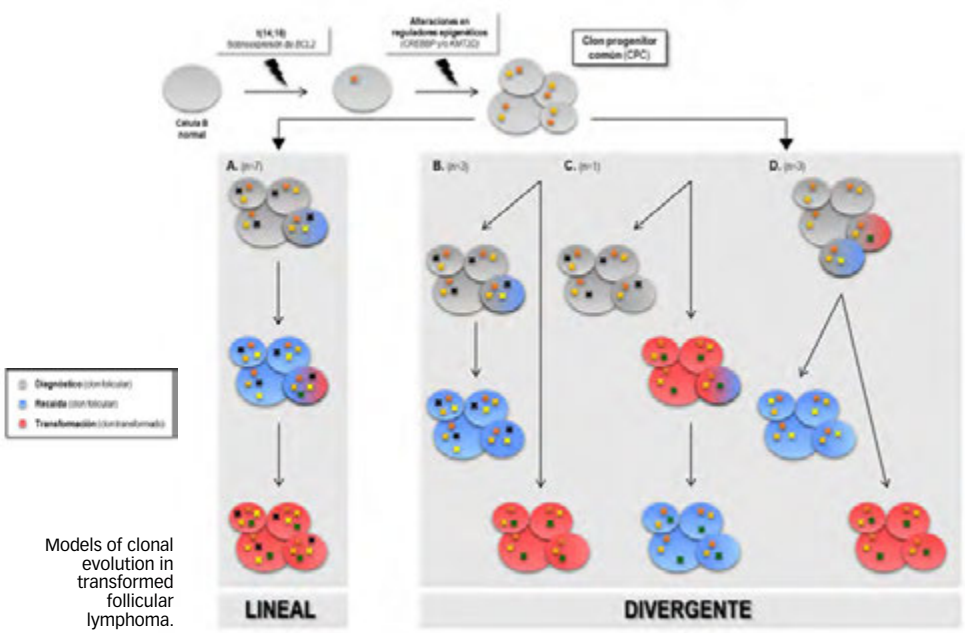
- **Valoración clínica en Linfoma no Hodgkin**. *Alejandro Martín García-Sancho.* Ed YOU & US S.A. ISBN: 978-84-948641-2-4. DL: M-17659-2018. Madrid 2018.
- **CRISPR-ERA for Switching Off (Onco) Genes. Book chapter** *Ignacio García-Tuñon, Elena Vuelta, Sandra Pérez-Ramos, Jesús M Hernández-Rivas, Lucía Méndez, María Herrero and Manuel Sánchez-Martin* 2018. DOI: 10.5772/intechopen.80245 Avilable at: IntechOpenhttp://dx.doi.org/10.5772/intechopen.80245
- **Don Agustín Ríos y la Hematología. En: Fernández Vallina E y Heredia Soriano A (eds).** *Cañizo C, González Díaz M, San Miguel JF, Sánchez-Guijo F.* Agustín Ríos González: Médico. Profesor. Sacerdote. Ediciones Universidad de Salamanca, Salamanca, 2019.Págs. 95-112. ISBN: 978-84-1311-035-6.
- **Mesenchymal stromal cells for graft-versus-host disease. En: Pham PV (ed). Stem cell therapy for autoimmune diseases and inflammation** *López-Parra M, Villaron EM, Sánchez-Guijo F.* Springer Nature, Cham (Switzerland) 2019. Págs: 77-88.ISBN 978-3-030-23420-1. ISBN online: 978-3-030-23421-8.
- **Linfoma difuso de células B grandes. En: Manual Práctico de Hematología Clínica 2019, 6ª edición. Editores: Miguel A Sanz, Enric Carreras.** *AM García-Sancho, MD Caballero.* Ediciones Escofet Zamora SL. Molins de Rei (España), 2019. ISBN: 978-84-88825-27-8. DL B 11250-2019. Páginas 347-356
- **Impacto de la sobrecarga férrica en la funcionalidad del paciente con síndrome mielodisplásico y dependencia transfusional.** *Remacha Sevilla A, Arrizabalaga Amuchastegui B, del Orbe Barreto R, Lopez Cadenas F. Martín García A, Olivier Cornacchia C, Díez Campelo M (coordinadora, autora).* Medea Medical Education Agency S.L. ISBN: 978-84-09-09716-6. DL: M-18010-2019
- **Chapter 10. Symptomatic therapy and management of complications in myeloma Leukaemia & Myeloma Essentials for Clinicians.** *MV Mateos, V González-Calle, P Rodríguez-Otero & EM Ocio.* 2019 European Society for Medical Oncology. ESMO press. ISBN: 978-88-941795-6-9. Editors: Veronika Ballova, Michele Ghielmini, Meletios-Athanassios Dimopoulos.
- **Macroglobulinemia de Waldenström / Enfermedades de las cadenas pesadas. En: Manual Práctico de Hematología Clínica 2019, 6ª edición.** *R García-Sanz*. Editores: Miguel A Sanz, Enric Carreras. Ediciones Escofet Zamora SL. Molins de Rei (España), 2019. ISBN: 978-84-88825-27-8. DL B 11250-2019. Páginas 431-438

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Valor diagnóstico y pronóstico del perfil de expresión génica, mutaciones somáticas y nivel de enfermedad mínima residual en la leucemia mieloblástica aguda (LMA) (AIOA13131395)	Marcos González Díaz	Spanish Association against Cancer (AECC)	2013-2018	135,000.00 €
Estudio de la infiltración de médula ósea y monitorización de enfermedad mínima residual mediante citometría de flujo en pacientes con linfoma difuso de células B grandes (PI13/02644)	Alejandro Martín	Carlos III Health Institute (ISCIII)	2013-2018	17,908.00 €
MDS RIGHT: Providing the right care to the right patient with myelodysplastic syndrome at the right time (MDS-RIGHT ; H2020-PHC-2014)	IP: T de Witte Jesús María Hernández Rivas	European Union	2015-2018	6,000,000.00 €
Restoring tissue regeneration in patients with visceral graft vs host disease, Node 6 (Proposal number RETHRIM. H2020-PHC-2014-RTD actividad PCH-15-2014	Fermín M. Sánchez-Guijo	European Union	2015-2019	314,850.00 €
Aristotle - Assessing the Risk of Transformation of Follicular Lymphoma in the Immunochemotherapy Era, and its Outcome (ELI)	Mª Dolores Caballero	European Lymphoma Institute (ELI)	2015-2020	
Estudio mediante secuenciación masiva de las mutaciones presentes en síndromes mielodisplásicos de bajo riesgo tratados con agentes estimulantes de la eritropoyesis. Evaluación de la respuesta terapéutica	Jesús María Hernández Rivas	Haematology and Haemoterapy Sapnish Foundation (FEHH)	2016-2018	36,000.00 €
Análisis genómico y funcional de la evolución clonal en los enfermos con leucemia linfática crónica y en un modelo "in vitro" de modificación genética dirigida (PI15/01471)	Jesús María Hernández Rivas	Carlos III Health Institute (ISCIII)	2016-2018	134,915.00 €
Caracterización genómica de la leucemia mieloblástica aguda. Utilidad clínica del perfil genético al diagnóstico y en la monitorización terapéutica (PI15/01706)	Marcos González Díaz	Carlos III Health Institute (ISCIII)	2016-2018	56,265.00 €
Estrategias de la nueva generación para la caracterización molecular global del clon tumoral en el mieloma multiple: implicaciones en diagnóstico clínico y patogenia de la enfermedad (PI15/01956)	Ramón García Sanz	Carlos III Health Institute (ISCIII)	2016-2018	87,120.00 €
Evaluación ultra-sensible de enfermedad mínima residual como biomarcador de curabilidad en dos modelos de mieloma múltiple (sintomático y quiescente de alto riesgo) (PI15/02049)	Mª Victoria Mateos	Carlos III Health Institute (ISCIII)	2016-2018	154,880.00 €
Mecanismos moleculares de la transformación clínico-histológica del linfoma folicular a linfoma agresivo, implicaciones pronósticas y su aplicación en el diseño de nuevas terapias (PI15/01393)	Mª Dolores Caballero	Carlos III Health Institute (ISCIII)	2016-2018	50,215.00 €
Design and standardization of a new NGS approach for integrated evaluation of IGH somatic hypermutation, gene mutations and copy-number variations in patients with CLL (GLD15/00348)	Marcos González Díaz	Gilead	2016-2018	44,405.00 €
Waldenström macroglobulinemia transformed into agressive forms of disease: evaluations of diagnostic and therapeutic possibilities of genomic changes (GLD16/00162)	Ramón García Sanz	Gilead	2016-2018	53,500.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Análisis de la leucemia aguda linfoblástica mediante un estudio transcriptómico (RNA-SEQ) y funcional (CRISPR) en un entorno Big Data (SA085U16)	Jesús María Hernández Rivas	Ministry of Education. Regional Government of Castilla and León	2016-2018	120,000.00 €
Regulación del microambiente en el mieloma múltiple por microRNAs: papel en la enfermedad y posibilidades terapéuticas (PI15/02156)	Mercedes Garayoa	Carlos III Health Institute (ISCIII)	2016-2019	110,715.00 €
Desarrollo de fármacos en nuevas dianas terapéuticas IDP para el tratamiento del mieloma múltiple (RTC-2016-5056-1)	Enrique Ocio	Spanish Ministry of Economy & Competitiveness	2016-2019	86,350.00 €
Función, valor diagnóstico e inhibición farmacológica de çR-RAS2, un nuevo "driver" oncogénico (GC16173472GARC)	Mª Dolores Caballero (PI Group 3)	Spanish Association against Cancer (AECC)	2016-2021	197,500.00 €
Genética Molecular en Oncohematología. Programa XIII	Jesús María Hernández Rivas	Salamanca University	2017	19,611.00 €
Predicción de la transformación histológica en linfoma folicular: papel de las alteraciones genómicas tumorales y composición del microambiente (CAS102P17)	Marcos González Díaz	Ministry of Education. Regional Government of Castilla and León	2017-2018	40,000.00 €
Estudio mediante secuenciación masiva y PCR-DIGITAL de la mutaciones de los genes implicados en Mielofibrosis (GRS 1343/A/16)	Jesús María Hernández Rivas	Regional Health Management.Regional Government of Castilla and León	2017-2018	16,966.00 €
Estudio del estado funcional de p53 en el mieloma multiple y de su reercusión en la respuesta terapéutica y en la supervivencia de los pacientes (PI16/01014)	Norma Gutiérrez Gutiérrez	Carlos III Health Institute (ISCIII)	2017-2019	154,275.00 €
Modelo integrado de citometría y ultrasecuenciación de nueva generación para desvelar la patogénesis de la leucemia mieloblástica aguda y definir nuevos criterios de respuesta (PI16/00517)	Mª Carmen Chillón	Carlos III Health Institute (ISCIII)	2017-2019	141,570.00 €
Tratamiento de enfermedades inmunes/inflamatorias con vesículas extracelulares derivadas de células mesenquimales preestimuladas: la enfermedad injerto contra huésped como modelo para el desarrollo clínico (PI16/01407)	Fermín M. Sánchez-Guijo	Carlos III Health Institute (ISCIII)	2017-2019	62,315.00 €
Optimización de las células mesenquimales para su empleo en trastornos inmunes: estudio in vitro e in vivo (CAS079P17)	Fermín M. Sánchez-Guijo	Ministry of Education. Regional Government of Castilla and León	2017-2019	118,600.00 €
From preclinical models to the patient: a holistic investigation of immunotherapies in multiple myeloma (FRA16/003)	Enrique Ocio	Ramón Areces Foundation	2017-2019	120,000.00 €
Red de Terapia Celular (RD16/0011/0015)	Fermín M. Sánchez-Guijo	Carlos III Health Institute (ISCIII)	2017-2021	310,750.00 €
HARMONY: Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology (Program Topic 4: "Development of an outcome-focused data platform to empower policy makers and clinicians to optimize care for patients with hematologic malignancies" (Innovative Medicines Initiative, «H2020-JTI-IMI2» Big Data for Better Outcomes)	Jesús María Hernández Rivas	European Union	2017-2021	2,200,000.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Cell therapy for knee osteoarthritis. Comparison of treatments with autologous and allogeneic mesenchymal stromal cells in a multicenter controlled randomized clinical trial (ARTROCELL)	Fermín M. Sánchez-Guijo	Carlos III Health Institute (ISCIII)	2018	767,962.80 €
Estudios de la ultrasecuenciación mediante las mutaciones genéticas en las rutas de señalización molecular asociadas a Leucemia Aguda linfoblástica	Jesús María Hernández Rivas	Fundación Castellano Leonesa de Hematologia y Hemoterapía (FUCALHH)	2018	6,000.00 €
Biomarcadores proteicos séricos en el desarrollo de enfermedad injerto contra huésped aguda y daño endotelial en receptores de trasplante alogénico de progenitores hematopoyéticos de donante haploidéntico (GRS 1632/A/17)	Lucía López-Corral	Regional Health Management.Regional Government of Castilla and León	2018	15,197.00 €
Estudio de enfermedad mínima residual en pacientes con linfoma folicular o linfoma difuso de célula grande B en ADN tumoral circulante mediante PCR digital (GRS 1652/A/17)	M. Eugenia Alonso	Regional Health Management.Regional Government of Castilla and León	2018	19,570.00 €
Estudio de la desregulación del transcriptoma inducida por la dexametasona en el mieloma múltiple como diana abordable para revertir la resistencia a glucocorticoides (GRS1654/A/17)	Norma Gutiérrez Gutiérrez	Regional Health Management.Regional Government of Castilla and León	2018	20,000.00 €
Microangiopatía trombótica intestinal tras trasplante alogénico hematopoyético. criterios diagnósticos, factores pron´soticos y posible relación con biomarcadores y polimorfismos en suero. Estudio retrospectivo y prospectivo en pacientes sometidos a trasplante hematopoyético (GRS 1644/A/17)	Mª Dolores Caballero	Regional Health Management.Regional Government of Castilla and León	2018	19,140.00 €

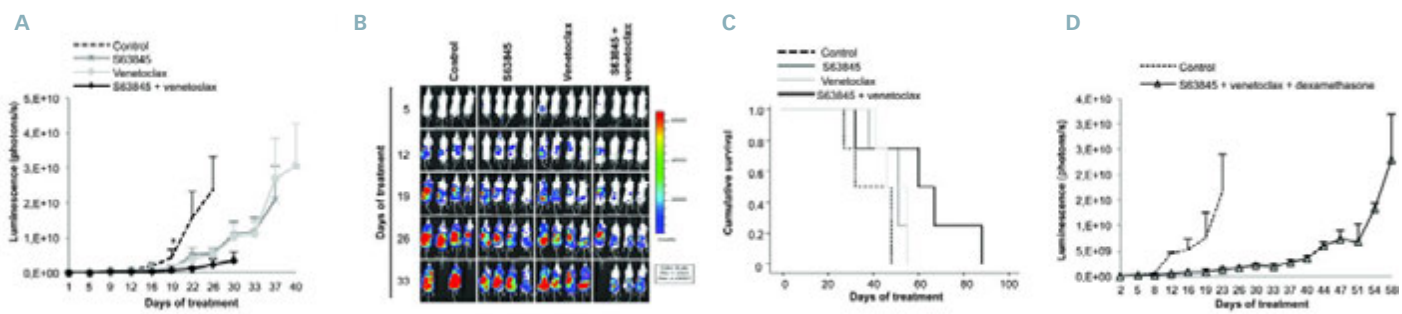


Models of clonal evolution in transformed follicular lymphoma.

PROJECT	PI	GRANT	TIME	FUNDING
Financiación grupos GIR. Biología molecular y celular en hemopatias	Marcos González Díaz	Salamanca University	2018	14,710.00 €
Enfermedad mínima residual en linfoma difuso de célula grande B en ADN tumoral circulante mediante PCR digital	Alejandro Martín	Fundación Castellano Leonesa de Hematologia y Hemoterapía (FUCALHH)	2018-2019	6,000.00 €
The role of microenvironment and tumoral genomic alterations in the prediction of histological tansformation in folicular lymphoma (GLD17/00334)	Mª Dolores Caballero	Gilead Spain	2018-2019	49,998.96 €
Análisis de la patogenicidad de nuevas mutaciones de RUNX1 en la génesis y evolución del trastorno plaquetario hereditario y en la predisposicion a desarrollar neoplasias mieloides (IBY1700006)	Jesús María Hernández Rivas	The Institute for Biomedical Research of Salamanca (IBSAL)	2018-2019	40,000.00 €
Validación de un modelo murino humanizado para el estudio de tratamientos inmunoterápicos en hemopatías malignas (IBY17/00008)	Teresa Paíno Gómez	The Institute for Biomedical Research of Salamanca (IBSAL)	2018-2019	40,000.00 €
Centro en Red de Medicina regenerativa y Terapia Celular de CyL	Fermín M. Sánchez-Guijo	Regional Government of Castilla and León	2018-2019	220,000.00 €
Estudio de las mutaciones genéticas en las rutas de señalización molecular asociadas a mielofibrosis (GRS 1653/A/17)	Jesús María Hernández Rivas	Regional Health Management.Regional Government of Castilla and León	2018-2019	18,280.00 €
Identificación de genes esenciales para la supervivencia de las células plasmáticas del mieloma múltiple mediante tecnología CRISPR-cas9 (GRS1833/A/18)	Norma Gutiérrez Gutiérrez	Regional Health Management.Regional Government of Castilla and León	2018-2019	16,853.00 €
Caracterizacion de los SMD de bajo riesgo sin sideroblastos en anillo: de las CPH a las vesículas extracelulares circulantes (PI17/01741)	María Díez Campelo	Carlos III Health Institute (ISCIII)	2018-2020	197,230.00 €
Plataforma de unidades de investigación clínica y ensayos clínicos	Mª Victoria Mateos	Cardiovascular Health Institute	2018-2020	120,450.00 €
Non-Invasive diagnostics and monitoring of minimal residual disease and clonal evolution in Waldenström´s macroglobulinemia (FIL_BIOWM)	Ramón García Sanz	International Waldenstrom's macroglobulinemia Foundation (IWMF) & Fondazione Italiana Linfomi (FIL)	2018-2020	100,000.00 $
Study of the functional status of p53 in multiple mieloma and its impact in therapeutic response and patient survival (CLJUN18010DERA)	Norma Gutiérrez Gutiérrez	Spanish Association against Cancer (AECC)	2018-2021	60,000.00 €
Valorización de cereales integrales para el desarrollo de alimentos de carácter inmunomodulador dirigidos a pacientes oncohematologicos	Mª Dolores Caballero	Spanish Ministry of Science, Innovation and Universities	2018-2022	223,850.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Early detection and intervention: understanding the mechanisms of transformation and hidden resistance of incurable haematological malignancies	Marcos González Díaz	Spanish Association against Cancer (AECC)	2018-2023	269,052.96 €
Mejora de la raza morucha a través de estudios citogenéticos	Jesús María Hernández Rivas	Salamanca University /Diputacion de Salamanca		10.000,00 €
Aplicabilidad y valor pronóstico de la caracterización molecular del linfoma de Hodgkin mediante biopsia líquida. Comparación con las técnicas de imagen (PET/TC) (GRS 1845/A/18)	Ramón García Sanz	Regional Health Management.Regional Government of Castilla and León	2019	18,876.00 €
Caracterización de las alteraciones genéticas en linfomas B de alto grado con doble/triple translocación MYC y BCL2 y/o BCL6 en pacientes de Castilla y León. Implicaciones clínico pronósticas (GRS 1846/A/18)	Alejandro Martín	Regional Health Management.Regional Government of Castilla and León	2019	17,753.00 €
Estudio de las mutaciones genéticas en las rutas de señalización molecular asociadas a leucemia aguda linfoblástica (GRS 1847/A/18)	Jesús María Hernández Rivas	Regional Health Management.Regional Government of Castilla and León	2019	18,876.00 €
Evaluación genómica y proteómica de mecanismos claves en el desarrollo de resistencias a fármacos inmunomoduladores en mieloma múltiple (GRS 1880/A/18)	Lucía López-Corral	Regional Health Management.Regional Government of Castilla and León	2019	17,978.00 €
Ultrasecuenciación del ARN (RNA-Seq) en pacientes con trombocitopenia inmune tratados con eltrombopag. Búsqueda de biomarcadores de respuesta y de nuevos mecanismos de acción de eltrombopag (GRS 1873/A/18)	Jose M. Bastida	Regional Health Management.Regional Government of Castilla and León	2019	17,753.00 €
Valor pronóstico de las alteraciones del cromosoma 1(ganancias de 1q y deleciones de 1p) en pacientes con mieloma múltiple de nuevo diagnóstico no candidatos a trasplante autólogo de progenitores hematopoyéticos (GRS1849/A/18)	Mª Victoria Mateos	Regional Health Management.Regional Government of Castilla and León	2019	20,000.00 €
Caracterización biológica de los pacientes con linfoma difuso de células B grandes (LDCBG) doble-hit MYC/BCL2 de Castilla y León (FUCALHH19/001)	Miguel Alcoceba	Fundación Castellano Leonesa de Hematología y Hemoterapía (FUCALHH)	2019-2020	6,000.00 €
Minimal residual disease in patients with non-Hodgkin´s lymphoma using imaging and molecular biology techniques. Total Metabolic volumen, tumor glycolysis and circulating tumor DNA (GLD18/00063)	Ramón García Sanz	Gilead	2019-2020	49,829,00 €
Mutational landscape of folicular lymphoma at late relapse, early failure and histological transformation (PROYE18020BEA)	Ramón García Sanz	Spanish Association against Cancer (AECC) & CIBERONC	2019-2021	150,000.00 €
Caracterización y seguimiento del sistema inmune en pacientes mayores con MM tratados dentro del ensayo GEM2017FIT: tratando de personalizar el tratamiento para maximizar la respuesta (PI18/01673)	Mª Victoria Mateos	Carlos III Health Institute (ISCIII)	2019-2021	209,330.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Estudio genómico y funcional de la concurrencia de alteraciones genéticas y de la resistencia a fármacos en pacientes de leucemia linfática crónica mediante modelos celulares y animales (PI18/01500)	Jesús María Hernández Rivas	Carlos III Health Institute (ISCIII)	2019-2021	135,520.00 €
Evaluación de estrategias de sensibilización a tratamientos inmunoterápicos en Mieloma Múltiple	Teresa Paíno Gómez	Carlos III Health Institute (ISCIII)	2019-2021	87,120.00 €
Identificación de marcadores pronósticos/ predictores de recaída/ progresión precoz en linfoma folicular (PI18/00410)	Mª Dolores Caballero	Carlos III Health Institute (ISCIII)	2019-2021	135,500.00 €
Perfil genómico integrado DNA/RNA como estrategia para el diagnóstico de la leucemia mieloblástica aguda. Monitorización molecular de EMR mediante técnicas de alta sensibilidad (PI18/01946)	Marcos González Díaz	Carlos III Health Institute (ISCIII)	2019-2021	123,420.00 €
SYNtherapy. Synthetic lethality for personalized therapy based stratification in acute leukemia (ERA PerMed "1st joint call for proposals on research projects on personalized medicine-smart combination of pre-clinical and clinical research with data and ICT soutions Ref: AC18/00093. ERAPERMED2018-275	Jesús María Hernández Rivas	European Union Spanish complementary actions-ISCIII (AC18/00093)	2019-2021	1,999,999.69 €
Medicina personalizada en la leucemia aguda linfoblástica. Uso clínico de las tecnologías de secuenciación masiva (SA271P186)	Jesús María Hernández Rivas	Ministry of Education. Regional Government of Castilla and León	2019-2021	120,000.00 €
Macroglobulinemia de Waldenström: identificación de la célula clonogénica e implicaciones en su diagnóstico y monitorización (PI18/01866)	Ramón García Sanz	Carlos III Health Institute (ISCIII)	2019-2022	220,000.00 €



The S63845 + venetoclax combination has potent *in vivo* anti-myeloma activity. (A) *In vivo* efficacy of S63845+venetoclax in an RPMI-8226-luc xenograft model of disseminated multiple myeloma (MM) in BRG mice. (B) Images representing the bioluminescence signal of each mouse by treatment group from day 5 to day 33 of treatment. (C) Kaplan-Meier curves for survival of each treatment group. (D) *In vivo* efficacy of the triple combination S63845+venetoclax+dexamethasone [from Algarín EM et al. Haematologica (2019) Jul 18. doi: 10.3324/haematol.2018.212308].

Team Leader

Isidro Sánchez García

Phone.: +34 923 294 813

E-mail: isg@usal.es

Research Team

Postdoctorals

Carolina Vicente Dueñas
Inés González Herrero

Predoctorals

Sara González de Tena-Dávila
Andrea Luengas Martínez
Guillermo Rodríguez Hernández
Ana Casado García
Alba Iglesias Ceacero
Marta Isidro Hernández
Javier Raboso Gallego

Master Student

Silvia Alemán Arteaga

LABORATORY 13

STEM CELLS, CANCER STEM CELLS AND CANCER BIOLOGY

The elucidation of the molecular mechanisms that underlie tumor development remains a tremendous challenge for basic science, but also represents an essential step in the development of new drugs. The origin of cancer within a particular tissue is often impossible to determine, due to the advanced stages when patients enter the clinic. Our knowledge about the etiology of cancer is therefore derived from animal models that recapitulate human disease.

Due to the clonal nature of human cancer evolution, all tumoral cells carry the same cancer-initiating genetic lesions, independently of the intrinsic tumoral cellular heterogeneity. However, our latest findings have shown that the mode of action of oncogenes is not homogeneous throughout the developmental history of the tumor. Studies on different types of hematopoietic tumors have shown that the contribution of oncogenes to cancer development is mainly mediated through the epigenetic reprogramming of the cancer-initiating target cell.

This driving of cancer by a malignant epigenetic stem cell rewiring is however not exclusive of the hematopoietic system, but rather represents a common tumoral mechanism that is also at work in epithelial tumors. Tumoral epigenetic reprogramming is therefore a new type of interaction between genes and their target cells, in which the action of the oncogene modifies the epigenome to prime cancer development by establishing a new pathological tumoral cellular identity.

This reprogramming may remain latent until it is afterwards triggered by either endogenous or environmental stimuli. This new view on oncogenesis not only reveals a novel function for oncogenes in cancer, but also provides evidence for a previously unconsidered model of tumorigenesis, in which the programming of the cancerous cellular identity has already occurred at the level of stem cells, therefore showing a role for oncogenes in the timing of cancer initiation. These findings on the mechanisms of cellular commitment to a tumoral fate are relevant also to regenerative medicine, since it will be essential to have full control over the potential malignancy of reprogrammed cells.

Our CSC-based mouse models are unique tools to address this challenge, and they will be used by our research team as the basis for understanding the molecular mechanisms that govern the development of cancer cells as a result of a reprogramming-like mechanism. We hope this investigation will result not only in new concepts in cancer biology and development, but it will also provide the basis for the development of both a new strategy in cancer therapy and new methods for assessing treatment efficacy.

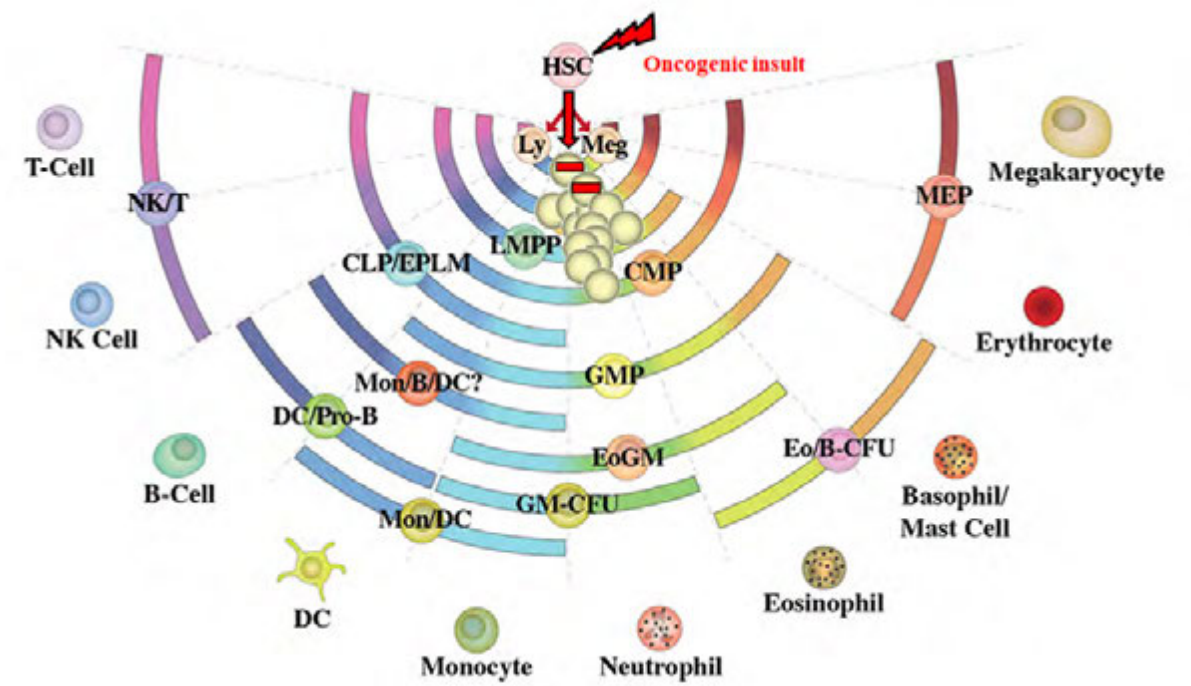
PUBLICATIONS

- **Loss of Pax5 Exploits Sca1-BCR-ABLp190 Susceptibility to Confer the Metabolic Shift Essential for pB-ALL.** *Martín-Lorenzo A, Auer F, Chan LN, García-Ramírez I, González-Herrero I, Rodríguez-Hernández G, Bartenhagen C, Dugas M, Gombert M, Ginzel S, Blanco O, Orfao A, Alonso-López D, Rivas JL, García-Cenador MB, García-Criado FJ, Müschen M, Sánchez-García I, Borkhardt A, Vicente-Dueñas C, Hauer J.* **Cancer Res. 2018 May 15;78(10):2669-2679. doi: 10.1158/0008-5472.CAN-17-3262.** PMID: 29490943. **IF: 8.378 / D1**
- **The Making of Leukemia.** *González-Herrero I, Rodríguez-Hernández G, Luengas-Martínez A, Isidro-Hernández M, Jiménez R, García-Cenador MB, García-Criado FJ, Sánchez-García I, Vicente-Dueñas C.* **Int J Mol Sci. 2018 May 17;19(5). pii: E1494. doi: 10.3390/ijms19051494. Review.** PMID: 29772764 **IF: 4.183 / D1**
- **Author Correction: Metabolic gatekeeper function of B-lymphoid transcription factors.** *Chan LN, Chen Z, Braas D, Lee JW, Xiao G, Geng H, Cosgun KN, Hurtz C, Shojaee S, Cazzaniga V, Schjerven H, Ernst T, Hochhaus A, Kornblau SM, Konopleva M, Pufall MA, Cazzaniga G, Liu GJ, Milne TA, Koeffler HP, Ross TS, Sánchez-García I, Borkhardt A, Yamamoto KR, Dickins RA, Graeber TG, Müschen M.* **Nature. 2018 Jun;558(7711):E5. doi: 10.1038/s41586-018-0164-5.** PMID: 29849140 **IF: 43.070 / D1**
- **Epigenetic Priming in Cancer Initiation.** *Vicente-Dueñas C, Hauer J, Cobaleda C, Borkhardt A, Sánchez-García I.* **Trends Cancer. 2018 Jun;4(6):408-417. doi: 10.1016/j.trecan.2018.04.007. Review.** PMID: 29860985 **IF: 8.884/D1**
- **LMO2 expression defines tumor cell identity during T-cell leukemogenesis.** *García-Ramírez I, Bhatia S, Rodríguez-Hernández G, González-Herrero I, Walter C, González de Tena-Dávila S, Parvin S, Haas O, Woessmann W, Stanulla M, Schrappe M, Dugas M, Natkunam Y, Orfao A, Domínguez V, Pintado B, Blanco O, Alonso-López D, De Las Rivas J, Martín-Lorenzo A, Jiménez R, García Criado FJ, García Cenador MB, Lossos IS, Vicente-Dueñas C, Borkhardt A, Hauer J, Sánchez-García I.* **EMBO J. 2018 Jul 13;37(14). pii: e98783. doi: 10.15252/embj.201798783.** PMID: 29880602 **IF: 11.227/D1**
- **T-cell leukemogenesis is an inappropriate lineage decision-making process: implications for precision oncology.** *Rodríguez-Hernández G, Bhatia S, Vicente-Dueñas C, Borkhardt A, Hauer J, Sánchez-García I.* **Mol Cell Oncol. 2018 Aug 7;5(4):e1497860. doi: 10.1080/23723556.2018.1497860. eCollection 2018.** PMID: 30250933 **IF: NI**
- **Lineage choice decisions in B-cell development and leukemia.** *Raboso-Gallego J, Casado-García A, Rodríguez-Hernández G, Vicente-Dueñas C, Sánchez-García I.* **Stem Cell Investig. 2018 Dec 7;5:46. doi: 10.21037/sci.2018.12.01. eCollection 2018.** PMID: 30701181 **IF: NI**
- **Dnmt1 links BCR-ABLp210 to epigenetic tumor stem cell priming in myeloid leukemia.** *Vicente-Dueñas C, González-Herrero I, Sehgal L, García-Ramírez I, Rodríguez-Hernández G, Pintado B, Blanco O, Criado FJG, Cenador MBG, Green MR, Sánchez-García I.* **Leukemia. 2018 Jun 28. doi: 10.1038/s41375-018-0192-z.** PMID: 29955131 **IF: 9.944/D1**
- **Novel ETV6-RUNX1 Mouse Model to Study the Role of ELF-MF in Childhood B-Acute Lymphoblastic Leukemia: a Pilot Study.** *Campos-Sánchez E, Vicente-Dueñas C, Rodríguez-Hernández G, Capstick M, Kuster N, Dasenbrock C, Sánchez-García I, Cobaleda C.* **Bioelectromagnetics. 2019 Jul;40(5):343-353. doi: 10.1002/bem.22193.** PMID: 31157932 **IF: 1.945/Q2**
- **Interplay between HGAL and Grb2 proteins regulates B-cell receptor signaling.** *Jiang X, Lu X, Zhang Y, Lacaria L, Schuchardt BJ, Mikles DC, Magistri M, García-Ramírez I, Sánchez-García I, Farooq A, Verdun RE, Abdulreda MH, Moy VT, Lossos IS.* **Blood Adv. 2019 Aug 13;3(15):2286-2297. doi: 10.1182/bloodadvances.2018016162.** PMID: 31362927 **IF: 2.484/D1**
- **LMO2 Confers Synthetic Lethality to PARP Inhibition in DLBCL.** *Parvin S, Ramirez-Labrada A, Aumann S, Lu X, Weich N, Santiago G, Cortizas EM, Sharabi E, Zhang Y, Sánchez-García I, Gentles AJ, Roberts E, Bilbao-Cortes D, Vega F, Chapman JR, Verdun RE, Lossos IS.* **Cancer Cell. 2019 Sep 16;36(3):237-249.e6. doi: 10.1016/j.ccell.2019.07.007.** PMID: 31447348 **IF: 23.916/D1**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Mecanismos moleculares responsables de la reprogramación tumoral de progenitores hematopoyéticos mediada por Bcl6 (TAMARA) (SAF2015-64420-R)	Isidro Sánchez García	Spanish Ministry of Economy & Competitiveness	2016-2018	290,400.00 €
Infectious trigger in childhood pB-ALL – new approaches for leukemia prevention. (DJCLS 02R/2016)	Isidro Sánchez García	German Carreras Foundation (DJCLS)	2016-2019	367,767.00 €

PROJECT	PI	GRANT	TIME	FUNDING
Identifying and targeting mechanisms of CREBBP mutation-driven lymphomagenesis (1R01CA201380-01A1)	Isidro Sánchez García	National Health Insitute. Universidad de Nebraska	2016-2021	237,600.00 €
Leukämie im Kindesalter – Einfluss des Immunnsystems auf die Entstehung der Erkankrung experimentelle Studie am einem geeigneten Tiernmodell (FRAUNHOFER-ITEM17-ISG)	Isidro Sánchez García	Fraunhofer Institut für Toxikologie und Experimentelle Medizin	2017-2018	50,000.00 €
Nuevas aproximaciones terapéuticas para la prevención de la leucemia aguda infantil (CSI234P18)	Isidro Sánchez García	Regional Government of Castilla and León	2018-2021	120,000.00 €
Desencadenante infecciosos en la PB-ALL Infantil – Descifrando los mecanismos responsables de la evolución clonal con el objetivo de prevenir la leucemia (RTI2018-093314-B-100)	Isidro Sánchez García	Spanish Ministry of Science, Research & Universities	2019-2021	
Einfluss von Niedrigdosisstrahlung auf die LeuKämieentwicklung bei genetischer Prädisposition in einem Mousmodell	Isidro Sánchez García	Universitätsklinikum **Düsseldorf**	2019-2022	280,000.00 €



Tumoral Reprogramming - Leukemia Stem Cells are reprogrammed by an oncogenic insult to an invariant cell lineage.

Team Leader

Rogelio González Sarmiento

Phone.: +34 923 294 814

E-mail: gonzalez@usal.es

Research Team

Postdoctorals

Eva María Sánchez Tapia
Jessica Pérez García
Elena Bueno Martínez
Ana Belén Herrero Hernández

Predoctorals

Carlos Gutiérrez Cerrajero
Pamela Vázquez Cárdenas
Nerea Gestoso Uzal
Abel Jesús Martel Martel

Master Students

Ana Casado García
Tania Sánchez-Bayuela Recio
Paula García Vallés
Sara Vallejo Fuente
Sheila Almaraz Postigo
María Ovejero Sánchez
Diego Iglesias Corral
Paloma Martín-Bejarano Soto

LABORATORY 14

HEREDITARY CANCER

The first aim of the laboratory 14 is the characterization of molecular abnormalities in patients with familiar cancer within the program of Genetic Counseling in Hereditary Cancer supported by the Junta de Castilla y León. Within this project, the laboratory is also characterizing molecular abnormalities in women with familiar breast cancer (more than 3 family members with breast or ovarian cancer) that do not carry BRCA mutations. We are also characterizing low penetration mutations in women with breast cancer under 40 years old as well as novel mutations in males with breast cancer. In colon cancer our aim is to characterize the molecular changes in tumor in patients under 50 years old. Actually we are part of a multidisciplinary group, involving different groups from different hospitals of the Country as well as other groups from Europe and EEUU.

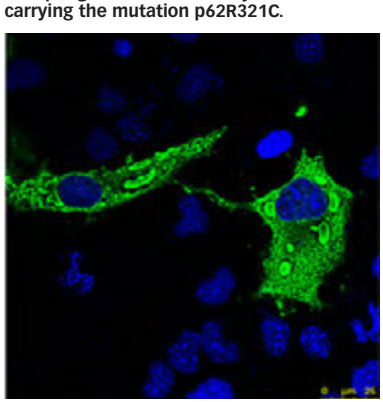
A second aim of the laboratory is the characterization of molecular abnormalities in brain and endometrial tumors and correlate them with abnormalities in colon cancer within Lynch Syndrome. In this aim we are collaborating with the Service of Neurosurgery of the Hospital Son Llatzer and with the Departments of Obstetrics and Gynecology, and pathology of the University Hospital of Salamanca.

A third aim is the analysis of the modifications induced in cell lines derived from different tumor after incubation with new drugs, some of them developed by the Department Pharmaceutical Chemistry of the University of Salamanca.

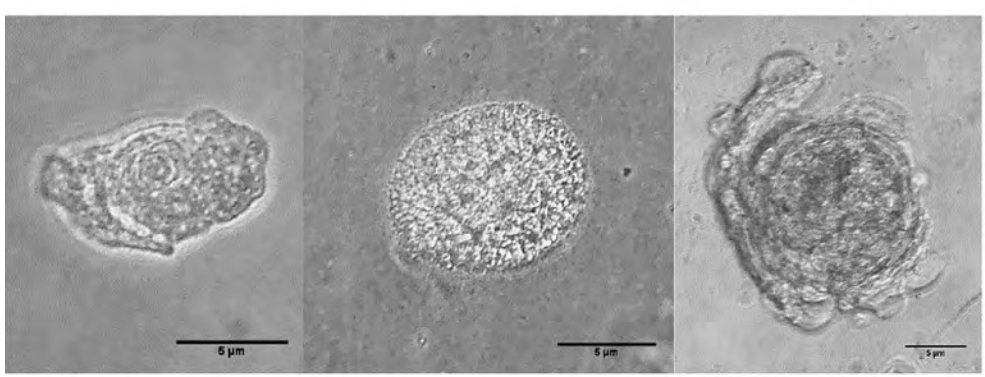
Finally, we are collaborating in a multicentric trial analyzing SNPs in candidate genes that could increase the risk to suffer head and neck cancer and characterizing novel mutations in these tumors.

All these projects are developed in collaboration with the Department of Oncology of the University Hospital of Salamanca directed by Prof. JJ Cruz.

Autophagosome abnormality in a cell line carrying the mutation p62R321C.



Organoids derived from head and neck cancer.



Maxilar (cavidad oral) **Laringe** **Lengua (cavidad oral)**

PUBLICATIONS

- **Novel clinical and molecular findings in Spanish patients with naevoid basal cell carcinoma syndrome.** *Alonso N, Cañueto J, Ciria S, Bueno E, Palacios-Álvarez I, Alegre M, Badenas C, Barreiro A, Pena L, Maldonado C, Nespeira-Jato MV, Peña-Penabad C, Azon A, Gavrilova M, Ferrer I, Sanmartin O, Robles L, Hernandez-Martin A, Urioste M, Puig S, Puig L, González-Sarmiento R.* **Br J Dermatol. 2018 Jan;178(1):198-206. doi: 10.1111/bjd.15835.** PMID: 28733979. **IF: 6.714 / Q1**

- **Identification of a novel locus on chromosome 2q13, which predisposes to clinical vertebral fractures independently of bone density.** *Alonso N, Estrada K, Albagha OME, Herrera L, Reppe S, Olstad OK, Gautvik KM, Ryan NM, Evans KL, Nielson CM, Hsu YH, Kiel DP, Markozannes G, Ntzani EE, Evangelou E, Feenstra B, Liu X, Melbye M, Masi L, Brandi ML, Riches P, Daroszewska A, Olmos JM, Valero C, Castillo J, Riancho JA, Husted LB, Langdahl BL, Brown MA, Duncan EL, Kaptoge S, Khaw KT, Usategui-Martín R, Del Pino-Montes J, González-Sarmiento R, Lewis JR, Prince RL, D'Amelio P, García-Giralt N, Nogués X, Mencej-Bedrac S, Marc J, Wolstein O, Eisman JA, Oei L, Medina-Gómez C, Schraut KE, Navarro P, Wilson JF, Davies G, Starr J, Deary I, Tanaka T, Ferrucci L, Gianfrancesco F, Gennari L, Lucas G, Elosua R, Uitterlinden AG, Rivadeneira F, Ralston SH.* **Ann Rheum Dis. 2018 Mar;77(3):378-385. doi: 10.1136/annrheumdis-2017-212469.** PMID: 29170203 **IF: 14.299 / D1**

- **Molecular analysis of thyroglobulin mutations found in patients with goiter and hypothyroidism.** *Siffo S, Adrover E, Citterio CE, Miras MB, Balbi VA, Chiesa A, Weill J, Sobrero G, González VG, Papendieck P, Martínez EB, González-Sarmiento R, Rivolta CM, Targovnik HM.* **Mol Cell Endocrinol. 2018 Sep 15;473:1-16. doi: 10.1016/j.mce.2017.12.009.** PMID: 29275168 **IF: 3.693 /Q1**

- **Gorlin Syndrome.** *Palacios-Álvarez I, González-Sarmiento R, Fernández-López E.* **Actas Dermosifiliogr. 2018 Apr;109(3):207-217. doi: 10.1016/j.ad.2017.07.018.** PMID: 29373110 **IF: NI**

- **Comment on 'Distinct clinical outcomes of two CIMP-positive colorectal cancer subtypes based on a revised CIMP classification system'.** *Tapial S, Rueda D, Arriba M, Luis García J, Brandáriz L, Pérez J, Rodríguez Y, García-Olmo D, González-Sarmiento R, Urioste M, Perea J.* **Br J Cancer. 2018 Feb 6;118(3):e3. doi: 10.1038/bjc.2017.343.** PMID: 29384528 **IF: 5.416/D1**

- **Analysis of the relationship between interleukin polymorphisms within miRNA-binding regions and alcoholic liver disease.** *Novo-Veleiro I, Cieza-Borrella C, Pastor I, González-Sarmiento R, Laso FJ, Marcos M.* **Rev Clin Esp. 2018 May;218(4):170-176. doi: 10.1016/j.rce.2018.02.005.** PMID: 29566963 **IF: 1.043/Q2**

- **Polymorphisms in genes implicated in base excision repair (BER) pathway are associated with susceptibility to Paget's disease of bone.** *Usategui-Martín R, Gutiérrez-Cerrajero C, Jiménez-Vázquez S, Calero-Paniagua I, García-Aparicio J, Corral-Gudino L, Del Pino-Montes J, González-Sarmiento R.* **Bone. 2018 Jul;112:19-23. doi: 10.1016/j.bone.2018.04.003.** PMID: 29630930 **IF: 4.360 /D1**

- **Differential clinicopathological and molecular features within late-onset colorectal cancer according to tumor location.** *Brandariz L, Arriba M, García JL, Cano JM, Rueda D, Rubio E, Rodríguez Y, Pérez J, Vivas A, Sánchez C, Tapial S, Pena L, García-Arranz M, García-Olmo D, Urioste M, González-Sarmiento R, Perea J.* **Oncotarget. 2018 Feb 15;9(20):15302-15311. doi: 10.18632/oncotarget.24502. eCollection 2018 Mar 16.** PMID: 29632645 **IF: NI**

- **Corrigendum: Association of VAV2 and VAV3 polymorphisms with cardiovascular risk factors.** *Perretta-Tejedor N, Fernández-Mateos J, García-Ortiz L, Gómez-Marcos MA, Recio-Rodríguez JI, Agudo-Conde C, Rodriguez-Sánchez E, Morales AI, López-Hernández FJ, López-Novoa JM, González-Sarmiento R, Martínez-Salgado C.* **Sci Rep. 2018 May 11;8:46977. doi: 10.1038/srep46977.** PMID: 29749392 **IF: 4.011/ D1**

- **Evidence of the high prevalence of neurological disorders in nonsyndromic X-linked recessive ichthyosis: a retrospective case series.** *Rodrigo-Nicolás B, Bueno-Martínez E, Martín-Santiago A, Cañueto J, Vicente A, Torrelo A, Noguera-Morel L, Duat-Rodríguez A, Jorge-Finnigan C, Palacios-Álvarez I, García-Hernández JL, Sebaratnam DF, González-Sarmiento R, Hernández-Martín A.* **Br J Dermatol. 2018 Oct;179(4):933-939. doi: 10.1111/bjd.16826.** PMID: 29901853 **IF: 6.714/Q1**

- **Changes in the Management and Prognosis of Ovarian Cancer Due to the New FIGO and WHO Classifications: A Case Series Observational Descriptive Study. Seven Years of Follow-up.** *Gomes Ferreira M, Sancho de Salas M, González Sarmiento R, Doyague Sánchez MJ.* **Int J Gynecol Cancer. 2018 Oct;28(8):1461-1470. doi: 10.1097/IGC.0000000000001331.** PMID: 30045138 **IF: 1.746/Q2**

- **Influence Of Angiogenic Mediators And Bone Remodelling In Paget´s Disease Of Bone.** *Fuentes-Calvo I, Usategui-Martín R, Calero-Paniagua I, Moledo-Pouso C, García-Ortiz L, Pino-Montes JD, González-Sarmiento R, Martínez-Salgado C.* **Int J Med Sci. 2018 Jul 30;15(11):1210-1216. doi: 10.7150/ijms.26580. eCollection 2018.** PMID: 30123059 **IF: 2.333/D1**

- **The impact of vascular burden on behavioural and psychological symptoms in older adults with dementia: the BEVASDE study.** *Manso-Calderón R, Cacabelos-Pérez P, Sevillano-García MD, Herrero-Prieto ME, González-Sarmiento R.* **Neurol Sci. 2019 Sep 7. doi: 10.1007/s10072-019-04071-3.** PMID: 3149482 **IF: 2.484/Q2**

- **Redefining synchronous colorectal cancers based on tumor clonality.** *Perea J, García JL, Corchete L, Lumbreras E, Arriba M, Rueda D, Tapial S, Pérez J, Vieiro V, Rodríguez Y, Brandáriz L, García-Arranz M, García-Olmo D, Goel A, Urioste M, Sarmiento RG.* **Int J Cancer. 2019 Apr 1;144(7):1596-1608. doi: 10.1002/ijc.31761.** PMID: 30151896 **IF: 4.982/D1**

- **Comparative genomic hybridization analysis of basal cell carcinoma.** *Palacios-Álvarez I, Bueno E, Fernández-López E, García JL, González-Sarmiento R.* **J Dtsch Dermatol Ges. 2019 Feb;17(2):197-200.**

doi: 10.1111/ddg.13740. PMID: 30629797
IF: 3.924/Q3

- **Clinical and Molecular Comparative Study of Colorectal Cancer Based on Age-of-onset and Tumor Location: Two Main Criteria for Subclassifying Colorectal Cancer.** Álvaro E, Cano JM, García JL, *Brandáriz L, Olmedillas-López S, Arriba M, Rueda D, Rodríguez Y, Cañete Á, Arribas J, Inglada-Pérez L, Pérez J, Gómez C, García-Arranz M, García-Olmo D, Goel A, Urioste M, González-Sarmiento R, Perea J.* **Int J Mol Sci. 2019 Feb 22;20(4). pii: E968. doi: 10.3390/ijms20040968.** PMID: 30813366 IF: 4.183/D1

