ANNUAL SCIENTIFIC REPORT 2013

IDIBAPS

ANNUAL SCIENTIFIC REPORT **2013**

IDIBAPS

Published by:
IDIBAPS
Rosselló, 149-153
08036 Barcelona

Editorial Board
Pastora Martínez, Managing Director
Laura González, Managing Director's Assistant
Gemma Llaverías, Head of Scientific Career Unit

Graphic Design
Gemma Alberich

Legal diposit
B-47.798-2005

© IDIBAPS 2014
http://creativecommons.org/licenses/by-nc-sa/4.0/

Institució CERCA
Centres de Recerca de Catalunya

ANNUAL SCIENTIFIC REPORT **2013**

Index

7 **Foreword IDIBAPS**
About IDIBAPS
IDIBAPS Researchers
Research and Innovation Outputs
Scientific Facilities
Training
Commitment to Society

54 **Area 1**
Biological aggression and response mechanisms

84 **Area 2**
Respiratory, cardiovascular and renal pathobiology and bioengineering

134 **Area 3**
Liver, digestive system and metabolism

196 **Area 4**
Clinical and experimental neuroscience

250 **Area 5**
Oncology and haematology

300 **Transversal Research groups**

311 **Team and group leaders index**

About IDIBAPS

The Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) is a public research center dedicated to translational research in the field of biomedicine.

It aims to integrate state-of-the-art basic research and quality clinical research in order to acquire and transfer knowledge regarding the main health problems present in our society, with the final purpose of improving their prevention and treatment. Therefore, innovation and technological progress are at the forefront of IDIBAPS. The IDIBAPS staff consists of more than 460 principal investigators, making IDIBAPS one of the most powerful translational research centers in Spain.

IDIBAPS is situated in a melting pot location for biomedical research, the Clínic Campus. Here the School of Medicine of the University of Barcelona, the Hospital Clínic of Barcelona and the Barcelona Institute of Biomedical Research (IIBB-CSIC) are found right next to one another. This strategic positioning is ideal for creating powerful synergies and ensuring that IDIBAPS research is effectively transferred to the patient and featured in the training of new health professionals.

IDIBAPS is accredited as an Instituto de Investigaciones Sanitarias by the Instituto de Salud Carlos III (ISCIII).

The research activities of the Institute are divided into five different areas, which encompass 59 top-level research teams. IDIBAPS researchers work in five different fields of activity:

AREA 1
Biological aggression and response mechanisms

AREA 2
Respiratory, cardiovascular and renal pathobiology and bioengineering

AREA 3
Liver, digestive system and metabolism

AREA 4
Clinical and experimental neuroscience

AREA 5
Oncology and haematology

Additionally, several transversal groups perform research in Primary Care, Nursing, Pharmacology and Clinical Trials.

Scientific breakthroughs are never the result of chance. They are the fruit of long-term commitments that involve not only researchers, but also society as a whole. IDIBAPS is a consortium that has made such a commitment, to encourage translational research, innovation and technological progress in the field of biomedicine, through different programmes addressing diseases with a high prevalence, morbidity and mortality in our society.

Focus on translational research

The data presented in this Annual Scientific Report details the ever-growing scientific achievements made by IDIBAPS investigators and their capacity for attracting public and private funding. This enormous potential for capturing resources and their conversion into results applicable to clinical practice constitute the best guarantee for securing the future of the Institute. With 7 submitted patents in 2013, and a growing number of transfer agreements, the research underway at IDIBAPS has a direct impact on society and industry.

In 2013 IDIBAPS researchers published 1,005 original articles in high-impact scientific journals. As detailed in other sections of this Report, the progression of the yearly IF figures show a growing trend, achieving 5,595 IF points in 2013. With a 72 % of the original papers published in journals pertaining to the upper quartile of impact in their respective fields, scientific production at IDIBAPS continues to grow in volume as well as in quality. The number of reviews (148), editorials (40) and clinical guidelines (38) that the Institute's researchers either led or participated in during 2013 is another indicator of their strong influence in the scientific community.

Funding sources

The economic figures of the Institute are another example of its high levels of competitiveness. The funding of IDIBAPS research, coming from multiple public sources but mainly from competitive research calls, ensures the sustainability and the leading capacity of the researchers and their scientific projects.

The funding of IDIBAPS during 2013 totalled more than 24 million Euros.

Around 23 % of this amount corresponds to the contribution of the Generalitat de Catalunya from the Departament d'Economia i Coneixement (DECO) and the Departament de Salut (DSalut). The rest of the funding obtained by IDIBAPS during 2013 corresponds to calls for research funding (62 %), as well as contracts and cooperative agreements with private entities (12 %), IDIBAPS core facility services (3 %), and financial income sources.

Organisation chart

IDIBAPS requires a solid administrative infrastructure to support the state-of-the-art research developed by its researchers.

For this reason, in addition to developing its own scientific management and administrative units, IDIBAPS works together with the Fundació Clínic per a la Recerca Biomèdica to ensure efficiency and quality in the services offered to its research staff, in particular, in the areas of research project management and administration.

Administration Units

DIRECTION
Ramon Gomis
Director
Gemma Pedrola
Assistant

MANAGING DIRECTION
Pastora Martínez
Managing Director
Laura González
Assistant

ADMINISTRATION UNITS

RESEARCH CAREER
Gemma Llaverias

INTERNATIONAL UNIT
Gemma Pascual

KNOWLEDGE MANAGEMENT
Marta Vidal

CORE FACILITIES MANAGEMENT
Anna Bosch

LABORATORIES MANAGEMENT
Sandra Piquer
Head
Cristina Canaleta
Labmanager
Maite Cazorla
Labmanager
Marta Diví
Labmanager
Marta Julià
Labmanager
Pepa Ros
Labmanager
M. Isabel Sánchez
Labmanager
Sonia Travé
Labmanager
Montserrat Rigol
Animal Welfare
Vicenç Rioja
Sterilization facility

Board of Governors

The Board of Governors' main responsibilities are: to supervise IDIBAPS actions, budget and results; to make key scientific decisions in consultation with the Scientific Advisory Board, and to evaluate the implementation of the strategic plan.

CHAIRMAN
Josep Maria Martorell
General Director, Direcció General de Recerca, Departament d'Economia i Coneixement, Generalitat de Catalunya

VICE-CHAIRMAN
Cristina Suñol
Director, Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC)

BOARD MEMBERS
Jordi Alberch
Research Vice-Dean, Universitat de Barcelona

Joan Bigorra
Director of Innovation, Hospital Clínic de Barcelona

Lluís Calvo
Institutional Coordinator, Consejo Superior de Investigaciones Científicas (CSIC) in Catalonia

Francesc Cardellach
Dean of the School of Medicine, Universitat de Barcelona

Carles Constante
General Director, Direcció General de Planificació i Recerca en Salut, Departament de Salut, Generalitat de Catalunya

Ramon Gomis
Director, IDIBAPS

Josep Maria Piqué
General Manager, Hospital Clínic de Barcelona

SECRETARY
Pastora Martínez
Managing Director, IDIBAPS

Scientific Advisory Board

The Scientific Advisory Board is comprised of external scientific leaders, many of which work abroad, who advise IDIBAPS on different scientific and political issues affecting its activities.

CHAIRMAN
Jesús Ávila
Centro de Biología Molecular Severo Ochoa (CBM), Madrid

BOARD MEMBERS
María Blasco
Centro Nacional de Investigaciones Oncológicas (CNIO), Madrid

Bartolomé Celli
Harvard University, Cambridge

Francisco Fernández Avilés
Hospital Gregorio Marañón, Madrid

Roberto Gallego
Instituto de Neurociencias de Alicante, Universidad Miguel Hernández - CSIC

Francisco Javier García-Sancho
Instituto de Biología y Genética Molecular, Valladolid

Guadalupe García-Tsao
Yale Liver Center, New Haven

Roberto Groszmann
Yale University School of Medicine, West Haven

José López Barneo
Instituto de Biomedicina de Sevilla (IBiS)

Carlos López Otín
Universidad de Oviedo

Carlos Macaya
Hospital Clínico San Carlos, Madrid

Óscar Marín
Instituto de Neurociencias de Alicante, Universidad Miguel Hernández - CSIC

José M. Mato
Centro de Investigación Cooperativa en Biociencias (CIC bioGUNE), Bizcaya

Federico Mayor
Centro de Biología Molecular Severo Ochoa, Madrid

Ginés Morata
Centro de Biología Molecular Severo Ochoa, Madrid

Miguel Ángel del Pozo
Centro Nacional de Investigaciones Cardiovasculares(CNIC), Madrid

Ciril Rozman
Hospital Clínic de Barcelona, Universitat de Barcelona

Jesús San Miguel
Hospital Clínico de Salamanca

Francisco Sánchez-Madrid
Hospital La Princesa, Madrid

Eugenio Santos
Centro de Investigación del Cáncer (CIC), Salamanca

Antonio Vidal-Puig
School of Clinical Medicine, University of Cambridge

Steering Committee

The Steering Committee is responsible for the supervision of the progress achieved by the five IDIBAPS research areas, the recruitment of new scientists within the framework of different programmes, and the evaluation of IDIBAPS training programmes.

CHAIRMAN
Ramon Gomis
Director, IDIBAPS

Elías Campo
Director of Research, Hospital Clínic de Barcelona and Director, Fundació Clínic per a la Recerca Biomèdica

Josep Maria Llovet
Head of the IDIBAPS Group "Translational research in hepatic oncology"

Anna Planas
Coordinator of the IDIBAPS Research Area 4

SECRETARY
Pastora Martínez
Managing Director, IDIBAPS

Internal Advisory Committee

On a daily basis, IDIBAPS' director is assessed by an Internal Advisory Committee formed by IDIBAPS researchers. This committee helps the director implement the strategic decisions made by the Board of Governors.

CHAIRMAN
Ramon Gomis
Director, IDIBAPS

STEERING COMMITTEE MEMBERS
Elías Campo
Director of Research, Hospital Clínic de Barcelona
Director, Fundació Clínic per a la Recerca Biomèdica

Josep Maria Llovet
Head of the IDIBAPS Group "Translational research in hepatic oncology"

Anna Planas
Coordinator of the IDIBAPS Area 4

INSTITUTIONAL REPRESENTATIVES
Manel Ramos
Doctors' Representatives, Hospital Clínic de Barcelona

Guadalupe Mengod
Deputy Director, Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC)

Cristina Suñol
Director, Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC)

Francesc Cardellach
Dean of the School of Medicine, Universitat de Barcelona

AREA REPRESENTATIVES

AREA 1
Josep Maria Miró, Coordinator
Maria Cinta Cid, Representative

AREA 2
Ramón Farré, Coordinator
Joan Albert Barberà, Representative

AREA 3
Julià Panés, Coordinator
Jorge Ferrer, Representative

AREA 4
Anna Planas, Coordinator
Pablo Villoslada, Representative

AREA 5
Dolors Colomer, Coordinator
Cristina Nadal, Representative

TRAINING COORDINATOR
Neus Agell
Vice-Dean of School of Medicine, Universitat de Barcelona

GUEST MEMBERS
Àlvar Agustí
CIBERes Scientific Director

Joan Bigorra
Director of Innovation, Hospital Clínic de Barcelona

Jaume Bosch
CIBERehd Scientific Director

Josep M. Gatell
National Coordinator of the RETIC on AIDS

Joan Rodés
Member of the IDIBAPS Scientific Council

Antonio Sisó
CAPSE-GESCLINIC Research Coordinator

SECRETARY
Pastora Martínez
Managing Director, IDIBAPS

IDIBAPS Researchers

IDIBAPS is firm in its belief that by investing in quality researchers, the benefits for the institute are multiple; from increased research capacity, to increased scientific impact and increased international recognition, thus helping towards its overall goal of becoming a European Centre of Excellence. The following table shows the distribution of IDIBAPS researchers. It is worth to mention that more than 400 IDIBAPS researchers come from Hospital Clínic de Barcelona (HCB), University of Barcelona (UB), IIBB-CSIC, and institutions other than IDIBAPS. The table below shows the origin of the 465 accredited investigators:

IDIBAPS researchers by Institution

HCB	200
HCB and UB	142
UB	31
CSIC-IIBB	33
IDIBAPS	49
ICREA	5
FCRB	5
Total	**465**

HCB
HCB AND UB
UB
CSIC-IIBB
IDIBAPS
FCRB
ICREA

Institució Catalana de Recerca i Estudis Avançats (ICREA)

ICREA, the Catalan Institute for Research and Advanced Studies, is a foundation supported by the Catalan Government through the Catalan Ministry of Economy and Knowledge that aims to recruit top scientists for the Catalan R&D system. Currently IDIBAPS has five ICREA Research Professors:

Dr. Josep M. Llovet
Translational research group in liver oncology

The Translational research group in liver oncology was created in 2006 by Dr. Josep M. Llovet, ICREA Research Professor of the IDIBAPS and Professor of Medicine of the Mount Sinai School of Medicine. The group is composed of 10 people from the IDIBAPS and leads an international consortium on genomic research in liver cancer, the HCC Genomic Consortium, with about 30 investigators.

In 2009 it received the AACR-Landon International Innovator Award, and was acknowledged as a Singular Research Group by the Catalan Government. In 2010 the group started the coordination of a European FP7-HEALTH project, the HEPTROMIC consortium, involving the coordination of 6 academic centres and 2 companies, with the purpose of identifying new oncogenes and treatment targets. In 2011, the group was awarded with the grant of the Spanish Association against Cancer (Asociación Española contra el Cancer, AECC). Finally, during 2012-2013 Dr. Llovet has been nominated as President of the International Liver Cancer Association (ILCA), and he received the Hans Popper International award (2012) and the Josep Trueta award (2013).

The fundamental contributions of the group during the last 5 years have been the following:

- Definition of a molecular classification of hepatocellular carcinoma (Hoshida, New England Journal of Medicine 2008); Chang, Can Res, 2008; Hoshida, Cancer Res 2009; Villanueva, Gastroenterology 2011; Minguez, J Hep 2011, Hoshida, Gastroenterology 2013) and cholangiocarcinoma (Sia, Gastroenterology 2013).

- Identification of key oncogenes in hepatocarcinogenesis, such as miRNA Let-7 (viswanathan, Nature Genetics 2009; Toffanin, Gastroenterology 2011), EGF and c-MET (Keng, Nature Biotech 2009), AEG-1 (Yoo, J Clin Invest, 2009) and the signalling pathway of IGFR1 (Tovar, J Hepatol 2010), Wnt (Lachenmayer, Clin Can Res 2012) and Notch (Villanueva, Gastroenterology 2012).

- Leadership of EASL-EORTC Guidelines: Dr Llovet has been working as Chair of the Clinical Practice Guidelines on Management of HCC endorsed by EASL and EORTC and published in J Hepatology 2012 and European Journal of Cancer 2012, and guidelines of design of clinical trials (Llovet, J Nat Can Inst 2008).

Dr. Antonio Postigo
Group of Regulation of Gene Expression in Cell Differentiation and Cancer

Dr. Postigo's group investigates the molecular mechanisms involved in the regulation of gene expression during normal cell differentiation and in cancer, focusing on the ZEB family of transcription factors. ZEB1 and ZEB2 modulate cell differentiation, maintain stemness in normal and cancer stem cells and participate in several stages of tumor initiation and progression. Thus, ZEB factors are essential effectors of the pro-oncogenic effects of several pathways involved in cancer, namely, Wnt, TGFbeta, Notch and Ras. ZEB1 and ZEB1 cooperate with gain-of-function mutations of these pathways in oncogenic transformation, induction of epithelial-mesenchymal transition (EMT) and tumor invasiveness and metastasis.

The group uses a wide number of vitro techniques and in vivo models to address two main research lines:

- Study the role of ZEB1 and ZEB2 in the regulation of normal differentiation in epithelial, skeletal muscle and hematopoietic cells

- Study of the mechanisms by which ZEB1 and ZEB2 regulate tumorigenesis, cancer cell stemness and EMT during cancer progression in colorectal and breast carcinomas.

Research of the group at IDIBAPS has been funded by public (Spanish Ministry of Economy and Competitiveness, the European Union, Catalan Agency for Universities and Research) and private (Spanish Association Against Cancer-AECC, O. Torres Foundation, AVON Cosmetics SAU, La Caixa Foundation, and the Academy of Medical Sciences of Catalonia and the Balearic Islands) grants.

Dr. Albert Pol
Cell proliferation and signalling

The aim of Dr. Pol's group is to characterize - in health and in illness - the cellular processes that are regulated or altered due to lipid accumulation within the cells. All prokaryote and eukaryote cells maintain the evolutive competence of accumulating lipids in organelles known as intracellular lipid droplets. In healthy cells, a small population of lipid droplets is present at all times, though these organelles become abundant in response to different physiopathological conditions such as obesity, diabetes, fatty liver disease (steatosis), liver cirrhosis, viral hepatitis, arteriosclerosis and even cancer. Globally, these disorders affect over half of the population in western countries. Recent advances in the cellular biology of lipid droplets have shown the latter to be multifunctional organelles that are metabolically very active and thus constitute key elements in the complex exchange of lipids and proteins in constant movement within the cells. In this scenario, the group is especially focused in the cellular cost of the accumulation of cholesterol in organelles and the role of the caveolin protein in the regulation of these fluxes.

Dr. Maria V. Sánchez-Vives
Cortical networks and EVENT Lab (Virtual Environments in Neuroscience and Technology)

Dr. Sánchez-Vives joined the IDIBAPS in 2008 and is the head of the Systems Neurosciences Group of the IDIBABS, acknowledged by the AGAUR as a Consolidated Research Group.

Understanding how the brain processes information and how brain activity is generated and modulated in neuronal networks is crucial for intervening in cerebral function when the latter has been altered. Neuron connectivity and the cellular and synaptic properties conform brain activity, and the latter at the same time has effects upon the network. The objective of the Dr. Sánchez-Vives' group is to determine how these processes take place, particularly as regards the generation of brain rhythms: how information is generated, synchronized or encoded. These activity patterns are altered under pathological conditions, and their restoration may contribute to recover function. The models of diseases in genetically modified mice allow us to carry out such studies.

Another line of research of the group is referred to the integration of information in the brain cortex, resulting in body representation. They use virtual reality and brain-computer interfaces with a view to understanding and acting upon these processes. At present, and within the setting of a project integrated in the European Union, the group is studying the usefulness of body representation in virtual reality for the treatment of pain and the restoration of motor function.

Dr. Josep Dalmau
Autoimmunity against synaptic antigens

The Autoimmunity Against Synaptic Antigens team is led by Dr. Josep Dalmau i Obrador, ICREA Research Professor of the IDIBAPS and Professor of Neurology at the University of Pennsylvania in Philadelphia. Dr. Dalmau is a clinical neurooncologist trained and working as Associate Professor of Neurology in the Memorial Sloan-Kettering Cancer Center in New York.

His research focuses on a group of diseases located at the intercrossing of autoimmunity, cancer and synaptic proteins. This includes the description of new syndromes, the associated immune mechanisms, isolation of the target antigens, and the development of diagnostic tests and treatment strategies. These studies have identified 17 autoantigens and have led to diagnostic tests - some of which are used all over the world.

In the last 5 years Dr. Dalmau has discovered a new category of autoimmune processes resulting in alterations of memory, behaviour and cognition, and which may cause psychosis. These processes are associated with autoimmune responses characterized by antibodies targeted to synaptic proteins and receptors such as for example the glutamate receptors (NMDA, AMPA) or the GABA(B) receptors, or to synaptic proteins related with epilepsy (LGI1, Caspr2), among others. Once the antigens have been identified, Dr. Dalmau's group studies focus on the cellular and molecular mechanisms whereby the antibodies alter the function of the synaptic proteins and receptors and produce the symptoms. The results of these studies have had an impact on many medical disciplines and on neuroscience, since they offer a link between immune processes and synaptic activity related to memory, behaviour, psychosis, epilepsy and neuron degeneration.

ISCIII ISIS Program

IDIBAPS is a research Institute accredited through the Spanish Government's Health Research Institutes Accreditation Programme. This initiative includes the ISIS contracts to attract senior researchers with a proven experience leading research teams.

Dr. Cristina Fillat
Gene Therapy and Cancer Group

The Gene Therapy and Cancer Group led by Dr. Fillat started at IDIBAPS in September 2011, with the support of the ISIS Programme from the Instituto de Salud Carlos III and acknowledged by the Catalan Government as a Singular Research Group. Dr. Fillat's group research focuses on the study of the molecular and cellular basis of pancreatic ductal adenocarcinoma and the development of novel experimental therapies based on gene transfer and virotherapy.

The main research lines are:

- Identify specific cellular pathways and molecular determinants altered in pancreatic tumors.

- Development of antitumoral therapies based on oncolytic adenovirus. Main interest is devoted to the search for sensitizers of adenoviral oncolysis and to study their mechanisms of synergie. Special emphasis is also applied to engineer tumor-selective oncolytic adenoviruses.

- Explore novel non-viral experimental therapies for pancreatic tumors.

Dr. Pere Santamaria
Pathogenesis and Treatment of Autoimmunity

Dr. Santamaria's laboratory has two distinct components: one for purely basic biomedical research which studies the role of particular genes and molecules in the development and functioning of the immune system; and another, more applied, based on the study of the immunological effects of a new therapeutic platform they have developed for the treatment of autoimmune diseases, which include type 1 diabetes, lupus and autoimmune diseases of the central nervous system. This treatment, based on nanotechnology, works by way of an immunological mechanism for protection against autoimmunity designed by mother nature, which they have learned to manipulate by using a new type of drug, also discovered by Santamaria's group. One of the main objectives is to start using this therapeutic platform with patients through the conducting of clinical trials.

IDIBAPS 50/50 Program

With the final mission to strengthen translational clinical research, IDIBAPS and Hospital Clinic of Barcelona started in 2012 this pioneering program designed to facilitate the combination of research and clinical activity. The 50/50 researchers are young medical staff specialists (MD) with a strong research career (PhD) built up, at least in part, in the most prestigious foreign research centers. These junior group leaders are called to be the future clinical research group leaders that this institution will need.

Dr. Felicia Alexandra Hanzu (ICMDM / IDIBAPS)

Endocrine disorders: crosstalk between molecular and metabolic determinants

Dr. Hanzu´s group studies the crosstalk between molecular and metabolic determinants in endocrine pathologies, respectively the molecular determinants underlying physiopathological mechanisms of endocrine tumors. The aim is to translate knowledge from the basic research, in endocrine tumors, into the clinical practice by focusing on the development of new treatment strategies.

Adrenal hormones secreted in an autonomous manner, as in endocrine tumors, determine disruption of the endocrine circadian rhythms inducing aberrant systemic tissue responses. Visceral adipose tissue, one of the targets of cortical and medulla adrenal hormones, has a primordial role in the development of cardiometabolic diseases.

The endocrine tumors group is studying the impact of adrenal hormone secreting tumours on the visceral adipose tissue plasticity, on the secreted adipokines and their effect on the endothelium. Patients with endogenous hypercortisolism present an increased risk of cardiovascular disease even after cure. The understanding of the epigenetic mechanisms, underlying the altered cardiometabolic memory, is a further goal of this group.

The group started up in 2012, after Dr. Hanzu was incorporated to IDIBAPS and Hospital Clinic.

Milestones of her scientific formation are the Rio Hortega fellowship and her trainings in translational research at the Free University of Brussels and the University of Medicine Munich.

Dr. Ignacio Revuelta (ICNU / IDIBAPS)

Translational research in posttransplant neoplasia

The Translational Research group in Posttransplant Neoplasia led by Ignacio Revuelta started up at the IDIBAPS in January 2012 after his stay at Harvard Medical School in Boston.

Cancer is the second leading cause of mortality in general and transplant population, and cancer rates are higher after kidney transplantation compared with the general population. Several pathogenic factors have been implicated in oncogenesis and metastasis development in transplant patients, such as the direct secondary effects of exposure to immunosuppressive drugs.

The use of mTOR inhibitors as immunosuppressive therapy with antioncogenic, antiproliferative and antiangiogenic properties plays a crucial role in the development of posttransplant neoplasms, tumoral progression, and the potential for metastasis. The group has been studying and characterizing the different behavior of posttransplant neoplasia. However, knowledge about the understanding of oncogenesis and metastasis development in this particular population is still unresolved, and information on longdistance communication between a tumor and the host organs is unknown.

Dr. Isabel Blanco
(ICT / IDIBAPS)
Translational research in pulmonary vascular diseases: cell proliferation and apoptotic mechanisms in pulmonary arterial hypertension.

Pulmonary arterial hypertension (PAH) is a disease of small pulmonary arteries, characterized by gradual obliteration of the arterial lumen due to the enlargement of the vessel wall. It results in a progressive increase of pulmonary vascular resistance (PVR) and, finally, right ventricular failure and death. While vasoconstriction contributes, especially in earlier stages, the obstructive vascular remodelling is the major cause of the elevated PVR and ultimately the right heart failure. Recent therapeutic advances increase survival and improve quality of life of patients with PAH. However, currently available drugs act primarily as vasodilators and do not alter the disease process or the structural lesions in the pulmonary arteries.

Therefore, there is a need to identify new signaling pathways in the pathogenesis of PAH, which may represent different more appropriate therapeutic targets. With the 50/50 program started in 2013 Dr. Blanco's group aims going from the bench to the bed side studying with cells, tissue samples, animal models and also human samples potential biomarkers of the disease activity and progression; as well as potential new drugs to reverse the proliferative remodelling phenotype in PAH.

Dr. Gisela Sugranyes
(ICN / IDIBAPS)
Multimodal neuroimaging in high risk and early psychosis.

Dr. Sugranyes' group was established in 2013 with the aim to understand the neural mechanisms underlying the development of psychotic disorders in children and adolescents. Specifically, it aims to identify structural and functional neural correlates which characterize youth at high risk for psychosis and during the early phase of the disorder. It also aims to explore the relationship between neuroimaging measures and clinical and neuropsychological phenotypes, in addition to the interaction with specific genotypes. Particular focus is given to the interaction between illness-related changes and processes associated to normative child and adolescent neurodevelopment, given the age range of this sample. On a translational level, priority is given to the identification of factors predicting transition to psychosis and functional outcomes, in addition to identification of treatment targets.

Dr. Carlos Fernández de Larrea
(ICMHO / IDIBAPS)
Mechanisms of progression in monoclonal gammopathies.

Dr. Fernández de Larrea's group is focused on a comprehensive study on patients with multiple myeloma in complete remission, in order to investigate whether or not immune restoration is associated with the emergence of oligoclonal bands and to a continued response, and to search common features that these patients can share with those with long-lasting stable monoclonal gammopaties of undetermined significance (MGUS). For this purpose, a wide spectrum of biological studies in peripheral blood and bone marrow are performed in patients after transplantation or induction chemotherapy only, in comparison with patients with active myeloma.

Research and Innovation Outputs

Scientific publications

Since its creation in 1996, IDIBAPS has shown constant growth of the main research outcomes: scientific publications, translation of knowledge and innovation, and capacity to get research funds.

Indicators are divided into three groups intended to reflect output (number of publications), quality (total impact factor, mean impact factor and %Q1) and intramural collaboration (% of publications carried out by one, two or more IDIBAPS teams). In 2013 these figures were as follows:

The number and quality of papers published by IDIBAPS have not stopped increasing since its creation in 1996 to 2012. Despite the number of publications have not increased in 2013 compared to 2012, an increase in the scientific impact of the research conducted is observed through an increase in the total impact factor (5,595 versus 5,334) and mean impact factor (5.6 versus 5.2).

	OUTPUT	TOTAL I.F.	Mean I.F.	%Q1
Original articles	1,005	5,595	5.6	72%
Reviews	148	628	4.2	51%
Editorials	40	278	6.9	78%
Clinical guidelines	38	225	5.9	50%

FIGURE TITLE
2013 publication outputs

FIGURE LEGEND
2013 number and quality of the publications.
Output – Total number of documents published in scholarly journals indexed in the ISI Web of Science.
Total IF – Accumulated impact factor of all the scientific publications.
Mean IF – Mean impact factor of all the scientific publications.
%Q1 – % of publications published in journals ranked in the first quartile (top 25%) of their category as ordered by the 2012 Journal Citation Reports.

SOURCE
2012 Journal Citation Reports, ISI Web of Science (Thomson Reuters, Inc.).

FIGURE TITLE
2013 intra-mural collaboration original articles.

FIGURE LEGEND
Distribution of the original articles authored by members of one, two, three and four or more IDIBAPS teams.

FIGURE TITLE

Evolution of the total number of original articles and the total number of original articles per area.

FIGURE LEGEND

Only original articles were taken into consideration. Publications resulting from collaboration between teams from two different areas have been counted once for each area, so the sum of the articles per area is higher than the total.

FIGURE TITLE

Evolution of the total impact factor and the mean impact factor.

FIGURE LEGEND

Only original articles were taken into consideration.

SOURCE

2012 Journal Citation Reports, ISI Web of Science (Thomson Reuters, Inc.).

The following table shows the peer-reviewed publications from IDIBAPS in the highest impact factor journals (impact factor > 10). It is noteworthy that the list reflects the 103 original articles published in 32 of the most relevant scientific journals during 2013, number that keeps increasing year by year.

JOURNAL	IF	TOTAL ORIGINAL ARTICLES
New Engl J Med	51.658	4
Lancet	39.06	1
Nature	38.597	2
Nat Genet	35.209	4
Cell	31.957	1
JAMA-J Am Med Assoc	29.978	1
Lancet Oncol	25.117	2
Nat Med	24.302	1
Lancet Neurol	23.917	3
Nat Cell Biol	20.761	1
Lancet Infect Dis	19.966	2
Immunity	19.795	1
J Clin Oncol	18.038	10
Circulation	15.202	4
Am J Psychiatry	14.721	1
Alzheimers Dement	14.483	2
JNCI-J Natl Cancer I	14.336	1
J Am Coll Cardiol	14.086	6
Dev Cell	12.861	1
Gastroenterology	12.821	9
Gene Dev	12.444	1
J Allergy Clin Immunol	12.047	1
Autophagy	12.042	1
Hepatology	12.003	14
Ann Neurol	11.193	2
Am J Respir Crit Care Med	11.041	4
J Cell Biol	10.822	1
Sci Transl Med	10.757	1
Gut	10.732	9
Eur Urol	10.476	1
Leukemia	10.164	9
Nat Commun	10.015	2

Find below a selection of these publications with main or contributing authors from IDIBAPS, a total of 50 original articles.

AUTHORS	TITLE	REFERENCE	GROUPS INVOLVED
Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Martínez-González MA, for the PREDIMED Study Investigators	**Primary prevention of cardiovascular disease with a Mediterranean diet**	New Engl J Med 368(14):1279-1290	2.4
Ramsay AJ, Quesada V, Foronda M, Conde L, Martínez-Trillos A, Villamor N, Rodríguez D, Kwarciak A, Garabaya C, Gallardo M, López-Guerra M, López-Guillermo A, Puente XS, Blasco MA, Campo E, López-Otín C	**POT1 mutations cause telomere dysfunction in chronic lymphocytic leukaemia**	Nat Genet 45(5):526-530	5.2; 5.8; 5.9
Schneeberger M, Dietrich MO, Sebastián D, Imbernón M, Castaño C, Garcia A, Esteban Y, Gonzalez-Franquesa A, Rodríguez IC, Bortolozzi A, Garcia-Roves PM, Gomis R, Nogueiras R, Horvath TL, Zorzano A, Claret M	**Mitofusin 2 in POMC neurons connects ER stress with leptin resistance and energy imbalance**	Cell 155(1):172-187	3.14; 3.15; 4.1
Martínez-García MA, Capote F, Campos-Rodríguez F, Lloberes P, Díaz de Atauri MJ, Somoza M, Masa JF, González M, Sacristán L, Barbé F, Durán-Cantolla J, Aizpuru F, Mañas E, Barreiro B, Mosteiro M, Cebrián JJ, de la Peña M, García-Río F, Maimó A, Zapater J, Hernández C, Grau SanMarti N, Montserrat JM; Spanish Sleep Network	**Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial**	JAMA-J Am Med Assoc 310(22):2407-2415	2.6
Titulaer MJ, McCracken L, Gabilondo I, Armangue T, Glaser C, Iizuka T, Honig LS, Benseler S, Kawachi I, Martinez-Hernandez E, Aguilar E, Gresa-Arribas N, Ryan-Florance N, Torrents A, Saiz A, Rosenfeld MR, Balice-Gordon R, Graus F, Dalmau J	**Treatment and prognostic factors for long-term outcome in patients with anti-N-Methyl-D-Aspartate (NMDA) receptor encephalitis: a cohort study**	Lancet Neurol 12(2):157-165	4.10
Iranzo A, Tolosa E, Gelpi E, Molinuevo JL, Valldeoriola F, Serradell M, Sanchez-Valle R, Vilaseca I, Lomeña F, Vilas D, Lladó A, Gaig C, Santamaria J	**Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study**	Lancet Neurol 12(5):443-53	4.3; 4.4
Llovet JM, Decaens T, Raoul JL, Boucher E, Kudo M, Chang C, Kang YK, Assenat E, Lim HY, Boige V, Mathurin P, Fartoux L, Lin DY, Bruix J, Poon RT, Sherman M, Blanc JF, Finn RS, Tak WY, Chao Y, Ezzeddine R, Liu D, Walters I, Park JW	**Brivanib in patients with advanced hepatocellular carcinoma who where intolerant to sorafenib or for whom sorafenib failed: results from the randomized Phase III BRISK-PS Study**	J Clin Oncol 31:3509-3516	3.5
Miro JM, Pericas JM, del Rio A; Heras M,Hospital Clinic Endocarditis Study Group	**A new era for treating Enterococcus faecalis endocarditis: ampicillin plus short-course gentamicin or ampicillin plus ceftriaxone: that is the question!**	Circulation 127(17):1763-1766	2.1
Valenzuela-Alcaraz B, Crispi F, Bijnens B, Cruz-Lemini M, Creus M, Sitges M, Bartrons J, Civico S, Balasch J, Gratacós E	**Assisted reproductive technologies are associated with cardiovascular remodeling in utero that persists postnatally**	Circulation 128(13):1442-50	2.2; 3.1; 3.2
Torrent C, Bonnin Cdel M, Martínez-Arán A, Valle J, Amann BL, González-Pinto A, Crespo JM, Ibáñez Á, Garcia-Portilla MP, Tabarés-Seisdedos R, Arango C, Colom F, Solé B, Pacchiarotti I, Rosa AR, Ayuso-Mateos JL, Anaya C, Fernández P, Landín-Romero R, Alonso-Lana S, Ortiz-Gil J, Segura B, Barbeito S, Vega P, Fernández M, Ugarte A, Subirà M, Cerrillo E, Custal N, Menchón JM, Saiz-Ruiz J, Rodao JM, Isella S, Alegría A, Al-Halabi S, Bobes J, Galván G, Saiz PA, Balanzá Martínez V, Selva G, Fuentes-Durá I, Correa P, Mayoral M, Chiclana G, Merchan-Naranjo J, Rapado-Castro M, Salamero M, Vieta E	**Efficacy of functional remediation in bipolar disorder: a multicenter randomized controlled study**	Am J Psychiatry 170(8):852-859	4.7; 4.8

Gauthier S, Molinuevo JL	**Benefits of combined cholinesterase inhibitor andmemantine treatment in moderate-severe Alzheimer's disease**	Alzheimers Dement 9(3):326-331	4.3
Castells A, Bessa X, Quintero E, Bujanda L, Cubiella J, Salas D, Lanas A, Carballo F, Morillas JD, Hernández C, Jover R, Montalvo I, Arenas J, Cosme A, Hernández V, Iglesias B, Castro I, Cid L, Sala T, Ponce M, Andrés M, Teruel G, Peris A, Roncales MP, González-Rubio F, Seoane-Urgorri A, Grau J, Serradesanferm A, Pellisé M, Ono A, Cruzado J, Pérez-Riquelme F, Alonso-Abreu I, Carrillo-Palau M, de la Vega-Prieto M, Iglesias R, Amador J, Blanco JM, Sastre R, Ferrándiz J, González-Hernández MJ, Andreu M; COLONPREV study investigators	**Risk of advanced proximal neoplasms according to distal colorectal findings: comparison of sigmoidoscopy-based strategies**	JNCI-J Natl Cancer 105(12):878-886	3.11
Penela D, Magaldi M, Fontanals J, Martin V, Regueiro A, Ortiz JT, Bosch X, Sabaté M, Heras M	**Hypothermia in acute coronary syndrome: brain salvage versus stent thrombosis?**	J Am Coll Cardiol 61(6):686-687	2.1
Penela D, Van Huls Vans Taxis C, Aguinaga L, Fernández-Armenta J, Mont L, Castel MA, Heras M, Tolosana JM, Sitges M, Ordóñez A, Brugada J, Zeppenfeld K, Berruezo A	**Neurohormonal, structural, and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction: a prospective multicenter study**	J Am Coll Cardiol 62(13):1195-1202	2.1
Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J	**Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies: the OVERCOME trial (preventiOn of left Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive ChemOtherapy for the treatment of Malignant hEmopathies)**	J Am Coll Cardiol 61(23):2355-2362	2.1; 2.2; 3.4; 5.3; 5.7; 5.8
Penela D, Van Huls Van Taxis C, Aguinaga L, Fernández-Armenta J, Mont L, Castel MA, Heras M, Tolosana JM, Sitges M, Ordóñez A, Brugada J, Zeppenfeld K, Berruezo A	**Neurohormonal, structural, and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction: a prospective multicenter study**	J Am Coll Cardiol 62(13):1195-1202	2.2
Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, Durand F, Gustot T, Saliba F, Domenicali M, Gerbes A, Wendon J, Alessandria C, Laleman W, Zeuzem S, Trebicka J, Bernardi M, Arroyo V; CANONIC Study Investigators of the EASL–CLIF Consortium	**Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis**	Gastroenterology 144(7):1426-1437	3.4
Revill K, Wang T, Lachenmayer A, Kojima K, Harrington A, Li J, Hoshida Y, Llovet JM, Powers S	**Genome-wide methylation analysis and epigenetic unmasking identify tumor suppressor genes in hepatocellular carcinoma**	Gastroenterology 145(6):1424-1435	3.5
Hoshida Y, Villanueva A, Sangiovanni A, Sole M, Hur C, Andersson KL, Chung RT, Gould J, Kojima K, Gupta S, Taylor B, Crenshaw A, Gabriel S, Minguez B, Iavarone M, Friedman SL, Colombo M, Llovet JM, Golub TR	**Prognostic gene expression signature for patients with hepatitis C-related early-stage cirrhosis**	Gastroenterology 144(5):1024-1030	3.5
Sia D, Hoshida Y, Villanueva A, Roayaie S, Ferrer J, Tabak B, Peix J, Sole M, Tovar V, Alsinet C, Cornella H, Klotzle B, Fan JB, Cotsoglou C, Thung SN, Fuster J, Waxman S, Garcia-Valdecasas JC, Bruix J, Schwartz ME, Beroukhim R, Mazzaferro V, Llovet JM	**Integrative molecular analysis of intrahepatic cholangiocarcinoma reveals 2 classes that have different outcomes**	Gastroenterology 144(4):829-840	3.5; 3.10
Berzigotti A, Seijo S, Arena U, Abraldes JG, Vizzutti F, García-Pagán JC, Pinzani M, Bosch J	**Elastography, Spleen Size, and Platelet Count Identify Portal Hypertension in Patients with Compensated Cirrhosis**	Gastroenterology 144(1):102-111	3.6