- **Meta-analysis of the rs243865 MMP-2 polymorphism and age-related macular degeneration risk.** *Usategui-Martín R, Pastor-Idoate S, Chamorro AJ, Fernández I, Fernández-Bueno I, Marcos-Martín M, González-Sarmiento R, Carlos Pastor J.* **PLoS One. 2019 Mar 7;14(3):e0213624. doi: 10.1371/journal.pone.0213624. eCollection 2019.** PMID: 30845235 IF: 2.776/D1

- **A new common functional coding variant at the DDC gene change renal enzyme activity and modify renal dopamine function.** *Miramontes-González JP, Hightower M, Zhang K, Kurosaki H, Schork AJ, Biswas N, Vaingankar S, Mahata M, Lipkowitz MS, Nievergelt CM, Baker DG, Ziegler MG, León-Jiménez D, González-Sarmiento R, Ichinose H, O'Connor DT.* **Sci Rep. 2019 Mar 25;9(1):5055. doi: 10.1038/s41598-019-41504-7.** PMID: 30911067 IF: 4.011/D1

- **Genetic Susceptibility in Head and Neck Squamous Cell Carcinoma in a Spanish Population.** *Fernández-Mateos J, Seijas-Tamayo R, Adansa Klain JC, Pastor Borgoñón M, Pérez-Ruiz E, Mesía R, Del Barco E, Salvador Coloma C, Rueda Dominguez A, Caballero Daroqui J, Fernández Ruiz E, Ocana A, González-Sarmiento R, Cruz-Hernández JJ.* **Cancers (Basel). 2019 Apr 7;11(4). pii: E493. doi: 10.3390/cancers11040493.** PMID: 30959967 IF: 6.162 / D1

- **VEGFR2 and OPG genes modify the risk of subclinical coronary atherosclerosis in patients with familial hypercholesterolemia.** *Miramontes-González JP, Usategui-Martín R, Pérez de Isla L, Alonso R, Muñiz-Grijalvo O, Díaz-Díaz JL, Zambón D, Jiménez FF, Martín-Vallejo J, Rodríguez Gude AE, Jiménez DL, Padro T, González-Sarmiento R, Mata P.* **Atherosclerosis. 2019 Jun;285:17-22. doi: 10.1016/j.atherosclerosis.2019.03.019.** PMID: 30991288 IF: 4.255 / D1

- **Intermediate-onset colorectal cancer: A clinical and familial boundary between both early and late-onset colorectal cancer.** *Arriba M, Sánchez C, Vivas A, Nutu OA, Rueda D, Tapial S, Rodríguez Y, Brandáriz L, García JL, García-Olmo D, Goel A, González-Sarmiento R, Urioste M, Perea J.* **PLoS One. 2019 May 16;14(5):e0216472. doi: 10.1371/journal.pone.0216472. eCollection 2019.** PMID: 31095598 IF: 2.776 / D1

- **Genetic study in patients operated dentally and anesthetized with articaine-epinephrine.** *López-Valverde N, López-Valverde A, Gómez de Diego R, Cieza-Borrella C, Ramírez JM, González-Sarmiento R.* **J Pain Res. 2019 Apr 29;12:1371-1384. doi: 10.2147/JPR.S193745. eCollection 2019.** PMID: 31118755 IF: 2.236 / Q1

- **Transdermal Buprenorphine for Controlling Pain in Patients with Critical Lower-Limb Ischemia.** *Blanco-Antona F, González-Sarmiento R, García-Cenador B, Lozano FS.* **Pain Med. 2019 Jul 17. pii: pnz165. doi: 10.1093/pm/pnz165.** PMID: 31313809 IF: 2.764 / Q1

- **Cimp-Positive Status is More Representative in Multiple Colorectal Cancers than in Unique Primary Colorectal Cancers.** *Tapial S, Olmedillas-López S, Rueda D, Arriba M, García JL, Vivas A, Pérez J, Pena-Couso L, Olivera R, Rodríguez Y, García-Arranz M, García-Olmo D, González-Sarmiento R, Urioste M, Goel A, Perea J.* **Sci Rep. 2019 Jul 19;9(1):10516. doi: 10.1038/s41598-019-47014-w.** PMID: 31324877 IF: 4.011 / D1

- **Multiple familial trichoepitheliomas: Ultrasonographic findings.** *Capusan TM, Noguera-Morel L, Bueno-Martínez E, Colmenero I, Torrelo A, González-Sarmiento R, Hernández-Martin A.* **Skin Res Technol. 2019 Jul 23. doi: 10.1111/srt.12746.** PMID: 31338873 IF: 1.657 / Q2

- **Imbalance in T-Helper 17 Cells and Targeted Therapy in an Infant with SAM-like Syndrome.** *Hernández-Martín A, Kennedy-Batalla R, Cañedo E, Bernaldo-de-Quirós E, Carazo-Gallego B, Vera A, Torrelo A, Noguera-Morel L, González-Sarmiento R, Bolling M, Martínez-Bonet M, Pion M, Correa-Rocha R.* **N Engl J Med. 2019 Nov 28;381(22):2176-2178. doi: 10.1056/NEJMc1908531.** PMID: 31774967 IF: 70,67 / D1

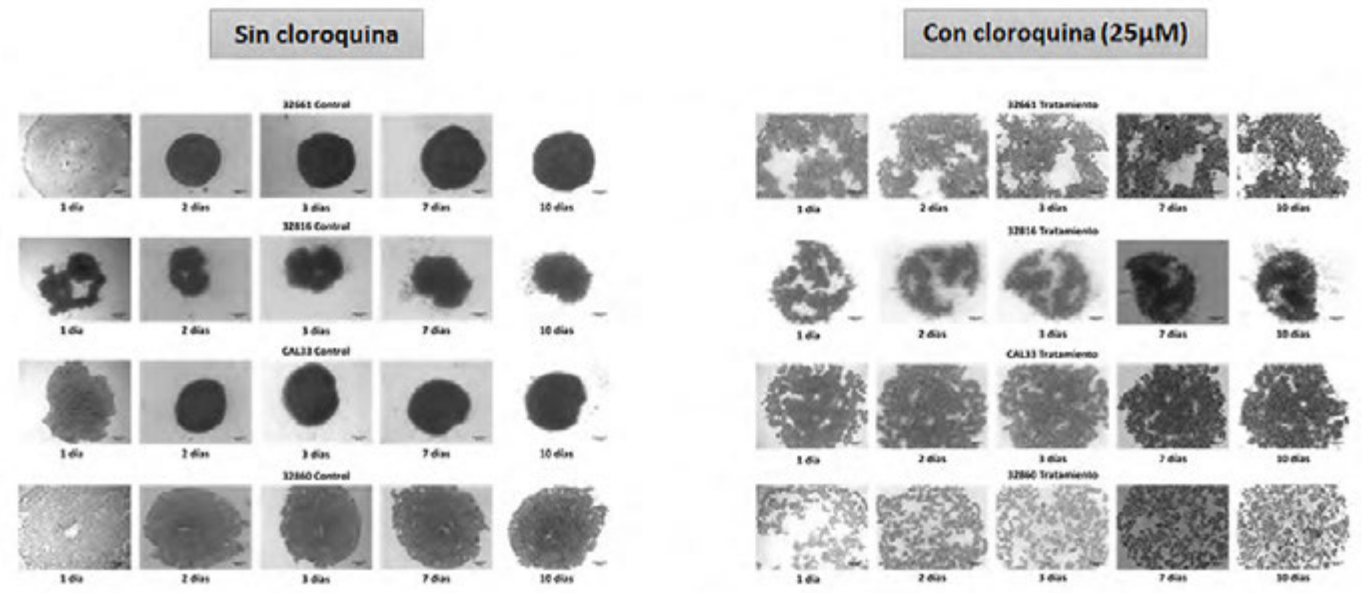
- **Association of Polyps with Early-Onset Colorectal Cancer and Throughout Surveillance: Novel Clinical and Molecular Implications.** *Perea García J, Arribas J, Cañete Á, García JL, Álvaro E, Tapial S, Narváez C, Vivas A, Brandáriz L, Hernández-Villafranca S, Rueda D, Rodríguez Y, Pérez-García J, Olmedillas-López S, García-Olmo D, Cavestro GM, Urioste M, Goel A, González-Sarmiento R.* **Cancers (Basel). 2019 Nov 29;11(12). pii: E1900. doi: 10.3390/cancers11121900.** PMID: 31795313 IF 6,160 / Q1

OTHER PUBLICATIONS & BOOK CHAPTERS

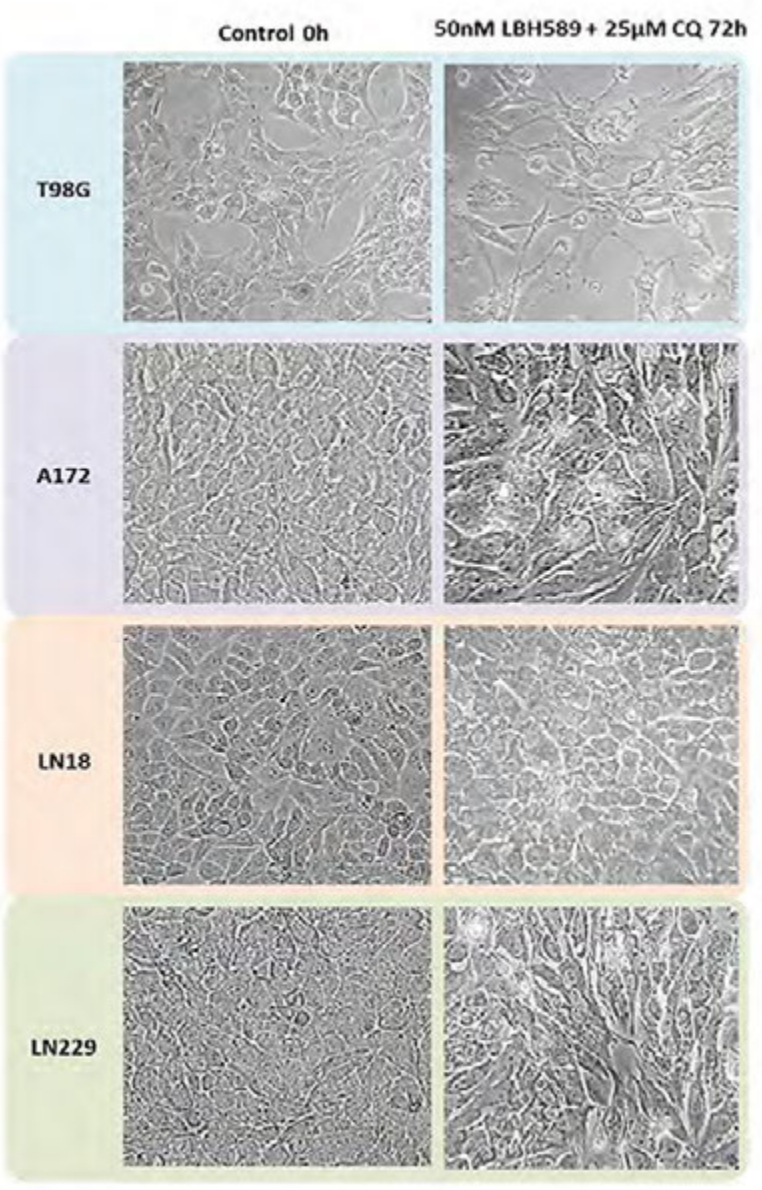
- **Biología celular y molecular del cáncer** **En: Lecciones de Oncología Clínica 6ª ed. Ed. Elsevier. pp: 5-11. 2018** Authors: J.J. Cruz Hernández, R. González-Sarmiento.

GRANTS FOR RESEARCH IN PROGRESS

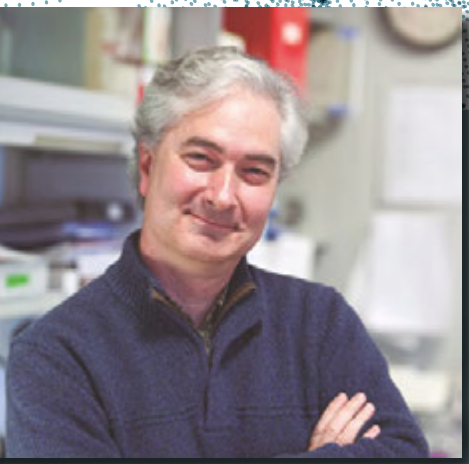
PROJECT	PI	GRANT	TIME	FUNDING
Correlación clínico-molecular del receptor de andrógenos y sus isoformas en pacientes con cáncer de próstata metastásico y resistente a castración farmacológica	Rogelio González Sarmiento	Spanish Association against Cancer (AECC)	2016-2018	40,000.00 €
Subvención directa Consejería Sanidad a la Fundación de Investigación del Cáncer	Rogelio González Sarmiento	Ministry of Health. Regional Government of Castilla and León	2018	120,000.00 €
Subvención directa Consejería Sanidad a la Fundación de Investigación del Cáncer	Rogelio González Sarmiento	Ministry of Health. Regional Government of Castilla and León	2019	120,000.00 €
Estudio clínico y molecular del complejo NOMO/NICALINA/ TEMEM147 y la vía Nodal en cáncer (PI16/01920)	Rogelio González Sarmiento	Carlos III Health Institute	2017-2020	98,615.00€



Spheroids from Head and Neck Cancer after treatment with Cloroquine.



Glioblastoma cell lines treated with histone acetilase inhibitor.



Team Leader

Atanasio Pandiella Alonso

Phone.: +34 923 294 815

E-mail: atanasio@usal.es

Research Team

Senior Researcher

Azucena Esparís Ogando

Postdoctorals

María Elena Díaz Rodríguez
Juan Carlos Montero González
Patricia Tomás Martín

Predoctorals

Ariana Centa
Laura Díaz Gil
Lucía Gandullo Sánchez
Sofía Matilla Vicente-Almazán
Inés Romero Pérez
Fany Verónica Ticona Pérez
Ana María Orive Ramos
Yolanda Mª Guillén Pérez
Sara García Alonso
Adrián Sánchez Fernández

Master Students

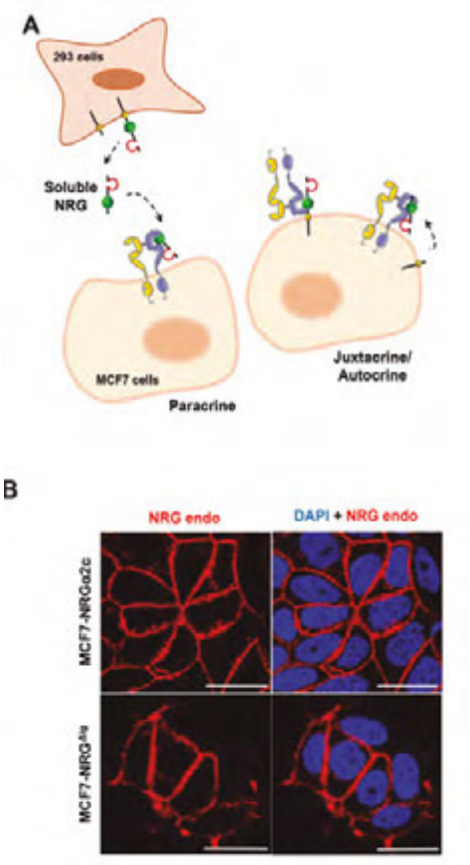
Jorge Alejo Mateo
Laura Sánchez Díaz

Visiting Researchers

Alberto Ocaña Fernández
Paulo Michel Pinheiro Ferreira
Elena Spinola Lasso
Javier Pérez Peña
Alessandro Tubita
Irene Cosi
Cristina Nieto Jiménez
Adeline Duvallet
Sabrina Fischer
Bachir Benarba

LABORATORY 15

KINASES IN ONCOLOGY. SIGNALING BY RECEPTOR TYROSINE KINASES



During the last few years our research has been centered in the understanding of the role of several receptor tyrosine kinases (RTKs) and their signal transduction routes in cell proliferation and oncogenesis.

Interest in the activation of RTKs by membrane anchored ligands has been a major focus of our laboratory with special emphasis on the study of the mechanisms responsible for the solubilization of membrane-anchored growth factors, and the biological properties of these factors in the membrane-anchored conformation. In addition, the role of novel RTK signaling intermediates, such as P-Rex1 or MMP13 are being analyzed.

In this area of research, an effort is being paid to an integral understanding of the role of RTKs, especially those of the ErbB/HER family in cancer, by analyzing how their activating ligands act, and how downstream signaling molecules participate in proliferative responses to RTK activation. Studies with drugs (small molecule kinase inhibitors as well as monoclonal antibodies) that target these receptors or their signal transduction pathways are carried out in parallel with biological studies.

During the last few years we have become especially interested in the major clinical problem of the establishment of resistances to targeted therapies, especially in the context of HER2 positive breast cancer. In line with this, we have made an effort to generate new in vitro and in vivo models of resistance to anti-HER2 therapies and have identified novel mechanisms of acquired resistance to these drugs. Taking all these into consideration we are investigating and developing new therapeutic approaches to be used in this context. In line with this, the identification of new targets and the development of new therapeutic agents against them is, in this moment, an important goal in our team.

Biological activity of NRGα2c and NRGΔIg. (A) Representation of the paracrine and juxtacrine/autocrine forms of intercellular communication of NRG. In the paracrine form, the soluble NRG produced by 293 cells activates the HER receptors on MCF7 cells that reside at a certain distance from where the NRG is synthesized. In the juxtacrine form, the transmembrane NRG produced in MCF7 cells is able to active the HER receptors present at the membrane of cells that are in physical contact with the cell that produces the NRG. In the autocrine form, the soluble NRG produced in MCF7 cells is able to activate HER receptors in the same cell that produced the NRG. (B) Subcellular distribution of proNRGα2c and proNRGΔIg in MCF7 cells was analyzed by immunofluorescence using the anti-endodomain antibody. Nuclear staining (in blue) was performed with DAPI. Images were captured using a Leica TCS SP5 confocal microscope. Bar, 25 μm.

SENIOR RESEARCHER

THE MEK5/ERK5 PATHWAY IN CANCER

Azucena Esparís Ogando

Phone.: +34 923 294 815

E-mail: esparis@usal.es

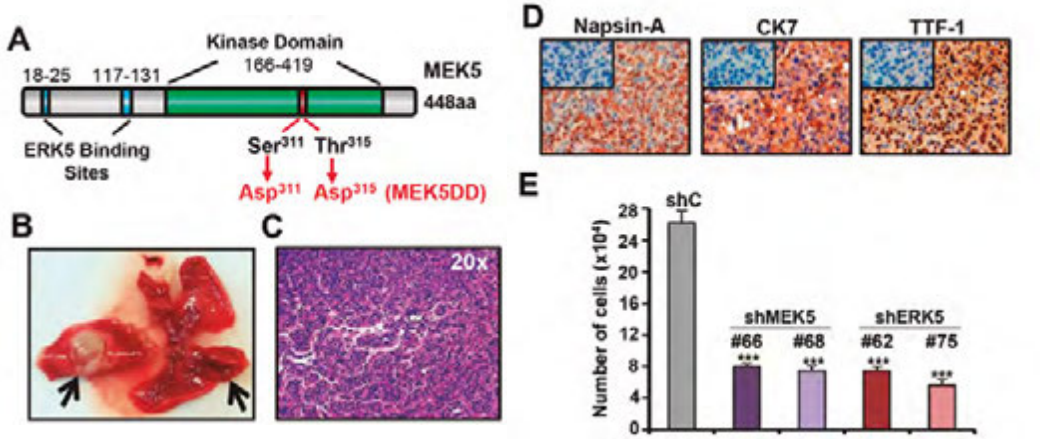
Mitogen-activated protein kinases (MAPKs) control multiple essential biological processes. In mammals, several MAPK families have been described. In the last years, the MEK5/ERK5 pathway has been reported to be deregulated in various types of cancer. However, whether activation of this route is sufficient to drive tumorigenesis was unknown. To answer this question, we generated a transgenic mouse engineered to express a constitutively active form of MEK5, and we show that this route contributes to the pathogenesis of lung cancer, opening the possibility of its targeting with therapeutic purposes.

Now, we are trying to:

i) Gain insights into the mechanism of activation of the MEK5 / ERK5 pathway in lung cancer. This will open new options for future clinical applications.

ii) Analyze the regulation of gene expression by MEK5 in lung cancer and determine if there is any type of molecular signature associated with the MEK5 activation.

On the other hand, proteomic studies from our group identified several ERK5-interacting proteins, some of them related to the intermediate metabolism, which may represent interesting anticancer targets. The role of those proteins in the actions of ERK5 is being unveiled.



The sole activation of MEK5 fosters the appearance of lung adenocarcinomas in mice and is pivotal for human lung adenocarcinoma. A) Schematic representation of MEK5 and the sites mutated to create constitutively active MEK5 (MEK5DD). B) Representative macroscopic image of a MEK5DD transgenic tumoral lung (tumours are indicated by arrows). C) Representative haematoxylin– eosin staining of a lung mass section from a MEK5DD mouse. D) 40× representative immunohistochemical images of napsin-A, cytokeratin (CK)-7 and thyroid transcription factor (TTF)-1 of a lung tumor from MEK5DD mouse. These markers are routinely used to identify the adenocarcinoma subtype. An inset image with an isotype control for each antibody was included. E) NCI-H23 (human lung adenocarcinoma cells) were infected with pLKO lentiviral vectors including short hairpin control (shC), shMEK5 or shERK5 interfering sequences. Proliferation was measured by cell counting. *** indicates: p<0.001.

PUBLICATIONS

- **Functional transcriptomic annotation and protein-protein interaction analysis identify EZH2 and UBE2C as key upregulated proteins in ovarian cancer.** *Martínez-Canales S, López de Rodas M, Nuncia-Cantarero M, Páez R, Amir E, Győrffy B, Pandiella A, Galán-Moya EM, Ocaña A.* **Cancer Med. 2018 May;7(5):1896-1907. doi: 10.1002/cam4.1406.** PMID: 29575713 **IF: 3.357 / D1**

- **Resistance to Antibody-Drug Conjugates.** *García-Alonso S, Ocaña A, Pandiella A.* **Cancer Res. 2018 May 1;78(9):2159-2165. doi: 10.1158/0008-5472.CAN-17-3671. Review.** PMID: 29653942 **IF: 8.378 / D1**

- **Antitumoral effect of Ocoxin, a natural compound-containing nutritional supplement, in small cell lung cancer.** *Díaz-Rodríguez E, Sanz E, Pandiella A.* **Int J Oncol. 2018 Jul;53(1):113-123. doi: 10.3892/ijo.2018.4373.** PMID: 29658597 **IF: 3.571 / Q1**

- **The immunoglobulin-like domain of neuregulins potentiates ErbB3/HER3 activation and cellular proliferation.** *Centa A, Rodríguez-Barrueco R, Montero JC, Pandiella A.* **Mol Oncol. 2018 Jun;12(7):1061-1076. doi: 10.1002/1878-0261.12310.** PMID: 29683256 **IF: 5.962 / D1**

- **Colorectal cancer and medicinal plants: Principle findings from recent studies.** *Benarba B, Pandiella A.* **Biomed Pharmacother. 2018 Nov;107:408-423. doi: 10.1016/j.biopha.2018.08.006. Review.** PMID: 30099345 **IF: 3.743 / Q1**

- **Dual targeting of HER2-positive breast cancer with trastuzumab emtansine and pertuzumab: understanding clinical trial results**. *Ocaña A, Amir E, Pandiella A.* **Oncotarget. 2018 Aug 7;9(61):31915-31919. doi: 10.18632/oncotarget.25739. eCollection 2018 Aug 7. Review.** PMID: 30159132 **IF: NI**

- **Epigenetic modulation of FOXM1-gene interacting network by BET inhibitors in breast cancer.** *Pérez-Peña J, Győrffy B, Amir E, Pandiella A, Ocaña A.* **Breast Cancer Res Treat. 2018 Sep 11. doi: 10.1007/s10549-018-4965-x.** PMID: 30206781 **IF: 3.471 / Q2**

- **Refining Early Antitumoral Drug Development.** *Ocaña A, García-Alonso S, Amir E, Pandiella A.* **Trends Pharmacol Sci. 2018 Nov;39(11):922-925. doi: 10.1016/j.tips.2018.09.003.** PMID: 30279003 **IF: 11.523 / D1**

- **Evaluation of transcriptionally regulated genes identifies NCOR1 in hormone receptor negative breast tumors and lung adenocarcinomas as a potential tumor suppressor gene.** *Noblejas-López MDM, Morcillo-García S, Nieto-Jiménez C, Nuncia-Cantarero M, Győrffy B, Galan-Moya EM, Pandiella A, Ocaña A.* **PLoS One. 2018 Nov 28;13(11):e0207776. doi: 10.1371/journal.pone.0207776. eCollection 2018.** PMID: 30485330 **IF: 2.776 / D1**

- **MEK5 promotes lung adenocarcinoma**. *Sánchez-Fdez A, Ortiz-Ruiz MJ, Re-Louhau MF, Ramos I, Blanco-Múñez Ó, Ludeña D, Abad M, Sánchez-Martín M, Pandiella A, Esparís-Ogando A.* **Eur Respir J. 2019 Feb 28;53(2). pii: 1801327. doi: 10.1183/13993003.01327-2018. Print 2019 Feb.** PMID: 30442718 **IF: 11.807 / D1**

- **Efficacy and safety of dasatinib with trastuzumab and paclitaxel in first line HER2-positive metastatic breast cancer: results from the phase II GEICAM/2010-04 study.** *Ocana A, Gil-Martin M, Antolín S, Atienza M, Montaño Á, Ribelles N, Urruticoechea A, Falcón A, Pernas S, Orlando J, Montero JC, Escudero MJ, Benito S, Caballero R, Carrasco E, Rojo F, Pandiella A, Ruiz-Borrego M.* **Breast Cancer Res Treat. 2019 Apr;174(3):693-701. doi: 10.1007/s10549-018-05100-z.** PMID: 30607629 **IF: 3.471 / Q2**

- **Resistance to MAPK Inhibitors in Melanoma Involves Activation of the IGF1R-MEK5-Erk5 Pathway.** *Benito-Jardón L, Díaz-Martínez M, Arellano-Sánchez N, Vaquero-Morales P, Esparís-Ogando A, Teixidó J.* **Cancer Res. 2019 May 1;79(9):2244-2256. doi: 10.1158/0008-5472.CAN-18-2762.** PMID: 30833419 **IF: 8.378 / D1**

- **TRAIL receptor activation overcomes resistance to trastuzumab in HER2 positive breast cancer cells.** *Díaz-Rodríguez E, Pérez-Peña J, Ríos-Luci C, Arribas J, Ocaña A, Pandiella A.* **Cancer Lett. 2019 Jul 1;453:34-44. doi: 10.1016/j.canlet.2019.03.042.** PMID: 30928382 **IF: 6.508 / D1**

- **Mapping Bromodomains in breast cancer and association with clinical outcome.** *Pérez-Pena J, Páez R, Nieto-Jiménez C, Sánchez VC, Galan-Moya EM, Pandiella A, Győrffy B, Ocana A.* **Sci Rep. 2019 Apr 5;9(1):5734. doi: 10.1038/s41598-019-41934-3.** PMID: 30952871 **IF: 4.011 / D1**

- **Genetic mutational status of genes regulating epigenetics: Role of the histone methyltransferase KMT2D in triple negative breast tumors.** *Morcillo-García S, Noblejas-Lopez MDM, Nieto-Jiménez C, Perez-Peña J, Nuncia-Cantarero M, Győrffy B, Amir E, Pandiella A, Galan-Moya EM, Ocana A.* **PLoS One. 2019 Apr 16;14(4):e0209134. doi: 10.1371/journal.pone.0209134. eCollection 2019.** PMID: 30990809 **IF: 2.776 / D1**

- **Central Role of Cell Cycle Regulation in the Antitumoral Action of Ocoxin.** *Pérez-Peña J, Díaz-Rodríguez E, Sanz E, Pandiella A.* **Nutrients. 2019 May 14;11(5). pii: E1068. doi: 10.3390/nu11051068**. PMID: 31091680 **IF: 4.171 / D1**

- **Bryonia dioica aqueous extract induces apoptosis and G2/M cell cycle arrest in MDA-MB 231 breast cancer cells.** *Benarba B, Elmallah A, Pandiella A.* **Mol Med Rep. 2019 Jul;20(1):73-80. doi: 10.3892/mmr.2019.10220.** PMID: 31115513 **IF: 1.851 / Q3**

- **Prognostic value of receptor tyrosine kinase-like orphan receptor (ROR) family in cancer: A meta-analysis**. *Saleh RR, Antrás JF, Peinado P, Pérez-Segura P, Pandiella A, Amir E, Ocaña A.* **Cancer Treat Rev. 2019 Jul;77:11-19. doi: 10.1016/j.ctrv.2019.05.006.** PMID: 31174180 **IF: 8.332 / D1**

- **Paclitaxel-Trastuzumab Mixed Nanovehicle to Target HER2-Overexpressing Tumors**. *Nieto C, Centa A, Rodríguez-Rodríguez JA, Pandiella A, Martín Del Valle EM.* **Nanomaterials (Basel). 2019 Jun 29;9(7). pii: E948. doi: 10.3390/nano9070948.** PMID: 31261957 **IF: 4.034 / Q1**

- **Screening and Preliminary Biochemical and Biological Studies of [RuCl(p-cymene)(N,N-bis(diphenylphosphino)-isopropylamine)][BF4] in Breast Cancer Models.** *Corrales Sánchez V, Nieto-Jiménez C, Castro-Osma JA, de Andrés F, Pacheco-Liñán PJ, Bravo I, Rodríguez Fariñas N, Niza E, Domínguez-Jurado E, Lara-Sánchez A, Ríos Á, Gómez Juárez M, Montero JC, Pandiella A, Shafir A, Alonso-Moreno C, Ocaña A.* **ACS Omega. 2019 Aug 1;4(8):13005-13014. doi: 10.1021/acsomega.9b00296. eCollection 2019 Aug 20.** PMID: 31460427 **IF: 2.584 / Q1**

- **Activity of BET-proteolysis targeting chimeric (PROTAC) compounds in triple negative breast cancer.** *Noblejas-López MDM, Nieto-Jiménez C, Burgos M, Gómez-Juárez M, Montero JC, Esparís-Ogando A, Pandiella A, Galán-Moya EM, Ocaña* **A. J Exp Clin Cancer Res. 2019 Aug 30;38(1):383. doi: 10.1186/s13046-019-1387-5.** PMID: 31470872 **IF: 5.645 / Q1**

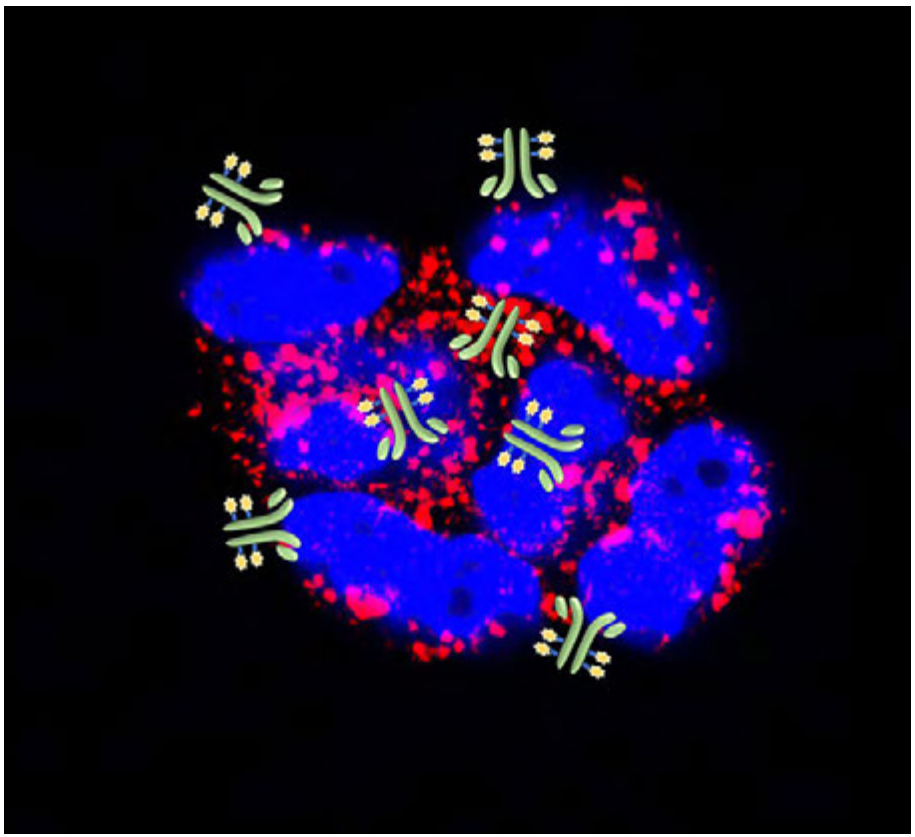
- **Expression of MHC class I, HLA-A and HLA-B identifies immune-activated breast tumors with favorable outcome.** *Noblejas-López MDM, Nieto-Jiménez C, Morcillo García S, Pérez-Peña J, Nuncia-Cantarero M, Andrés-Pretel F, Galán-Moya EM, Amir E, Pandiella A, Győrffy B, Ocana A.* **Oncoimmunology. 2019 Jul 3;8(10):e1629780. doi: 10.1080/2162402X.2019. 1629780. eCollection 2019.** PMID: 31646075 **IF: 5.333 / Q1**

- **Prognostic Value of Lymphocyte-Activation Gene 3 (LAG3) in Cancer: A Meta-Analysis.** *Saleh RR, Peinado P, Fuentes-Antrás J, Pérez-Segura P, Pandiella A, Amir E, Ocaña A.* **Front Oncol. 2019 Oct 15;9:1040. doi: 10.3389/fonc.2019.01040. eCollection 2019.** PMID: 31681578 **IF:4.137 / Q2**

- **A Transcriptomic Immunologic Signature Predicts Favorable Outcome in Neoadjuvant Chemotherapy Treated Triple Negative Breast Tumors.** Pérez-Pena J, Tibor Fekete J, Páez R, Baliu-Piqué M, García-Saenz JÁ, García-Barberán V, Manzano A, Pérez-Segura P, Esparís-Ogando A, *Pandiella A, Gyorffy B, Ocana A.* **Front Immunol. 2019 Dec 18;10:2802. doi: 10.3389/fimmu.2019.02802. eCollection 2019.** PMID: 31921107 **IF: 4.716 / Q2**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Nuevas estrategias para tratar el cáncer de mama positivo para HER2	Atanasio Pandiella Alonso (Coordinated with Joaquín Arribas)	Spanish Association against Cancer (AECC)	2012-2019	600,000.00 €
Nuevas terapias en cáncer de ovario	Atanasio Pandiella Alonso	CRIS Foundation	2015-2018	18,000.00 €
La ruta de MEK5/ERK5 como diana terapéutica en cáncer (PI15/01180)	Azucena Esparís Ogando	Carlos III Health Institute	2016-2019	110,715.00 €
Búsqueda de nuevas dianas moleculares en cáncer de mama triple negativo (PI15/00684)	Juan Carlos Montero	Carlos III Health Institute	2016-2018	92,565.00 €
Señalización por receptores ERBB/HER en cáncer (BFU2015-71371-R)	Atanasio Pandiella Alonso	Spanish Ministry of Economy & Competitiveness	2016-2020	369,050.00 €
Señalización por receptores ERBB/HER en cáncer (CSI002U16)	Atanasio Pandiella Alonso	Regional Government of Castilla and León	2016-2018	120,000.00 €
Center of Biomedical Research on Cancer (CIBERONC) (CB16/12/00317)	Atanasio Pandiella Alonso	Carlos III Health Institute	2018-2019	100,000.00 €
Implicación de la vía de señalización MEK5/ERK5 en liposarcoma y otros sarcomas de partes blandas (FS/39-2017)	Azucena Esparís Ogando	Solórzano Foundation	2018	1,697.08 €



Composite image illustrating six breast cancer cells which are resistant to anti-HER2 therapies used in the clinic. We used those cells to explore novel therapeutic strategies to fight these resistances. One such strategy consists in the use of an antibody that recognizes the cell surface cognate receptor HER3. The antibody to HER3 has been modified to include a highly cytotoxic payload. The whole complex of antibody-cytotoxic drug (termed EV20/MMAF) is internalized in the tumoral cells, and this process is followed by specific death of the tumoral cells.

Team Leader

José María de Pereda Vega
Phone.: +34 923 294 817
E-mail: pereda@usal.es

Research Team

Senior Researcher
Carmen Guerrero Arroyo

Postdoctorals
Sergio de Cima Martín
Sara Ortíz Rivero

Predoctorals
Sara Gutiérrez Herrero
Arturo Carabias del Rey
Luis Hernández Cano
Antonio Rodríguez Blázquez
Cristina Fernández Infante
Alba Morán Vaquero

Master Students
Óscar Herranz Varea
Isabel Cuesta Almagro

Visiting researcher
Laura Niehaus

LABORATORY 17

STRUCTURAL BIOLOGY OF CELL ADHESION AND SIGNALING

The interaction of cell with their environment, including extracellular matrix and other cells, through adhesion molecules is essential in a wide range of cellular and tissue functions. Our group is interested in understanding the organization and regulation of cell adhesions mediated by a group of receptors named integrins. Such adhesions not only participate in physiological processes, but are also altered or involved in diverse pathologies including coagulation disorders, skin blistering diseases, and multiple types of cancer. In our research, we study the the structural and mechanistic basis of the function of proteins involved in cell adhesion. Our work involves the application of mutidisciplinary approaches that include complementary structural biology methods and the use of quantitative biophysical and biochemical techniques.

We study the structure and regulation of hemidesmosomes, which are multiprotein adhesion complexes that mediate the stable attachment of epithelial cells to the basement membrane. Defects in the proteins that form the hemidesmosomes cause different variants of epidermolysis bullosa, a group of severe blistering diseases characterized by fragility of the skin. Hemidesmosomes are dynamic complexes that disassemble when epithelial cells migrate, for example during wound healing and in invasive carcinoma cells. The integrin α6β4 is a central component of the hemidesmosomes. In the skin and other complex epithelia, two proteins of the plakin family, plectin and BP230, connect α6β4 to the cytokeratins, of the intermediate filament system. We had previously elucidated the mechanism and structural basis of the interaction between α6β4 and plectin. Recently, we have characterized in detail the structural basis of the binding of BP230 to the integrin β4 subunit. A short sequence located at the beginning of BP230 binds to a region of β4 formed by the third and fourth Fibronectin type-III domain (FnIII-3,4). The crystal structure of the complex revealed that BP230 in placed between the two FnIII domains. Using double electron-electron resonance, a methods that allows to measure long range distances, we showed that binding of BP230 induces a conformational change in the FnIII-3,4 of β4; this suggests that binding of BP230 to α6β4 might be allosterically regulated. We have also shown that the interaction between BP230 and β4 is necessary for the recruitment of BP230 to hemidesmosomes in human keratinocytes. Finally, we have identified a residue in BP230, Ser46, which is critical for the interaction. Substitution of this residue by Asp, which resembles its phosphorylation, prevents the binding to α6β4. This suggests that the interaction between BP230 and α6β4 might be regulated by phosphorylation by Ser/Thr-kinases. This is reminiscent of the disruption of the α6β4/plectin interaction by phosphorylation of the β4 subunit. Thus, we provide a first potential mechanism that regulates the disruption of the α6β4/BP230 interaction during hemidesmosome disassembly.

Our group also studies mechanisms of cellular signaling that regulate adhesion by integrin receptors. In particular, we are interested in mechanisms that regulate the small GTPase Rap1, which is an activator of integrins. In collaboration with the group of Dr Carmen Guerrero, we study the regulation of the protein C3G, which is a guanine nucleotide exchange factor (GEF) of Rap1 proteins. C3G promotes the active form of Rap1 in response to tyrosine-phosphorylation signaling. We have identified the main mechanism of autoregulation of C3G. We are also interested in understanding potential alterations in the C3G-Rap1 signaling pathway linked to human diseases.

SENIOR RESEARCHER

C3G REGULATION OF PLATELET FUNCTION USING ANIMAL MODELS AND ITS IMPACT ON ISCHEMIA AND TUMOR METASTASIS

Carmen Guerrero Arroyo

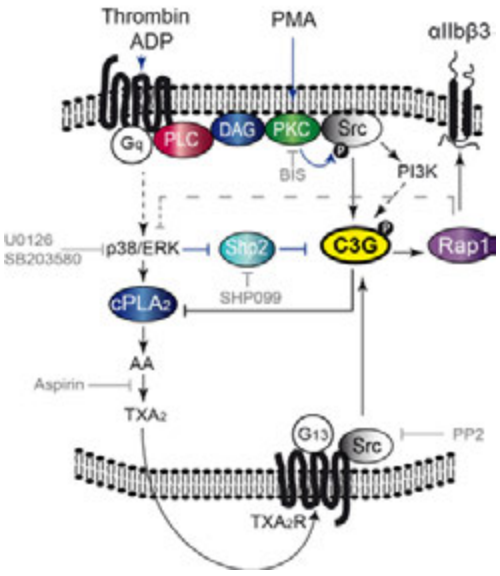
Phone.: +34 923 294 817

E-mail: cguerrero@usal.es

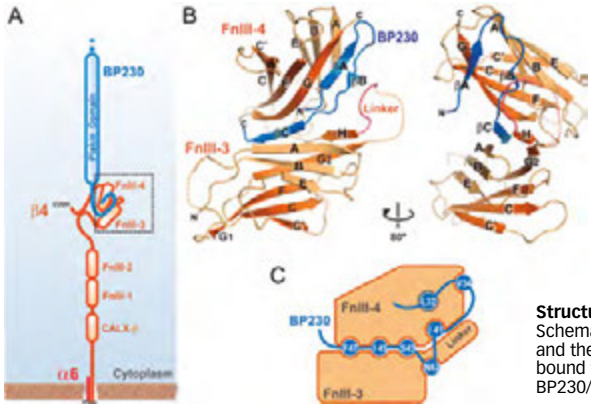
Our group is focused on the role of C3G in platelet function and its relationship with tumor development and metastasis. Using mouse models with platelet-specific overexpression or ablation of C3G, we have uncovered new functions of C3G in regulating different aspects of platelet biology. C3G participates in the differentiation of immature hematopoietic cells to megakaryocytes. In addition, C3G contributes to the activation of the platelet integrin αIIbβ3 through the regulation of the main signaling pathways leading to Rap1 activation, including thrombin-PKC-Src, thrombin-ERK/p38-Shp2 and ADP-P2Y12-PI3K. Moreover C3G is a mediator of thrombin-TXA2 activities and inhibits the synthesis of TXA2 through cPLA2 regulation.

C3G contributes to platelet-mediated angiogenesis in tumors and other contexts, through the modulation of α-granule secretion, via Rap1b-dependent and independent mechanisms. Additionally, overexpression of C3G in platelets greatly increases mouse melanoma cell metastasis. This is mediated by its interaction with proteins of the secretory machinery and actin cytoskeleton remodeling. Consequently, C3G plays an important role in platelet spreading. Decreased secretion of thrombospondin-1 is probably the most important event that contributes to the tumorigenesis mediated by platelet C3G.

At present, we are analyzing the role of platelet C3G in ischemia-induced neovascularization. Also, we are investigating the mechanisms by which C3G regulates platelet secretion.



Proposed model for the participation of C3G in platelet signaling. C3G participates in the second wave of Rap1 activation induced by thrombin, which leads to its activation by phosphorylation in Tyr504 through a PKC-Src pathway. C3G phosphorylation is also regulated by ERKs and p38 MAPKs: ERKs inhibits Shp2 tyrosine phosphatase, allowing C3G phosphorylation, and both MAPKs control the production of TXA2. C3G, via Rap1-dependent or independent mechanisms, regulate TXA2 synthesis through a negative feedback loop, involving inhibition of cPLA2. PLC: phospholipase C; DAG: diacylglycerol; AA: arachidonic acid; TXA2: Tromboxane A2; TXA2R: TXA2 receptor; cPLA2: cytosolic phospholipase A2; BIS: bisindolylmaleimide, inhibitor of PKC; PP2: Src inhibitor; wortmannin: PI3K inhibitor; SHP099: Shp2 inhibitor; U0126: ERKs inhibitor; SB203580: p38α/β MAPK inhibitor; aspirin: cyclooxygenase inhibitor. Dashed grey blocking lines indicates a hypothetical Rap1-dependent pathway that could regulate the activation of ERKs and p38 MAPKs.



Structural basis of the interaction between BP230 and integrin β4 in hemidesmosomes. **(A)** Schematic representation of the cytoplasmic domain of β4 and the N-terminal region of BP230, and their interaction. **(B)** Structure of the complex formed by the N-terminal region of BP230 (blue) bound to the region FnIII-3,4 of integrin β4 (orange) (PDB entry 6GVL). **(C)** Simplified diagram of the BP230/β4 complex and the main contacts.

PUBLICATIONS

- **How Rap and its GEFs control liver physiology and cancer development. C3G alterations in human hepatocarcinoma**. *Sequera C, Manzano S, Guerrero C, Porras A.* **Hepat Oncol. 2018 Apr 16;5(1):HEP05. doi: 10.2217/hep-2017-0026. eCollection 2018 Jan. Review.** PMID: 30302196 IF: NI
- **Ferredoxin-linked flavoenzyme defines a family of pyridine nucleotide-independent thioredoxin reductases**. *Buey RM, Fernández-Justel D, de Pereda JM, Revuelta JL, Schürmann P, Buchanan BB, Balsera M.* **Proc Natl Acad Sci U S A. 2018 Dec 3. pii: 201812781. doi: 10.1073/pnas.1812781115.** PMID: 30510005 IF: 9.580 / D1
- **C3G, through its GEF activity, induces megakaryocytic differentiation and proplatelet formation.** *Ortiz-Rivero S, Baquero C, Hernández-Cano L, Roldán-Etcheverry JJ, Gutiérrez-Herrero S, Fernández-Infante C, Martín-Granado V, Anguita E, de Pereda JM, Porras A, Guerrero* C. Cell Commun Signal. **2018 Dec 19;16(1):101. doi: 10.1186/s12964-018-0311-5.** PMID: 30567575 IF: 5.111 / Q1
- **Integrin α6β4 Recognition of a Linear Motif of Bullous Pemphigoid Antigen BP230 Controls Its Recruitment to Hemidesmosomes.** *Manso JA, Gómez-Hernández M, Carabias A, Alonso-García N, García-Rubio I, Kreft M, Sonnenberg A, de Pereda JM.* **Structure. 2019 Jun 4;27(6):952-964.e6. doi: 10.1016/j.str.2019.03.016.** PMID: 31006587 IF: 4.576 / Q1

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Bases estructurales y mecanísticas de la regulación del activador de RAP1 C3G (BFU2015-69499-P)	José María de Pereda	Spanish Ministry of Economy & Competitiveness	2016-2018	130,438.00 €
Papel de C3G en la regulación de la función plaquetaria: implicaciones en angiogénesis y aplicación al diagnóstico y tratamiento de la enfermedad trombótica (SA017U16)	Carmen Guerrero Arroyo	Ministry of Education. Regional Government of Castilla and León	2016-2018	119,999.00 €
Función de C3G en el desarrollo tumoral y en la patofisiología del hígado. Implicación del C3G plaquetario en la angiogénesis y en enfermedades hepáticas y cardiovasculares (SAF2016-76588-C2-2-R)	Carmen Guerrero Arroyo	Spanish Ministry of Economy & Competitiveness	2017-2019	121,000.00 €
New connections - A novel cytoskeletal linkage that connects cell matrix adhesions to intermediate filaments (IES\ R3\170232).	Benjamin Goult	The Royal Society, International Exchanges	2018-2020	12,000.00 £

Team Leader

Felipe X. Pimentel-Muiños

Phone.: +34 923 294 818

E-mail: fxp@usal.es

Research Team

Postdoctoral

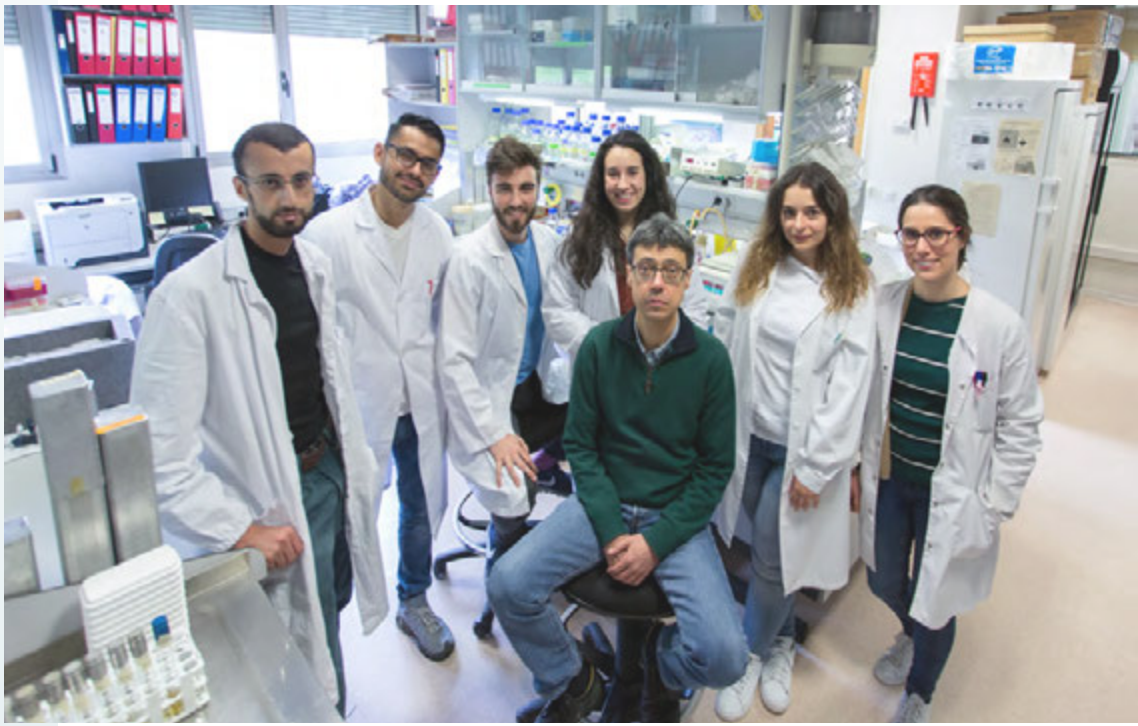
Jose Luis Cedillo Mireles

Predoctoral

Álvaro Fernández Cabrera
Inmaculada Serramito Gómez
Rachid Taouil Hammouti
Raquel Villamuera del Sordo
Elena Terraza Silvestre

Master Student

Claudia María Rejano Gordillo

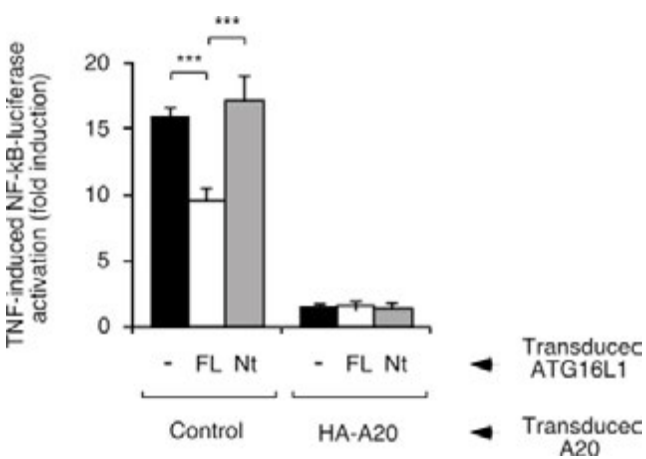


LABORATORY 18

UNCONVENTIONAL AUTOPHAGY IN HEALTH AND DISEASE

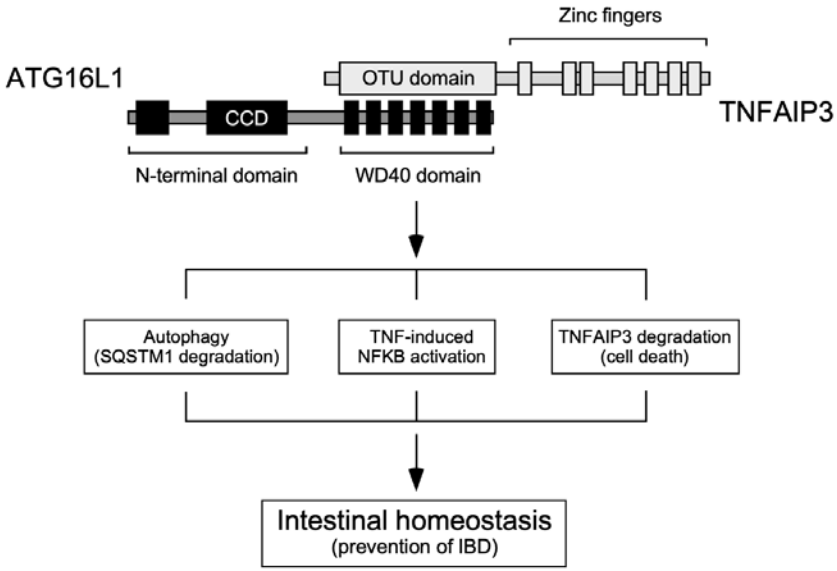
The main focus of our laboratory is the study of unconventional forms of autophagy and the implications that this growing collection of processes may have in human disease.

In its most canonical version, autophagy is a catabolic process that promotes degradation of cytoplasmic components for metabolic homeostasis and quality control. This phenomenon involves sequestration of the items to be degraded into double membrane vesicles that become labeled with the autophagic marker LC3 and fuse with lysosomes for degradation of their contents. Due to well-established roles in stress management and quality control, autophagy is widely viewed as a mechanism that helps maintain a healthy cellular homeostasis. However, in the last few years a number of atypical forms of autophagy have been described where either autophagy itself or the molecular machinery that regulates this process play biological roles that seem unrelated to the canonical activities originally described. The molecular mechanisms governing these novel functions are largely unknown.



Our interest in unconventional autophagy comes from our previous characterization of the autophagic activity induced by the transmembrane protein TMEM59. This molecule activates an atypical autophagic process where its own single membrane vesicles become labeled with LC3 and are more efficiently targeted for lysosomal degradation, a phenomenon that seems to be involved in the innate defense against invading microorganisms. TMEM59 directly engages the canonical autophagic mediator ATG16L1 through a minimal aminoacid motif present in its intracellular domain. Notably, a polymorphic allele of ATG16L1 (T300A) that increases the risk of suffering Crohn's disease alters the ability of ATG16L1 to bind TMEM59, raising the idea that at least part of the pathological features caused by the T300A allele may be due to dysfunctions in the normal biology of TMEM59 or other proteins with a similar activity. Therefore, identification of autophagic regulators that function through a TMEM59-like mechanism may point to the molecular and cellular activities whose alteration increases susceptibility to disease.

In our laboratory we are trying to identify such molecules, study the common mechanisms that they utilize to trigger autophagy and analyze their functional relevance in a variety of unconventional processes where the autophagic machinery has been involved. These processes range from the secretion of leaderless proteins, regulation of vesicle trafficking or control of innate and adaptive immunity. Since many of these events are tightly linked to physiopathological processes like inflammation, immune responses or microbial infections, their detailed characterization holds substantial interest in human health. We are also exploring how the normal activity of these molecules may be altered by the ATG16L1-T300A allele to favor disease onset. We are using animal models lacking the relevant molecules to confirm their relevance in disease and possible value as therapeutic targets.



PUBLICATIONS

- **TMEM59 potentiates Wnt signaling by promoting signalosome formation.** *Gerlach JP, Jordens I, Tauriello DVF, van 't Land-Kuper I, Bugter JM, Noordstra I, van der Kooij J, Low TY, Pimentel-Muiños FX, Xanthakis D, Fenderico N, Rabouille C, Heck AJR, Egan DA, Maurice MM.* **Proc Natl Acad Sci U S A. 2018 Apr 24;115(17):E3996-E4005. doi: 10.1073/pnas.1721321115.** PMID: 29632210 **IF: 9.580 / D1**

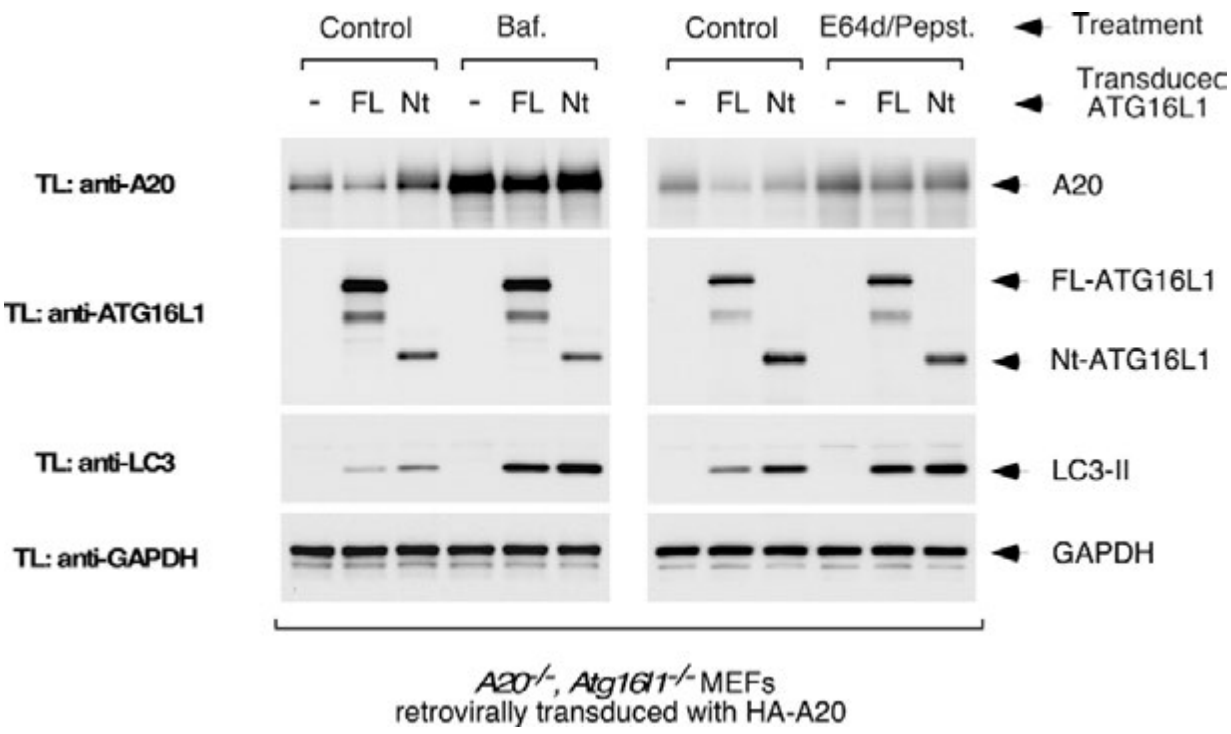
- **Biochemical analyses reveal amino acid residues critical for cell cycle-dependent phosphorylation of human Cdc14A phosphatase by cyclin-dependent kinase 1**. *Ovejero S, Ayala P, Malumbres M, Pimentel-Muiños FX, Bueno, A, Sacristán, MP*. **Sci. Rep. 2018 Aug 8;8(1):11871. doi: 10.1038/s41598-018-30253-8.** PMID: 30089874 **IF: 4,011 / Q1**

- **Physical and functional interaction between A20 and ATG16L1-WD40 domain in the control of intestinal homeostasis.** *Slowicka K, Serramito-Gómez I, Boada-Romero E, Martens A, Sze M, Petta I, Vikkula HK, De Rycke R, Parthoens E, Lippens S, Savvides SN, Wullaert A, Vereecke L, Pimentel-Muiños FX (*), van Loo G (*).* **Nat Commun. 2019 Apr 23;10(1):1834. (*) Co-corresponding authors. doi: 10.1038/s41467-019-09667-z.** PMID: 31015422 **IF: 11.878 / D1**

- **The anti-inflammatory protein TNFAIP3/A20 binds the WD40 domain of ATG16L1 to control the autophagic response, NFKB/NF-κB activation and intestinal homeostasis**. *Serramito-Gómez I, Boada-Romero E, Slowicka K, Vereecke L, Van Loo G, Pimentel-Muiños FX*. **Autophagy. 2019 Sep;15(9):1657-1659. doi: 10.1080/15548627.2019.1628549.** PMID: 31184523 **IF: 11.059 / D1**

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Transautophagy European Network (Participación como miembro del equipo de investigación) (COST Action; CA15138)	Felipe X. Pimentel Muiños	European Union	2016-2018	500,000.00 €
Nuevas actividades del regulador autofágico ATG16L1 y su relevancia en patología (SAF2017-88390-R)	Felipe X. Pimentel Muiños	Spanish Ministry of Economy & Competitiveness	2018-2020	205,700.00 €
Mechanisms and manipulation of immunogenic cell death (IDEAS18093PIME)	Felipe X. Pimentel Muiños	Spanish Association against Cancer (AECC)	2019-2020	20,000.00 €



Team Leader

Javier De Las Rivas

Phone.: +34 923 294 819

E-mail: jrivas@usal.es

Research Team

Postdoctoral

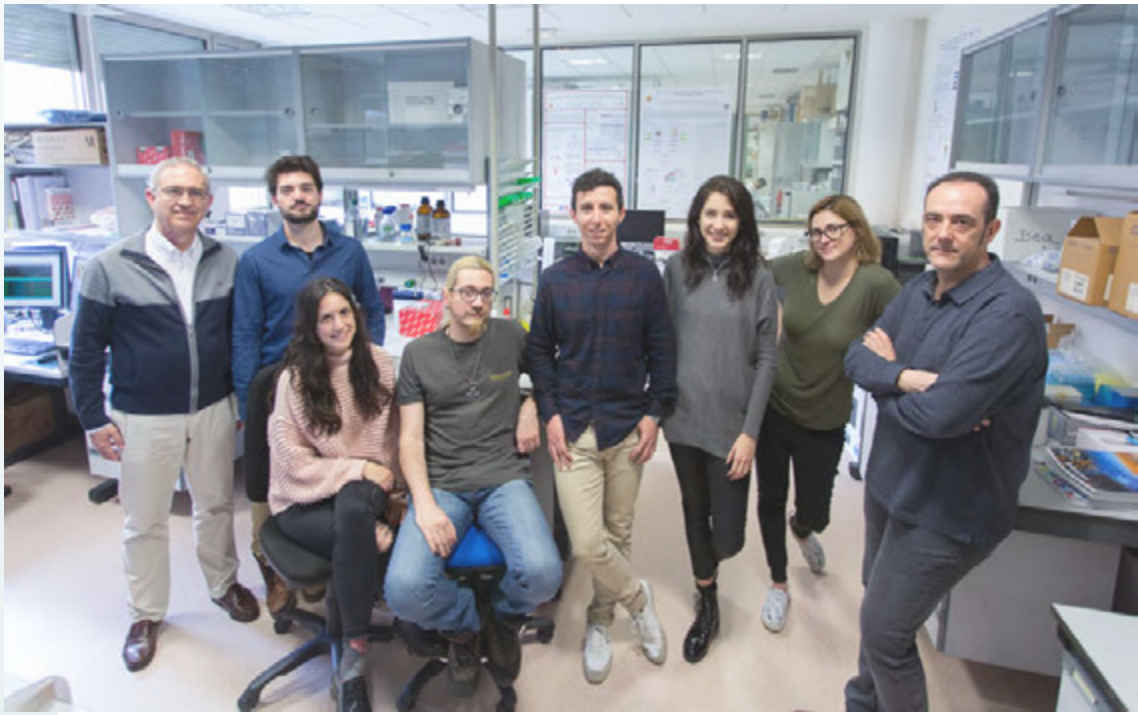
José Manuel Sánchez Santos

Predoctoral

Francisco José Campos Laborie
Santiago Bueno Fortes
Óscar González Velasco
Elena Sánchez Luis
Alberto Berral González
Fernando Bueno Gutiérrez

Visiting researcher

Lauren J. Antrim
Alberto J. Martín
Álvaro Andrades Delgado
Mónica M. Arroyo Cabán
Carolina Cortés Urrea
Cecilia López Martínez

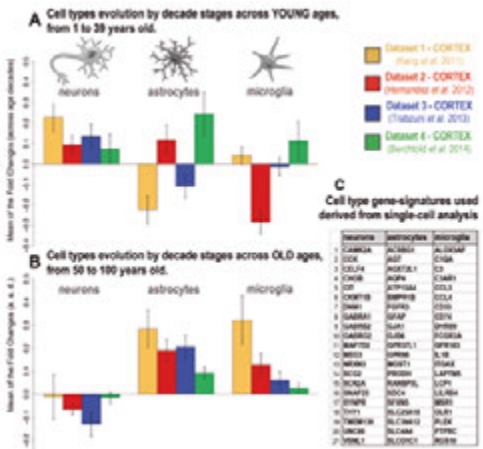


LABORATORY 19

BIOINFORMATICS AND FUNCTIONAL GENOMICS OF CANCER

Research framed within the field of Bioinformatics and Functional Genomics applied to the biomedical area of Cancer and Oncology:

- Functional Genomics and Bioinformatics: Development of methods and strategies for the analysis of genomic data derived from different large-scale technologies (such as RNA-seq, DNA-seq, etc) to determine expression of genes, miRNAs and ncRNAs; or to identify gene splicing, copy-number alterations, changes in the methylation pattern, etc. Data mining, integration and analysis of genomic profiles to achieve robust assignment of signal values and identify gene signatures associated to specific biological or pathological stages. Focus on cancer samples from patients to identify disease subtypes, disease evolution and treatment responses (always in close collaboration with medical groups).
- Big Data, Machine Learning and Computational Omics: Application of methods of big data mining and artificial intelligence (such as Machine and Deep Learning, Reverse Engineering, Non-linear Dimensionality Reduction, etc) to omics data for: (i) the discovery of biomolecular signatures associated to specific pathological states; (ii) to build prognosis predictors derived from survival analysis; (ii) to build treatment response predictors. At present our studies are focused on the study of cancer and and also on neurodegenerative disorders (based in our participation in several EU projects). Also, as indicated above, most of the work is done on samples derived from patients and always in close collaboration with medical groups.



Analysis, based on single-cell gene signatures, of the evolution of cell types (neurons, astrocytes and microglia) in the human brain with age: (A) changes in the cerebral cortex from young children to adults (1-39 years); (B) changes in the cerebral cortex from adults to elderly (50-100 years); (C) gene signatures used to detect the 3 cell types (derived from single-cell data analysis).

- Proteomics, Interactomics and Network Biology: Development of a biomolecular database of experimentally determined protein-protein interactions (PPIs) including strategies for quality control and validation. Use of this PPIs-DB to build comprehensive human interactome networks and derive cancer-related networks. Integration of genome-wide co-expression data and proteomic interaction data to build multiplex human biomolecular networks. Identification of regulatory circuits associated to these networks to identify causal genes (gene drivers) in specific disease subtypes or pathological states. Construction of bipartite interaction networks between drugs and proteins using pharmacogenomc data. Analysis of these networks for drug-target predictions.

PUBLICATIONS

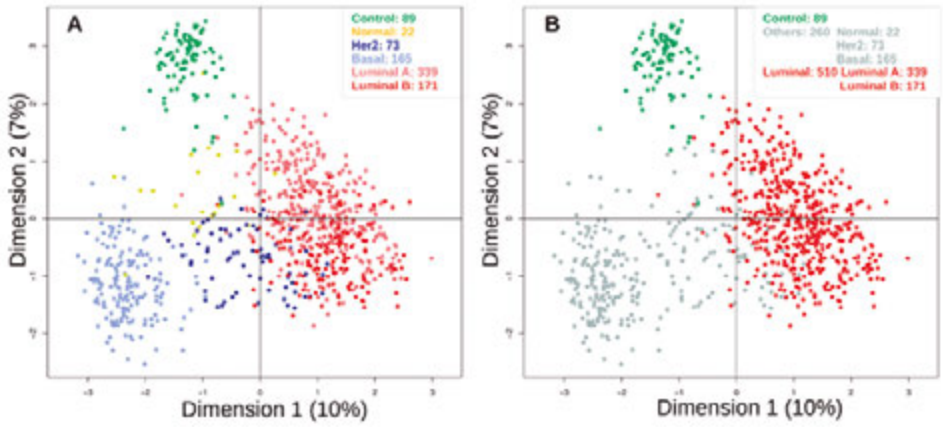
- **Bioinformatics in Latin America and SoIBio impact, a tale of spin-off and expansion around genomes and protein structures.** *De Las Rivas J, Bonavides-Martínez C, Campos-Laborie FJ.* **Brief Bioinform. 2019; 20(2):390-397. doi: 10.1093/bib/bbx064. Erratum in: Brief Bioinform. 2017 Nov 1;18(6):1091.** PMID: 28981567 IF: 9.101 / Q1

- **Human Interactomics: Comparative Analysis of Different Protein Interaction Resources and Construction of a Cancer Protein-Drug Bipartite Network.** *De Las Rivas J, Alonso-López D, Arroyo MM.* **Adv Protein Chem Struct Biol. 2018; 111:263-282. doi: 10.1016/bs.apcsb.2017.09.002.** PMID: 29459035 IF: 3.783 / Q2

- **Loss of Pax5 Exploits Sca1-BCR-ABLp190 Susceptibility to Confer the Metabolic Shift Essential for pB-ALL.** *Martín-Lorenzo A, Auer F, Chan LN, García-Ramírez I, González-Herrero I, Rodríguez-Hernández G, Bartenhagen C, Dugas M, Gombert M, Ginzel S, Blanco O, Orfao A, Alonso-López D, Rivas JL, García-Cenador MB, García-Criado FJ, Müschen M, Sánchez-García I, Borkhardt A, Vicente-Dueñas C, Hauer J.* **Cancer Res. 2018; 78(10):2669-2679. doi: 10.1158/0008-5472.CAN-17-3262.** PMID: 29490943. IF: 8.378 / D1

- **Encompassing new use cases - level 3.0 of the HUPO-PSI format for molecular interactions.** *Sivade Dumousseau M, Alonso-López D, Ammari M, Bradley G, Campbell NH, Ceol A, Cesareni G, Combe C, De Las Rivas J, Del-Toro N, Heimbach J, Hermjakob H, Jurisica I, Koch M, Licata L, Lovering RC, Lynn DJ, Meldal BHM, Micklem G, Panni S, Porras P, Ricard-Blum S, Roechert B, Salwinski L, Shrivastava A, Sullivan J, Thierry-Mieg N, Yehudi Y, Van Roey K, Orchard S.* **BMC Bioinformatics. 2018;19(1):134. doi: 10.1186/s12859-018-2118-1.** PMID: 29642841 IF: 2.511 / Q1

- **JAMI: a Java library for molecular interactions and data interoperability.** *Sivade Dumousseau M, Koch M, Shrivastava A, Alonso-López D, De Las Rivas J, Del-Toro N, Combe CW, Meldal BHM, Heimbach J, Rappsilber J, Sullivan J, Yehudi Y, Orchard S.* **BMC Bioinformatics. 2018;19(1):133. doi: 10.1186/s12859-018-2119-0.** PMID: 29642846 IF: 2.511 / Q1



Comparative analysis of the RNA-seq global expression profiles of 770 Breast Ductal Carcinomas samples obtained from TCGA, marking the 5 main subtypes of breast cancer and the control samples.

- **LMO2 expression defines tumor cell identity during T-cell leukemogenesis.** *García-Ramírez I, Bhatia S, Rodríguez-Hernández G, González-Herrero I, Walter C, González de Tena-Dávila S, Parvin S, Haas O, Woessmann W, Stanulla M, Schrappe M, Dugas M, Natkunam Y, Orfao A, Domínguez V, Pintado B, Blanco O, Alonso-López D, De Las Rivas J, Martín-Lorenzo A, Jiménez R, García Criado FJ, García Cenador MB, Lossos IS, Vicente-Dueñas C, Borkhardt A, Hauer J, Sánchez-García I.* **EMBO J. 2018; 37(14). pii: e98783. doi: 10.15252/embj.201798783.** PMID: 29880602 IF: 11.227/D1

- **Searching the overlap between network modules with specific betweeness (S2B) and its application to cross-disease analysis.** *García-Vaquero ML, Gama-Carvalho M, Rivas JL, Pinto FR.* **Sci Rep. 2018 8(1):11555. doi: 10.1038/s41598-018-29990-7.** PMID: 30068933 IF: 4.011 / D1

- **Regulatory motifs found in the small heat shock protein (sHSP) gene family in tomato.** *Arce D, Spetale F, Krsticevic F, Cacchiarelli P, Las Rivas J, Ponce S, Pratta G, Tapia E.* **BMC Genomics. 2018;19 (Suppl 8):860. doi: 10.1186/s12864-018-5190-z.** PMID: 30537925 IF: 3.501 / Q1

- **Survival marker genes of colorectal cancer derived from consistent transcriptomic profiling.** *Martínez-Romero J, Bueno-Fortes S, Martín-Merino M, Ramirez de Molina A, De Las Rivas J.* **BMC Genomics. 2018 19(Suppl 8):857. doi: 10.1186/s12864-018-5193-9.** PMID: 30537927 IF: 3.501 / Q1

- **APID database: redefining protein-protein interaction experimental evidences and binary interactomes.** *Alonso-López D, Campos-Laborie FJ, Gutiérrez MA, Lambourne L, Calderwood MA, Vidal M, De Las Rivas J.* **Database (Oxford). 2019; 2019. doi: 10.1093/database/baz005.** PMID: 30715274 IF: 3.683 / D1

- **DECO: decompose heterogeneous population cohorts for patient stratification and discovery of sample biomarkers using omic data profiling.** *Campos-Laborie FJ, Risueño A, Ortiz-Estévez M, Rosón-Burgo B, Droste C, Fontanillo C, Loos R, Sánchez-Santos JM, Trotter MW, De Las Rivas J.* **Bioinformatics. 2019; 35(19):3651-3662. doi: 10.1093/bioinformatics/btz148.** PMID: 30824909 IF: 4.531 / D1

- **OMICfpp: a fuzzy approach for paired RNA-Seq counts.** *Berral-González A, Riffo-Campos AL, Ayala G.* **BMC Genomics. 2019; 20(1):259. doi: 10.1186/s12864-019-5496-5.** PMID: 30940089 IF: 3.501 / Q1
- **Maximizing binary interactome mapping with a minimal number of assays.** *Choi SG, Olivet J, Cassonnet P, Vidalain PO, Luck K, Lambourne L, Spirohn K, Lemmens I, Dos Santos M, Demeret C, Jones L, Rangarajan S, Bian W, Coutant EP, Janin YL, van der Werf S, Trepte P, Wanker EE, De Las Rivas J, Tavernier J, Twizere JC, Hao T, Hill DE, Vidal M, Calderwood MA, Jacob Y.* **Nat Commun. 2019;10(1):3907. doi: 10.1038/s41467-019-11809-2.** PMID: 31467278 IF: 11.878 / D1
- **Proteomic and Transcriptomic Profiling Identifies Early Developmentally Regulated Proteins in Dictyostelium Discoideum.** *González-Velasco Ó, De Las Rivas J, Lacal J.* **Cells. 2019; 8(10). pii: E1187. doi: 10.3390/cells8101187.** PMID: 31581556 IF: 5.656/ Q1
- **Transcriptomic analysis of patients with immune thrombocytopenia treated with eltrombopag.** *Hernández-Sánchez JM, Bastida JM, Alonso-López D, Benito R, González-Porras JR, De Las Rivas J, Hernández Rivas JM, Rodríguez-Vicente AE.* **Platelets. 2019:1-8. doi: 10.1080/09537104.2019.1702156.** PMID: 31838946 IF: 3.106 / Q2

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Fly-SMALS: Common RNA-dependent pathways for motor neuron degeneration in spinocerebellar muscular atrophy and amyotrophic lateral sclerosis. (Project Refs. AC14/00024 and JPND_CD_FP-688-085)	Javier De Las Rivas	EU Joint Programme - Neurodegenerative Disease Research (JPND) & Spanish Ministry of Health and Consumer Affairs & Carlos III Health Institute	2015-2018	49,610.00 €
Genómica y proteómica integrativa de hemopatías malignas mieloides y mieloma múltiple: estudio bioinformático de datos ómicos de muestras clínicas de pacientes (PI15/00328)	Javier De Las Rivas	Carlos III Health Institute	2016-2018	92,565.00 €
3-O-sulfated heparan sulfate translocation in altered membrane biology: A new strategy for early population screening and halting Alzheimer's neurodegeneration -ArrestAD (Project Ref. 737390)	Javier De Las Rivas	European Union – Horizon 2020	2017-2020	452,375.00 €
Plataforma de Bioinformática: Bioinformatics and Functional Genomics in Cancer (PT17/0009/0008)	Javier De Las Rivas	Carlos III Health Institute	2017-2019	31,899.00 €
Onco-proteogenómica personalizada aplicada a hemopatías malignas e inmunomodulación: desarrollo y uso de métodos bioinformáticos para búsqueda de marcadores, predictores de riesgo y dianas en pacientes y donantes (PI18/00591)	Javier De Las Rivas	Carlos III Health Institute	2019-2021	99,220.00 €

OTHER ACTIVITIES & RELEVANT FACTS

- President of the Sociedad Iberoamericana de Bioinformática / Iberoamerican Society for Bioinformatics (SOIBIO), from Oct.2016 (second mandate 2019-21). (www.soibio.org)
- Member & Vice-Chair of European COST ACTION CA17104: STRATAGEN, New diagnostic and therapeutic tools against multidrug resistant tumors (4 years Action). From December.2018 https://www.cost.eu/actions/CA17104/
- Member of European COST ACTION CA17118: TRANSCOLONCAN, Identifying biomarkers through translational research for prevention & stratification of Colorectal Cancer (4 years Action). From December.2018 https://www.cost.eu/actions/CA17118/
- Member of the Executive Board of the Global Organisation for Bioinformatics Learning, Education & Training (GOBLET) (Member from 2012, in the Executive Board from 2019). www.mygoblet.org

Team Leader

Juan Jesús Cruz Hernández
Phone: +34 923 291 200 Ext 55342
E-mail: jjcruz@usal.es

Research Team

Medical Oncologists
Amalia Gómez Bernal
Emilio Fonseca Sánchez
Rocío García Domínguez
Germán Martín García
César Rodríguez Sánchez
Elvira del Barco Morillo
Teresa Martín Gómez
Lorena Bellido Hernández
Luis Miguel Navarro Martín
Rosario Vidal Tocino
María Aránzazu Amores Martín
Raquel Seijas Tamayo
Marta Belén Navalón Jiménez
María García Muñoz
Belén Cigarral García
Beatriz Barrios Collado
Diego Casado Elia
Elena Escalera Martín
Juncal Claros Ampuero
Alejandro Olivares Hernández
Luis Figuero Pérez
Eduardo Terán Brage
Álvaro López Gutiérrez
Beatriz María Rivas López

Nurse
Aline Rodrigues Françoso

Administrative Staff
Felicidad Alisente Frías

Biologist
Cristina Gómez Rapela

Visiting Researchers
Roberto Andrés Escala Cornejo
Soledad Medina Valdivieso
Leydy Mallerling Paredes Durán
Belén Cigarral García
Julia Ayuso Martín-Romo

CLINICAL AND MOLECULAR ANALYSIS OF SOLID TUMORS

The research group collaborate with the main national and international cooperative groups such as GEICAM (Spanish research group in breast cancer), SOLTI (Spanish group treatment of solid tumors), TTD (Spanish group treatment of gastrointestinal tumors), Group ONCOPAZ, BCIRG (Breast Cancer International Research Group), the Spanish Group for Head and Neck Cancer (TTCC), GECP (Spanish Group for Lung Cancer), BCIRG (Breast Cancer International Research Group) among others.

Research in hereditary cancer. It is carried out by our group in collaboration with the group of Dr. González Sarmiento, having a clinical unit of genetic counseling and the laboratory 14 of the Cancer Research Center (CIC / IBSAL) for molecular studies. These studies have focused on the clinical-pathological characteristics and their correlation with molecular alterations, mainly in the syndrome of hereditary breast and ovarian cancer and in Lynch Syndrome.

Translational research lines in head and neck tumors. Polymorphism studies in relation to the susceptibility and response to medical and radiotherapy treatment of Head and Neck tumors. Coordinating studies at the national level. Polymorphism studies are carried out in collaboration with the Molecular Medicine Unit of Prof. González Sarmiento. Following the previous line, we have initiated other projects: studies of genetic mutations through massive sequencing techniques in head and neck tumors and their relationship with response and survival in patients with a pre-established treatment, in collaboration with the Molecular Medicine Unit of Prof. González Sarmiento and with the HUSA Cytogenetics Unit of Prof. Hernández Rivas.

The research group has focused on the development of a global program in different solid tumors to study genomic alterations using liquid fluids, mainly in blood samples, what has been called "liquid biopsy in solid tumors".

This new line of research has been designed as a mid-long term effort that is based on the strengths that our group has acquired during the last years. Previous projects and key collaborations with local research groups provide the bases for the development of this new proposal. We have previously collaborated exploring circulating tumor cells, as prognostic and possibly predictive factors of response in patients with breast, colon and prostate cancer. We began this line 15 years ago with the CIC / IBSAL group led by Dr. Isidro Sánchez, and since two years ago it is our own independent line that we developed within our group, since Dr. Juan joined the group.

In addition, based on a collaboration with AMGEN-Biocartis, as an external partner, and with the Service of pathology directed by Dr. Ludeña, we started the implementation of Liquid BIOPSY in some tumors like colon, lung, and prostate cancer. Results of these efforts have been the based of scientific publications in national and international journals and congresses.

With this background our group has started a new project in the last months in which we pretend to perform whole exome sequencing analysis in ctDNA from patients diagnosed with breast, colon and lung cancer. The project has been approved and all resources has been put in place. Patients will be monitored to explore novel mutations and to assess response to treatment when a targeted agent is given, like in the case of PI3K inhibitors in hormone receptor positive breast cancer. Identification of primary resistant patients and molecular vulnerabilities associated with resistance to a given therapy ▸

▸ are key goals of this project. In addition, modifications of treatment based on the identified genomic alterations can help physicians to provide a personalized medicine strategy, a clear necessity for the future oncology. We expect that new patients will be included in the study during this year and first results will be obtained during 2021-2022. Finally, we will expect to export this personalized medicine approach to other hospitals of influence and be a referent for internal and external initiatives.

Characterization of the molecular subtypes of breast cancer, in collaboration with the Pathological Anatomy Service directed by Dr. Ludeña, through the agreement of the Regional Health and Prosignation Management. It is coordinated from our service for the entire community of Castilla y León. The first results were presented at the next congress of the SEOM to be held in Madrid in October.

PUBLICATIONS

- **Oncologist's knowledge and implementation of guidelines for breakthrough cancer pain in Spain: CONOCE study.** *López López R, Camps Herrero C, Khosravi-Shahi P, Guillem Porta V, Carrato Mena A, García-Foncillas J, Cruz Hernández JJ, Gascón Vilaplana P, Antón Torres A, Díaz-Rubio E, Feyjoo Saus M, Aranda Aguilar E.* **Clin Transl Oncol. 2018 May;20(5):613-618. doi: 10.1007/s12094-017-1756-5.** PMID: 28975575. IF: 2.441 / Q2
- **SEOM clinical guideline in nasopharynx cancer (2017).** *Pastor M, Lopez Pousa A, Del Barco E, Perez Segura P, Astorga BG, Castelo B, Bonfill T, Martínez Trufero J, Grau JJ, Mesia R .***Clin Transl Oncol. 2018 Jan;20(1):84-88. doi: 10.1007/s12094-017-1777-0.** PMID: 29098554; IF: 2.441 / Q2
- **SEOM clinical guidelines for the treatment of head and neck cancer (2017).** *Iglesias Docampo LC, Arrazubi Arrula V, Baste Rotllan N, Carral Maseda A, Cirauqui Cirauqui B, Escobar Y, Lambea Sorrosal JJ, Pastor Borgoñón M, Rueda A, Cruz Hernández JJ.* **Clin Transl Oncol. 2018 Jan;20(1):75-83. doi: 10.1007/s12094-017-1776-1.** PMID: 29159792 IF: 2.441 / Q2
- **Outcomes of single versus double hormone receptor-positive breast cancer. A GEICAM/9906 sub-study.** *Ethier JL, Ocaña A, Rodríguez Lescure A, Ruíz A, Alba E, Calvo L, Ruíz-Borrego M, Santaballa A, Rodríguez CA, Crespo C, Ramos M, Gracia Marco J, Lluch A, Álvarez I, Casas M, Sánchez-Aragó M, Carrasco E, Caballero R, Amir E, Martin M. Eur J* **Cancer. 2018 May;94:199-205. doi: 10.1016/j.ejca.2018.02.018.** PMID: 29573665. IF: 6.680 / D1
- **Renal Cell Carcinoma Associated with Xp11.2 Translocation/TFE3 Gene-fusion: A Long Response to mammalian target of rapamycin (mTOR) Inhibitors.** Rua *Fernández OR, Escala Cornejo R, Navarro Martín M, García Muñoz M, Antunez Plaza P, García Dominguez AR, Cruz Hernández JJ.* **Urology. 2018 Jul;117:41-43. doi: 10.1016/j.urology.2018.03.032.** PMID: 29702156 IF: 1.861 / Q2
- **A survey of perceptions, attitudes, knowledge and practices of medical oncologists about cancer pain management in Spain.** García-Mata J, *Álamo C, de Castro J, Contreras J, Gálvez R, Jara C, Llombart A, Pérez C, Sánchez P, Traseira S, Cruz JJ.* **Clin Transl Oncol. 2018 Aug;20(8):1061-1071. doi: 10.1007/s12094-017-1826-8.** PMID: 29721765 IF: 2.441 / Q2
- **GEICAM 9906 Study Investigators. Prognostic role for the derived neutrophil-to-lymphocyte ratio in early breast cancer: a GEICAM/9906 substudy.** *Templeton AJ, Rodríguez-Lescure Á, Ruíz A, Alba E, Calvo L, Ruíz-Borrego M, Santaballa A, Rodríguez CA, Crespo C, Ramos M, Gracia-Marco JM, Lluch A, Álvarez I, Casas MI, Sánchez-Aragó M, Caballero R, Carrasco E, Amir E, Martin M, Ocaña A.* **Clin Transl Oncol. 2018 Dec;20(12):1548-1556. doi: 10.1007/s12094-018-1885-5.** PMID: 29766456. IF: 2.441 / Q2
- **Combined assessment of the TNM stage and BRAF mutational status at diagnosis in sporadic colorectal cancer patients**. *Sayagués JM, Del Carmen S, Del Mar Abad M, Corchete LA, Bengoechea O, Anduaga MF, Baldeón MJ, Cruz JJ, Alcazar JA, Angoso M, González M, García J, Muñoz-Bellvis L, Orfao A, Sarasquete ME.* **Oncotarget. 2018 May 8;9(35):24081-24096. doi: 10.18632/oncotarget.25300. eCollection 2018 May 8.** PMID: 29844874 IF: NI
- **Large cell neuroendocrine carcinoma of the lung with atypical evolution and a remarkable response to lutetium Lu 177 dotatate.** *Escala Cornejo RA, García-Talavera P, Navarro Martin M, Pérez López B, García Muñoz M, Tamayo Alonso MP, Cruz Hernández JJ.* **Ann Nucl Med. 2018 Oct;32(8):568-572. doi: 10.1007/s12149-018-1276-6.** PMID: 30051167 IF: 1.648 / Q2
- **The Medical Oncology resident mentor: situation and workload.** *Elez E, Quintanar T, Bosch-Barrera J, Corral J, Lainez N, Moreno V, Rodriguez CA, González-Flores E, Cervantes A.* **Clin Transl Oncol. 2019 Mar;21(3):304-313. doi: 10.1007/s12094-018-1923-3.** PMID: 30062521. IF: 2.441 / Q2
- **Phase II pilot study of the prednisone to dexamethasone switch in metastatic castration-resistant prostate cancer (mCRPC) patients with limited progression on abiraterone plus prednisone (SWITCH study).** *Romero-Laorden N, Lozano R, Jayaram A, López-Campos F, Saez MI, Montesa A, Gutiérrez-Pecharoman A, Villatoro R, Herrera B, Correa R, Rosero A, Pacheco MI, Garcés T, Cendón Y, Nombela* **MP, Van de Poll F, Grau G, Rivera L, López PP, Cruz JJ, Lorente D, pub 2018 A Attard G, Castro E, Olmos D. Br J Cancer. 2018 Oct;119(9):1052-1059. doi: 10.1038/s41416-018-0123-9.** PMID: 30131546 IF: 5.416 / D1
- **Long-term response to first-line bevacizumab-based therapy in patients with metastatic breast cancer: results of the observational "LORENA" study.** *Redondo A, Ramos Vázquez M, Manso L, Gil Gil MJ, Garau Llinas I, García-Garre E, Rodríguez CA, Chacón JI, López-Vivanco G.* **Onco Targets**

Ther. 2018 Sep 17; 11:5845-5852. doi: 10.2147/OTT.S170303. PMID: 30271167. IF: 3.046 / Q1

- **Late Administration of Trastuzumab Emtansine Might Lead to Loss of Chance for Better Outcome in Patients with HER2-Positive Metastatic Breast Cancer.** *Manso L, Sánchez-Muñoz A, Calvo I, Izarzugaza Y, Plata J, Rodriguez C.* Breast Care (Basel). 2018 Aug;13(4):277-283. doi: 10.1159/000488794. PMID: 30319330. IF: 2.087 / Q2

- **A phase 2 trial of neoadjuvant metformin in combination with trastuzumab and chemotherapy in women with early HER2-positive breast cancer: the METTEN study.** *Martin-Castillo B, Pernas S, Dorca J, Álvarez I, Martínez S, Pérez-García JM, Batista-López N, Rodríguez-Sánchez CA, Amillano K, Domínguez S, Luque M, Stradella A, Morilla I, Viñas G, Cortés J, Cuyàs E, Verdura S, Fernández-Ochoa Á, Fernández-Arroyo S, Segura-Carretero A, Joven J, Pérez E, Bosch N, García M, López-Bonet E, Saidani S, Buxó M, Menendez JA.* Oncotarget. 2018 Nov 2;9(86):35687-35704. doi: 10.18632/oncotarget.26286. PMID: 30479698 IF: NI

- **Biomarkers and polymorphisms in pancreatic neuroendocrine tumors treated with sunitinib.** *Jiménez-Fonseca P, Martín MN, Carmona-Bayonas A, Calvo A, Fernández-Mateos J, Redrado M, Capdevila J, Lago NM, Lacasta A, Muñarriz J, Segura Á, Fuster J, Barón F, Llanos M, Serrano R, Castillo A, Cruz Hernández JJ, Grande E.* Oncotarget. 2018 Dec 11;9(97):36894-36905. doi: 10.18632/oncotarget.26380. eCollection 2018 Dec 11. PMID: 30651923 IF: NI

- **Phase II, Multicenter, Single-arm Trial of Eribulin as First-line Therapy for Patients With Aggressive Taxane-pretreated HER2-Negative Metastatic Breast Cancer: The MERIBEL Study.** *Ortega V, Antón A, Garau I, Afonso N, Calvo L, Fernández Y, Martínez-García M, Blanco E, Zamora P, García M, Illarramendi JJ, Rodríguez Sánchez CA, Sampayo M, Aguirre E, Pérez-García JM, Cortés J, Llombart-Cussac A.* Clin Breast Cancer. 2019 Apr;19(2):105-112. doi: 10.1016/j.clbc.2018.12.012. PMID: 30679100. IF: 2.762 / Q2

- **Neoadjuvant Management of Early Breast Cancer: A Clinical and Investigational Position Statement.** *Colomer R, Saura C, Sánchez-Rovira P, Pascual T, Rubio IT, Burgués O, Marcos L, Rodríguez CA, Martín M, Lluch A.* Oncologist. 2019 May;24(5):603-611. doi: 10.1634/theoncologist.2018-0228. PMID: 30710068 IF: 5.252 / Q1

- **Genetic Susceptibility in Head and Neck Squamous Cell Carcinoma in a Spanish Population.** *Fernández-Mateos J, Seijas-Tamayo R, Adansa Klain JC, Pastor Borgoñón M, Pérez-Ruiz E, Mesía R, Del Barco E, Salvador Coloma C, Rueda Dominguez A, Caballero Daroqui J, Fernández Ruiz E, Ocana A, González-Sarmiento R, Cruz-Hernández JJ.* Cancers (Basel). 2019 Apr 7;11(4). pii: E493. doi: 10.3390/cancers11040493. PMID: 30959967 IF: 6.162/ D1

- **The C Allele of ATM rs11212617 Associates with Higher Pathological Complete Remission Rate in Breast Cancer Patients Treated With Neoadjuvant Metformin.** *Cuyàs E, Buxó M, Ferri Iglesias MJ, Verdura S, Pernas S, Dorca J, Álvarez I, Martínez S, Pérez-García JM, Batista-López N, Rodríguez-Sánchez CA, Amillano K, Domínguez S, Luque M, Morilla I, Stradella A, Viñas G, Cortés J, Joven J, Brunet J, López-Bonet E, García M, Saidani S, Queralt Moles X, Martin-Castillo B, Menendez JA.* Front Oncol. 2019 Mar 28;9:193. doi: 10.3389/fonc.2019.00193. PMID: 30984619. IF: 4.137/ Q1

- **Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer.** *Im SA, Lu YS, Bardia A, Harbeck N, Colleoni M, Franke F, Chow L, Sohn J, Lee KS, Campos-Gómez S, Villanueva-Vazquez R, Jung KH, Chakravartty A, Hughes G, Gounaris I, Rodriguez-Lorenc K, Taran T, Hurvitz S, Tripathy D.* N Engl J Med. 2019 Jul 25;381(4):307-316. doi: 10.1056/NEJMoa1903765. PMID: 31166679. IF: 70.670 / D1

- **A retrospective, multicenter study of the efficacy of lapatinib plus trastuzumab in HER2-positive metastatic breast cancer patients previously treated with trastuzumab, lapatinib, or both: the Trastyvere study.** *Gavilá J, De La Haba J, Bermejo B, Rodríguez-Lescure Á, Antón A, Ciruelos E, Brunet J, Muñoz-Couselo E, Santisteban M, Rodríguez Sánchez CA, Santaballa A, Sánchez Rovira P, García Sáenz JÁ, Ruiz-Borrego M, Guerrero-Zotano AL, Huerta M, Cotes-Sanchís A, Lao Romera J, Aguirre E, Cortés J, Llombart-Cussac A.* Clin Transl Oncol. 2020 Mar;22(3):420-428. doi: 10.1007/s12094-019-02145-4. PMID: 31203575. IF: 2.441 / Q2

- **Development and validation of a sexual relations satisfaction scale in patients with breast cancer - "SEXSAT-Q".** *Mancha RG, Muñoz M, de la Cruz-Merino L, Calvo L, Cruz J, Baena-Cañada JM, Fernandez Y, Ramos M, Rodriguez CA, Chacón JI, Palomero I, Llinares J, Rivero M, Ruiz MÁ.* Health Qual Life Outcomes. 2019 Aug 17;17(1):143. doi: 10.1186/s12955-019-1197-7. PMID: 31420041 IF: 2.318 / Q1

- **Working towards a consensus on the oncological approach of breakthrough pain: a Delphi survey of Spanish experts.** *Camps Herrero C, Antón Torres A, Cruz-Hernández JJ, Carrato A, Constenla M, Díaz-Rubio E, Feyjoo Saus M, García-Foncillas J, Gascón P, Guillem V.* J Pain Res. 2019 Jul 29;12:2349-2358. doi: 10.2147/JPR.S203903. eCollection 2019. PMID: 31534359 IF: 2.236 / Q1

- **Lung cancer in Spain: information from the Thoracic Tumors Registry (TTR study).** *Provencio M, Carcereny E, Rodríguez-Abreu D, López-Castro R, Guirado M, Camps C, Bosch-Barrera J, García-Campelo R, Ortega-Granados AL, González-Larriba JL, Casal-Rubio J, Domine M, Massutí B, Sala MÁ, Bernabé R, Oramas J, Del Barco E.* Transl Lung Cancer Res. 2019 Aug;8(4):461-475. doi: 10.21037/tlcr.2019.08.05. PMID: 31555519. IF: 4.806 / Q1

- **Situation, challenges, and SEOM recommendations for the future of undergraduate education in Oncology in Spain.** *Segui MA, Cruz JJ, Alba E, Feliu J, Jara C, Rivera F, Rodriguez Lescure A, Lorenzo A, Martin M.* Clin Transl Oncol. 2019 Nov 8. doi: 10.1007/s12094-019-02230-8. Review. PMID: 31701365 IF: 2.441 / Q2

- **Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer.** *Slamon DJ, Neven P, Chia S, Fasching PA, De Laurentiis M, Im SA, Petrakova K, Bianchi GV, Esteva FJ, Martín M, Nusch A, Sonke GS, De la Cruz-Merino L, Beck JT, Pivot X, Sondhi M, Wang Y, Chakravartty A, Rodriguez-Lorenc K, Taran T, Jerusalem G.* N Engl J Med. 2020 Feb 6;382(6):514-524. doi: 10.1056/NEJMoa1911149. PMID: 31826360. IF: 70.670 / D1

- **The economic burden of metastatic breast cancer in Spain.** *Bermejo de Las Heras B, Cortes Ramon Y Cajal J, Galve Calvo E, de la Haba Rodriguez J, García Mata J, Moreno Anton F, Pelaez Fernandez I, Rodriguez-Lescure A, Rodriguez Sánchez CA, Ruiz-Borrego M, Remak E, Barra M, Rivero M, Soto Alvarez J.* Eur J Hosp Pharm. 2020 Jan;27(1):19-24. doi: 10.1136/ejhpharm-2017-001453. PMID: 32064084. IF: 0,717 / Q3

OTHER PUBLICATIONS & BOOK CHAPTERS

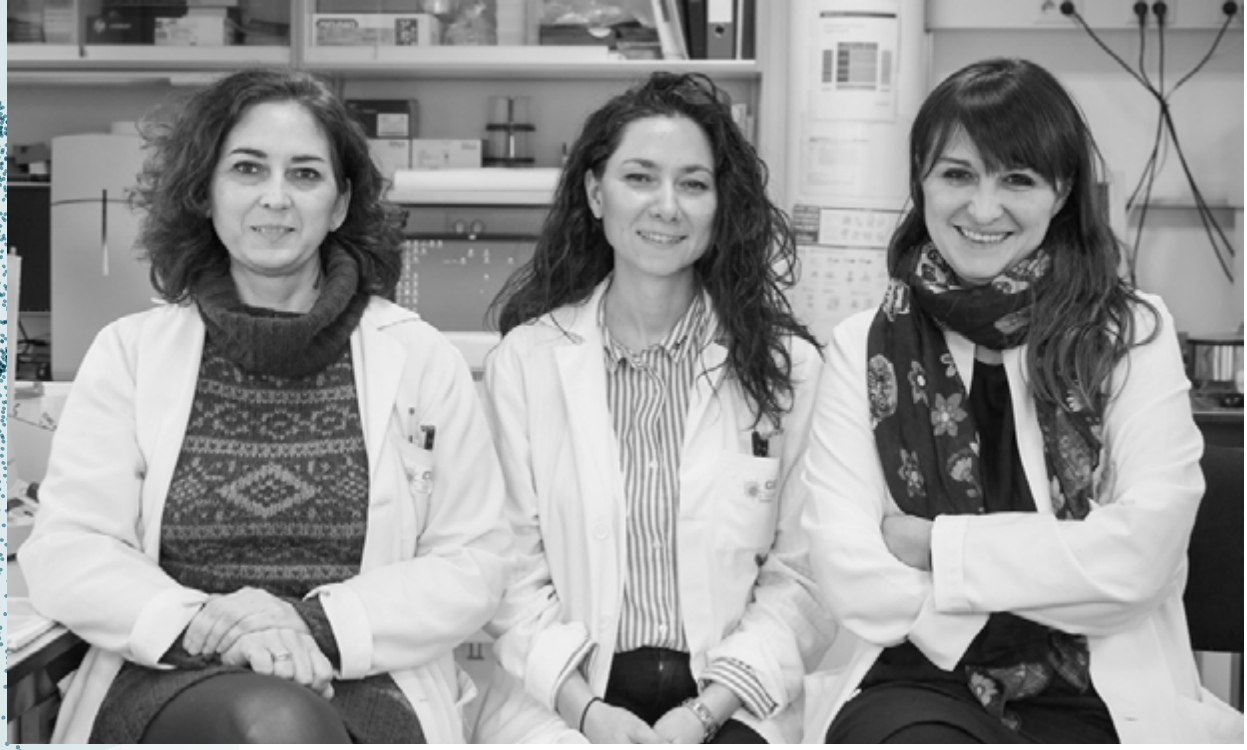
- **Síndrome de neoplasia endocrina múltiple: revisión radiológica.** *Ignacio Martín García, Rosario Vidal Tocino, Elisabeth Martín García, Manuel Angel Martín Pérez, José Martín Marín Balbín:.* Rev Argent Radiol 2018; June 82(03): 124-130 DOI: 10.1055/s-0038-1656560.
- **Urinary transferrin detects subclinical tubular dysfunction predisposing to AKI in rats and predicts nephrotoxicity in oncological patients treated with platinum-based antineoplastics.** *Alfredo G. Casanova, Laura Vicente-Vicente, M. Teresa Hernández-Sánchez, Marta Prieto, M Isabel Rihuete, Laura M. Ramis, Elvira del Barco, Juan J. Cruz, Alberto Ortiz, Carlos Martínez-Salgado, Moisés Pescador, Francisco J Lopez-Hernandez; Ana I. Morales.* Archives of Toxicology ATOX-D-18-01099
- **Cómo seleccionar un biosimilar para su incorporación en la práctica clínica.** *C.A. Rodríguez Sánchez.* Revisiones en cáncer Vol. 33. Supl 1. Pp 138-140, 2019 ISSN: 0213-8573/2019/138-140
- **Analysis of care for cancer patients with opioid-induced constipation in clinical practice: EIO-PRAXIS Project.** *Enrique Aranda, Jesús García-Foncillas, Antonio Antón, Carlos Camps, Alfredo Carrato, Manuel Constenla, Juan J Cruz-Hernandez, Eduardo Díaz-Rubio, Pere Gascón, Vicente Guillem, Rafael López, Margarita Feyjoo, Begoña Soler, Javier Puente.* Open J Pain Med 3(1): 027-033. DOI: https://dx.doi.org/10.17352/ojpm.000015
- **Clinical practice evaluation of opioids induced constipation management in patients with cancer: The EIO-50 project.** *Vicente Guillem, Francisco Javier Salvador Bofill, Margarita Feyjoo, Antonio Antón, Enrique Aranda, Carlos Camps, Alfredo Carrato, Manuel Constela, Juan Jesús Cruz-Hernández, Eduardo Díaz-Rubio, Jesús García-Foncillas, Pere Gascón, Rafael López, Begoña Soler,Yolanda Escobar.* Open J Pain Med 3(1): 034-040. DOI: https://dx.doi.org/10.17352/ojpm.000016

GRANTS FOR RESEARCH IN PROGRESS

PROJECT	PI	GRANT	TIME	FUNDING
Análisis mutacional de BRCA1/BRCA2 en línea somática en cáncer de ovario. Evaluación de implicaciones pronósticas y terapéuticas. GRS1637/A/17	Teresa Martín Gómez	Regional Health Management. Regional Government of Castilla and León	2017-2018	13,710.00 €
Aplicación de la detección mediante biopsia líquida de isoformas del receptor de andrógenos y su perfil genmómico en pacietes con cáncer de próstata. GRS1863/A/18	Juan Jesús Cruz Hernández	Regional Health Management. Regional Government of Castilla and León	2018-2019	15,730.00 €
Análisis integrado de las alteraciones en el número de copias, ADN Metilado y carga mutacional en pacientes con cáncer epidermoide de cabeza y cuello localmente avanzado. Importancia pronóstica y predictiva de respuesta al ensayo clínico TTCC-2007-01. PI18/01476	Juan Jesús Cruz Hernández	Carlos III Health Institute	2018-2020	111,320.00 €

4

SCIENTIFIC SERVICES UNITS



SCIENTIFIC SERVICE UNITS

GENOMICS

Scientific Coordinator

Xosé R. Bustelo

Office phone: (+34) 663 194 634
Lab phone: (+34) 923 29 4802
E-mail: xbustelo@usal.es

Genomics Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Unit Coordinator

M. Encarnación Fermiñán Benito
Phone: (+34) 923 294 816
E-mail: encarnaf@usal.es

Personnel

M. Encarnación Fermiñán Benito
Eva María García
M. Estela Hernández

DESCRIPTION

This CIC facility provides full services for: (a) Genome-wide expression profiling and genotyping using Affymetrix technology. (b) Printing and processing of home-made chips not available commercially. (c) DNA Sequencing. (d) Genomics-related techniques (e.g., quantitative RT-PCR).