Panés J, López-Sanromán A, Bermejo F, García-Sánchez V, Esteve M, Torres Y, Domènech E, Piqueras M, Gomez-García M, Gutiérrez A, Taxonera C, Sans M, AZTEC Study Group	**Early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's Disease**	Gastroenterology 145(4): 766-774	3.7
van Arensbergen J1, García-Hurtado J, Maestro MA, Correa-Tapia M, Rutter GA, Vidal M, Ferrer J	**Ring1b bookmarks genes in pancreatic embryonic progenitors for repression in adult β cells**	Gene Dev 27(1):52-63	3.13
Fernández-Bertolín L, J Mullol, M Fuentes-Prado, I Alobid, J Roca-Ferrer, C Picado, L Pujols	**Deficient glucocorticoid induction of anti-inflammatory genes in nasal polyp fibroblasts of asthmatic patients with and without aspirin intolerance**	J Allergy Clin Immunol 132(5):1243-1246	2.8
Rosich L, Colomer D, Roue G	**Autophagy controls everolimus (RAD001) activity in mantle cell lymphoma**	Autophagy 9(1):115-117	5.9
Benítez C, Londoño MC, Miquel R, Manzia TM, Abraldes JG, Lozano JJ, Martínez-Llordella M, López M, Angelico R, Bohne F, Sese P, Daoud F, Larcier P, Roelen DL, Claas F, Whitehouse G, Lerut J, Pirenne J, Rimola A, Tisone G, Sánchez-Fueyo A	**Prospective multicenter clinical trial of immunosuppressive drug withdrawal in stable adult liver transplant recipients**	Hepatology 58(5):1824-1835	3.10
Acevedo J, Fernández J, Prado V, Silva A, Castro M, Pavesi M, Roca D, Jimenez W, Ginès P, Arroyo V	**Relative adrenal insufficiency in decompensated cirrhosis: Relationship to short-term risk of severe sepsis, hepatorenal syndrome, and death**	Hepatology 58(5):1757-1765	3.4
Bañares R, Nevens F, Larsen FS, Jalan R, Albillos A, Dollinger M, Saliba F, Sauerbruch T, Klammt S, Ockenga J, Pares A, Wendon J, Brünnler T, Kramer L, Mathurin P, de la Mata M, Gasbarrini A, Müllhaupt B, Wilmer A, Laleman W, Eefsen M, Sen S, Zipprich A, Tenorio T, Pavesi M, Schmidt HH, Mitzner S, Williams R, Arroyo V; RELIEF study group	**Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: the RELIEF trial**	Hepatology 57(3):1153-1162	3.4; 3.8
Morales-Ibanez O, Domínguez M, Ki SH, Marcos M, Chaves JF, Nguyen-Khac E, Houchi H, Affò S, Sancho-Bru P, Altamirano J, Michelena J, García-Pagán JC, Abraldes JG, Arroyo V, Caballería J, Laso FJ, Gao B, Bataller R	**Human and experimental evidence supporting a role for osteopontin in alcoholic hepatitis**	Hepatology 58(5):1742-1756	3.4; 3.9
Reig M, Rimola J, Torres F, Darnell A, Lope CR, Forner A, Llarch N, Ríos J, Ayuso C, Bruix J	**Post progression survival of patients with advanced hepatocellular carcinoma. Rationale for second line trial design**	Hepatology 58(6):2023-2031	3.5
La Mura V, Pasarín M, Meireles CZ, Miquel R, Rodriguez-Vilarrupla A, Hide D, Gracia-Sancho J, García-Pagán JC, Bosch J, Abraldes JG	**Effects of simvastatin administration on rats with LPS induced liver microvascular dysfunction**	Hepatology 57(3):1172-1181	3.6
Ripoll C, Genescà J, Araujo IK, Graupera I, Augustin S, Tejedor M, Cirera I, Aracil C, Sala M, Hernandez-Guerra M, Llop E, Escorsell A, Catalina MV, Cañete N, Albillos A, Villanueva C, Abraldes JG, Bañares R, Bosch J	**Rebleeding prophylaxis improves outcomes in patients with hepatocellular carcinoma. A multicenter case-control study**	Hepatology 58(6):2079-2088	3.6
Rosado E, Rodríguez-Vilarrupla A, Gracia-Sancho J, Tripathi D, García-Calderó H, Bosch J, García-Pagán JC	**Terutroban, A TP-receptor antagonist, reduces portal pressure in cirrhotic rats**	Hepatology 58(4):1424-1435	3.6
Guañabens N, Monegal A, Cerdá D, Muxí Á, Gifre L, Peris P, Parés A	**Randomized trial comparing monthly ibandronate and weekly alendronate for osteoporosis in patients with primary biliary cirrhosis**	Hepatology 58(6):2070-2078	3.8; 5.3
Boronat A, Gelfand JM, Gresa-Arribas N, Jeong H-Y, Walsh M, Roberts K, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R, Graus F, Rudy B, Dalmau J	**Encephalitis and antibodies to DPPX, a subunit of Kv4.2 potassium channels**	Ann Neurol 73(1):120-128	4.10
Podlesniy P, Figueiro-Silva J, Llado A, Antonell A, Sanchez-Valle R, Alcolea D, Lleo A, Molinuevo JL, Serra N, Trullas R	**Low cerebrospinal fluid concentration of mitochondrial DNA in preclinical Alzheimer disease**	Ann Neurol 74(5):655-668	4.3; 4.11
Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, Duran-Cantolla J, Peña Mde L, Masdeu MJ, Gonzalez M, Campo Fd, Gallego I, Marin JM, Barbe F, Montserrat JM, Farre R; Spanish Sleep Network	**Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort**	Am J Respir Crit Care Med 187(1):99-105	2.5; 2.6

Sellares J, López-Giraldo A, Lucena C, Cilloniz C, Amaro R, Polverino E, Ferrer M, Menéndez R, Mensa J, Torres A	**Influence of Previous Use of Inhaled Corticoids on the Development of Pleural Effusion in Community-Acquired Pneumonia**	Am J Respir Crit Care Med 187(11):1241-1248	2.6
Kassan A, Herms A, Fernández-Vidal A, Bosch M, Schieber NL, Reddy BJ, Fajardo A, Gelabert-Baldrich M, Tebar F, Enrich C, Gross SP, Parton RG, Pol A	**Acyl-CoA synthetase 3 promotes lipid droplet biogenesis in ER microdomains**	J Cell Biol 203(6):985-1001	5.12
García F, Climent N, Guardo AC, Gil C, León A, Autran B, Lifson JD, Martínez-Picado J, Dalmau J, Clotet B, Gatell JM, Plana M, Gallart T; DCV2/MANON07-ORVACS Study Group.	**A dendritic cell-based vaccine elicits T cell responses associated with control of HIV-1 replication.**	Sci Transl Med 5(166):166ra2	1.3
Reichenbach V, Muñoz-Luque J, Ros J, Casals G, Navasa M, Fernández-Varo G, Morales-Ruiz M, Jiménez W	**Bacterial lipopolyshaccaride inhibits CB2 receptor expression in human monocytic cells**	Gut 62(7):1089-1091	3.3; 3.4
Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF, Soria G, Tudela R, Planas AM, Fernández-Hernando C, Arroyo V, Jiménez W, Morales-Ruiz M	**Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats**	Gut 62(1):138-145	3.4
Affò S, Dominguez M, Lozano JJ, Sancho-Bru P, Rodrigo-Torres D, Morales-Ibanez O, Moreno M, Millán C, Loaeza-del-Castillo A, Altamirano J, García-Pagán JC, Arroyo V, Ginès P, Caballería J, Schwabe RF, Bataller R	**Transcriptome analysis identifies TNF superfamily receptors as potential therapeutic targets in alcoholic hepatitis**	Gut 62(3):452-460	3.4; 3.6; 3.9
Planell N, Lozano JJ, Mora-Buch R, Masamunt MC, Jimeno M, Ordás I, Esteller M, Ricart E, Piqué JM, Panés J, Salas A	**Transcriptional analysis of the intestinal mucosa of patients with ulcerative colitis in remission reveals lasting epithelial cell alterations**	Gut 62(7):967-976	3.7
Ordás I, Rimola J, García-Bosch O, Rodríguez S, Gallego M, Etchevers MJ, Pellisé M, Feu F, González-Suárez B, Ayuso C, Ricart E, Panés J	**Diagnostic accuracy of magnetic resonance colonography for the evaluation of disease activity and severity in ulcerative colitis: a prospective study**	Gut 62(11): 1566-1572	3.7; 3.11
Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF, Soria G, Tudela R, Planas AM, Fernández-Hernando C, Arroyo V, Jiménez W, Morales-Ruiz M (2013)	**Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats**	Gut 62(1):138-145	4.2
Villamor N, Conde L, Martínez-Trillos A, Cazorla M, Navarro A, Beà S, López C, Colomer D, Pinyol M, Aymerich M, Rozman M, Abrisqueta P, Baumann T, Delgado J, Giné E, González-Díaz M, Hernández JM, Colado E, Payer AR, Rayon C, Navarro B, Terol MJ, Bosch F, Quesada V, Puente XS, López-Otín C, Jares P, Pereira A, Campo E, López-Guillermo A	**NOTCH1 mutations identify a genetic subgroup of chronic lymphocytic leukemia patients with high risk of transformation and poor outcome**	Leukemia 27(5):1100-1106	5.2; 5.9
Díaz-Beyá M, Navarro A, Ferrer G, Díaz T, Gel B, Camós M, Pratcorona M, Torrebadell M, Rozman M, Colomer D, Monzo M, Esteve J	**Acute myeloid leukemia with translocation (8;16)(p11;p13) and MYST3-CREBBP rearrangement harbors a distinctive microRNA signature targeting RET proto-oncogene**	Leukemia 27(3):595-603	5.3; 5.8; 5.9
Herman SE, Sun X, McAuley EM, Hsieh MM, Pittaluga S, Raffeld M, Liu D, Keyvanfar K, Chapman CM, Chen J, Buggy JJ, Aue G, Tisdale JF, Pérez-Galán P,* Wiestner A*	**Modeling tumor-host interactions of chronic lymphocytic leukemia in xenografted mice to study tumor biology and evaluate targeted therapy**	Leukemia 27(12):2311-2321	5.9
Liu Y, Sánchez-Tilló E, Lu X, Huang L, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A*, Dean DC*	**Rb1 family mutation is sufficient for sarcoma initiation**	Nat Commun 4:2650-2661	5.2

Translation of knowledge and innovation

Clinical Guidelines

With the aim of improving health in our society, the IDIBAPS is firmly committed to the translation of results within the healthcare sector. Above and beyond evaluating research and protecting knowledge, IDIBAPS is concerned with promoting the use of new medical protocols and technologies that will improve patients' state of health, their quality of life and the efficiency of healthcare processes.

As a general perspective of IDIBAPS' impact in society, it is worth mentioning that every year our researchers participate in the elaboration of international clinical guides. These guidelines have a tremendous impact in patients' care and medical practice.

The list below reflects the participation of IDIBAPS researchers in 38 clinical guidelines published in 2013.

AUTHORS	TITLE	REFERENCE	Q; IF	GROUPS INVOLVED
Martí MJ, Tolosa E	**Parkinson disease: New guidelines for diagnosis of Parkinson disease**	Nat Rev Neurol. 9(4):190-1	Q1; 15.518	4.3
Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, et al.	**2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA).**	Eur Heart J. 34(29):2281-2329	Q1; 14.097	3.15
Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, et al.	**ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD)**	Eur Heart J. 34(39):3035-87	Q1; 14.097	2.1
Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al.	**2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology.**	Eur Heart J. 34(38):2949-3003	Q1; 14.097	2.2
Seeger W, Adir Y, Barberà JA, Champion H, Coghlan JG, et al.	**Pulmonary hypertension in chronic lung diseases**	J Am Coll Cardiol. 62: D109-116	Q1; 14.086	2.7
Vachiéry JL, Adir Y, Barberà JA, Champion H, Coghlan JG, et al.	**Pulmonary hypertension due to left heart diseases**	J Am Coll Cardiol. 62: D100-108	Q1; 14.086	2.7
Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, et al.	**Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, GOLD Executive Summary**	Am J Respir Crit Care Med. 187: 347-365	Q1; 11.041	2.7
Gakis G, Witjes JA, Compérat E, Cowan NC, De Santis M, et al.	**EAU Guidelines on primary urethral carcinoma**	Eur Urol. 64(5):823-30	Q1; 10.476	2.10
Fernández de Larrea C, Kyle RA, Durie BG, Ludwig H, Usmani S, et al.	**Plasma cell leukemia: consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group**	Leukemia. 27(4):780-91	Q1; 10.164	5.8
Baccarani M, Deininger MW, Rosti G, Hochhaus A, Soverini S, et al.	**European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013**	Blood. 122(6):872-84	Q1; 9.06	5.8
Barosi G, Mesa RA, Finazzi G, Harrison C, Kiladjian JJ, et al.	**Revised response criteria for polycythemia vera and essential thrombocythemia: a ELN and IWG-MRT consensus project**	Blood. 121(23):4778-81	Q1; 9.06	5.8
Tefferi A, Cervantes F, Mesa RA, Passamonti F, Verstovsek S, et al.	**Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) & European LeukemiaNet (ELN) consensus report**	Blood. 122(8):1395-8	Q1; 9.06	5.8
Balmaña J, Balaguer F, Cervantes A, Arnold D; ESMO Guidelines Working Group	**Familial risk-colorectal cancer: ESMO Clinical Practice Guidelines**	Ann Oncol. 24 Suppl 6:vi73-80	Q1; 7.384	5.2

Dreyling M, Thieblemont C, Gallamini A, Arcaini L, Campo E, et al.	**ESMO Consensus conferences: guidelines on malignant lymphoma, part 2: marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma**	Ann Oncol. 24(4):857-77	Q1; 7.384	5.8
Ghielmini M, Vitolo U, Kimby E, Montoto S, Walewski J, et al.	**ESMO Guidelines consensus conference on malignant lymphoma 2011 part 1: diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL)**	Ann Oncol. 24 (3): 561-76	Q1; 7.384	3.11
Giammarile F, Alazraki N, Aarsvold JN, Audisio RA, Glass E, et al.	**The EANM and SNMMI practice guideline for lymphoscintigraphy and sentinel node localization in breast cancer.**	Eur J Nucl Med Mol Imaging. 40: 1932–47	Q1; 5.114	5.3
Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, et al.	**HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes:document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013.**	Heart Rhythm. 10(12):1932-1963	Q1; 5.045	2.2
Bauer M, Pfennig A, Severus E, Whybrow PC, Angst J, et al.	**Task Force on Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of unipolar depressive disorders, part 1: update 2013 on the acute and continuation treatment of unipolar depressive disorders**	World J Biol Psychiatry. 14(5):334-85	Q1; 3.571	4.7
Grunze H, Vieta E, Goodwin GM, Bowden C, Licht RW, et al.	**The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2012 on the long-term treatment of bipolar disorder**	World J Biol Psychiatry. 14(3):154-219	Q1; 3.571	4.7
Van Assche G, Dignass A, Bokemeyer B, Danese S, Gionchetti P, et al.	**Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations.**	J Crohns Colitis. 7(1):1-33	Q2; 3.385	3.7
Panes J, Bouhnik Y, Reinisch W, Stoker J, Taylor SA, et al.	**Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines**	J Crohns Colitis. 7(7): 556-85	Q2; 3.385	3.7
Camm AJ, Lip GY, Caterina RD, Savelieva I, Atar D, et al.	**Actualización de las guías de la Sociedad Europea de Cardiología (ESC) para el manejo de la fibrilación auricular de 2010 Elaborada en colaboración con la Asociación Europea del Ritmo Cardiaco.**	Rev Esp Cardiol. 66(1):54.e1-54.e24	Q2; 3.204	2.1
Worner F, Cequier A (coordinators)	**Comments on the ESC Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting With ST-Segment Elevation.**	Rev Esp Cardiol. 66(1):5-11	Q2; 3.204	2.2
Caballero D, Campo E, López-Guillermo A, Martín A, Arranz-Sáez R, et al.	**Clinical practice guidelines for diagnosis, treatment, and follow-up of patients with mantle cell lymphoma. Recommendations from the GEL/TAMO Spanish Cooperative Group**	Ann Hematol. 92(9):1151-79	Q2; 2.866	5.2; 5.8
Blomström Lundqvist C, Auricchio A, Brugada J, Boriani G, Bremerich J, et al.	**The use of imaging for electrophysiological and devices procedures: a report from the first European Heart Rhythm Association Policy Conference, jointly organized with the European Association of Cardiovascular Imaging (EACVI), the Council of Cardiovascular Imaging and the European Society of Cardiac Radiology.**	Europace. 15(7):927-36	Q2; 2.765	2.2
Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, et al.	**Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement.**	Europace. 15(9):1337-1382 (I.F.: 2.765)	Q2; 2.765	2.2
Kirchhof P, Breithardt G, Aliot E, Al Khatib S, Apostolakis S, et al.	**Personalized management of atrial fibrillation: Proceedings from the fourth Atrial Fibrillation competence NETwork/European Heart Rhythm Association consensus conference.**	Europace. 15(11):1540-1556	Q2; 2.765	2.2
Bousquet J, Antó J, Sunyer J, Nieuwenhuijsen M, Vrijheid M, et al.	**Pooling birth cohorts in allergy and asthma: European Union-funded initiatives - a MeDALL, CHICOS, ENRIECO, and GA²LEN joint paper**	Int Arch Allergy Immunol 161(1):1-10	Q2; 2.248	2.8
Martínez J, Abad-González A, Aparicio JR, Aparisi L, Boadas J, et al.	**The Spanish Pancreatic Club recommendations for the diagnosis and treatment of chronic pancreatitis: part 1 (diagnosis)**	Pancreatology. 13(1):8-17	Q3; 2.043	3.11
de-Madaria E, Abad-González A, Aparicio JR, Aparisi L, Boadas J, et al.	**The Spanish Pancreatic Club's recommendations for the diagnosis and treatment of chronic pancreatitis: part 2 (treatment)**	Pancreatology. 13(1):18-28	Q3; 2.043	3.11

Vázquez-Sequeiros E, González-Panizo-Tamargo F, Barturen A, Calderón A, Esteban JM, et al.	**The role of endoscopic ultrasound guided fine needle aspiration (EUS-FNA) in non small cell lung cancer (NSCLC) patients: SEED-SEPD-AEG Joint Guideline**	Rev Esp Enferm Dig. 105(4):215-224	Q3; 1.652	3.11
Blasco AJ, Llibre JM, Arribas JR, Boix V, Clotet B, et al.	**Analysis of costs and cost-effectiveness of preferred GESIDA/ NationalAIDS Plan regimens for initial antiretroviral therapy in human immunodeficiency virus infected adult patients in 2013**	Enferm Infec Micr Cl. 31(9):568-578	Q4; 1.478	1.3
Torres A, Barberán J, Falguera M, Menéndez R, Molina J, et al.	**[Multidisciplinary guidelines for the management of community-acquired pneumonia]**	Med Clin (Barc). 140(5):223 e1-223 e19	Q4; 1.399	2.6
García-Río F, Calle M, Burgos F, Casan P, Del Campo F, et al.	**Normativa SEPAR Espirometría**	Arch Bronconeumol. 49: 388-401	Q4; 1.372	2.7
Maurel J, Grávalos C, Rivera F, Vera R, González Flores E	**SEOM clinical guidelines for the adjuvant treatment of colorectal cancer 2013**	Clin Transl Oncol. 15(12):991-5	Q4; 1.276	5.11
Mesía R, Pastor M, Grau JJ, Del Barco E	**SEOM clinical guidelines for the treatment of head and neck cancer (HNC) 2013**	Clin Transl Oncol. 15(12):1018-24	Q4; 1.276	5.11
Cabriada JL, Vera I, Domènech E, Barreiro-de Acosta M, Esteve M, et al.	**[Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis on the use of anti-tumor necrosis factor drugs in inflammatory bowel disease]**	Gastroent Hepat-Barc. 36(3): 127-46	Q4; 0,567	3.7
Gisbert JP, Calvet X, Bermejo F, Boixeda D, Bory F, et al.	**III Spanish Consensus Conference on Helicobacter pylori infection**	Gastroent Hepat-Barc. 36(5):340-74	Q4; 0,567	3.11

Clinical Trials

The IDIBAPS constitutes the ideal setting for completing a number of the crucial steps in the development of new medicinal products. Basic biomedical research and applied clinical research, together with specialized healthcare practice, are aspects of IDIBAPS that may be very useful for the development of drugs.

The adjacent graphics summarize the number of clinical trials approved by the Clinical Research Ethics Committee (CREC) in the past years. Of note is the number of clinical trials designed and promoted by the IDIBAPS researchers themselves:

FIGURE TITLE:

Evolution of the number of clinical trials approved by CREC and promoted by IDIBAPS researchers.

- Approved by CREC
- Promoted by IDIBAPS researchers

FIGURE TITLE

Evolution of the type of clinical trials approved every year.

- Single-center trial
- Multicenter (reference CREC)
- Multicenter (concerned CREC)
- Observetional / non comparative phase IV study
- Medical devices
- Other

Patents

A list is provided below of the patent applications during 2013:

Spanish patent applications

TITLE
Métodos y kits para el diagnóstico de la diabetes tipo 2
OWNERS
IDIBAPS, HCB, UB
IDIBAPS INVENTORS
Silvia Canivell, Ramon Gomis
PATENT NUMBER (APPLICATION DATE)
P201330814 (03/06/2013)

European patent applications

TITLE
4-amino-6-(2,6-dichlorophenyl)-2-(phenylamino)-pyrido[2,3-d] pyrimidin-7(8h)-one derivatives, synthesis and uses thereof
OWNERS
IDIBAPS, HCB, FCRB, IQS
IDIBAPS INVENTORS
Dolors Colomer, Patricia Pérez-Galán, Gael Roué,
EUROPEAN PATENT NUMBER (APPLICATION DATE)
EP13382225.4 (14/06/2013)

TITLE
Genetic variant in the CX3CR1 gene as prognosis marker for amyotrophyc lateral sclerosis (ALS)
OWNERS
IDIBAPS, UB, Hospital Vall Hebron, FUND RIOJA SALUD
IDIBAPS INVENTORS
Alan López, Nicole Mahy, Manuel Rodríguez
EUROPEAN PATENT NUMBER (APPLICATION DATE)
EP13382200 (30/05/2013)

TITLE
Method for predicting the onset of extrapyramidal symptoms induced by an antipsychotic-based treatment
OWNERS
IDIBAPS, HCB, UB, CIBERSAM
IDIBAPS INVENTORS
Miguel Bernardo, Patricia Gassò, Amalia Lafuente
EUROPEAN PATENT NUMBER (APPLICATION DATE)
EP13382027.4 (25/01/2013)

PCT extension applications

TITLE
Use of the soluble form of axl in the diagnosis and/or prognosis of heart failure sindrome
OWNERS
IDIBAPS, CSIC
IDIBAPS INVENTORS
Montserrat Batlle, Pablo García de Frutos
PCT NUMBER
PCT/EP2013/052743

TITLE
Tungstat sodic com a potencial estrategia farmacologica antiplaquetaria
OWNERS
IDIBAPS, HCB, UB
IDIBAPS INVENTORS
Maribel Díaz-Ricart, Ginés Escolar, Ramon Gomis
PCT NUMBER
PCT/ES2013/070905

National phase applications

TITLE
Stent amb fàrmac per evitar reestenosi vascular en angioplastia
OWNERS
HCB, Universidad de Valladolid
IDIBAPS INVENTORS
Magdalena Heras, Mercè Roqué
PCT NUMBER
PCT/EP2009/063099

Spin-Off Companies

The knowledge dealt with from the IDIBAPS usually completes its cycle when transferred to the industry. In other cases the link with the centre is maintained through the creation of spin-off companies. Spin-off companies created by IDIBAPS researchers are:

Immunnovative Developments S.L. (2010)
Spin-off company promoted by Dr. Francisco Lozano for the development of new biological therapies for the prevention and treatment of inflammatory disorders with an immune basis.
www.immunnovative.com

Bionure (2009)
Spin-off company promoted by by Dr. Pablo Villoslada for the development of new neuro-protective drugs for the treatment of multiple sclerosis and other neurological diseases.
www.bionure.com

Transmural Biotech (2009)
Spin-off company promoted by Dr. Eduard Gratacós for the development and commercialization of different diagnostic devices in the gynecology field.
www.transmuralbiotech.com

Linkcare (2009)
Spin-off company promoted by Dr. Josep Roca that has developed an Open Source platform that links clinical data from different systems such as Primary Care Information (PCIS), Hospital Information (HIS), Electronic Health Record (EHR) and Enterprise Resource Programming (ERP) Systems with a library of customized patient profile protocols.
info@linkcare.es

Neurotec Pharma (2006)
Spin-off company promoted by Dr. Nicole Mahy for the development of new diagnostic and therapeutic tools for acute and chronic central nervous system diseases that occur with inflammation and/or neurodegeneration such as Stroke, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, Parkinson and Alzheimer disease.
www.neurotec-pharma.com

Research projects

Research Funding

The IDIBAPS collaboration network is wide reaching, spanning the five continents and more than 40 countries. IDIBAPS' researchers participate in hundreds of national and international consortia:

- **IDIBAPS participates in all nine Spanish Biomedical Research Centres from the Instituto de Salud Carlos III (ISCIII).** A total number of 27 research groups from IDIBAPS participate in these national networks, and 2 of them are coordinated by an IDIBAPS researcher: CIBER of Hepatic and Gastrointestinal Diseases, and CIBER of Respiratory Diseases.

- **IDIBAPS' researchers also participate in 11 National Networks from ISCIII,** and 2 of them are coordinated by IDIBAPS: AIDS and Multiple Sclerosis National Networks.

- In the **7th Framework Programme and Executive Agency for Health and Consumers Protection Programme,** IDIBAPS participates in 61 projects and coordinates 13 of them.

- IDIBAPS' researchers also participate in **many international consortia** such as: Colorectal Cancer Genetics (COGENT), International Cancer Genome Consortium (ICGC), International Consortium for inflammatory bowel disease genetics, European Clinical Research Infrastructures Network (ECRIN) and Hepatoellular Carcinoma International (HCC) Genomic Consortium.

The funding obtained from public and private institutions is one of the main driving forces of research 2013 that make the excellence of the IDIBAPS possible. The table below shows the large number of new projects initiated in 2013:

It is worth to mention that many projects as well as IDIBAPS facilities and equipments have been co-funded by the European Regional Development Fund (ERDF).

	NUMBER OF PROJECTS
COMPETITITVE PUBLIC FUNDING	**115**
Catalan institutions	**2**
Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR)	1
Associació Catalana d'Universitats Públiques (ACUP)	1
Spanish institutions	**88**
Instituto de Salud Carlos III (ISCIII)	69
Ministerio de Economía y Competitividad	18
Ministerio de Sanidad, Política Social e Igualdad	1
International institutions	**25**
European Commission	18
European Science Foundation	2
National Institutes of Health (NIH)	4
Netherlands Organisation for Scientific Research	1

COMPETITIVE PRIVATE FUNDING	**21**
Catalan institutions	**7**
Fundació La Marató de TV3	7
Spanish institutions	**6**
Asociación Española Contra el Cáncer (AECC)	1
Fundación Contra la Hipertensión Pulmonar	1
Fundación de Investigación Médica Mútua Madrileña	1
Fundación Mapfre	1
Fundación Salud 2000	1
Sociedad Española de Tasplante	1
International institutions	**8**
Brain and Behavior Research Foundation	2
CHDI Foundation	1
European Foundation for the Study of Diabetes	1
Michael J. Fox Foundation for Parkinson's Research	4

Spanish Biomedical Networks

In the last few years much of the economical effort from the Instituto de Salud Carlos III (Spanish Ministry of Economy and Competitiveness) has been focused in the consolidation of the Spanish National Research Networks, an initiative that includes the Networked Biomedical Research Centres (Centros de Investigación Biomédica en Red, CIBERs) and the Cooperative Research Topic Networks (Redes Temáticas de Investigación Cooperativa en Salud, RETICs).

These structures represent a modern and cooperative way of understanding biomedical research and have achieved excellent results. IDIBAPS participates in most of these virtual research structures and leads four of them, as described below:

CIBER FOR HEPATIC AND DIGESTIVE DISEASES (Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, CIBERehd)

DIRECTOR

Dr. Jaume Bosch, IDIBAPS team leader

www.ciberehd.org

CIBERehd was created in 2006, and is currently integrates 46 research groups (1 of them associated) from 26 organisations throughout Spain.

CIBERehd objectives are:

- To promote top level research in liver and digestive diseases, in an international context, fostering interaction among the best Spanish groups.
- Focused on translation research, in order to facilitate a rapid transferral of the results that to clinical practice and biotechnological applications.

The scientific activity of the CIBERehd is fundamentally focused on its research programs and strategic actions, and is complemented by the training programme, the scientific and technological platforms and common resources. The CIBERehd has its own platforms in genomics, transcriptomics, proteomics, metabolomics, gene silencing and bioinformatics, as well as a biobank (integrated within the IDIBAPS biobank), a bank of steatotic livers and telemedicine platforms for diagnostic and therapeutic support in liver cancer, genetic counselling in colorectal cancer; a database of chronic hepatitis B patients and a national Registry of patients with Vascular Liver Diseases.

The CIBERehd has 6 major research programs:

- Portal hypertension and mechanisms of transition to cirrhosis
- Hepatitis viruses
- Cholestasis and metabolic disorders
- Liver immunology, cell therapy and transplantation
- Liver and digestive cancer
- Gastrointestinal inflammation and motility

CIBER FOR RESPIRATORY DISEASES (Centro de Investigación Biomédica en Red de Enfermedades Respiratorias, CIBERes)

DIRECTOR

Dr. Àlvar Agustí, IDIBAPS team leader

www.ciberes.org

CIBERes, created in 2006, is currently formed by 35 research groups from 23 organisations throughout Spain.

The research activity of CIBERes is structured upon the basis of Corporate Research Programmes (Programes Corporatius de Investigació - PCI). Each PCI comprises a series of projects that in a cooperative and integrated manner address a relevant healthcare problem in the field of respiratory disease, such as:

- Asthma
- Pulmonary fibrosis
- Chronic obstructive pulmonary disease (COPD)
- Lung Cancer – Thoracic Neoplasms
- Acute lung injuries
- Sleep Apnea Hypopnea Syndrome
- Tuberculosis
- Pneumonia and sepsis of respiratory origin
- Pathogen-Host Interactions
- H1N1 influenza

In parallel to these PCIs, CIBERes has organized a series of research support platforms, such as: (1) Pulmonary biobank; (2) Technological development and transference; (3) Training program; and (4) Communications Department.

AIDS RESEARCH NETWORK (Red de Investigación en Sida, RIS)

DIRECTOR

Dr. Josep Maria Gatell, IDIBAPS team leader

www.retic-ris.net

The AIDS Research Network was created in 2003, and established the bases for driving original and innovative research in the field of AIDS.
The AIDS network is composed by 19 core research groups, 17 associate clinical groups and includes groups with different experience in virology, immunology, and cellular and molecular biology.

The AIDS network aims to address original problems through novel technological approaches. A series of large scale projects have been defined. The strategies used to reach the established objectives are based on references which can only be addressed through network-based effort and the creation of different platforms.
A large cohort has been defined, corresponding to different groups of patients of homogeneous characteristics which allows us to evaluate the efficacy of new treatment protocols and intervention strategies, and to carry out studies on toxicity, resistance and pathogenesis.
The particular characteristics of the HIV epidemic in our country allows the study of certain pathologies associated to HIV infection, such as hepatitis C coinfection.

SPANISH MULTIPLE SCLEROSIS NETWORK (Red Española de Esclerosis Múltiple, REEM)

DIRECTOR

Dr. Pablo Villoslada, IDIBAPS group leader

www.reem.es

The Spanish Multiple Sclerosis Network was created in 2008. REEM is composed of basic and clinical investigators at national level, interested in the aetiopathogenesis of multiple sclerosis and in the development of new diagnostic and treatment methods with which to combat the disease.

REEM has three objectives:

- Development of a cooperative research programme on the aetiology, diagnosis and treatment of multiple sclerosis.
- Promotion of the creation of shared resources among the different centres participating in the REEM, such as biobanks or clinical databases.
- Training of young investigators in the knowledge of multiple sclerosis, based on courses, conferences and stays in other laboratories.

European Projection

IDIBAPS researchers are currently participating in 61 projects funded by the European Commission (from FPVII and EAHC programmes). From these 61 projects, 13 are coordinated by IDIBAPS researchers, in 43 of them IDIBAPS RESEARCHERS participate as partners, and 5 are monocontract Marie Curie projects.

The 13 European projects led by IDIBAPS researchers are presented below:

COOPERATION

HEPTROMIC - Genomic predictors and oncogenic drivers in hepatocellular carcinoma
Dr. Josep M. Llovet
2010 - 2013
Call: CE-FP7-HEALTH-2ST-10
Official code: 259744

AMPHORA - Alcohol Measures for Public Health Research Alliance
Dr. Antoni Gual
2009 - 2014
Call: CE_FP7_Health_B_07
Official code: 223059

ODHIN - Optimizing delivery of health care interventions
Dr. Antoni Gual
2011 - 2014
Call: CE-FP7-HEALTH-2ST-10
Official code: 259268

ALICE RAP - Addictions and Lifestyles In Contemporary Europe - Reframing Addictions Project
Dr. Antoni Gual
2011 - 2016
Call: CE_FP7-SSH-2010-1
Official code: 266813

iHIVarna - Therapeutic TriMix / mRNA based Vaccine in Chronic HIV-1 Infected Patients Receiving Antiretroviral Therapy
Dr. Felipe Garcia
2013 - 2017
Call: CE-FP7-HEALTH-IN1-13
Official code: 602570

CORTICONIC - Computations and Organization of Retes Through the Interaction of Computational, Optical and Neurophysiological Investigations of the Cerebral
Dr. Maria Victoria Sánchez Vives
2013 - 2015
Call: CE-FP7-ICT-2011-9
Official code: 600806

EuCOLONGENE – Cooperation Studies on Inherited Susceptibility to Colorectal Cancer
Dr. Sergi Castellví
2013 - 2017
Call: CE-COST-2012
Official code: OC-2012-1-11711

PEOPLE

ENDO-VV - EndoVascularVision: new endoscopic tools for real time vascular assisted vision
Dr. Eduard Gratacós
2010 - 2014
Call: CE_FP7_PPOLE_09_IAPP
Official code: 251356

REPROTRAIN - Reproductive Biology Early Research Training
Dr. Rafael Oliva
2012 - 2015
Call: CE-FP7-PEOPLE-ITN-11
Official code: 289880

CLEVER - Contrast-enhanced uLtrasound for livEr-disease eValuation: development and validation of a novel E-Health-software for Risk-stratification
Dr. Jaume Bosch
2013 - 2018
Call: CE_PEOPLE-2013-IAPP
Official code: 612273

SANCO - EAHC

ELIPSY - European Living Donor Psychosocial Follow-up
Dr. Martí Manyalich
2009 - 2013
Call: CE_SANCO08
Official code: 20081104

ENERCA III - European reference network of expert centres in rare anaemias
Dr. Juan Luis Vives-Corrons
2009 - 2013
Call: CE_SANCO08
Official code: 20081210

e-ENERCA - New e-Health Services for the European Reference Network on Rare Anaemias
Dr. Juan Luis Vives-Corrons
2013 - 2016
Call: CE_SANCO_12
Official code: 295882

Coordinated international initiatives

CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) GENOME PROJECT

SCIENTIFIC DIRECTORS

Dr. Elías Campo, IDIBAPS team leader, and Dr. Carlos López-Otín, University of Oviedo

www.cllgenome.es

The Chronic Lymphocytic Leukemia (CLL) Genome Project aims to generate a comprehensive catalogue of genomic alterations involved in the development and progression of the disease. This information will improve our ability to diagnose and categorize the patients and will promote the advance in new therapeutic approaches. The CLL Genome Project, as a contributing member of the International Cancer Genome Consortium (ICGC), has the purposes of creating diagnostic tools, discovering therapeutic targets and developing new strategies that will allow a customized therapy for CLL in order to make it more precise and effective. The overall objective of the CLL Genome Project is to generate a comprehensive catalogue of genomic alterations in 500 independent tumors, including clinical, biological, and epidemiological information. The ultimate goal is to decipher the enormous diversity and complexity of the changes in the human cancer genome, mostly still unknown, which are responsible for the development and progression of the different types of the disease with the aim of improving its prevention, diagnosis and treatment.

HEALTH CONNECT-EU GROUP

COORDINATOR

Gemma Pascual, IDIBAPS International Unit

www.connecteusalut.org

The Health Connect-EU Group is a network led by IDIBAPS and made up of nearly sixty organisations that focus their activity on health in Catalonia. The group's components are compromised to join their efforts to improve the recognition of the Catalan research and development in the international environment. It is an initiative supported by ACCIO and AGAUR from the Generalitat de Catalunya.

The members of this network belong to different sectors, both academia and industry. The promoters of the Health Connect-EU Group are: ANAXOMICS, CATALONIABIO, CRG, FARMAINDUSTRIA, FENIN, Fundació ACE, Fundació IMIM - PARC DE SALUT MAR, ICO, IDIBAPS, IDIBELL and IRSICAIXA.

In 2013, the Health Strategic Research Agenda (SRA) of the Health Connect-EU Group has been launched. This document expects to make known research areas being developed in Catalonia with the aim of inspiring and finding similarities with forthcoming calls in Horizon 2020. Nearly a hundred research topics have been included in the document and split into seven sections related to the Societal Challenge "Health, demographic change and wellbeing": 1) Understanding health, wellbeing and disease; 2) Preventing disease; 3) Treating and managing disease; 4) Active ageing, independent and assisted living; 5) Methods and data; 6) Healthcare provision and integrated care; and 7) Global health.

The SRA's contents have been presented to several departments of the European Commission. Moreover, the final document has been spread in Catalonia as well as nationally and internationally. The effort of promoting the SRA of the Health Connect-EU Group is expected to help improving the Catalan participation and success rates in Horizon 2020.

Scientific Facilities

The task developed by IDIBAPS and its researchers is only possible thanks to tough work, enthusiasm and also research infrastructures such as the Esther Koplowitz and the CELLEX Research Centers, as well as the Scientific Core Facilities.

Traditionally, IDIBAPS researchers were distributed in spaces within the three scientific institutions forming the consortium. Some of the research lines summarized in this Report are still developed in these institutions, but today IDIBAPS researchers have two new reference facilities were all the research areas interact and grow together.

In addition, excellent biomedical research requires the use of high-cost techniques and equipment. IDIBAPS promotes the setting up of common core facilities to support research for use by all researchers, with the purpose of improving the performance and profitability of investments and efficiency in the use of available resources.