The philosophy of this Unit is to provide full services to both internal and external customers. By full services we understand carrying out the whole analytic process: starting with the experimental sample provided by the customer (total RNA, genomic DNA), the Facility's personnel carries out all the required analytical and quality control steps as well as the standard bioinformatics analysis of the data obtained. Further analyses (e.g., functional annotation) will be done using the services of the Bioinformatics Unit.

The facility work and protocols are ISO9001-certified. The occupational health and safety management system of the facility are also OHSAS18001-certified.

SERVICES

– DNA Sequencing using the ABI-3130xl sequencer (Applied Biosystems). This system is able to do both genotyping and SNPs analysis.

– Genomics studies using Affymetrix technology in different species. The main array services included in this category are:
  - Gene Chip Human Genome U133 Plus 2.0
  - Gene Chip Mouse Genome 430 2.0
  - Gene Chip Rat Genome 230 2.0 array
  - Gene Chip Arabidopsis ATH1 Genome array
  - Gene Chip Drosophila Genome 2.0 array
  - Gene Chip Yeast Genome 2.0 array
  - Prime View Human Genome

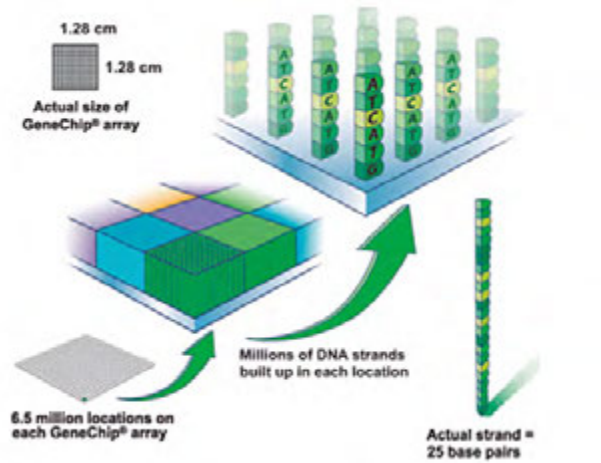
– Analysis of expression profiles using the Gene ST System of Affymetrix in different organisms. The main arrays used are:
  - Gene Chip Human Gene 1.0 and 2.0 ST array
  - Gene Chip Mouse Gene 1.0 and 2.0ST array
  - Gene Chip Rat Gene 1.0 and 2.0 ST array
  - Clariom S human/mouse arrays

– Analysis of expression profiles and splicing alternative using the Exon ST System of Affymetrix. The main arrays used are:
  - Gene Chip Human Exon 1.0 and 2.0 ST array
  - Gene Chip Mouse Exon 1.0 and 2.0 ST array
  - Gene Chip Rat Exon 1.0 and 2.0 ST array
  - HTA Array
  - MTA Array
  - Clariom D human/mouse arrays

– Identification of regulatory promoter sites using immunoprecipitation (ChIP on chip) and other techniques that involve complete genome analyses. The main arrays used are:
  - Gene Chip S. pombe Tiling 1.0 FR array
  - Gene Chip S. cerevisiae Tiling 1.0 FR array
  - Gene Chip Human Tiling 1.0 R array

– SNP and copy number analyses. The main arrays used are:
  - Gene Chip Human Mapping 250K NspI/StyI arrays
  - Genome-Wide Human SNP array 6.0
  - CytoScan 750K array
  - CytoScan HD array
  - OncoScan CNV array

– Analysis of miRNAs and biosynthestic precursors using the Gene Chip miRNA 2.0, 3.0 and 4.0 arrays



Affymetrix GeneChip Structure

– Printing and processing home-made chips: We provide services to prepare home-made microarrays using the MGII Arrayer (Biorobotics). The samples are provided by the user (oligonucleotides, cDNAs, DNA cloned in BACs, antibodies, purified proteins or cellular lysates). Once generated, the microarrays are hybridized using the automatized system hs4800pro (Tecan) and scanned using the GenePix4000 system (Axon).

EQUIPMENT

– 16-capillary ABI Prism 3130xl (Applied Biosystems) for DNA sequencing

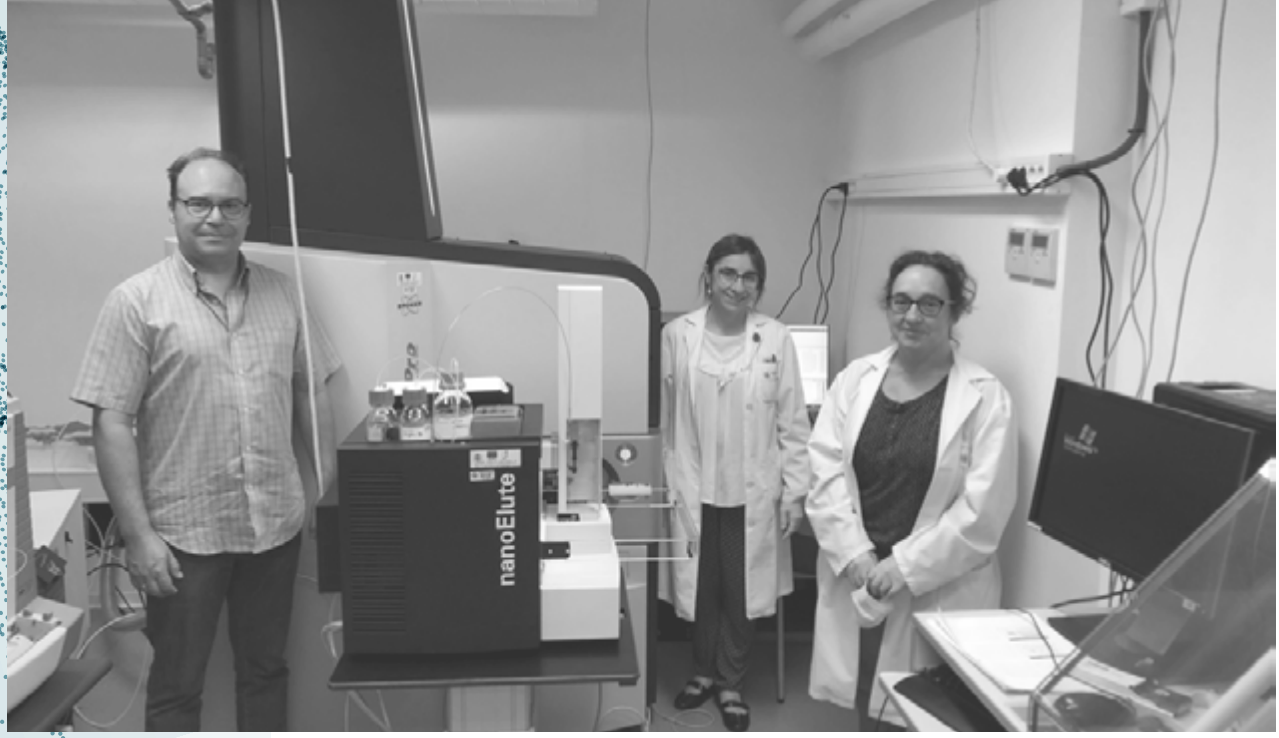
– Agilent 2100 Bioanalyzer for quality control of RNA samples

– Affymetrix equipment, composed of the GeneChip Hybridization Oven 640, the GeneChip Fluidics Station 450, and the Gene Array Scanner 3000 7G

– Biorobot 3000 (Qiagen) and Arrayer (Biorobotics) for home-made array manufacturing

– HS4800Pro Hybridization station (Tecan) for hybridization of home-made microarrays

– GenePix 4000B (Axon) for scanning of data from both home-made and commercial (double colored) chips



SCIENTIFIC SERVICE UNITS

PROTEOMICS

Scientific Coordinator
Xosé R. Bustelo
Office phone: (+34) 663 194 634
Lab phone: (+34) 923 294 802
E-mail: xbustelo@usal.es

Proteomics Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Unit Coordinator
Nieves Ibarrola de Andrés
Phone: (+34) 923 294 720 Ext 1904
E-mail: nibarrola@usal.es

Personnel
Nieves Ibarrola de Andrés
Rosa M. Dégano Blázquez
Raúl Manzano Román

DESCRIPTION

This CIC facility offers advanced proteomics services to support research with optimized costs. To maintain a high level of quality in our services, we have developed standard operating procedures and carry out quality controls of our equipment (ISO 9001 Quality Certification). The Occupational Health and Safety Management System of the Facility has been also OHSAS18001-certified.

The Facility provides consultancy service for many biological research goals involving mass spectrometry or protein arrays and adapts its services to meet projects' requirements and objectives.

To keep up with the state of art of the rapidly evolving mass spectrometry based proteomics field, services are modified according to the latest methods and technologies, and new services are implemented through input and request from our users.

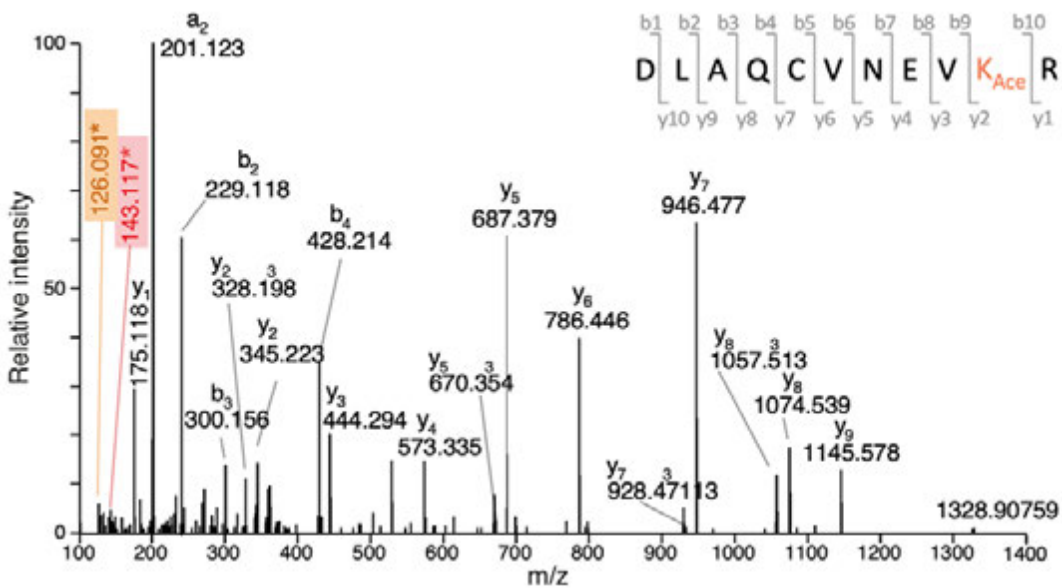
The Facility is part of the Technological Platform for Biomolecular and Bioinformatics resources (PRB3) by the Carlos III Health Institute (https://prb3.org).

MAIN SERVICES

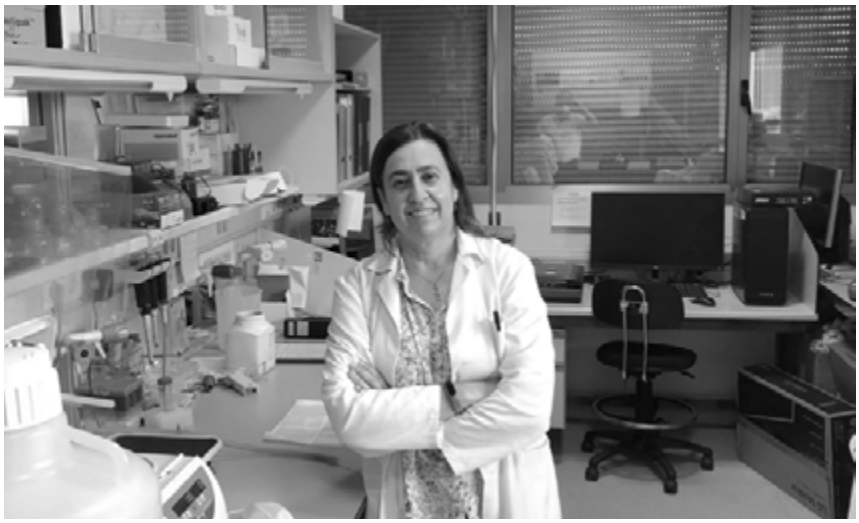
- Protein and peptide separation
  - Electrophoresis. SDS-PAGE gels can be processed (10.0 x 8.0, 16.0 x14.0, 18.5 x 20.0, and 26.0 x22.0 cm) and stained using mass spectrometry-compatible techniques
  - Bidimensional Electrophoresis. Before protein separation in SDS-PAGE gels, we perform a first protein separation by isoelectrophocusing using different strip lengths (7, 13, 18 or 24 cm)
  - Isoelectrofocusing fractionation. Proteins and peptides are fractionated in 12 or 24 cm stripes according to their pI using the Agilent OFFGEL 3100
  - HPLC fractionation using an the HPLC 1100 equipment (Agilent)
- Protein identification by LC MS/MS. Peptides derived from trypsin or other protease sample digestion are separated by a chromatographic gradient in a nano-UPLC system before analysis by mass spectrometer. The gradient length is chosen to meet the depth of analysis required by the different sample complexities
- Relative protein quantitation by using label-free LC-MS/MS and SILAC
- Protein postranslational modification characteryzation by LC MS/MS
- Protein array generation and analyses

EQUIPMENT

- Separation equipment:
  - Ettan IPGPHOR, Ettan Dalt-6 Electrophoresis, Hoefer miniVE, and Hoefer SE 600 Ruby equipment (all from GE Healthcare) to carry out both 2D and vertical gel electrophoresis
  - HPLC 1100 (Agilent) for liquid chromatography analyses
  - 3100 OFFGEL (Agilent) for in solution peptide and protein separation based on isoelectric point
- LC-MS/MS EQUIPMENT composed of an in tandem arrangement of a NanoAcquity nanoUPLC chromatography system (Waters) and an LTQ velos Orbitrap with ETD mass spectrometer (Thermo)
- Brüker timsTOF-PRO
- PROTEIN MICROARRAYS
  - Ultra-Marathon Microarray Printer (Arrayjet)
  - Scanner Sensovation
  - Array Processor M2



Example of mass spec determination done in our facility. Identification of acetylation sites in an oncogenic driver



SCIENTIFIC SERVICE UNITS

TRASLATIONAL ONCOPHARMACOLOGY

DESCRIPTION

The Traslational Oncopharmacology Laboratory (LOT) was created in april 2007 in response to the needs of several groups of our institute that work on antitumor drug development. This unit performs screening of antitumoral activities of drugs in solid tumors and hematological disorders. The unit has given support to both internal research groups, but also to some pharma and biotech companies, as well as to researchers from other academic/government institutions outside our Institute.

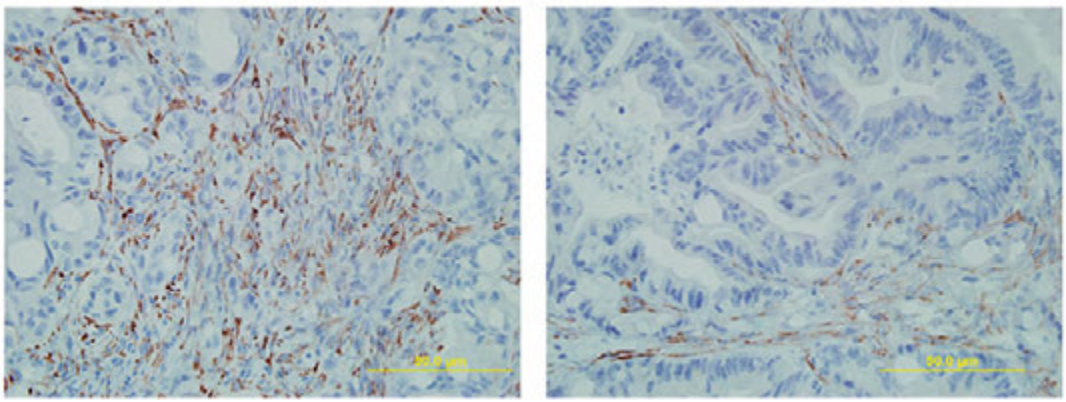
SERVICES

- MTT uptake assay in 24w, 48 w and 96 w microtiter plates. MTT uptake experiments are used to initially assess drug activity on tumoral cells.
- BrdU Cell Proliferation Assay. BrdU uptake experiments are used to assess drug activity on tumoral cells.
- Bioluminescence Assay. Two types of protocols are usually performed. One is based on the incubation of the agent of interest in the presence of bone marrow (BM) cells. In this case, BM cells from patients or the HS-5 cell line can be used. The latter is preferred as it gives more consistent and less variable results. The second experimental setting consists on the incubation of the agent together with growth factors, such as IL-6 or IGF-I. Both protocols are designed to test whether

Scientific Coordinator
Atanasio Pandiella
Phone: (+34) 923 294 815
E-mail: atanasio@usal.es

Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Personnel
Elena Díaz Rodríguez
Phone: (+34) 923 294 815
E-mail: ediaz@usal.es



IHQ analysis of a murine tumor with an antibody produced and purified at the service and directed against an stromal protein.

drug was able to overcome the protective effect of the BM microenvironment.

- Apoptosis assays (Annexin V-FITC). Annexin V staining experiments are used to initially asses the action of drugs on apoptosis of tumoral cells.
- Cell cycle analyses (Propidium Iodide). Cell cycle experiments are used to initially assess whether a drug interferes with cell cycle progression.
- Western blot. The effect induced by the drug(s) treatment on the most important cell signaling and proliferation pathways as Erk, PI3K/AKT, NFkB or JAK/STAT are evaluated by Western-Blot. Besides this technique is also used to complement the apoptosis and/or cell cycle analyses.
- Senescence determination by β-galactosidase activity measurement.
- Biochemical determination of caspase activity.
- Analyses of the results. Once the data are available, most of the external customers ask for counseling about how to further proceed based on the data generated.
- Antibody generation. If required, rabbit polyclonal antibodies will be prepared and affinity purified following protocols previously optimized in our laboratory. Their performance in several experimental settings will also be determined (see, for example, an immunohistochemistry staining in the accompanying figure).
- Murine Model Assay. In vivo studies of the activity of some drugs and drug combinations using mouse models may be required. Usually a set is required for control, placebo-treated animals, and several additional sets for different doses of a single drug or combination of drugs.
- Design of strategic assays (advice and acquisition of material and reagents) In addition to the advice once the data have been generated, sometimes new and specialized assays have to be set-up. This, together with counseling for unexperienced customers, is provided.

A detailed description of the experimental protocols is listed as Standard Operating Procedure (SOP) of the unit.

A web page is already prepared detailing the services offered by the unit. http://www.cicancer.org/lot/screening.php

The Occupational Health and Safety Management System of the facility has been also certified using the OHSAS18001 system.

STRATEGIC OBJECTIVES

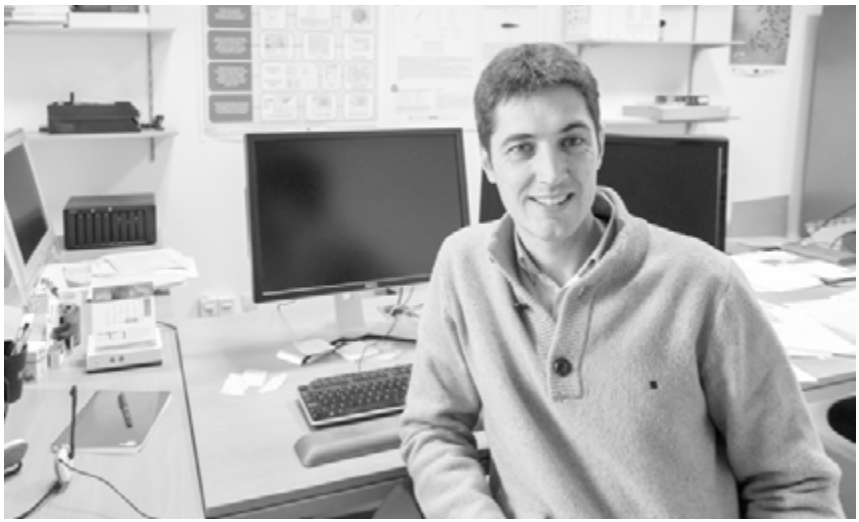
We offer a suitable service to the demand that allows the translation into the clinics of new clinical antitumor drugs acting on different cellular targets. In addition, an increase in the ability to predict their biological behavior in different tumor types is also pursued.

ACHIEVEMENTS

In addition to counseling services performed and conducted by staff of the unit it has also been implemented in 2009 the Quality Certification ISO 9001 to improve the scientific output of the unit and provide reliability and traceability studies.

GOALS FOR THE FUTURE

To ensure quality services and fulfill the purpose of the LOT indicated above in this document.



SCIENTIFIC SERVICE UNITS

BIOINFORMATICS

Scientific Coordinator

Javier De Las Rivas

Phone: (+34) 923 294 819

E-mail: jrivas@usal.es

Bioinformatics Unit

Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Unit Coordinator

Diego Alonso López

Phone: (+34) 923 294 821

E-mail: diego.alonso@usal.es

Personnel

Diego Alonso López

DESCRIPTION

The Bioinformatics Unit works in the CiC-IBMCC with the help and support of the Bioinformatics and Functional Genomics Research Group, to provide technical and scientific service on bioinformatic and computational data analyses to scientists and research groups from the CiC, the University of Salamanca or from outside. The Unit has major expertise in the analysis of omic data (such as transcriptomic, genomic, proteomic, interactomic, etc.) derived from the study of complex biological systems that generally apply to cancer research.

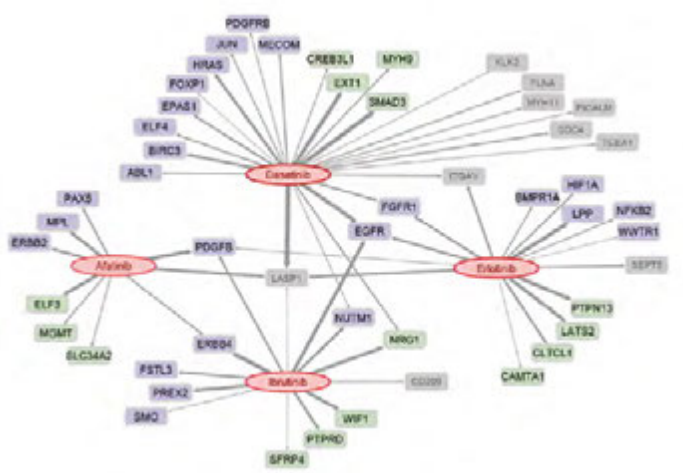
The Bioinformatics Unit was launched to provide services in June 2008 and, since then, more than 5000 samples coming from different labs and including a broad spectrum of experimental platforms (high throughput sequencing, custom panels, microarrays, etc.) have been analyzed.

SERVICES

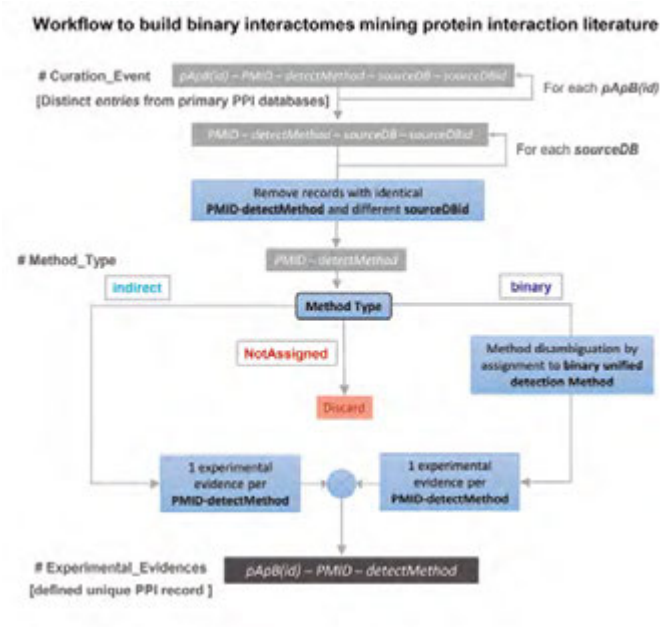
- Multivariate analyses and comparison of biological states using omic data. Analysis to search and identify genes (or other biomolecular entities such as miRNAs, ncRNAs, proteins, etc.) that show statistically significant

changes using robust techniques of differential contrast of two states (Normal versus Altered) or between different classes.

- Biomarker profiling and pharmacogenomic studies. Integrated analysis of omic data across multiple states, conditions or individuals for the identification of biological feature profiles (biomarkers), such as those derived from genome-wide expression studies. Search and analysis on drug-to-target data.
- Functional enrichment analysis. Annotation and assignment of biological functions based on enrichment studies and clustering analyses. These types of analysis vary widely according to the objectives of each study and generally provide complex results that also require the Unit's help in interpretation.
- Bioinformatics tools and big data management. The unit facilitates the use of various bioinformatics software tools and the access to scientific data repositories:
  - Tools and databases provided to the scientific community by other research institutions, for example: TCGA, NCI-GDC Data Portal, NCBI-GEO, NCBI-SRA, Bioconductor, etc.



Generation of weighted networks of cancer drugs and predicted target genes



Some of the largest interactomes included in APID

Organisms	PROTEOME (UniProt)	Proteins in the INTERACTOME	Interactions in the INTERACTOME	Proteome Coverage (%)
Homo sapiens	73,099	**30,632**	**385,438**	**41.9**
Mus musculus	53,451	**19,759**	**67,567**	**37.0**
Arabidopsis thaliana	39,389	**11,274**	**50,597**	**28.6**
Rattus norvegicus	29,959	**5,991**	**10,154**	**20.0**
Caenorhabditis elegans	26,805	**5,388**	**13,736**	**20.1**
Drosophila melanogaster	21,937	**11,806**	**67,249**	**53.8**
S. cerevisiae (strain ATCC 204508 / S288c)	6,049	**7,331**	**141,431**	121.1
Escherichia coli (strain K12)	4,313	**3,834**	**37,930**	**88.9**

  - Open Access Software developed within the CiC-IBMCC: GeneTerm-Linker, FGNet, APID Interactomes, DECO, GEDA, etc.
- Custom analysis and data integration. The unit also offers customized analyses for data from non-standard platforms as well as new analysis of datasets that have been studied previously and the integration with other accessible series.
- Advice and assistance. Frequently the unit also provides support and assistance to the scientists and researchers of the CIC-IBMCC and the University Campus who ask for help in Bioinformatics.

Scientific Coordinator:
Alberto Orfao
Phone: (+34) 923 294 811
E-mail: orfao@usal.es

Cytometry Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Personnel:
Julia Almeida Parra
Martín Pérez Ándres
Sergio Matarraz Sudón
Juana Ciudad Pizarro
Antonio López Fernández
Lourdes Martín Martín
Carolina Pontes Caldas
Susana Barrena Delfa
Laura Gutiérrez Troncoso
Carlos Fernández Giménez
Miriam Fierro
Miriam Santos
María González González
Virginia Herráez
Elisa Menchini

SCIENTIFIC SERVICE UNITS

CYTOMETRY

DESCRIPTION

The Cytometry Service (SGC) is a common research platform of open use to all members of the Institute (Cancer Research Centre) as well as to other external research and clinical groups. It is aimed at supporting research and education in cytometry. The most relevant activities include cell analysis and sorting for research purposes with more than 50 different techniques being currently set up and available in the area of immunophenotyping, cell cycle analysis, apoptosis, drug resistance and screening, quantification of phosphorylated proteins and their associated intracellular signalling pathways, among others. In addition, it provides tests to support the diagnosis of cancer acting as a common platform for the immunophenotypic diagnosis of leukemias and lymphomas for the Spanish RTICC from the Instituto de Salud Carlos III. In parallel, at the SGC

there are several ongoing technologically oriented research projects. Finally, the SGC has an important role in education in Cytometry with more than 35 researches from all over the world being trained during the last year, and more than 350 in the last 15 years.

ISO Certifications: The SGC is certified with the ISO-9001:2000, applied to "Molecular, Genetic and immunophenotypic studies to support the diagnosis and monitoring of haematological malignancies, using flow cytometry, FISH and molecular biology" since the 3rd of August 2007.

SERVICES

- Screening of monoclonal gammapathy
- Screening of lymphocytosis or suspect of mature T-cell lymphoid neoplasms in peripheral blood, cerebrospinal fluid, bone marrow, lymph node or other tissue
- Immunophenotypic characterization of Mature B-cell lymphoid neoplasms y Waldenstrom's macroglobulinemia
- Screening of clonality of mature alfa-beta T-and gamma-delta T cells lymphoid neoplasms by flow cytometry
- Immunophenotypic characterization of mature T and NK-cell neoplasm
- Screening of acute leukemias
- Immunophenotypic characterization of myeloid acute leukemias and myelodysplastic syndromes
- Screening and immunophenotypic characterization of B-precursor lymphoblastic leukaemia and T-cell lineage acute lymphoblastic leukaemia
- Immunophenotypic characterization of chronic myeloid leukaemia
- Detection of minimal residual diseases in acute and chronic leukaemias studied at diagnosis in our service
- Detection of minimal residual diseases in acute and chronic leukaemias and acute myeloid leukaemias
- Screening of mastocytosis
- Immunophenotypic screening of histiocytosis and Reed Stenberg cells
- Screening of primary immunodeficiency and paroxymal nocturnal hemoglobinuria
- Immunophenotypic characterization of the platelets
- Detection of antiplatelet autoantibodies in platelets and plasma
- Quantitation of CD34+ cells
- Control of leucodepletion
- Antigenic quantitation
- Spherocytosis
- DNA quantitation in mature and immature B cell, plasma cells and epithelial cells
- Evaluation of Zap70
- Evaluation of viability by DRAQ5 or Dye Cycle
- DNA quantitation with phenotype and DRAQ5 or Dye Cycle in myeloid leukemia or myelodisplastic syndromes
- Evaluation of each individual antigen
- Study of the presence of one, two or three genetic abnormalities by in situ hybridization
- Study of the presence of prognostic genetic abnormalities in B-cell chronic lymphocytic leukemia
- Evaluation of each individual genetic abnormality by in situ hybridization
- Sample purification for molecular biology techniques
- Evaluation of CKIT mutations by molecular biology
- Humara PCR test for one cell population
- Sorting of cell populations
- Acquisition and analysis at the flow cytometer
- Immunobead protein assays Equipment
- Cytometer Analyzer FACScanto II (BDB) for analysis in 8 fluorescence
- 2 Cytometer Analyzer FACScalibur I (BDB) for analysis in 4 fluorescence
- 1 Cytometer LSR-Fortessa X20 (BDB) for analysis in 13 fluorescence
- Termocyclers
- Fluorescence microscopies
- Other equipment: centrifuges, refrigerators, freezers, bathrooms…

Scientific Coordinator
Jesús María Hernández Rivas
Phone: (+34) 923 294 312
E-mail: jmhr@usal.es

Cytogenetics Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Personnel
Jesús María Hernández Rivas
Norma C. Gutiérrez
Juan Luis García Hernández
Teresa González
Eva Lumbreras González
M Rocío Benito Sánchez
María J. del Pozo Hernández
Ana Belén Díaz Martín
Sara González Briones
Mª Ángeles Hernández García
Mª Almudena Martín Martín
Mª Ángeles Ramos Rodríguez
Irene Rodríguez Iglesias
Ana María Simón Muñoz
Isabel Mª Isidro Hernández
Vanesa Gutiérrez Moreta
Mª Teresa Prieto Martín
Sandra Santos
Sandra Pujante
Jesús M Hernández Sánchez
Marta Martín

SCIENTIFIC SERVICE UNITS

CYTOGENETICS

The Molecular Cytogenetic Service (MCU) is a facility devoted to the karyotypic analysis, fluorescence *«in situ» hybridization, comparative genomic* hybridization, microarrays and next generation sequencing of cancer patients. More than 100 hospitals in Spain, and occasionally others from the EU, have used the MCU services. The Unit collaborates with the most relevant groups in the treatment of the hematological malignancies such as Pethema, GEL-TAMO, GEM or GETH providing technical support and characterization of the genetic abnormalities in the patients included in clinical trials. In addition, the MCU is involved in several international projects related such as oncNGS with aim at developing an integrated solution for predictive, prognostic and diagnostic analysis in liquid biopsies of solid tumours (including appropriate haematological indications) based on Next Generation sequencing (NGS) technology; HARMONY, which through the use of Big Data will help improve the care of patients with

hematologic malignancies; SYNTHERAPY, which aim is to develop a machine learning-based model to predict personalized treatment and to identify novel therapeutic strategies based on synthetic lethality approach for relapsed or refractory acute leukemia patients by using multilayer analysis of omics data, including RNA-Seq, Copy Number Alterations by SNP array and DNA targeted NGS)

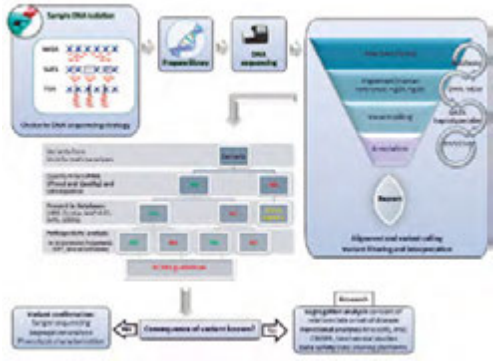
SERVICES

- Bone Marrow Cytogenetic: leukemia, lymphoma and myeloma.
- Peripheral blood cytogenetic: leukemia, lymphoma and myeloma.
- Lymph node and spleen cytogenetics: lymphoma.
- Solid tumour cytogenetics.
- Centromeric «in situ» hybridization: FISH performed with centromeric probes to analyse numerical abnormalities.
- Painting «in situ» hybridization: FISH performed with libraries of DNA to analyse structural abnormalities.
- Loci specific «in situ» hybridizations: FISH performed with probes to analyse either losses or gains of genetic material or fusion genes.
- Genomic microarrays highest resolution gene-level. Genotyping, methylation, transcriptomics and pharmacogenomics assays. High quality and Formalin Fixed Paraffin Embedded (FFPE) samples.
- Next generation sequencing to analyses genetic alterations by flexible and scalable methodology for target regions, genes, individual exons or hot spots. Available disease-focused panels (custom and commercial), fusion gene panels and RNA seq.
- High-Depth next-generation sequencing for somatic variant detection.
- Germline variant detection by next-generation sequencing in key genes involved in severe congenital coagulation bleeding disorders.
- DNA/RNA shearing service for NGS.
- Ultra–sensitive droplet digital PCR for detecting low prevalence somatic mutations.
- Absolute quantification of gene expression and alternatively spliced transcripts with digital PCR.
- DNA and Protein Liquid Biopsy.

EQUIPMENT

- Full authomatised system for karyotyping and FISH (Cytovision) with 3 analysis stations.
- Full authomatised system for karyotyping and FISH (Metasystems) including a karyotype finder with 3 analysis stations.
- Microbeads-based system for cellular isolation (Miltenyi).
- Microscopes of light and fluorescence.
- Veriti 96W Thermal Cycler.
- Pyrosequencer (Pyromark Q24, Qiagen).
- Affymetrix GeneChip® *Instrument System: Hybridization* Oven 646/Fluidics Station 450 and GeneChip® *Scanner* 3000 7G.
- Droplet Digital PCR QX200 system (Bio–Rad Laboratories, Hercules, CA, USA).
- Bioanalyzer for fragment analysis: 4200 Tapestation system (Agilent technologies Santa Clara, CA).
- Covaris M220 Focused Ultrasonicator (Covaris, Woburn, MA, USA).
- Next-generation sequencing facilities (Illumina), MiSeq sequencer
- Automated capillary nano-immunoassay—Simple Western assay "WES™ ProteinSimple"

Oncoscan analysis of a solid tumour cancer sample showing CN-LOH on chromosome 1. Plots shown the loss of heterozygosity (LOH), track top and allele difference (B-Allele Frequency (BAF) track bottom).



Overview of the NGS flow chart in inherited bleeding disorders (IBDs) from DNA extraction to clinical interpretation of molecular data.

Scientific Coordinator
Marcos González Díaz
Phone: (+34) 923 291 100 Ext. 55384
E-mail: margondi@usal.es

Molecular Biology Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Personnel

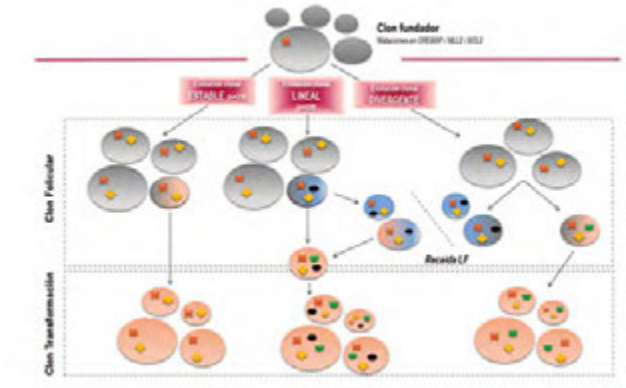
Marcos González Díaz,
Ramón García-Sanz
Verónica González de la Calle
Rocío Corral
Francisco Boix
Ana Balanzategui
M. Carmen Chillón
M. Eugenia A. Sarasquete
Miguel Alcoceba
Cristina Jiménez
M. Isabel Prieto Conde,
María García-Álvarez
Alejandro Medina
Alicia Antón
Montserrat Hernández-Ruano
Rebeca Maldonado
Estrella Arnés
Inmaculada Villares
Pilar Terradillos
Isabel Jiménez
Sandra Lucas
Leticia Gallo
Ana Isabel Sánchez

SCIENTIFIC SERVICE UNITS

MOLECULAR BIOLOGY

DESCRIPTION

The Molecular Biology Unit (MBU) is a facility with the aim of providing molecular analysis for cancer patients, with special focus on patients with haematological malignancies (leukaemia, lymphoma, and myeloma). In addition, the MBU carries out HLA typing for histocompatibility studies in receptors candidates to allogeneic stem-cell transplantation, as well as chimerism monitorization in those who finally undergo it, molecular studies in coagulopathies, and HLA typing for disease association. The MBU is the reference centre for Castilla y León Hospitals. Furthermore, more than 50 hospitals in Spain, multicentric clinical trials, and some occasional foreign institutions, have used the MBU services. The Unit actively collaborates with the most relevant Spanish groups in both research and in the treatment



of the haematological malignancies such as SEHH, PETHEMA, GELTAMO, GEM, GELLC, GETH, or GBMH by characterizing molecular abnormalities and carrying out studies on molecular monitoring of drug efficacy (Minimal Residual Disease -MRD- Studies) for patients included in clinical trials. In addition, the MBU has participated in several international projects focused on methodological standardization (Biomed I, Biomed II, Europe Against Cancer and Eurochimerism projects), and it is involved in several international projects related to clonality assessment (EuroClonality), next generation sequencing (EuroClonality-NGS Consortium), and TP53 sequencing (European Research Initiative in CLL- ERIC TP53 Network, and RED53 from the Spanish group for the study of CLL, GELLC).

The total number of samples received in 2018 and 2019 were 15779 and 17482, respectively.

SERVICES

- Screening and quantification of chromosomal translocations (qualitative and real-time quantitative PCR, RT-PCR) for diagnosis and MRD monitoring in haematological malignancies.
- Gene expression: RT-PCR for diagnosis, prognosis and MRD detection.
- B-cell and T-cell clonality for diagnosis or MRD detection in fresh cells (bone marrow, peripheral blood, lymph node, spleen, etc...) and/or formalin-fixed paraffin-embedded.
- Analysis of somatic mutations: diagnosis, prognostic value, screening of potential MRD markers and/or identification of therapeutic targets (Sanger sequencing, allelic-specific PCR, etc.).
- Next generation sequencing: Analysis of genetic alterations using commercial kits (i.e. AML panel) and custom panels for diagnosis and prognostic value.
- Digital PCR for low allele frequency mutation detection.
- Liquid biopsy. Analysis of circulating tumour DNA in lymphoproliferative disorders.
- Fragment analysis and Sanger sequencing.
- Genetic polymorphisms (single nucleotide polymorphisms [SNP], short tandem repeats [STR]) analysis: SNP array, SNP assays. Identification of patients with different drug sensibility, susceptibility to second neoplasia, etc.
- Hematopoietic chimerism analysis and cell-lines characterization with STR polymorphisms.
- Low- and high-resolution HLA typing: donor typing, disease association.

EQUIPMENT

- Real-time quantitative (4): One7900HT, two StepOnePlus (Applied Biosystems) and one LightCycler (Roche Diagnostics)
- Next generation sequencing systems: MiSeq and MiniSeq (Illumina; CA)
- Digital PCR system: QX200 Droplet Digital PCR system (Bio-Rad Laboratories, Hercules, California, USA)
- Bioanalyzer for fragment analysis: 4200 Tapestation system (Agilent technologies Santa Clara, CA)
- Automatic sequencer (1): ABI3500 XL (16-capillary, Applied Biosystems)
- Fluoroanalyzer (2): Luminex XYP (Luminex Corp.) and FluoVista (Inno-train)
- Thermocyclers (11): seven Veriti 96-Well Thermal Cycler and one GeneAmp PCR System 9700 (Applied Biosystems), and three Biometra (T1, T3, and T Professional Thermocycler)
- Automatic nucleic acid extractor (2): one Maxwell16 and one Maxwell RSC (Promega)

Scientific Coordinator

Mª del Carmen García Macías

Phone: (+34) 923 295 227

E-mail: janagm@usal.es

Comparative Molecular Pathology Unit

Centro de Investigación del Cáncer (CSIC-USAL)

Campus Miguel de Unamuno s/n

37007Salamanca (Spain)

Phone: (+34) 923 294 832

E-mail: lpmc@usal.es

Personnel

Mª del Carmen García Macías

Susana Fraile Martín

Jairo Nieto Castro

Telmo Rodrigues Teixeira

Sonia Andrés Recio

Irene González Valero

SCIENTIFIC SERVICE UNITS

COMPARATIVE MOLECULAR PATHOLOGY

DESCRIPTION

PMC has two different functions of interest for the entire University Community.

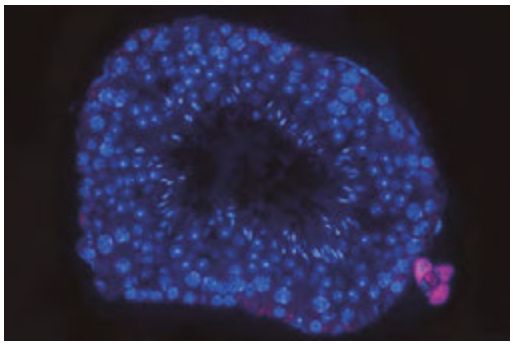
1) The **Compared Molecular Pathology Unit** analyzes samples of human, transgenic murine animal models and plants. Offers a complete and variable range, designed and adapted to each request, of histological, immunohistochemical and molecular analysis techniques.

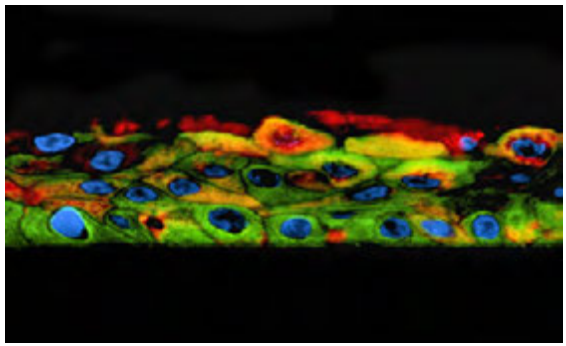
The PMC Unit is certified in Quality by ISO9001:2015.

SERVICES OFFERED:

Tissue processing and routine stain (each paraffin block). Our service processes animal models provided by other CSIC researchers to produce hematoxylin-eosin stained sections. Animal tissues are prepared for inclusion and paraffin embedding, and then cut and stained. Approximately 5.240 samples are processed per year, from 556 job applications.