© MARC VERGÉS

CEK, Esther Koplowitz Research Center

The Esther Koplowitz Research Center (CEK) building is a wonderful example of public and private co-responsibility, since it benefits from the participation of the Generalitat de Catalunya, the Ministerio de Economía y Competitividad, and the Instituto de Salud Carlos III, as well as from the support of other donors such as the Fundación Esther Koplowitz, Fundació Privada Cellex, Acció Sardà Farriol para la Investigación en Diabetes and Laboratorios Esteve.

Inaugurated by the end of 2010 and with space for more than 350 researchers, the CEK building receives international scientists and PhD students, fostering the exchange of experience and professional synergies. The building includes a ground floor, mezzanine and five floors with a total area of 6,500 m2 on the ground. In the basement three underground floors offer a total area of 2,485 m2, including space for scientific core facilities and a parking. In 2011 it reached its full operating capacity.

The CEK building homes 18 of the IDIBAPS teams, including an enormous range of research lines.

CELLEX Biomedical Research Center

The CELLEX Biomedical Research Center is a new space with five floors equipped for last generation biomedical research located in the UB School of Medicine. Thanks to the collaboration between the public and private sectors 5,150 m2 of laboratories, scientific and technological services and other spaces have been reformed and equipped to support the research developed at IDIBAPS and the University of Barcelona. The new facilities were inaugurated in January 2013.

The renovation and adaptation of these areas is mainly the result of a donation from the CELLEX Foundation to the University of Barcelona, which offers to IDIBAPS four floors with laboratories for biomedical research. IDIBAPS added around one million euros to complete the purchase of scientific equipment. Part of the contribution of the IDIBAPS has been funded with FEDER funds from the Generalitat de Catalunya and the rest comes from specific calls by the Instituto de Salud Carlos III.

These new IDIBAPS facilities home over 200 researchers from 18 different research teams. It is a space equipped with the latest technology and comforts, and it respects the original external centenary architecture of the UB School of Medicine.

Scientific Core Facilities

IDIBAPS has 6 scientific core facilities of its own, mostly located in the CEK building:

- **Biobank of Hospital Clínic – IDIBAPS**
- **Bioinformatics**
- **Biostatistics and Data Management**
- **Cytometry and Cell Sorting**
- **Functional Genomics**
- **Magnetic Resonance Imaging**

© MARC VERGÉS

Biobank of Hospital Clínic - Idibaps

LOCATION

NEUROLOGICAL TISSUE BANK
UB School of Medicine

TUMOUR BANK
CEK building
HCB building

BLOOD AND FLUID BANK
CEK building

FOR FURTHER INFORMATION
www.clinicbiobanc.org
biobanc@idibaps.org

PEOPLE
Anna Bosch Comas, PhD (IDIBAPS)
Scientific Coordinator
Joan Albert Barberà, MD, PhD (HCB)
Director
Meritxell Rufet (FCRB)
Assistant Manager
Ángela Martín (FCRB)
Informed Consent Manager
Esther Barnadas (IDIBAPS)
Lab Manager

NEUROLOGICAL TISSUE BANK
Ellen Gelpí, MD, PhD(IDIBAPS)
Manager
Maria Jesús Rey, MD, PhD (UB)
Neuropathologist. Senior Technician
Carina Antiga (IDIBAPS)
Secretary
Sara Charif (IDIBAPS)
Laboratory Technician
Verónica Santiago (IDIBAPS)
Specialised Technician
Abel Muñoz (IDIBAPS)
Autopsy Assistant
Leire Etxarri (IDIBAPS)
Autopsy Assistant

TUMOUR BANK
Miriam Cuatrecasas MD, PhD (HCB)
Manager
Raquel Bermudo Gascón, PhD (FCRB)
Tumour Bank Manager
Laura Gelabert (IDIBAPS)
Laboratory Technician
Mónica Marín (HCB)
Laboratory Technician
Blanca Noemí Luján, MD, PhD (HCB)
Pathologist and Website Manager for the Catalan Tumour Bank Network

BLOOD AND FLUID BANK
Verónica Fernandez Pascual, PhD (IDIBAPS)
Manager
Anna Morales (IDIBAPS)
Laboratory Technician
Regina Cañaveras (FCRB)
Laboratory Technician

DESCRIPTION

The Biobank is a centralised core facility for coordinating the collection, processing, storage and transfer of human biological samples to promote biomedical research of the highest standard. All the procedures performed at the Biobank are carried out under ISO9001 certification.

The Biobank's catalogue of samples is formed by the samples collected by three large banks, all of which have extensive experience in research with human samples and which are available for scientific purposes for the consolidation of personalised medicine:

1. **Neurological Tissue Bank**
   A nervous tissue repository (brain and spinal cord) created from donations from deceased donors with or without neurological conditions, helping to facilitate research into neurological illnesses in order to improve diagnoses and enhance patient care.

2. **Tumour Bank and Anatomical Pathology Collections**
   A repository of tumoural and non-tumoural tissue samples from patients affected by a neoplasia, as well as tissue samples from other diseases, all surplus to diagnostic requirements from the Department of Anatomical Pathology in Hospital Clínic. This material is essential to providing current large-scale tissue research projects with the samples they require.

3. **Blood and Fluid Bank**
   This repository contains samples of,

among others, metabolic, inflammatory bowel, oncological, digestive, psychiatric and maternal and foetal diseases. It houses a large range of samples of scientific interest, primarily DNA, serum and plasma, which are provided by doctors' surgeries and laboratories where blood and fluid are taken for lab tests and blood and fluid donation.

SERVICES

The Biobank of Hospital Clínic – IDIBAPS offers a wide variety of human biological samples along with services. The scientific community may make full use of the bank's equipment and professional staff to achieve their most ambitious goals. The work of the biobank goes beyond simply providing samples; they offer support to researchers during the various stages of projects requiring the use of biological samples.

Human Biological Sample Provision

- Brain and spinal cord tissue from deceased donors affected by neurologic diseases.
- Frozen and paraffin-embedded tissues representing the most common neoplasms and paraffin-embedded samples from a wide variety of diseases.
- DNA, serum, plasma and PBMCs from different diseases as well as from control donors.

Technical And Scientific Advice

- Creation and management of new collections.
- Methodology (technical guidance).
- Experimental design with human and animal tissue samples.
- Design and interpretation of immunohistochemical studies.
- Quality management programmes.
- Harmonization of quality procedures for the handling of DNA samples.
- Technical assessment for the handling of the Biobank equipment (laser microdissector, multiobserver microscope equipped with software for morphometric analysis and a histological slide scanner with analysis software).

Private Collections Management

- Collection management for multicentre studies.
- Storage of pre-existing collections.

Histological Techniques

- Processing of frozen and paraffin-embedded tissues (macroscopy, cryopreservation, paraffin blocks, histological sections).
- Histological staining.
- Definitive neuropathological diagnosis of neurological diseases.
- Lasser microdissection.
- Tissue microarray construction (TMA).
- Slide scan and morphometric analysis.

Cellular Techniques

- Purification and cryopreservation of mononuclear cells.
- Immortalization of B lymphocytes.
- Erythrocyte isolation from whole blood.
- Cell counting.

Molecular Techniques

- DNA extraction from peripheral blood.
- DNA/RNA/protein extraction from tissue (frozen and paraffin- embedded).
- WGA.
- Serum and plasma isolation.
- Immunohistochemistry.

EQUIPEMENT

- -20ºC, -80ºC and -150ºC freezers with safety systems.
- Vapour phase liquid nitrogen tanks.

Neurological Tissue Bank

- Biological safety cabinets for processing brain tissue in fresh state.
- Microtomes and equipment for formalin fixation and paraffin embedding
- Gas filtration cabinet.
- Automated immunostainer.
- Refrigerator and -20ºC freezer for preserving fungibles.
- Autoclave for sterilising autopsy material.

Tumour Bank

- Equipment for preparing tissue microarrays (TMAs): TMA Master (3Dhistech) (UB Faculty of Medicine / FEDER)
- Laser microdissector system LMD7000 (Leica Microsystems)
- Microtomes and cryostat (Leica Microsystems)
- Tissue processor (Leica Microsystems)
- Bond Max III for automated immunohistochemistry (Leica Microsystems)
- Digital slide scanner Pannoramic Desk (3Dhistech)
- Multiobserver microscope BX43 with a 12Mpx photographic camera and the morphometric analysis software CellSens Dimension (Olympus)
- "QIAcube" for automatization of QIAGEN spin columns (DNA, RNA, Protein extraction from different sample origin)

Blood And Fluid Biobank

- Programmable freezer with a controlled freezing ramp.
- "Chemagic MSM1®" automated device for obtaining DNA from large volumes of blood.
- "QIAcube" for automatization of QIAGEN spin columns (DNA, RNA, Protein extraction from different sample origin
- "Tecan EvO150®" automated station for the aliquoting of samples.
- "CoulterZ1®" cells and particles counter.
- TC Automated Cell Counter (Bio Rad).
- Cabinets for isolating cells under sterile conditions.
- Cell immortalisation platform.
- Computer systems for managing samples and related data.
- Epoch Micro-Volume Spectrophotometer System.
- Trinean DropSense96 UV/VIS droplet reader.
- ABF500 Automated Blood Fractionation system (RTS).

PUBLICATIONS

Originals in collaboration with IDIBAPS teams / IF: 102.081

1. Iranzo A, Tolosa E, Gelpi E, Molinuevo JL, Valldeoriola F, Serradell M, Sanchez-Valle R, Vilaseca I, Lomeña F, Vilas D, Lladó A, Gaig C, Santamaria J. **Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study.** *Lancet Neurol* 12(5):443-453 I.F.: 23.917

2. Pera M, Alcolea D, Sánchez-Valle R, Guardia-Laguarta C, Colom-Cadena M, Badiola N, Suárez-Calvet M, Lladó A, Barrera-Ocampo AA, Sepulveda-Falla D, Blesa R, Molinuevo JL, Clarimón J, Ferrer I, Gelpi E, Lleó A. **Distinct patterns of APP processing in the CNS in autosomal-dominant and sporadic Alzheimer disease.** *Acta Neuropathol* 125(2):201-213 I.F.: 9.734

3. Sánchez-Tilló E; de Barrios O; Siles L; Amendola PG; Darling DS; Cuatrecasas M; Castells A; Postigo A. **ZEB1 Promotes invasiveness of colorectal carcinoma cells through the opposing regulation of uPA and PAI-1.** *Clin Cancer Res* 19(5):1071-1082 I.F.: 7.837

4. Marqués N; Sesé M; Cánovas V; Valente F; Bermudo R; de Torres I; Fernández Y; Abasolo I; Fernández PL; Contreras H; Castellón E; Celià-Terrassa T; Méndez R; Ramón Y Cajal S; Thomson TM; Paciucci R. **Regulation of protein translation and c-Jun expression by prostate tumor overexpressed 1.** *Oncogene* 33(9):1124-1134 I.F.: 7.357

5. Giráldez MD; Lozano JJ; Cuatrecasas M; Alonso-Espinaco V; Maurel J; Mármol M; Hörndler C; Ortego J; Alonso V; Escudero P; Ramírez G; Petry C; Lasalvia L; Bohmann K; Wirtz R; Mira A; Castells A. **Gene-expression signature of tumor recurrence in patients with stage II and III colon cancer treated with 5'fluoruracil-based adjuvant chemotherapy.** *Int J Cancer* 132(5):1090-1097 I.F.: 6.198

6. Rué L, López-Soop G, Gelpi E, Martínez-Vicente M, Alberch J, Pérez-Navarro E. **Brain region- and age-dependent dysregulation of p62 and NBR1 in a mouse model of Huntington's disease.** *Neurobiol Dis* 52:219-228 I.F.: 5.624

7. Córdova H; San José Estépar R; Rodríguez-D'Jesús A; Martínez-Pallí G; Arguis P; Rodríguez de Miguel C; Navarro-Ripoll R; Perdomo JM; Cuatrecasas M; Llach J; Vosburgh KG; Fernández-Esparrach G. **Comparative study of NOTES alone versus NOTES guided by a new image registration system for navigation in the mediastinum: a study in a porcine model.** *Gastrointest Endosc* 77(1):102-107 I.F.: 5.210

8. Gutiérrez-Repiso C, Rojo-Martínez G, Soriguer F, García-Fuentes E, Vendrell J, Vázquez JA, Valdés S, Urrutia I, Serrano-Rios M, Pascual-Manich G, Ortega E, Mora-Peces I, Menéndez E, Martínez-Larrad MT, López-Alba A, Gutiérrez G, Gomis R, Goday A, Girbés J, Gaztambide S, Franch J, Delgado E, Catalá M, Castell C, Castaño L, Casamitjana R, Carmena R, Calle-Pascual A, Bordiú E, Bosch-Comas A. **Factors affecting levels of urinary albumin excretion in the general population of Spain: the Di@bet.es study.** *Clin Sci (Lond)* 124(4):269-277 I.F.: 4.859

9. Liu Y; Sánchez-Tilló E; Lu X; Huang L; Clem B; Telang S; Jenson AB; Cuatrecasas M; Chesney J; Postigo A; Dean DC. **Sequential inductions of the ZEB1 transcription factor caused by mutation of Rb and then Ras proteins are required for tumor initiation and progression.** *J Biol Chem* 288(16):11572-11580 I.F.: 4.651

10. Marcuello C, Calle-Pascual AL, Fuentes M, Runkle I, Rubio MA, Montañez C, Rojo-Martinez G, Soriguer F, Bordiu E, Goday A, Bosch-Comas A, Carmena R, Casamitjana R, Castaño L, Castell C, Catalá M, Delgado E, Franch J, Gaztambide S, Girbés J, Gomis R, Urrutia I, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Serrano-Rios M, Valdés S, Vázquez JA, Vendrell J. **Prevalence of the metabolic syndrome in Spain using regional cutoff points for waist circumference: the di@bet.es study.** *Acta Diabetol* 50(4):615-623 I.F.: 4.631

11. Camacho L; Meca-Cortés O; Abad JL; García S; Rubio N; Díaz A; Celià-Terrassa T; Cingolani F; Bermudo R; Fernández PL; Blanco J; Delgado A; Casas J; Fabriàs G; Thomson TM. **Acid ceramidase as a therapeutic target in metastatic prostate cancer.** *J Lipid Res* 54(5):1207-1220 I.F.: 4.386

12. Colom-Cadena M, Gelpi E, Charif S, Belbin O, Blesa R, Martí MJ, Clarimón J, Lleó A. **Confluence of α-Synuclein, Tau, and β-Amyloid Pathologies in Dementia With Lewy Bodies.** *J Neuropathol Exp Neurol* 72(12):1203-1212 I.F.: 4.345

13. Grau-Rivera O, Gelpi E, Rey MJ, Valldeoriola F, Tolosa E, Compta Y, Martí MJ. **Prominent psychiatric symptoms in patients with Parkinson's disease and concomitant argyrophilic grain disease.** *J Neurol* 260(12):3002-3009 I.F.: 3.578

14. Rojo-Martínez G, Valdés S, Colomo N, Lucena MI, Gaztambide S, Gomis R, Casamitjana R, Carmena R, Catalá M, Martínez-Larrad MT, Serrano-Ríos M, Castaño L, Vendrell J, Girbés J, Franch J, Vázquez JA, Mora-Peces I, Urrutia I, Pascual-Manich G, Ortega E, Menéndez E, Delgado E, Bordiú E, Castell C, López-Alba A, Goday A, Calle A, Bosch-Comas A, Soriguer F. **Use of Drugs Related to the Treatment of Diabetes Mellitus and Other Cardiovascular Risk Factors in the Spanish Population. The Di@bet.es Study.** *Rev Esp Cardiol* 66(11):854-863 I.F.: 3.204

15. Soriguer F, Rojo-Martínez G, Goday A, Bosch-Comas A, Bordiú E, Caballero-Díaz F, Calle-Pascual A, Carmena R, Casamitjana R, Castaño L, Castell C, Catalá M, Delgado E, Franch J, Gaztambide S, Girbés J, Gomis R, Gutiérrez G, López-Alba A, Teresa Martínez-Larrad M, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Serrano-Rios M, Urrutia I, Valdés S,

Antonio Vázquez J, Vendrell J. **Olive oil has a beneficial effect on impaired glucose regulation and other cardiometabolic risk factors. Di@bet.es study.** *Eur J Clin Nutr* 67(9):911-916 I.F.: 2.756

16. Llorens F, Ansoleaga B, Garcia-Esparcia P, Zafar S, Grau-Rivera O, López-González I, Blanco R, Carmona M, Yagüe J, Nos C, Del Río JA, Gelpí E, Zerr I, Ferrer I. **PrP mRNA and protein expression in brain and PrPc in CSF in Creutzfeldt-Jakob disease MM1 and VV2.** *Prion* 18;7(5):383-393 I.F.: 2.133

17. Ortega E, Franch J, Castell C, Goday A, Ribas-Barba L, Soriguer F, Vendrell J, Casamitjana R, Bosch-Comas A, Bordiú E, Calle-Pascual A, Carmena R, Castaño L, Catalá M, Delgado E, Gaztambide S, Girbés J, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Pascual-Manich G, Rojo-Martínez G, Serrano-Rios M, Urrutía I, Valdés S, Vázquez JA, Gomis R. **Mediterranean diet adherence in individuals with prediabetes and unknown diabetes: the Di@bet.es Study.** *Ann Nutr Metab* 62(4):339-346 I.F.: 1.661

Originals in collaboration with other Institutions / I.F.: 84.148

1. Heneka MT, Kummer MP, Stutz A, Delekate A, Schwartz S, Vieira-Saecker A, Griep A, Axt D, Remus A, Tzeng TC, Gelpi E, Halle A, Korte M, Latz E, Golenbock DT. **NLRP3 is activated in Alzheimer's disease and contributes to pathology in APP/PS1 mice.** *Nature* 493(7434):674-678 I.F.: 38.597

2.Gomez-Martin C; Plaza JC; Pazo-Cid R; Salud A; Pons F; Fonseca P; Leon A; Alsina M; Visa L; Rivera F; Galan MC; Del Valle E; Vilardell F; Iglesias M; Fernandez S; Landolfi S; Cuatrecasas M; Mayorga M; Jose Paulés M; Sanz-Moncasi P; Montagut C; Garralda E; Rojo F; Hidalgo M; Lopez-Rios F. **Level of HER2 gene amplification predicts response and overall survival in HER2-positive advanced gastric cancer treated with trastuzumab.** *J Clin Oncol* 31(35):4445-4452 I.F.: 18.038

3. Kovacs GG, Milenkovic I, Wöhrer A, Höftberger R, Gelpi E, Haberler C, Hönigschnabl S, Reiner-Concin A, Heinzl H, Jungwirth S, Krampla W, Fischer P, Budka H. **Non-Alzheimer neurodegenerative pathologies and their combinations are more frequent than commonly believed in the elderly brain: a community-based autopsy series.** *Acta Neuropathol* 126(3):365-384 I.F.: 9.734

4. Gelpi E, Cullel F, Navarro-Otano J, Lladó A. **Globular glial-like inclusions in a patient with advanced Alzheimer's disease.** *Acta Neuropathol* 126(1):155-157 I.F.: 9.734

5. Respondek G, Roeber S, Kretzschmar H, Troakes C, Al-Sarraj S, Gelpi E, Gaig C, Chiu WZ, van Swieten JC, Oertel WH, Höglinger GU. **Accuracy of the National Institute for Neurological Disorders and Stroke/Society for Progressive Supranuclear Palsy and Neuroprotection and Natural History in Parkinson Plus Syndromes Criteria for the Diagnosis of Progressive Supranuclear Palsy.** *Mov Disord* 28(4):504-509 I.F.: 4.588

6. Boeve BF, Silber MH, Ferman TJ, Lin SC, Benarroch EE, Schmeichel AM, Ahlskog JE, Caselli RJ, Jacobson S, Sabbagh M, Adler C, Woodruff B, Beach TG, Iranzo A, Gelpi E, Santamaria J, Tolosa E, Singer C, Mash DC, Luca C, Arnulf I, Duyckaerts C, Schenck CH, Mahowald MW, Dauvilliers Y, Graff-Radford NR, Wszolek ZK, Parisi JE, Dugger B, Murray ME, Dickson DW. **Clinicopathologic correlations in 172 cases of rapid eye movement sleep behavior disorder with or without a coexisting neurologic disorder.** *Sleep Med* 14(8):754-762 I.F.: 3.487

Citation in aknowledgments

Antonell A, Lladó A, Altirriba J, Botta-Orfila T, Balasa M, Fernández M, Ferrer I, Sánchez-Valle R, Molinuevo JL. **A preliminary study of the whole-genome expression profile of sporadic and monogenic early-onset Alzheimer's disease.** *Neurobiol Aging* 34(7):1772-1778

Canivell S, Ruano EG, Sisó-Almirall A, Kostov B, González-de Paz L, Fernandez-Rebollo E, Hanzu F, Párrizas M, Novials A, Gomis R. **Gastric inhibitory polypeptide receptor methylation in newly diagnosed, drug-naïve patients with type 2 diabetes: a case-control study.** *PLoS One* 8(9):e75474

Merino-Serrais P, Benavides-Piccione R, Blazquez-Llorca L, Kastanauskaite A, Rábano A, Avila J, DeFelipe J. **The influence of phospho-τ on dendritic spines of cortical pyramidal neurons in patients with Alzheimer's disease.** *Brain* 136(6):1913-1928

Michael R, Rosandić J, Montenegro GA, Lobato E, Tresserra F, Barraquer RI, Vrensen GF. **Absence of beta-amyloid in cortical cataracts of donors with nd without Alzheimer's disease.** *Exp Eye Res* 106:5-13

Villar-Menéndez I, Blanch M, Tyebji S, Pereira-Veiga T, Albasanz JL, Martín M, Ferrer I, Pérez-Navarro E, Barrachina M. **Increased 5-methylcytosine and decreased 5-hydroxymethylcytosine levels are associated with reduced striatal A2AR levels in Huntington's disease.** *NeuroMolecular Med* 15(2):295-309

GRANTS FOR RESEARCH IN PROGRESS

Barberà, JA. **Red Nacional de Biobancos Hospitalarios (RETIC BIOBANCOS).** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD09/0076/00038 Duration 01/01/2010-31/12/2013

Bioinformatics

LOCATION
CEK building

FOR FURTHER INFORMATION
www.bioinformatics.fcrb.es
bioinformatica@idibaps.org

PEOPLE
Susana Kalko, PhD (IDIBAPS)
Scientific coordinator
Teresa Casserras (IDIBAPS)
Bioinformatician

DESCRIPTION

The Bioinformatics Platform is mainly devoted to analysis and support in the interpretation of data coming from OMICS disciplines (transcriptomics, genomics, proteomics and metabolomics). The integration of data from these fields requires huge efforts in the development of common languages, tools, and specific databases.

Differential expression or classification studies in every OMICS field usually face two big challenges: the high dimensionality and the small number of samples. Furthermore, biomedical research is frequently aimed at understanding very complex biological problems for the discovery of specific biological markers. It is then necessary to use sophisticated tools with complex statistical methodologies to derive information from the usual conditions of high-throughput experiments.

At present, the emerging field of Systems Biology is aimed at analysing and integrating data from the entire OMICS field to ultimately create working models of entire biological systems.

SERVICES

Bioinformatics support in different areas of biomedical research, particularly in OMICS technologies; development of new tools and diffusion:

- Consultancy and Analysis: counselling in experimental design; low-level and quality-control analyses; orientation on biostatistical resources; assistance in tools utilisation; intensive analysis of OMICS technology data in collaborative settings; interpretation of results.
- Administration of Bioinformatics resources and development of new tools: access to proprietary computer resources on Linux servers (especially in NGS projects); software management; development of customized tools and databases, particularly in web settings.
- Dissemination: courses and seminars organisation.

EQUIPMENT

- 2 rack Servers HP ProLiant DL580 G7 4P Intel® Xeon® E7-4870 10-cores, 2,40GHz, Hyper-Threading Technology (80 threads per node), 30 MB CPU cache, 192 GB RAM. Internal Hard disk: 2 x 300GB 6G SAS 10K SFF. O.S.: 64b Suse Linux Enterprise Server configured with SGE System (Sun Grid Engine).
- Rack Server HP ProLiant DL580 G7 4P Intel® Xeon® E7-4850 10-cores, 2,00GHz, Hyper-Threading Technology (80 threads per node), 24 MB CPU cache, 128 GB RAM. Internal Hard disk: 2 x 300GB 6G SAS 10K SFF. O.S.: 64b Suse Linux Enterprise Server configured with SGE System (Sun Grid Engine).
- Rack Server HP ProLiant DL580 G7 2P Intel® Xeon® E7-4830 8-cores, 2,13GHz, Hyper-Threading Technology (32 threads per node), 24 MB CPU cache, 64 GB RAM. Internal Hard disk: 2 x 300GB 6G SAS 10K SFF. O.S.: 64b Suse Linux Enterprise Server.
- IBM eServer BladeCenter HS21 Server. 1P Intel® Xeon® E5-345 4-cores, 2,33 GHz. 8 MB CPU cache, 16GB RAM. Attached Hard Disk DAS: 500 GB (Raid 5). O.S.: 64b Suse Linux Enterprise Server.
- Rack Server HP ProLiant DL580 G5 4P Intel® Xeon® X7350 4-cores, 2,93GHz, 8 MB CPU cache, 32 GB RAM. Internal Hard disk: 2 x 146GB 6G SAS 10K SFF. O.S.: 64b Red Hat Enterprise Linux Server.
- High Performance Storage System (HPSS) for High Performance Computing (HPC) EMC-Isilon, 3 nodes X200, 24 TB (72 Tb, Raid 5), 12GB CPU cache, with internal infiniband connection. Scalability up to 15PB. O.S.: OneFS configured with Parallel NFS.
- External SAS storage HP MSA60, 8 TB 2U Serial Attach SCSI.
- Back up rack-mount tape autoloader - HP LTO-5 Ultrium. Capable up to 24TB of compressed capacity with hp p212/256 smart array controller.

PUBLICATIONS

Originals in collaboration with other Institutions / IF: 3.730

1. Paco S.; Kalko S.G.; Jou C.; Rodríguez M. A.; Corbera J. R.; Muntoni F.; Feng L.; Rivas E.; Torner F.; Gualandi F.; Gómez-Foix A.M.; Ferrer A.; Ortez C.I.; Nascimento A.; Colomer J.; Jimenez-Mallebrera C. **Gene expression profiling identifies molecular pathways associated with collagen VI deficiency and provides novel therapeutic targets.** *PLoS ONE* 8(10): e77430 I.F.: 3.730

Citation in aknowledgments

Lopez F.J.; Bernabeu M.; Fernandez-Becerra C.; del Portillo H. **A new computational approach redefines the subtelomeric vir superfamily of Plasmodium vivax.** *BMC Genomics* 14:8

Lucas M.; Mato E.; Barceló-Batllori S.; Gomis R.; Novials A. **Proteomics Characterization of the Secretome from Rat Pancreatic Stellate Cells with ATP-Binding Cassette Transporters (ABCG2) and NCAM Phenotype.** *ISRN Cell Biology* ID 828060

Biostatistics and Data Management

LOCATION
183, Mallorca st.

FOR FURTHER INFORMATION
bioestadistica@idibaps.org

PEOPLE
Ferran Torres MD, PhD (IDIBAPS)
Scientific Director
José Ríos (IDIBAPS)
Scientific coordinator. Training and Consultancy Manager
Abiguei Torrents (FCRB)
Junior Statistician
José Fernández Sardiña (FCRB)
Data Management Manager
Sandra Serrano (FCRB)
Data Management

DESCRIPTION

The Biostatistics and Data Management Platform provides methodological and statistical support for research projects.

The platform's main objective is to promote cutting edge clinical research and to facilitate the necessary resources to carry it out.

The platform's tasks are conducted in compliance with the International Conference of Harmonisation guidelines, European and local laws, as well as with the regulatory recommendations. Standard Operating Procedures (SOPs) are in place to fulfil those standards.

SERVICES

Consulting Services
Short-term consulting services in methodology and statistics. Specific consultations are free to departments and institutes of Hospital Clínic and similar institutions. They include, but are not limited to: (a) statistical study design; (b) sample size calculation; (c) consulting on information collection methods for analysis; (d) methodological and statistical consulting for research projects.

A maximum duration of 2 hours is established for each session and service may be provided for a maximum of 2 sessions. Consultations requiring additional attention shall receive the same consideration as a project.

Projects
Any services required by the client above and beyond those specified in the section on consulting services shall be rendered upon formal acceptance of the estimate and timetable provided.
Sample projects:
- Creation and maintenance of a clinical trial data base: (a) creation of the eCRF (electronic case report form); (b) creation and consensus of Data Management and validation Plans with the research team; (c) traceable data export to analysis systems.
- Statistical analysis of clinical trials or other projects: (a) creation and consensus of the most appropriate Statistical Analysis Plan depending on data type and study objective; (b) creation of the most appropriate statistical program according to the objective of the study, with emphasis on the traceability of results; (c) creation of a statistical report and collaboration in writing and supervising subsequent follow-up articles.

EQUIPMENT

- Equipment includes a personal computer and statistics and data management programmes: nQuery, SAS, SPSS, EAST, jMP, MACRO.

PUBLICATIONS

Originals in collaboration with IDIBAPS teams / I.F.: 73.309

1. Titulaer M.J.; McCracken L.; Gabilondo I.; Armangué T.; Glaser C.; Iizuka T.; Honig L.S.; Benseler S.M.; Kawachi I.; Martinez-Hernandez E.; Aguilar E.; Gresa-Arribas N.; Ryan-Florance N.; Torrents A.; Saiz A.; Rosenfeld M.R.; Balice-Gordon R.; Graus F.; Dalmau J. **Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis:an observational cohort study.** *Lancet Neurol* 12(2):157-165 I.F.: 23.917

2. Reig M.; Rimola J.; Torres F.; Darnell A.; Lope C.R.; Forner A.; Llarch N.; Ríos J.; Ayuso C.; Bruix. **Post-progression survival of patients with advanced hepatocellular carcinoma. Rationale for second line trial design.** *Hepatology* 58(6):2023-2031 I.F.: 12.003

3. Maduell F.; Moreso F.; Pons M.; Ramos R.; Mora-Macià J.; Carreras J.; Soler J.; Torres F.; Campistol J.M.; Martinez-Castelao A.; ESHOL Study Group. **High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients.** *J Am Soc Nephrol* 24(3):487-97 I.F.: 8.987

4. Blanco I.; Santos S.; Gea J.; Güell R.; Torres F.; Gimeno-Santos E.; Rodriguez D.A.; Vilaró J.; Gómez B.; Roca J.; Barberà J.A. **Sildenafil to improve respiratory rehabilitation outcomes in COPD: a controlled trial.** *Eur Respir J* 42(4):982-992 I.F.: 6.355

5. Castel M.A.; Roig E.; Ríos J.; Tomas C.; Mirabet S.; Cardona M.; Brossa V.; López L.; Vargas L.; Sionis A.; Vallejos I.; Pérez-Villa F. **Long-term prognostic value of elevated heart rate one year after heart transplantation.** *Int J Cardiol* 168(3):2003-2007 I.F.: 5.509

6. Compta Y.; Pereira J.B.; Ríos J.; Ibarretxe-Bilbao N.; Junqué C.; Bargalló N.; Cámara A.; Buongiorno M.; Fernández M.; Pont-Sunyer C.; Martí M.J. **Combined dementia-risk biomarkers in Parkinson's disease:a prospective longitudinal study.** *Parkinsonism Relat Disord.* 2013;19 (8):717-24 I.F.: 3.274

7. Dodd C.N.; Romio S.A.; Black S.; Vellozzi C.; Andrews N.; Sturkenboom M.; Zuber P.; Hua W.; Bonhoeffer J.; Buttery J.; Crawford N.; Deceuninck G.; de Vries C.; De Wals P.; Gimeno M.V.; Heijbel H.; Hughes H.; Hur K.; Hviid A.; Kelman J.; Kilpi T.; Chuang S.K.; Macartney K.; Rett M.; Lopez-Callada

V.R.; Salmon D.; Sanchez F.G.; Sanz N.; Silverman B.; Storsaeter J.; Thirugnanam U.; van der Maas N.; Yih K.; Zhang T.; Izurieta H. Global H1N1 GBS Consortium. **International collaboration to assess the risk of Guillain BarréSyndrome following Influenza A (H1N1) 2009 monovalent vaccines.** *Vaccine* 31(40):4448-4458 I.F.: 3.274

8. Adán A.; Pelegrín L.; Rey A.; Llorenç V.; Mesquida M.; Molins B.; Ríos J.; Keller J. **Dexamethasone intravitreal implant for treatment of uveitic persistent cystoid macular edema in vitrectomized patients.** *Retina* 33 (7):1435-1440 I.F.: 2.825

9. Ogbah Z.; Visa L.; Badenas C.; Ríos J.; Puig-Butille J.A.; Bonifaci N.; Guino E.; Augé J.M.; Kolm I.; Carrera C.; Pujana M.A.; Malvehy J.; Puig S. **Serum 25-hydroxyvitamin D3 levels and vitamin D receptor variants in melanoma patients from the Mediterranean area of Barcelona:25-hydroxyvitamin D3 levels and VDR variants in melanoma patients from Barcelona.** *BMC Med Genet* 14(1):26 I.F.: 2.536

10. Alvarez G.; Rey A.; Sanchez-Dalmau F.B.; Muñoz E.; Ríos J.; Adán A. **Optical coherence tomography findings in spinocerebellar ataxia-3.** *Eye* (Lond) 27 (12):1376-81 I.F.: 1.818

11. Rey A.; Llorenç V.; Pelegrín L.; Mesquida M.; Molins B.; Ríos J.; Arévalo J.F.; Adán A. **Clinical pattern of toxoplasmic retinochoroiditis in a Spanish referral center.** *Ophthalmologica* 229(3):173-178 I.F.: 1.412

12. Mena G.; Sequera V.G.; Nogué-Xarau S.; Ríos J.; Bertran M.J.; Trilla A. **[Translation and cross-cultural adaptation of the Quick Environmental Exposure and Sensitivity Inventory for use in the Spanish population].** *Med Clin* (Barc) 140(7):302-304 I.F.: 1.399

Originals in collaboration with other Institutions / I.F.: 21.051

1. Palomar M.; Alvarez-Lerma F.; Riera A.; Díaz M.T.; Torres F.; Agra Y.; Larizgoitia I.; Goeschel C.A.; Pronovost P.J. **Impact of a National Multimodal Intervention to Prevent Catheter-Related Bloodstream Infection in the ICU:The Spanish Experience.** *Crit Care Med* 41(10):2364-2372 I.F.: 6.124

2. Domingo P.; Cabeza Mdel C.; Torres F.; Salazar J.; Gutierrez Mdel M.; Mateo M.G.; Martínez E.; Domingo J.C.; Fernandez I.; Villarroya F.; Ribera E.; Vidal F.; Baiget M. **Association of Thymidylate Synthase Polymorphisms with Acute Pancreatitis and/or Peripheral Neuropathy in HIV-Infected Patients on Stavudine-Based Therapy.** *PLoS One* 8(2):e57347 I.F.: 3.730

3. Domingo P.; Mateo M.G.; Pruvost A.; Torres F.; Salazar J.; Gutierrez M.D.; Ma Carmen Cabeza.; Domingo J.C.; Fernandez I.; Villarroya F.; Vidal F.; Baiget M.; de la Calle-Martín O. **Polymorphisms of Pyrimidine Pathway Enzymes Encoding Genes and HLA-B*40:01 Carriage in Stavudine-Associated Lipodystrophy in HIV-Infected Patients.** *PLoS One* 8(6):e67035 I.F.: 3.730

4. Llupià A.; Mena G.; Olivé V.; Quesada S.; Aldea M.; Sequera V.G.; Ríos J.; García-Basteiro A.L.; Varela P.; Bayas J.M.; Trilla A. **Evaluating influenza vaccination campaigns beyond coverage:a before-after study among health care workers.** *Am J Infect Control* 41(8):674-678 I.F.: 2.731

5. Armengou L.; Jose-Cunilleras E.; Ríos J.; Cesarini C.; Viu J.; Monreal L. **Metabolic and endocrine profiles in sick neonatal foals are related to survival.** *J Vet Intern Med* 27(3):567-575 I.F.: 2.064

6. Malouf J.; Digregorio S.; Rio L.D.; Torres F.; Marin A.M.; Farrerons J.; Herrera S.; Domingo P. **Fat Tissue Measurements by Dual-Energy X-Ray Absorptiometry:Cross-Calibration of 3 Different Fan-Beam Instruments.** *J Clin Densitom* 16(2):212-222 I.F.: 1.713

7. Escanilla N.; Leiva M.; Monreal L.; Ríos J.; Peña T. **Aqueous humor fibrinolytic activity in dogs with cataracts.** *Vet Ophthalmol* 16(6):409-415 I.F.: 0.959

Cytometry and cell sorting

LOCATION
CEK building

FOR FURTHER INFORMATION
citometria@idibaps.org

PEOPLE
Isabel Crespo, PhD (IDIBAPS)
Scientific coordinator
Cristina López (IDIBAPS)
Specialist Technician
Laia Llinas (IDIBAPS)
Specialist Technician

DESCRIPTION

Flow cytometry is a technique for multiparametric analysis of particles, such as cells, by suspending them in a stream of fluid and passing them through a LASER. It allows for the simultaneous multiparametric analysis of the physical and/or chemical characteristics of up to thousands of particles per second. Each suspended particle passing through the beam scatters the LASER, and fluorescent chemicals found in the particle or attached to the particle may be excited into emitting light at a longer wavelength than the light source.

Fluorescence-activated cell sorting is a specialised type of flow cytometry. It provides a method for sorting a heterogeneous mixture of biological cells, one cell at a time, based on the specific light-scattering and fluorescent characteristics of each cell. It provides fast, objective and quantitative recording of fluorescent signals from individual cells as well as physical separation of cells of particular interest.

This technology has applications in molecular biology, pathology, immunology, plant biology and marine biology. It has broad application in medicine (especially in transplantation, haematology, tumour immunology and chemotherapy, prenatal diagnosis, genetics, etc.).

The Facility is subdivided into three rooms: FACS analysis and high-resolution images

Functional genomics

in flow room; data analysis room; and cell sorting room.

SERVICES

- Analysis of population of interest.
- Apoptosis.
- Cell cycle, proliferation.
- Functional analysis.
- Stem cells.
- viability.
- Analysis of microorganisms.
- Multiparameter quantitative trials on soluble molecules and phosphoproteins (CBA and CBA Flex Set), cell signalling.
- Cell sorting.
- Microparticles.
- High resolution microscopy in flow (cell signalling and molecular translocation, internalization, co-localization, cell-cell Interaction, morphology analysis, cell death and autophagy, cell cycle and mitosis, DNA damage and repair).
- User training.

EQUIPMENT

- BD FACSCalibur: 2 LASER, Up to 4 fluorescence.
- BD FACSCantoI : 2 LASER, Up to 6 fluorescence.
- BD FACSCantoII: 3 LASER, Up to 8 fluorescence.
- BD LSRFortessa SORP + HTS: 4 LASER, Up to 16 fluorescence.
- BD LSRFortessa SORP: 5 LASER, Up to 18 fluorescence.
- AMNIS ISX: 2 digital cameras, Up to 12 fluorescence channels.
- BD FACSAriaII: 3 LASER, Up to 9 fluorescence.
- BD FACSAria SORP: 5 LASER, Up to 18 fluorescence.
- Magnetic cell sorter autoMACSPro.
- Data analysis: DIvA v6.1.3, CellQuestPro v6.0.3, ModFit LT v3.2, Flowjo v7.6.1, FCAPArray v1.0.1, IDEAS V.6.0

PUBLICATIONS

Originals in collaboration with IDIBAPS teams / I.F.: 5.076

1. Ferreira CB, Merino-Mansilla A, Llano A, Pérez I, Crespo I, Llinas L, Garcia F, Gatell JM, Yuste E, Sanchez-Merino V. **Evolution of Broadly Cross-Reactive HIV-1-Neutralizing Activity:Therapy-Associated Decline, Positive Association with Detectable Viremia, and Partial Restoration of B-Cell Subpopulations.** *J. Virol* 87(22):12227 I.F.: 5.076

Citation in aknowledgments

Martín-Jaular L, Elizalde-Torrent A, Thomson-Luque R, Ferrer M, Segovia JC, Herreros-Aviles E, Fernández-Becerra C, del Portillo HA. **Reticulocyte-prone malaria parasites predominantly invade CD71hi immature cells: implications for the development of an in vitro culture for Plasmodium vivax.** *Malar* J 12:434

Perez-Asensio FJ, Perpiñá U, Planas AM, Pozas E. **Interleukin-10 regulates progenitor differentiation and modulates neurogenesis on adult brain.** *J Cell Sci* 126:4208-4219

Pérez-de Puig I.; Miró F, Salas-Pérdomo A., Bonfill-Teixidor E.; Ferrer-Ferrer M.; Márquez-Kisinousky L.; Planas AM. **IL-10 deficiency exacerbates the brain inflammatory response to permanent ischemia without preventing resolution of the lesion.** *J Cereb Blood Flow Metab* 33:1955-1966

LOCATION
CEK building

FOR FURTHER INFORMATION
genomica@idibaps.org

PEOPLE
Pedro Jares, PhD (HCB-UB)
Scientific coordinator
Elías Campo, MD, PhD (HCB-UB)
Scientific director
Magda Pinyol, PhD (IDIBAPS)
Unit manager
Anna Enjuanes, PhD (IDIBAPS)
Specialist technician
Helena Suárez, PhD (IDIBAPS)
Specialist technician
Laura Plà (IDIBAPS)
Technician
Montse Sánchez (IDIBAPS)
Technician

DESCRIPTION

The unit provides access to different genome-wide protocols.
The platform manages samples for genomic projects starting from quantitative and qualitative analysis of nucleic acids up to genome-wide gene expression, genotyping, gene dose analysis and sequencing using different platforms including real-time PCR, microarrays and next generation sequencing.

SERVICES

- Quantification of nucleic acids
- Qualitative analysis of nucleic acids
- Expression analysis by Real-time PCR (Fluidigm)
- Genotyping analysis by Real-time PCR (Fluidigm)
- Digital PCR (Fluidigm)
- Genome-wide expression analysis (Affymetrix microarrays)
- Genome-wide genotyping analysis (Affymetrix microarrays)
- High-throughput expression analysis (GeneTitan Affymetrix)
- High-throughput genotyping analysis

(GeneTitan Affymetrix)
- CGH-Arrays (Agilent).
- Pyrosequencing (Quiagen)
- Next-generation sequencing (Illumina)

In addition to these services, the Core Facility offers advice on experimental design for different gene expression profile transcriptomic studies, and next generation sequencing.

EQUIPMENT

- NanoDrop (ND1000)
- Qubit
- Bioanalyzer 2100 (Agilent)
- BioMark (Fluidigm)
- GeneChip Affymetrix genetic analysis system.
- GeneTitan Affymetrix genetic analysis system.
- Agilent platform
- Axon 4000B scanner
- PyroMark Q96 ID
- MiSeq (Illumina)

PUBLICATIONS

Originals in collaboration with IDIBAPS teams / I.F.: 35.159

1. Villamor N, Conde L, Martínez-Trillos A, Cazorla M, Navarro A, Beà S, López C, Colomer D, Pinyol M, Aymerich M, Rozman M, Abrisqueta P, Baumann T, Delgado J, Giné E, González-Díaz M, Hernández JM, Colado E, Payer AR, Rayon C, Navarro B, José Terol M, Bosch F, Quesada V, Puente XS, López-Otín C, Jares P, Pereira A, Campo E, López-Guillermo A. **NOTCH1 mutations identify a genetic subgroup of chronic lymphocytic leukemia patients with high risk of transformation and por outcome.** *Leukemia* 27(5):1100-1106 I.F.: 10.164

2. Beà S, Valdés-Mas R, Navarro A, Salaverria I, Martín-Garcia D, Jares P, Giné E, Pinyol M, Royo C, Nadeu F, Conde L, Juan M, Clot G, Vizán P, Di Croce L, Puente DA, López-Guerra M, Moros A, Roue G, Aymerich M, Villamor N, Colomo L, Martínez A, Valera A, Martín-Subero JI, Amador V, Hernández L, Rozman M, Enjuanes A, Forcada P, Muntañola A, Hartmann EM, Calasanz MJ, Rosenwald A, Ott G, Hernández-Rivas JM, Klapper W, Siebert R, Wiestner A, Wilson WH, Colomer D, López-Guillermo A, López-Otín C, Puente XS, Campo E. **Landscape of somatic mutations and clonal evolution in mantle cell lymphoma.** *Proc Natl Acad Sci U S A* 110(45):18250-18255 I.F.: 9.737

3. Vegliante MC, Palomero J, Pérez-Galán P, Roué G, Castellano G, Navarro A, Clot G, Moros A, Suárez-Cisneros H, Beà S, Hernández L, Enjuanes A, Jares P, Villamor N, Colomer D, Martín-Subero JI, Campo E, Amador V. **SOX11 regulates PAX5 expression and blocks terminal B-cell differentiation in aggressive mantle cell lymphoma.** *Blood* 121(12):2175-2185 I.F.: 9.060

4. Enjuanes A, Albero R, Clot G, Navarro A, Beà S, Pinyol M, Martín-Subero JI, Klapper W, Staudt LM, Jaffe ES, Rimsza L, Braziel RM, Delabie J, Cook JR, Tubbs RR, Gascoyne R, Connors JM, Weisenburger DD, Greiner TC, Chan WC, López-Guillermo A, Rosenwald A, Ott G, Campo E, Jares P. **Genome-wide methylation analyses identify a subset of mantle cell lymphoma with a high number of methylated CpGs and aggressive clinicopathological features.** *Int J Cancer* 133(12):2852-2863 I.F.: 6.198

Magnetic resonance imaging

LOCATION
HCB building
CEK building

FOR FURTHER INFORMATION
imatge@idibaps.org

PEOPLE
Núria Bargalló Alabart, MD, PhD (HCB)
Scientific coordinator
Clinical Imaging Research (3T MRI Unit)
Guadalupe Soria Rodríguez, PhD. (IDIBAPS)
Experimental Imaging Research (7T MRI Unit)
Anna Calvo (IDIBAPS)
Image Analysis Advisor
Raúl Tudela, PhD (CIBER-BBN)
Image Analysis Advisor

DESCRIPTION

The main objectives of this Core Facility are:
- To provide services related to medical imaging techniques for researchers from IDIBAPS and other institutions, and to industries connected with health.
- To perform first-rate basic and clinical research into medical imaging using structural and functional magnetic resonance imaging, magnetic resonance spectroscopy, molecular imaging, other types of medical imaging and image processing.
- Researcher training in techniques and basic research to enable them to conduct experimental and clinical studies, thereby allowing them to explore the advantages of translational research.

SERVICES

- Clinical Imaging Research (3T MRI Unit).
- Experimental Imaging Research (7T MRI Unit).
- Imaging Processing Lab.

EQUIPMENT

Clinical Imaging Research (3T MRI Unit):
- RM 3T- Siemens 3T TRIO, B17 software

- 32 phased-array head coil
- 8 phased-array head coil
- Body coil
- Others phase array coil

Experimental Imaging Research (7T MRI Unit):

- Bruker BioSpec 70/30 (gradient system of 400 mT/m)
- Imaging volume coils for mice, rat and small cats or rabbits
- Surface coil for rat and mouse brain imaging
- Surface coil for rat heart imaging (with CINE acquisition sequence)
- volume coils for 1H/13C, 1H/31P and 1H/19F spectroscopy
- Surface coil for 1H/13C spectroscopy
- Electric stimulator for fMRI
- Inhalation anaesthetic system including animal monitoring
- 4 PC for image processing and analysis

Image Processing Lab:

- 3 dedicated workstations (1 Mac, 2 linux) and 7 high performance
- PC (5 dual windows-linux, 2 windows) for image postprocessing
- 10 standard PC
- Software licences: 10 Matlab, 2 LcModel, 1 AnalyzeDirect

PUBLICATIONS

Originals in collaboration with IDIBAPS teams / I.F.: 131.950

1. Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF, Soria G, Tudela R, Planas AM, Fernández-Hernando C, Arroyo V, Jiménez W, Morales-Ruiz M. **Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats.** *Gut* 62(1):138-145 I.F.: 10.732

2. Penadés R, Pujol N, Catalán R, Massana G, Rametti G, García-Rizo C, Bargalló N, Gastó C, Bernardo M, Junqué C. **Brain Effects of Cognitive Remediation Therapy in Schizophrenia: A Structural and Functional Neuroimaging Study.** *Biol Psychiatry* 73(10):1015-1023 I.F.: 9.247

3. Toledano P, Sarbu N, Espinosa G, Bargalló N, Cervera R. **Neuropsychiatric systemic lupus erythematosus: magnetic resonance imaging findings and correlation with clinical and immunological features.** *Autoimmun Rev* 12(12):1166-70 I.F.: 7.975

4. Palacios EM, Sala-Llonch R, Junque C, Roig T, Tormos JM, Bargallo N, Vendrell P. **Resting-state functional magnetic resonance imaging activity and connectivity and cognitive outcome in traumatic brain injury.** *JAMA Neurol* 70(7):845-851 I.F.: 7.685

5. Alemán-Gómez Y, Janssen J, Schnack H, Balaban E, Pina-Camacho L, Alfaro-Almagro F, Castro-Fornieles J, Otero S, Baeza I, Moreno D, Bargalló N, Parellada M, Arango C, Desco M. **The human cerebral cortex flattens during adolescence.** *J Neurosci* 33(38):15004-15010 I.F.: 6.908

6. Batalle D, Muñoz-Moreno E, Figueras F, Bargallo N, Eixarch E, Gratacos E. **Normalization of similarity-based individual brain networks from gray matter MRI and its association with neurodevelopment in infants with intrauterine growth restriction.** *Neuroimage* 83:901-11 I.F.: 6.252

7. Jovicich J, Marizzoni M, Sala-Llonch R, Bosch B, Bartrés-Faz D, Arnold J, Benninghoff J, Wiltfang J, Roccatagliata L, Nobili F, Hensch T, Tränkner A, Schönknecht P, Leroy M, Lopes R, Bordet R, Chanoine V, Ranjeva JP, Didic M, Gros-Dagnac H, Payoux P, Zoccatelli G, Alessandrini F, Beltramello A, Bargalló N, Blin O, Frisoni GB; The PharmaCog Consortium. **Brain morphometry reproducibility in multi-center 3T MRI studies: A comparison of cross-sectional and longitudinal segmentations.** Neuroimage 83C:472-484 I.F.: 6.252

8. Palacios EM, Sala-Llonch R, Junque C, Fernandez-Espejo D, Roig T, Tormos JM, Bargallo N, Vendrell P. **Long-term declarative memory deficits in diffuse TBI: Correlations with cortical thickness, white matter integrity and hippocampal volume.** *Cortex* 49(3):646-657 I.F.: 6.161

9. Palacios EM, Sala-Llonch R, Junque C, Roig-Rovira T, Tormos JM, Bargallo N, Vendrell P. **White Matter/Gray Matter Contrast Changes in Chronic and Diffuse Traumatic brain Injury.** *J Neurotrauma* 30(23):1991-1994 I.F.: 4.295

10. Segura B, Ibarretxe-Bilbao N, Sala-Llonch R, Baggio HC, Martí MJ, Valldeoriola F, Vendrell P, Bargalló N, Tolosa E, Junqué C. **Progressive changes in a recognition memory network in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(4):370-378 I.F.: 4.924

11. Zarei M, Ibarretxe-Bilbao N, Compta Y, Hough M, Junque C, Bargallo N, Tolosa E, Martí MJ. **Cortical thinning is associated with disease stages and dementia in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(8):875-882 I.F.: 4.924

12. Segura B, Baggio HC, Solana E, Palacios EM, Vendrell P, Bargalló N, Junqué C. **Neuroanatomical correlates of olfactory loss in normal aged subjects.** *Behav Brain Res* 246:148-153 I.F.: 4.924

13. Sala-Llonch R, Fortea J, Bartrés-Faz D, Bosch B, Lladó A, Peña-Gómez C, Antonell A, Castellanos-Pinedo F, Bargalló N, Molinuevo JL, Sánchez-Valle R. **Evolving brain functional abnormalities in PSEN1 mutation carriers: a resting and visual encoding fMRI study.** *J Alzheimers Dis* 36(1):165-175 I.F.: 4.174

14. Donaire A, Capdevila A, Carreño M, Setoain X, Rumià J, Aparicio J, Campistol J, Padilla N, Sanmartí F, Vernet O, Pintor L, Boget T, Ortells J, Bargalló N. **Identifying the cortical substrates of interictal epileptiform activity in patients with extratemporal epilepsy: An EEG-fMRI sequential analysis and FDG-PET study.** *Epilepsia* 54(4):678-690 I.F.: 3.909

15. Sierra-Marcos A, Maestro I, Falcón C, Donaire A, Setoain J, Aparicio J, Rumià J, Pintor L, Boget T, Carreño M, Bargalló N.

Ictal EEG-fMRI in localization of epileptogenic area in patients with refractory neocortical focal epilepsy. *Epilepsia* 54(9):1688-1698 I.F.: 3.909

16. Egaña-Ugrinovic G, Sanz-Cortes M, Figueras F, Bargalló N, Gratacós E. **Differences in cortical development assessed by fetal MRI in late-onset intrauterine growth restriction.** *Am J Obstet Gynecol* 209(2):126 e1-8 I.F.: 3.877

17. Muñoz-Moreno E, Batallé D, Eixarch E, Soria G, Prat-Galino A, Gratacós E. **A Magnetic Resonance Image Based Atlas of the Rabbit Brain for Automatic Parcellation.** *Plos One* 8(7):e67418 I.F.: 3.730

18. Sanz-Cortes M, Ratta GA, Figueras F, Bonet-Carne E, Padilla N, Arranz A, Bargallo N, Gratacos E. **Automatic quantitative MRI texture analysis in small-for-gestational-age fetuses discriminates abnormal neonatal neurobehavior.** *PLoS One* 8(7):e69595 I.F.: 3.730

19. Soria G, Tudela R, Márquez-Martín A, Camón L, Batalle D, Muñoz-Moreno E, Eixarch E, Puig J, Pedraza S, Vila E, Prats-Galino A, Planas AM. **The ins and outs of the BCCAo model for chronic hypoperfusion: a multimodal and longitudinal MRI approach.** *Plos One* 8(9):e74631 I.F.: 3.730

20. Solé-Padullés C, Bartrés-Faz D, Lladó A, Bosch B, Peña-Gómez C, Castellví M, Rami L, Bargalló N, Sánchez-Valle R, Molinuevo JL. **Donepezil treatment stabilizes functional connectivity during resting state and brain activity during memory encoding in Alzheimer's disease.** *J Clin Psychopharmacol* 33(2):199-205 I.F.: 3.513

21. Compta Y, Pereira JB, Ríos J, Ibarretxe-Bilbao N, Junqué C, Bargalló N, Cámara A, Buongiorno M, Fernández M, Pont-Sunyer C, Martí MJ. **Combined dementia-risk biomarkers in Parkinson's disease: A prospective longitudinal study.** *Parkinsonism Relat Disord* 19(8):717-724 I.F.: 3.274

22. González-Ortiz S, Oleaga L, Pujol T, Medrano S, Rumiá J, Caral L, Boget T, Capellades J, Bargalló N. **Simple fMRI postprocessing suffices for normal clinical practice.** *Am J Neuroradiol* 34(6):1188-1193 I.F.: 3.167

23. Lázaro L, Andrés S, Calvo A, Cullell C, Moreno E, Plana MT, Falcón C, Bargalló N, Castro-Fornieles J. **Normal gray and white matter volume after weight restoration in adolescents with anorexia nervosa.** *Int J Eat Disord* 46(8):841-8 I.F.: 2.877

24. Gil-Navarro S, Lladó A, Rami L, Castellví M, Bosch B, Bargalló N, Lomeña F, Reñé R, Montagut N, Antonell A, Molinuevo JL, Sánchez-Valle R. **Neuroimaging and biochemical markers in the three variants of primary progressive aphasia.** *Dement Geriatr Cogn Disord* 35(1-2):106-17 I.F.: 2.787

25. Pujol N, Penadés R, Rametti G, Catalán R, Vidal-Piñeiro D, Palacios E, Bargallo N, Bernardo M, Junqué C. **Inferior frontal and insular cortical thinning is related to dysfunctional brain activation/deactivation during working memory task in schizophrenic patients.** *Psychiatry Res* 214(2):94-101 I.F.: 2.456

26. Rumià J, Marmol F, Sanchez J, Giménez-Crouseilles J, Carreño M, Bargalló N, Boget T, Pintor L, Setoain X, Donaire A, Saez GT, Ribalta T, Ferrer E, Puig-Parellada P. **Oxidative stress markers in the neocortex of drug-resistant epilepsy patients submitted to epilepsy surgery.** *Epilepsy Res* 107(1-2):75-81 I.F.: 2.241

27. Sanz-Cortés M, Figueras F, Bonet-Carne E, Padilla N, Tenorio V, Bargalló N, Amat-Roldan I, Gratacós E. **Fetal brain MRI texture analysis identifies different microstructural patterns in adequate and small for gestational age fetuses at term.** *Fetal Diagn Ther* 33(2):122-129 I.F.: 1.902

28. de Notaris M, Topczewski T, de Angelis M, Enseñat J, Alobid I, Gondolbleu AM, Soria G, Gonzalez JB, Ferrer E, Prats-Galino A. **Anatomic skull base education using advanced neuroimaging techniques.** *World Neurosurg* 79(2 Suppl):S16 I.F.: 1.765

Originals in collaboration with other Institutions / IF: 9.453

1. Puig J, Blasco G, Daunis-I-Estadella J, Thomalla G, Castellanos M, Soria G, Prats-Galino A, Sánchez-González J, Boada I, Serena J, Pedraza S. **Increased corticospinal tract fractional anisotropy can discriminate stroke onset within the first 4.5 hours.** *Stroke* 44(4):1162-1165 I.F.: 6.158

2. Alemany S, Mas A, Goldberg X, Falcón C, Fatjó-Vilas M, Arias B, Bargalló N, Nenadic I, Gastó C, Fañanás L. **Regional gray matter reductions are associated with genetic liability for anxiety and depression: an MRI twin study.** *J Affect Disord* 149(1-3):175-181 I.F.: 3.295

GRANTS FOR RESEARCH IN PROGRESS

Soria G. **Biomarcadores de neuroimagen y moleculares del deterioro cognitivo vascular.** Sponsored by: MICINN-ERANET Neuron (PRI-PIMNEU-2011-1340). Duration: 01/12/2011-31/11/2014

Bargallo N. **Utilidad de los estudios de perfusión cerebral obtenidos mediante ASL en pacientes con epilepsia refractaria.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/00465. Duration 01/01/2013-31/12/2015

Training

Doctoral Theses

The PhD training dedication of IDIBAPS is reflected by the large number of doctoral theses that are driven and supported by IDIBAPS researchers. A list is provided below of the 93 doctoral theses presented during 2013:

THESIS AUTHOR	TITLE	THESIS DIRECTORS
Diego Agustín Rodríguez	**Effects of training in patients with chronic obstructive pulmonary disease: a systems approach**	Roca J
Clara Alsinet Armengol	**Characterization of driver pathways in hepatocellular carcinoma through genomic profiling and animal models**	Llovet J.M
Marta Anglada Huguet	**Characterization of mechanisms underlying neuronal survival and plasticity in Huntington's disease**	Alberch J
Mircea Balasa	**Enfermedad de alzheimer de inicio presenil esporádica: caracterización clínico-biológica y diagnóstico precoz**	Sánchez-Valle R, Lladó A
Ferran Ballesteros Alonso	**Sordera súbita neurosensorial idiopática. Análisis de los factores de riesgo vascular clásicos y genéticos**	Bernal-Sprekelsen M, Tàssies D
Cristina Baylo Gazquez	**Biomarcadores de estadiaje molecular y de respuesta terapéutica en pacientes con cáncer de vejiga músculo invasivo**	Ribal MJ, Mengual L
Jesús Benito Penalva	**Entrenamiento de la marcha en el lesionado medular. Uso de sistemas electromecánicos y estimulación transcraneal no invasiva**	Valls-Sole J
Miquel Bioque Alcázar	**Neuroinflammation in first episodes of psychosis**	Bernardo, M
Lizette Bonet Rosello	**Estudio de variantes estructurales (naturales e inducidas) de los receptores linfocitarios CD5 y CD6**	Lozano F
Felipe Burgos Rincón	**Impact of Information and Communication Technologies on Remote Testing, Forced Spirometry as a Use Case**	Roca J
Andreu Caballero David	**Utilidad de la resonancia magnética con realce tardío en la ablación de arritmias ventriculares**	Berruezo A, Mont L
Naiara Calvo Galiano	**Análisis sistemático de las diferentes estrategias de tratamiento en la práctica clínica habitual e impacto de la instauración de protocolos de actuación para el tratamiento de la fibrilación auricular**	Mont L
María Cano Colino	**Serotonergic neuromodulation and schizophrenia dysfunctions in a spatial working memory model**	Compte A
Cristina Carrera Alvarez	**Efectos de la radiación ultravioleta en lesiones melanocíticas. Implicaciones en diagnóstico precoz y prevención de melanoma**	Estrach T, Puig S
Gregori Casals Mercada	**Mecanismes moleculars de secreció miocardíaca: remodelat ventricular i secreció de pèptid natriurètictipus B**	Jiménez W
Gemma Chiva Blanch	**Balanç benefici/risc del contingut en polifenols i alcohol del vi: bases científiques dels efectes del consum moderat de vi sobre el sistema cardiovascular**	Estruch R
Yaroslau Compta Hirnyj	**Cerebrospinal fluid biomarkers in parkinson's disease dementia: clinico-pathological rationale and clinical correlates**	Martí MJ
Henry Nelson Córdova Guevara	**Utilidad de un sistema de navegación endoscópica basado en la tomografía computarizada para la cirugía endoscópica transluminal a través de orificios naturales (NOTES)**	Fernández-Esparrach, Mª G
Mairene Coto Llerena	**Polimorfismos del gen de la IL28B en la respuesta al tratamiento contra el virus de la hepatitis c en receptores de trasplante hepático**	Pérez del Pulgar S, Forns X
Mónica Cruz-Lemini	**Fetal cardiovascular dysfunction in intrauterine growth restriction as a predictive marker of perinatal outcome and cardiovascular disease in childhood**	Gratacós E, Crispi F

Marta Diví Oriol	**Mecanismes involucrats en la regularització del to vascular hepatic en la cirrosi: paper dels antioxidants en la biodisponibilitat de l'òxid nítric**	García-Pagán JC, Bosch J
Antonio Jesús Donaire Pedraza	**Identificación de las estructuras corticales implicadas en la generación de la actividad epiléptica crítica e intercrítica en pacientes con epilepsia fármacorresistente: un estudio de resonancia magnética funcional con EEG simultáneo**	Bargalló N
Cristina Embid López	**Nuevas estrategias para el diagnóstico y tratamiento del Síndrome de apnea-hipopnea del Sueño**	Montserrat JM
Bibiana J Escobar Suárez	**Repercusión de la capacidad de respuesta cardiovascular en la estabilidad hemodinámica y en la aparición de complicaciones en el trasplante hepático**	Fondevila C
María Florencia Etcheverry Rufino	**Identificación y seguimiento de cohortes de alto riesgo de infección por el virus de la inmunodeficiencia humana para futuros estudios de vacunas preventivas**	Gatell JM
Laia Fernández Barat	**Estudio del biofilm en un modelo porcino de neumonía asociada al ventilador: papel de la antibioterapia sistémica en su microbiología y morfología microscópica**	Torres A
Laura Fernández Bertolín	**Mecanismes involucrats en la resposta als glucocorticoides en malalties inflamatòries de les vies aèries**	Picado C, Pujols L
Joana Figueiro Silva	**Regulation of synapse density and mitochondrial dynamics by Neuronal Pentraxin 1**	Trullàs R
Blanca de la Fuente Capdevila	**Estudio de los decomisos de sustancias psicoactivas en los centros penitenciarios de Catalunya (1991-2010)**	To-Figueras J
Roland Galgoczy	**Study of the diffusive properties of extracellular matrix gels used in 3D cultures**	Reguart N, Alcaraz J
Francesc Josep García García	**Regulació del metabolisme de l'àcid araquidònic i senyalització cel·lular en un model d'asma i intolerància als aines**	Picado C, Roca-Ferrer J
Ana García Miralles	**Efecto de la activación de receptores de serotonina 5-ht4 sobre la patología amiloide y el deterioro cognitivo en el modelo triple transgénico 3xTg-AD de la enfermedad de alzehimer**	Vilaró MT
Silvia Gil Navarro	**Afasias primarias progresivas: caracterización clínica y marcadores biológicos**	Sánchez-Valle R, Lladó A
Eduard Graell i Martin	**Factors pronòstics en l'artritis reumatoide d'inici recent**	Sanmartí R
Iria Grande Fullana	**Desenvolupament i validaciód'unmodeld'estadificació en el trastorn bipolar: variables clíniques, funcionals i biomarcadorsperifèrics**	Vieta E
Enrique Gutiérrez Martínez	**Función de la fosfatasa de fosfolípidos 3 (LPP3) en las etapas tempranas de la vía secretora**	Egea G
Jorge Huguet Pérez	**Afectación extravesical en varones con carcinoma urotelial de vejiga sometidos a cistectomía radical**	Alcaraz A
Stefan Iliev Savchev	**Development of biomarkers to predict adverse outcomes in fetal growth restriction**	Gratacós E, Figueras F
Valentina Isetta	**Advances in the application of information and communication technologies in healthcare at the patient's home**	Farré R
Suha Jabr	**Contribution to the study of the role of arachidonic acid metabolism in inflammatory airway diseases (nasal polyps, asthma and cystic fibrosis)**	Picado C
Daniel Alejandro Jercog	**Dynamics of spontaneous activity in the cerebral cortex across brain states**	Compte A, De la Rocha J
Laura Jiménez Sánchez	**Papel de la corteza prefrontal en la fisiopatología y tratamiento de la depresión. Estudios en modelos animales**	Adell A
Gianluigi Li Bassi	**New insights into the role of the semirecumbent position in the pathogenesis of ventilator-associated pneumonia and potential preventive measures**	Torres A

Alba Llopis Gómez	**Reguladores del checkpoint de replicación en células no transformadas**	Agell N
Víctor Llorens Bellés	**Estudio clínico y experimental de las uveítis relacionadas con la tuberculosis**	Adán A
Sara Llufriu Duran	**Estudios de resonancia magnética y técnicas electrofisiológicas para evaluar y predecir la discapacidad en pacientes con esclerosis múltiple**	Blanco Y, Saiz A
María Lombraña Mencía	**Impacto de la prostatectomía radical en la incontinencia urinaria y disfunción eréctil. Influencia de un programa de intervención para la educación sanitaria**	Alcaraz A, Izquierdo L
Cristina López González	**Identificación, estratificación y adquisición de nuevas alteraciones citogenéticas en el curso evolutivo de la leucemia linfática crónica**	Colomer D
Diego López Pigozzi	**Brain mechanisms underlying the tracking and localization of dynamic cues**	Sánchez-Vives MV
María López-Cerón Pinilla	**La utilidad del Narrow Band Imaging para el estudio de las enfermedades con alto riesgo de cáncer digestivo**	Llach J, Pellisé Mª
Berta Martí Fuster	**Image processing of emission tomography studies in refractory epilepsy**	Pavía J
Joan-Daniel Martí Romeu	**Efficacy and safety assessment of ventilatory strategies and respiratory therapy techniques to improve mucociliary clearance during invasive mechanical ventilation**	Torres A
Josep Martí Sánchez	**Análisis de los resultados y factores pronósticos en el retrasplante hepático**	Fuster J
Marta Martín Llahí	**Estudis sobre la insuficiència renal en la cirrosi hepàtica: anàlisi del pronòstic i investigació en el tractament farmacològic de la síndrome hepatorenal**	Ginés P
Eider Martínez de Arenaza Urquijo	**Structural and functional brain correlates of education and cognitive activities in healthy aging and elders at higher risk for Alzheimer's disease**	Bartrés D
Margot Martínez Moreno	**Efecte de l'activació del canal KATP al perfil d'expressió microglial durant la neurodegeneració a l'hipocamp de la rata**	Rodríguez MJ
Sara Martínez Pasamar	**Dinámica del linfocitos T en autoinmunidad**	Villoslada P
Claudia Mendoza Pinto	**Bone mineral density and vertebral fractures in women with systemic lupus erythematosus**	Cervera R
Cristina Miró Julià	**Caracterització fenotípica i funcional de membres solubles de la superfamília de receptors scavenger rics en cisteïna (SF-SRCR)**	Lozano F
Joana Raquel Moitinho de Oliveira	**Targeting B-cell death in type 2 diabetes: the effect of sodium tungstate in IRS2 knochkout mice**	Gomis R
Eva Morán Salvador	**Papel del receptor nuclear PPARg en la inflamación y la esteatosis hepática**	Clària J
Leticia Moreira Ruiz	**Nueva caracterización clínica y molecular del síndrome de Lynch**	Balaguer F
Rosa Maria Muñoz Cano	**Efecte de la inhibició del factor d'activació de plaquetes (PAF) sobre la resposta al·lèrgica: model in vivo i in vitro**	Mullol J, Valero A
Andrea Murru	**Treatment adherence in schizoaffective disorder**	Vieta E, Colom F
Serena Orlando	**Analysys of the role of p27 kip1 in the recruitment of cyclins and cdks on the promoters of the target genes**	Bachs O
Eva M. Palacios Martinez	**Structural and functional connectivity alterations and their relationship with cognitive impairment in traumatic brain injury**	Junqué C
Aikaterini Papageorgiou	**Impact of adipose tissue on endothelial cells: effect of metabolic disorders**	Gomis R
Montserrat Pauta Puig	**Nuevos mecanismos de regulación hepática mediados por miR-33 y el receptor de las lipoproteinas de baja densidad**	Morales M

María Pérez Zabala	**Synaptic and intrinsic mechanisms involved in the generation of cortical slow rhythms**	Sánchez-Vives MV
Anna Plaza Estradé	**Efecto de las adversidades en la infancia en la patología depresiva y tiroidea en el posparto**	García-Esteve L, Valdés M
Pilar Prats Rodriguez	**Cribado de aneuploidías de primer trimestre en las gestaciones gemelares**	Puerto B
Nuria Pujol Giménez	**Functional and structural correlates of cognitive impairments in schizophrenia disorder and brain effects of cognitive remediation therapy**	Junqué C, Penadés R
Sílvia Quer Palomas	**Anàlisi de la relació entre variables fisiològiques i conductuals del nadó prematur**	Botet F
Rosa Anna Quiroga Varela	**Caracterización de un modelo progresivo y bilateral de enfermedad de Parkinson con administración intraventricular de 6-OHDA en la rata**	Marin C
María Elisa Reig Monzón	**Tratamiento del carcinoma hapatocelular con sorafenib: Perfil de seguridad, evaluación de marcadores de respuesta e impacto hemodinámico en la circulación sistémica y portal. Correlación de los eventos secundarios, tiempo a progresión y supervivencia de esta cohorte de pacientes para definir criterios de respuesta al tratamiento**	Bruix J
Susana Revilla Ortueta	**Neuroprotection by Physical Exercise and GDNF Transfection Therapies in the 3xTg-AD Mouse and MC65 Cell Models of Alzheimer's Disease**	Sanfeliu C, Cristofol RM, Adell A
Amanda Rey Torrente	**Factores predictores clínicos y biológicos de severidad en la toxoplasmosis ocular**	Adán A
Susana Rives Solá	**Caracterización clínica y factores pronósticos en subgrupos de pacientes pediátricos con leucemia linfoblástica aguda de alto riesgo de recaída**	Esteve J
Eugenio Rosado Mateo	**Mecanismes involucrats en la regulació del to vascular heoàtic en la cirrosi: paper dels prostanoids vasoconstrictors i biodisponibilitat d'òxid nítric**	García-Pagán JC, Bosch J
Cristina Royo Moreno	**Caracterización genética y molecular del linfoma de células del manto y sus implicaciones clínicas**	Beà S, Campo E
Marcel Ruiz Mejías	**Oscillations in the cerebral cortex: mechanisms of control and alterations in a transgenic model of down syndrome**	Sánchez-Vives MV
José Manuel de Salort	**Ly9, un regulador de la tolerancia inmunológica**	Engel P
Santiago Sánchez Cabús	**Importancia de la monitorización hemodinámica en el trasplante hepático de donante vivo**	García-Valdecasas JC
Susana Seijo Ríos	**Avances en el diagnóstico, etiopatogenia y pronóstico de la hipertensión portal no cirrótica**	García-Pagán JC, Bosch J
Elsa Solà Vergés	**Contribució a l´estudi de la hiponatrèmia a la cirrosi hepàtica: descripció d´una nova causa i implicacions sobre la qualitat de vida dels pacients**	Ginés P
Eva Troyano Rodríguez	**Alteració dels Circuits Talamocorticals en el Model NMDA d'Esquizofrènia. Reversió per Antipsicòtics**	Artigas F
Marc Udina Bonet	**Estudi de la incidència, factors de risc (sociodemogràfics, clínics i genètics), i resposta al tractament profilàcticamb antidepressius de la depressió induïda per interferó alfa en la hepatitis C crònica**	Marín-Santos, R
Juan Pablo Undurraga Fourcade	**Uso de antidepresivos y suicidio en el trastorno bipolar**	Vieta E
Alexandra Valera Barros	**Implicació de l'oncogen MYC en la patogènesi dels limfomes B agressius**	Campo E, Colomo L
María Carmela Vegliante	**SOX11 transcription factor functional analysis in aggressive MCL**	Amador V, Campo E
Marina Ventayol Espinazo	**Paper del miRNA en la diferenciació de les cèl·lules mare**	Hotter G, Viñas JL
Luis E Zapata Raboso	**Uso de la realidad virtual en violencia de género: tecnología al servicio de la rehabilitación de conductas violentas**	Sánchez-Vives MV, Slater M
Leire Zubiaurre Elorza	**Long-term brain MRI morphological patterns and cognitive performance in subjects born pretemp at low and high risk for neurodevelopmental deficits**	Junqué C

BIOTRACK, IDIBAPS mobility action

BIOTRACK, Professional Training and Career Development in Biomedicine, is an IDIBAPS initiative co-funded by the Marie Curie Actions of the European Commission, 7th Framework Program. It is composed by two schemes, a Post-doctoral in-coming mobility action and a Reintegration programme. The objective of BIOTRACK is improving the scientific production and quality of IDIBAPS by strengthening its existing research programmes.

BIOTRACK in-coming mobility scheme - Post-doctoral programme

The BIOTRACK in-coming mobility scheme - Post-doctoral programme wants to recruit excellent young researchers with a good track record in scientific publications that have acquired experience in other countries.

2013 facts and figures:

- 6 researchers previously selected have started their contract at IDIBAPS.
- 3 fellows have finished their contract.

BIOTRACK has recruited in total 18 fellows, 17 of them have coincided in 2013 at IDIBAPS:

FELLOW	RESEARCH PROJECT
Elena Garreta	Modulation of Stem Cell differentiation by biophysical stimuli: Effect of acellular lung matrix scaffold and oxygen tension on the pulmonary differentiation of stem cells
Elisabeth Calderon	Microbial specific T cells in Crohn's Disease
Sara Cervantes	Understanding the molecular determinants of beta-cell specification and expansion
Esther Carreras	Functional and therapeutical implications of exogenous and endogenous ligand recognition by scavenger-like lymphocyte receptors
Meritxell Rovira	REST inactivation during pancreas development and adult
Eduardo Fernández	LncRNAs regulation in insulina resistance of the adipose tissue
Maria Laura Pérez	New nanomedicines for the treatment of Systemic Lupus Erythematosus
Ester Valls	Role of ZEB transcription factors in DLBCL malignancy and Germinal Center reaction regulation
Vicente Ribas	Development of genetic tools to modify the expression of target genes steatohepatitis in hepatocytes
Juan Rodríguez	Therapeutic potential of new Akt/PKB targets in liver fibrosis
Virginia Hernández-Gea	Identification of molecular drivers of tumor dissemination and poor prognosis in hepatocellular carcinoma
Olga Tura	Identification of the causes that result to dysfunctional endothelial cells in COPD patients
Ekaterina Kotelnikova	A new method for drug discovery based on systems biology: combination therapy and biomarkers for Multiple Sclerosis (CombiMS)
Andrés Miguez	Study of the neuroprotective effect of Fingolimod mediated by BDNF release in a Huntington's Disease mouse model
Anja Meissner	Hypertension in cerebrovascular disease
Joel Montane	The role of chaperones in the ER stress response induced by human IAPP overexpression
Aritz Lopategi	Role of omega-3 fatty acids derived bioactive lipid mediators in the modulation of the NLRP3 inflammasome in macrophages during diet induce inflammation

BIOTRACK reintegration programme

BIOTRACK also includes a Reintegration prorgamme that provides some senior researchers with start-up incentives. The reintegrated scientists through some specific competitive calls who accomplish some mobility requirements can access to them.

It is expected that these incentive will help to enhance their excellent research.

6 researchers have received at this stage an institutional start-up co-funded by BIOTRACK.

IDIBAPS Research Seminars

Traditionally, the institutional seminars program consisted in the so-called IDIBAPS Seminars organized in a monthly basis (from October to June). In addition to the IDIBAPS Seminars, two new lines of seminars were started in the fall term, the IDIBAPS In-House Seminars and the IDIBAPS Core Facility Seminars. The overall objective of this new seminar program was to promote lively discussion and debate about the latest research news on every field.

- **IDIBAPS Seminars.** With a clear translational vocation, these seminars are imparted by top scientists of international prestige who are invited to share their most recent scientific findings.

- **IDIBAPS In-House Seminars.** Imparted by IDIBAPS researchers, especially those who have just published high impact results on their scientific field or those holding a tenure-track position. The main objective of this program is to share in-house knowledge and encourage the establishment of intramural collaborations.

- **IDIBAPS Core Facility Seminars.** The program aims to become a tool to introduce new techniques and services offered by the IDIBAPS Core Facilities (Biobank, Bioinformatics, Biostatistics and data management, Cytometry and cell sorting, Functional genomics and Medical imaging).