- Paraffin embedding. Previously fixed tissue is embedded in paraffin.
- Sectioning/staining. Tissue previously embedded in paraffin is sectioned and stained.





- Immunohistochemistry (each stain). The process includes setting up an assay for a particular antibody, as well as the performance of an actual immunohistochemical stain. In the last two years, 97 antibodies have been prepared for murine tissues, at the request of the different researchers from both the CIC and the rest of the Units of Campus.
- Tissue microarray. 1-mm Tissue Cores from 100-200 human or animal tumors are arrayed into a paraffin block. This allows the simultaneous study of a series of cases with minimal interobserver biopses.
- Diagnostic samples processed in the Service by the Responsible Pathologist, when they are required by the researchers.
- Microscopy Service offered:
  - Multihead Optical Microscope.
  - One automated scanning microscope and image analysis system, ARIOL.
  - Virtual Microscope DOT SLIDE, to scan and processed samples.
  - Microscope laser microdissection: essential for molecular characterization of individual cells of complex solid tissues to identify differences that show respect to other cell lines to identify new molecular targets that reveal the altered cellular pathways and study the origin of the equipment disease and possible treatment.
- The Service Comparative Molecular Pathology imparts teaching to:
  - Students in practice, as a Senior Technician of Pathological Anatomy of the Institute "IES Ramon y Cajal" of Valladolid, of School Aloya of Vigo, and Institute "CIFP Río Ebro" of Miranda de Ebro of Burgos.
  - Master students in Biobanks.
  - Collaborates with the Communication Service of the Center for Cancer Research in the program of guided tours to the CIC, to different groups such as Schools, Universities, Businesses, Associations and Town Hall.
- The Compared Molecular Pathology Unit is a Research Support Service and is associated with the NUCLEUS Service of the University of Salamanca. CMP offers its services to all the Researchers of the Cancer Research Center, where it is located, and to all the Centers of the University of Salamanca (IBFG, Departmental, INCyL, Hospital Clínico Universitario...) and to other Spanish Centers.

2) This Unit is also a **Coordinating Node of the Biobank in Network of Oncological Diseases of Castilla y León (**BEOCyL). The Compared Molecular Pathology Unit coordinates all requests for tissue samples from the seven Biobanks that make up the Network and from researchers.

- Tissue request from a Cancer Cooperative Biobank Network Requests from researchers are evaluated by the external committees of the Biobank, and served, if ethical and scientific standards are accomplished, and enough tissue is banked in the network.
- Tissue banking (each individual case aliquot). In each of the Hospitals affiliated to the Biobank Network, cases are collected, interesting tissue areas are selected, prepared and stored. In addition, this process includes getting all basic clinical information linked to the sample, which is stored in a central database. Collection can take place only when a written informed consent has been taken from the patient after detailed information has been provided to him/her.

The tissue of the Biobank is given, if there are enough samples, if the Project meets the appropriate ethical and scientific requirements.

http://www.cicancer.org/en/compared-molecular-pathology-service-and-main-beocyl-node

SCIENTIFIC SERVICE UNITS

STRUCTURAL BIOLOGY

Scientific Coordinator

José María de Pereda

Phone: (+34) 923 294 817

E-mail: pereda@usal.es

Structural Biology Unit

Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Personnel

José María de Pereda

DESCRIPTION

The primary mission of the Macromolecular Crystallography Facility (MXF) is to provide access to X-ray crystallography methods to researchers interested in elucidating the 3D atomic structure of macromolecules and molecular complexes of biological relevance.

SERVICES

Crystallization: the MXF offers dedicated space for setting up and for storage of crystallization experiments in temperature controlled environments. The Facility has stereo microscopes for visualization and manipulation of crystals. Equipment for cryo-cooling, storage, and transportation of crystals at cryo-temperatures (liquid nitrogen) is also available at the MXF.

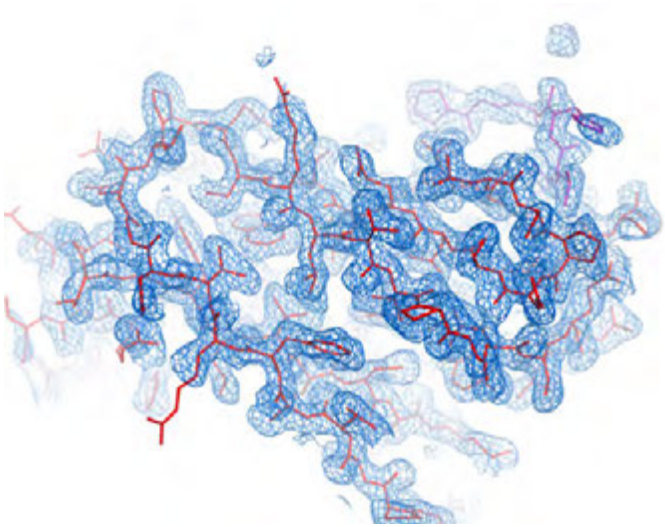
Data collection and analysis: the MXF provides access to equipment for X-ray data collection and analysis from macromolecular crystals. The Facility houses a Microstar (Bruker AXS) rotating anode micro-focus X-ray generator equipped with a large-area Image-plate detector mar345 (Marresearch) and a Cryostream 700 low temperature system (Oxford Cryosystems). The MXF also provides consultations and assistance on optimization of crystallization, data collection, processing, and structure solution.

Remote data collection: In recent years, the use of MX beamlines at synchrotrons has increased. Third generation synchrotrons allow performing experiments that can not be addressed in house. Most experiments at synchrotron beamlines are done remotely from the home laboratories, which improves the accessibility. To address this growing demand, the MXF is equipped with a computer setup for remote data collection at synchrotron laboratories. A workstation with two screens provides a large desktop area that has greatly improved the remote operation of the synchrotron beamlines. This has been extensively used to easily collect data at the synchrotrons ALBA (Barcelona, Spain) and Diamond Light Source (Didcot, UK).

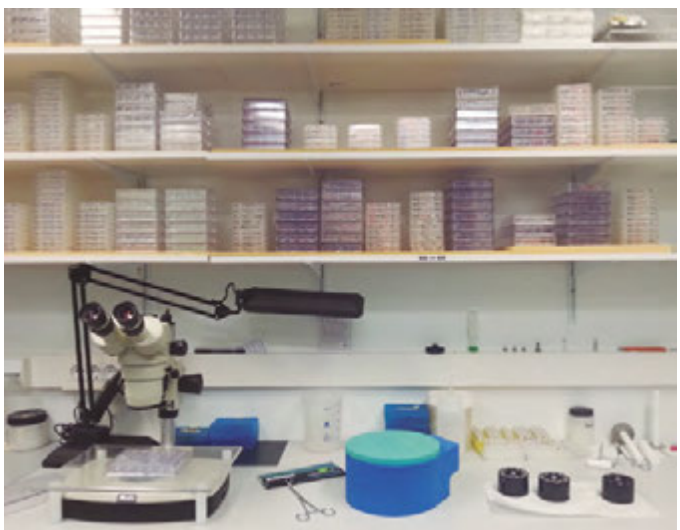
The activities at the MXF during this period have resulted in 10 protein structures solved with the support from the Facility (Table 1). All these structures are available in the Protein Data Bank.

PDB CODE	DESCRIPTION	REFERENCE
6GVK 6GVL	Complexes of integrin β4 bound to BP230	Manso et al. (2019) Structure 27, 952-964.
6RPU	Complex of the IMPDH dehydrogenase (*Ashbya gossypii*) bound to the dinucleoside polyphosphate Ap5G and GDP	Fernández-Justel et al. (2019) J.Biol.Chem. 294: 14768-14775.
6I0M 6I0O	Human IMP dehydrogenase 2	Fernández-Justel et al. (2019) J Mol Biol 431, 956-969.
6GN9	Thioredoxin from *Clostridium acetobutylicum*	Buey et al. (2018) PNAS 115, 12967-12972.
6GNA 6GNB	Ferredoxin-Flavin Thioredoxin Reductase from *Clostridium acetobutylicum*	Buey et al. (2018) PNAS 115, 12967-12972.
6GND	Complex of a Ferredoxin-Flavin Thioredoxin Reductase and a Thioredoxin from *Clostridium acetobutylicum*	Buey et al. (2018) PNAS 115, 12967-12972.
4ZN0	NADPH-dependent thioredoxin reductase from *Methanosarcina mazei*	Buey et al. (2018) Antioxidants 7, 166.

Table 1. Protein structures solved with support from the Facility, published in the Protein Data Bank (PDB) in this period.



Electron density map of a protein structure determined at the MXF.



Equipment for crystallization of biological macromolecules at the MXF

SCIENTIFIC SERVICE UNITS

MICROSCOPY

Scientific Coordinators

Alberto Martín Pendás
Miguel Vicente Manzanares

Phone: (+34) 923 294 809
(+34) 923 294 806
E-mail: amp@usal.es
Email: miguel.vicente@csic.es

Microscopy Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Unit Coordinators

Ángel Luis Prieto Martín
Ana Isabel García Vega

Phone: (+34) 923 492 720 Ext: 3016
E-mail: microscopia_cic@usal.es

Personnel

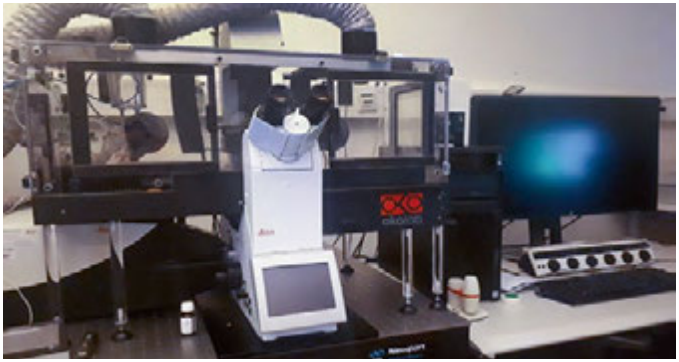
Ángel Luis Prieto Martín
Ana Isabel García Vega
Sara González Armenteros

DESCRIPTION

During last two years CIC-IBMCC Microscopy and Cytometry Unit has improved their services with the incorporation of a new super-resolution equipment allow to get new images with an unprecedented resolution.

SERVICES

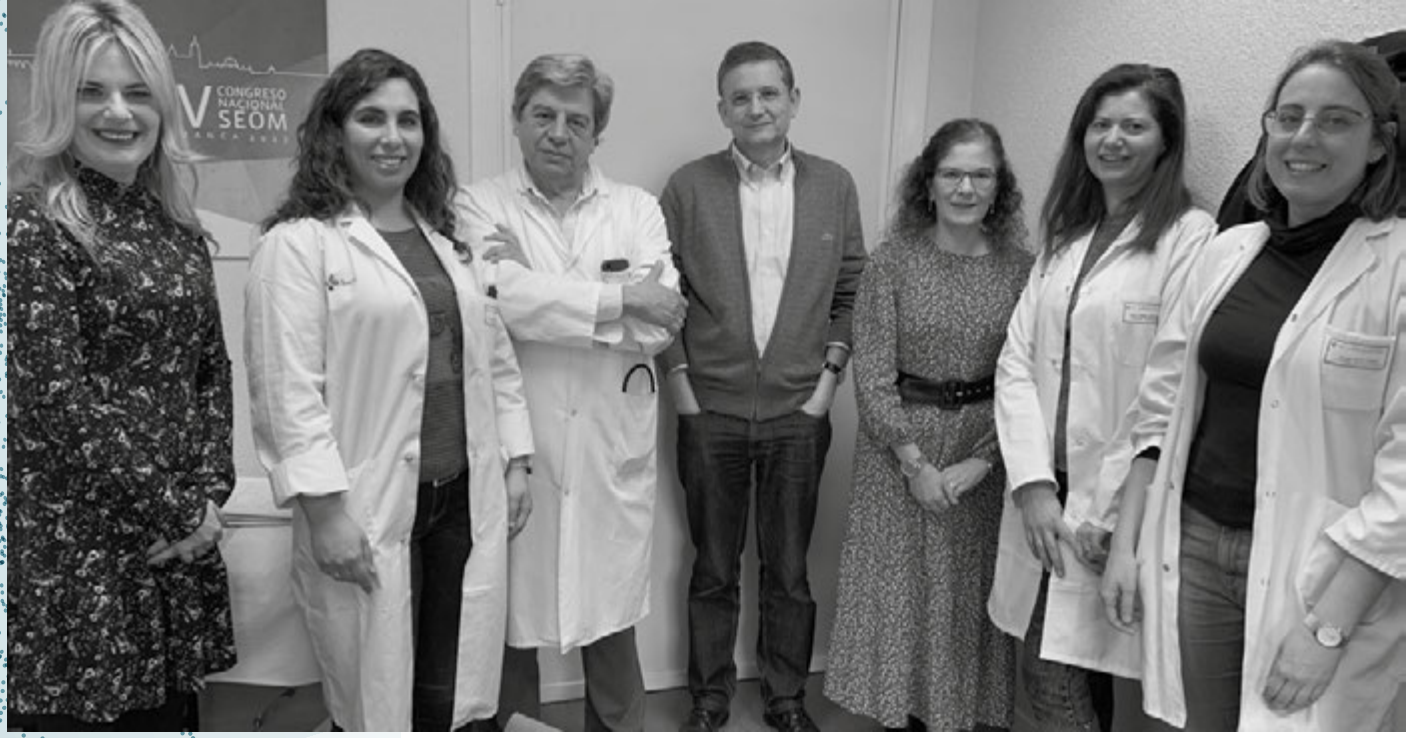
- Confocal imaging: Fixed samples, time-lapse, Z-Series, quantitative co-localization, FRAP and FRET experiments.
- Flow cytometry: BDFACS-Aria-III and AccuriC6 systems. Multicolor sorting and immunophenotypic analysis.
- Widefield live cell imaging: Olympus IX71 and Nikon Eclipse TE2000 microscopes, CO2- and temperature-controlled. Image processing and deconvolution of images available upon request.
- Conventional widefield microscopy for fixed samples (upright) and for tissue culture (inverted).
- Monthly revisions of the microscopes, including phase adjustment, Kohler adjustment, objective cleaning and weekly revisions.
- Training and advising regarding image capture software and hardware (Metamorph, Leica LAS AF, LSM Image Browser, ImageJ, Openlab, etc.), as we as image analysis.
- Creating, updating and maintaining the Web Unit, including updates of technical specifications or new equipment incorporated by the Center. Quality assessment. Certifications: ISO-9001 and OHSAS-18001.



EQUIPMENT.

The Microscopy Unit of the Cancer Research Centre with its variety of equipments offers a high range of possibilities. There are seven main equipments:

- Laser Scan Confocal Microscopy Leica SP5. Funded by FEDER, Ministerio de Sanidad y Consumo and Instituto de Salud Carlos III. It has four lasers with seven excitation lines, which in combination with the spectral detection technology, allows any fluorochrome to be detected in the visible range. Due to its confocal module, it is highly demanded to obtain high resolution images of cell cultures or tissues.
- Flow cytometer and sorter BD FACS-AriaIII. Co-funded by CSIC-MINECO and FEDER. It supports up to 6 excitation lasers combined with 20 detectors. Cell damage is minimized by a temperature controlled system.
- Live Cell Microscopy Delta-Vision. FEDER and CSIC founding. It is mainly used for in vivo time-lapse experiments. The microscopy main advantages are the ultra-precise stage; the lighting system which combines a xenon lamp with an excitation filters wheel. Deconvolution module contributes to a more complex image processing.
- Laser Scan Confocal Microscopy Zeiss LSM 510.
- Microscope Nikon TE2000 for in vivo analysis combined with Metamorph
- Cell analyzer cytometer BD Accuri-C6®. Co-founded by CSIC-MINECO and FEDER. Accuri-C6® is a simple and easy platform that offers an optimum configuration which detects four fluorochromes simultaneously.
- Laser Scan Confocal/ STED Microscopy Leica SP8. Co-founded by FEDER, Ministerio de Economía, Industria y Competitividad and Universidad de Salamanca. It has a powerfull white laser that is able to excite ever wavelength into a width range. In combination with the spectral detection technology, allows any fluorochrome to be detected in the visible range. In addition, it can do depletion (STED)-based superresolution in the green and red channels, up to 50 nanometres. The equipment is completed with a Huygens Deconvolution Software provides a significant increase in the contrast and resolution.
- 9 fluorescence microscopes, 11 inverted microscopes for cell culture, 1 microinjector, 1microscope for cytogenetic and 1 microscope for histological analysis.
- During the 2020-21 period, the unit will incorporate several improvements for existing machines plus two new microscopes:
- The Leica SP5 Confocal will be updated with a hybrid detector that will improve the signal detection and a 100x objective.
- SP8 Confocal will be actualized to optimize the applications in the Hyvolution and Lightning environment. A new depletion laser of 775nm that allow to depletion far red and a 405nm laser will be added.
- Thunder® microscope for transmitted light and fluorescence with opto-digital technology that uses a new computational clearing method to generate high resolution (0.05um) and high contrast images.
- An inverted microscope for in vivo microscopy equipped with a TIRF module, a photo-manipulation module for FRAT, FRET, photo conversion and uncaging experiments and high intensity lasers for single molecule localization experiments PALM/STORM and photo ablation.



Scientific Coordinators:

Rogelio González Sarmiento
Phone: (+34) 923 294 814
E-mail: gonzalez@usal.es

Juan Jesús Cruz Hernández
Phone: (+34) 923 291 342
E-mail: jjcruz@usal.es

Hereditary Cancer &
Genetic Counseling Unit
Centro de Investigación
del Cáncer (CSIC-USAL)
Campus Miguel de Unamuno s/n
37007 Salamanca (Spain)

Unit Coordinators
Eva Mª Sánchez Tapia
Jéssica Pérez García
Phone: (+34) 923 294 814
E-mail: emstapia@usal.es
jessipg4@hotmail.com

Personnel
Eva María Sánchez Tapia
Jéssica Pérez García
Teresa Martín Gómez
Rosario Vidal Tocino
Raquel Seijas Tamayo

SCIENTIFIC SERVICE UNITS

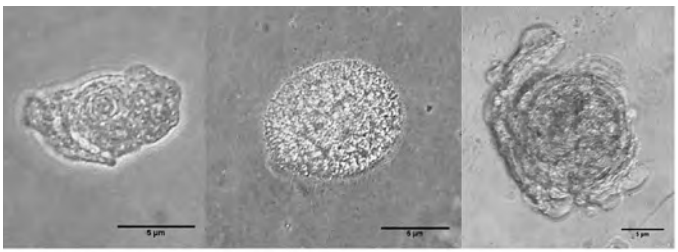
HEREDITARY CANCER & GENETIC COUNSELING

DESCRIPTION

Cancer is a very heterogeneous disease caused by different factors. Those factors can be environmental and genetic and both are responsible for its etiopathogeny. It is estimated that between 5% and 10% of all tumors are hereditary. In those cases, the genetic alterations which determine the appearance of a series of cancer types can be transmitted from parents to their off spring together with a high possibility that the carriers of this particular mutation can therefore develop a tumor. This implies the necessity to carry out a genetic check-up of the entire family who then will be informed not only about the probability of a neoplasm appearance and transmitting the cancer predisposition to the descendants, but also about the prognosis, early detection strategies and proper treatment.

Therefore, the study of hereditary cancer is currently one of the most developing areas within oncology. The possibility of detecting people with high risk of suffering from cancer is going to help us progress in two directions. On the one hand, the possibility of reducing the risk of suffering from certain neoplasmic types or at least of detecting

Organoids derived from head and neck cancer



them early, and on the other hand, the possibility of having a better knowledge of the disease that will help transfer this information onto other types of tumors.

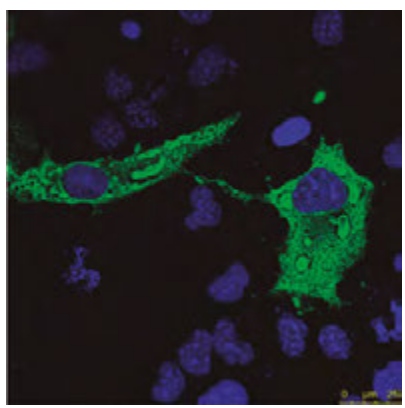
The thorough knowledge of the genetic factors related to cancer will be helpful in estimating more precisely the risk of developing it by each individual. It will also help establish precautionary measures which will be personalized and therefore efficient. Talking about the hereditary cancer is closely connected to genetic counseling. Except for clearly investigatory situations, anything that can be even remotely related to the hereditary cancer should be inscribed into the proper genetic counseling. This will imply a series of communication phases with the person and/ or relatives who are going to require an expert specialized in the concrete area.

The main objective of the Laboratory of Hereditary Cancer of CIC-IBMCC (Institute of Molecular and Cellular Biology of Cancer) is to pay attention, prevent from and investigate the hereditary and family cancer. It can be fulfilled through counseling, evaluation, and study of the family with an increased genetic susceptibility to cancer. For this reason the Laboratory collaborates with the Genetic Counseling Unit of Hereditary Cancer that is part of the Clinical Oncology Department at the University Hospital of Salamanca. Both the Genetic Counseling Unit and the Laboratory of Hereditary Cancer are supported by the "Consejería de Sanidad" of the"Junta de Castilla y León". Among their shared objectives are (i) to carry out an early diagnosis among people with a medical record that could suggest hereditary transmission. In those cases there can be no existing clinical indication of suffering from cancer but they can show high probability of developing one at any time in their lives or be carriers of a certain genetic mutation currently known to be involved in the development of hereditary tumors, (ii) chooses families at a considerable risk of suffering from hereditary cancer by means of defining the genetic mutations implicated in each case and (iii) finally, offers genetic counseling to the affected individuals.

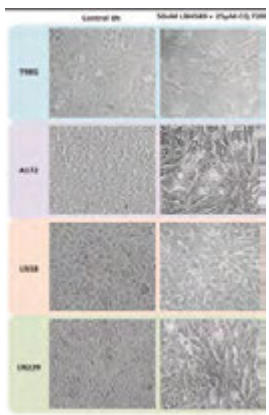
The Laboratory collaborates closely also with professionals from other hospitals in order to assist and monitor patients by means of offering their service to hospitals and professionals in any part of Spain. In the laboratories of the Cancer Genetic Units of CIC-IBMCC genetic and cytogenetic studies are being carried out.

The work procedures of the Laboratory of Hereditary Cancer of CIC-IBMCC in coordination with the Genetic Counseling Unit of the Clinical Oncology Department include: 1) Evaluation of a personal and family record of cancer, 2) Evaluation of the risk and choosing the most appropriate genetic study taking characteristics of the family into account and 3) Collecting biological samples necessary to carry out one or more different genetic studies. The Genetic Counseling Unit of the Clinical Oncology Department offers Genetic counseling, planning a family research depending on the results obtained from the genetic testing and recommendations of how to reduce the risk, and in case of already existing one, recommending the clinical monitoring of patients.

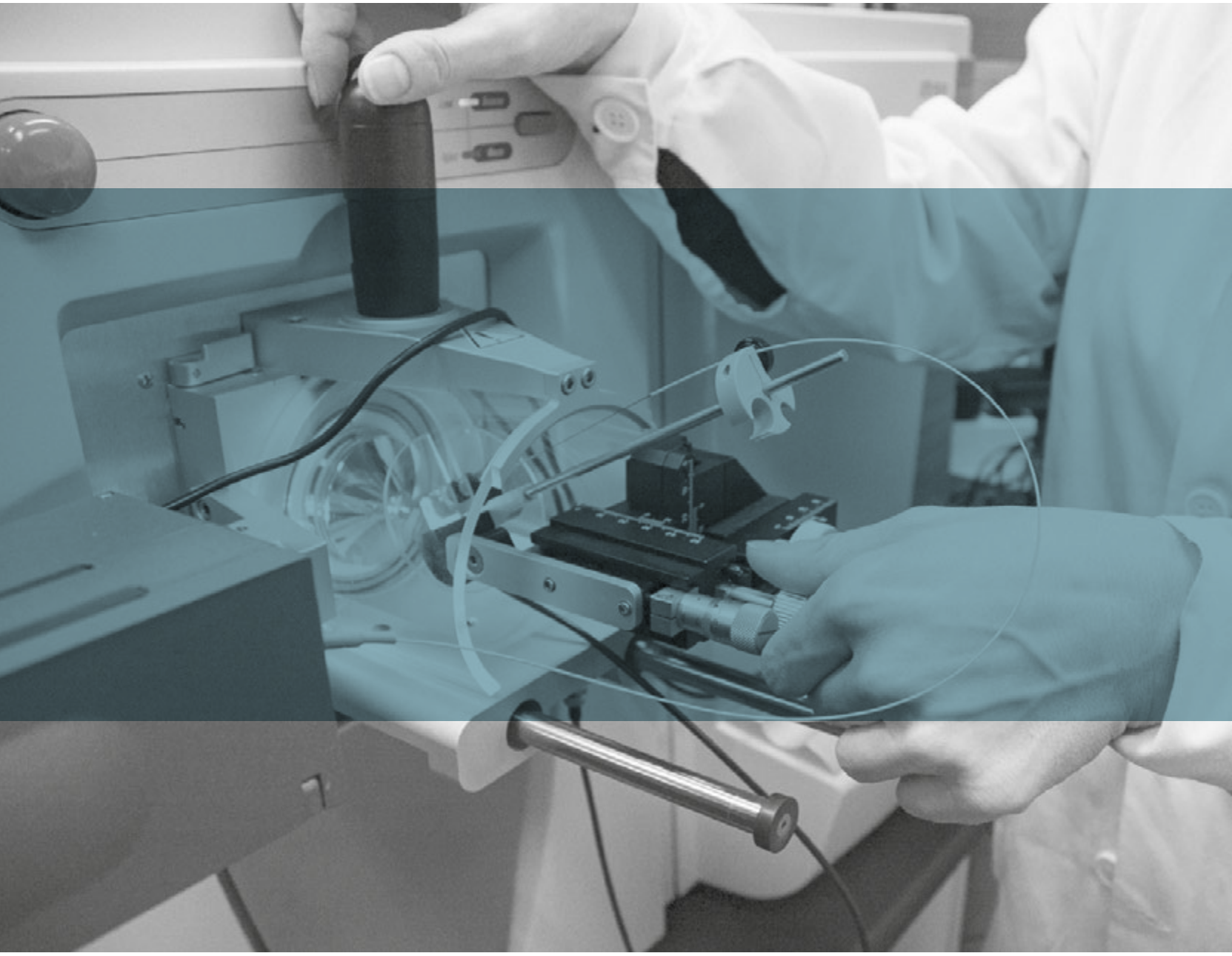
Even though the programs that currently have the highest level of development, at the Laboratory of Hereditary Cancer are mainly focused to the detection of the mutations of the hereditary breast and ovarian familial cancer and colorectal cancer, the laboratory analyze any syndrome of a hereditary cancer should undergo genetic study.



Autophagosome abnormality in a cell line carrying the mutation p62R321C



Glioblastoma cell lines treated with histone acetilase inhibitor



5

TECHNICAL SUPPORT UNITS

Personnel
Gerardo Arévalo Vicente

TECHNICAL SUPPORT UNITS
FICUS MANAGER

The manager, with the broadest of powers of the Board, develops:

- The management and implementation of the agreements and guidelines adopted by the Board of the FICUS.
- The management of existing services in the FICUS and as many management functions are accurate to the best achievement of the aims of FICUS.
- Oversee the accounting of FICUS and formulate draft reports; budgets and annual accounts.
- Directing the human resources policy of staff employed by the FICUS.
- Formal monitor compliance with fiscal and tax obligations of FICUS.
- Advise the Board on economic or tax legal issues that may affect the Foundation
- Acts of complete implementation of the agreements of the Board as may be ordered by the member of the Board in each case be responsible for the implementation of the same.
- Formulate proposals to the Board deemed appropriate for the smooth running of the Foundation

Personnel
Nuria Morán Aguirre

TECHNICAL SUPPORT UNITS
SECRETARY

- Administrative and logistic assistance to the personnel and visitors (travels, meetings, events, bookings…).
- Processing of internship programs for students in the center.
- Preparation of annual and semi-annual reports of activities of the center.
- Implementation and control of the Annual Training Plan for FICUS employees
- Processing (Customs, Project Authorizations, Bioethics Certificates ...)

Personnel

Antonio Mata Domínguez
Cristina Santos Gallego
Álvaro Menéndez Sánchez
Margarita Villamor Carba
Miguel Ángel Moreno Valle
Mª Manuela Calvo González

TECHNICAL SUPPORT UNITS

ADMINISTRATION

The Administration Unit in coordination with other institutions is responsible for the operation of the services to FICUS, such as:

- Budgetary and financial management: (i) annual budget institutional and financial management operations, (ii) budget and justification of competitive grants, (iii) management of contracts and agreements with public and private institutions and (iv)administration of revenues derived from direct services delivered by our technical scientific units.
- Human resources: (i) recruitment of scientific, technical, and administrative personnel and (ii) payroll and social security obligations management for staff employed by each of the institutions.
- Administrative management: (i) presentation of national and international scientific and the corresponding economic justification dossiers to the granting agencies, (ii) administrative coordination with the USAL, CSIC, FICUS and other institutions and (iii) administrative work related to Ph.D. and Master program of the Institute.

Personnel

Juan Pablo Clavero Herrero

TECHNICAL SUPPORT UNITS

IBMCC-CSIC MANAGER

The IBMCC-CSIC manager performs the operation of the services related to the competencies of the CSIC within the institute (staff and budget) as:

- Economics and financial management
- Personnel management
- Management accounting
- Advice on the preparation and justification for projects
- Elaboration of the IBMCC budget

Personnel

Almudena Timón Sánchez

TECHNICAL SUPPORT UNITS

COMMUNICATION & MARKETING

The essential target of the Communication and Marketing Unit of the Cancer Research Center is to improve the scientific culture in society through scientific dissemination and social marketing development.

The Communication and Marketing unit of the CIC holds four main services:

- Management of the scientific culture unit (belonging UCC+i Network) of the Cancer Research Center (2016-2021).
- Social marketing to achieve behavioral goals for a social benefit: enhancing cancer research. Some projects have improved the scientific culture in order to interact with the general public, young people and media. Communication activities have been developing to reinforce the positioning of CIC.
- Corporate public communications that includes: media relations, press releases, press conferences, social networking services, media monitoring and evaluation.
- Internal communications

SERVICES:

- Promotion of scientific culture through educational projects.
- Attention to the guided tours request to visit of schools, university students and society in general.
- Attention to the media.
- Attention to the consults and managements of the donations to the CIC through its foundation (FICUS).
- Elaboration of press releases and organization of press conferences.
- Follow up of news published in newspapers and journals.
- CIC Scientific seminars series.
- Internal support to the meetings organized by scientists at the center.
- Management of training and commercial activities requested by entities outside the center.

EQUIPMENT & BUILDING MAINTENANCE

Personnel

Celso Collazo López
Carlos M. de los Dolores Redondo

The Equipment & Building Maintenance unit has the following functions:

- Modification, reparation and maintenance programs of laboratory equipment and building facilities.
- Oversees and management maintenance contracts and externals for repairs by outside contractors and supplies for laboratory equipment and building facilities.
- Helps research laboratories and core services units in verification and internal calibration of laboratory equipment for Quality Management System and/or purchases, replacement or any technical problem.
- Registration into the management software for equipment inventory, instruction manuals and work orders.

Although not considered as a service for external users, sporadically the unit gives support to other centers on the university campus. The unit has the ISO Certifications: ISO 9001 and OSHAS 18001

SERVICES

- Installation and initial setup of new equipment
- Modification and repairs of simple lab equipment.
- Complex repair of laboratory equipment using some specific maintenance tools or equipment.
- Programmed routine maintenance, corrective and preventive building facilities (fancoil filters, oil vacuum replacement, CO_2 cell culture incubators, spectrophotometer etc.) and steam checkout
- Verification/calibration of balances, pipettes, dry heat incubators, refrigerators, thermoblocks, etc.
- Request of an intervention, overseeing of the work of outside contractors and management of repairs made by external companies

QUALITY CONTROL & RISK PREVENTION

Personnel

María José Campo Beneítez

The Quality & Risk Unit Labor is responsible for:

- Management of ISO 9001 and OSHAS 18001 standard, elaboration of general quality procedures applicable to all Units and review of standard operation protocols. Quality control, assurance and improvement in the center
- Control of occupational and environmental safety and health in the institute and elaboration of customized procedures for labor risks prevention and safety instructions according current regulations on safety and health
- Training and education of newly incorporated personnel on occupational safety and emergency procedures and all personnel with regards to Environmental Safety and Health programs
- Organization of annual drills, annual revision and update of Emergency Plans and health monitoring and checkups and communication between centralized Risk Prevention Services of center and the USAL
- Record keeping and management of occupational accidents/incidents

SERVICES

- Follow-up control of the units and laboratories certified to check for the compliance of rules under the OHSAS 18001 and ISO 9001 requirements
- Preparation, follow-up and modification of quality procedures and occupational risks prevention
- Internal and external quality and prevention audits. Yearly health monitoring and preparation of paperwork, data filling, and elaboration of annual report to be reviewed by the Direction.
- Training of new personnel joining the center and emergency drill preparation and execution.

Personnel

María Sonia Pérez Díez
Mª Eugenia Fdez. de la Torre

CENTRAL WAREHOUSE & RADIOLOGICAL PROTECTION

SERVICES

- Supply of fungible material, reactive materials, solvents, liquid nitrogen and various gases and monitoring of user expenses, internal invoicing and information. Files and acquisitions of inventorial material
- Management of the acquisition of radioisotopes and means, equipment and instruments of prevention and protection. Acquisition of safety equipment and edition of procedures.
- Management of hazardous waste. Controlled disposal of disclassified radioactive waste
- Evaluations, previous and periodic, of biological, chemical and radiological risk. Maintenance of medical and dosimetric reports of the exposed personnel.
- Acting in incidents, accidents and emergency situations following the previously established procedures.
- Training, information, safety, health seminars and permanent practical advising for the personnel exposed to potential risk agents.

Personnel

Ana Brufau Redondo
Mª del Rosario García Rubia
Vanessa Centeno Talayero

TECHNICAL SUPPORT UNITS

GLASSWARE CLEANING AND STERILIZATION

The Washing and Sterilization unit performs its services for the research units and service units of the institute in the following areas:

- Ordering and storage of reagents and research materials. Stock management.
- Decontamination, cleaning of labware and sterilization of material.
- Preparation of different media and solutions usually required in the laboratories of our center, and some media and solutions specifically required from certain laboratories.

The unit has the ISO Certification: ISO 9001:2000 since 2007and it having successfully passed the successive external audits required.

SERVICES

- Sterilization of biological waste
- Media preparation
- Cleaning and sterilization of material needed in laboratories
- Stocking of reagents and research material

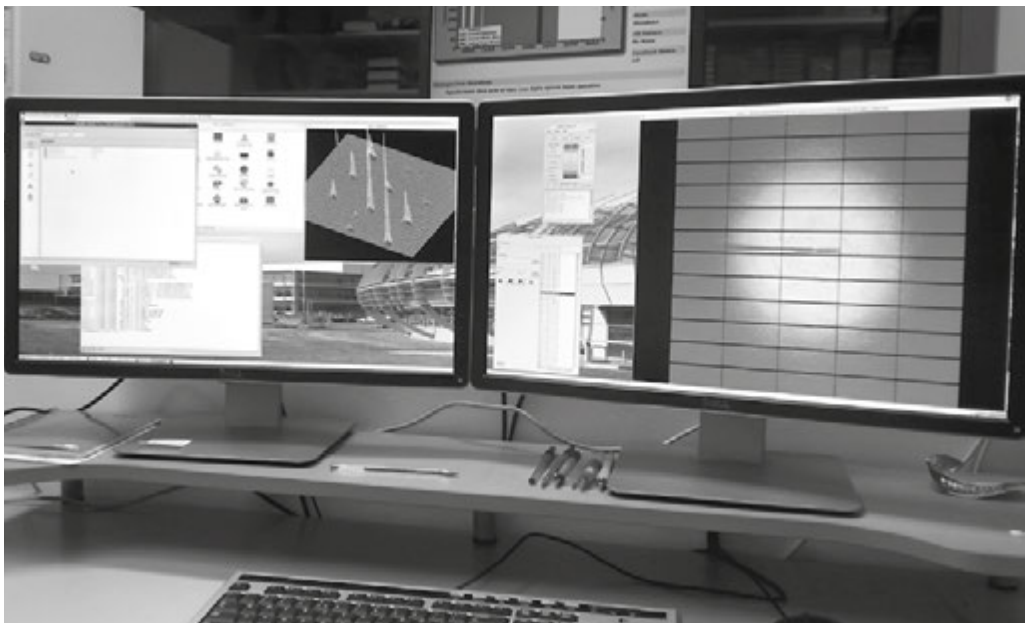
Personnel

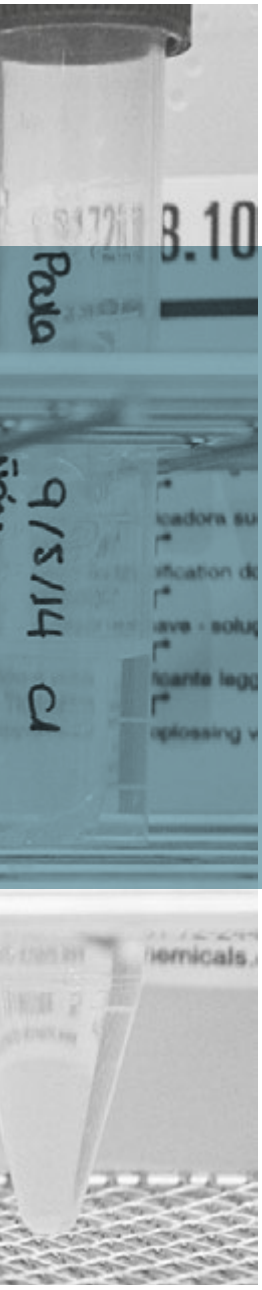
Sonia Pedraza Flores
Pablo González Delgado

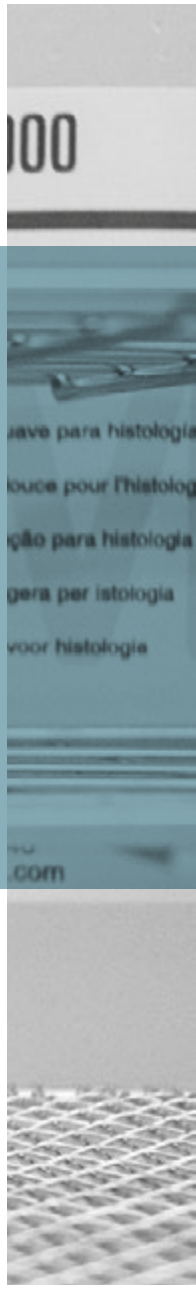
INFORMATION TECHNOLOGIES SERVICE (IT)

The Computer Service is responsible for the development, maintenance, management, and control information technology resources and communications as well as providing technical support to users, works to provide the following services:

- Guidance, negotiation, and follow-up on the purchase of corporation hardware.
- Management of network users, e-mail accounts and distribution lists.
- Installation, maintenance and repair of end-user computer equipment, software and hardware.
- Incident management, technical support, user help and assistance.
- Development and maintenance of the data network infrastructure, wireless network, and audiovisual media.
- Installation, configuration and maintenance of local servers (file server, domain controllers, web server, etc.).
- Network data and database administration department.
- Application Development.(Analysis, design, implementation and maintenance of custom software)







6

SCIENTIFIC ACTIVITIES

LIST OF JOURNALS

This list reflects all the journal in which the investigators of the CIC-IBMCC have published original articles during 2018-2019. The publications with an impact factor over 10 points are highlighted.

JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
ACS Medicinal Chemistry Letters	**1**	**3,737**	**3,737**	**Q1**
ACS Omega	1	2,584	2,584	Q1
Acta Neuropathologica	**1**	**18,174**	**18,174**	**Q1/D1**
Actas Dermo-Sifiliográficas	1	NI	NI	NI
Advances in Hematology	1	NI	NI	NI
Advances in Protein Chemistry and Structural Biology	1	3,783	3,783	Q2
Allergy	1	6,771	6,771	Q1
American Journal of Hematology	1	6,137	6,137	Q1
American Journal of Respiratory and Critical Care Medicine	**1**	**16,494**	**16,494**	**Q1/D1**
Andrology	1	3,259	3,259	Q1
Annals of Hematology	**2**	**2,850**	**5,7**	**Q2**
Annals of Medicine	**1**	**3,049**	**3,049**	**Q1/D1**
Annals of Nuclear Medicine	1	1,648	1,648	Q2
Annals of Oncology	1	14,196	14,196	Q1/D1
Annals of The Rheumatic Diseases	**3**	**14,299**	**42,897**	**Q1/D1**
Annals of Translational Medicine	1	3,689	3,689	Q2
Atherosclerosis	1	4,255	4,255	Q1/D1
Autophagy	**1**	**11,059**	**11,059**	**Q1/D1**
Biochemical Society Transactions	1	4,291	4,291	Q1
Biochimica et Biophysica Acta-Gene Regulatory Mechanisms	1	4,599	4,599	Q1/D1
Bioelectromagnetics	1	1,945	1,945	Q2
Bioinformatics	1	4,531	4,531	Q1/D1
Biology of Blood and Marrow Transplantation	6	3,599	21,594	Q1
Biomed Research International	1	2,197	2,197	Q2

JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
Biomedicine & Pharmacotherapy	1	3,743	3,743	Q1
Blood	**7**	**16,562**	**115,934**	**Q1/D1**
Blood Advances	5	2,484	12,42	Q1/D1
Blood Cancer Journal	8	7,895	63,16	Q1
BMC Bioinformatics	2	2,511	5,022	Q1
BMC Biotechnology	1	2,303	2,303	Q2
BMC Genomics	3	3,501	10,503	Q1
BMC Medical Education	1	1,870	1,87	Q1
Bone	1	4,36	4,36	Q1/D1
Bone Marrow Transplantation	8	4,674	37,392	Q2
Brain and Behavior	1	2,072	2,072	Q2
Breast Cancer Research and Treatment	2	3,471	6,942	Q2
Briefings in Bioinformatics	1	9,101	9,101	Q1
British Journal of Cancer	2	5,416	10,832	Q1/D1
British Journal of Dermatology	2	6,714	13,428	Q1
British Journal of Haematology	12	5,206	62,472	Q1
Cancer	2	6,102	12,204	Q1
Cancer Cell	**2**	**23,916**	**47,832**	**Q1/D1**
Cancer Letters	1	6,508	6,508	Q1/D1
Cancer Medicine	2	3,357	6,714	Q1/D1
Cancer Research	4	8,378	33,512	Q1/D1
Cancer Treatment Reviews	1	8,332	8,332	Q1/D1
Cancers (Basel)	4	6,162	24,648	Q1/D1
Case Reports in Hematology	1	NI	NI	NI
Cell Communication and Signaling	1	5,111	5,111	Q1
Cell Death & Disease	1	5,959	5,959	Q1
Cell Death Discovery	1	NI	NI	NI
Cell Reports	2	7,815	15,63	Q1/D1
Cells	3	5,656	16,968	Q1
Cellular and Molecular Life Sciences	2	7,014	14,028	Q1/D1
Cellular Signalling	1	3,388	3,388	Q2
Chromosoma	1	3,530	3,53	Q2
Clinical Cancer Research	1	8,911	8,911	Q1/D1
Clinical & Translational Oncology	4	2,441	9,764	Q2
Clinical and Experimental Dermatology	1	1,771	1,771	Q3

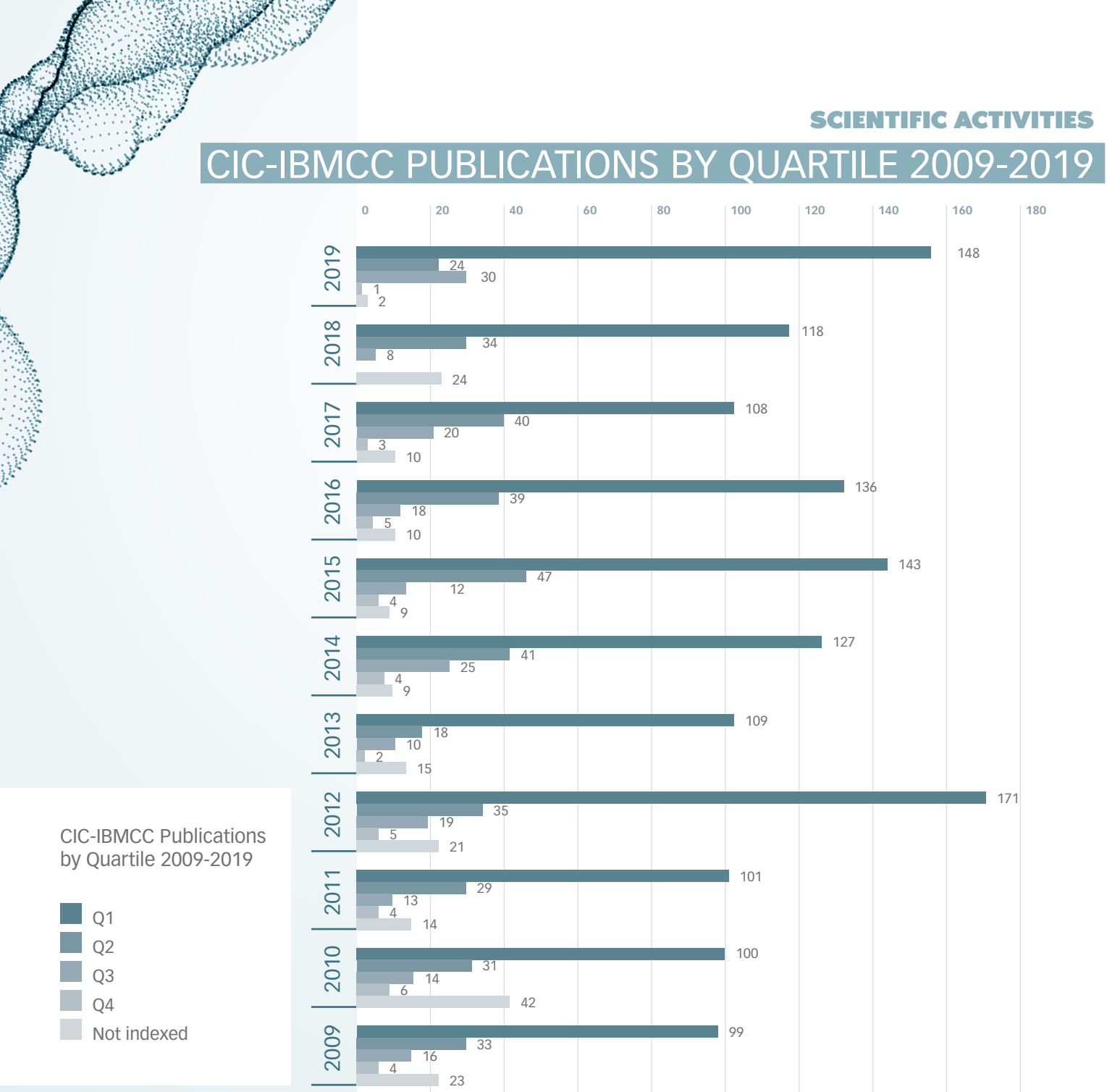
JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
Clinical and Experimental Medicine	1	2,642	2,642	Q2
Clinical Immunology	1	3,548	3,548	Q2
Clinical Lymphoma Myeloma & Leukemia	1	2,274	2,274	Q2
Computer Methods and Programs in Biomedicine	1	3,424	3,424	Q1
Critical Reviews in Oncology/Hematology	1	5,012	5,012	Q1/D1
Current Biology	1	9,193	9,193	Q1/D1
Current Medicinal Chemistry	1	3,894	3,894	Q1
Current Opinion in Cell Biology	3	8,233	24,699	Q1/D1
Current Opinion in Genetics & Development	1	5,288	5,288	Q1
Cytometry Part B-Clinical Cytometry	2	2,938	5,876	Q1
Data in Brief	1	NI	NI	NI
Database-The Journal of Biological Databases and Curation	1	3,683	3,683	Q1/D1
Drug Metabolism and Personalized Therapy	1	NI	NI	NI
EMBO Journal	**3**	**11,227**	**33,681**	**Q1/D1**
European Journal of Haematology	4	2,217	8,868	Q2

JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
European Journal of Immunology	2	4,695	9,39	Q1
European Journal of Internal Medicine	1	3,660	3,66	Q2
European Respiratory Journal	**1**	**11,807**	**11,807**	**Q1/D1**
Experimental Hematology	1	2,462	2,462	Q2
Expert Opinion on Drug Safety	1	3,220	3,22	Q1
Free Radical Biology and Medicine	1	5,657	5,657	Q1/D1
Frontiers in Bioengineering and Biotechnology	1	5,122	5,122	Q1
Frontiers in Cell and Developmental Biology	1	5,206	5,206	Q1
Frontiers in Immunology	7	4,716	33,012	Q1
Frontiers in Oncology	1	4,137	4,137	Q1
Frontiers in Pharmacology	1	3,845	3,845	Q1
Future Oncology	1	2,279	2,279	Q3
Genes Chromosomes & Cancer	1	2,94	2,94	Q2
Haematologica	15	7,570	113,55	Q1/D1
Hemasphere	1	NI	NI	NI
Hematological Oncology	4	3,439	13,756	Q3
Hematology/ Oncology and Stem Cell Therapy	1	NI	NI	NI
Hepatic Oncology	1	NI	NI	NI
Infection and Immunity	1	3,160	3,16	Q1
International Journal of Cancer	1	4,982	4,982	Q1/D1
International Journal of Dermatology	1	1,794	1,794	Q2
International Journal of Gynecological Cancer	1	1,746	1,746	Q2
International Journal of Laboratory Hematology	1	2,073	2,073	Q2
International Journal of Medical Sciences	1	2,333	2,333	Q1/D1
International Journal of Molecular Sciences	4	4,183	16,732	Q1/D1
International Journal of Oncology	1	3,571	3,571	Q1
JAMA Oncology	**1**	**22,416**	**22,416**	**Q1/D1**
Journal der Deutschen Dermatologischen Gesellschaft	2	3,924	7,848	Q3
Journal of Allergy and Clinical Immunology	**4**	**14,110**	**56,44**	**Q1/D1**
Journal of Allergy and Clinical Immunology-In Practice	2	7,55	15,1	Q2
Journal of Biological Chemistry	1	4,106	4,106	Q1
Journal of Cell Biology	2	8,891	17,782	Q1/D1
Journal of Clinical Gastroenterology	1	2,724	2,724	Q2
Journal of Clinical Oncology	**6**	**28,245**	**169,47**	**Q1/D1**
Journal of Endocrinology	1	4,381	4,381	Q1

JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
Journal of Experimental & Clinical Cancer Research	3	5,645	16,935	Q1
Journal of Hematology & Oncology	3	8,731	26,193	Q1/D1
Journal of Immunological Methods	10	1,913	19,13	Q3
Journal of Leukocyte Biology	1	4,012	4,012	Q2
Journal of Medical Case Reports	1	NI	NI	NI
Journal of Medical Economics	1	1,885	1,885	Q2
Journal of Molecular Biology	1	5,067	5,067	Q1
Journal of Neuroscience	1	6,074	6,074	Q1/D1
Journal of Pain Research	2	2,236	4,472	Q1
Journal of Pathology	1	5,942	5,942	Q1/D1
Journal of Proteome Research	1	3,78	3,78	Q1
Journal of Proteomics	2	3,537	7,074	Q1
Journal of The American Academy of Dermatology	1	7,102	7,102	Q1/D1
Journal of the American Heart Association	1	4,660	4,66	Q1/D1
Journal of Tissue Engineering and Regenerative Medicine	1	3,319	3,319	Q1
Journal of Translational Medicine	1	4,098	4,098	Q1
Lancet	**1**	**59,102**	**59,102**	**Q1/D1**
Lancet Haematology	**7**	**11,990**	**83,93**	**Q1/D1**
Lancet Oncology	**4**	**35,386**	**141,544**	**Q1/D1**
Leukemia	23	9,944	228,712	Q1/D1
Leukemia & Lymphoma	10	2,674	26,74	Q2
Leukemia Research	2	2,036	4,072	Q2
Malaria Journal	1	2,798	2,7982	Q1
Medical Oncology	1	3,252	3,252	Q1
Medicina Clínica	1	1,277	1,277	Q3
Methods in Molecular Biology	3	NI	NI	NI
Modern Pathology	1	6,365	6,365	Q1/D1
Molecular and Cellular Biology	1	3,735	3,735	Q2
Molecular and Cellular Endocrinology	1	3,693	3,693	Q1
Molecular and Cellular Oncology	2	NI	NI	NI
Molecular Medicine Reports	1	1,851	1,851	Q3
Molecular Oncology	2	5,962	11,924	Q1/D1
Nanomaterials (Basel)	2	4,034	8,068	Q1
Nature	**2**	**43,070**	**86,14**	**Q1/D1**
Nature Communications	**5**	**11,878**	**59,39**	**Q1/D1**

JOURNAL	Nº PAPERS	IF	TOTAL IF	QUARTILE
Neurobiology of Disease	1	5,160	5,16	Q1/D1
Neurological Sciences	1	2,484	2,484	Q2
New England Journal of Medicine	**3**	**70,670**	**212,01**	**Q1/D1**
Non-Coding RNA	1	NI	NI	NI
Nutrients	1	4,171	4,171	Q1/D1
Ocular Surface	1	9,108	9,108	Q1/D1
Oncogene	1	6,634	6,634	Q1/D1
Oncogenesis	1	5,995	5,995	Q1
Oncotarget	9	NI	NI	NI
Pain Medicine	1	2,764	2,764	Q1
Pharmacogenomics Journal	1	3,503	3,503	Q2
Platelets	3	3,106	9,318	Q2
Plos Biology	1	8,386	8,386	Q1/D1
Plos Genetics	2	5,224	10,448	Q1/D1
Plos One	7	2,776	19,432	Q1/D1
Proceedings of The National Academy of Sciences of The United States of America	3	9,580	28,74	Q1/D1
Proteomes	1	NI	NI	NI
Proteomics Clinical Applications	1	2,324	2,324	Q2
Revista Clínica Española	1	1,043	1,043	Q2
Revista Española de Cardiologia	2	5,078	10,156	Q3
RNA	1	3,949	3,949	Q2
Science Signaling	2	6,481	12,962	Q3
Scientific Reports	7	4,011	28,077	Q1/D1
Seminars in Hematology	1	3,738	3,738	Q1
Seminars in Thrombosis and Hemostasis	1	3,401	3,401	Q1
Skin Research and Technology	1	1,657	1,657	Q2
Small GTPases	1	NI	NI	NI
Stem Cell Investigation	2	NI	NI	NI
Stem Cell Research & Therapy	2	4,627	9,254	Q1/D1
Stem Cells	1	5,614	5,614	Q1
Structure	1	4,576	4,576	Q1
The Lancet Infectious Diseases	**1**	**27,516**	**27,516**	**Q1/D1**
Trends in Cancer	2	8,884	17,768	Q1/D1
Trends in Pharmacological Sciences	**1**	**11,523**	**11,523**	**Q1/D1**
Urology	1	1,861	1,861	Q2

CIC-IBMCC PUBLICATIONS BY QUARTILE 2009-2019



NATIONAL AND INTERNATIONAL COLLABORATIONS

NATIONAL COLLABORATIONS

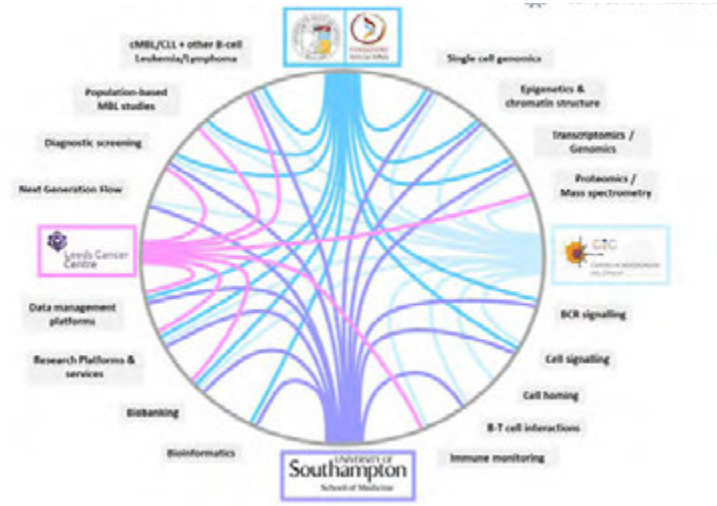
CENTER	PROVINCE	RESEARCHERS
Centro Singular de Investigación en Medicina Molecular y Enfermedades Crónicas (CIMUS) / Universidad de Santiago de Compostela	A Coruña	Carlos Diéguez / Rubén Nogueiras / José Tubío
Hospital Clínico Universitario de Albacete	Albacete	Eva María Galán Moya
Hospital Universitario Central de Asturias, Oviedo University, Oviedo	Asturias	Juan P. Rodrigo
Instituto de Nanomaterials (CSIC) / Instituto de Investigación Sanitaria del Principado de Asturias (ISPA)	Asturias	Mario F. Fraga
Universidad de Extremadura	Badajoz	Pedro Fernández Salguero
Centro Nacional de Análisis Genómico (CNAG) / Centro de Regulación Genómica (CRG)	Barcelona	Marc Martí-Renom
Instituto Josep carreras contra la Leucemia	Barcelona	Manel Esteller / Alex Vaquero
Hospital Sant Joan de Deu	Barcelona	Carme Fons
Instituto de Investigación Biomédica (IRB)	Barcelona	Salvador Aznar-Benitah / Núria López-Bigas
Instituto Hospital del Mar de Investigaciones Médicas (IMIM) / Parque de Salud MAR (PSMar)	Barcelona	Anna Bigas / Lluis Espinosa
Universidad Pompeu Fabra	Barcelona	Pura Muñoz
Centro de Investigación Cooperativa en Biociencias (CIC bioGUNE)	Bilbao	Arkaitz Carracedo
Instituto de Parasitología y Biomedicina López Neyra -CSIC	Granada	Fuencisla Matesanz
Centro de Investigación Biomédica de La Rioja (CIBIR)	La Rioja	Juan Cabello
Centro de Investigaciones Biológicas (CIB)	Madrid	Rodrigo Bermejo
Centro Nacional de Investigaciones Oncológicas (CNIO)	Madrid	Marcos Malumbres / Maríano Barbacid / Tomaso Di Domenico
Centro de Biología Molecular Severo Ochoa-CSIC	Madrid	Paulino Gómez-Puertas / Balbino Alarcón
Instituto de Investigaciones Biomédicas "Alberto Sols"	Madrid	Jorge Martín Pérez
Universidad Complutense	Madrid	Sonia Castillo Lluva / Almudena Porras
Hospital Clínico San Carlos	Madrid	Alberto Ocaña

CENTER	PROVINCE	RESEARCHERS
Fundación Jiménez Díaz	Madrid	José Perea / Damián García Olmo
Hospital Niño Jesús	Madrid	Ángela Hernández
Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	Madrid	Jesús M. Paramio
Universidad de Murcia	Murcia	Senena Corbalán-García
Clínica Universidad de Navarra-Centro de Investigaciones Médicas Aplicadas (CIMA), Universidad de Navarra	Navarra	Jesús San Miguel / Bruno Paiva / Luis Montuenga
Universidad de Salamanca	Salamanca	Rubén Martínez Buey / Manuel A. Sánchez Martín / Francisco S. Lozano Sánchez
Instituto de Recursos Naturales y Agrobiología de Salamanca IRNASA)	Salamanca	Mónica Balsera
Hospital Universitario de Salamanca	Salamanca	José Ramón González Porras / Francisco Martín Herrero
Instituto de Biomedicina y Biotecnología de Cantabria (IBBTEC)	Santander	Piero Crespo
Centro Andaluz de Biología Molecular y Medicina Regenerativa (CABIMER)	Sevilla	José C. Reyes /A. Aguilera
Instituto de Biomedicina de Sevilla (IBIS)	Sevilla	Jesús de la Cruz
Hospital Nacional de Parapléjicos	Toledo	Diego Clemente
Spanish Network on Mastocytosis, Toledo	Toledo	Álvarez-Twose I. / Escribano L.
Instituto de Biología y Genética Molecular (IBGM)	Valladolid	Andrés Alonso
Instituto Oftalmobiología Aplicada (IOBA)	Valladolid	José Carlos Pastor / Ricardo Usategui
Universidad de Zaragoza	Zaragoza	Inés García Rubio

INTERNATIONAL COLLABORATIONS

CENTER	PROVINCE	RESEARCHERS
University of Mascara	Argelia	Bachir Benarba
Cátedra de Genética Universidad de Buenos Aires	Argentina	Hector Targovnik
CONICET, Buenos Aires	Argentina	Pablo Lorenzano-Mena /Mauricio Menacho-Márquez
European Competence Network on Mastocytosis	Austria	Gotlib J Valent P
VIB Center for Inflammation Research, Ghent	Belgium	Geert Van Loo
Universidade do Vale de Itajaì	Brazil	Valdir Cechinel
Princess Margaret Hospital, Toronto	Canada	Eitan Amir
Institute de Biologie, Paris	France	Katja Wassmann
CNRS/Montpellier	France	Anna Castro/T. Lorca
Laboratoire Cell Growth and Tissue Repair / Université Paris-Est Créteil Val-de-Marne , Paris	France	Dulce Papy-García
German Cancer Research Center	Germany	Angel Cid
University of Munich	Germany	Stephan Imreh
Johannes Gutenberg University Mainz, Institute for Pharmacy and Biochemistry, Mainz	Germany	Mark Helm
Institute for Medical Informatics and Biometry, Medical School, University of Technology Dresden	Germany	Lars Kaderalli
University of Bayreuth	Germany	Olaf Stemmann
Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Pokfulam,	Hong Kong. - China	Yao Q / Bai Y /Chim CS
Hebrew University of Jerusalem	Israel	Ephrat Levy-Lahad / Paul Renbaum
Department of Pathology, University of Florence	Italy	Elisabetta Rovida
Mediapharma s.r.l.	Italy	Stefano Iacobelli
Department of Oral Biology, University of Chieti	Italy	Gianluca Sala
Oncological Pharmacology Lab, Department of Oncology, University of Torino (UNITO)	Italy	Chiara Riganti
Computational Genomics Lab, Center for Genomic Sciences (CCG), Universidad Nacional Autonóma de México (UNAM)	Mexico	Julio Collado-Vides
Biological Systems and Integrative Sciences Institute (BioISI), Faculty of Sciences, University of Lisbon (ULISBOA)	Portugal	Margarida Gama-Carvalho
iMM, Lisbon	Portugal	Joao Barata
University of Porto	Portugal	Sandra Macedo-Ribeiro
University of Genève, Genève	Switzerland	Roberto Coppari
University of Utrecht	The Netherlands	Dir de Rooij

CENTER	PROVINCE	RESEARCHERS
Netherlands Cancer Institute-NKI	The Netherlands	Arnoud Sonnenberg
Department of Immunohematology and Blood Transfusion (IHB), Leiden University Medical Center, Leiden.	The Netherlands	Van Dongen JJM / Van Der Velden VHJ
University of Newcastle	United Kingdom	Owen Davies
Department of Biology, University of Manchester	United Kingdom	Cathy Tournier
Crick Institute	United Kingdom	Jernej Ule
Wellcome Trust – MRC Stem Cell Institute	United Kingdom	Sabine Dietmann
Hutchison/MRC Research Centre. Cambridge	United Kingdom	Ashok Venkitaraman
University of Kent	United Kingdom	Benjamin T Goult
Instituto Pasteur de Montevideo	Uruguay	Eduardo Osinaga
Center for Cancer Systems Biology (CCSB) at the Dana-Farber Cancer Institute, Harvard Medical School (DFCI-HMS)	USA	Marc Vidal
University of Ohio	USA	Sarah Heissler
NIH, Bethesda	USA	James R. Sellers
Department of Medicine and Cardiovascular Institute Stanford University School of Medicine. CA. USA.	USA	Mark Mercola
Center for Molecular Medicine. Maine Medical Center Research Institute. Scarborough, ME	USA	Thomas Gridley
Lawrence Berkeley National Laboratory (LBNL). University of California. Berkeley. CA.	USA	Jian Hua Mao
University of Oklahona	USA	Dean S. Dawson
University California at Los Angeles, CA	USA	María L. Iruela-Arispe
Rowan University School of Osteopathic Medicine, Stratford, NJ	USA	Dimitri G. Pestov



ECRIN M3
Early Cancer Research Initiative Network

ONCOLOGY BIOMEDICAL RESEARCH NETWORKING CENTRE (CIBERONC)

CIBER (Biomedical Research Networking Centers) are stable, co-operative research structures that, in the form of public research consortia with recognized legal status, were created under an initiative by the Instituto de Salud Carlos III with the aim of promoting research of excellence in priority areas of Biomedicine and Health Science, carried out in the National Health System and in the National Science and Technology System. The importance of this goal for science, health and society as a whole requires the ISCIII to undertake the promotion and financial support of these CIBER.

Currently, the consortia CIBER (www.ciberisciii.es) and CIBERNED (www.ciberned.es) consist of over 400 research groups working in hospitals, universities and public research institutions, with a broad geographical distribution, which are collaborating for research excellence in the different fields, among which is cancer research.

The proven improvement of the scientific quality and the maturation of the cooperative activity in cancer of the Spanish scientific community that took place within the RTICC in its successive editions since 2003 constituted an essential factor for the decision of the Management of the Institute of Health Carlos III (ISCIII) in the sense of changing, from 2017, the structure of cooperative research in cancer in Spain (previously in RTICC format) to a structure of organization and more stable format within the organizational chart of the ISCIII as it is a new area of Cancer (named CIBERONC) of the CIBER of ISCIII.

The main aim of the Consorcio Centro de Investigación Biomédica en Red de Cáncer (CIBERONC) is to promote excellence in oncology research in Spain, as well as to incorporate new findings to clinical practice. In order to attain excellence, CIBERONC promotes the cooperation of 50 of the best national research groups in cancer. CIBERONC pursues also an increase in the quality of its researchers by means of a transversal training and mobility program.

In order to ensure the integration of the results of our research in patients' treatment, there is a balance between basic and clinical researchers in all CIBERONC structures. The central objectives of each program are furthermore intended to improve the diagnosis and treatment of cancer patients.

Last, but not least, the CIBERONC center wishes to narrow the gap between scientific knowledge and society and clearly explain the benefits of our research to the general public by means of different endeavors.

CIBERONC has adopted a structure with the following specific aims:

- To carry out joint programs for research, development and innovation in the cancer area.
- To contribute to solving the problems faced by healthcare in the field of oncology.
- To promote the participation of research groups in national and international research activities, especially the ones included in European R+D+I Framework Programs.
- To promote the transfer of results of research processes to society and in particular to the production sector.
- To promote the dissemination of its activities and the training of researchers in the cancer field.

Five groups of the CIC-IBMCC, led by Dr. Eugenio Santos, Xosé R. Bustelo (Coordinator of the Tumour Progression Mechanisms program), Alberto Orfao, Marcos González (Coordinator of the Haematological Tumours program) and Atanasio Pandiella Alonso are involved in several programs of the CIBERONC.

GROUPS OF CIC-IBMCC RECOGNIZED AS "UNIDAD DE INVESTIGACIÓN CONSOLIDADA" (UIC) FOR CASTILLA-LEÓN AUTONOMOUS GOVERNMENT

Nº	PI	RESEARCHERS
002	**Xosé Ramón García Bustelo**	María Josefa Montero Gómez / Mercedes Dosil Castro / María Ángeles Sevilla Toral / Javier Robles Valero / Myriam Cuadrado López
009	**Atanasio Pandiella Alonso**	María Azucena Esparís Ogando / Juan Carlos Montero González / María Elena Díaz Rodríguez / Alberto Ocaña Fernández
017	**Isidro Sánchez García**	Rafael Jiménez Fernández / Francisco Javier García Criado / Jesús Pérez Losada / Carolina Vicente Dueñas
066	**Alberto Martín Pendás**	Elena Llano Cuadra / Manuel Sánchez Martín / José Luis Barbero Esteban
076	**Eugenio Santos de Dios**	Javier De Las Rivas Sanz / Alberto Fernández Medarde / José María Rojas Cabañeros / Carmela Gómez Rodríguez
106	**Mª del Carmen Guerrero Arroyo**	José Ramón González Porras / Francisco Santiago Lozano Sánchez / Francisco Martín Herrero / José María de Pereda Vega / Jose María Bastida Bermejo / Almudena Porras Gallo
110	**Norma Carmen Gutiérrez Gutiérrez**	María Victoria Mateos Manteca / Enrique María Ocio San Miguel / Mercedes Garayoa Berrueta / Noemí Puig Morón / Ana Belén Herrero Hernández / Irena Misiewick-Krzeminska / María Teresa Paíno Gómez
143	**Jesús María Hernández Rivas**	Juan Luis García Hernández / José Luis Ordóñez García / Ana Eugenia Rodríguez Vicente / M. Rocío Benito Sánchez / Ignacio García-Tuñón Llanio / María Abaigar Alvarado / María Hernández Sánchez / Verónica Alonso Pérez / María Teresa González Martínez
151	**José Alberto Orfao de Matos Correia e Vale**	Julia Mª Almeida Parra / Manuel Fuentes García / Mª Dolores Tabernero Redondo / Andrés Celestino García Montero / José María Sayagués Manzano
155	**Marcos González Díaz**	Ramón García Sanz / Cristina Jiménez Sánchez / María del Carmen Chillón Santos / María Eugenia Alonso Sarasquete / María Belén Vidriales Vicente
252	**Andrés Avelino Bueno Núñez**	Felipe Xosé Pimentel Muiños / María Sacristán Martín / Rodrigo Bermejo Moreno
258	**Pedro Alfonso Lazo-Zbikowski Taracena**	Juan Jesús Cruz Hernández /Rogelio González Sarmiento / Sandra Blanco Benavente
265	**María Dolores Caballero Barrigón**	Alejandro Martín García-Sancho / Pilar Tamayo Alonso / Miguel Alcoceba Sánchez / Lucía López Corral

GROUPS OF CIC-IBMCC RECOGNIZED AS "GRUPOS DE INVESTIGACIÓN RECONOCIDA" (GIR) FOR THE SALAMANCA UNIVERSITY (USAL)

NAME	PI	RESEARCHERS	COLLABORATIONS	RESEARCH LINES
Inestabilidad Genética y Autofagia	Bueno Núñez, Andrés Avelino	Sacristán Martín, María / Pimentel Muiños, Felipe / Bermejo Moreno, Rodrigo		- Identificación y estudio del significado biológico de los mecanismos que revierten la tolerancia al daño en el DNA - Estudio de la fosforilación de proteínas en respuesta a daño en el DNA - Mecanismos de estabilización de horquillas de replicación - El papel de la autofagia en la prevención de patologías inflamatorias graves
Linfomas y Trasplantes	Caballero Barrigón, Dolores	Martín García-Sancho, Alejandro / Alcoceba Sánchez, Miguel / Tamayo Alonso, Mª Pilar / López Corral, Lucía		- Promoción y desarrollo de ensayos clínicos controlados en LNH para la investigación de nuevos fármacos - Mejorar los procedimientos del trasplante autólogo y alogénico, la eficacia y tolerancia de los regímenes de acondicionamiento pre-trasplante, así como la prevención y manejo de la enfermedad injerto contra huésped - Identificación de biomarcadores clínicos y genéticos que permitan identificar subgrupos de LNH con diferente evolución clínico/ pronóstica - Identificación de biomarcadores clínicos y genéticos asociados a complicaciones del trasplante: EICH, infecciones, miroangiopatía trombótica, etc - Monitorización de la respuesta terapéutica de los síndromes linfoproliferativos e impacto de la misma en la supervivencia mediante la prueba metabólica PET/TC, así como citometría de flujo y biología molecular

NAME	PI	RESEARCHERS	COLLABORATIONS	RESEARCH LINES
Señalización, División y Crecimiento Celular	Dosil Castro, Mercedes	Llano Cuadra, Elena/ Lacal Romero, Jesús	Martín Pendás, Alberto / García Bustelo, Xosé Ramón / Vicente Manzanares, Miguel	- Papeles de moléculas de señalización celular en procesos tumorales y en otras enfermedades de alta incidencia - Regulación de la tolerancia al daño en el DNA durante su replicación y relación con la estabilidad del genoma - Formación de ribosomas y regulación del crecimiento celular - Análisis funcional de genes implicados en segregación cromosómica y su implicación en enfermedades humanas: cáncer, envejecimiento e infertilidad - División celular y estabilidad genómica: papel de las proteínas fosfatasas Cdc14 en la regulación del ciclo de división celular y en la respuesta de daño al DNA
Biología Molecular y Celular en Hemopatías	González Díaz, Marcos	García Sanz, Ramón / Vidriales Vicente, Mª Belén	Chillón Santos, Mª del Carmen / Alonso Sarasquete, Mª Eugenia / Jiménez Sánchez, Cristina	- Alteraciones genéticas/moleculares de la célula tumoral de las hemopatías malignas - Factores pronósticos clínico-biológicos y fenotípicos/moleculares de las hemopatías malignas - Monitorización terapéutica mediante técnicas Fenotípicas y de Biología molecular (estudio de enfermedad mínima residual -EMR) - Polimorfismos genéticos en hemopatías malignas - Biología del Trasplante de precursores hematopoyéticos: Mecanismos de la Enfermedad Injerto Contra Huésped y Enfermedad Injerto Contra Leucemia
Mecanismos de Señalización en Enfermedades Cardiovasculares y otras Patologías: De la Investigación Básica a la Clínica	Guerrero Arroyo, Carmen	Lozano Sánchez, Francisco Santiago / González Porras, José Ramón / Martín Herrero, Francisco / Hernández Cano, Luis / Fernández Infante, Cristina / Rodríguez Blázquez, Antonio	Porras Gallo, Almudena / Pereda Vega, José María de / Bastida Bermejo, Jose Mª	- Modelos animales para el estudio de la ruta de señalización C3G-Rap1 en plaquetas - Implicación del C3G plaquetario en isquemia cardiaca y angiogénesis utilizando modelos murinos - Implicación de C3G en la patología cardiovascular humana - Papel de la ruta C3G-Rap1 en la diferenciación megacariocítica - Mecanismos de regulación intramolecular de PCa3pGel de C3G en la regulación de los procesos de migración/invasión y en las metástasis. Implicación de C3G en la transición epitelio-mesénquima - Fenotipo y Genotipo plaquetario

NAME	PI	RESEARCHERS	COLLABORATIONS	RESEARCH LINES
Genética Molecular en Oncohematología	Hernández Rivas, Jesús Mª	García Hernández, Juan Luis / Robledo Montero, Cristina / Rodríguez Vicente, Ana E. / Benito Sánchez, M. Rocío / del Rey González, Mónica / García-Tuñón Llanio, Ignacio	Lumbreras González, Eva / Hernández Sánchez, María / Montaño Brioso, Adrián / Janusz, Kamila / Quijada Álamo, Miguel / Martín Izquierdo, Marta / Hernández Sánchez, Jesús María / Abáigar Alvarado, María / Alonso Pérez, Verónica / Ordóñez García, José Luis / Marín Quilez, Ana	- Determinación de marcadores moleculares con interés diagnóstico y pronóstico en las hemopatías malignas y en los tumores sólidos - Identificación de mecanismos genéticos relacionados con la patogénesis de las hemopatías - Incorporación de las nuevas metodologías de análisis genético masivo (microarrays y secuenciación) al estudio de las neoplasias humanas
Citómica	Orfao de Matos, José Alberto	Almeida Parra, Julia / García Montero, Andrés Celestino / Fuentes García, Manuel / Tabernero Redondo, Mª Dolores / Sayagués Manzano, José Mª / Corrales Hernández, Juan J / Pérez Andrés, Martín		- Definición de los patrones de expresión proteica aberrantes en células neoplásicas y la relación con su origen genético. Implicaciones clínicas en el diagnóstico, monitorización de enfermedad residual y resistencia a drogas, e identificación de potenciales dianas terapéuticas en hemopatías. - Análisis de las vías de adquisición de alteraciones genéticas a nivel intra-tumoral en tumores sólidos y hemopatías malignas y sus implicaciones en el rastreo e identificación de alteraciones pre-malignas y en el diagnóstico precoz de transformación maligna. - Estudio del papel del sistema inmunológico en el control y progresión de la enfermedad en hemopatías malignas y en procesos no tumorales (infección por el VIH, alcoholismo y enfermedades autoinmunes).
CANCIRMED	García Criado, Francisco J.	González Sarmiento, Rogelio / Jiménez Fernández, Rafael / Cruz Hernández, Juan Jesús / García Cenador, Mª Begoña	Vicente Dueñas, Carolina / Pérez Losada, Jesús / Sánchez J. García, Isidro / Lazo-Zbikowski Taracena, Pedro A	- Programa de oncología traslacional: Biología de células madre tumorales y su aplicabilidad clínica
GTPASAS y Cáncer: Señalización mediada por RAS	Santos de Dios, Eugenio	Rivas Sanz, Javier de las / Fernández Medarde, Alberto / Gómez Rodríguez, Carmela / Jimeno García, David / Fuentes Mateos, Rocío / Castellano Sánchez, Esther	Calvo Baltanás, Fernando / M García Navas, Rósula	

7

TRAINING ACTIVITIES

POSTGRADUATE PROGRAM: MASTER DEGREE IN "BIOLOGY AND CLINIC OF CANCER"

The Master´s Degree "*Biology and Clinic of Cancer*" is a distinctly and selective Master Research focused on specialized training on basic, translational and clinical aspects of cancer research. It is aimed at the basic training necessary for graduates with an interest in Cancer Biology without prior experimental experience in the fields of molecular and cell biology that allow students to continue doctoral studies in the field.

The title is related to the Degrees taught in the Faculties of Biology (Biology, Biotechnology, Biomedicine, etc.), Medicine and Pharmacy, which could be called powers of the biomedical area.

This Master´s Degree provides an introduction to the study of tumor processes through an integrated approach that begins with an analysis of these processes at the molecular level and continues with the application of these basic skills to the clinic. The integration of molecular and clinical contents in the same program gives an extremely unique character and training key for future researchers in this field.

The rationale for this Master Program is determined by the need to integrate modern studies of cancer at the molecular level with the body of knowledge of this disease clinically. The progress generated in this field of study ranges from basic research (in the microbiological, biochemical or molecular biology fields) to clinical research areas related to diagnosis, prognosis and experimental treatment. This knowledge breaks down barriers between traditionally separated biomedical fields such as Medicine, Pharmacy and Biology. In this sense, the training consists of proposing an interdisciplinary approach to graduate with academic interest and /or applied in the medical, pharmaceutical, biological, biotechnological or bioinformatics fields.

The Master´s Academic Program is taught by professors and researchers specialized in each of the subjects, most of them belonging to the CIC-IBMCC but also by visiting researchers, experts on specific topic, invited for that purpose.

An important characteristic is its high practical profile, which constitutes one of its most attractive points. Thus, of its 60 total ECTS, 18 of them correspond to the subject "Practicum Biology and Cancer Clinic" in which the student carries out, under the direct supervision of a tutor, a research project in one of the CIC-IBMCC research groups throughout the academic year. This project leads to the development of the final Master´s Thesis, which will be presented and defended at the end of academic course.

One of the academic additional activities of the Master is the active participation of the students in the Scientific Seminar Program prepared annually by the CIC. Students have the opportunity to meet prestigious researchers invited by the Center as well as to know the research projects carried out by the different laboratories at the CIC.

The CIC makes available to the students all facilities and technological units. The goal is to provide them with the most complete research training.

The orientation of this teaching is therefore preferentially a postgraduate research program, which aims to prepare students for inclusion in doctoral programs and the completion of the PhD. The Master "*Biology and Clinic of Cancer*" aims also to transfer to future doctors the experience and knowledge generated about the different diseases that collectively we call cancer as well as introduce the culture of cutting-edge research that will cure or turn into chronic these diseases in the future.

ACHIEVEMENTS:

-The Master´s Degree "*Biology and Clinic of Cancer*" maintains an average enrollment of 85% of the places offered.

-In 2019, it has been evaluated by the board of "Agencia para la calidad del Sistema Universitario de Castilla y León" and has achieved its renovation with an excellent rating.

TRAINING ACTIVITIES

STUDENTS MASTER PROGRAM

2017 / 2018	2018 / 2019	2019 / 2020
Jorge Alejo Mateo	María Carranza Jiménez	Vanessa Acebes Fernández
Sara Armenteros González	Daniel García Ruano	Marta Alcón Pérez
Esla Natividad Astorga Simón	Paula García Vallés	Silvia Alemán Arteaga
Judith Jeniffer Azaña Yupanqui	Marta Isidro Hernández	Ana Macrina Añazco Guenkova
Marina Belver Jiménez	Pablo Juanes Velasco	Blanca Ayuso Íñigo
Beatriz Benayas López	Judith López Luis	David Bastante Rodríguez
Ana Casado García	Jimena Álvarez Freile	Víctor Coca Ruiz
Claudia Cifuentes Caballero	Francisco Javier Morán Plata	Alejandro Crespo Carazo
Cristina Fernández Infante	Alba Morán Vaquero	Celia Gálvez Merchán
Natalia Fernández Parejo	Cynthia Mucientes Valdivieso	Ángela Patricia Hernández García
Blanca Fuentes Herrero	Lorena Ochoa Garayoa	Óscar Herranz Varea
Natalia García Sancha	Claudia Alarcón Torrecillas	Diego Iglesias Corral
Nerea Gestoso Uzai	Alonso Rodríguez Pescador	Alejandro Jiménez Navas
Luis González Moreno	Lydia De La Torre Quintana	Mauro Lorenzo Mohamed
Carlos Gutiérrez Cerrajero	Sara Vallejo Fuente	Marcos Manrique Crespo
Marta López Yus	Javier Zamarreño Lozano	Paloma Martín Bejarano Soto
Gerardo Javier Martí Chillón	Sheila Almaraz Postigo	María Matorra Miguel
María Millán Salanova	Rosa Ayala Bueno	Verónica Salgado Pacheco
Guillermo Oliva Ariza	Ignacio Jesús Cardona Benavides	Sandra Santos Mínguez
Ana Ordiales Talavero	Rocío Anahi Martínez Correa,	Tatiana Ugalde Catarinella
Niyireth Peñaloza Castañeda	Juan Carlos Fernández Izquierdo	
Claudia Pérez Carretero		
Claudia María Rejano Gordillo		
Antonio Rodríguez Blázquez		
Laura Sánchez Díaz		
Tania Sánchez-Bayuela Recio		
Laura Silva Sousa		
Darnel Alfonso Marchena Mendoza		

MASTER THESES

MASTER STUDENT	DIRECTOR	TITLE MASTER THESES	DATE
Ana Casado García	Rogelio González-Sarmiento	*Nuevas aportaciones a la caracterización del cáncer de mama en mujeres jóvenes*	25/06/2018
María Millán Salanova	Miguel Vicente-Manzanares	*Papel funcional de los parálogos de la NMII en la activación de los linfocitos T*	25/06/2018
Guillermo Oliva Ariza	Alberto Orfao / Martín Pérez Andrés	*Identificación y caracterización de linfocitos B con cambio de isotipo en la sangre de cordón*	25/06/2018
Niyireth Peñaloza Castañeda	Alberto Orfao/ Sergio Matarraz	*Caracterización inmunofenotípica de nuevos marcadores candidatos para seguimiento de EMR en LMA*	25/06/2018
Claudia Pérez Carretero	Jesús Mª Hernández-Rivas / Ana E. Rodríguez Vicente	*Mutational analysis of chronic lymphocytic leukemia patients with IGH rearrangements reveals a unique mutational profile that differs from the rest of CLL patients and refines their clinical outcome*	25/06/2018
Claudia María Rejano Gordillo	Felipe X Pimentel Muiños	*Regulación autofágica mediada por miembros pro-apoptóticos de la familia Bcl-2*	25/06/2018
Antonio Rodríguez Blázquez	José Mª de Pereda Vega	*Caracterización de la interacción de la proteína adaptadora NCK1 y el factor de intercambio de nucleótidos C3G*	25/06/2018
Jorge Alejo Mateo	Azucena Esparís Ogando	*Genes regulados por MEK5/ERK5 en cáncer de pulmón y ovario. Implicaciones terapéuticas*	26/06/2018
Sara Armenteros González	Julia Almeida Parra / Mª Laura Gutiérrez Troncoso	*Estudio de los cambios genéticos y del micro-medioambiente tumoral asociados al grado de diferenciación histológica en el adenocarcinoma ductal de páncreas*	26/06/2018
Elsa Natividad Astorga Simón	Xosé R. Bustelo / Javier Robles Valero	*Caracterización funcional de mutaciones del protooncogén VAV1 descritas por primera vez en tumores humanos*	26/06/2018
Judith Jeniffer Azaña Yupanqui	Alberto Orfao / Susana Barrena / Juana Ciudad	*Optimización del método de evaluación de enfermedad mínima residual de leucemia linfoblástica aguda de células T mediante el estudio inmunofenotípico por citometría de flujo*	26/06/2018
Marina Belver Jiménez	Manuel Fuentes García	*Inmunoproteogenómica*	26/06/2018
Tania Sánchez-Bayuela Recio	Rogelio González-Sarmiento	*Nueva aproximación al perfil mutacional del cáncer de ovario*	26/06/2018
Laura Silva Sousa	Alicia Rodríguez / Miguel Pericacho	*Efecto de la sobreexpresión de endoglina en la estabilización y maduración de los vasos sanguíneos*	26/06/2018
Beatriz Benayas López	Mercedes Garayoa / Teresa Paíno Gómez / Enrique M. Ocio San Miguel	*Evaluación de la actividad de isatuximab sobre el microambiente en el mieloma múltiple: potencial papel en las lesiones osteolíticas y efecto sobre la producción de exosomas*	27/06/2018
Claudia Cifuentes Caballero	Miguel Vicente-Manzanares	*Miosina no muscular de claseII-B: efectos específicos sobre la migración del modelo de melanoma B16-F10 y caracterización de su región promotora*	27/06/2018

MASTER STUDENT	DIRECTOR	TITLE MASTER THESES	DATE
Cristina Fernández Infante	Carmen Guerrero Arroyo	*Análisis de la interacción entre C3G y proteínas de la maquinaria de* secreción	27/06/2018
Natalia Fernández Parejo	Xosé R. Bustelo	*Vav2 as a regulator of ribosome biogenesis in squamous lineages*	27/06/2018
Blanca Fuentes Herrero	Julia Almeida / María Aránzazu Rodríguez Caballero	*Estudio molecular y genético de la Linfocitosis B Monoclonal de alto recuento*	27/06/2018
Ana Ordiales Talavero	María P. Sacristán Martín	*Estudio del papel de las fosfatasas Cdc14A/B en el checkpoint de respuesta a estrés replicativo*	27/06/2018
Laura Sánchez Díaz	Atanasio Pandiella Alonso / Juan Carlos Montero González	*Resistencia a Neratinib en cáncer de mama HER2-positivo*	27/06/2018
Natalia García Sancha	Jesús Pérez-Losada	*Protección parcial frente al cáncer de mama mediante la potenciación de la involución postlactancia con agonistas dopaminérgicos*	28/06/2018
Nerea Gestoso Uzal	Rogelio González-Sarmiento	*Aproximación preliminar a la caracterización funcional de la pérdida del gen NOMO-1*	28/06/2018
Luis González Moreno	Mercedes Dosil Castro	*Estudio de los defectos de síntesis de ribosomas causados por mutaciones en RPS19 que originan la anemia de Diamond-Blackfan*	28/06/2018
Carlos Gutiérrez Cerrajero	Rogelio González-Sarmiento	*Estudio de nuevos biomarcadores en glioblastoma multiforme*	28/06/2018
Marta López Yus	Eugenio Santos / Fernando Calvo Baltanás	*Estudio de la función de las proteínas sos en el mantenimiento de la homeostasis del bazo*	28/06/2018
Darnel Alfonso Marchena Mendoza	Jesús Mª Hernández-Rivas/ Maribel Forero-Castro / Mª Rocío Benito Sánchez	*Estudio de la incidencia y valor pronóstico de las mutaciones somáticas del gen JAK2 en enfermos con LAL-B*	28/06/2018
Gerardo Javier Martí Chillón	Fermín Sánchez-Guijo	*Estudio de los microRNAs de vesículas extracelulares plasmáticas en pacientes con síndromes mielodisplásicos de alto riesgo y leucemia mieloide aguda*	28/06/2018
María Carranza Jiménez	Alberto Fernández-Medarde / Eugenio Santos	*Screening de inhibidores de la activación de RAS por SOS*	24/06/2019
Daniel García Ruano	Sergio Moreno	*Construcción y caracterización funcional de mutantes de la CDK PEF1 de Schizosaccharomyces Pombe*	24/06/2019
Paula García Vallés	Rogelio González-Sarmiento	*Nuevas aportaciones a la caracterización de NOMO1 en cáncer colorrectal*	24/06/2019
Marta Isidro Hernández	Isidro Sánchez García	*Inhibición transitoria de la vía JAK/STAT en células preleucémicas*	24/06/2019
Pablo Juanes Velasco	Manuel Fuentes García	*Caracterización sistemática del perfil proteico de la leucemia linfocítica crónica de célula B mediante estrategias de proteómica funcional*	24/06/2019
Judith López Luis	Sandra Blanco Benavente	*Role of aberrant deposition of 5methylcytosine in ribosomal RNA in prostate cancer*	24/06/2019

MASTER STUDENT	DIRECTOR	TITLE MASTER THESES	DATE
Jimena Álvarez Freile	Alberto Orfao / Elena Blanco	*Desarrollo de un protocolo para la identificación de células B específicas de antígeno mediante citometría de flujo*	25/06/2019
Francisco Javier Morán Plata	Julia Almeida Parra	*Aproximación al origen celular de los síndromes linfoproliferativos crónicos de células T CD4*	25/06/2019
Alba Morán Vaquero	José Mª de Pereda	*Desarrollo de inhibidores de la proteína C3G para el análisis de su función en modelos celulares*	25/06/2019
Cynthia Mucientes Valdivieso	Fernando Calvo Baltanás / Eugenio Santos	*Papel funcional de las proteínas SOS1 y SOS2 en cultivos primarios de queratinocitos*	25/06/2019
Lorena Ochoa Garayoa	Alicia Rodriguez / Miguel Pericacho	*Efecto de la expresión de Endoglina sobre las uniones adherentes de VE-Cadherina en células endoteliales en cultivo*	25/06/2019
Claudia Alarcón Torrecillas	Alicia Rodríguez / Miguel Pericacho	*Efecto de las MSC en modelos de angiogénesis in vitro*	26/06/2019
Alonso Rodríguez Pescador	Fermín Sánchez-Guijo	*Estudio de los efectos inducidos en células endoteliales por la incorporación de vesículas extracelulares procedentes de células mesenquimales de pacientes con neoplasias mieloproliferativas*	26/06/2019
Lydia De La Torre Quintana	Alberto Orfao / Martín Pérez Andrés	*Análisis de las subpoblaciones de linfocitos T en pacientes con inmunodeficiencia variable común*	26/06/2019
Sara Vallejo Fuente	Rogelio González-Sarmiento	*Estudio del gen SEZ6L en cáncer de endometrio*	26/06/2019
Javier Zamarreño Lozano	Avelino Bueno	*Papel de UBP1 en la tolerancia al daño en DNA mediante la desubiquitinación de PCNA*	26/06/2019
Sheila Almaraz Postigo	Rogelio González-Sarmiento	*Estudio de la posible implicación del gen HTRA4 en cáncer de mama en mujeres jóvenes*	27/06/2019
Rosa Ayala Bueno	Alberto Orfao / Sergio Matarraz	*Caracterización inmunofenotípica de la leucemia mieloide aguda con mutación en el gen nucleofosmina 1 (NPM1)*	27/06/2019
Ignacio Jesús Cardona Benavides	Marcos González Díaz	*Screenings a escala genómica mediante la tecnología CRISPR-CAS9 en mieloma múltiple: búsqueda de nuevas vulnerabilidades y terapias dirigidas*	27/06/2019
Rocío Anahi Martínez Correa,	Jesús Mª. Hernández-Rivas	*Estudio del perfil mutacional y su impacto pronóstico en pacientes con mielofibrosis*	27/06/2019
Juan Carlos Fernández Izquierdo	Carmela Gómez / Eugenio Santos	*Importancia de las proteínas sos en el desarrollo de la leucemia mieloide crónica en ratones C57BL/6*	19/07/2019

TRAINING ACTIVITIES

POSTGRADUATE PROGRAM: PHD PROGRAM ENTITLED "BIOSCIENCE: BIOLOGY AND CLINIC OF CANCER AND TRANSLATIONAL MEDICINE"

The PhD program entitled "*Bioscience: Biology and Clinic of Cancer and Translational Medicine*" is academically sponsored by the Department of Microbiology and Genetics (Faculty of Biology) and the Department of Medicine (Medical School), and involves the adaptation to the Education European Space of the PhD programs.

The program aims among its objectives to provide the students an interdisciplinary approach to the study of cancer. Thus, the PhD program offers two initial courses focused on topics related to cellular and molecular biology of cancer, as well as to the basic knowledge for diagnosis, prognosis and cancer treatment. In addition, genetic, development, and clinical pathology of various human solid or hematologic tumors are analyzed. These subjects integrate "molecular" and "clinical" approaches with an emphasis on the molecular links with the disease.

Additional training activities are also offer to postgraduate students, among which we highlight the following: 1) participation in the Scientific Seminar Program prepared annually by the CIC, where students have the opportunity to meet prestigious researchers in the oncology field invited by the Center, as well as to know the research projects carried out by the different laboratories at the CIC; 2) work meetings for research project monitoring and analysis of results; 3) assistance to national or international conferences, and 4) mobility: short stays in foreign research groups related with their projects.

Together with the Master´s Degree "*Biology and Clinic of Cancer*", the aim of these two Programs is to give the students a complete training in the oncology field, ranging from the most recent knowledge generated in both basic research and areas of clinical research related with the diagnosis, prognosis and experimental treatments. We believe that this view jumps the barriers between traditionally separate biomedical areas such as Medicine, Pharmacy and Biology. This Postgraduate training Program is indeed of interest to professionals in the area and to academics in the medical, pharmaceutical or biological fields.

ACHIEVEMENTS:

-The mentioned PhD program generates an average of 20 new PhD annually.

-In 2019, it has been evaluated by the board of "Agencia para la Calidad del Sistema Universitario de Castilla y León" and has achieved its renovation with an excellent rating.