IDIBAPS SEMINARS

January 28th, 2013
Epigenetics in oncology
Manel Esteller, PhD
ICREA Research Professor.
IDIBELL, Barcelona.

May 6th, 2013
Genomic profiling and sequence analysis of B-cell lymphomas: From pathogenesis to clinics
Prof. Reiner Siebert
Institute of Human Genetics.
Christian-Albrechts-Universität zu Kiel

June 17th, 2013
Understanding Colorectal Cancer as a Stem Cell hierarchy
Eduard Batlle, PhD
ICREA Research Professor. IRB Barcelona

July 1st, 2013
Novel mechanisms of intercellular communication of immune cells
Paco Sánchez-Madrid, PhD
Hospital de la Princesa.
Universidad Autónoma de Madrid.

October 14th, 2013
New genomic strategies for the identification of genes involved in colorrectal cancer
Angel Carracedo MD, PhD
Director of Centro Nacional de Genotipado.
Universidad Santiago de Compostela.

November 25th, 2013
The role of microRNAs as metabolic stress regulators
Markus Stoffel MD, PhD
Institute of Molecular Health Science. Swiss Federal Institute of Technology (ETH) Zürich

IDIBAPS IN-HOUSE SEMINARS

October 24th, 2013
Autoimmune encephalitis: From symptom to synapse
Josep Dalmau MD, PhD
IDIBAPS Group Leader and ICREA Research Professor

November 28th, 2013
Molecular characterization of posttransplant malignancies
Ignacio Revuelta MD, PhD
IDIBAPS Researcher – 50/50 Program

December 12th, 2013
Mitofusin 2 in POMC neurons connects ER stress with leptin resistance and energy imbalance
Marc Claret, PhD
IDIBAPS Researcher

IDIBAPS CORE FACILITY SEMINARS

November 6th, 2013
Novetats a les plataformes IDIBAPS
Anna Bosch, Ferran Torres, Susana Kalko, Cristina López, Madga Pinyol, Núria Bargalló.
IDIBAPS Core Facilities Coordinators

Commitment to Society

These are just a few examples of IDIBAPS' commitment to society. By informing the public about advancements made in biomedical research and healthcare innovation, IDIBAPS shows its dedication to people, based upon the principle that a well-informed person is a healthier person.

The Center of Contemporary Culture of Barcelona (CCCB) hosted the first edition of the ICREA-CCCB Debates in June, featuring two IDIBAPS researchers, Dr. Josep Maria Llovet, who leads the Translational Research in Liver Oncology group, and Dr. Josep Dalmau, head of the Autoimmunity Against Synaptic Antigens group.

In November, IDIBAPS teamed up with Casal Infantil Urgell, a children's recreational facility within the local Urgell Civic Centre, to organize the filming of a family-oriented SceneMob, or live lipsync performance, in celebration of the TV3 Telethon, which raised money for neurodegenerative disease research.

Also at the same civic centre, during the last trimester of 2013, IDIBAPS researcher Dr. Maria Victoria Sánchez-Vives coordinated a series of lectures entitled "Health and the Brain", with tips on healthy ageing and mental wellness.

Finally, the IDIBAPS Neuroimmunology team hosted 23 local high school students for a week in March, offering them a first-hand view of Optical Coherence Tomography technology and one-on-one interaction with the IDIBAPS Neuroimmunology team

AREA 1

Biological aggression and response mechanisms

1.1 **Inflammatory joint diseases (IJDs)** 56
Raimon Sanmartí

1.2 **Systemic autoimmune diseases** 58
Ricard Cervera

1.3 **Infectious diseases and AIDS** 65
Josep Maria Gatell

1.4 **Immune receptors of the innate and adaptive system** 72
Francisco Lozano

1.5 **Musculoskeletal repair and plasticity** 74
Joaquim Forés

1.6 **Immunogenetics of the autoinflammatory response** 76
Jordi Yagüe

1.7 **Emergencies: Processes and pathologies** 78
Oscar Miró

1.8 **Molecular and cellular bases of inflammation. Structural and biological mass spectrometry** 81
Daniel Closa

1.1 Inflammatory joint diseases (IJDs)

LOCATION
HCB building

KEYWORDS
1. **Rheumatoid arthritis**
2. **Psoriatic arthritis**
3. **Pathogenesis**
4. **Biomarkers**
5. **Targeted therapies**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	36.45	8	5	3
2012	70.08	13	8	3
2013	26.54	6	4	2

TEAM INVOLVED IN
RIER

TEAM LEADER
Raimon Sanmartí (HCB)
T. 93 227 54 00 (Ext.: 2236/2604)
sanmarti@clinic.cat

RESEARCHERS
Juan D. Cañete (HCB)

POST-DOCTORAL RESEARCHERS
Raquel Celis (FCRB)
María Victoria Hernández (FCRB)
Virginia Ruiz-Esquide (FCRB)

PRE-DOCTORAL RESEARCHERS
Julio Ramírez (FCRB)
Sónia Cabrera-Villalba (FCRB)

COLLABORATORS
Guadalupe Ercilla (HCB)
Jaume Pomés (HCB)
Xavier Tomas (HCB)
Odette Viñas (HCB)

STRATEGIC OBJECTIVES

Promotion of research into the most prevalent chronic forms of immune mediated inflammatory arthritis: rheumatoid arthritis (RA) and spondyloarthritis, including psoriatic arthritis.

MAIN LINES OF RESEARCH

1. Prognostic factors in early arthritis
- Prognostic factors (clinical and immunogenetic) in patients with recent-onset rheumatoid arthritis.
- Production of new synthetic citrullinated peptides for the design of immunoassays with diagnostic and prognostic value in recent-onset rheumatoid arthritis and palindromic rheumatism.
- Effect of tobacco on the phenotype of recent-onset rheumatoid arthritis

2. Clinical and sonographic characterization of clinical remission
- Definition and clinical characterization of subclinical "active synovitis"
- Immunopathological and molecular characterization of subclinical "active synovitis".
- Search of biomarkers of clinical reactivation and radiographic progression.

3. Immunopathology of synovitis in chronic arthritis
- Utility in pathogenesis, differential diagnosis and prognosis of rheumatoid arthritis and psoriatic arthritis. Immunopathological changes induced by biological treatments. Mechanism of action of targeted therapies. Synovial response biomarkers.

4. Pharmacogenomics of chronic arthritis
- Genetic biomarkers associated to biological therapy response in rheumatoid arthritis and psoriatic arthritis

5. Role of autoinflammatory genes in the pathogenesis of chronic arthritis
- MEFV gene mutations in the diagnosis and treatment of undifferentiated intermittent arthritis. Utility of the test in a clinical setting.

PUBLICATIONS

Originals / I.F.: 26.542

1. Yeremenko N, Noordenbos T, Cantaert T, van Tok M, van de Sande M, Cañete JD, Tak PP, Baeten D. **Disease-specific and inflammation-independent stromal alterations in spondylarthritis synovitis.** *Arthritis Rheum.* 65(1):174-185. I.F. 7.477

2. Gómez-Puerta JA, Celis R, Hernández MV, Ruiz-Esquide V, Ramírez J, Haro I, Cañete JD, Sanmartí R. **Differences in synovial fluid cytokine levels but not in synovial tissue cell infiltrate between anti-citrullinated peptide/ protein antibody-positive and -negative rheumatoid arthritis patients.** *Arthritis Res Ther.* 7;15(6):R182. I.F. 4.302

3. Descalzo MÁ, Garcia VV, González-Alvaro I, Carbonell J, Balsa A, Sanmartí R, Lisbona P, Hernandez-Barrera V, Jiménez-Garcia R, Carmona L; SERAP Study Group. **Tackling missing radiographic progression data: multiple imputation technique compared with inverse probability weights and complete case analysis.** *Rheumatology.* 52(2):331-336. I.F. 4.212

4. Acosta-Colman I, Palau N, Tornero J, Fernández-Nebro A, Blanco F, González-Alvaro I, Cañete JD, Maymó J, Ballina J, Fernández-Gutiérrez B, Olivé A, Corominas H, Erra A, Canela-Xandri O, Alonso A, López Lasanta M, Tortosa R, Julià A, Marsal S. **GWAS replication study confirms the association of PDE3A-SLCO1C1 with anti-TNF therapy response in rheumatoid arthritis.** *Pharmacogenomics.* 14(7):727-734. I.F. 3.857

5. Hernández MV,Sanmartí R, Cañete JD, Descalzo MA; Alsina M; Carmona L; Gomez-Reino JJ. **Cutaneous Adverse Events During Treatment of Chronic Inflammatory Rheumatic Conditions With Tumor Necrosis Factor Antagonists: Study Using the Spanish Registry of Adverse Events of Biological Therapies in Rheumatic Diseases.** *Arthritis Care Res* 65 (12): 2024-2031. I.F. 3.,731

6. Fischer S, Agmon-Levin N, Shapira Y, Porat Katz BS, Graell E, Cervera R, Stojanovich L, Gómez Puerta JA, Sanmartí R, Shoenfeld Y. **Toxoplasma gondii: bystander or cofactor in rheumatoid arthritis.** *Immunol Res* 56(2-3):287-292. I.F. 2.963

Reviews / I.F.: 11.106

1. Pablos JL, Cañete JD. **Immunopathology of rheumatoid arthritis.** *Curr Top Med Chem* 13(6):705-711 I.F. 3.702

2. Cañete JD, Pablos JL. **Biologic therapy in rheumatoid arthritis.** *Curr Top Med Chem* 13(6):752-759. I.F. 3.702

3. Sanmartí R, Ruiz-Esquide V, Hernández MV. **Rheumatoid arthritis: a clinical overview of new diagnostic and treatment approaches.** *Curr Top Med Chem* 13(6):698-704. I.F. 3.702

Editorials/ I.F.: 3.702

1. Haro I, Sanmartí R. **Rheumatoid arthritis: current advances in pathogenesis, diagnosis and therapy.** *Curr Top Med Chem* 13(6):697. I.F. 3.702

Multicenter/ I.F.: 39.060

1. Gabay C, Emery P, van Vollenhoven R, Dikranian A, Alten R, Pavelka K, Klearman M, Musselman D, Agarwal S, Green J, Kavanaugh A; **ADACTA Study Investigators. Tocilizumab monotherapy versus adalimumab monotherapy for treatment of rheumatoid arthritis (ADACTA): a randomised, double-blind, controlled phase 4 trial.** *Lancet.* 381(9877):1541-1550. I.F.: 39.060

GRANTS FOR RESEARCH IN PROGRESS

Cañete J. **Caracterización ecográfica e inmunohistología de la sinovitis subclínica en pacientes con artritis reumatoide en remisión clínica: Implicaciones pronósticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01890. Duration 01/01/2012-31/12/2014.

Cañete, J. **Red de investigación en inflamación y enfermedades reumáticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD08/0075/0006. Duration: 23/02/2009-31/12/2014.

Cañete, J. **Red de investigación en inflamación y enfermedades reumáticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0009/0016. Duration: 01/01/2013-31/12/2016.

DOCTORAL THESES

Sanmartí, R. **Factors pronòstics en l'artritis reumatoide d'inici recent.** PhD student : Eduard Graell i Martin.

1.2 Systemic autoimmune diseases

LOCATION
HCB building
Cellex building

KEYWORDS
1. **Systemic autoimmune diseases**
2. **Systemic lupus erythematosus**
3. **Systemic vasculitis**
4. **Uveitis**
5. **Antiphsopholipid syndrome**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	185.01	37	19	13
2012	264.16	50	32	8
2013	200.50	43	19	20

AWARDS

APS ACTION Award
Institution: Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION)
Awardee: Ignasi Rodríguez-Pintó

PANLAR Granted Award for Junior Rheumatologists
Institution: PanAmerican League Against Rheumatism (PANLAR
Awardee: Guillermo Pons-Estel

TEAM LEADER
Ricard Cervera Segura (HCB)
T. 93 227 57 74
rcervera@clinic.cat

GROUP LEADERS
Alfredo Adán (HCB)
Maria Cinta Cid (HCB)

RESEARCHERS
Albert Bové (UB)
Ricardo P. Casaroli (HCB)
Gerard Espinosa Garriga (HCB)
José Hernández Rodríguez (HCB)
Elena Millá (HCB)
Manuel Ramos Casals (HCB)

PRE-DOCTORAL RESEARCHERS
Marco Alba (IDIBAPS)
Montserrat Butjosa (HCB)
Emmanuel Coloma (HCB)
Marc Corbera (IDIBAPS)
Nerea Iniesta (HCB)
Juan Carlos Mejía (IDIBAPS)
Ester Planas (IDIBAPS)
Sergio Prieto (HCB)
Ignasi Rodríguez (HCB)
Itziar Tavera (HCB)
Nekane Terrades (IDIBAPS)

ADMINISTRATIVE STAFF
Isabel Chaves (HCB)

COLLABORATORS
Xavier Bosch Aparici (HCB)
Pilar Brito-Zerón (IDIBAPS)
Cándido Díaz-Lagares (HCB)
Georgina Espígol (IDIBAPS)
Ana García Martínez (HCB)
María Soledad Retamozo (IDIBAPS)
María Teresa Sainz de la Maza (HCB)
Antoni Sisó (GESCLINIC)

VISITING SCIENTISTS
Aruna Chakrabarty
(Leeds, United Kingdom)
Daniela de la Garza
(México DF, México)
Hoda Gheitasi (Iran)
Sarah Mackie (Leeds, United Kingdom)
Claudia Mendoza (Puebla, México)
Guillermo Pons-Estel (Barcelona)
Rosa Serrano (Barcelona)
Mauricio Vera-Recabarren
(Santiago, Chile)

STRATEGIC OBJECTIVES

The Systemic Autoimmune Diseases research group promotes basic, clinical and translational research in these diseases in a multidisciplinary manner, with the participation of members of the following Departments: Autoimmune Diseases, Ophthalmology, Internal Medicine, Nephrology, Immunology, Hemostasis, Hepatology, Obstetrics and Dermatology, among others. These activities are carried out in close collaboration with different international work groups, of which the team members are national and/or international coordinators: European Working Party on Systemic Lupus Erythematosus (EWPSLE), European Forum on Antiphospholipid Antibodies (EFAPL), Catastrophic Antiphospholipid Syndrome (CAPS) Registry Project Group, International Pediatric Register of Antiphospholipid Syndrome (Ped-APS Register), Systemic Lupus International Collaborative Centers (SLICC), Sjögren's Syndrome-Hepatitis C Virus (SS-HCV) Study Group, HISPAMEC Study Group, Systemic Autoimmune Disease Study Group – Use of Biological Therapies (BIOGEAS), Spanish Sjögren's Syndrome Multicenter Study Group (GEMESS), European Vasculitis Study Group (EUVAS), European League Against Rheumatism (EULAR) Systemic Vasculitis Task Force, EULAR Standing Committee for International Clinical Studies Including Therapeutics, and the American College of Rheumatology (ACR) Work Group for Development of Classification Criteria for Rheumatic Polymyalgia, among others.

MAIN LINES OF RESEARCH

1. Systemic lupus erythematosus, antiphospholipid syndrome and systemic sclerosis:
- Epidemiological multicenter studies on the clinical manifestations and long-term evolution of these diseases.
- Clinical trials in new biological therapies.
- Study of genetic polymorphisms as risk factors of the different clinical manifestations of these diseases.
- Study of the cardiovascular and endothelial damage risk factors found in these diseases.
- Basic research in animal models on the mechanism of action of antiphospholipid antibodies.

2. Sjögren's syndrome, autoimmune manifestations of hepatitis C virus infection and biological therapies:
- Epidemiological multicenter studies on the clinical manifestations and long-term evolution of these diseases.
- Study of IgG4 disease associated with Sjögren's syndrome.
- Validation of ESSDAI and ESSPRI activity scores,
- European Task Force for the characterization of Sjögren's syndrome systemic manifestations (EULAR-SS Task Force).
- Development of new international classification criteria for Sjögren's syndrome (ACR-EULAR Task Force Group).
- Study of the cardiovascular and endothelial damage risk factors found in this syndrome.
- Clinical and basic studies in mixed cryoglobulinemia.
- Development of new international classification criteria for mixed cryoglobulinemia.
- International registry of treatments with biological drugs for systemic autoimmune disorders (BIOGEAS).

3. Systemic vasculitis:
- Investigation of the mechanisms involved and the clinical consequences of the persistence of vascular inflammation in giant cell arteritis. Identification of new therapeutic targets.
- Study of the mechanisms involved in the development of abnormal vascular remodelling (occlusion or dilatation) and its clinical consequences.
- Development of an organ culture model for studying the factors implicated in the perpetuation of inflammation and in vascular remodelling.
- Study of the prevalence of large vessel inflammatory involvement at the start and during the course of giant cell arteritis.
- Genetic studies on giant cell arteritis.
- Clinical trials promoted fundamentally for investigating new biological therapies in the management of systemic vasculitis.
- Spanish systemic vasculitis registry.
- Spanish Behçet's disease registry.

4. Autoimmune ophthalmopathy:
- Clinical trials in new biological therapies.
- Study of genetic polymorphisms in uveitis as risk factors of the different clinical manifestations of such ophthalmological disorders.
- Treatment with anti-Vascular Endothelial Growth Factor (VEGF) drugs for choroid neovascularization and cystic macular edema secondary to uveitis.

RESEARCH GROUP
AUTOIMMUNE OPHTHALMOPATHY

GROUP LEADER
Alfredo Manuel Adán (HCB)

This group studies the clinical, diagnostic and therapeutic aspects of autoimmune diseases. The scientific contribution of this line of research is very competitive and is internationally renowned. The group also studies the genetic polymorphisms of uveitis as risk factors for the different clinical manifestations of the disease, and participates in different clinical trials involving novel biological treatments.

RESEARCH GROUP
SYSTEMIC VASCULITIS

GROUP LEADER
Maria Cinta Cid (HCB)

This group studies the clinical, diagnostic and therapeutic aspects of systemic vasculitic disorders, as well as the mechanisms producing vascular damage in these diseases.

The scientific contribution of this line of research is very competitive and is internationally renowned. Clinical studies are also made of the systemic vascular lesions characterizing giant cell arteritis, exploring the mechanisms that produce these vascular lesions in this disease, and participating in different clinical trials involving new biological treatments. The group also coordinates the Spanish registries of vasculitis associated with antineutrophil cytoplasmic antibodies (ANCA) and Behçet's disease.

PUBLICATIONS

Originals / I.F.: 200.504

1. Bossini-Castillo L, Martin JE, Broen J, Simeon CP, Beretta L, Gorlova OY, Vonk MC, Ortego-Centeno N, Espinosa G, Carreira P, García de la Peña P, Oreiro N, Román-Ivorra JA, Castillo MJ, González-Gay MA, Sáez-Comet L, Castellví I, Schuerwegh AJ, Voskuyl AE, Hoffmann-Vold AM, Hesselstrand R, Nordin A, Lunardi C, Scorza R, van Laar JM, Shiels PG, Herrick A, Worthington J, Fonseca C, Denton C, Tan FK, Arnett FC, Assassi S, Koeleman BP, Mayes MD, Radstake TR, Martin J; Spanish Scleroderma Group. **Confirmation of TNIP1 but not RHOB and PSORS1C1 as systemic sclerosis risk factors in a large independent replication study.** *Ann Rheum Dis.* 72(4): 602-607. I.F.:9.111

2. Diaz-Gallo LM, Simeon CP, Broen JC, Ortego-Centeno N, Beretta L, Vonk MC, Carreira PE, Vargas S, Román-Ivorra JA, González-Gay MA, Tolosa C, López-Longo FJ, Espinosa G, Vicente EF, Hesselstrand R, Riemekasten G, Witte T, Distler JH, Voskuyl AE , Schuerwegh AJ, Shiels PG, Nordin A, Padyukov L, Hoffmann-Vold AM, Scorza R, Lunardi C, Airo P, van Laar JM, Hunzelmann N, Gathof BS, Kreuter A, Herrick A, Worthington J, Denton CP, Zhou X, Arnett FC, Fonseca C, Koeleman BP, Assasi S, Radstake TR, Mayes MD, Martín J; Spanish Scleroderma Group. **Implication of IL-2/IL-21 region in systemic sclerosis genetic susceptibility.** *Ann Rheum Dis.* 72(7): 1233-1238. I.F.:9.111

3. Espígol-Frigolé G, Corbera-Bellalta M, Planas-Rigol E, Lozano E, Segarra M, García-Martínez A, Prieto-González S, Hernández-Rodríguez J, Grau JM, Rahman MU, Cid MC. **Increased IL-17A expression in temporal artery lesions is a predictor of sustained response to glucocorticoid treatment in patients with giant-cell arteritis.** *Ann Rheum Dis.* 72(9): 1481-1487. I.F.:9.111

4. Parker B, Urowitz MB, Gladman DD, Lunt M, Bae SC, Sanchez-Guerrero J, Romero-Diaz J, Gordon C, Wallace DJ, Clarke AE, Bernatsky S, Ginzler EM, Isenberg DA, Rahman A, Merrill JT, Alarcón GS, Fessler BJ, Fortin PR, Hanly JG, Petri M, Steinsson K, Dooley MA, Manzi S, Khamashta MA, Ramsey-Goldman R, Zoma AA, Sturfelt GK, Nived O, Aranow C, Mackay M, Ramos-Casals M, van Vollenhoven RF, Kalunian KC, Ruiz-Irastorza G, Lim S, Kamen DL, Peschken CA, Inanc M, Bruce IN. **Clinical associations of the metabolic syndrome in systemic lupus erythematosus: data from an international inception cohort.** *Ann Rheum Dis.* 72(8): 1308-1314. I.F.:9.111

5. Serrano A, Carmona FD, Castañeda S, Solans R, Hernández-Rodríguez J, Cid MC, Prieto-González S, Miranda-Filloy JA, Rodríguez-Rodríguez L, Morado IC, Gomez-Vaquero C, Blanco R, Sopeña B, Ortego-Centeno N, Unzurrunzaga A, Marí-Alfonso B, Sánchez-Martín J, García-Villanueva MJ, Hidalgo-Conde A, Pazzola G, Boiardi L, Salvarani C, González-Gay MA, Martín J. **Evidence of association of the NLRP1 gene with giant cell arteritis.** *Ann Rheum Dis.* 72(4): 628-630 I.F.:9.111

6. Serrano A, Márquez A, Mackie SL, Carmona FD, Solans R, Miranda-Filloy JA, Hernández-Rodríguez J, Cid MC, Castañeda S, Morado IC, Narváez J, Blanco R, Sopeña B, García-Villanueva MJ, Monfort J, Ortego-Centeno N, Unzurrunzaga A, Marí-Alfonso B, Sánchez-Martín J, de Miguel E, Magro C, Raya E, Braun N, Latus J, Molberg O, Lie BA, Moosig F, Witte T, Morgan AW, González-Gay MA, Martín J; UK GCA Consortium Spanish GCA Consortium. **Identification of the PTPN22 functional variant R620W as susceptibility genetic factor for giant cell arteritis.** *Ann Rheum Dis.* 72(11): 1882-1886. I.F.:9.111

7. Vitali C, Bootsma H, Bowman SJ, Dorner T, Gottenberg JE, Mariette X, Ramos-Casals M, Ravaud P, Seror R, Theander E, Tzioufas AG. **Classification criteria for Sjogren's syndrome: we actually need to definitively resolve the long debate on the issue.** *Ann Rheum Dis.* 72(4): 476-478. I.F.:9.111

8. Berman H, Rodríguez-Pintó I, Cervera R, Morel N, Costedoat-Chalumeau N, Erkan D, Shoenfeld Y, Espinosa G, for the Catastrophic Antiphospholipid Syndrome (CAPS) Registry Project Group (European Forum on Antiphospholipid Antibodies). **Rituximab use in the catastrophic antiphospholipid syndrome: Descriptive analysis of the CAPS registry patients receiving rituximab.** *Autoimmun Rev.* 12(11): 1085-1090. I.F.:7.975

9. Chamorro AJ, Marcos M, Hernández-García I, Calvo A, Mejía JC, Cervera R, Espinosa G. **Association of allelic variants of factor V Leiden, prothrombin and methylenetetrahydrofolate reductase with thrombosis or ocular involvement in Behçet's disease: A systematic review**

and meta-analysis. *Autoimmun Rev.* 12(5): 607-616. I.F.:7.975

10. Toledano P, Sarbu N, Espinosa G, Bargalló N, Cervera R. **Neuropsychiatric systemic lupus erythematosus: magnetic resonance imaging findings and correlation with clinical and immunological features.** *Autoimmun Rev.* 12(12): 1166-1170. I.F.:7.975

11. Martin JE, Assassi S, Diaz-Gallo LM, Broen JC, Simeon CP, Castellvi I, Vicente-Rabaneda E, Fonollosa V, Ortego-Centeno N, González-Gay MA, Espinosa G, Carreira P; Spanish Scleroderma Group; SLEGEN consortium; U.S. Scleroderma GWAS group; BIOLUPUS, Camps M, Sabio JM, D'alfonso S, Vonk MC, Voskuyl AE, Schuerwegh AJ, Kreuter A, Witte T, Riemekasten G, Hunzelmann N, Airo P, Beretta L, Scorza R, Lunardi C, Van Laar J, Chee MM, Worthington J, Herrick A, Denton C, Fonseca C, Tan FK, Arnett F, Zhou X, Reveille JD, Gorlova O, Koeleman BP, Radstake TR, Vyse T, Mayes MD, Alarcón-Riquelme ME, Martin J. **A systemic sclerosis and systemic lupus erythematosus pan-meta-GWAS reveals new shared susceptibility loci.** *Hum Mol Genet.* 22(19): 4021-4029. I.F.:7.692

12. Hanly JG, Urowitz MB, O'Keeffe AG, Gordon C, Bae SC, Sanchez-Guerrero J, Romero-Diaz J, Clarke AE, Bernatsky S, Wallace DJ, Ginzler EM, Isenberg DA, Rahman A, Merrill JT, Petri M, Fortin PR, Gladman DD, Fessler BJ, Alarcón GS, Bruce IN, Dooley MA, Steinsson K, Khamashta MA, Ramsey-Goldman R, Manzi S, Sturfelt GK, Nived O, Zoma AA, van Vollenhoven RF, Ramos-Casals M, Aranow C, Mackay M, Ruiz-Irastorza G, Kalunian KC, Lim SS, Inanc M, Kamen DL, Peschken CA, Jacobsen S, Theriault C, Thompson K, Farewell V. **Headache in systemic lupus erythematosus: results from a prospective, international inception cohort study.** *Arthritis Rheum.* 65(11): 2887-2897. I.F.:7.477

13. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, Hoffman GS, Jayne DR, Kallenberg CG, Lamprecht P, Langford CA, Luqmani RA, Mahr AD, Matteson EL, Merkel PA, Ozen S, Pusey CD, Rasmussen N, Rees AJ, Scott DG, Specks U, Stone JH, Takahashi K, Watts RA. **2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides.** *Arthritis Rheum.* 65(1): 1-11. I.F.:7.477

14. Petri MA, van Vollenhoven RF, Buyon J, Levy RA, Navarra SV, Cervera R, Zhong ZJ, Freimuth WW, on behalf of the BLISS-52 and BLISS-76 Study Groups. **Baseline predictors of systemic lupus erythematosus flares. Data from the combined placebo groups in the phase III belimumab trials.** *Arthritis Rheum.* 65(8): 2143-2153. I.F.:7.477

15. Pérez-Alvarez R, Pérez-de-Lis M, Ramos-Casals M; BIOGEAS study group. **Biologics-induced autoimmune diseases.** *Curr Opin Rheumatol.* 25(1): 56-64. I.F.:5.191

16. Pinazo MJ, Espinosa G, Cortes-Lletget C, Posada Ede J, Aldasoro E, Oliveira I, Muñoz J, Gállego M, Gascon J. **Immunosuppression and Chagas disease: a management challenge.** *PLoS Neglect Trop Dis.* 7(1): e1965. I.F.:4.569

17. Montes-Cano M, Conde-Jaldón M, García-Lozano J, Ortiz-Fernández L, Ortego-Centeno N, Castillo-Palma M, Espinosa G, Graña-Gil G, González-Gay M, Barnosi-Marín A, Solans R, Fanlo P, Camps T, Castañeda S, Sánchez-Bursón J, Núñez-Roldán A, Martín J, González-Escribano M. **HLA and non-HLA genes in Behçet's disease: a multicentric study in the Spanish population.** *Arthritis Res Ther.* 15(5): R145. I.F.:4.302

18. Recarte-Pelz P, Tàssies D, Espinosa G, Hurtado B, Sala N, Cervera R, Reverter JC, García de Frutos P. **Vitamin K-dependent proteins GAS6 and Protein S and TAM receptors in patients of systemic lupus erythematosus: correlation with common genetic variants and disease activity.** *Arthritis Res Ther.* 15(2): R41. I.F.:4.302

19. Gómez-Puerta JA, Peris P, Reverter JC, Espinosa G, Martinez-Ferrer A, Monegal A, Monteagudo J, Tàssies D, Guañabens N. **High prevalence of prothrombotic abnormalities in multifocal osteonecrosis: description of a series and review of the literature.** *Medicine* 92(6): 295-304. I.F.:4.233

20. Espinosa G, Rodríguez-Pintó I, Gómez-Puerta JA, Pons-Estel G, Cervera R, for the Catastrophic Antiphospholipid Syndrome (CAPS) Registry Project Group (European Forum on Antiphospholipid Antibodies). **Relapsing catastrophic antiphospholipid syndrome – Potential role of microangiopathic hemolytic anemia in disease relapses.** *Semin Arthritis Rheu* 42(4): 417-423. I.F.:3.806

21. Cénit MC, Márquez A, Cordero-Coma M, Gorroño-Echebarría MB, Fonollosa A, Adán A, Martínez-Berriotxoa A, Díaz Valle D, Pato E, Blanco R, Cañal J, Díaz-Llopis M, García Serrano JL, de Ramón E, Del Rio MJ, Martín-Villa JM, Molins B, Ortego-Centeno N, Martín J. **No evidence of association between common autoimmunity STAT4 and IL23R risk polymorphisms and non-anterior uveitis.** *PLoS One* 8(11):e72892. I.F.:3.730

22. Márquez A, Cénit MC, Cordero-Coma M, Ortego-Centeno N, Adán A, Fonollosa A, Díaz Valle D, Pato E, Blanco R, Cañal J, Díaz-Llopis M, de Ramón E, Del Rio MJ, García Serrano JL, Artaraz J, Martín-Villa JM, Llorenç V, Gorroño-Echebarría MB, Martín J. **Two functional variants of IRF5 influence the development of macular edema in patients with non-anterior uveitis.** *PLoS One.* 8(10):e76777. I.F.:3.730

23. Coloma Bazán E, Donate López C, Moreno Lozano P, Cervera R, Espinosa G. **Discontinuation of anticoagulation or antiaggregation treatment may be safe in patients with primary antiphospholipid syndrome when antiphospholipid antibodies became persistently**

negative. *Immunol Res.* 56(2-3): 358-361. I.F.: 2.963

24. Fischer S, Agmon-Levin N, Shapira Y, Porat Katz BS, Graell E, Cervera R, Stojanovich L, Gómez-Puerta JA, Sanmartí R, Shoenfeld Y. **Toxoplasma gondii: bystander or cofactor in rheumatoid arthritis.** *Immunol Res.* 56(2-3): 287-292. I.F.:2.963

25. Adán A, Pelegrín L, Rey A, Llorenç V, Mesquida M, Molins B, Ríos J, Keller J. **Dexamethasone intravitreal implant for treatment of uveitic persistent cystoid macular edema in vitrectomized patients.** *Retina-J Ret Vit Dis.* 33(7):1435-40. I.F.:2.825

26. Agmon-Levin N, Rosário C, Porat Katz BS, Zandman-Goddard G, Meroni P, Cervera R, Stojanovich L, Blank M, Pierangeli SS, Praprotnik S, de Meis E, Parente Seguro L, Ruffatti A, Pengo V, Tincani A, Doria A, Shoenfeld Y. **Ferritin in the antiphospholipid syndrome and its catastrophic variant (cAPS).** *Lupus.* 22(13): 1327-1335. I.F.:2.783

27. Mendoza-Pinto C, García-Carrasco M, Etchegaray-Morales I, Jiménez-Hernández M, Méndez-Martínez S, Jiménez-Hernández C, Briones-Rojas R, Ramos-Alvarez G, Rodríguez-Gallego A, Montiel-Jarquin A, López-Colombo A, Cervera R. **Bone mineral density in systemic lupus erythematosus women one year after rituximab therapy.** *Lupus.* 22(11): 1128-1134. I.F.:2.783

28. Wallace DJ, Navarra S, Petri MA, Gallacher A, Thomas M, Furie R, Levy RA, van Vollenhoven RF, Cooper S, Zhong ZJ, Freimuth W, Cervera R, for the BLISS-52 and -76 and LBSL02 Study Groups. **Safety profile of belimumab: pooled data from placebo-controlled phase 2 and 3 studies in patients with systemic lupus erythematosus.** *Lupus.* 22(2): 144-154. I.F.:2.783

29. Rey A, Molins B, Llorenç V, Pelegrín L, Mesquida M, Adán A. **Cytokine profiling reveals decreased serum levels of CCL2 in active ocular toxoplasmosis.** *Brit J Ophthalmol.* 97(10):1338-42. I.F.:2.725

30. Belenguer-Prieto R, Morales-Espinoza EM, Martín-González RM, Brito-Zerón P, Pastor-Oliver JF, Kostov B, Buss D, Gómez-Gálvez C, Salazar-Cifre A, Sisó-Almirall A, Ramos-Casals M. **Specificity and sensitivity of objective tests to detect possible malingering in fibromyalgia: a case-control study in 211 Spanish patients.** *Clin Exp Rheumatol.* 31(6): 86-93. I.F.:2.655

31. Berman H, Ugarte-Gil MF, Espinosa G, Tàssies D, Monteagudo J, Reverter JC, Cervera R. **Can inherited thrombophilia modulate the clinical phenotype of patients with antiphospholipid syndrome?** *Clin Exp Rheumatol.* 31(6): 926-932. I.F.:2.655

32. Brito-Zerón P, Akasbi M, Bosch X, Bové A, Pérez-De-Lis M, Diaz-Lagares C, Retamozo S, Gandía M, Pérez-Alvarez R, Soto-Cárdenas MJ, Sisó A, Valls-Solé J, Graus F, Ramos-Casals M. **Classification and characterisation of peripheral neuropathies in 102 patients with primary Sjögren's syndrome.** *Clin Exp Rheumatol.* 31(1): 103-110. I.F.:2.655

33. Serrano A, Carmona FD, Castañeda S, Miranda-Filloy JA, Morado IC, Gomez-Vaquero C, Solans R, Sopeña B, Blanco R, Unzurrunzaga A, Ortego-Centeno N, Marí-Alfonso B, Hidalgo-Conde A, Hernández-Rodríguez J, Cid MC, Martín J, Gonzalez-Gay MA. **A case-control study suggests that the CCR6 locus is not involved in the susceptibility to giant cell arteritis.** *Clin Exp Rheumatol.* 31(1): S5-8. I.F.:2.655

34. Cénit MC, Márquez A, Cordero-Coma M, Fonollosa A, Adán A, Martínez-Berriotxoa A, Llorenç V, Díaz Valle D, Blanco R, Cañal J, Díaz-Llopis M, García Serrano JL, de Ramón E, del Rio MJ, Begoña Gorroño-Echebarría M, Martín-Villa JM, Ortego-Centeno N, Martín J. **Evaluation of the IL2/IL21, IL2RA and IL2RB genetic variants influence on the endogenous non-anterior uveitis genetic predisposition.** *BMC Med Genet.* 14:52. I.F.:2.536

35. Llorenç V, González-Martin J, Keller J, Rey A, Pelegrín L, Mesquida M, Adán A. **Indirect supportive evidence for diagnosis of tuberculosis-related uveitis: from the tuberculin skin test to the new interferon gamma release assays.** *Acta Ophthalmol.* 91(2):e99-e107. I.F.:2.345

36. Cénit MC, Ortego-Centeno N, Raya E, Callejas JL, García-Hernandez FJ, Castillo-Palma MJ, Fernandez-Sueiro JL, Magro C, Solans R, Castañeda S, Camps M, Hidalgo A, Espinosa G, González-Gay MA, González-Escribano MF, Martín J. **Influence of the STAT3 genetic variants in the susceptibility to psoriatic arthritis and Behcet's disease.** *Hum Immunol.* 74(2): 230-233. I.F.:2.298

37. Millá E, Mañé B, Duch S, Hernan I, Borràs E, Planas E, Dias Mde S, Carballo M, Gamundi MJ; Spanish Multicenter Glaucoma Group-Estudio Multicéntrico Español de Investigación Genética del Glaucoma, EMEIGG. **Survey of familial glaucoma shows a high incidence of cytochrome P450, family 1, subfamily B, polypeptide 1 (CYP1B1) mutations in non-consanguineous congenital forms in a Spanish population.** *Mol Vis.* 19:1707-22. I.F. 1.987

38. Adán A, Mesquida M, Llorenç V, Espinosa G, Molins B, Hernández MV, Pelegrín L. **Tocilizumab treatment for refractory uveitis-related cystoid macular edema.** Graef Arch Clin Exp Ophthalmol. 251(11): 2627-2632. I.F.:1.932

39. Alvarez G, Rey A, Sanchez-Dalmau FB, Muñoz E, Ríos J, Adán A. **Optical coherence tomography findings in spinocerebellar ataxia-3.** *Eye.* 27(12):1376-81. I.F.:1.818

40. Casaroli-Marano RP, Nieto-Nicolau N, Martínez-Conesa EM. **Progenitor cells for ocular surface regenerative therapy.** *Ophthalmic Res.* 49(3):115-21. I.F. 1.562

41. Rey A, Llorenç V, Pelegrín L, Mesquida M, Molins B, Rios J, Arévalo JF, Adán A. **Clinical pattern of toxoplasmic retinochoroiditis in a Spanish referral center.** *Ophthalmologica.* 229(3):173-8. I.F.:1.412

42. Mesquida M, Llorenç V, Cervera C, Adán A. **[Ocular brucellosis]**. *Med Clin-Barcelona* 16;140(6):284. I.F.:1.399

43. Llorenç V, Molins B, Rey A, Mesquida M, Adán A. **Adalimumab in serpiginous choroiditis.** *Ocul Immunol Inflamm.* 21(3):237-40. I.F.:1.082

Reviews / I.F.: 16.013

1. Cuadrado MJ, Sciascia S, Bosch X, Khamashta MA, Ramos-Casals M. **Is it time for biosimilars in autoimmune diseases?** *Autoimmun Rev.* 12(10): 954-957. I.F.:7.975

2. Retamozo S, Brito-Zerón P, Bosch X, Stone JH, Ramos-Casals M. **Cryoglobulinemic disease.** *Oncology (Williston Park).* 27(11): 1098-1105, 1110-6. I.F.: 3.188

3. Brito-Zerón P, Sisó-Almirall A, Bové A, Kostov BA, Ramos-Casals M. **Primary Sjögren syndrome: an update on current pharmacotherapy options and future directions.** *Expert Opin Pharmacother.* 14(3): 279-289. I.F.:2.860

4. Gómez-Puerta JA, Espinosa G, Cervera R. **Catastrophic antiphospholipid syndrome. Diagnosis and management in pregnancy.** *Clin Lab Med.* 33(2): 391-400. I.F.:1.990

Editorials / I.F.: 8.424

1. Cervera R, Espinosa G. **The anti-phospholipid syndrome: 30 years in the forefront (1983-2013).** *Rheumatology (Oxford).* 52(8): 1347-1348. I.F.:4.212

2. Ramos-Casals M. **The B-lymphocyte stimulator connection in Sjogren's syndrome.** *Rheumatology (Oxford).* 52(2): 223-225. I.F.:4.212

Clinical Guidelines

1. Ramos-Casals M, Ruiz-Irastorza G, Jiménez-Alonso J, Khamashta MA; Comité de Consenso sobre el uso de belimumab, Grupo de Trabajo de Enfermedades Autoinmunes Sistémicas (GEAS) de la Sociedad Española de Medicina Interna (SEMI). **Recomendaciones sobre el uso de rituximab en el lupus eritematoso. Guía de Práctica Clínica GEAS-SEMI.** *Rev Clin Esp.* 213(1): 42-58.

Multicenter / I.F.: 15.496

1. Carmona FD, Cénit MC, Diaz-Gallo LM, Broen JAC, Simeón CP, Carreira PE, Callejas-Rubio JL; Spanish Scleroderma Group (Espinosa G). **New insights on the Xq28 association with systemic sclerosis.** *Ann Rheum Dis.*72(12):2032-8. I.F.:9.111

2. Carmona FD, Martin JE, Beretta L, Simeón CP, Carreira PE, Callejas JL, Fernández-Castro M, Sáez-Comet L, Beltrán E, Camps MT, Egurbide MV; Spanish Scleroderma Group (Espinosa G), Airó P, Scorza R, Lunardi C, Hunzelmann N, Riemekasten G, Witte T, Kreuter A, Distler JH, Madhok R, Shiels P, van Laar JM, Fonseca C, Denton C, Herrick A, Worthington J, Schuerwegh AJ, Vonk MC, Voskuyl AE, Radstake TR, Martín J. **The systemic lupus erythematosus IRF5 risk haplotype is associated with systemic sclerosis.** *PLoS One.* 8(1): e54419. I.F.:3.730

3. Guillevin L, Hunsche E, Denton CP, Krieg T, Schwierin B, Rosenberg D, Matucci-Cerinic M; DUO Registry Group (Espinosa G). **Functional impairment of systemic scleroderma patients with digital ulcerations: results from the DUO Registry.** *Clin Exp Rheumatol.* 31(2): 71-80. I.F.:2.655

GRANTS FOR RESEARCH IN PROGRESS

Adan A. **Prevención, detección precoz y tratamiento de la patología ocular prevalente, degenerativa y crónica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0034/0005. Duration: 01/01/2013-31/12/2016

Adan A. **Estudio de factores predictores para el desarrollo de recurrencias en la toxoplasmosis ocular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00479. Duration: 01/01/2011-30/04/2014

Casaroli R. **Cell Therapy in ocular surface: Role and biosubstitutive applications of human adult mesenchymal stem cells (ADS and BMDS) for corneal regeneration.** Sponsored by: Fundació La Marató de TV3. 120630. Duration: 21/01/2013-20/01/2016

Cervera R. **Grup de recerca de malalties autoimmunes sistèmiques. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR).** 2009_SGR_1421. Duration: 15/09/2009-30/04/2014

Cid M.C. **Mecanismos implicados en la persistencia de la inflamación y la oclusión vascular en la arteritis de células gigantes, biomarcadores de actividad y remodelado vascular.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-30073. Duration: 01/01/2012-31/12/2014

Cid M.C. **Mecanismos implicados y consecuencias clínicas de la persistencia de la inflamación vascular en la arteritis de células gigantes. Identificación de posibles dianas terapéuticas.** Sponsored by: Ministerio de Economía y Competitividad. SAF2008-04328. Duration: 01/01/2009-30/04/2013

Ramos M. **Activación del inmunoreceptor linfocitario CD5 en la patogenia del síndrome de Sjogren: alteraciones**

genéticas y funcionales implicadas en la expresión fenotípica de la enfermedad.
Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01009.
Duration: 01/01/2013-31/12/2015

Ramos M. **Grup de Recerca en la Síndrome de Sjögren (GRESS).**
Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1357.
Duration: 28/09/2009-30/04/2014

Ramos M. **Susceptibilitat immunogenètica i alteracions metabòliques com a factors etiopatogènics de dolor crònic en pacients amb síndrome de Sjörgen en comparació amb pacients atesos a l'àmbit de l'atenció primària (Immunogenetic susceptibility and metabolic alterations as etiopathogenic factors of chronic pain in patients with Sjörgen's syndrome in comparison with primary health care patients).**
Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 071810.
Duration: 13/02/2008-31/12/2013

DOCTORAL THESES

Adán, A. **Factores predictores clínicos y biológicos de severidad en la toxoplasmosis ocular.**
PhD student: Amanda Rey Torrente

Adán, A. **Estudio clínico y experimental de las uveítis relacionadas con la tuberculosis.**
PhD student: Víctor Llorens Bellés

Cervera, R. **Bone mineral density and vertebral fractures in women with systemic lupus erythematosus.**
PhD student: Claudia Mendoza Pinto

1.3 Infectious diseases and AIDS

LOCATION
CELLEX building

FOR FURTHER INFORMATION
www.idibaps.org/aidsresearch

KEYWORDS
1. **HIV**
2. **AIDS**
3. **Endocarditis**
4. **Nosocomial infections**
5. **Immune suppressed patients**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	359.35	91	37	19
2012	294.46	66	39	14
2013	194.72	28	19	7

TEAM INVOLVED IN
RIS

TEAM LEADER
Josep M. Gatell (HCB)
T. 93 227 54 30
jmgatell@clinic.cat

GROUP LEADERS
Josep M. Gatell (HCB)
José M. Miró (HCB)
Asunción Moreno (HCB)
Alex Soriano (HCB)

RESEARCHERS
Mireia Arnedo (IDIBAPS)
Miguel Caballero (HCB)
Felipe García (HCB)
Montserrat Laguno (FCRB)
Josep Mallolas (HCB)
Esteban Martínez (HCB)
José Antonio Martínez (HCB)
José Mensa (HCB)
Montserrat Plana (IDIBAPS)
M. Eloisa Yuste (IDIBAPS)

PRE-DOCTORAL RESEARCHERS:
Hodei Arneras (FCRB)
Carolina Ferreira (IDIBAPS)
Irma Hoyo (UB)
Laura Linares (IDIBAPS)
Christian Manzardo (FCRB)
Gemma Sanclemente (HCB)
Berta Torres (Fundació Clinic)

TECHNICIANS
Carmen Álvarez (FCRB)
Yolanda Armero (FCRB)
Manuel Enric Bargalló (IDIBAPS)
Pilar Callau (FCRB)
Alberto Crespo (IDIBAPS)
Tuixent Escriba (IDIBAPS)
Ana García (FCRB)
Maria Teresa García (FCRB)
Carmen Hurtado (FCRB)
M. José Maleno (FCRB)
Alberto Merino (IDIBAPS)
Laia Miralles (IDIBAPS)
Sara Nieto (IDIBAPS)
Cristina Rovira (FCRB)

NURSING STAFF
Emmanuela Fernandez (FCRB)

ADMINISTRATIVE STAFF
Carmen Mensa (IDIBAPS)
Irene Ruiz (FCRB)

STATISTICIAN
Jose Ignacio Pérez (FCRB)

COLLABORATORS
Valentin Araunde (CAPSE)
Pilar Arrabal (GESCLINIC)
José Luis Blanco (HCB)
Olga Barba (CAPSE)
Luisa Benito Serrano (GESCLINIC)
Dani Cararach (GESCLINIC)
Marta Catalan (CAPSE)
Carlos Cervera (HCB)
Nuria Climent (IDIBAPS)
Nazaret Cobos (IDIBAPS)
Ana del Rio (HCB)
Teresa Gallart (HCB)
Cristina García de la María (FCRB)
Mª Jose Giner (GESCLINIC)
Ana Gonzalez (FCRB)
Zoe Herreras Pérez (CAPSE)
Jordi Hoyo (GESCLINIC)
Joan Joseph (FCRB)
Agathe León (FCRB)
Montserrat Loncà (FCRB)
Laura Maroto (FCRB)
María Martínez (IDIBAPS)
Ignacio Menacho Pascual (GESCLINIC)
Eloisa Molés (GESCLINIC)
Mª Luisa Moro (GESCLINIC)
Mª Angeles Moreno Ubiedo (CAPSE)
Ana Picas (GESCLINIC)
Víctor Sánchez-Merino (FCRB)
Sonsoles Sánchez-Palomino (FCRB)
Narcís Saubí (IDIBAPS)
Ethel Sequeira Aymar (CAPSE)
Laura Zamora (FCRB)

VISITING SCIENTISTS
Gilles Mirambeau (UB)

STRATEGIC OBJECTIVES

1. In the AIDS field:

- Immunotherapy of the disease and natural and acquired defense mechanisms, including the development of therapeutic and preventive vaccines.
- Efficacy and resistance and tolerance mechanisms of new antiretrovirals.
- Immunopathogenesis, treatment response and resistance mechanisms of certain opportunistic infections, including tuberculosis, pneumocystis carinii pneumonia (PCP) and toxoplasmosis.
- Non-AIDS defining complications related with age and residual viral replication, inflammation and immuneactivation

2. In the general infections field:

- Prevention and treatment of endocarditis due to multiresistant microrganisms, including animal models.
- Infection in solid-organ transplant recipients.
- Interactions between nosocomial infections and antibiotic use.

MAIN LINES OF RESEARCH

1. In the AIDS field:

- The most important line focuses on the peripheral (blood) and central response (lymphatic tissue and cerebrospinal fluid) to different antiretroviral therapies when administered in very early evolutive stages (CD4 > 500 mm3). We have developed ultrasensitive techniques for the determination of viral load in plasma and tissues, as well as techniques for the determination of genotypic resistance and for immunophenotyping and the evaluation of CD4+ lymphocyte proliferation in response to antigens of the HIV virus. Techniques for the determination of drug levels have also been developed in collaboration with the clinical pharmacology group. Having ruled out the possibility of eradicating the HIV virus, the working hypothesis is to see whether it is possible to almost completely suppress HIV replication over the long term, recover the host immune system and quantify the degree of such recovery. The interruption of treatment leads to a rapid disease rebound effect, which could be avoided partially or totally (functional recovery).
- The mechanism by which the virus is able to escape the cytotoxic immune response subject to study subject to study, and could correspond to the selection of quasispecies different from the reservoirs(immunological resistance). For this reason we have started a research line aimed at developing techniques for stimulating the immune system, with a view to associating them with antiretroviral therapy. Cyclic interruption of them treatment and therapeutic vaccines can induce recovery of the specific immune response to HIV antigens, associated with a spontaneous decrease in viral load, which is correlated to the degree of proliferative and specific cytotoxic response against HIV-1 in a small percentage of patients.
- We have also developed an immunotherapeutic technique based on the dministration of autologous dendritic cells stimulated ex vivo with the virus of the patient. The first three Phase I clinical trials have already been finished and published. We are also developing different immunogens which may be potential candidates for therapeutic or preventive vaccines in the setting of an FP7 program.

2. In the general infections field:

- Clinical and experimental endocarditis, including endocarditis in illegal drug abusers (Dr. J.M. Miró).
- Infections in transplant recipients. Microbiological diagnosis and prognostic markers (Dr. A. Moreno).
- Predictive factors and markers of treatment response in nosocomial infections (Dr. A. Soriano).
- Response to treatment, resistance and transmission of tuberculosis.
- Prognostic factors of communityacquired and nosocomial respiratory infections in both immunocompetent and immune depressed individuals.
- The genetic fundaments of host susceptibility and the biochemical, molecular and replicative capacity bases of the resistant strains.

RESEARCH GROUP
ENDOCARDITIS. CARDIOVASCULAR INFECTIONS. EXPERIMENTAL MODEL

GROUP LEADER
Josep Maria Miro (HCB)

This group studies the epidemiological, clinical, diagnostic, preventive and therapeutic aspects of infectious endocarditis. This is done based on studies of local, national or international cohorts (ICE) that have revealed an increase in endocarditis produced by methicillin-sensitive and -resistant Staphylococcus aureus (MSSA and MRSA, respectively). Studies using the experimental model of endocarditis due to MRSA and glycopeptide intermediate-resistant Staphylococcus aureus (GISA) have evaluated the activity of new antibiotic combinations (phosphomycin and imipenem), or new antibiotics such as daptomycin and telavancin.

RESEARCH GROUP
INFECTIONS IN SOLID-ORGAN TRANSPLANT RECIPIENTS

GROUP LEADER
Asuncion Moreno (HCB)

In the last years, this group has studied the clinical and evolutive characteristics of bacteremias in patients subjected to different solid organ transplants (kidney, liver, heart and renal-pancreatic). We have shown that mannose binding to lectin polymorphisms (MBL) condition an increase in the prevalence of cytomegalovirus (CMV) disease, and have analyzed the mortality risk factors of pneumonia in transplant patients.Studies have been made of the prevalence of other viruses of the herpes group (HHV-6 and -7) in the transplant population, as well as their pathogenic role in the post-transplantation period. These studies have been made jointly with I investigators specialized in Microbiology and Immunology, and with the different Transplantation Units (Institutes of Digestive, Renal and Thoracic Diseases). Its components are members of the REIPI (Spanish Research Network in Infectious Disease), and participate actively in multicenter projects financed by the FIS.

RESEARCH GROUP
AIDS AND HIV INFECTION

GROUP LEADER
Josep Maria Gatell (HCB)

This group studies the clinical, diagnostic, therapeutic and preventive aspects of HIV infection. The scientific contribution of this line of research is very competitive and is internationally renowned. This group of investigators focuses on exploration of the potential for eradicating HIV infection and on reconstruction of the immune system, including the development of preventive and therapeutic vaccines. Since its start in 2002, Dr. Gatell has coordinated the Spanish network of research groups in AIDS (RIS), funded by the FIS, and since 2007 has coordinated the HIVACAT project on research therapeutic and preventive vaccines against HIV infection.

EMERGENT GROUP
NOSOCOMIAL INFECTION STUDY GROUP

GROUP LEADER
Alex Soriano (HCB)

This group studies the clinical, diagnostic, therapeutic and preventive aspects of nosocomial (in-hospital) infections. The scientific contribution is particularly notorious in the treatment and management of bacteremia, infections in Intensive Care Units, and infections related to orthopedic implants.

PUBLICATIONS

Originals / I.F.: 194.724

1. SPARTAC Trial Investigators, Fidler S, Porter K, Ewings F, Frater J, Ramjee G, Cooper D, Rees H, Fisher M, Schechter M, Kaleebu P, Tambussi G, Kinloch S, Miro JM, Kelleher A, McClure M, Kaye S, Gabriel M, Phillips R, Weber J, Babiker A. **Short-course antiretroviral therapy in primary HIV infection.** *New Engl J Med.* 368(3):207-217 I.F.: 51.658

2. Eron JJ, Cooper DA, Steigbigel RT, Clotet B, Gatell JM, Kumar PN, Rockstroh JK, Schechter M, Markowitz M, Yeni P, Loutfy MR, Lazzarin A, Lennox JL, Strohmaier KM, Wan H, Barnard RJ, Nguyen BY, Teppler H; BENCHMRK Study Teams. **Efficacy and safety of raltegravir for treatment of HIV for 5 years in the BENCHMRK studies: final results of two randomised, placebo-controlled trials.** *Lancet Infect Dis.* 13(7):587-596 I.F.:19.966

3. García F, Climent N, Guardo AC, Gil C, León A, Autran B, Lifson JD, Martínez-Picado J, Dalmau J, Clotet B, Gatell JM, Plana M, Gallart T; DCV2/MANON07-ORVACS Study Group. **A dendritic cell-**

based vaccine elicits T cell responses associated with control of HIV-1 replication. *Sci Transl Med.* 5(166):166ra2 I.F.: 10.757

4. Mocroft A, Furrer HJ, Miro JM, Reiss P, Mussini C, Kirk O, Abgrall S, Ayayi S, Bartmeyer B, Braun D, Castagna A, d'Arminio Monforte A, Gazzard B, Gutierrez F, Hurtado I, Jansen K, Meyer L, Muñoz P, Obel N, Soler-Palacin P, Papadopoulos A, Raffi F, Ramos JT, Rockstroh JK, Salmon D, Torti C, Warszawski J, de Wit S, Zangerle R, Fabre-Colin C, Kjaer J, Chene G, Grarup J, Lundgren JD; Opportunistic Infections Working Group on behalf of the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study in EuroCOORD. **The incidence of AIDS-defining illnesses at a current CD4 count ≥ 200 cells/μL in the post combination antiretroviral therapy era.** *Clin Infect Dis.* 57(7):1038-1047 I.F.:9.374

5. Rotger M, Glass TR, Junier T, Lundgren J, Neaton JD, Poloni ES, van 't Wout AB, Lubomirov R, Colombo S, Martinez R, Rauch A, Günthard HF, Neuhaus J, Wentworth D, van Manen D, Gras LA, Schuitemaker H, Albini L, Torti C, Jacobson LP, Li X, Kingsley LA, Carli F, Guaraldi G, Ford ES, Sereti I, Hadigan C, Martinez E, Arnedo M, Egaña-Gorroño L, Gatell JM, Law M, Bendall C, Petoumenos K, Rockstroh J, Wasmuth JC, Kabamba K, Delforge M, De Wit S, Berger F, Mauss S, de Paz Sierra M, Losso M, Belloso WH, Leyes M, Campins A, Mondi A, De Luca A, Bernardino I, Barriuso-Iglesias M, Torrecilla-Rodriguez A, Gonzalez-Garcia J, Arribas JR, Fanti I, Gel S, Puig J, Negredo E, Gutierrez M, Domingo P, Fischer J, Fätkenheuer G, Alonso-Villaverde C, Macken A, Woo J, McGinty T, Mallon P, Mangili A, Skinner S, Wanke CA, Reiss P, Weber R, Bucher HC, Fellay J, Telenti A, Tarr PE; MAGNIFICENT Consortium; INSIGHT; Swiss HIV Cohort Study. **Contribution of genetic background, traditional risk factors, and HIV-related factors to coronary artery disease events in HIV-positive persons.** *Clin Infect Dis.* 57(1):112-121 I.F.: 9.374

6. McLaren PJ, Coulonges C, Ripke S, van den Berg L, Buchbinder S, Carrington M, Cossarizza A, Dalmau J, Deeks SG, Delaneau O, De Luca A, Goedert JJ, Haas D, Herbeck JT, Kathiresan S, Kirk GD, Lambotte O, Luo M, Mallal S, van Manen D, Martinez-Picado J, Meyer L, Miro JM, Mullins JI, Obel N, O'Brien SJ, Pereyra F, Plummer FA, Poli G, Qi Y, Rucart P, Sandhu MS, Shea PR, Schuitemaker H, Theodorou I, Vannberg F, Veldink J, Walker BD, Weintrob A, Winkler CA, Wolinsky S, Telenti A, Goldstein DB, de Bakker PI, Zagury JF, Fellay J. **Association study of common genetic variants and HIV-1 acquisition in 6,300 infected cases and 7,200 controls.** *PLoS Pathog.* 9(7):e1003515 I.F.:8.136

7. Letang E, Lewis JJ, Bower M, Mosam A, Borok M, Campbell TB, Naniche D, Newsom-Davis T, Shaik F, Fiorillo S, Miro JM, Schellenberg D, Easterbrook PJ. **Immune reconstitution inflammatory syndrome associated with Kaposi sarcoma: higher incidence and mortality in Africa than in the UK.** *AIDS.* 27(10):1603-1613 I.F.: 6.407

8. Podlekareva DN, Panteleev AM, Grint D, Post FA, Miro JM, Bruyand M, Furrer H, Obel N, Girardi E, Vasilenko A, Losso MH, Arenas-Pinto A, Caylá J, Rakhmanova A, Zeltina I, Werlinrud AM, Lundgren JD, Mocroft A, Kirk O; HIV/TB study group. **Short- and long-term mortality and causes of death in HIV/tuberculosis patients in Europe.** *Eur Respir J.* 43(1):166-177 I.F.:6.355

9. Bernardino JI, Pulido F, Martinez E, Arrizabalaga J, Domingo P, Portilla J, Ocampo A, Muñoz J, Torres R, Arribas JR; GESIDA-6008-KRETA Study Group. **Switching to lopinavir/ritonavir with or without abacavir/lamivudine in lipoatrophic patients treated with zidovudine/abacavir/lamivudine.** J *Antimicrob Chemoth.* 68(6): 1373-1381 I.F.:5.338

10. Ferreira CB, Merino-Mansilla A, Llano A, Pérez I, Crespo I, Llinas L, Garcia F, Gatell JM, Yuste E, Sanchez-Merino V. **Evolution of broadly cross-reactive HIV-1-neutralizing activity: therapy-associated decline, positive association with detectable viremia, and partial restoration of B-cell subpopulations**. *J Virol.* 87(22):12227-12236 I.F.:5.076

11. Massanella M, Esteve A, Buzón MJ, Llibre JM, Puertas MC, Gatell JM, Domingo P, Stevenson M, Clotet B, Martinez-Picado J, Blanco J; IntegRal **Collaborative Group. Dynamics of CD8 T-cell activation after discontinuation of HIV treatment intensification.** *JAIDS-J Acq Imm Def.* 63(2):152-160 I.F.: 4.653

12. Chirouze C, Athan E, Alla F, Chu VH, Ralph Corey G, Selton-Suty C, Erpelding ML, Miro JM, Olaison L, Hoen B; International Collaboration on Endocarditis Study Group. **Enterococcal endocarditis in the beginning of the 21st century: analysis from the International Collaboration on Endocarditis-Prospective Cohort Study.** *Clin Microbiol Infec.* 19(12):1140-1147 I.F.:4.578

13. Manzardo C, Esteve A, Ortega N, Podzamczer D, Murillas J, Segura F, Force L, Tural C, Vilaró J, Masabeu A, Garcia I, Guadarrama M, Ferrer E, Riera M, Navarro G, Clotet B, Gatell JM, Casabona J, Miró JM; PISCIS Investigators. **Optimal timing for initiation of highly active antiretroviral therapy in treatment-naïve human immunodeficiency virus-1-infected individuals presenting with AIDS-defining diseases: the experience of the PISCIS Cohort.** *Clin Microbiol Infec.* 19(7):646-653 I.F.: 4.578

14. Carugati M, Bayer AS, Miró JM, Park LP, Guimarães AC, Skoutelis A, Fortes CQ, Durante-Mangoni E, Hannan MM, Nacinovich F, Fernández-Hidalgo N, Grossi P, Tan RS, Holland T, Fowler VG Jr, Corey RG, Chu VH; International Collaboration on Endocarditis. **High-dose daptomycin therapy for left-sided infective endocarditis: a prospective study from the international collaboration**

on endocarditis. *Antimicrob Agents Ch.* 57(12):6213-6222 I.F.:4.565

15. García-de-la-Mària C, Pericas JM, Del Río A, Castañeda X, Vila-Farrés X, Armero Y, Espinal PA, Cervera C, Soy D, Falces C, Ninot S, Almela M, Mestres CA, Gatell JM, Vila J, Moreno A, Marco F, Miró JM; Hospital Clinic Experimental Endocarditis Study Group. **Early in vitro and in vivo development of high-level daptomycin resistance is common in mitis group Streptococci after exposure to daptomycin.** *Antimicrob Agents Ch.* 57(5):2319-2325 I.F.:4.565

16. Tattevin P, Saleh-Mghir A, Davido B, Ghout I, Massias L, Garcia de la Maria C, Miró JM, Perronne C, Laurent F, Crémieux AC. **Comparison of six generic vancomycin products for treatment of methicillin-resistant Staphylococcus aureus experimental endocarditis in rabbits.** *Antimicrob Agents Ch.* 57(3):1157-1162 I.F.:4.565

17. Gould IM, Miró JM, Rybak MJ. **Daptomycin: the role of high-dose and combination therapy for Gram-positive infections.** *Int J Antimicrob Ag.* 42(3):202-210 I.F.: 4.415

18. Guardo AC, Alvarez-Fernández C, Arberas H, García-Pérez J, García F, Bargalló ME, Maleno MJ, Gatell JM, Mothe B, Alcami J, Sánchez-Palomino S, Plana M. **Use of RT-defective HIV virions: new tool to evaluate specific response in chronic asymptomatic HIV-infected individuals.** *PLoS One.* 8(3):e58927 (I.F.: 3.730)

19. Millet JP, Shaw E, Orcau A, Casals M, Miró JM, Caylà JA; Barcelona Tuberculosis Recurrence Working Group. **Tuberculosis recurrence after completion treatment in a European city: reinfection or relapse?** *PLoS One.* 8(6):e64898 I.F.:3.730

20. Regueiro A, Falces C, Cervera C, Del Rio A, Paré JC, Mestres CA, Castañeda X, Pericàs JM, Azqueta M, Marco F, Ninot S, Almela M, Moreno A, Miró JM; Hospital Clínic Endocarditis Study Group. **Risk factors for pericardial effusion in native valve infective endocarditis and its influence on outcome.** *Am J Cardiol.* 112(10):1646-1651 .F.:3.209

21. Menacho I, Sequeira E, Muns M, Barba O, Leal L, Clusa T, Fernandez E, Moreno L, Raben D, Lundgren J, Gatell JM, Garcia F, Cayuelas L, Aragunde V, Vergara M, Catalan M, Moreno MA, Hormigo G, Siso A, Herreras Z, Sebastian L, Benito L, Picas A, Hoyo J, Giner MJ, Cararach D, Moles E, Moro ML, Arrabal P, Roca D, Prego S, Ferrer X, Egido A, Ventosa C, Garcia S, Muñoz S, Massana A, Sole J, Curiel M,Heras F, Leon **A. Comparison of two HIV testing strategies in primary caremcentres: indicator-condition-guided testing vs. testing of those with non-indicator conditions.** *HIV Med.* 14 Suppl 3:33-37 I.F.:3.155

22. Monge S, Alejos B, Dronda F, Del Romero J, Iribarren JA, Pulido F, Rubio R, Miró JM, Gutierrez F, Del Amo J; CoRIS. **Inequalities in HIV disease management and progression in migrants from Latin America and sub-Saharan Africa living in Spain.** *HIV Med.* 14(5):273-283 I.F.:3.155

23. Efsen AM, Panteleev AM, Grint D, Podlekareva DN, Vassilenko A, Rakhmanova A, Zeltina I, Losso MH, Miller RF, Girardi E, Caylá J, Post FA, Miro JM, Bruyand M, Furrer H, Obel N, Lundgren JD, Mocroft A, Kirk O; HIV/TB Study Group. TB **Meningitis in HIV-Positive Patients in Europe and Argentina: Clinical Outcome andFactors Associated with Mortality.** *Biomed Res Int.* 22013:373601 I.F. : 2.880

24. Lucero C, Torres B, León A, Calvo M, Leal L, Pérez I, Plana M, Arnedo M, Mallolas J, Gatell JM, García F. **Rate and predictors of non-AIDS events in a cohort of HIV-infected patients with a CD4 T cell count above 500 cells/mm³.** *AIDS Res Hum Retrov.*29(8):1161-7 I.F.: 2.705

25. Podlekareva DN, Grint D, Post FA, Mocroft A, Panteleev AM, Miller RF, Miro JM, Bruyand M, Furrer H, Riekstina V, Girardi E, Losso MH, Caylá JA, Malashenkov EA, Obel N, Skrahina AM, Lundgren JD, Kirk O; HIV-TB Study Group. **Health care index score and risk of death following tuberculosis diagnosis in HIV-positive patients.** *Int J Tuberc Lung* D. 17(2):198-206 I.F.:2.610

26. Martínez-Rebollar M, Muñoz A, Pérez I, Hidalgo S, Brunet M, Laguno M, González A, Calvo M, Loncà M, Blanco JL, Martínez E, Gatell JM, Mallolas J. **Pharmacokinetic study of dual therapy with raltegravir 400 mg twice daily and Darunavir/ Ritonavir 800/100 mg once daily in HIV-1-infected patients.** *Ther Drug Monit.* 35(4):552-556 I.F.:2.234

27. Blasco AJ, Llibre JM, Arribas JR, Boix V, Clotet B, Domingo P,González-García J, Knobel H, López JC, Lozano F, Miró JM, Podzamczer D,Santamaría JM, Tuset M, Zamora L, Lázaro P, Gatell JM; en representación de GESIDA. **Analysis of costs and cost-effectiveness of preferred GESIDA/NationalAIDS Plan regimens for initial antiretroviral therapy in human immunodeficiency virus infected adult patients in 2013.** *Enferm Infec Micr Cl.* 31(9):568-578 I.F.:1.478

28. Rivero A, Pulido F, Caylá J, Iribarren JA, Miró JM, Moreno S, Pérez-Camacho I; Grupo de Estudio de Sida (GESIDA). **The Spanish AIDS study group and Spanish national AIDS plan (GESIDA/Secretaría del plan nacional sobre el Sida) recommendations for the treatment of tuberculosis in HIV-infected individuals (Updated January 2013).** *Enferm Infec Micr* Cl. 31(10):672-684 I.F.:1.478

Reviews / I.F.: 5.848

1. Gupta RK, Wainberg MA, Brun-Vezinet F, Gatell JM, Albert J, Sönnerborg A, Nachega JB. **Oral antiretroviral drugs as public health tools for HIV prevention: global implications for adherence, drug resistance, and the success of HIV treatment programs.** *J Infect Dis.* 207 Suppl 2:S101-106 I.F.: 5.848

Editorials / I.F.: 18.406

1. Falces C, Miró JM. **Prevention of Infective Endocarditis From the Dentist's Perspective. Response.** *Rev Esp Cardiol.* 66(5):417 I.F.: 3.204

2. Miro JM, Pericas JM, del Rio A; Hospital Clinic Endocarditis Study Group. **A new era for treating Enterococcus faecalis endocarditis: ampicillin plus short-course gentamicin or ampicillin plus ceftriaxone: that is the question!** *Circulation.* 127(17):1763-6 I.F.: 15.202

Clinical Guidelines / I.F.: 1.478

1. Blasco AJ, Llibre JM, Arribas JR, Boix V, Clotet B, Domingo P,González-García J, Knobel H, López JC, Lozano F, Miró JM, Podzamczer D,Santamaría JM, Tuset M, Zamora L, Lázaro P, Gatell JM; en representación de GESIDA. **Analysis of costs and cost-effectiveness of preferred GESIDA/NationalAIDS Plan regimens for initial antiretroviral therapy in human immunodeficiency virus infected adult patients in 2013.** *Enferm Infec Micr Cl.* 31(9):568-578 I.F.:1.478

GRANTS FOR RESEARCH IN PROGRESS

Arnedo M. **Implicación de los miRNA y el metabolismo del colesterol en la infección por el VIH y el riesgo cardiovascular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00866.
Duration: 01/01/2013-31/12/2015

Castro P. **Caracterización de la disfunción endotelial en los sindromes septicos e influencia del defibrotide.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00832.
Duration: 01/01/2013-31/12/2015

Garcia F. **Therapeutic TriMix / mRNA based Vaccine in Chronic HIV-1 Infected Patients Receiving Antiretroviral Therapy.** Sponsored by: European Commission. 602570.
Duration: 01/12/2013-30/11/2017

Garcia F. **Relevancia de las células dendríticas en los mecanismos de protección en no infectados y en el control inmunológico de la replicación viral en infectados por VIH.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-39075.
Duration: 01/01/2013-31/12/2015

Garcia F. **Design of multifunctional nanoparticles targeting TLR or Nod receptors for dendritic cell immune therapy.** Sponsored by: European Commission. ERA-NET_NANOMED10_01.
Duration: 01/01/2011-31/12/2013

Garcia F. **Design of multifunctional nanoparticles targeting TLR or Nod receptors for dendritic cell immune therapy.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/02984(NANO-MED).
Duration: 01/01/2011-31/12/2013

Gatell J.M. **Red de Sida.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0017/0001.
Duration: 01/01/2013-31/12/2016

Gatell J.M. **Targeting the HIV-1 Nucleocapsid Protein to fight Antiretroviral Drug Resistance.** Sponsored by: European Commission. 601969-2.
Duration: 01/09/2013-31/08/2016

Gatell J.M. **European Network of HIV/AIDS Cohort Studies to Coordinate at European and International level Clinical Research on HIV/AID.** Sponsored by: European Commission. 260694.
Duration: 01/01/2011-31/12/2015

Gatell J.M. **Papel de las células dendríticas en la protección y control de la infección por el VIH. Avanzando hacia la remisión sin tratamiento antirretroviral o la curación funcional.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01247.
Duration: 01/01/2013-31/12/2015

Gatell J.M. **Programa HIVACAT para el desarrollo de vacunas preventivas y terapéuticas frente al VIH.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2012-0325-010000.
Duration: 01/01/2013-31/12/2015

Gatell J.M. **New Generation of Anti-RetroVirals by targeting HIV-cellular cofactors interactions.** Sponsored by: European Commission. 305137.
Duration: 01/10/2012-30/09/2015

Gatell J.M. **Grup de recerca VIH/sida. Hospital Clinic. Barcelona.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1159.
Duration: 23/09/2009-30/04/2014

Gatell J.M. **Red de SIDA.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0006/0000.
Duration: 01/01/2007-31/12/2013

Gatell J.M. Gatell Artigas, Josep M. - **RETICS A 2006.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0006.
Duration: 01/01/2007-31/12/2013

Gatell J.M. **La Nucleocapside du VIH-1: Structure, maturation et architecture.** Sponsored by: AGENCE NATIONALE DE RECHERCHES SUR LE SIDA ET LES HÉPATITES VIRALE. SF/CRM/Nº1458.
Duration: 01/12/2011-31/12/2013

Gatell J.M. **NoE - European AIDS Treatment Network.** Sponsored by: European Commission. LSHP-CT-2006-037570.
Duration: 01/02/2007-31/07/2013

Laguno M. **Hipertensión Portal Idiopática en el paciente infectado por el VIH. Prevalencia, curso clínico, identificación de métodos diagnósticos no invasivos y factores pronóstico.** Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE) 36-0963-10.
Duration: 16/02/2011-15/06/2014

Martinez E. **Seguridad virológica**

e inmunológica de una estratégia de reducción de dosis con la pauta antirretroviral efavirenz/tenofovir/ emtricitabina. Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01217. Duration: 01/01/2013-31/12/2015

Martinez J.A. **Evaluación farmacocinética y farmacodinámica del tratamiento inicial con meropenem, ceftazidima, piperaciclina-tazobactam y colistina en pacientes críticos con sepsis.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00479. Duration: 01/01/2012-31/12/2014

Miro J.M. **Supervivencia de los pacientes con infección por el VIH en terapia renal sustitutiva o trasplante renal en España.** Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE) 24-0858-09. Duration: 04/01/2010-03/01/2015

Miro J.M. **Estudio de la eficacia de la daptomicina asociada a otros antibióticos en el tratamiento de la endocarditis experimental por Staphylococcus aureus resistentes o no a mecilina (SARM/ SASM) y S. epidermidis resistentes a meticilina (SERM) y a vancomicina (VR).** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01131. Duration: 01/01/2012-31/12/2014

Miro J.M. **Trasplante hepático en pacientes coinfectados por el VIH y VHC: Historia natural de la recurrencia del VHC y factores pronosticos de supervivencia.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-150. Duration: 01/01/2012-31/12/2014

Miro J.M. **A Phase III multi-center, randomized, open-label, comparative study to assess the efficacy of a treatment algorithm to reduce the use of vancomycin in patients with intravenous catheter-associated bloodstream infections (BSI) due to Staphylococci.** Sponsored by: National Institute of Health (NIH). NIHAI2008025. Duration: 23/05/2011-07/08/2014

Moreno A. **Impacto de las variaciones genéticas de los TLR 2, 4 y 9 en el riesgo de infección por citomegalovirus postrasplante y su utilidad en la prevención.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01743. Duration: 01/01/2013-31/12/2015

Moreno A. **Evaluar la eficacia y la seguridad de la cambinación de fosfomicina (F) e imipenem (I) para el tratamiento de la endocarditis (EI) sobre la válvula nativa o protésica por S.aureus resistente a meticilina (MRSA).** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00190. Duration: 01/01/2009-30/06/2014

Moreno A. **Infecciones en el Trasplante de órgano sólido (INFTOS). Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1341.** Duration: 15/09/2009-30/04/2014

Plana M. **Papel de los microRNAs en la regulación de la respuesta inmune antiviral y en el control y / o progresión de la infección por el VIH-1.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00969. Duration: 01/01/2013-31/12/2015

Yuste E. **Diseño, síntesis y estudio anti-HIV-1 de dominios peptídices del GB virus C.** Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE) 36-0735-09. Duration: 09/03/2010-30/11/2013

DOCTORAL THESES

Gatell JM. **Identificación y seguimiento de cohortes de alto riesgo de infección por el virus de la inmunodeficiencia humana para futuros estudios de vacunas preventivas.** PhD student: María Florencia Etcheverry Rufino

1.4 Immune receptors of the innate and adaptive system

LOCATION
CEK building

KEYWORDS
1. **Innate and adaptive immune response**
2. **Immune receptor-ligand interactions**
3. **Immunomodulation and immunotherapy**
4. **Host-pathogen interaction**
5. **Immunevasion**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	92.77	16	11	-
2012	44.53	7	5	2
2013	44.86	6	5	-

TEAM INVOLVED IN
REIPI

AWARDS
Program for Promotion of the Academic Entrepreneurship
Institution: Red Emprendia, Santander Universitades and Spanish Ministerio de Educación, Cultura y Deportes
Awardee: Lozano F

TEAM LEADER
Francisco Lozano (HCB/UB)
T. 93 227 42 17
flozano@clinic.cat

RESEARCHERS
Ana Angulo (IDIBAPS)
Pablo Engel (UB)
Carles Serra (HCB/UB)

POST-DOCTORAL RESEARCHERS
Lyzette Bonet (FCRB)
Esther Carrasco Miguel (FCRB)
Esther Carreras Margalef (IDIBAPS)
Domènec Farré Marimon (IDIBAPS)
Vanesa G. Martínez (FCRB)
Mario Martínez Florensa (AGAUR)
Xavier Romero (IDIBAPS)
Jose de Salort (UB)

PRE-DOCTORAL RESEARCHERS
Marta Consuegra (AGAUR)
Marta Cuenca (IDIBAPS)
M. Carmen Diaz-Ramos (IDIBAPS)
Cristina Escoda (FCRB)
Pablo Martínez Vicente (MEC)
Marc Orta (Fundació Clínic)
Natalia Pérez Carmona (UB)
Inês Simoês (FCyT)
Ángela Zarama (IDIBAPS)

TECHNICIANS
Noelia Armiger Borràs (IDIBAPS)
Adriana Lázaro (FCRB)

STRATEGIC OBJECTIVES

1. Genetic and molecular characterization of immune receptors from both the innate and adaptive system.
2. Functional characterization of the ligand-receptor interactions responsible for intercellular communication between components from the innate and adaptive immune system.
3. Molecular characterization of pathogen-host interactions.
4. Characterization of cytomegalovirus (CMV) biology and pathogenesis.