STUDENTS PHD PROGRAM

2017 / 2018	2018 / 2019	2019 / 2020
Adrián Ricardo Montaño Brioso	Abel Jesús Martel Martel	Abel Jesús Martel Martel
Adrián Sánchez Fernández	Adriá Casanovas Fernández	Adrián Ricardo Montaño Brioso
Alberto Rocha De Losada	Adrián Ricardo Montaño Brioso	Adrián Sánchez Fernández
Alejandro Hernández Delgado	Adrián Sánchez Fernández	Alba Morán Vaquero
Alejandro Medina Herrera	Afonso Fernandes de Abreu Alves Chaves	Alba Pérez Pons
Alfonso Fernandes De Abreu Alves Chaves	Alba García Pérez	Alba Torres Valle
Aline Rodrigues Françoso	Alba Pérez Pons	Alberto Berral González
Álvaro Casado Blanco	Alberto Rocha de Lossada	Alberto Conde Ferreiros
Álvaro Fernández Cabrera	Alejandro Hernández Delgado	Alberto Rocha De Lossada
Álvaro Muñoz Galindo	Alejandro Jiménez Rihuete	Alberto Ruíz Gómez
Álvaro Veiga Vaz	Alejandro Medina Herrera	Alejandro Hernández Delgado
Ana África Martín López	Alicia Landeira Viñuela	Alejandro Medina Herrera
Ana Alejandra Cordero Vaquero	Álvaro Casado Blanco	Alejandro Olivares Hernández
Ana María Gavilán García	Álvaro Fernández Cabrera	Alex Viñolas Cuadros
Ana María Mateos Díaz	Álvaro Muñoz Galindo	Alfredo Barrio Rodríguez
Ana María Orive Ramos	Ana África Martin López	Alicia Landeira Viñuela
Ana Marín Quilez	Ana Casado García	Álvaro Casado Blanco
Ana Rico Sorli	Ana Elisa Rodríguez Gude	Álvaro Fernández Cabrera
Andrea Díaz Tejedor	Ana María Marín Cassinello	Álvaro Veiga Vaz
Andrés Achury Murcia, Carlos	Ana María Mateos Díaz	Ana África Martin López
Andrés Barbosa Ventura	Ana María Orive Ramos	Ana Casado García
Aránzazu García Mateo	Ana Marín Quílez	Ana Elisa Rodríguez Gude
Ariana Centa	Ana Rico Sorli	Ana María Marín Cassinello
Arturo Carabias Del Rey	Andre Barbosa Ventura	Ana María Mateos Díaz
Aurora Gómez Vecino	Andrea Díaz Tejedor	Ana María Orive Ramos
Beatriz Loureiro Rodríguez	Andrea Noya Mourullo	Ana María Vaquero Campos
Beatriz María Rivas López	Angie Alejandra Díaz Baquero	Ana Marín Quílez
Bianca Paz Renau Mínguez	Antonio Rodríguez Blázquez	Ana Rico Sorli
Blanca Nieto Bernáldez	Aránzazu García Mateo	Anda Magdalena Ciocea
Carlos Fabián Castaño Romero	Arturo Carabias del Rey	Andre Barbosa Ventura
Carlos Llanes Álvarez	Aurora Gómez Vecino	Andrea Díaz Tejedor
Catalina Gil Restrepo	Belén Cigarral García	Angie Alejandra Díaz Baquero
Catia Daniela Quintas Faria	Bianca Paz Renau Mínguez	Antonio Rodríguez Blázquez

2017 / 2018	2018 / 2019	2019 / 2020
Cecilia Higueruela Mínguez	Blanca Fuentes Herrero	Aurora Gómez Vecino
César Augusto Rodríguez Sánchez	Carlos Fabián Castaño Romero	Beatriz María Rivas López
Conrado Jorge Finnigan	Carlos Gutiérrez Cerrajero	Belén Cigarral García
Cristina Carbonell Muñoz	Carlos Llanes Álvarez	Berta Bote Bonaechea
Cristina Cigarral García	Catalina Gil Restrepo	Bianca Paz Renau Mínguez
Cristina De Ramón Sánchez	Cátia Daniela Quintas Faria	Blanca Fuentes Herrero
Cristina Egido Turrión	Cecilia Higueruela Mínguez	Borja Miguel López
Dalia Salim Quwaider	Clara Llorente González	Carlos Fabián Castaño Romero
Daniel Esteban Rivera Delgado	Clara Sánchez Pablo	Carlos Gutiérrez Cerrajero
Daniela Pinto Damasceno	Claudia Pérez Carretero	Carlos Llanes Álvarez
David González Calle	Conrado Jorge Finnigan	Catalina Gil Restrepo
Diana Esther Castilla Perera	Consolación Rosado Rubio	Cátia Daniela Quintas Faria
Elena Blanco Álvarez	Cristina Carbonell Muñoz	Clara Llorente González
Elena Díaz Peláez	Cristina de Ramón Sánchez	Clara Sánchez Pablo
Elena Martín Doncel	Cristina Egido Turrión	Claudia Pérez Carretero
Elena Martín González	Cristina Fernández Infante	Cristian Morillo Losada
Elena Navarro Carrasco	Cristina Juliá Álvarez	Cristina Carbonell Muñoz
Elena Orgaz Rivas	Cristina Sofía Baz Villoria	Cristina Cigarral García
Elizabeta De Los Ángeles Rojas Ricardo	Dalia Salim Quwaider	Cristina De Ramón Sánchez
Esperanza Macarena Algarín Pachón	Daniel Esteban Rivera Delgado	Cristina Egido Turrión
Ester Laso Lucas	Daniela Pinto Damasceno	Cristina Fernández Infante
Ester Parra Vidales	David González Calle	Cristina Juliá Álvarez
Eva García Piney	Diana Esther Castilla Perera	Daniela Pinto Damasceno
Eva María Bravo Barba	Elena de Dios Rodríguez	David González Calle
Eva María Diez Baeza	Elena Díaz Peláez	Diana Esther Castilla Perera
Félix López Cadenas	Elena Gómez Barragues	Eduardo Sobejano Fuertes
Francisco Javier Ortega García	Elena Martín Doncel	Elena De Dios Rodríguez
Francisco Javier Peñalver Parraga	Elena Martín González	Elena Díaz Peláez
Francisco José Campos Laborie	Elena Navarro Carrasco	Elena Martín González
Guillermo Rodríguez Hernández	Elena Orgaz Rivas	Elena Navarro Carrasco
Henar Pérez Ramos	Elena Sánchez Luis	Elena Sánchez Luis
Hernán Juan Llorente Cancho	Elena Vuelta Ramos	Elena Terraza Silvestre
Idoia García Ramírez	Eliana María Taveras Domínguez	Elena Vuelta Ramos
Ignacio Campillo Marcos	Elísabet González DEL Portillo	Eliana María Taveras Domínguez
Ignacio Criado García	Elizabeta de los Ángeles Rojas Ricardo	Elizabeta De Los Ángeles Rojas Ricardo
Inmaculada Serramito Gómez	Esperanza Macarena Algarín Pachón	Esperanza Macarena Algarín Pachón
Irene Andrés Ramos	Estanislao Arana Fernández de Moya	Estanislao Arana Fernández De Moya
Isabel Corbacho Cambero	Ester Parra Vidales	Ester Parra Vidales
Isabel Valriberas Herrero	Eva García Piney	Eva García Piney
Javier Ignacio Muñoz González	Eva María Bravo Barba	Eva Monte Serrano
Jésica Pérez García	Eva Monte Serrano	Félix López Cadenas

2017 / 2018	2018 / 2019	2019 / 2020
Jesús María Hernández Sánchez	Fany Verónica Ticona Pérez	Fernando Sánchez Sáez
José Carlos Moreno Samos	Félix López Cadenas	Francisco Javier García García
José Javier Garrido Sánchez	Fernando Sánchez Sáez	Francisco Javier Morán Plata
Josepa Sebastia Morant	Francisco Javier Ortega García	Gerardo Javier Martí Chillón
Juan Carlos Caballero Berrocal	Francisco Javier Peñalver Parraga	Guillermo Oliva Ariza
Julie Milena Galvis Jiménez	Gerardo Javier Martí Chillón	Ignacio Jesús Cardona Benavides
Julio Davila Valls	Guillermo Oliva Ariza	Inés Romero Pérez
Kamila Magdalena Janusz	Guillermo Rodríguez Hernández	Inmaculada Serramito Gómez
Laura Clavaín Mateo	Henar Pérez Ramos	Irene Andrés Ramos
Laura Díaz Gil	Idania de los Santos Ventura	Irene Esparcia Arnedo
Laura Gómez Hernández	Ignacio Campillo Marcos	Isabel Valriberas Herrero
Laura Manzanedo Bueno	Inés Romero Pérez	Itzel Rivera Santos
Laura Ruiz Remolina	Inmaculada Serramito Gómez	Javier Ignacio Muñoz González
Laura Sánchez Montori	Irene Andrés Ramos	Javier Raboso Gallego
Leticia Gómez Sánchez	Irene Gil Torres	Javier Zamarreño Lozano
Lorena Bellido Hernández	Isabel Corbacho Cambero	Jendri Manuel Pérez Perozo
Lucía Gandullo Sánchez	Isabel Valriberas Herrero	Jesús Manuel Sampedro Gómez
Lucía Pinzón Uribe	Javier Ignacio Muñoz González	José Andrés Lorenzo Martín
Luis Francisco Lorenzo Martín	Javier Raboso Gallego	José Javier Garrido Sánchez
Luis Gonzaga Díaz González	Jendri Manuel Pérez Perozo	José Luis Revuelta Herrero
Luis Hernández Cano	Jésica Pérez García	Josepa Sebastia Morant
Luis Ignacio Martin Leal	Jesús Manuel Sampedro Gómez	Juan Alejandro Cascón Hernández
Luzalba Del Carmen Sanoja Flores	Jesús María Hernández Sánchez	Juan Carlos Caballero Berrocal
M.De La Paz Vaquero Herrero	José Javier Garrido Sánchez	Juan Carlos Fiorini Talavera
Marco López Zubizarreta	José Luis Revuelta Herrero	Judith López Luis
María Auxiliadora Brenes Fernández	Josepa Sebastia Morant	Julie Milena Galvis Jiménez
María Carmela Rodríguez Martín	Juan Alejandro Cascon Hernandez	Julio Davila Valls
María Del Pilar Leoz	Juan Carlos Caballero Berrocal	Laura Clavaín Mateo
María Fernández Regueras	Juan Luis Muñoz Sánchez	Laura Díaz Gil
María García Álvarez	Julie Milena Galvis Jiménez	Laura Gómez Hernández
María González González	Julio Davila Valls	Lorena Carrascal Laso
María González-Tablas Pimenta	Kamila Magdalena Janusz	Lucía Fernández Nevado
María Isabel Garavís Vicente	Laura Clavaín Mateo	Lucia Gandullo Sánchez
María Isabel Prieto Conde	Laura Díaz Gil	Luis Figuero Pérez
María Jesús Canal Boyero	Laura Gómez Hernández	Luís Gómez-Lechón Quirós
María Mercedes Alperi López	Laura Manzanedo Bueno	Luis Hernández Cano
María Teresa Cano Mozo	Lorena Bellido Hernández	Luzalba Del Carmen Sanoja Flores
María Teresa González Sánchez	Lorena Carrascal Laso	M.De La Paz Vaquero Herrero
Marta Alonso Fernández De Gatta	Lucía Fernández Nevado	Mª Concepción Piñero Pérez
Marta Gómez Iglesias	Lucia Gandullo Sánchez	Manuel Domínguez Gómez
Marta Martín Izquierdo	Lucia Pinzón Uribe	Marco López Zubizarreta

2017 / 2018	2018 / 2019	2019 / 2020
Martina Vanova	Luis Francisco Lorenzo Martín	María Ángeles Fidalgo Fernández
Mercedes Garzón Martínez	Luís Gómez-Lechón Quirós	María Auxiliadora Brenes Fernández
Miguel Quijada Álamo	Luis Hernández Cano	María Carmela Rodríguez Martín
Miriam López Parra	Luzalba del Carmen Sanoja Flores	María Cristina Hidalgo Calleja
Mónica Baile González	Manuel Domínguez Gómez	María Del Carmen Martín Gómez
Mónica Morais Gomes Ferreira	Marco López Zubizarreta	María Del Pilar Leoz Allegretti
Natalia Eugenia Espinosa Lara	María Amparo Mateos Diego	María Dolores Calabria Gallego
Natalia Felipe Medina	María Ángeles Fidalgo Fernández	María Elena Tundidor Sanz
Natalia Sánchez Aguadero	María Asunción Juanes Bellido	María Elisa Acosta De La Vega
Noelia Dasilva Freire	María Auxiliadora Brenes Fernández	María García Duque
Noemí Muñoz García	María Carmela Rodríguez Martín	María González-Tablas Pimenta
Oscar González Velasco	María Cristina Hidalgo Calleja	María Isabel Garavís Vicente
Pablo Álvarez Vega	María del Pilar Leoz	María Jesús Baldeón Conde
Pablo Segovia Alonso	María Dolores Calabria Gallego	María Jesús Canal Boyero
Pamela Vázquez Cárdenas	María Elena Tundidor Sanz	María Millán Salanova
Paola María Fradejas Salazar	María Fernández Regueras	María Ovejero Sánchez
Patricia Martínez Pérez	Maria García Álvarez	María Paulina Pérez Yuste
Patricia Morejón García	María González-Tablas Pimenta	María Teresa González Sánchez
Pedro Mogollón Arroyo	María Isabel Garavís Vicente	Mariana Sánchez Magdaleno
Rachid Taouil	María Jesús Baldeón Conde	Marta Gómez Iglesias
Rafael Hipola Muñoz	María Jesús Canal Boyero	Marta Gómez Sánchez
Ramón Rodríguez Borrego	María Mercedes Alperi López	Marta Isidro Hernández
Raquel García Vilchez	María Millán Salanova	Marta López Serna
Raquel Jiménez Gómez	María Ovejero Sánchez	Marta Martín Izquierdo
Raquel Moreno Mayordomo	María Paulina Pérez Yuste	Marta Ortiz Aneiros
Raquel Villamuera Del Sordo	María Teresa González Sánchez	Mauricio Molinari Ulate
Raúl García González	Marta Alonso Fernández de Gatta	Miguel Quijada Álamo
Rebeca Lozano Mejorada	Marta Gómez Iglesias	Miriam López Parra
Rebeca Sánchez González	Marta Martín Izquierdo	Natalia Eugenia Espinosa Lara
Roberto Corchado Cobos	Marta Ortiz Aneiros	Natalia Felipe Medina
Rocío Fuentes Mateos	Mercedes Garzón Martínez	Natalia Fernández Parejo
Ronald Paul Macías Casanova	Miguel Quijada Álamo	Natalia García Sancha
Rosa Ana Marcos Sánchez	Miriam Álvarez Álvarez	Nerea Gestoso Uzal
Rosario Alonso Domínguez	Miriam López Parra	Noemí Muñoz García
Rubén Fernández Caloto	Mónica Baile González	Olga Durán Bobín
Santiago José Bueno Fortes	Mónica Morais Gomes Ferreira	Oscar González López
Sara García Alonso	Natalia Eugenia Espinosa Lara	Oscar González Velasco
Sara Gutiérrez Herrero	Natalia Felipe Medina	Pablo Juanes Velasco
Sara Teresa González De Tena-Dávila	Natalia Fernández Parejo	Pablo Luengo Mondéjar
Silvia Preciado Pérez	Natalia García Sancha	Pablo Segovia Alonso
Silvio Ragozzino	Nerea Gestoso Uzal	Pamela Vázquez Cárdenas

2017 / 2018	2018 / 2019	2019 / 2020
Sonia Gómez Gaspar	Noemí Muñoz García	Patricia Morejón García
Sonia Rodríguez Fernández	Olga Durán Bobín	Paula García Vallés
Soraya Jodra Sánchez	Oscar González Velasco	Pedro Mogollón Arroyo
Soraya Merchán Gómez	Pablo Luengo Mondéjar	Pilar Andrés Olivera
Susana Hernández García	Pablo Segovia Alonso	Rachid Taouil Hammouti
Susana Riesco Riesco	Pamela Vázquez Cárdenas	Rafael Hipola Muñoz
Svetlana Zhilina	Paola María Fradejas Salazar	Rafael Roberto Rodríguez Calzada
Tamara Jiménez Solas	Patricia Morejón García	Ramón Rodríguez Borrego
Vega Riesco Cuadrado	Paula García Vázquez	Raquel García Vilchez
Verónica González De La Calle	Pedro Mogollón Arroyo	Raquel Jiménez Gómez
Verónica Temprado Moreno	Rachid Taouil	Raquel Sainz Urruela
Víctor Miguel Martín Granado	Rafael Benito Melero González	Raquel Villamuera Del Sordo
Yazmine Bejarano Condezo	Rafael Hipola Muñoz	Raúl García González
Yolanda María Guillen Pérez	Rafael Roberto Rodríguez Calzada	Rebeca Lozano Mejorada
Yuliana Mónica Jamanca Poma	Ramón Rodríguez Borrego	Roberto Corchado Cobos
	Raquel García Vilchez	Rocío Fuentes Mateos
	Raquel Jiménez Gómez	Rocío Taboada Taboada
	Raquel Moreno Mayordomo	Rubén Fernández Caloto
	Raquel Villamuera del Sordo	Sara Marcos Asensio
	Raúl García González	Sofía María Toribio Castelló
	Rebeca Lozano Mejorada	Sofía Matilla Vicente Almazán
	Roberto Corchado Cobos	Soledad Medina Valdivieso
	Rocío Fuentes Mateos	Sonia Gómez Gaspar
	Rocío Taboada Taboada	Sonia Miguel Criado
	Rosa Ana Marcos Sánchez	Sonia Peña Balbuena
	Rosario Alonso Domínguez	Tamara Jiménez Solas
	Rubén Fernández Caloto	Tomas Fernando Benito González
	Ruth García García	Valentina Ramírez Maldonado
	Santiago José Bueno Fortes	Víctor Eduardo Vallejo García
	Sara Teresa González DE Tena-Dávila	Víctor Manuel Pérez Rosa
	Silvia Preciado Pérez	Yazmine Bejarano Condezo
	Soledad Medina Valdivieso	Yolanda María Guillen Pérez
	Sonia Gómez Gaspar	
	Sonia Rodríguez Fernández	
	Tamara Jiménez Solas	
	Tatiana Mallely Matajira Chia	
	Tomas Fernando Benito González	
	Vega Riesco Cuadrado	
	Verónica Temprado Moreno	
	Yazmine Bejarano Condezo	
	Yolanda María Guillén Pérez	

TRAINING ACTIVITIES

DOCTORAL THESES

PhD STUDENT	DIRECTOR	TITLE	DATE
Vanessa Carolina Rivero Perdomo	Rogelio González-Sarmiento	*Nuevas aproximaciones en el estudio de la ruta autofágica en cáncer colorrectal*	19/01/2018
Sara García Alonso	Atanasio Pandiella Alonso	*Anticuerpos conjugados a fármacos frente a receptores ErbB: Nuevas indicaciones y mecanismos de resistencia*	13/03/2018
Aline Rodrigues Françoso	Juan Jesús Cruz Hernández / Rosa González del Rio / Raquel Seijas Tamayo	Análisis de posibles diferencias clínicoanatomopatológicas y de supervivencia entre las pacientes con cáncer de mama con criterios de asociación al Síndrome de Cáncer de Mama y Ovario Hereditario (con y sin mutación en BRCA1/2) y con cáncer de mama esporádico	24/04/2018
Sara Gutiérrez Herrero	Carmen Guerrero Arroyo	*Función de C3G en la señalización plaquetaria, utilizando modelos de ratón transgénicos*	7/05/2018
Verónica González De La Calle	Mª Victoria Mateos Manteca/ Norma Carmen Gutiérrez Gutiérrez	*Factores pronósticos en el mieloma múltiple en fase asintomática y sintomática*	28/05/2018
Susana Hernández García	Enrique M. Ocio San Miguel / Mercedes Garayoa Berrueta / Teresa Paíno Gómez	*Evaluación del efecto sinérgico del inhibidor de las "Kinesin Spindle Proteins" Filanesib (arry-520) en combinación con fármacos inmunomoduladores en modelos preclínicos de mieloma múltiple*	19/06/2018
Ignacio Criado García	Julia Almeida Parra / Alberto Orfao de Matos	*Caracterización fenotípica, citogenética y molecular de pequeños clones de linfocitos B de individuos sanos frente a su contrapartida maligna de la leucemia linfática crónica B*	4/07/2018
Mª Isabel Prieto Conde	Marcos González Díaz / Mª del Carmen Chillón Santos	*Caracterización genómica de la leucemia mieloblástica aguda: utilidad clínica del perfil molecular en el diagnóstico, pronóstico y monitorización terapéutica*	6/07/2018
Elena Blanco Álvarez	Martín Pérez Andrés / Alberto Orfao de Matos	*Desarrollo de nuevas estrategias para diagnóstico y clasificación de inmunodeficiencias predominantemente de anticuerpos*	12/07/2018
Oriana Jimena López Godino	Mª Dolores Caballero Barrigón / Lucía López-Corral	*Transplante alogénico de progenitores hematopoyéticos en el Hospital Universitario de Salamanca: eficacia, complicaciones e impacto de los nuevos procedimientos tras 20 años de experiencia*	19/07/2018
Blanca Nieto Bernáldez	Mercedes Dosil Castro	*Intermediate maturation stages of the human 40S ribosomal subunit*	20/07/2018
Eva María Díez Baeza	Alejandro Martín García-Sancho / Mª Dolores Caballero Barrigón / Emilia Pardal de la Mano	*Análisis de pacientes ancianos con linfoma B agresivo: Estudio observacional retrospectivo sobre características clínicas, factores pronósticos y eficacia del tratamiento*	6/09/2018
Francisco José Campos Laborie	Javier de las Rivas Sanz / José Manuel Sánchez Santos	*Bioinformatics applied to human genomics and proteomics: development of algorithms and methods for the discovery of molecular signatures derived from omic data and for the construction of co-expression and interaction networks*	14/09/2018

PhD STUDENT	DIRECTOR	TITLE	DATE
María González González	Alberto Orfao de Matos / José María Sayagués Manzano / Manuel Fuentes García / Luis Muñoz Bellvis	*Identificación de biomarcadores genómicos en el cáncer colorrectal esporádico*	17/09/2018
Luis López Mesonero	Rogelio González Sarmiento / José Carlos Gómez Sánchez	*Longitud del telómero, polimorfismos de la telomerasa y autofagia en el pronóstico funcional de pacientes con ictus*	20/09/2018
Ester Laso Lucas	Rogelio González Sarmiento / Ricardo Usategui Martín	*Polimorfismos genéticos implicados en la respuesta al tratamiento de deshabituación tabáquica*	21/09/2018
Ariana Centa	Atanasio Pandiella Alonso / Juan Carlos Montero González	*Dominios funcionales de las neuregulinas y su uso como dianas terapéuticas*	28/09/2018
Marta Alonso Fernández De Gatta	Ana Martín García / María Díez Campelo, como tutor D. Rogelio González Sarmiento	*Cardiopatía estructural y cardiotoxicidad por depósito de hierro en pacientes con síndrome mielodisplásico de bajo riesgo*	11/03/2019
Mónica Morais Gomes Ferreira	Rogelio González Sarmiento / Mª José Doyagüe Sánchez	*Cáncer de ovario: Cambios en el manejo y en el pronóstico debido a las nuevas clasificaciones FIGO y OMS y análisis de genes reparadores de DNA*	18/03/2019
Fany Verónica Ticona Pérez	Atanasio Pandiella Alonso / María Elena Díaz Rodríguez	*Dianas terapéuticas en mieloma múltiple: desregulación de miRNAs y TRAIL*	9/04/2019
Consolación Rosado Rubio	Rogelio González Sarmiento	*Análisis clínico y genético del síndrome de Alport y la nefropatía del colágeno IV (α3/α4)*	24/05/2019
Miriam Álvarez Álvarez	Rogelio González Sarmiento / Raquel Manso Calderón	*Análisis de polimorfismos de genes relacionados con la reparación de DNA, La apoptosis, la autofagia y gen PRNP en pacientes con demencia vascular y enfermedad del Alzheimer*	31/05/2019
Luis Francisco Lorenzo Martín	Xosé Ramón García Bustelo y como tutora Dª Mercedes Dosil Castro	*Rho Exchange Factors in the Regulation of Squamous Cell Stemness and Carcinogenesis*	21/06/2019
María García Álvarez	Marcos González Díaz / Miguel Alcoceba Sánchez / Ramón García Sanz	*Caracterización del linfoma folicular y predicción de la transformación histológica a linfoma agresivo: mecanismos moleculares e implicaciones pronósticas*	24/06/2019
Jésica Pérez García	Rogelio González Sarmiento	*Cáncer colorrectal en el adulto joven, una entidad diferente*	28/06/2019
Sonia Rodríguez Fernández	Xosé Ramón García Bustelo y Mercedes Dosil Castro (como tutora)	*Characterization of new regulatory mechanisms and metabolic roles for VAV proteins*	5/07/2019
Kamila Janusz	Jesús Mª Hernández Rivas / María Díez Campelo / María Abáigar Alvarado	*Characterization by Next Generation Sequencing of mutations of spliceosome genes and bone marrow mesenchymal cells in patients with myelodysplastic syndromes*	24/07/2019

PhD STUDENT	DIRECTOR	TITLE	DATE
Lorena Bellido Hernández	Juan Jesús Cruz Hernández / Óscar Bengoechea Miranda / Raquel Seijas Tamayo	*Estudio de moléculas de adhesión y migración en cáncer colorrectal*	24/07/2019
Arturo Carabias Del Rey	José Mª de Pereda Vega / Carmen Guerrero Arroyo	*Mechanisms of auto-regulation and activation of the guanine nucleotide exchange factor C3G*	25/07/2019
Ignacio Campillo Marcos	Pedro A. Lazo-Zbikowski Taracena	*Nuevas funciones de la quinasa humana VRK1 en la respuesta al daño en el ADN y la estructura de la cromatina*	26/07/2019
Jesús Mª Hernández Sánchez	Jesús Mª Hernández Rivas / Mª del Rocío Benito Sánchez / Ana Eugenia Rodríguez Vicente	*Therapy-induced changes in the gene expression profile of patients with hematological diseases*	2/09/2019
Elena Martín Doncel	Pedro A. Lazo-Zbikowski Taracena	*Implicación de la quinasa humana VRK1 en enfermedades neurodegenerativas*	3/09/2019
Aránzazu García Mateo	Mª Victoria Mateos Manteca y como tutor D. Alberto Orfao de Matos Correia e Vale	*Gammapatia Monoclonal de Significado Incierto en la provincia de Segovia: Estudio poblacional y factores pronósticos (células plasmáticas en sangre periférica por inmunofenotipo y ensayo de cadena pesada-ligera de las inmunoglobulinas)*	3/09/2019
Santiago Bueno Fortes	Javier de las Rivas Sanz / Manuel Martín-Merino Acera	*Development and application of bioinformatic methods to analyse genome-wide expression and survival data from cancer patients*	5/09/2019
Guillermo Rodríguez Hernández	Isidro Sánchez García / Carolina Vicente Dueñas	*Mecanismos moleculares implicados en la génesis de la leucemia linfoblástica aguda B infantil*	6/09/2019
Silvia Preciado Pérez	Fermín Sánchez-Guijo Martín / Mª Dolores Caballero Barrigón / Sandra Muntión Olave	*Papel del estroma medular en la mejora de la función hematopoyética: Desde la irradiación hasta las vesículas extracelulares*	6/09/2019
Ana María Orive Ramos	Atanasio Pandiella Alonso	*Implicación de los receptores ERBB/HER y sus ligandos en la búsqueda de nuevas estrategias terapéuticas en cáncer de mama*	25/09/2019
Vitor Dessanti Botafogo Gonçalves	Alberto Orfao de Matos / Julia Almeida Parra	*Identificação de múltiplas supopulações de células T CD4+ funcionalmente relevantes através da citometría de fluxo de 14 cores: Desenvolvimento, padronização e validação do método*	15/10/2019
Laura Gómez Hernández	Alberto Martín Pendás / Elena Llano Cuadra	*Functional analysis of mammalian gametogenesis*	4/12/2019
Inmaculada Serramito Gómez	Felipe Xosé Pimentel Muiños	*Mecanismos autofágicos no convencionales implicados en la regulación del tráfico endocítico y la señalización celular*	17/12/2019

CONFERENCE MEETINGS & SCIENTIFIC COURSES

1. ESPECTROMETRÍA DE MASAS EN INVESTIGACIÓN BIOMÉDICA

(http://www.cicancer.org/es/eventos/269/espectrometria-de-masas-en-investigacion-biomedica)

Speakers: Dr. Arndt Asperger Bruker Applications Group leader MALDI-TOF, Dr. Francesc Márquez. Especialista en Blociencias

Organization: ProteoRed-Bruker / Centro de Investigación del Cáncer de Salamanca

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

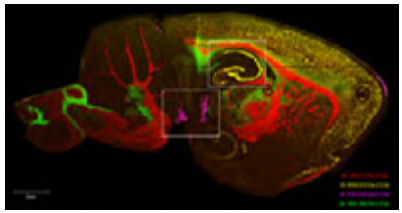
Date: 20/02/2018

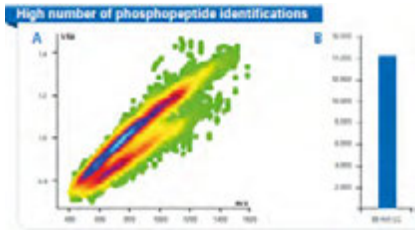
Summary: El objetivo fundamental de la jornada es dar a conocer las nuevas herramientas disponibles basadas en espectrometría de masas en el campo de imagen molecular MALDI y proteómica, orientadas a la resolución de los retos actuales en la investigación biomédica.

Se presentarán diferentes soluciones basadas en espectrometría de masas, especialmente la técnica de imagen molecular MALDI IMAGING. Esta técnica emergente permite detectar y localizar proteínas, péptidos o metabolitos directamente sobre un tejido. La combinación de la imagen molecular con las técnicas histológicas tradicionales ofrece un salto adelante en el campo de la histopatología.

En la sesión de proteómica se mostrarán datos de la última innovación tecnológica de Bruker: El sistema timsTOF PRO con tecnología PASEF. Gracias a la adopción de la tecnología PASEF se ha producido un importante avance en la cantidad y calidad de datos obtenidos en estudios de proteómica, lo que proporciona una mayor proporción de péptidos y proteínas identificados y cuantificados, hasta ahora muy difícil de alcanzar en muestras con poca cantidad de material de partida. Asímismo la tecnología PASEF ofrece ventajas en el estudio de modificaciones post-traduccionales como las fosforilaciones

Program: https://www.bruker.com/events/2018/mass-spectrometry/seminario-bruker.html





2. JORNADA INFORMATIVA EN EL CENTRO DE INVESTIGACIÓN DEL CÁNCER " LA OPCIÓN DE DEDICARSE A LA INVESTIGACIÓN EN BIOMEDICINA O BIOLOGÍA FUNDAMENTAL"

(http://www.cicancer.org/es/eventos/276/jornadas-informativas-en-el-centro-de-investigacion-del-cancer)

Speaker: Mercedes Dosil

Organization: Centro de Investigación del Cáncer de Salamanca

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 27-28 /02/2018

3. ÚLTIMOS AVANCES EN ESPECTROMETRÍA DE MASAS Y EN ANÁLISIS DE DATOS PARA PROTEÓMICA CUANTITATIVA

(http://www.cicancer.org/es/eventos/279/ultimos-avances-en-espectrometria-de-masas-y-en-analisis-de-datos-para-proteomica-cuantitativa)

Speakers: Bernabé Bodas; Manuel Fuentes; Javier Lago; Bruno Manadas; Antonio Serna

Organization: ProteoRed-SCIEX / Centro de Investigación del Cáncer

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 21/03/2018

Summary:

- Puesta en valor de una tecnología sólida y ampliamente probada.
- Presentación de los últimos avances tecnológicos en Espectrometría de Masas, TTOF 6600®.
- Capacidad de análisis, tanto cualitativos como cuantitativos, simultáneamente, SWATH®.
- Solución total integrada, con el software completo de tratamiento de datos.

Program: (http://www.cicancer.org/es/eventos/279/ultimos-avances-en-espectrometria-de-masas-y-en-analisis-de-datos-para-proteomica-cuantitativa)

4. HARNESSING THE POWER OF EXOSOMES: BIOMARKER DISCOVERY & ENGINEERING

(http://www.cicancer.org/es/eventos/284/harnessing-the-power-of-exosomes-biomarker-discovery-engineering)

Speaker: Dra. Elena Miñones-Moyano (Technical Specialist, System Biosciences - SBI (Palo Alto, CA)

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 09/05/2018

5. X SIMPOSIUM BASES BIOLÓGICAS DEL CÁNCER Y TERAPIAS PERSONALIZADAS

(http://www.cicancer.org/es/eventos/285/x-simposium-de-bases-biologicas-del-cancer-y-terapias-personalizadas)

Date: 17/05/2018 to 18/05/2018

Scientific Director: Prof. Juan Jesús Cruz Hernández (Hospital Clínico Universitario / Universidad de Salamanca)

Coordinator: Dr. César A. Rodríguez (Hospital Clínico Universitario / Universidad de Salamanca)

Venue: Centro de Investigación del Cáncer de Salamanca. Salón de Actos, Campus Miguel de Unamuno s/n. Salamanca

Program:

MAY 17, 2018

09:00-09:15
BIENVENIDA Y PRESENTACIÓN
Dr. Juan Jesús Cruz, Hospital Clínico Universitario de Salamanca-IBSAL /
Dr. Eugenio Santos de Dios, Centro de Investigación del Cáncer de Salamanca

09:00-09:45
CONFERENCIA INAUGURAL

Moderador: Dr. Emilio Alba, Hospital Universitario Regional Virgen de la Victoria, Málaga

Diez años de avances en el conocimiento sobre la biología y el tratamiento del cáncer / Dr. Eduardo Díaz-Rubio, Académico de la RANM. Prof Emérito Universidad Complutense de Madrid

09:45-10:15
CONFERENCIA EDUCACIONAL 1

Moderadores: Dr. José Enrique Alés, Hospital de Nuestra Señora de Sonsoles, Ávila / Dra. Amalia Gómez Bernal, Hospital Clínico Universitario de Salamanca-IBSAL

Bases biológicas del cáncer ovario en el siglo XXI / Dr. Javier de Castro, Hospital Universitario La Paz, Madrid

10:15-11:15
MESA REDONDA 1

Diez años de avances en el tratamiento del cáncer ginecológico

Moderadores: Dra. Beatriz Esteban, Complejo Asistencial de Segovia / Dr. José Valero Álvarez, Complejo Asistencial de Zamora

Estrategia terapéutica actual del cáncer de ovario / Dr. Andrés Redondo, Hospital Universitario La Paz, Madrid

Optimizando el tratamiento del cáncer de cérvix / Dr. Andrés Redondo, Hospital Universitario La Paz, Madrid

11:45-12:15
CONFERENCIA EDUCACIONAL 2

Moderador: Dr. Rogelio González Sarmiento, Instituto de Investigación Biomédica de Salamanca (IBSAL)

Bases biológicas del cáncer: biología molecular y microambiente tumoral en

melanoma maligno / Dr. Alfonso Berrocal, Hospital General Universitario de Valencia

12:15-13:15
MESA REDONDA 2

Diez años de avances en el tratamiento del melanoma maligno

Moderadores: Dr. José Luis González Larriba, Hospital Clínico San Carlos, Madrid / Dr. Salvador Martín Algarra, Hospital Clínica de Navarra, Pamplona

Avances en inmunoterapia / Dr. Enrique Espinosa, Hospital Universitario La Paz, Madrid

Otras moléculas y combinaciones / Dra. Lorena Bellido, Hospital Clínico Universitario de Salamanca-IBSAL

13:15-14:00
COMPARTIENDO CONOCIMIENTO

La biopsia líquida, del laboratorio a la práctica clínica

Moderadores: Dr. Enrique Grande, MD Anderson Cancer Center, Madrid / Dr. Pedro Lazo-Zbikowski, Centro de Investigación del Cáncer de Salamanca

¿Qué nos ofrece el laboratorio? técnicas disponibles, ventajas e inconvenientes / Dr. Isidro Sánchez, Centro de Investigación del Cáncer, Salamanca

¿Qué espera un clínico de la biopsia líquida? aplicaciones reales y potenciales de la biopsia líquida / Dr. César A. Rodríguez, Hospital Clínico Universitario de Salamanca-IBSAL

15:15-15:45
CONFERENCIA EDUCACIONAL 3

Moderadores: Dr. Jesús García Mata, Hospital Santa María de Nai, Ourense / Dr. Ignacio Chacón, Hospital Virgen de la Salud, Toledo

Bases biológicas del cáncer de mama: heterogeneidad tumoral. Perspectiva actual y retos inmediatos / Dr. Atanasio Pandiella, Centro de Investigación del Cáncer, Salamanca

15:45-17:00
MESA REDONDA 3

Diez años de avances en el tratamiento del cáncer de mama

Moderadores: Dr. Miguel Martín, Hospital General Universitario Gregorio Marañón, Madrid / Dra. Ana Lluch, Hospital Clínico Universitario de Valencia

Enfermedad luminal / Dr. Andrés García Palomo, Complejo Asistencial Universitario de León

Cáncer de mama HER2 positivo / Dr. Juan A. Virizuela, Hospital Universitario Virgen de la Macarena, Sevilla

Cáncer de mama triple negativo / Dra. Manuel Ruiz Borrego, Hospital Universitario Virgen del Rocío, Sevilla

17:30-18:00
CONFERENCIA EDUCACIONAL 4

Moderadores: Dr. Enrique Aranda, Hospital Universitario Reina Sofía, Córdoba / Dr. Antonio Antón, Hospital Universitario Miguel Servet, Zaragoza

Bases biológicas del cáncer colorrectal: diversidad biológica y sus repercusiones en la práctica clínica / Dra. Ruth Vera, Complejo Hospitalario de Navarra, Pamplona

18:00-19:45
MESA REDONDA 4

Diez años de avances en el tratamiento de los tumores digestivos

Moderadores: Dr. Alfredo Carrato, Hospital Universitario Ramón y Cajal, Madrid / Dr. Emilio Fonseca, Hospital Clínico Universitario de Salamanca-IBSAL

Cáncer de colon / Dra. Pilar García Alfonso, Hospital General Universitario Gregorio Marañón, Madrid

Cáncer gástrico / Dr. Juan Carlos Torrego, Hospital Río Hortega, Valladolid

Tumores neuroendocrinos / Dr. Miguel Navarro, Hospital Clínico Universitario de Salamanca-IBSAL

Cáncer de páncreas / Dr. Fernando Rivera, Hospital Universitario Marqués de Valdecilla, Santander

MAY 18, 2019

09:00-9:30
CONFERENCIA EDUCACIONAL 5

Moderadores: Dra. Pilar Garrido, Hospital Universitario Ramón y Cajal, Madrid / Dr. Emilio Esteban, Hospital Universitario Central de Asturias, Oviedo

Bases biológicas del cáncer de pulmón: el largo viaje de los subtipos histológicos a la clasificación molecular / Dr. David Vicente, Hospital Universitario Virgen de la Macarena, Sevilla

09:30-10:30
MESA REDONDA 5

Diez años de avances en el tratamiento del cáncer de pulmón no microcítico

Moderador: Dr. Carlos García Girón, Complejo Asistencial Universitario de Burgos

La Inmunoterapia en el tratamiento del CPNM avanzado. ¿Cuál, cómo, cuándo y a quienes? / Dra. Rosario García Campelo, Complejo Hospitalario Universitario de A Coruña

Otras terapias biológicas en CPMN: selección y secuencia óptima del tratamiento / Dra. Dolores Isla, Hospital Clínico Universitario Lozano Blesa, Zaragoza

10:30-11:00
CONFERENCIA EDUCACIONAL 6

Moderadores: Dr. Juan Jesús Cruz, Hospital Clínico Universitario de Salamanca-IBSAL / Dr. Diego Soto de Prado, Hospital Clínico Universitario de Valladolid

Bases biológicas del cáncer de cabeza y cuello: una visión actualizada / Dr. Rogelio González Sarmiento, Instituto de Investigación Biomédica de Salamanca (IBSAL)

11:00-12:00
MESA REDONDA 6

Diez años de avances en el tratamiento del cáncer de cabeza y cuello

Moderadores: Dra. Elvira del Barco, Hospital Clínico Universitario de Salamanca-IBSAL / Dr. Alberto Arizcun, Hospital Río Carrión, Palencia

Incorporación de la inmunoterapia a la estrategia de tratamiento del cáncer de cabeza y cuello / Dr. Ricard Mesía, Hospital Universitari German Trias i Pujol, Badalona

Quimioterapia y otras terapias biológicas en cáncer de cabeza y cuello / Dra. Yolanda Escobar, Hospital General Universitario Gregorio Marañón, Madrid

12:30-13:00
CONFERENCIA EDUCACIONAL 7
Moderadores: Dr. Germán Martín, Hospital Clínico Universitario de Salamanca-IBSAL / Dr. Vicente Guillem, Instituto Valenciano de Oncología, Valencia

Bases biológicas del cáncer de próstata / Dra. Rebeca Lozano, CNIO-IBIMA, Madrid

13:00-14:00
MESA REDONDA 7
Diez años de avances en el tratamiento del cáncer genitourinario
Moderadores: Dr. Javier Cassinello, Hospital Universitario de Guadalajara / Dra. Rocío García Domínguez, Hospital Clínico Universitario de Salamanca-IBSAL

Cáncer de próstata. Ofreciendo una secuencia óptima de tratamiento / Dr. Enrique Gallardo, Hospital Universitari Parc Taulí, Sabadell

Nuevos paradigmas en el tratamiento del cáncer vesical avanzado / Dr. Martín Lázaro, Hospital Álvaro Cunqueiro, Vigo

Una aproximación actual a las diferentes líneas de tratamiento en cáncer renal / Dr. José Ángel Arranz, Hospital General Universitario Gregorio Marañón, Madrid

6. SEMINARIO PMC "PATOLOGÍA MOLECULAR COMPARADA, APOYANDO A LA INVESTIGACIÓN"

(http://www.cicancer.org/es/eventos/288/seminario-pmcpatologia-molecular-comparada-apoyando-a-la-investigacion)

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 01/06/2018

Summary: Mediante este Seminario se da a conocer la Cartera de Servicios y el Flujo de Trabajo de la Unidad de Servicios de Patología Molecular Comparada y está dirigido a la Comunidad Científica (Centros de Investigación, Hospitales y Universidades).

- Presentación: Dra. Carmen García Macías, Directora Científica del Servicio de PMC.
- Técnicas Histológicas: Telmo Rodrigues Teixeira, Técnico Especialista de Anatomía Patológica.
- Técnicas Inmunohistoquímicas: Susana Fraile Martín, Técnica Especialista de Laboratorio.
- Equipos de Microscopía: Óptico, Dot-slide, Ariol, Microscopio Láser Microdisección: Telmo Rodrigues Teixeira / Susana Fraile Martín / Sonia Andrés Recio, Técnica Especialista de Laboratorio.
- Gestión, Documentación y Tarifas: Solicitud, Tarifas, Facturación: Jairo Nieto Castro, Técnico Administrativo.
- Diagnóstico Anatomopatológico, Docencia en PMC y Coordinación Técnica del BEOCyL: Dra. Carmen García Macías, Directora Científica del Servicio de PMC y Coordinadora Técnica del BEOCyL.

7. SEBBM-ASEICA-CIBERONC SYMPOSIUM ON GENOMICS, BIOINFORMATICS AND HIGH-THROUGHPUT METHODS FOR THE ANALYSIS OF TUMORIGENIC PATHWAYS.

(https://congresosebbm.santander2018.es/programa/programa-cientifico/simposios/)

Organization: Xosé R. Bustelo

Venue: Hotel Santemar (Calle Joaquín Costa, 28, 39005 Santander, Cantabria)

Date: 13/09/2018

8. CON-CIENCIA-CON-ARTE

(https://concienciaconarte.csic.es/)

Organization: Sandra Blanco Benavente / Almudena Timón

Date: 2019

Summary: **A través de** *Con-ciencia-con-arte* abordaremos aspectos científicos con diversas formas de trabajado multidisciplinar y el fruto de esta colaboración se expondrá al público.

Mediante el proyecto *Con-ciencia-con-arte* pretendemos acercar la ciencia a través del arte, y esperamos concienciar a la sociedad de que el desarrollo científico y tecnológico es uno de los motores del progreso social. Con esta iniciativa queremos crear un espacio donde los científicos y los artistas podamos trabajar juntos, comunicarnos y aprender unos de otros, para finalmente transmitir al público general el conocimiento científico que generamos en un formato más comprensible y sugerente; y mucho menos abstracto. Los científicos y artistas exploraremos la misma cuestión científica a través de con-ciencia-con-arte. Sus diferentes formas de trabajar y abordar el mismo estudio serán posteriormente presentadas al público.

Tanto el arte como la ciencia comparten la creatividad y la abstracción como elementos fundamentales en la búsqueda del deseo de conocimiento. En definitiva, el arte y la ciencia se retroalimentan donde los límites entre ellas se disuelven. Además el arte es un buen formato para desarrollar la cultura científica, en ciencia a menudo la selección de determinadas imágenes busca un criterio estético que armoniza con el contenido científico desarrollado.

Comité Evaluador
Francisco Antequera Márquez
Mercedes Dosil Castro
Sergio Fuentes Rafful
Aquilino Gónzalez Barrio
José Gómez Isla
María del Carmen Guerrero Arroyo
Óscar Lorenzo
Miguel Elías Sánchez Sánchez

Comité Suplente

Comité científico
Julia Almeida Parra
Sandra Blanco Benavente
José María de Pereda
José Ángel Agudo
Montserrat Martínez Ortega
Fernando Silla Cortés
Ántonio González
Mª Jesús Martín Martínez
Raúl Rengel Estévez
Beatriz Rodríguez Vázquez de Aldana
Juan Francisco de Paz Santana
José Manuel Sánchez Santos
Margarita Díaz Martínez
Fernando Leal
David Díez Martín
Esther Fernández Laespada
María Jesús Almendral
Félix Torres Gónzalez

Comité artístico
Miguel Ángel Gasco
Ángel González Quesada
José María Corvo
Mª Ángeles Triana Pascual
Lara Díaz Pérez

9. JORNADA INFORMATIVA EN EL CENTRO DE INVESTIGACIÓN DEL CÁNCER "DECIDIENDO MI POSGRADO ¿TE GUSTA LA BIOMEDICINA?"

Organization: Centro de Investigación del Cáncer de Salamanca

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 14/03/2019

10. XVI CONGRESS OF THE IBERIAN SOCIETY OF CYTOMETRY

(http://www.sic2019.com/)

Date: 09-11/05/ 2019

Place: Hospedería Fonseca / Calle Fonseca, 2 – 37002 Salamanca

Organizing Committee

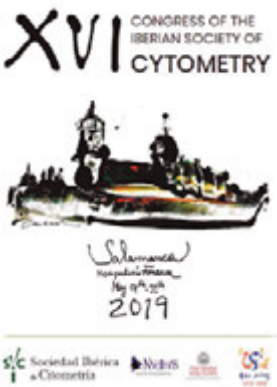
Chair: Julia Almeida Parra
Co-chair: Martín Pérez Andrés

Vocals:
Susana Barrena Delfa
Elena Blanco Álvarez
Juana Ciudad Pizarro
Ignacio Criado García
Carlos Fernández Giménez
Juan A. Flores Montero
Antonio López Fernández
Lourdes Martín Martín
Catarina Martins
Sergio Matarraz Sudón
Alberto Orfao de Matos

Scientific Committee
Julia Almeida Parra (Chair)
Alberto Álvarez Barrientos
Teresa Caballero
Joana Caetano
Mª Ángeles Cid
Juana Ciudad
Enrique Colado
Juan A. Flores Montero

João Loureiro
Lola Martínez
Catarina Martins
Enrique O'Connor
Alberto Orfao de Matos
Martín Pérez Andrés
Jordi Petriz
Noemí Puig
José Carlos Segovia

Program: (http://www.sic2019.com/wp-content/uploads/2019/05/programa-cientfico-sic2019_30_04_19_web.pdf)



11. RAMÓN ARECES FOUNDATION INTERNATIONAL SYMPOSIUM ON "THE RAS SUPERFAMILY AND RELATED PATHWAYS IN HEALTH AND DISEASE"

(https://www.fundacionareces.es/fundacionareces/en/events/the-ras-superfamily-and-related-pathways-in-health-and-disease.html

Date: 16-18/05/2019

Coordinator: Luis Miguel Lozano (IBBTEC-University of Cantabria-CSIC. SODERCAN.)

Organizers: Piero Crespo (IBBTEC-University of Cantabria. CSIC.) / Maríano Barbacid (Centro Nacional de Investigaciones Oncológicas-CNIO) / Xosé R. Bustelo (Centro de Investigación del Cáncer-IBMCC. CSIC-USAL) / Eugenio Santos (Centro de Investigación del Cáncer-IBMCC. CSIC-USAL) / Silvestre Vicent (CIMA University of Navarra)

Venue: Palacio de La Magdalena. Avenida de la Magdalena s/n. 39005. Santander. Cantabria.

Summary: RAS subfamily constitute the gene family most frequently mutated in human cancer: 22%, 8.2% and 3.7% for KRAS, NRAS and HRAS respectively. To these figures must be added those cases in which mutational activation is detected in downstream effectors. Overall, the proportion of human neoplasias harboring oncogenic mutations in RAS induced pathway constituents exceeds 50%. This fraction, significant as is, somewhat undervalues those referring to specific tumors: 99% of pancreatic carcinomas show KRAS mutational activation; 80% of melanomas harbor mutations in RAS-related pathways; while in thyroid cancer this figure reaches 75% of the cases. In addition, a wealth of gain- and loss-of-function genetic approaches using animal and cellular models mechanistically links RAS-induced pathways to cancer initiation, promotion and progression. It is therefore hardly surprising that these biochemical pathways rank among the most scrutinized in search of targets for oncological therapeutic intervention.

The members of the RAS superfamily behave as ''molecular switches" that fluctuate between inactive and active states, two conformations that depend on the binding of either GDP or GTP, respectively. Based on structural and functional criteria, this superfamily can be subdivided in several groups, including the RAS, RAP and RHO/RAC families. In the active, GTP-bound state, these GTPases bind to a large collection of effector molecules that, in turn, lead to the stimulation of signaling cascades that promote general cellular responses such as cytoskeletal changes, cell cycle progression and cell proliferation and survival, among many others.

The plasticity of RAS superfamily members in terms of subcellular localization, regulation, binding to effectors, and crosstalk with other cellular pathways has put them in a central regulatory point for a quite large number of cellular processes. Unfortunately, the toll that we have to pay for such important functions in vivo is the development of diseases when these routes become dysfunctional. Indeed, activating mutations of RAS or of components of its effector pathways are common in human cancers, with special incidence in some of the most aggressive tumors for which there are no efficacious treatments. Tumor types frequently harboring RAS oncogenes include pancreatic ductal adenocarcinoma (PDAC) one of the deadliest human cancer; non-small cell lung carcinoma, a tumor type for which the five year survival is less than 10%; and metastatic melanoma, with a survival rate of about 5%, among others.

Not surprisingly, for more than two decades, this has led to a colossal, comprehensive and multidimensional scrutiny of RAS-mediated signaling pathways. In order to understand how these signals impinge on the different biological processes involved in carcinogenesis, with the aim of finding molecular targets for the potential development of therapeutic agents whereby aberrant RAS signals, and, subsequently, tumor progression, could be inhibited.

With the perspective provided by more than thirty years of progress in the field, we are now in an excellent position to review the state-of-the-art of some of these developments, the challenges that have arisen during preclinical and clinical stages and how novel venues of research on the RAS field make conceivable new strategies towards the development of antitumor agents, alternative or complementary, to those currently in use and, for the first time in the history of biomedicine, the design of new therapies based on the specific blockage of molecular targets of RAS superfamilydependent routes. Some of these new therapeutic approaches have been already moved from the bench to the bedside.

In this context, this meeting aims at providing a format for the exchange of ideas and information, to discuss the latest research findings and methodological advances in the RAS-mediated signaling pathways, and to foster interactions amongst groups that investigate these signal transduction pathways at the structural, biochemical, signaling, physiological and/or pathological level. Special topics of attention will be those related to the systems biology of these routes, the analysis of their mechanism of regulation and action, the information derived from animal models, their role in human carcinogenesis, and the new therapeutic avenues that are being developed to manipulate their function.

From other perspective, this meeting will constitute a continuation of the Fundación Ramón Areces-sponsored meeting "Antitumoral targets upstream and downstream of RAS GTPases" held in the same venue in 2012 and remembered in the field as a highly successful gathering.