MAIN LINES OF RESEARCH

1. Study of the structure and function of the SLAM (Signaling Lymphocytic Activation

Molecule) and SAP (SLAM-Associated Protein) leukocyte molecule families.
2. Study of the molecules that intervene in leukocyte adhesion and inflammation.
3. Immunogenetics of receptors and molecules implicated in the regulation of innate and adaptive immune responses.
4. Study of the role of the lymphoid scavenger-like receptors CD5 and CD6 as immunomodulators in infection, autoimmunity and cancer.
5. Molecular and functional characterization of nonlymphoid members of the superfamily of receptors with extracellular domains rich in cysteine (SRCR, Scavenger Receptor Cysteine-Rich) residues.
6. Characterization of the mechanisms that regulate CMV gene expression and identification of functions encoded by CMV.
7. Study of CMV modulation of the immune response and viral immune evasion strategies.

PUBLICATIONS

Originals / I.F.: 44.859

1. Blanc M, Hsieh WY, Robertson KA, Kropp KA, Forster T, Shui G, Lacaze P, Watterson S, Griffiths SJ, Spann NJ, Meljon A, Talbot S , Krishnan K, Covey DF, Wenk MR, Craigon M, Ruzsics Z, Haas J, Angulo A, Griffiths WJ, Glass CK, Wang Y, Ghazal P. **The transcription factor STAT-1 couples macrophage synthesis of 25-hydroxycholesterol to the interferon antiviral response.** *Immunity.* 38: 106-118 I.F. 19.795

2. Garcia-Recio S, Fuster G, Fernandez-Nogueira P, Pastor-Arroyo EM, Yeon Park S, Mayordomo C, Ametller E, Mancino M, Gonzalez-Farre X, Russnes H, Engel P, Costamagna D, Fernandez PL, Gascon P, Almendro V. **Substance P autocrine signaling contributes to persistent HER2 activation that drives malignant progression and drug resistance in breast cancer.** *Cancer Res.* 73:6424-6434. I.F. 8.650

3. Sintes J, Cuenca M, Romero X, Bastos R, Terhorst C, Angulo A, Engel P. **LY9 (CD229), a SLAM family receptor, negatively regulates the development of thymic innate memory-like CD8+ T and invariant NKT cells.** *J Immunol.* 190(1): 21-26. I.F. 5.520

4. Julià M, Guilabert A, Lozano F, Suárez-Casasús B, Moreno N, Carrascosa JM, Ferándiz C, Pedrosa E, Alsina-Gibert M, Mascaró JM Jr. **The role of Fc gamma polymorphisms in the response to anti-TNF-α therapy in Psoriasis: a pharmacogenetic study.** *J Am Acad Dermatol.* 149 (9): 1033-1039. I.F. 4.906

5. Bonet L, Farnós M, Martínez-Florensa M, Martínez VG, Lozano F. **Identification of Functionally Relevant phoshorylatable Serine Clusters in the Cytoplasmic region of the human CD6 Lymphocyte Surface Receptor.** *FEBS Lett* 587(14):2205-2213. I.F. 3.582

6. Roa NS, Ordoñez-Rueda D, Chávez-Rios JR, Raman C, García-Zepeda EA, Lozano F, Soldevila G. **The carboxy-terminal region of CD5 is required for c-CBL mediated TCR signaling downmodulation in thymocytes.** *Biochem Bioph Res Co.* 432(1):52-59. I.F. 2.406

Reviews / I.F.: 4.970

1. Muntasell A, Vilches C, Angulo A, López-Botet M. **Adaptive reconfiguration of the human NK cell compartment in response to cytomegalovirus: a different perspective of the host-pathogen interaction.** *Eur J Immunol.* 43(5): 1133-1141 I.F. 4.970

GRANTS FOR RESEARCH IN PROGRESS

Lozano F. **Red Española de Investigación en Patología Infecciosa.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0015/0018. Duration: 01/01/2013-31/12/2016

Lozano F. **Implicaciones funcionales y terapéuticas del reconocimiento de ligandos exógenos y endógenos por parte de receptores linfocitarios tipo Scavenger.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-19717. Duration: 01/01/2011-30/09/2014

Angulo A. **Identificación y caracterización de genes del citomegalovirus con propiedades inmunomoduladoras.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-25155. Duration: 01/01/2012-31/12/2014

Lozano F. **Immunoreceptors of the Innate and Adaptive System.** Sponsored by Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), 2009/SGR/00252. Duration 01/01/2009-31/12/2013.

Engel P. **Función de la molécula CD229 (Ly9), un miembro de la famila SLAM, en el desarrollo de los linfocitos T y B de tipo innato inducida por patógenos.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-39536. Duration 01/01/2011-31/12/2015.

Engel P. **SLAM Gene Family Controlled Pathways to SLE.** Sponsored by: NIH (USA). 2P01AI065687-06A1. Duration 01/08/2012-31/07/2017

DOCTORAL THESES

Engel P. **Ly9, un regulador de la tolerancia inmunológica.** PhD. student: José Manuel de Salort

Lozano F. **Estudio de variantes estructurales (naturales e inducidas) de los receptores linfocitarios CD5 y CD6.** PhD student: Lizette Bonet Rosello

Lozano F. **Caracterització fenotípica i funcional de membres solubles de la superfamília de receptors scavenger rics en cisteïna (SF-SRCR).** PhD student: Cristina Miró Julià.

1.5 Musculoskeletal repair and plasticity

LOCATION
HCB building

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	62.94	21	7	6
2012	4.97	3	1	-
2013	16.132	5	3	2

TEAM LEADER
Joaquim Forés i Viñeta (HCB)
T. 93 227 93 14
jfores@clinic.cat

RESEARCHERS
Jesús Benito (HCB)
Andrés Combalía (HCB)
Sebastián García (HCB)
Luis M. Lozano (HCB)
Francisco Maculé (HCB)
Montserrat Nuñez (HCB)
Jaume Pomés (HCB)
Sergi Sastre (HCB)
Josep M. Segur (HCB)
Santiago Suso (HCB)

ADMINISTRATIVE STAFF
Antònia Bayo (HCB)

COLLABORATORS
M. Teresa Anglada (HCB)
Jordi Asunción (HCB)
Misericordia Basora (HCB)
Guillem Bori (HCB)
Xavier Carné (HCB)
Ana Carreño (HCB)
Adela Faulí (HCB)
Jenaro A. Fernández-Valencia (HCB)
Joan Xavier Fontdevila (HCB)
Salvador Fuster (HCB)
Xavier Gallart (HCB)
Eloy M. García Díez (HCB)
Ruben García Elvira (HCB)
Raquel García Tarriño (HCB)
Anna López Gutiérrez (HCB)
Felipe Orient (HCB)
Lluis Peidro (HCB)
Daniel Poggio (HCB)
Dragos Popescu (HCB)
Salvi Prat (HCB)
Josep Riba (HCB)
Moisés Rios (HCB)
Xavier Sala (HCB)
Isabel Sañudo (HCB)
Xavier Tomás (HCB)
Pere Torner (HCB)
Antoni Trilla (HCB)
Raquel Vilarrasa (HCB)
Josep M. Serra (HCB)
Alex Soriano (HCB)

STRATEGIC OBJECTIVES

Our research group, which was incorporated to the IDIBAPS in 2007, aims to agglutinate and generate synergies among specialists in different disciplines that work in the field of the locomotor system. This is a field with a growing social and technological demand, but with scant incidence in the research setting of this institution. There are many aspects of new knowledge related to the musculoskeletal system: cellular, genic and pharmacological therapies; new materials and implants; robotics; top-level surgical and anesthetic technology; and sophisticated imaging techniques. The lack of clinical scientific evidence relating to much of the new knowledge, and the great volume of patients in our setting, with limited resources, represent an important source of work from which to derive intellectual benefit. Working with humbleness but "thinking big" seems to us to be the best strategy for reaching the objective of being a reference group in our setting.

MAIN LINES OF RESEARCH

1. Bone physiopathology, pathological variation with age, evaluation of fracture setting techniques and bone substitutes.
2. Cartilage, degeneration and repair through tissue engineering.
3. Evaluation and design of new prosthetic implants.
4. Minimally invasive surgery with new technology and instruments.
5. Infections of the locomotor apparatus, their prevention and treatment.
6. Acute postoperative pain and chronic musculoskeletal pain.
7. Functional re-adaptation, prevalence and evaluation of health results in degenerative arthropathies.
8. Biology of autologous adipose tissue grafts.
9. Musculoskeletal system tissue bank.
10. Imaging diagnosis, new technologies in diagnosis and follow-up.
11. Collaboration in joint projects with the UASP.
12. Acute-phase response in open fractures. Use of IL-6, C-reactive protein and CK in predicting results, and correlation with the Gustilo classification.
13. Vascular anatomy of the upper extremity applied to reconstructive procedures.
14. Surgical management of facial lipoatrophy based on the injection of autologous adipose tissue in HIVinfected patients.
15. Nervous system:
- Tubulization repair of peripheral nervous system damage.
- Experimental reimplantation of nerve root preganglionic avulsions.

PUBLICATIONS

Originals / I.F.: 16.132

1. Torres-Espin A, Corona-Quintanilla DL, Fores J, Allodi I, Gonzalez F, Udina E, Navarro X. **Neuroprotection and Axonal Regeneration After Lumbar Ventral Root Avulsion by Re-implantation and Mesenchymal Stem Cells Transplant Combined Therapy.** *Neurotherapeutics* 10(2): 354-368 I.F.: 5.904

2. Dubreuil M, Ruiz-Gaspà S, Guañabens N, Peris P, Alvarez L, Monegal A, Combalia A, Parés A. **Ursodeoxycholic acid increases differentiation and mineralization and neutralizes the damaging effects of bilirubin on osteoblastic cells.** *Liver Int* 33(7):1029-1038 I.F.: 3.870

3. Ares O, Castellet E, Maculé F, León V, Montañez E, Freire A, Hinarejos P, Montserrat F, Amillo JR. **Translation and validation of 'The Knee Society Clinical Rating System' into Spanish.** *Knee Surg Sports Traumatol Arthrosc* 21(11):2618-2624 I.F.: 2.676

4. Muñoz-Mahamu E, Bori G, Garcia S, Ramirez J, Riba J, Soriano A. **Usefulness of histology for predicting infection at the time of hip revision for the treatment of Vancouver B2 periprosthetic fractures.** *J Arthroplasty.*28 (8):1247-50. I.F.: 2.110

5. Boeckstyns MEH, Sørensen AI, Fores J, Rosén B, Navarro X, Archibald SJ, Valls-Solé J, Moldovan M, Krarup C. **Collagen Conduit Versus Microsurgical Neurorrhaphy: 2-Year Follow-Up of a Prospective, Blinded Clinical and Electrophysiological Multicenter Randomized, Controlled Trial.** *J Hand Surg Am.* 38:2405-2411. I.F.: 1.572

GRANTS FOR RESEARCH IN PROGRESS

Fores J. **Eficacia del tratamiento con condroitin sulfato en la rizartrosis. Medicion con test sensoriales y funcionales cuantitativos y analisis de concordancia con escalas subjetivas de dolor.** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00079. Duration: 01/01/2009-30/06/2013

Nuñez M. **Fall Detector for the Elder.** Sponsored by: European Commission. 297178. Duration: 01/09/2013-31/05/2015

Sastre S. **Determinación de los niveles plasmáticos de substancia P en pacientes afectos de patología tendinosa degenerativa del hombro tributarios de cirugía.** Sponsored by: Fundacion Española de Artroscopia. AEA2011-SASTRE. Duration: 04/05/2011-03/05/2013

Suso S. **Estudio clínico piloto de terapia alogénica con células madre adultas expandidas "ex vivo" conjugadas en matriz ósea de origen alogénico en el tratamiento de fracturas de fémur proximal en ancianos.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-158. Duration: 01/01/2012-31/12/2014

1.6 Immunogenetics of the autoinflammatory response

LOCATION
HCB building

KEYWORDS
1. **Autoinflammation**
2. **Immunogenetics**
3. **Inflammasome**
4. **Immunotherapy**
5. **Immunodeficiencies**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	70.42	9	5	1
2012	68.60	11	7	2
2013	37.91	8	5	1

TEAM LEADER
Jordi Yagüe (HCB)
T. 93 227 54 00 (Ext: 2155)
jyague@clinic.cat

RESEARCHERS
Juan Ignacio Aróstegui (HCB)
Manel Juan Otero (HCB)

COLLABORATORS
Eva Gonzalez Roca (HCB)
Estíbaliz Ruiz Ortiz de Arrizabaleta (FCRB)
Azucena González Navarro (HCB)

STRATEGIC OBJECTIVES

In the field of autoinflammatory diseases:
Promotion of basic, clinical and translation research in the physiopathology of autoinflammatory diseases as a model for gaining in-depth knowledge of the regulation of the normal inflammatory response, its dysfunctions, and its repercussions upon the immune response.

In the field of immune response:
Determination of the components of normal and pathological inflammatory response is essential for modulating the specific recognition phenomena of the immune response.

MAIN LINES OF RESEARCH

In the field of autoinflammatory diseases:
- Determination of the genetic and molecular bases of the autoinflammatory process.
- Characterization of the regulatory mechanisms of the inflammasome and its dysfunction.
- Characterization of the specific transcriptional profiles of

autoinflammatory diseases.
- Isolation of new genes responsible for hereditary autoinflammatory diseases and identification of genetic susceptibility factors for the development of polygenic autoinflammatory processes.
- Definition of new therapeutic targets for the treatment of autoinflammatory diseases.

In the field of immune response:
- Assessing the role of HLA-DRB3/4/5 loci in the immune response against infection, transplantation and autoimmune response.
- Assessing the role of the mutation E52del in MyD88 in normal population as well as in relation to the lack of MyD88.

PUBLICATIONS

Originals / I.F.: 37.909

1. Bea, Silvia; Valdes-Mas, Rafael; Navarro, Alba; Salaverria, Itziar; Martin-Garcia, David; Jares, Pedro; Gine, Eva; Pinyol, Magda; Royo, Cristina; Nadeu, Ferran; Conde, Laura; Juan, Manel; Clot, Guillem; Vizan, Pedro; Di Croce, Luciano; Puente, Diana A.; Lopez-Guerra, Monica; Moros, Alexandra; Roue, Gael; Aymerich, Marta; Villamor, Neus; Colomo, Lluis; Martinez, Antonio; Valera, Alexandra; Martin-Subero, Jose I.; Amador, Virginia; Hernandez, Luis; Rozman, Maria; Enjuanes, Anna; Forcada, Pilar; Muntanola, Ana; Hartmann, Elena M.; Calasanz, Maria J.; Rosenwald, Andreas; Ott, German; Hernandez-Rivas, Jesus M.; Klapper, Wolfram; Siebert, Reiner; Wiestner, Adrian; Wilson, Wyndham H.; Colomer, Dolors; Lopez-Guillermo, Armando; Lopez-Otin, Carlos; Puente, Xose S.; Campo, Elias. **Landscape of somatic mutations and clonal evolution in mantle cell lymphoma.** *P Natl Acad Sci USA* 110:18250-18255 I.F.: 9.737

2. Tovar, N, de Larrea, CF, Aróstegui, JI, Cibeira, MT, Rosiñol, L, Rovira, M, Elena, M, Filella, X, Yagüe, J, Bladé, J. **Natural history and prognostic impact of oligoclonal humoral response in patients with multiple myeloma after autologous stem cell transplantation: Long-term results from a single institution.** *Haematologica* 98 (7):1142-1146 I.F.: 5.935

3. Vazquez-Ortiz M, Pascal M, Juan M, Alsina L, Martín-Mateos MA, Plaza AM. **Serum allergen-specific IgA is not associated with natural or induced tolerance to egg in children.** *Allergy* 68(10):1327-1332 I.F.: 5.883

4. van de Vosse E, Haverkamp MH, Ramirez-Alejo N, Martinez-Gallo M, Blancas-Galicia L, Metin A, Garty BZ, Sun-Tan Ç, Broides A, de Paus RA, Keskin Ö, Çağdaş D, Tezcan I, Lopez-Ruzafa E, Arostegui JL, Levy J, Espinosa-Rosales FJ, Sanal Ö, Santos-Argumedo L, Casanova JL, Boisson-Dupuis S, van Dissel JT, Bustamante J. **IL-12Rβ1 deficiency: mutation update and description of the IL12RB1 variation database.** *Hum Mutat.*34:1329-39. I.F.: 5.213

5. Retamozo S, Díaz-Lagares C, Bosch X, Bové A, Brito-Zerón P, Gómez M-E, Yagüe J, Forns X, Cid MC, Ramos-Casals M. **Life-threatening cryoglobulinemic patients with hepatitis C: Clinical description and outcome of 279 patients.** *Medicine (United States)* 92(5):273-284 I.F.: 4.233

6. Tovar N, Fernández de Larrea C, Pedrosa F, Aróstegui JL, Cibeira MT, Rosiñol L, Elena M, Filella X, Yagüe J, Bladé J.**Differential humoral responses against heat-shock proteins after autologous stem cell transplantation in multiple myeloma.** *Ann Hematol.* 93(1):107-11. I.F.: 2.866

7. Llorens F, Ansoleaga B, Garcia-Esparcia P, Zafar S, Grau-Rivera O, López-González I, Blanco R, Carmona M, Yagüe J, Nos C, Del Río JA, Gelpí E, Zerr I, Ferrer I. **PrP mRNa and protein expression in brain and PrPc in CSF in Creutzfeldt-Jakob disease MM1 and VV2.** *Prion* 7(5):383-393 I.F.: 2.133

8. Gelpi E, Soler Insa JM, Parchi P, Saverioni D, Yagüe J, Nos C, Martínez- Saez E, Ribalta T, Ferrer I, Sanchez-Valle R. **Atypical neuropathological sCJD-MM phenotype with abundant white matter Kuru-type plaques sparing the cerebellar cortex.** *Neuropathology* 33(2):204-208 I.F.: 1.909

GRANTS FOR RESEARCH IN PROGRESS

Juan M. **Reevaluación del papel de HLA-DRB3 (DR52) en la respuesta de los linfocitos T CD4+.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01404. Duration: 01/01/2011-31/12/2013

Yagüe J. **Immunogenetica en la resposta autoinflamatoria. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca** (AGAUR). 2009_SGR_1260. Duration: 23/09/2009-30/04/2014

1.7 Emergencies: Processes and pathologies

LOCATION
HCB building

KEYWORDS
1. **Emergency department**
2. **Organization**
3. **Toxicology**
4. **Chest pain**
5. **Arrhythmia**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	49.13	20	4	5
2012	52.02	16	12	2
2013	38.00	15	9	5

AWARDS

Pepe Millà Award 2013.
Best paper in Emergency Medicine published by Spanish emergency physicians during 2012
Institution: Sociedad Española de Medicina de Urgencias y Emergencias
Awardee/s: Miró O, Gil V, Herrero P, Martín-Sánchez FJ, Jacob J, Llorens P; ICA-SEMES Research Group.

Award to the second best Presentation at XXV SEMES National Congress
Institution: Sociedad Española de Medicina de Urgencias y Emergencias
Awardee/s: Jiménez Hernández S, Ruiz-Artacho P, Merlo Loranca M, Llorens Soriano P, Antolín Santaliestra A, Carrizosa Bach M

Award to the second best Oral Presentation at XXV SEMES National Congress
Institution: Sociedad Española de Medicina de Urgencias y Emergencias
Awardee/s: Ruiz-Artacho P, Merlo Loranca M, Llorens Soriano P, Aguillo García A, Franco Sorolla JM, Jiménez Hernández S.

TEAM LEADER
Òscar Miró Andreu (HCB)
T. 93 227 54 00 (Ext. 3153)
omiro@clinic.cat

RESEARCHERS
Santiago Nogué Xarau (HCB)
Miguel Sánchez Sánchez (HCB)
Blanca Coll-Vinent Puig (HCB)
Sònia Jiménez Hernández (HCB)
Rafel Perelló Carbonell (HCB)

PRE-DOCTORAL RESEARCHERS
Sira Aguiló Mir (HCB)
Xavier Alemany González (HCB)
Montserrat Amigó Tadín (HCB)
Maria Luisa Benito (CAP Les Corts)
Pablo Busca Ostolaza (UB)
Núria Díaz Miranda (Escola Molina)
Francesc Xavier Escalada Roig (SEM)
Rosa Escoda Turón (HCB)
Carolina Fuenzalida Inostroza (UB)
Victor Gil Espinosa (HCB)
Beatriz López Barbeito (HCB)
Arrate Placer López de Alda (HCB)
María Teresa Ruiz (HCB)

NURSING STAFF
Berta Calvo (HCB)
Eva Gómez Rodríguez (HCB)
Verónica Peinado (HCB)
Carolina Fuenzalida Inostoza (FCRB)
Natalia Alcolea (FCRB)

COLLABORATORS
Josep Ramon Alonso Viladot (HCB)
Albert Antolín Santaliestra (HCB)
Francesc Xavier Jiménez Fábrega (SEM)
Miguel Galicia Paredes (HCB)
Ana García Martínez (HCB)
Elisenda Gómez Angelats (HCB)
Mila Perea Gainza (HCB)
Emilio Salgado García (HCB)
Mar Ortega Romero (HCB)

STRATEGIC OBJECTIVES

The group has a general interest in the study of all processes and pathologies inherent to the emergency setting - in all cases adopting a patient-centered approach and focusing on the acute process leading to emergency consultation. This approach is absolutely unique in Catalonia and in Spain, in view of the topic involved and the perspective from which it is addressed. The processes seen in the Emergency Department are

exclusive and unique, and improvement in their knowledge leads to healthcare and organizational implications with considerable scope and repercussion. While the transverse characteristics of emergency disease conditions cause them to be dealt with by other disciplines, in the first few hours of their presentation they are exclusively addressed by the Emergency Department, where clinical research has not classically been considered. As a result, the possibilities for gaining in-depth and new knowledge on the part of the group are immense.

MAIN LINES OF RESEARCH

1. Functional aspects of Hospital Emergency Departments.
2. Clinical aspects of intoxicated patients.
3. Treatment of arrhythmias in the emergency room.
4. Evaluation of chest pain in the Emergency Department.
5. Diffusion of the teaching of cardiopulmonary resuscitation maneuvers among the general population
6. Emergency medical care for problems caused by drug abuse.
7. Acute heart failure
8. Attention to infectious diseases in Emergency Departments.
9. Dynamics of teaching and research in Emergency Medicine.

PUBLICATIONS

Originals / I.F.: 38.005

1. Batalla A, Bhattacharyya S, Yücel M, Fusar-Poli P, Crippa JA, Nogué S, Torrens M, Pujol J, Farré M, Martin-Santos R. **Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings.** *PLoS One* 8(2):e55821 I.F: 3.730

2. Said MA, Johnson HL, Nonyane BA, Deloria-Knoll M, O'Brien KL; AGEDD Adult Pneumococcal Burden Study Team, Andreo F, Beovic B, Blanco S, Boersma WG, Boulware DR, Butler JC, Carratalà J, Chang FY, Charles PG, Diaz AA, Domínguez J, Ehara N, Endeman H, Falcó V, Falguera M, Fukushima K, Garcia-Vidal C, Genne D, Guchev IA, Gutierrez F, Hernes SS, Hoepelman AI, Hohenthal U, Johansson N, Kolek V, Kozlov RS, Lauderdale TL, Mareković I, Masiá M, Matta MA, Miró Ò, Murdoch DR, Nuermberger E, Paolini R, Perelló R, Snijders D, Plečko V, Sordé R, Strålin K, van der Eerden MM, Vila-Corcoles A, Watt JP. **Estimating the burden of pneumococcal pneumonia among adults: a systematic review and meta-analysis of diagnostic techniques.** *PLoS One* 8(4):e60273 I.F: 3.730

3. Martín-Sánchez FJ, Marino-Genicio R, Rodríguez-Adrada E, Jacob J, Herrero P, Miró Ò, Llorens P, Ribera-Casado JM; ICA-SEMES Group. **Management of acute heart failure in spanish emergency departments based on age.** *Rev Esp Cardiol* 66(9):715-720 I.F: 3.204

4. Calvo-Sanchez M; Perello R; Perez, I; Mateo MG; Junyent M; Laguno M; Blanco JL; Martinez-Rebollar M; Sánchez M; Mallolas J; Mas A. **Differences between HIV-infected and uninfected adults in the contributions of smoking, diabetes and hypertension to acute coronary syndrome: two parallel case-control studies.** *HIV Medicine* 14:40-48 I.F: 3.155

5. Amigó Tadín M, Ríos Guillermo J, Nogué Xarau S. **Demanda al servicio de urgencias de profilaxis para infecciones de transmisión sexual tras prácticas sexuales de riesgo.** *Emergencias* 25:437-444 I.F: 2.578

6. Burbano P, Martín-Sánchez FJ, Burillo-Putze G, Fernández Pérez C, Del Prado González N, Miró Ò. **Producción y repercusión científica de un grupo de urgenciólogos españoles seleccionados por su trayectoria investigadora.** *Emergencias* 25:245-254 I.F: 2.578

7. Bustamante P, Avendaño D, Camacho B, Ochoa E, Alemany FX, Romero MA, Tariq KM, Sánchez M. **Evaluación de la satisfacción del paciente con la atención recibida en un servicio de urgencias hospitalario y sus factores asociados.** *Emergencias* 25:171-176 I.F: 2.578

8. Perelló R, Miró Ò, Camón S, Sánchez M, Miró JM, Marcos MA, Moreno A. **Aproximación al valor pronóstico de diferentes marcadores identificables en urgencias en pacientes VIH con neumonía: Valor de la PCR.** *Emergencias* 25:268-272 I.F: 2.578

9. Puiguriguer J, Nogué S, Echarte JL, Ferrer A, Dueñas A, García L, Córdoba F, Burillo-Putze G. **Mortalidad hospitalaria por intoxicación aguda en España (EXITOX 2012).** *Emergencias* 25:467-471 I.F: 2.578

10. Sánchez M, Asenjo M, Gómez E, Zabalegui A, Brugada J. **Reorganización asistencial de un área de urgencias en niveles de urgencia: impacto sobre la efectividad y la calidad.** *Emergencias* 25:85-91 I.F: 2.578

11. Sánchez M, Vázquez J, Temboury R, Capdepon C, Povar J, Santaló M. **El síndrome coronario agudo inclasificable en los servicios de urgencias españoles. Aportaciones del registro MUSICA.** *Emergencias* 25:263-267 I.F: 2.578

12. Smithson A, Ruiz J, Perello R, Valverde M, Ramos J, Garzo L. **Diagnostic and management of spontaneous rectus sheath hematoma.** Eur J Intern Med. 24(6):579-82. I.F: 2.049

13. Jacob J, Martín-Sanchez FJ, Herrero P, Miró Ò, Llorens P; miembros del grupo ICA-SEMES. **Prognostic value of troponin in patients with acute heart failure attended in Spanish Emergency Departments: TROPICA study (TROPonin in acute heart failure).** *Med Clin (Barc)* 140(4):145-151 I.F: 1.399

14. Mena G, Sequera VG, Nogué-Xarau S, Ríos J, Bertran MJ, Trilla A. **Translation and cross-cultural adaptation of the Quick Environmental Exposure and Sensitivity**

Inventory for use in the Spanish population. *Med Clin* (Barc) 140(7):302-304 I.F: 1.399

15. Morén C, Garrabou G, Noguera-Julian A, Rovira N, Catalán M, Hernández S, Tobías E, Cardellach F, Fortuny C, Miró Ò. **Study of oxidative, enzymatic mitochondrial respiratory chain function and apoptosis in perinatally HIV-infected pediatric patients.** *Drug Chem Toxicol* 36(4):496-500 I.F: 1.293

Reviews / I.F: 3.599

1. Sánchez M, Escolar G, Reverter JC. **Hemorragias en pacientes anticoagulados: utilidad real de los antídotos y modo de actuación con los nuevos anticoagulantes orales.** *Emergencias* 25:482-490 I.F: 2.578

2. Coll-Vinent B, Fuenzalida C, García A, Martín A, Miró Ò. **Management of acute atrial fibrillation in the emergency department: a systematic review of recent studies.** *Eur J Emerg Med* 20(3):151-159 I.F: 1.021

Editorials / I.F: 6.177

1. Miró Ò. **¡Y ahí estamos de nuevo!** *Emergencias* 25:241-242 I.F: 2.578

2. Miró Ò. **25 años de EMERGENCIAS.** *Emergencias* 25:1-6 I.F: 2.578

3. Gonzalez Armengol, JJ, Miró Ò, Graham, CA. **From Spain, to Europe.** *Eur J Emerg Med.* 20(6): 373-374. I.F: 1.021

Clinical Guidelines / I.F:1.372

1. Uresandi F, Monreal M, García-Bragado F, Domenech P, Lecumberri R, Escribano P, Zamorano JL, Jiménez S, Ruiz-Artacho P, Lozano F, Romera A, Jiménez D; National Consensus on Diagnosis, Risk Stratification and Treatment of Patients With Pulmonary Thromboembolism, Bellmunt S, Cuenca J, Fernández Á, Fernández F, Ibáñez V, Lozano F, March JR, Romera A, Almenar L, Castro A, Escribano P, Lázaro M, Luis Zamorano J, Alonso JR, Ramón Casal J, Miguel Franco J, Jiménez S, Merlo M, Perales R, Piñera P, Ruiz-Artacho P, Suero C, Barba R, Fernández-Capitán C, García-Bragado F, Gómez V, Monreal M, Nieto JA, Riera-Mestre A, Suárez C, Trujillo-Santos J, Conget F, Jara L, Jiménez D, Lobo JL, de Miguel J, Nauffal D, Oribe M, Otero R, Uresandi F, Domenech P, González-Porras JR, Lecumberri R, Llamas P, Mingot E, Pina E, Rodríguez-Martorell J. **National Consensus on the Diagnosis, Risk Stratification and Treatment of Patients with Pulmonary Embolism.** *Arch Bronconeumol* 49(12):534-547 I.F: 1.372

GRANTS FOR RESEARCH IN PROGRESS

Miro O. **European Drug Emergencies Network.** Sponsored by: European Commission. JUS/11-12/DPIP/AG_01. Duration: 01/04/2013-31/03/2015

Miro O. **Identificación de los factores asociados a reconsulta, ingreso y mortalidad precoz en pacientes dados de alta directamente de urgencias por un episodio de insuficiencia cardiaca aguda: estudio español multicéntrico.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/01021. Duration: 01/01/2012-31/12/2014

1.8

Molecular and cellular bases of inflammation. Structural and biological mass spectrometry

LOCATION
IIBB-CSIC labs

KEYWORDS
1. **Inflammation**
2. **Fibrosis**
3. **Proteomics**
4. **Macrophages**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	24.86	5	3	-
2012	7.87	2	2	-
2013	30.86	6	5	-

TEAM LEADER
Daniel Closa (IIBB-CSIC)
T. 93 363 83 43
daniel.closa@iibb.csic.es

RESEARCHERS
Joaquín Abián (IIBB-CSIC-UAB)
Oriol Bulbena (IIBB-CSIC)
Montserrat Carrascal (IIBB-CSIC)
Emma Folch (IBB-CSIC)

PRE-DOCTORAL RESEARCHERS
L. Bonjoch (CIBEREHD)
R. Guillamat (CIBERES)
C. Lebrero (GENAME)

TECHNICIANS
Edita Bueno (JAE-TEC)
V. Casas (TS- MICINN)
Ana González (Proteored)
D. Ovelleiro (Proteored)
L. Ignacio Sánchez (IIBB-CSIC)
V. Sirenko (IDIBAPS)
Joan Villanueva (Proteored)

COLLABORATORS:
G. Gay (IIBB-CSIC)
M. Gay (JAE-DOC)
F. Pí (IIBB-CSIC)
A. Salas (RC)
A. Serrano (IIBB-CSIC)

STRATEGIC OBJECTIVES

1. **Molecular and cellular bases of inflammation:**
   Study of inflammatory response in general.

2. **Structural and biological mass spectrometry:**
   Development of techniques for solving problems in proteomics and in the analysis of biomolecules in general. Application to the study of antigen presentation in autoimmune diseases and to the investigation of therapeutic targets and markers of the disease.

MAIN LINES OF RESEARCH

1. **Molecular and cellular bases of inflammation:**
   - Mechanisms involved in the development of systemic inflammatory processes.

- New therapies for idiopathic pulmonary fibrosis.
- Study of the lipid alterations associated with pancreatitis.

2. Structural and biological mass spectrometry:

- Phosphoproteomics of the human T lymphocyte.
- Diagnostic and prognostic markers in cancer and other diseases.
- External scientific-technical services. Proteomics Services and Coordination of Proteored Network.

PUBLICATIONS

Originals / I.F.: 30.857

1. Gironella M, Calvo C, Fernandez A, Closa D, Iovanna JL, Rosello-Catafau J, Folch-Puy E. **Reg3 beta Deficiency Impairs Pancreatic Tumor Growth by Skewing Macrophage.** *Cancer Research.* 73(18):5682-5694 I.F. 8.650

2. Franco-Pons N, Casas J, Fabriàs G, Gea-Sorlí S, de-Madaria E, Gelpí E, Closa D. **Fat necrosis generates proinflammatory halogenated lipids during acute pancreatitis.** *Ann Surg.* 257(5):943-951 I.F. 6.329

Segura V, Medina-Aunon JA, Guruceaga E, Gharbi SI, González-Tejedo C, Sánchez del Pino MM, Canals F, Fuentes M, Casal JI, Martínez-Bartolomé S, Elortza F, Mato JM, Arizmendi JM, Abian J, Oliveira E, Gil C, Vivanco F, Blanco F, Albar JP, Corrales FJ. **Spanish human proteome project: dissection of chromosome 16**. *J Proteome Res.* 12(1):112-122 I.F. 5.056

3. Collado JA, Alvarez I, Ciudad MT, Espinosa G, Canals F, Pujol-Borrell R, Carrascal M, Abian J, Jaraquemada D. **Composition of the HLA-DR-associated human thymus peptidome.** *Eur J Immunol.* 43(9):2273-2282 I.F. 4.970

4. Amézqueta S, Galán E, Vila-Fernández I, Pumarola S, Carrascal M, Abian J, Ribas-Barba L, Serra-Majem L, Torres JL. **The presence of D-fagomine in the human diet from buckwheat-based foodstuffs.** *Food Chem.* 136(3-4):1316-1321 I.F. 3.334

5. Pavón EJ, Zumaquero E, Rosal-Vela A, Khoo KM, Cerezo-Wallis D, García-Rodríguez S, Carrascal M, Abian J, Graeff R, Callejas-Rubio JL, Ortego-Centeno N, Malavasi F, Zubiaur M, Sancho J. **Increased CD38 expression in T cells and circulating anti-CD38 IgG autoantibodies differentially correlate with distinct cytokine profiles and disease activity in systemic lupus erythematosus patients**. *Cytokine.* 62(2):232-243 I.F. 2.518

Reviews / I.F.: 3.279

1. Closa D. **Free radicals and acute pancreatitis: much ado about ... something.** *Free Radic Res.* 47(11):934-940 I.F. 3.279

GRANTS FOR RESEARCH IN PROGRESS

Abian J. **Desarrollo de una herramienta de diagnóstico molecular para la obtención de aves con mayor valor añadido.** Sponsored by: Proyectos INNPACTO 2011, MICINN. Laboratorios Dr. Larrasa S.L. Duration: 01/01/2011-31/12/2014.

Abian J. **Desarrollo de una vacuna global frente a Brachyspira hyodysenteriae y Brachyspira pilosicoli mediante análisis pan-genómico estructural y funcional combinado con tecnologías de producción de proteínas recombinantes (brachVac).** Sponsored by: Proyectos INNPACTO 2011, MICINN. Laboratorios Dr. Larrasa S.L. Duration: 01/01/2011-31/12/2014.

Bulbena O. **Trasplante de células alveolares tipo II, derivadas de células madre adultas, para el tratamiento de la fibrosis pulmonar idiopática.** Sponsored by: FIS, PS09/02362. Duration: 01/01/2010-31/12/2013.

Closa D. **Regulació de la Inflamació Aguda i Crónica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_966. Duration: 16/09/2009-30/04/2014

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

2.1 **Atherosclerosis, coronary disease and heart failure** 86
Manel Sabaté

2.2 **Arrhythmias, resynchronization and cardiac imaging** 92
Josep Brugada

2.3 **Nephro-urological diseases and kidney transplantation** 99
Josep Maria Campistol

2.4 **Hypertension, lipids and cardiovascular risk** 103
Emili Ros

2.5 **Respiratory biophysics and bioengineering** 108
Ramon Farré

2.6 **Applied research in infectious respiratory diseases, critically ill patients and lung cancer** 111
Antoni Torres

2.7 **Physiopathological mechanisms of respiratory illnesses** 117
Joan Albert Barberà

2.8 **Clinical and Experimental Respiratory Immunoallergy** 121
Joaquim Mullol

2.9 **Inflammation and repair in respiratory illnesses** 127
Alvar Agustí

2.10 **Genetic and urological tumours** 130
Antonio Alcaraz

2.1 Atherosclerosis, coronary disease and heart failure

LOCATION
CELLEX building

KEYWORDS
1. **Acute myocardial infarction**
2. **Percutaneous coronary intervention. Stent. Biodegradable device.**
3. **Therapeutic hypothermia**
4. **Stem cell therapy**
5. **Heart failure.**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	97.59	26	6	12
2012	217.51	31	19	8
2013	193.24	36	22	9

TEAM INVOLVED IN
Red HERACLES

TEAM LEADER
Manel Sabaté Tenas (HCB)
T. 93 227 93 05
masabate@clinic.cat

RESEARCHERS
Xavier Bosch (HCB)
Salvatore Brugaletta (HCB)
Ana Paula Dantas (IDIBAPS)
Carles Falces (HCB)
Magda Heras Fortuny (HCB)
Victoria Martín Yuste (HCB)
Carles Paré (HCB)
Félix Pérez Villa (HCB)
José Luis Pomar (HCB)
Montserrat Rigol (IDIBAPS)
Mercè Roqué (HCB)

POST-DOCTORAL RESEARCHERS
Laura Novensà (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Diego Fernández Rodriguez (HCB)
Ander Regueiro Cueva (HCB)

TECHNICIANS
Nadia Castillo (FCRB)

NURSING STAFF
Anna Barrabés (FCRB)
Elisabet de Mingo (IDIBAPS)

ADMINISTRATIVE STAFF
Mª Angeles Alvarez (HCB)
Eva Trellisó (FCRB)

COLLABORATORS
Rut Andrea (HCB)
Manel Azqueta (HCB)
Montserrat Batlle (IDIBAPS)
Montserrat Cardona (HCB)
Xavier Freixa (HCB)
Ana García Álvarez (HCB)
Mònica Masotti (HCB)
África Muxí (HCB)
José Ortiz Pérez (HCB)
Susanna Prat (HCB)
Mª José Pulgarín (IDIBAPS)
Núria Solanes (FCRB)

STRATEGIC OBJECTIVES

- To identify the pathophysiological mechanisms involved in the process of accelerated atherosclerosis.
- To evaluate the clinical efficacy of regenerative cell therapy and carry out further in-depth study of the regulatory mechanisms of the exogenous and endogenous stem cells in ischaemic heart disease and heart failure.
- To gain an increased understanding of the genetics, pathophysiology, diagnosis and treatment of heart failure.
- To gain an increased understanding of the organisational models for the care of cardiovascular patients in the community.
- To gain a more in-depth understanding of the pathophysiology, diagnostic methods and results of new treatments for acute and chronic ischaemic heart disease.
- To evaluate the repercussions of the new diagnostic techniques and types of treatment in structural heart disease.
- To study the applicability of the invasive and non-invasive imaging techniques in ischaemic heart disease, heart failure, structural heart disease and cell therapy.