Program: https://www.fundacionareces.es/fundacionareces/en/events/the-ras-superfamily-and-related-pathways-in-health-and-disease.html#pestanas-programa2

12. XI SIMPOSIUM BASES BIOLÓGICAS DEL CÁNCER Y TERAPIAS PERSONALIZADAS

(https://basesbiologicascancer.com/)

Date: 23-24/05/2019

Scientific Director: Prof. Juan Jesús Cruz Hernández

Coordinator: Dr. César A. Rodríguez

Venue: Centro de Investigación del Cáncer de Salamanca. Salón de Actos, Campus Miguel de Unamuno s/n. Salamanca

Program:

MAY 23, 2019

08:50-09:00
BIENVENIDA Y PRESENTACIÓN

Dr. Juan Jesús Cruz, Hospital Clínico Universitario de Salamanca-IBSAL / Dr. Eugenio Santos de Dios, Centro de Investigación del Cáncer de Salamanca / Dr. Rogelio González Sarmiento, Instituto de Investigación Biomédica de Salamanca (IBSAL)

09:00-09:45
CONFERENCIA INAUGURAL

Moderadores: Dr. Vicente Guillem, Instituto Valenciano de Oncología, Valencia / Dr. Rafael López, Complejo Hospitalario Universitario de Santiago

CAR-T Cells: una nueva realidad en el tratamiento del cáncer / Dra. Dolores Caballero, Hospital Clínico Universitario de Salamanca-IBSAL

09:45-10:20
CONFERENCIA EDUCACIONAL 1

Moderadores: Dr. Emilio Esteban, Hospital Universitario Central de Asturias, Oviedo / Dr. Pedro Lazo-Zbikowski, Centro de Investigación del Cáncer de Salamanca

Bases biológicas del cáncer de pulmón. Caracterización molecular y su repercusión en las decisiones terapéuticas / Dr. Javier de Castro, Hospital Universitario La Paz, Madrid

10:20-11:25
MESA REDONDA 1

Estrategia terapéutica en cáncer de pulmón. Una visión integral

Moderadores: Dr. Carlos Camps, Hospital General Universitario de Valencia / Dr. Carlos García Girón, Complejo Asistencial Universitario de Burgos

Selección individualizada del tratamiento en adenocarcinoma de pulmón avanzado con mutaciones "driver" / Dra. Dolores Isla, Hospital Clínico Universitario Lozano Blesa, Zaragoza

Inmunoterapia en NSCLC. Una revisión actualizada / Dr. Maríano Provencio, Hospital Universitario Puerta del Hierro, Madrid

Cáncer microcítico de pulmón: ¿el final de la sequía? / Dra. Rosario García Campelo, Complejo Hospitalario Universitario de A Coruña

11:50-12:30
CONFERENCIA EDUCACIONAL 2

Moderadores: Dr. Andrés García Palomo, Complejo Asistencial Universitario de León / Dr. Diego Soto de Prado, Hospital Clínico Universitario de Valladolid

Inhibición de PARP. Bases biológicas, aplicaciones actuales y perspectivas de futuro / Dr. Antonio González Martín, Clínica Universidad de Navarra de Madrid

12:30-13:15
MESA REDONDA 2

Estrategia terapéutica en tumores ginecológicos

Moderadores: Dra. Beatriz Esteban, Complejo Asistencial de Segovia / Dr. José Valero Álvarez, Complejo Asistencial de Zamora

Tratamiento del cáncer de ovario en 2019 / Dr. Andrés Redondo, Hospital Universitario La Paz, Madrid

Actualización del abordaje terapéutico del cáncer de cérvix / Dra. Ana de Juan,

Hospital Universitario Marqués de Valdecilla, Santander

13:15-14:00
COMPARTIENDO CONOCIMIENTO

Mecanismos de resistencia a terapia anti-HER2. Experiencia investigadora del CIC de Salamanca

Moderadores: Dr. Germán Martín, Hospital Clínico Universitario de Salamanca-IBSAL / Dr. Jesús García Mata, Hospital Santa María de Nai, Ourense

Mecanismos de resistencia a terapia anti-HER2: una visión desde el laboratorio / Dr. Atanasio Pandiella, Centro de Investigación del Cáncer, Salamanca

Repercusión en la práctica clínica / Dr. Alberto Ocaña, Hospital Clínico San Carlos, Madrid

15:00-15:30
CONFERENCIA EDUCACIONAL 3

Moderadores: Dr. Alfredo Carrato, Hospital Universitario Ramón y Cajal, Madrid / Dra. Amalia Gómez Bernal, Hospital Clínico Universitario de Salamanca-IBSAL

Desarrollo de biosimilares de anticuerpos monoclonales en oncología: el ejemplo de Trastuzumab / Dr. César A. Rodríguez, Hospital Clínico Universitario de Salamanca-IBSAL

15:30-16:50
MESA REDONDA 3

Novedades en el tratamiento del cáncer de mama. Puesta al día

Moderadores: Dr. Miguel Martín, Hospital General Universitario Gregorio Marañón, Madrid / Dra. Ana Lluch, Hospital Clínico Universitario de Valencia

Enfermedad luminal / Dr. José Ángel García Sáenz, Hospital Clínico San Carlos, Madrid

Cáncer de mama HER2 positivo / Dr. Fernando Moreno, Hospital Clínico San Carlos, Madrid

Cáncer de mama triple negativo / Dra. Eva Ciruelos, Hospital Universitario 12 de Octubre, Madrid

16:50-17:35
MESA REDONDA 4

Tumores digestivos I. Cáncer de colon y recto

Moderadores: Dr. Enrique Aranda, Hospital Universitario Reina Sofía, Córdoba / Dr. Juan Jesús Cruz, Hospital Clínico Universitario de Salamanca-IBSAL

¿Qué hay de nuevo en el cáncer de recto localizado? / Dra. Rosario Vidal, Hospital Clínico Universitario de Salamanca-IBSAL

Algoritmo terapéutico actual en cáncer colorrectal metastásico / Dra. Pilar García Alfonso, Hospital General Universitario Gregorio Marañón, Madrid

18:00-19:20
MESA REDONDA 5

Tumores digestivos II. Avances en el tratamiento

Moderadores: Dra. Ruth Vera, Complejo Hospitalario de Navarra, Pamplona / Dr. Emilio Fonseca, Hospital Clínico Universitario de Salamanca-IBSAL

Cáncer de páncreas / Dr. Fernando Rivera, Hospital Universitario Marqués de Valdecilla, Santander

Colangiocarcinoma / Dr. Miguel Navarro, Hospital Clínico Universitario de Salamanca-IBSAL Hepatocarcinoma / Dr. Carlos Gómez, Hospital Universitario 12 de Octubre, Madrid

Cáncer gástrico / Dr. Juan Carlos Torrego, Hospital Río Hortega, Valladolid

19:20-20:00
CONFERENCIA EDUCACIONAL 4

Moderadores: Dr. José Enrique Alés, Hospital de Nuestra Señora de Sonsoles, Ávila / Dr. Ignacio Chacón, Hospital Virgen de la Salud, Toledo

Predisposición genética y prevención en cáncer / Dr. Isidro Sánchez, Centro de Investigación del Cáncer, Salamanca

MAY 24, 2019

08:45-09:30
MESA REDONDA 6

Perspectiva actual en el tratamiento de los tumores neuroendocrinos y cáncer de tiroides

Moderadores: Dr. Alberto Arizcun, Hospital Río Carrión, Palencia / Dr. Miguel Navarro, Hospital Clínico Universitario de Salamanca-IBSAL

Tumores neuroendocrinos / Dra. Teresa Alonso Gordoa, Hospital Universitario Ramón y Cajal, Madrid

Cáncer de tiroides / Dr. José Manuel Trigo, Hospital Regional Universitario y Virgen de la Victoria, Málaga

09:30-10:05
CONFERENCIA EDUCACIONAL 5

Moderador: Dr. César A. Rodríguez, Hospital Clínico Universitario de Salamanca-IBSAL

Análisis de expresión de múltiples genes mediante nuevas plataformas en tejido tumoral y biopsia líquida. ¿Todo a punto? / Dr. Jesús García Foncillas, Hospital Universitario Fundación Jiménez Díaz, Madrid

10:05-11:25
MESA REDONDA 7

Puesta al día en el tratamiento del cáncer genitourinario

Moderadores: Dr. Javier Cassinello, Hospital Universitario de Guadalajara / Dra. Rocío García, Hospital Clínico Universitario de Salamanca-IBSAL

Cáncer de próstata. Bases biológicas del CPRC / Dr. Javier Puente, Hospital Clínico San Carlos, Madrid

Cáncer de próstata avanzado. Algoritmo terapéutico global / Dra. Rebeca Lozano, CNIO-IBIMA, Madrid

Cáncer vesical avanzado. La revolución de la moderna inmunoterapia / Dr. Martín Lázaro, Complexo Hospitalario Universitario de Vigo

Cáncer renal avanzado. Optimizando la secuencia de tratamiento / Dr. José Ángel Arranz, Hospital General Universitario Gregorio Marañón, Madrid

11:50-12:25
CONFERENCIA EDUCACIONAL 6

Moderadores: Dr. Pedro Pérez Segura, Hospital Clínico San Carlos, Madrid / Dra. Yolanda Escobar, Hospital General Universitario Gregorio Marañón, Madrid

Tratamiento del cáncer de cabeza y cuello recurrente y/o metastásico. Papel de las diversas terapias disponibles / Dr. Ricard Mesía, Institut Català de Oncologia - Hospital Duran i Reynals, l'Hospitalet de Llobregat

12:25-13:30
MESA REDONDA 8

Melanoma maligno: de la biología a la clínica

Moderadores: Dr. Salvador Martín Algarra, Hospital Clínica de Navarra, Pamplona / Dr. José Luis González Larriba, Hospital Clínico San Carlos, Madrid

Avanzando en el conocimiento de la biología molecular del melanoma / Dr. Alfonso Berrocal, Hospital General Universitario de Valencia

Adyuvancia en melanoma maligno. Hacia un nuevo estándar / Dra. Lorena Bellido, Hospital Clínico Universitario de Salamanca-IBSAL

Estrategia global del tratamiento del melanoma en estadios avanzados / Dr. Enrique Espinosa, Hospital Universitario La Paz, Madrid

13:30-14:15
MESA REDONDA 9

Tratamiento de soporte en el paciente oncológico

Moderador: Dra. Marta Navalón, Hospital Clínico Universitario de Salamanca-IBSAL

Optimizando la profilaxis y el tratamiento de la emesis inducida por quimioterapia / Dra. Maribel Ruiz, Hospital Río Carrión, Palencia

Nuevas estrategias en la evaluación y tratamiento del paciente con neutropenia febril / Dra. Arantxa Amores, Hospital Clínico Universitario de Salamanca-IBSAL

13. I ASEICA-ASPIC INTERNATIONAL MEETING "CURRENT TRENDS IN IMMUNOTHERAPY RESEARCH AND TREATMENT"

(https://www.aseica.es/i-aseica-aspic-international-meeting)

Organization: ASEICA-ASPIC

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 12-13/09/2019

Scientific Coordinators: Dr. Xosé R. Bustelo (ASEICA's president; CSIC and University of Salamanca) / Dr. Luis Paz-Ares (ASEICA's President elect) / Dr. Luís Costa (ASPIC's president) / Dra. Joana Paredes (ASPIC's Vice President) / María José Oliveira (i3S-Porto) / Júlio Oliveira (IPO Porto) / Karine Serra (IMM-Lisbonn)

Program: https://www.aseica.es/wp-content/uploads/2019/09/Program_I_ASEICA_ASPICInternationalMeeting.pdf

14. COMPLEMENTARY TECHNOLOGIES TO DELIVER DEEPER INSIGHT IN DRUG DISCOVERY: SPR & HCA

(http://www.cicancer.org/es/eventos/392/complementary-technologies-to-deliver-deeper-insight-in-drug-discovery-spr-hca)

Speakers: Philippe Wurtz (GEHC); Manuel Fuentes (Centro de Investigación del Cáncer); Mabel Saiz (GEHC)

Venue: Salón de Actos. Centro de Investigación del Cáncer de Salamanca. Campus Miguel de Unamuno s/n. Salamanca

Date: 18/10/2019

Summary: Orthogonal approaches enable better prioritization of lead drug candidates by delivering greater understanding, reducing risk and increasing efficiency.

A target-driven hypothesis-based approach where large compound/Ab libraries are tested against a specific target of interest. High throughput screening is used to identify leads which pharmacologically modulate a specific component or target.

The focus of phenotypic drug discovery is to 'measure a clinically meaningful phenotype in a physiological relevant system such as an animal or cell; the assays do not require prior understanding of the molecular mechanism of action (MMOA).

Program: http://www.cicancer.org/es/eventos/392/complementary-technologies-to-deliver-deeper-insight-in-drug-discovery-spr-hca

15. SIMPOSIO CIENTÍFICO VIII CENTENARIO UNIVERSIDAD DE

SALAMANCA "NUEVOS RETOS EN INVESTIGACIÓN ONCOLÓGICA"

(http://www.cicancer.org/es/eventos/334/simposio-cientifico-viii-centenario-universidad-de-salamanca)

Organization: Xosé R. Bustelo, Atanasio Pandiella, Almudena Timón

Venue: Salón de actos del Edificio Dioscórides (Campus Miguel de Unamuno, Paseo Universidad de Coimbra, 7, Salamanca)

Date: 26-27/11/2018

Summary: Los días 26 y 27 de noviembre de 2018 se celebró el "Simposio Científico sobre Nuevos Retos en Investigación Oncológica" dentro del programa de actividades organizado para conmemorar el VIII Centenario de la Universidad de Salamanca. El evento se está coordinado por la Fundación Diz-Pintado contra el Cáncer y el Centro de Investigación del Cáncer (CIC-IBMCC) de Salamanca.

Dimensión social del cáncer. Mesas redondas abiertas a la sociedad

Los avances en investigación permiten mejorar la asistencia médica. Los pacientes y familiares muestran un especial interés por las novedades que provienen de la investigación biomédica. Además, los medios de comunicación canalizan muchas de las novedades que se generan en los laboratorios de investigación de todo el mundo.

Teniendo en cuenta a los colectivos que tienen un papel destacado en la generación del conocimiento, en la transmisión y recepción de la información y el compromiso de la Universidad de Salamanca con la sociedad, el "Simposio Científico VIII Centenario Universidad de Salamanca: nuevos retos en investigación oncológica" celebrará el 26 de noviembre una sesión destinada al debate de aspectos de investigación biomédica teniendo presente la dimensión social del cáncer. En esta sesión se han organizado dos mesas redondas que están dirigidas no sólo a los investigadores, sino a la sociedad en general.

En las mesas redondas, moderadas por el periodista Aimar Bretos de la cadena Ser, se debatirán por una parte la relación entre investigación y medios de comunicación y por otra los retos actuales que presentan el entendimiento, diagnóstico y tratamiento del cáncer. Este último acto está especialmente dirigido a discutir cuestiones de interés particular para pacientes de cáncer.

La primera mesa de periodistas e investigadores estará integrada por Ángela Bernado, que trabaja en CIVIO (https://civio.es); el Dr. Arkaitz Carracedo, investigación en el CICbioGUNE de Bilbao; Nuño Domínguez, periodista de Materia/El País; Verónica Fuentes, de la Agencia Servicio de Información y Noticias Científicas (SINC) y Coral Larrosa, periodista de informativos Telecinco y actual vicepresidenta de la Asociación Nacional de Informadores de la Salud.

En la segunda mesa se debatirán aspectos que preocupan a investigadores y a las asociaciones de pacientes y familiares. Estará integrada por el Dr. Maríano Barbacid, investigador del Centro Nacional de Investigaciones Oncológicas de Madrid; el Dr. Juan Jesús Cruz, jefe del Servicio de Oncología del Hospital Universitario de Salamanca; el Dr. Adolfo Ferrando, profesor de pediatría y patología de la Universidad de Columbia (Nueva York); la Dra. María Victoria Mateos, del Servicio de Hematología del Hospital Universitario de Salamanca; la Dra. Marisol Soengas, investigadora del Centro Nacional de Investigaciones Oncológicas y la Dra. Marta Puyol, de la Fundación Científica de la Asociación Española Contra el Cáncer.

SIMPOSIO CIENTÍFICO

El día 27 de noviembre se celebrará en el edificio Dioscórides el encuentro científico que contará con las ponencias de investigadores de reconocido prestigio del ámbito de la investigación básica y clínica del cáncer. En él participarán los Dres. Maríano Barbacid, del Centro Nacional de Investigaciones Oncológicas de Madrid; Eduardo Batlle, del Instituto de Investigación Biomédica de Barcelona; Joan Seoane del Instituto de Investigación en Oncología de Vall d´Hebron de Barcelona; Manel Esteller, del Instituto de Investigación Biomédica Bellvitge de Barcelona; Arkaitz Carracedo, del CICbioGUNE de Bilbao; Amparo Cano, de la Universidad Autónoma de Madrid; Óscar Fernández-Capetillo, del Centro Nacional de Investigaciones Oncológicas de Madrid; Marisol Soengas, también del Centro Nacional de Investigaciones Oncológicas de Madrid y Adolfo Ferrando, de la Universidad de Columbia, Nueva York.

16. 2ND ASEICA EDUCATIONAL SYMPOSIUM

(https://www.aseica.es/2nd-aseica-educational-symposium)

Scientific Coordinators: Dr. Xosé R. Bustelo; Dr. Carlos Camps; Dr. Rafael López, Dr. Luis Paz-Ares; Dr. María M. Caffarel; Dr. Gema Moreno-Bueno; Dr. Héctor Peinado; Dr. María S. Soengas

Organization: ASEICA

Venue: Facultad de Medicina. Universidad Autónoma de Madrid

Date: 28-29/11/2019

Program: https://www.aseica.es/wp-content/uploads/2019/11/programa_aseica_educational_symposium_v22.pdf

SCIENTIFIC SEMINAR PROGRAM

DATE	TITLE	SPEAKER	AFFILIATION
11/01/2018	**tRNA modifications in evolution, metazoan physiology, and human disease**	*Lluis Ribas de Pouplana*	Institute for Research in Biomedicine (IRB), [Barcelona]
17/01/2018	**Live-cell structural biology: towards the mechanism of exocytosis**	*Oriol Gallego*	European Molecular Biology Laboratory (EMBL) (Heidelberg, Germany)
18/01/2018	**Genome Architecture Mapping: discovering chromatin contacts in rare cell types**	*Ana Pombo*	Max Delbruck Center for Molecular Medicine [Berlin, Germany]
25/01/2018	**Exploring amino acid vulnerabilities in cancer with differential ribosome codon reading**	*Fabricio Loayza Puch*	Netherlands Cancer Institute (NKI) [Amsterdam, Netherlands]
01/02/2018	**Diagnóstico inmunofenotípico de mastocitosis y LMA**	*Alberto Orfao de Matos*	CIC-IBMCC (CSIC-USAL) Lab 11
08/02/2018	**A mechanosensitive G1 checkpoint monitors cortical branched actin**	*Alexis Gautreau*	Ecole Polytechnique- Universite Paris-Saclay [Paris, France]
15/02/2018	**Mecanismos autofágicos implicados en la regulación del tráfico endocítico y la señalización celular**	*Inmaculada Serramito*	CIC-IBMCC (CSIC-USAL) Lab 18
22/02/2018	**Deconstructing K-Ras signalling in cancer: Identification and functional validation of therapeutic targets**	*Maríano Barbacid*	Spanish National Cancer Research Center (CNIO) [Madrid, Spain]
01/03/2018	**DECO: a method to decompose heterogeneous omic data for patient stratification and discovery of specific biomarkers**	*Francisco Campos-Laborie*	CIC-IBMCC (CSIC-USAL) Lab 19
08/03/2018	**Novel insights into the role of homologous recombination during DNA damage tolerance**	*Félix Prado*	Centro Andaluz de Biología Molecular y Medicina Regenerativa-CSIC (CABIMER), (Seville)
15/03/2018	**Proteostasis. Modulación y eficacia en patologías hematológicas**	*Diego Fernández Monjil*	Senior RML de Hematología de Celgene España (Madrid)
22/03/2018	**Computational modeling of protein interactions for biomedical applications**	*Juan Fernández-Recio*	Instituto de Biología Molecular de Barcelona (IBMB), CSIC; Barcelona Supercomputing Center (BSC) [Barcelona]

DATE	TITLE	SPEAKER	AFFILIATION
12/04/2018	**The Tousled like kinases: suppressors of replication stress and potential targets in cancer therapy.**	*Travis Stracker*	Institute for Research in Biomedicine (IRB), [Barcelona]
19/04/2018	**Vav2 shows muscle: new roles for this Rho-GEF in skeletal muscle and the development of metabolic syndrome.**	*Sonia Rodríguez Fernández*	CIC-IBMCC (CSIC-USAL) Lab 2
26/04/2018	**Differential role of the RasGEFs SOS1 and SOS2 in mouse skin homeostasis and carcinogenesis**	*Fernando Calvo Baltanás*	CIC-IBMCC (CSIC-USAL) Lab 1
03/05/2018	**Restoration of chromatin based information behind replication forks**	*Constance Alabert*	School of Life Sciences / Universidad de Dundee (Dundee, UK)
10/05/2018	**Simulating nucleic acids: from pure to applied science**	*Modesto Orozco*	Institute for Research in Biomedicine (IRB) [Barcelona]
21/05/2018	**Gut microbiota and energy homeostasis**	*Salvatore Fabbiano*	University of Geneva (Geneva, Switzerland)
24/05/2018	**Pot-holes and tailor-made ubiquitin ligases: damage signalling and damage processing during DNA replication**	*Helle Ulrich*	Institute of Molecular Biology (IMB-Mainz) / University of Mainz (Mainz, Germany)
31/05/2018	**Understanding mutations in AML and MDS to identify novel therapies**	*Ken Mills*	Queen´s University Belfast, [Belfast, UK]
07/06/2018	**El papel de la terapia celular en la leucemia linfocítica crónica**	*Julio Delgado*	Hospital Clinic de Barcelona [Barcelona]
14/06/2018	**Signalling by small GTPases : from allosteric regulation to inhibition by small molecules**	*Jacqueline Cherfils*	CNRS and Ecole Normale Supérieure Paris-Saclay (Paris, France)
18/06/2018	**Investigación traslacional en células madre cancerígenas: biomarcadores diagnósticos y terapias dirigidas**	*Juan Antonio Marchal*	Faculty of Medicine Biosanitary Research Institute of Granada (IBS) [Granada]
28/06/2018	**VRK1-mediated phosphorylation of TIP60 promotes its accumulation and activity in response to DNA damage**	*Raúl García González*	CIC-IBMCC (CSIC-USAL) Lab 4
05/07/2018	**NADPH oxidasas y señalización redox en hematopoyesis y leucemogénesis**	*Ángel Hernández Hernández*	Universidad de Salamanca
19/07/2018	**Avances en la investigación y desarrollo de nuevas dianas y opciones terapéuticas en Onco-Hematología**	*María Carmen Castillo / Ignacio Polo*	Janssen
27/09/2018	**Epigenetic management of cancer: promise versus practice**	*María Berdasco Menéndez*	Instituto de Investigación Biomédica de Bellvitge (IDIBELL) [Barcelona]
04/10/2018	**Retos de la Bioinformática en el diagnóstico clínico**	*Ángela del Pozo Maté*	Instituto de Genética Medica y Molecular – INGEMM / Hospital La Paz [Madrid]
11/10/2018	**Targeting Hepatic Stellate Cells to ameliorate liver inflammation**	*Manuel Fernández Rojo*	Institute IMDEA Food [Madrid]
18/10/2018	**Investigación traslacional de nuevos fármacos en oncología**	*Enrique M. Ocio*	Hospital Universitario Marqués de Valdecilla (HUMV-IDIVAL). Universidad de Cantabria. Santander
25/10/2018	**Ser or Leu - Functional and Structural impact of ambiguous translation in Candida albicans**	*Sandra de Macedo Ribeiro*	Instituto de Biologia Molecular e Celular - IBMC [Porto Portugal]

DATE	TITLE	SPEAKER	AFFILIATION
08/11/2018	**Los ratones carentes de espermatoproteasoma no presentan alteraciones en reparación del DNA, pero muestran defectos en la salida de meiosis**	*Laura Gómez*	CIC-IBMCC (CSIC-USAL) Lab 9
15/11/2018	**Understanding the dual role of WIP as oncogene and tumor suppressor**	*Inés Antón*	Centro Nacional de Biotecnología (UAM/CSIC) [Madrid]
16/11/2018	**Unfolding anti-cancer immunity: New roles for ER stress sensors in the tumor microenvironment**	*Juan Cubillos*	Weill Cornell Medicine [New York, USA]
22/11/2018	**The NO signaling pathway in aortic disease**	*Juan Miguel Redondo*	Centro Nacional de Investigaciones Cardiovasculares (CNIC) [Madrid]
29/11/2018	**Actomyosin-based mechanosensation controls T cell activation by shaping antigenic presentation**	*Miguel Vicente Manzanares*	CIC-IBMCC (CSIC-USAL) Lab 6
13/12/2018	**Regulating cell fate decisions through RNA epigenetics**	*Diana Guallar*	Center for Research in Molecular Medicine and Chronic Diseases (CiMUS), [Santiago de Compostela-A Coruña]
18/12/2018	**The Journey of Hematopoietic Stem Cells: From birth to death and beyond**	*Mikel Ganuza*	St. Jude Children's Research Hospital (Memphis, USA)
20/12/2018	**Neuronal proteome remodeling by microexons and their misregulation in autism spectrum disorder**	*Manuel Irimia*	Centro de Regulación Genómica (CRG) [Barcelona]
10/01/2019	**Identification of genetic and molecular determinants associated with cardiotoxicity by anthracyclines and taxanes**	*Aurora Gómez Vecino*	CIC-IBMCC (CSIC-USAL) Lab 7
15/01/2019	**Short-term activation of the Jun-N terminal Kinase pathway in apoptosis-deficient cells of Drosophila induces tumorigenesis**	*Noelia Pinal Seoane*	Centro de Biología Molecular "Severo Ochoa" (CBMSO) [Madrid]
17/01/2019	**Chromatin Conformation in Development and Disease**	*Juan Manuel Vaquerizas*	Max Planck Institute for Molecular Biomedicine [Münster, Germany]
21/01/2019	**Secreted factors and their role in Regeneration: Discovery and Therapeutic Applications**	*Pilar Ruiz Lozano*	Regencor, Inc. y del Departamento de Pediatría (Cardiología) de la Stanford University School of Medicine, California (USA)
24/01/2019	**Desarrollo de nuevas estrategias para diagnóstico y clasificación de inmunodeficiencias predominantemente de anticuerpos**	*Elena Blanco Álvarez*	CIC-IBMCC (CSIC-USAL) Lab 11
31/01/2019	**Nuevas dianas terapéuticas y papel de la medicina de precisión en inmunooncología**	*Víctor Moreno*	Clinical Research Phase 1 Trials Unit START MADRID-FJD / Hospital Fundación Jiménez Díaz [Madrid]
07/02/2019	**Enhancer defects in acute myeloid leukemia (AML): The Evil-side of gene regulation**	*Ruud Delwel*	Erasmus MC hospital [Rotterdam, Netherlands]
12/02/2019	**Role of microRNAs in B cell differentiation and neoplastic transformation**	*Virginia García de Yébenes Mena*	Centro Nacional de Investigaciones Cardiovasculares (CNIC). Madrid
14/02/2019	**Clonal evolution of pre-malignant B-cells in the absence of AID**	*Guillermo Rodríguez-Hernández*	CIC-IBMCC (CSIC-USAL) Lab 13
21/02/2019	**An epigenetic journey into the origin and evolution of B cell tumors**	*José Ignacio Martín Subero*	IDIBAPS, Universidad de Barcelona [Barcelona]

CANCER RESEARCH CENTER (CIC- IBMCC)
SCIENTIFIC SEMINAR SERIES
SALAMANCA 2017-2018
2017
2018
CANCER RESEARCH CENTER (CIC- IBMCC)
SCIENTIFIC SEMINAR SERIES
SALAMANCA 2018/2019
2018
2019
CANCER RESEARCH CENTER (CIC- IBMCC)
SCIENTIFIC SEMINAR SERIES
SALAMANCA 2019/2020
2019
2020

DATE	TITLE	SPEAKER	AFFILIATION
26/02/2019	**Nuevas terapias con actividad anti-tumoral en células madre tumorales de sarcomas**	*René Rodríguez*	Instituto de Investigación Sanitaria del Principado de Asturias (ISPA) /Hospital Universitario Central de Asturias (HUCA) [Oviedo]
28/02/2019	**Thirty years of biochemistry ,of the small GTPases of the RHO family: Current status, challenges, and future directions**	*Reza Ahmadian*	Heinrich Heine University [Dusseldorf, Germany]
07/03/2019	**Feedback loops controlling migration and invasion in healthy and cancerous cells**	*Laura Machesky*	Beatson Institute [Glasgow, UK]
14/03/2019	**El Banco de Tejidos Neurológicos del INCYL, una herramienta útil de apoyo a la investigación**	*M. Javier Herrero Turrión*	Instituto de Neurociencias de Castilla y León (INCYL); Banco de Tejidos Neurológicos del INCYL (BTN-INCYL)
21/03/2019	**The ins and outs of IL-7R-mediated signaling in leukemia**	*João Barata*	Instituto Medicina Molecular [Lisboa, Portugal]
28/03/2019	**How can 3D structure knowledge help systems biology?**	*Baldo Oliva Miguel*	Universidad Pompeu Fabra (UPF) [Barcelona]
04/04/2019	**Inmunoterapia de síndromes linfoproliferativos y enfermedad de injerto contra huésped con anticuerpos contra el receptor de quimiocinas CCR7.**	*Cecilia Muñoz Calleja*	Instituto de Investigación Sanitaria Hospital Universitario de La Princesa [Madrid]
11/04/2019	**Cáncer Colorrectal en el adulto joven, una entidad diferente**	*Jéssica Pérez García*	CIC-IBMCC (CSIC-USAL) Lab 14
25/04/2019	**MHC CLASS I LOSS AND CANCER IMMUNE ESCAPE**	*Federico Garrido*	Universidad de Granada [Granada]
02/05/2019	**Novel targeted therapies in lymphoid neoplasia: from apoptosis activation to microenvironment harnessing**	*Patricia Pérez Galán*	IDIBAPS- Hospital Clinic, Barcelona
09/05/2019	**CLINICAL IMPACT OF DNA REPAIR DEFECTS IN PROSTATE CANCER**	*Elena Castro Marcos*	Spanish National Cancer Research Centre (CNIO) [Madrid]
16/05/2019	**Cell-of-origin of prostate cancer and clinical heterogeneity**	*Esther Baena Chaparro*	Cancer Research UK Manchester Institute [Manchester, UK]
30/05/2019	**KRAS driven lung adenocarcinoma depends on ERBB signaling**	*Emilio Casanova-Hevia*	Ludwig Boltzmann Institute Cancer Research [Vienna, Austria]
05/06/2019	**Host-Microbiota Interactions in Health and Disease**	*Gabriel Núñez*	University of Michigan [Michigan, USA]
06/06/2019	**Regnase-1, a key endoribonuclease responsible for the inflammatory and immune responses**	*Shizuo Akira*	Laboratory of Host Defense, WPI Immunology Frontier Research Center & Department of Host Defense, Research Institute for Microbial Diseases, University of Osaka [Osaka, Japan]
13/06/2019	**MEK5 as a driver in lung cancer**	*Adrián Sánchez Fernández*	CIC-IBMCC (CSIC-USAL) Lab 15
27/06/2019	**Comparison between stem cell renewal and spermatogonial multiplication in humans and mice**	*Dirk de Rooij*	Utrecht University [Utrecht, The Netherlands]
28/06/2019	**Cuantificación de interacciones inmunes célula-célula a tiempo real mediante pinzas ópticas**	*Oriol Nos Aguilà*	Product Manager at Impetux Optics

DATE	TITLE	SPEAKER	AFFILIATION
04/07/2019	**Vascular checkpoints for cancer immunotherapy**	*Santos Mañes*	Centro Nacional de Biotecnologia (CNB) [Madrid]
11/07/2019	**La ciencia que subyace bajo la selección de linfocitos para la producción del CAR-T**	*Segundo González Rodríguez*	Universidad de Oviedo / Instituto Universitario de Oncología del Principado de Asturias (IUOPA) [Oviedo]
18/07/2019	**Mechanisms of regulation of the guanine nucleotide exchange factor C3G**	*Arturo Carabias del Rey*	CIC-IBMCC (CSIC-USAL) Lab 17
05/09/2019	**Measuring mitochondrial function and glycolysis using the Seahorse XF analyzers**	*Alfredo Caro-Maldonado*	Seahorse XF Consumables Product Specialist Cell Analysis, Agilent Technologies
26/09/2019	**Molecular perspectives on short-term fasting as a nutritional strategy against aging-related diseases**	*Pablo José Fernández Marcos*	Molecular perspectives on short-term fasting as a nutritional strategy against aging-related diseases
03/10/2019	**Human aneuploidy, sex chromosomes and infertility**	*James Turner*	The Francis Crick Institute [London, UK]
10/10/2019	**Estudios de transcriptómica y supervivencia en series de pacientes de cáncer de mama**	*Santiago Bueno Fortes*	CIC-IBMCC (CSIC-USAL) Lab 19
17/10/2019	**Implicación de la quinasa humana VRK1 en enfermedades neurodegenerativas**	*Elena Martín Doncel*	CIC-IBMCC (CSIC-USAL) Lab 4
24/10/2019	**Novel insights into KRas biology identify potential therapeutic strategies**	*David Santamaría*	Institut Européen de Chimie et Biologie [Pessac / Bordeaux, France]
31/10/2019	**Retrieval of endosomal cargo via protein scaffolds**	*Aitor Hierro*	CIC bioGUNE [Vizcaya]
07/11/2019	**Concomitant deletion of HRAS and NRAS leads to pulmonary immaturity, respiratory failure and neonatal death in mice**	*Rocío Fuentes Mateos*	CIC-IBMCC (CSIC-USAL) Lab 1
14/11/2019	**Tissue-specific and time-dependent mechanisms of metastasis**	*Roger Gomis*	Institute for Research in Biomedicine (IRB) [Barcelona]
21/11/2019	**Unveiling unexpected tumor suppressor functions for Vav3 in nonsmall cell lung cancer**	*Myriam Cuadrado*	CIC-IBMCC (CSIC-USAL) Lab 2
28/11/2019	**Filopodia and the metastatic cascade**	*Guillaume Jacquemet*	Turku Centre for Biotechnology, University of Turku [Turku, Finland]
05/12/2019	**Unconventional autophagic mechanisms involved in intracellular trafficking control and cell signalling**	*Inmaculada Serramito Gómez*	CIC-IBMCC (CSIC-USAL) Lab 18
12/12/2019	**The non-receptor tyrosine kinase ACK: signalling pathways and opportunities for therapeutic intervention**	*Darerca Owen*	University of Cambridge [Cambridge, UK]
19/12/2019	**Somatic structural variation and cancer**	*José Manuel C. Tubio*	CIMUS - University of Santiago de Compostela [Santiago de Compostela]

8

SCIENCE OUTREACH

THE MOST RELEVANT ACTIVITIES 2018-2019

During 2018 and 2019, communication planning has followed the guidelines established during all these years. The institutional communication is combined (press releases and press conferences), with activities of attention to different targets, such as patient and family associations, the organization of training events.

The Scientific Culture and Innovation unit of the Cancer Research Center (included in the UCC+i Network of the Spanish Foundation for Science and Technology (FECYT)) brings together all the communication activities of the CIC.

If the planning of the UCC+i is taken into account, the most relevant activities of 2018-2019 are:

PRESS RELEASES

- **02/2018.** The Cancer Research Center celebrates the International Day of Women and Girls in Science:

  http://www.cicancer.org/es/actualidad/132/el-centro-de-investigacion-del-cancer-celebra-el-dia-internacional-de-la-mujer-y-la-nina-en-ciencia

- **02/18.** The CIC receives new funding for predoctoral training:

  http://www.cicancer.org/es/actualidad/133/el-cic-recibe-nueva-ayuda-para-formacion-predoctoral

- **03/18.** Progress in understanding the genesis of B-cell acute lymphoblastic:

  http://www.cicancer.org/es/actualidad/135/avance-en-la-comprension-de-la-genesis-de-la-leucemia-linfoblastica-aguda-precursora-de-celulas-b

- **03/18.** The Cancer Research Center (FICUS) renews as an accredited member of the UCC+i Network:

  http://www.cicancer.org/es/actualidad/136/el-centro-de-investigacion-del-cancer-a-traves-de-la-ficus-renueva-como-miembro-acreditado-de-la-red-ucci

- **05/18.** Biological age, determined according to oxidative stress, modifies the aggressiveness of breast cancer:

  http://www.cicancer.org/es/actualidad/137/la-edad-biologica-determinada-segun-el-estres-oxidativo-modifica-la-agresividad-del-cancer-de-mama

- **05/18.** Sergio Matarraz exposes the results obtained through the project funded by the AECC Scientific Foundation:

  http://www.cicancer.org/es/actualidad/138/sergio-matarraz-expone-los-resultados-obtenidos-mediante-el-proyecto-financiado-por-la-fundacion-cientifica-de-la-aecc

- **06/18.** New paradigm for the generation of T-cell acute lymphoblastic leukemia:

  https://www.facebook.com/permalink.php?story_fbid=2300480726663874&id=1149031891808769&notif_id=1543827448810286&notif_t=page_post_reaction

- **08/18.** Solidarity route against cancer:

  http://www.cicancer.org/es/actualidad/142/marcha-solidaria-contra-el-cancer

- **09/18.** One of the most frequent genes mutated in cancer can become an antitumor agent, depending on its location within the cells:

  http://www.cicancer.org/es/actualidad/144/uno-de-los-genes-protumorales-mas-frecuentes-mutados-en-cancer-puede-convertirse-en-agente-antitumoral-dependiendo-de-su-localizacion-dentro-de-las-celulas

- **10/18.** Press conference: The Cancer Research Center accredited as a Research Center of Excellence in Castilla y León:

  http://www.cicancer.org/es/actualidad/145/convocatoria-de-rueda-de-prensa

  http://www.cicancer.org/es/actualidad/146/el-centro-de-investigacion-del-cancer-cic-ibmcc-acreditado-como-centro-de-investigacion-de-excelencia-de-castilla-y-leon

- **10/18.** Press conference: Presentation of the charity concert of María Espada and "De Mvsica Antiqva"

  http://www.cicancer.org/es/actualidad/147/concierto-benefico

- **8/10/18.** The award conditions of VIII Premio Nacional de Investigación en Cáncer "DOCTORES DIZ PINTADO»

  http://www.cicancer.org/es/actualidad/148/viii-premio-nacional-de-investigacion-en-cancer-doctores-diz-pintado

?fbclid=IwAR1rHkImoEYDLNvQuPTw4bTPdNqsAcrfHDZ2_Mj4cbIqFZK9rpJVwWnmM6I

- **10/18.** Local activation of mammalian separase in interphase promotes double-strand break repair and prevents oncogenic transformation

  http://www.cicancer.org/es/actualidad/149/la-proteasa-separasa-facilita-la-reparacion-fiel-del-adn-en-celulas-humanas

- **11/18.** Press conference: Presentation of the Symposium: New challenges in cancer research

  The Symposium held a session on November 26 to discuss aspects of biomedical research aimed not only at researchers, but at society in general.

  http://www.cicancer.org/es/actualidad/151/simposio-cientifico-viii-centenario-universidad-de-salamanca-nuevos-retos-en-investigacion-oncologica

  http://www.cicancer.org/es/actualidad/153/presentacion-del-simposio-nuevos-retos-en-investigacion-oncologica

- **01/19.** Xosé R. Bustelo holds the presidency of the Spanish Association for Research on Cancer (ASEICA)

  http://www.cicancer.org/es/actualidad/157/el-dr-xose-r-bustelo-investigador-del-cic-ocupa-la-presidencia-de-la-asociacion-espanola-de-investigacion-sobre-el-cancer

- **01-19.** Raúl Rabadán was awarded VIII Premio Nacional de Investigación en Cáncer "DOCTORES DIZ PINTADO"

  http://www.cicancer.org/es/actualidad/156/raul-rabadan-recibe-el-viii-premio-nacional-de-investigacion-en-cancer-doctores-diz-pintado

- **01-19.** Vav proteins maintain epithelial traits in breast cancer cells using miR-200c-dependent and independent mechanisms

  http://www.cicancer.org/es/actualidad/158/identifican-una-ruta-implicada-en-la-estructura-y-respuesta-terapeutica-del-cancer-de-mama

- **01-19.** Post-transcriptional regulation by cytosine-5 methylation of RNA

  http://www.cicancer.org/es/actualidad/159/revisada-la-aparicion-de-m5c-en-el-arn

- **03-19.** Deciding my postgraduate. Do you like biomedicine?

  http://www.cicancer.org/es/actualidad/162/jornada-informativa-decidiendo-mi-posgrado-te-gusta-la-biomedicina

- **04-19.** Press conference. Presentation of the Con-Ciencia-Con-Arte project. Con-science-with-art is a scientific dissemination project that uses art to bring science closer together. The project has been funded by the CSIC General Foundation.

  http://www.cicancer.org/es/actualidad/163/con-ciencia-con-arte

- **04-19.** Researchers at the Cancer Research Center describe how two identified proteins interact with the mechanical resistance of the skin

  http://www.cicancer.org/es/actualidad/165/describen-como-interaccionan-dos-proteinas-que-contribuyen-a-la-resistencia-mecanica-de-la-piel

- **04-19.** XVI Congress of Iberian Society of Cytometry

  http://www.cicancer.org/es/actualidad/166/xvi-congress-of-iberian-society-of-cytometry

- **04-19.** New molecular mechanism that prevents inflammatory bowel disease

  http://www.cicancer.org/es/actualidad/167/desvelado-un-nuevo-mecanismo-molecular-que-previene-la-enfermedad-inflamatoria-intestinal

- **05-19.** CRISPR / Cas9 improves its efficiency to cancel oncogenes in cells of cancer patients

  http://www.cicancer.org/es/actualidad/170/mejora-la-eficiencia-de-las-herramientas-crisprcas9-para-anular-oncogenes-en-celulas-de-pacientes-con-cancer

- **06-19.** Zumba solidarity masterclass raises funds for Cancer Research Center

  http://www.cicancer.org/es/actualidad/173/masterclass-solidaria-de-zumba-a-favor-del-cic

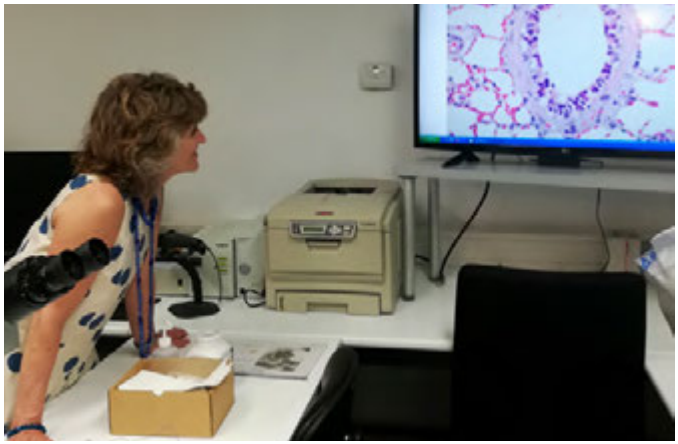
- **07-19.** Sonia Rodríguez Fernández awarded the "Primer premio Nacional Fin de Carrera" in the area of Science (2012/2013).

  http://www.cicancer.org/es/actualidad/174/sonia-rodriguez-fernandez-recibe-el-primer-premio-nacional-fin-de-carrera-en-el-area-de-ciencias-curso-20122013

- **07-19.** The IDIAL-NET project begins with a meeting at the Cancer Research Center

  http://www.cicancer.org/es/actualidad/176/meeting-proyecto-0639-idial-net-3-e

- **07-19.** The Cancer Research Foundation of the University of Salamanca (FICUS) starts the process, established by



the European Commission, to obtain the Human Resources Award

http://www.cicancer.org/es/actualidad/177/la-ficus-inicia-el-proceso-establecido-por-la-comision-europea-para-obtener-el-sello-human-resources-award

- **09-19.** Spermatoproteasome is essential for fertility in male mice

  http://www.cicancer.org/es/actualidad/178/el-espermatoproteasoma-es-esencial-para-la-fertilidad-en-ratones-machos

- **09-19.** Conference - Panel of experts: Strategies aimed at promoting health research in Cancer in Castilla y León

  http://www.cicancer.org/es/actualidad/180/jornada-panel-de-expertos-estrategias-dirigidas-a-potenciar-la-investigacion-sanitaria-del-cancer-en-castilla-y-leon

- **09-19.** Researchers at the Cancer Research Center discover a panel of biomarkers (autoantibodies) for the early diagnosis of knee osteoarthritis

  http://www.cicancer.org/es/actualidad/179/descubierto-un-panel-de-biomarcadores-autoanticuerpos-para-el-diagnostico-temprano-de-la-osteoartritis-de-rodilla

- **09-19.** Support for the Distinguished Gentleman Ride (DGR).

  http://www.cicancer.org/es/actualidad/183/semana-de-la-ciencia-2019

- **10-19.** The award conditions of IX Premio Nacional de Investigación en Cáncer "DOCTORES DIZ PINTADO"

  http://www.cicancer.org/es/actualidad/184/ix-premio-nacional-de-investigacion-en-cancer-doctores-diz-pintado?fbclid=IwAR3QYob5jOdWcZlOQu1kHJiTvtelqEtPQXcjdryjbJjoz9ithVjV6aZ7kOA

- **10-19.** New drugs (PROTAC subtype inhibitors) are effective in triple negative breast cancer

  http://www.cicancer.org/es/actualidad/185/nuevos-farmacos-inhibidores-del-subtipo-protac-son-efectivos-en-cancer-de-mama-triple-negativo

- **10-19.** Two new research projects of the Cancer Research Center receive funding from the AECC

  http://www.cicancer.org/es/actualidad/186/dos-nuevos-proyectos-de-investigacion-del-centro-de-investigacion-del-cancer-cic-ibmcc-reciben-financiacion-de-la-fundacion-cientifica-de-la-aecc

- **10-19.** The Cancer Research Foundation of the University of Salamanca «Excellence in Human Research Resources» (HRS4R)

  http://www.cicancer.org/es/actualidad/187/la-fundacion-para-la-investigacion-del-cancer-de-la-universidad-de-salamanca-excelencia-en-recursos-humanos-de-investigacion-hrs4r

- **10-19.** PCNA Deubiquitylases Control DNA Damage Bypass at Replication Forks.

  http://www.cicancer.org/es/actualidad/188/un-nuevo-estudio-explica-como-se-desactiva-la-ruta-de-la-tolerancia-al-dano-durante-la-sintesis-de-adn-en-las-horquillas-de-replicacion

- **11-19.** Proteomic and Transcriptomic Profiling Identifies Early Developmentally Regulated Proteins in Dictyostelium Discoideum

  http://www.cicancer.org/es/actualidad/190/un-nuevo-estudio-identifica-proteinas-reguladas-por-amp-ciclico-en-el-organismo-modelo-dictyostelium-discoideum

- **12-19.** Concomitant deletion of HRAS and NRAS leads to pulmonary immaturity, respiratory failure and neonatal death in mice

  http://www.cicancer.org/es/actualidad/193/la-eliminacion-simultanea-de-hras-y-nras-provoca-inmadurez-pulmonar-fallo-respiratorio-y-muerte-neonatal-en-ratones

- **12-19.** The increase in mechanical stress is related to a worse prognosis of lung cancer.

  http://www.cicancer.org/es/actualidad/192/el-aumento-del-estres-mecanico-esta-relacionado-con-un-peor-pronostico-del-cancer-de-pulmon

- **12-19.** New model that explains the development of B-cell acute lymphoblastic leukemia

  http://www.cicancer.org/es/actualidad/194/nuevo-modelo-que-explica-el-desarrollo-de-leucemia-linfoblastica-aguda-de-celulas-b

SCIENTIFIC CULTURE & FUNDRAISING

ACTIVITIES TO PROMOTE SCIENTIFIC CULTURE

- **February 11th.** World Day of Women and Girls in Science. The Cancer Research Center has organized seventeen talks in colleges and institutes in February 2018 and 2019. The objective was to emphasize the role of women in science.
- **Science week 2018-2019.** The Cancer Research Center has organized with the Animal Facility of the University of Salamanca two activities aimed at students to show the importance of using mice in biomedicine research.
- The Cancer Research Center participated in 2018-2019 at the University of Salamanca Summer Camp, attending guided visits to children between 6 and 14 years old.
- **The European Researchers' Night**

The Cancer Research Center organized activities in 2018 and 2019 to bring their work closer through outreach activities. The offer was incorporated into all activities organized by the University of Salamanca.

GUIDED TOURS FOR STUDENTS.

Throughout 2018 and 2019, more than two thousand students have been attended with guided visits. The fundamental objective is to explain what daily work is like in a biomedical research center. Before starting the visit, a talk is given to explain the fundamental characteristics of the Cancer Research Center, and later it shows how the research support services work.

INSTITUTIONAL VISITS.

- **08-19.** María Luisa Carcedo Roces, the Minister of Health, Consumption and Social Welfare, visited the Cancer Research Center. After explaining the characteristics of the center, the research support services were shown and to finish the activity an informal meeting was held with the center staff.
- **11-19.** Carlos García Carbayo, mayor of Salamanca, visited the Cancer Research Center. All research support services were toured and shown.

COMMUNICATION SUPPORT FOR FUNDRAISING

In 2018 and 2019, the Cancer Research Center received € 257,520.13 through donations made to FICUS.

Donations are often made by patient associations. The Communication and Marketing unit frequently organizes guided visits to associations and helps disseminate activities to capture the funds they organize.

PROFILES OF THE CENTER FOR CANCER RESEARCH IN NETWORKS:

The Cancer Research Center has a Twitter, Facebook and LinkedIn account.

PROFILES OF THE CENTER FOR CANCER RESEARCH IN NETWORKS

The Cancer Research Center has a Twitter, Facebook and LinkedIn account.

CIC
Centro de Investigación del Cáncer

SCIENTIFIC REPORT

2018 | 2019

iBMCC
Instituto de Biología Molecular y Celular del Cáncer (USAL - CSIC)

Universidad de Salamanca
Campus de Excelencia Internacional

800 años
1218 - 2018

CSIC
Consejo Superior de Investigaciones Científicas

HR EXCELLENCE IN RESEARCH

Fondo Europeo de Desarrollo Regional
Unión Europea
Junta de Castilla y León
Consejería de Educación
Europa impulsa nuestro crecimiento

PROGRAMA DE FORTALECIMIENTO DE ESTRUCTURAS DE INVESTIGACIÓN DE CASTILLA Y LEÓN "ESCALERA DE EXCELENCIA" COFINANCIADO POR EL P.O. FEDER DE CASTILLA Y LEÓN 14-20 *(Ref. CLC-2017-01)*

El objetivo temático de este tipo de actuaciones es promover el desarrollo tecnológico, la innovación y una investigación de calidad (OT.1)