MAIN LINES OF RESEARCH

- Study of the mechanisms of hyperplasia of the intima following coronary revascularisation procedures experimental models.

- Study of the biocompatibility of the materials and the endothelialisation process in the design of intracoronary devices.

- Study of the influence of hormonal factors and aging on the regulation of the nitric oxide and superoxide systems in the healthy and population with cardiovascular disease.

- Determination of the mechanisms involved in the regulation of the nitric oxide and superoxide systems.

- Study of hypothermia in patients with cardiac arrest.

- Study of the efficacy of cell therapy in patients with chronic refractory angina pectoris.

- Analysis of the regulatory mechanisms and the efficacy of the administration of mesenchymal stem cells on myocardial regeneration in an experimental model.

- Role of the mechanisms of vascular inflammation and thrombosis (circulating endothelial and the progenitor endothelial cells).

- Study of the impact of gender differences on ischaemic heart disease.

- Clinical studies evaluating the efficacy and safety of drug-eluting stents coated with everolimus in patients with ST-segment elevation myocardial infarction.

- Clinical evaluation of the fully bioresorbable coronary device in ischaemic heart disease.

- Chronic total occlusion of coronary arteries in humans: from the pathophysiology to the clinical implications of successful recanalisation.

- Study of neurohormonal activation and the fibrotic process associated with ventricular remodelling in dilated cardiomyopathy.

- Genetic study of familial idiopathic cardiomyopathy.

- Prevention of ventricular dysfunction in chemotherapy patients.

- Study of heart failure with normal ejection fraction.

- Evaluation of efficacy of mechanical circulatory support devices.

- Integration of care models between cardiology and primary care in patients with chronic heart disease.

- Outpatient characterisation of newonset heart failure using high-resolution imaging.

- Study of the efficacy and efficiency, of surgical and transcatheter treatment of aortic valve disease.

- Percutaneous closure of the left atrial appendage in patients with non-valvular atrial fibrillation requiring anticoagulant treatment.

- Evaluation of the impact of the use of MitraClip in patients with mitral regurgitation.

- Role of cardiac imaging in the indications, diagnosis, treatment and follow-up of patients with structural heart disease.

- Utility of the new imaging techniques and biomarkers for the early diagnosis of cardiac involvement in Chagas disease and response to antiparasitic treatment.

- Utility of cardiac magnetic resonance imaging in pulmonary hypertension and in the detection of right ventricular dysfunction. Evaluation of new pharmacological and invasive treatments for pulmonary hypertension.

PUBLICATIONS

Originals / I.F.: 193.241

1. Miro JM, Pericas JM, del Rio A; Heras M.,Hospital Clinic Endocarditis Study Group.: **'A new era for treating Enterococcus faecalis endocarditis: ampicillin plus short-course gentamicin or ampicillin plus ceftriaxone: that is the question!'** *Circulation.* 127(17):1763-1766 I.F.:15.202

2. Heras M, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. **Enalapril And Carvedilol for Preventing Chemotherapy-Induced Left Ventricular Systolic Dysfunction in Patients with Malignant Hemopathies. The OVERCOME Trial. (preventiOn of left**

Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive ChemOtherapy for the treatment of Malignant hEmopathies). *J Am Coll Cardiol.* 61(23):2355-2362 I.F.:14.086

3. Bosch X, Sitges M, Rovira M, Ortiz-Pérez JT, Esteve J. **Reply: Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies.** *J Am Coll Cardiol.* 62(25):2452 I.F.: 14.086

4. Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Sabaté M, Valgimigli M, Frati G, Kedhi E, Smits PC, Kaiser C, Genereux P, Galatius S, Kirtane AJ, Stone GW. **Clinical outcomes with drug-eluting and bare-metal stents in patients with ST-segment elevation myocardial infarction: evidence from a comprehensive network meta-analysis.** *J Am Coll Cardiol.* 62(6):496-504 I.F.: 14.086

5. Penela D, Magaldi M, Fontanals J, Martin V, Regueiro A, Ortiz JT, Bosch X, Sabaté M, Heras M. **Hypothermia in acute coronary syndrome: brain salvage versus stent thrombosis?** *J Am Coll Cardiol.* 61(6):686-687 I.F.: 14.086

6. Penela D, Van Huls Vans Taxis C, Aguinaga L, Fernández-Armenta J, Mont L, Castel MA, Heras M, Tolosana JM, Sitges M, Ordóñez A, Brugada J, Zeppenfeld K, Berruezo A.: **'Neurohormonal, structural, and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction: a prospective multicenter study.'** *J Am Coll Cardiol.* 62(13):1195-1202 I.F.: 14.086

7. Martí JD, Li Bassi G, Rigol M, Saucedo L, Ranzani OT, Esperatti M, Luque N, Ferrer M, Vilaro J, Kolobow T, Torres A. **"Effects of manual rib cage compressions on expiratory flow and mucus clearance during mechanical ventilation".** *Crit Care Med* 41(3):850-856 I.F.: 6.124

8. Brugaletta S, Sabate M, Martin-Yuste V, Masotti M, Shiratori Y, Alvarez-Contreras L, Cequier A, Iñiguez A, Serra A, Hernandez-Antolin R, Mainar V, Valgimigli M, Tespili M, den Heijer P, Bethencourt A, Vazquez N, Gomez-Lara J, Backx B, Serruys PW. **Predictors and clinical implications of stent thrombosis in patients with ST-segment elevation myocardial infarction: Insights from the EXAMINATION trial.** *Int J Cardiol.* 168(3):2632-2636 I.F.: 5.509

9. Fernández D, Brugaletta S, Martín-Yuste V, Regueiro A, de Mingo A, Santos A, Masotti M, Sabaté M. **First experience of a bioresorbable vascular scaffold implantation in left main stenosis.** *Int J Cardiol* 168(2):1566-1568 I.F.: 5.509

10. Pujadas S, Martin V, Rosselló X, Carreras F, Barros A, Leta R, Alomar X, Cinca J, Sabate M, Pons-Llado G. **Improvement of myocardial function and perfusion after successful percutaneous revascularization in patients with chronic total coronary occlusion.** *Int J Cardiol.* 169(2):147-52 I.F.: 5.509

11. Sabaté M, Brugaletta S, Abizaid A, Banning A, Bartorelli A, Džavík V, Ellis S, Holmes D, Gao R, Jeong MH, Legrand V, Neumann FJ, Nyakern M, Spaulding C, Stoll HP, Worthley S, Urban P; e-SELECT Investigators. **Drug eluting stent implantation in patients requiring concomitant vitamin K antagonist therapy. One-year outcome of the worldwide e-SELECT registry.** *Int J Cardiol.* 168(3):2522-2527 I.F.: 5.509

12. Batlle M, Roig E, Pulgarin MJ, Campos B, Ramírez J, Pomar JL, Farrero M, Castel MA, Cardona M, Roqué M , Orús J, Cartaña R, Perez-Villa F. **Molecular changes of the angiotensin converting enzyme 2 pathway in myocardial tissue from heart failure patients undergoing heart transplantation.** *J Clin Exp Cardiolog* S9:004 I.F.: 5.332

13. Sanchis J, Buenos C, Novella S, Rider M, Dapecre,Heras M, Hermenegildo C. **An affordable method to obtain cultured endothelial cells from peripheral blood" in its current form for publication.** *J Cell Mol Med.* 17(11):1475-1483 I.F.: 4.753

14. Garcia-de-la-Maria C, Pericas J, del Rio A, Castaneda X, Vila-Farres X, Armero Y, Espinal P, Cervera C, Soy D, Falces C, Ninot S, Almela M, Mestres C, Gatell JM, Vila J, Moreno A, Marco F, Miró JM. **Early In Vitro and In Vivo Development of High-Level of Daptomycin Resistance (HLDR) is Common in Mitis Group Streptococci After Exposure to Daptomycin.** *Antimicrob Agents Ch.* 66:419-425 I.F.:4.565

15. Gomez-Lara J, Brugaletta S, Gomez-Hospital JA, Ferreiro JL, Roura G, Romaguera R, Martin-Yuste V, Masotti M, Iñiguez A, Serra A, Hernandez-Antolin R, Mainar V, Valgimigli M, Tespili M, den Heijer P, Bethencourt A, Vazquez N, Serruys P, Sabate M, Cequier A. **Everolimus-eluting stent versus bare metal stent in proximal left anterior descending ST-elevation myocardial infarction: insights from the EXAMINATION trial.** *Am Heart J.* 166(1):119-126 I.F.: 4.497

16. Sambola A, Montoro JB, Del Blanco BG, Llavero N, Barrabés JA, Alfonso F, Bueno H, Cequier A, Serra A, Zueco J, Sabaté M, Rodríguez-Leor O, García-Dorado D. **Dual antiplatelet therapy versus oral anticoagulation plus dual antiplatelet therapy in patients with atrial fibrillation and low-to-moderate thromboembolic risk undergoing coronary stenting: design of the MUSICA-2 randomized trial.** *Am Heart J.* 166(4):669-675 I.F.:4.497

17. Jiménez-Altayó F, Onetti Y, Heras M, Dantas AP, Vila E. **'Western-style diet modulates contractile responses to phenylephrine differently in mesenteric arteries from senescence-accelerated prone (SAMP8) and resistant (SAMR1) mice.'** *Age (Dordr).* 35(4):1219-1234 I.F.:4.084

18. Novella S, Dantas AP, Segarra G, Novensa L, Heras M, Hermenegildo C, Medina P.: '**Aging enhances contraction to thromboxane A2 in aorta from female**

senescence-accelerated mice.' *Age (Dordr).* 35(1):117-128 I.F.: 4.084

19. Onetti Y, Jiménez-Altayó F, Heras M, Vila E, Dantas AP. **Western-type diet induces senescence, modifies vascular function in non-senescence mice and triggers adaptive mechanisms in senescent ones.** Exp Gerontol. 48(12):1410-1419 I.F.: 3.911

20. Ortiz-Pérez JT, Riera M, Bosch X, De Caralt TM, Perea RJ, Julio Pascual, María José Soler. **Role of Circulating Angiotensin Converting Enzyme 2 in Left Ventricular Remodeling following Myocardial Infarction: A Prospective Controlled Study.** *PLoS ONE* 8(4): e61695 I.F.: 3.730

21. P Beltran-Alvarez, AEspejo, R Schmauder, C Beltran, R Mrowka,T Linke, M Batlle, F Pérez-Villa, GJ. Pérez, FS. Scornik, K Benndorf , S Pagans, T Zimmer, R Brugada. **Protein arginine methyl transferases-3 and -5 increase cell surface expression of cardiac sodium channel.** FEBS Letters 587:3159–3165 I.F.: 3.730

22. Fernández-Rodríguez D, Vannini L, Martín-Yuste V, Brugaletta S, Robles R, Regueiro A, Masotti M, Sabaté M. **Medical management of connector pin thrombosis with the Amplatzer cardiac plug left atrial closure device.** *World J Cardiol.* 5(10):391-3 I.F.: 3.571

23. Regueiro A, Falces C, Cervera C, Del Río A, Paré JC, Mestres CA, Castañeda X, Pericàs JM, Azqueta M, Marco F, Ninot S, Almela M, Moreno A, Miró JM and the Hospital Clínic Endocarditis Study Group. **Risk Factors for Pericardial Effusion in Native Valve Infective Endocarditis and Its Influence on Outcome.** *Am J Cardiol* 112:1646-1651 I.F.: 3.209

24. Sabaté M, Cánovas S, García E, Hernández Antolín R, Maroto L, Hernández JM, Alonso Briales JH, Muñoz García AJ, Gutiérrez-Ibañes E, Rodríguez-Roda J; collaborators of the TAVI National Group. **In-hospital and Mid-term Predictors of Mortality After Transcatheter Aortic Valve Implantation: Data From the TAVI National Registry 2010-2011.** *Rev Esp Cardiol* 66(12):949-958 I.F.: 3.204

25. Di Mario C, Eltchaninoff H, Moat N, Goicolea J, Ussia GP, Kala P, Wenaweser P, Zembala M, Nickenig G, Alegria Barrero E, Snow T, Iung B, Zamorano P, Schuler G, Corti R, Alfieri O, Prendergast B, Ludman P, Windecker S, Sabate M, Gilard M, Witowski A, Danenberg H, Schroeder E, Romeo F, Macaya C, Derumeaux G, Maggioni A, Tavazzi L; Transcatheter Valve Treatment Sentinel Registry (TCVT) Investigators of the EURObservational Research Programme (EORP) of the European Society of Cardiology. **The 2011-12 pilot European Sentinel Registry of Transcatheter Aortic Valve Implantation: in-hospital results in 4,571 patients.** *EuroIntervention.* 8(12):1362-1371 I.F.: 3.173

26. Hamon M, Pristipino C, Di Mario C, Nolan J, Ludwig J, Tubaro M, Sabate M, Mauri-Ferré J, Huber K, Niemelä K, Haude M, Wijns W, Dudek D, Fajadet J, Kiemeneij F; European Association of Percutaneous Cardiovascular Interventions; Working Group on Acute Cardiac Care of the European Society of Cardiology; Working Group on Thrombosis on the European Society of Cardiology. **Consensus document on the radial approach in percutaneous cardiovascular interventions: position paper by the European Association of Percutaneous Cardiovascular Interventions and Working Groups on Acute Cardiac Care** and Thrombosis of the European Society of Cardiology.** *EuroIntervention.*8(11):1242-1251 I.F.: 3.173

27. Jiménez-Quevedo P, Hernando L, Gómez-Hospital JA, Iñiguez A, SanRoman A, Alfonso F, Hernández-Antolín R, Angiolillo DJ, Bañuelos C, Escaned J, Gonzalo N, Fernández C, Macaya C, Sabaté M; DIABETES Investigators. **Sirolimus-eluting stent versus bare metal stent in diabetic patients: the final five-year follow-up of the DIABETES trial.** *EuroIntervention.* 9(3):328-335 I.F.:3.173

28. Lüscher TF, de Feyter P, Sabate M, Van Mieghem NM, Mahfoud F, Serruys PW. **The European Heart Journal and EuroIntervention: information and education in interventional cardiology.** *EuroIntervention.* 9(6): 669-680 I.F.: 3.173

29. Rigol M, Solanes N, Fernández-Armenta J, Silva E, Doltra A, Duchateau N, Barceló A, Berruezo A, Brugada J, Sitges M. **"Development of a swine model of left bundle branch block for experimental studies of cardiac resynchronization therapy".** *J Cardiovasc Transl Res* 6(4):616-622 I.F.: 3.062

30. Brugaletta S, Garcia-Garcia HM, Gomez-Lara J, Radu MD, Pawar R, Khachabi J, Bruining N, Sabaté M, Serruys PW. Reproducibility of qualitative assessment of stent struts coverage **by optical coherence tomography.** *Int J Cardiovas Imag.* 29(1):5-11 I.F.: 2.648

31. Shiratori Y, Brugaletta S, Alvarez-Contreras L, Azpeitia Y, Ospino N, Gaido S, Delahanty A, Santos A, Martin-Yuste V, Masotti M, Serruys PW, Windecker S, Sabaté M. **One-year head to head comparison of the neointimal response between sirolimus eluting stent with reservoir technology and everolimus eluting stent: an optical coherence tomography study.** *Catheter Cardiovasc Inte.* 82(4):E428-36 I.F.: 2.514

32. Andrea R, Falces C, Sanchis L, Sitges M, Heras M, Brugada J. **Diagnóstico de la insuficiencia cardiaca con fracción de eyección preservada o reducida mediante una consulta de alta resolución. Diagnosis of heart failure with preserved or reduced ejection fraction in a one-stop clinic.** *Aten Primaria.* 45:184-192 I.F.: 1.850

33. Avanzas P, Heras M, Sanchis J.: **'The year 2011 in interventional cardiology.'** *Arq Bras Cardiol.* 101(6):571 I.F.:1.130

34. Cevallos J, Andrea R, Falces C, Martin-Yuste V, Freixa X, Vidal B, Brugaletta S, Castellá M, Masotti M, Sabaté M. **Transcatheter aortic valve implantation in patients with left main percutaneous coronary intervention.** *J Heart Valve Dis.* 22(6):874-7 I.F.: 1.071

35. Moreno R, García E, Teles R, Rumoroso JR, Cyrne Carvalho H, Goicolea FJ, Moreu J, Mauri J, Sabaté M, Mainar V, Patricio L, Valdés M, Fernández Vázquez F, Sánchez-Recalde A, Galeote G, Jimenez-Valero S, Almeida M, Lopez de Sa E, Calvo L, Plaza I, Lopez-Sendón JL, Martín JL; CIBELES Investigators. **Randomized comparison of sirolimus-eluting and everolimus-eluting coronary stents in the treatment of total coronary occlusions: results from the chronic coronary occlusion treated by everolimus-eluting stent randomized trial.** *Circ Cardiovasc Inte.* 6(1):21-8 I.F.: 0.871

36. Moreno R, García E, Teles R, Rumoroso JR, Cyrne Carvalho H, Goicolea FJ, Moreu J, Mauri F, Sabaté M, Mainar V, Patricio L, Valdés M, Cuellas C, Almeida M, Sánchez-Recalde A, Galeote G, Jimenez-Valero S, Calvo L, Plaza I, Lopez-Sendón JL, Martín JL; investigators of the CIBELES trial. **Techniques and material used in the percutaneous treatment of chronic coronary occlusions. Data from the CIBELES study.** *Rev Port Cardiol.* 32(7-8):593-599 I.F.: 0.592

Reviews / I.F.: 8.218

1. Bosch X Marrugat J, Sanchis J. **Platelet glycoprotein IIb/IIIa blockers during percutaneous coronary intervention and as the initial medical treatment of non-ST segment elevation acute coronary syndromes.** *Cochrane DB Syst Rev* 11:CD002130 I.F.: 5.785

2. Fernández D, Cevallos J, Brugaletta S, Martín-Yuste V, Freixa X, Andrea R, Falces C, Regueiro-Cueva A, Masotti M, Sabaté M. **Percutaneous transcatheter aortic valve implantation: present and future perspective.** *Expert Rev Med Devic.* 10(2):185-199 I.F.: 2.433

Editorials / I.F.: 13.159

1. Avanzas P, Bayes-Genis A, Pérez de Isla L, Sanchis J, Heras M.: **'Keeping Its Finger on the Pulse of the Digital Age.'** *Rev Esp Cardiol.* 66(12):996-998 I.F.: 3.204

2. Heras M, Avanzas P, Bayes-Genis A, Isla LP, Sanchis J.: **'2012 annual summary and new projects in revista española de cardiología.'** *Rev Esp Cardiol.* 66(3):231-240 I.F.: 3.204

3. Martin-Yuste V, Brugaletta S, Sabaté M. **Organized thrombus, disorganized heart.** *Circ J.* 77(5):1152-3 I.F.: 3.578

4. Brugaletta S, Sabaté M. **First-in-man, last in evidence?** *EuroIntervention.* 8(9):999-1001 I.F.: 3.173

Clinical Guidelines / I.F.: 17.301

1. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabaté M, Senior R, Taggart DP, van der Wall EE, Vrints CJ; ESC Committee for Practice Guidelines, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Rydén L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. **2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology.** *Eur Heart J.* 34(38):2949-3003 I.F.: 14.097

2. Coordinadores: Worner F, Cequier A; Grupo de Trabajo de la Sociedad Española de Cardiología para la guía de práctica clínica sobre el síndrome coronario agudo con elevación del segmento ST:, Bardají A, Bodí V, Bover R, Martínez-Sellés M, Sabaté M, Sionis A, Vázquez de Prada JA; Grupo de Revisores Expertos para la guía de síndrome coronario agudo con elevación del segmento ST:, Arós F, Arribas F, Barrabés J, Díaz de Castro O, Heras M, López Palop R, López-Sendón JL, Manito N, de Pablo MC, Ripoll T, San Román A, de la Torre JM; Comité de Guías de Práctica Clínica de la Sociedad Española de Cardiología:, Fernandez-Ortiz A, Alonso Gómez AM, Anguita M, Cequier A, Comín J, Diaz-Buschmann I, Fernández Lozano I, Gómez de Diego JJ, Pan M, Worner F.: **'Comments on the ESC Guidelines for the Management of Acute Myocardial Infarction in Patients Presenting With ST-Segment Elevation.'** *Rev Esp Cardiol.* 66(1):5-11 I.F.: 3.204

Multicenter / I.F.: 29.978

1. Steg PG, Mehta SR, Pollack CV Jr, Bode C, Cohen M, French WJ, Hoekstra J, Rao SV, Ruzyllo W, Ruiz-Nodar JM, Sabaté M, Widimsky P, Kiss RG, Navarro Estrada JL, Hod H, Kerkar P, Guneri S, Sezer M, Ruda M, Nicolau JC, Cavallini C, Ebrahim I, Petrov I, Kim JH, Jeong MH, Ramos Lopez GA, Laanmets P, Kovar F, Gaudin C, Fanouillere KC, Minini P, Hoffman EB, Moryusef A, Wiviott SD, Sabatine MS; TAO Investigators. **Anticoagulation with otamixaban and ischemic events in non-ST-segment elevation acute coronary syndromes: the TAO randomized clinical trial.** *JAMA.* 310(11):1145-55 I.F.: 29.978

GRANTS FOR RESEARCH IN PROGRESS

Heras M/ M Sabaté. **Red Cardiovascular. CARDIO-ISQ-IDIBAPS.** Funded by: Instituto de Salud Carlos III (ISCIII). RD12/0042/0006.
Duration: 01/01/2013-31/12/2016

Heras M. **HERACLES - Determinantes Genéticos y Ambientales de la Disfunción Vascular en la Hipertensión y Cardiopatía Isquémica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0009/0008.
Duration: 01/01/2007-31/12/2014

Perez-Villa F. Insuficiencia cardiaca con fracción de eyección preservada: Análisis de la relación entre hipertensión pulmonar, disfunción endotelial periférica y metalopreteinasas circulantes. Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01905.
Duration: 01/01/2012-31/12/2014

Rigol M. **Allogeneic adipose tissue-derived stem cells therapy in a porcine model of myocardial infarction: paracrine mechanisms, immune response and functional effects at short and long-term follow-up.** Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 122230.
Duration: 21/01/2013-20/01/2016

Roque M. **Efecto del bloqueo del canal iónico Kv 1.3 en la restenosis y la vasculopatía del injerto.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00225.
Duration: 01/01/2012-31/12/2014

2.2 Arrhythmias, resynchronization and cardiac imaging

LOCATION
CELLEX building

KEYWORDS
1. **Atrial Fibrillation**
2. **Ventricular Tachycardia**
3. **Sudden Death**
4. **Cardiac Imaging**
5. **Resynchronization Therapy**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	120.18	27	11	8
2012	105.86	24	14	3
2013	238.78	35	20	8

TEAM INVOLVED IN
REDINSCOR

AWARDS
2º Premio a la mejor comunicación de la Reunión Anual de la Sección de Electrofisiología y Arritmias. Santander, 17-19/May/2013.
Institution: Sociedad Española de Cardiología.
Awardees: Bisbal F, Guiu E, Cabanas P, Berruezo A, Prat-González S, Vidal B, De Caralt TM, Brugada J, Mont L.

Premio de la Sección de Electrofisiología y Arritmias a la Mejor Comunicación del Congreso de las Enfermedades Cardiovasculares, SEC. Valencia, 24-26/Oct/2013.
Institution: Sociedad Española de Cardiología.
Awardees: A Díaz-Garzón, D Penela, L Aguinaga, J Fernández-Armenta, L Mont, J Brugada, K Zeppenfeld, A Berruezo.

TEAM LEADER
Josep Brugada (HCB)
T. 93 227 57 03
jbrugada@clinic.cat

GROUP LEADERS
Gustavo Egea (UB)
Lluis Mont (HCB)
Marta Sitges (HCB)

RESEARCHERS
Elena Arbelo (HCB)
Antonio Berruezo (HCB)
Teresa M. de Caralt (HCB)
Mª Àngels Castel (HCB)
José Tomás Ortiz (HCB)
Rosario Jesús Perea (HCB)
Bárbara Vidal (HCB)

POST-DOCTORAL RESEARCHERS
David Andreu (FCRB)
Montserrat Batlle (IDIBAPS - FCRB)
Eduard Guasch (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Juan Acosta (FCRB)
Eva Benito (FCRB)
Mireia Calvo (FCRB)
Federico Gómez (FCRB)
Gonzalo Grazioli (HCB)
Aleksandra Mas-Stachurska (HCB – FCRB)
Silvia Montserrat (HCB - FCRB)
Diego Penela (FCRB)
Cira Rubies (FCRB)
Laura Sanchis (HCB)
Maria Sanz (FCRB)

TECHNICIANS
Nadia Castillo (FCRB)

NURSING STAFF
Vanesa Hervas (FCRB)
Sara Hevia (FCRB)
Mariona Matas (HCB)
Raquel Nuñez (FCRB)
Silvia Poyatos (FCRB)
Silvia Vidorreta (FCRB)

ADMINISTRATIVE STAFF
Neus Portella (FCRB)
Gemma Pros (FCRB)

STATISTICIAN
Roger Borras (FCRB)

COLLABORATORS
Bart Bijnens (ICREA, UPF)
Susanna Prat (HCB)
Nuria Soriano (FCRB)
José Mª Tolosana (HCB)

VISITING SCIENTISTS
Andrés A. Díaz Garzón (Argentina)
Viatcheslav Korshunov (European Heart Rhythm Association fellow)
M Emilce Trucco (Argentina)

STRATEGIC OBJECTIVES

The aims for the coming year is to continue and stabilize the six main research lines of the group: genetic in cardiovascular diseases, atrial fibrillation, cardiac resynchronization, ventricular tachycardias, experimental models of etiological factors in atrial fibrillation, and Sports Cardiology. Furthermore, we wish to continue promoting prospective multicenter projects without abandoning practical clinical research, to improve patient care. On the other hand, we will keep on working with the Bioengineering team at the UPF and Galgo Medical in modeling and software development for image processing.

MAIN LINES OF RESEARCH

1. **Cardiovascular genetic diseases:** The group is focused in recruiting patients and following them, in order to analyze prognosis of several genetic arrhythmias. The incorporation of Dr. Elena Arbelo has increased the activity and opened new research projects. Furthermore, genetic testing will continue to be done in collaboration with the group of Dr. Ramón Brugada

2. **Experimental models for the study of etiological factors in atrial fibrillation:**
- We wish to continue analyzing the mechanisms that promote atrial and ventricular fibrosis in the rat model of endurance exercise.

3. **Atrial fibrillation (AF):**
- On one hand we are continuing the study of etiological factors in primary atrial fibrillation.
- Several multicentric studies about new ablation techniques and new antiarrhythmic drugs are in course: EAST, FIRE AND ICE and RAFAELLO.
- We are also developing new ablation approaches based on imaging techniques such as MRI.

4. **Ventricular tachycardia (VT):**
- Multicenter study of antiarrhythmic drugs versus ablation in ischemic patients with automated implantable defibrillators.
- Different prospective studies are being conducted, evaluating the clinical usefulness of epicardial ablation in different substrates.
- Software has been developed to delimit the slow conduction zones within myocardial scars by means of magnetic resonance studies and their fusion with images obtained from three-dimensional navigation systems.
- Siemens has sponsored a prospective study to evaluate remodelling and sudden death risk predictive capacity with MRI and biomarker levels in patients with structural heart disease.

RESEARCH GROUP
CARDIAC IMAGING

TEAM LEADER
Marta Sitges (HCB)

Our group has a pluridisciplinary team of people dedicated to non-invasive cardiac imaging and its application in the knowledge and research into cardiovascular pathophysiology and therapy within the field of cardiac mechanics and remodelling in cardiovascular diseases. Our lines of research include:

- Application of cardiac imaging in the study of cardiac mechanics in patients with cardiac dyssynchrony treated with resynchronisation therapy.
- Study of atrial morphology and function in patients with atrial fibrillation and elite sportsmen and women.
- Study of right ventricular morphology and function in elite athletes at rest and exercising.
- Detection of latent ventricular dysfunction in different disorders such as Chagas disease, cirrhosis of the liver and cardiotoxicity caused by chemotherapy in blood disorders.
- Analysis of post-infarction remodelling using three-dimensional echocardiography and cardiac magnetic resonance imaging.
- Utility of multi-slice CT in the diagnosis of chest pain in Accident and Emergency.
- Non-invasive analysis of endothelial function through ultrasoundof the humeral artery in myocardial infarction patients with pulmonary hypertension.

RESEARCH GROUP
ATRIAL FIBRILLATION BIOPATHOLOGY AND THERAPY

TEAM LEADER
Lluis Mont (HCB)

Our grup is focusing in the study of etiologic factors, with the aim to understand the development of the disease and prevent its development. Furthermore, we are focused in improving therapy improving ablation techniques and participating in multicenter studies pursuing improvements in AF management.

- Analysis of the effects of endurance exercise in a murine model, to study the limits of healthy adaptation to exercise, vs excesive training leading to atrial disease.
- Estudi of the sympathetic/

parasympathetic balance in healthy volunteers, to analyze the relationship of stature and autonomic balance.
- Development of an custom made semiauthomatic software, devoted to identification of fibrosis at the atrial level, to guide ablation.
- Multicenter studies, establishing the usefulness of early rythm management strategy in atrial fibrillation.

RESEARCH GROUP
VASCULAR CELL BIOLOGY

TEAM LEADER
Gustavo Egea (UB)

The main objective of this group is to understand which are the molecular bases impaired in the formation and progression of syndromic aortic aneurysms particularly in Marfan syndrome. In addition, we are also interested in the crosstalk between vascular smooth muscle cells and extracellular matrix in terms of mechano-transduction. On the other hand, we keep on the study about the interaction of the transport intermediaries (vesicles and tubules) with the actin cytoskeleton and lipid homeostasis associated with membrane trafficking at the Golgi apparatus level.

PUBLICATIONS

Originals / I.F.: 238.784

1. Ruschitzka F, Abraham WT, Singh JP, Bax JJ, Borer JS, Brugada J, Dickstein K, Ford I, Gorcsan J 3rd, Gras D, Krum H, Sogaard P, Holzmeister J; EchoCRT Study Group. **Cardiac-resynchronization therapy in heart failure with a narrow QRS complex.** *New Engl J Med.* 369(15):1395-405 (I.F.: 51.658)

2. Nava S, Morales JL, Márquez MF, Barrera F, Gómez J, Colín L, Brugada J, Iturralde P. **Reuse of pacemakers: comparison of short and long-term performance.** *Circulation.* 127(11):1177-1183 I.F.: 15.202

3. Valenzuela-Alcaraz B, Crispi F, Bijnens B, Cruz-Lemini M, Creus M, Sitges M, Bartrons J, Civico S, Balasch J, Gratacós E. **Assisted reproductive technologies are associated with cardiovascular remodeling in utero that persists postnatally.** *Circulation.* 128(13):1442-1450 I.F.: 15.202

4. Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, De Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. **Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies: the OVERCOME trial (preventiOn of left Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive ChemOtherapy for the treatment of Malignant hEmopathies).** *J Am Coll Cardiol.* 61(23):2355-2362 I.F.: 14.086

5. Guasch E, Benito B, Qi X, Cifelli C, Naud P, Shi Y, Mighiu A, Tardif JC, Tadevosyan A, Chen Y, Gillis MA, Iwasaki YK, Dobrev D, Mont L, Heximer S, Nattel S. **Atrial fibrillation promotion by endurance exercise: demonstration and mechanistic exploration in an animal model.** *J Am Coll Cardiol.* 62(1):68-77 I.F.: 14.086

6. Penela D, Van Huls Van Taxis C, Aguinaga L, Fernández-Armenta J, Mont L, Castel MA, Heras M, Tolosana JM, Sitges M, Ordóñez A, Brugada J, Zeppenfeld K, Berruezo A. **Neurohormonal, structural, and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction: a prospective multicenter study.** *J Am Coll Cardiol.* 62(13):1195-202 I.F.: 14.086

7. Esther Bertran; Eva Crosas-Molist; Patricia Sancho; Laia Caja; Judit Lopez-Luque; Estanislao Navarro; Gustavo Egea; Raquel Lastra; Teresa Serrano; Emilio Ramos; Isabel Fabregat. A**utocrine expression of TGF-β confers a mesenchymal phenotype and CXCR4-dependent migratory properties to human hepatocellular carcinoma cells.** *Hepatology* 58:2032-2044 I.F.: 12.003

8. Planavila A, Redondo I, Hondares E, Vinciguerra M, Munts C, Iglesias R, Gabrielli LA, Sitges M, Giralt M, van Bilsen M, Villarroya F. **Fibroblast growth factor 21 protects against cardiac hypertrophy in mice.** *Nat Commun.* 4:2019 I.F.: 10.015

9. Gutiérrez-Martínez E., I. Fernández-Ulibarri, F. Lázaro-Diéguez, E. Martínez-Alonso, S. Pyne, E. Sarri, and G. Egea. **Lipid phosphate phosphatase 3 participates in the transport carrier formation and protein trafficking in the early secretory pathway.** *J Cell Sci* 126:2641-2655 I.F.: 5.877

10. Calvo N, Bisbal F, Guiu E, Ramos P, Nadal M, Tolosana JM, Arbelo E, Berruezo A, Sitges M, Brugada J, Mont L. **Impact of atrial fibrillation-induced tachycardiomyopathy in patients undergoing pulmonary vein isolation.** *Int J Cardiol.* 168(4):4093-4097 I.F.: 5.509

11. Castel MÁ, Roig E, Rios J, Tomas C, Mirabet S, Cardona M, Brossa V, López L, Vargas L, Sionis A, Vallejos I, Pérez-Villa F. **Long-term prognostic value of elevated heart rate one year after heart transplantation.** *Int J Cardiol.* 168(3):2003-2007 I.F.: 5.509

12. Regueiro A, García-Álvarez A, Sitges M, Ortiz-Pérez JT, De Caralt MT, Pinazo MJ, Posada E, Heras M, Gascón J, Sanz G. **Myocardial involvement in Chagas disease: insights from cardiac magnetic resonance.** Int J Cardiol. 165(1):107-112 I.F.: 5.509

13. Sarkozy A, Paparella G, Boussy T, Casado-Arroyo R, Yazaki Y, Chierchia GB, De Asmundis C, Bayrak F, Namdar M, Richter S, Brugada J, Brugada P.

The usefulness of the consensus clinical diagnostic criteria in Brugada syndrome. *Int J Cardiol.* 2013 Sep 10;167(6):2700-2704 I.F.: 5.509

14. Tobaldini E, Brugada J, Benito B, Molina I, Montserrat J, Kara T, Leinveber P, Porta A, Macedo PG, Montano N, Somers VK. **Cardiac autonomic control in Brugada syndrome patients during sleep: the effects of sleep disordered breathing.** *Int J Cardiol.* 168(4):3267-3272 I.F.: 5.509

15. Cinca J, Mendez A, Puig T, Ferrero A, Roig E, Vazquez R, Gonzalez-Juanatey JR, Alonso-Pulpon L, Delgado J, Brugada J, Pascual-Figal D; Investigators of the Spanish Heart Failure Network (REDINSCOR). **Differential clinical characteristics and prognosis of intraventricular conduction defects in patients with chronic heart failure.** *Eur J Heart Fail.* 15(8):877-884 I.F.: 5.247

16. Tolosana JM, Trucco E, Khatib M, Doltra A, Borras R, Castel MÁ, Berruezo A, Arbelo E, Sitges M, Matas M, Guasch E, Brugada J, Mont L. **Complete atrioventricular block does not reduce long-term mortality in patients with permanent atrial fibrillation treated with cardiac resynchronization therapy.** *Eur J Heart Fail.* 15(12):1412-1418 I.F.: 5.247

17. Riuró H, Beltran-Alvarez P, Tarradas A, Selga E, Campuzano O, Vergés M, Pagans S, Iglesias A, Brugada J, Brugada P, Vázquez FM, Pérez GJ, Scornik FS, Brugada R. **A missense mutation in the sodium channel β2 subunit reveals SCN2B as a new candidate gene for Brugada syndrome.** *Hum Mutat.* 34(7):961-966 I.F.: 5.213

18. Salcedo-Sicilia L., S. Granell, M. Jovic, A. Sicart, E. Mato, L. Johannes, T. **Balla and** G. Egea**. PI4P is a major determinant for the association of bIII spectrin to the Golgi complex.** *J Biol Chem* 288:2157-2166 I.F.: 4.651

19. Ortiz-Pérez JT, Riera M, Bosch X, De Caralt TM, Perea RJ, Pascual J, Soler MJ. **Role of circulating angiotensin converting enzyme 2 in left ventricular remodeling following myocardial infarction: a prospective controlled study.** *PLoS One.* 8(4):e61695 I.F.: 3.730

20. Bisbal F, Guiu E, Calvo N, Marin D, Berruezo A, Arbelo E, Ortiz-Pérez J, De Caralt TM, Tolosana JM, Borràs R, Sitges M, Brugada J, Mont L. **Left atrial sphericity: a new method to assess atrial remodeling. Impact on the outcome of atrial fibrillation ablation.** *J Cardiovasc Electrophysiol.* 24(7):752-759 I.F.: 3.475

21. Doltra A, Bijnens B, Tolosana JM, Gabrielli L, Castel MÁ, Berruezo A, Brugada J, Mont L, Sitges M. **Effect of cardiac resynchronization therapy on left ventricular diastolic function: implications for clinical outcome.** *J Card Fail.* 19(12):795-801 I.F.: 3.320

22. Penela D, Bijnens B, Doltra A, Silva E, Castel MA, Berruezo A, Mont L, Weidemann F, Brugada J, Sitges M. **Noncompaction cardiomyopathy is associated with mechanical dyssynchrony: a potential underlying mechanism for favorable response to cardiac resynchronization therapy.** *J Card Fail.* 19(2):80-86 I.F.: 3.320

23. Doménech M, Berruezo A, Molina I, Mont L, Coca A. **Nighttime Ambulatory Blood Pressure is Associated With Atrial Remodelling and Neurohormonal Activation in Patients With Idiopathic Atrial Fibrillation.** *Rev Esp Cardiol.* 66(6):458-463 I.F.: 3.204

24. Evertz R, Merschón F, Berruezo A, Mont L. **Dual ventricular response: another road to supraventricular tachycardia in dual atrioventricular nodal physiology.** *Rev Esp Cardiol.* 66(2):145-146 I.F.: 3.204

25. Rigol M, Solanes N, Fernandez-Armenta J, Silva E, Doltra A, Duchateau N, Barcelo A, Gabrielli L, Bijnens B, Berruezo A, Brugada J, Sitges M. **Development of a swine model of left bundle branch block for experimental studies of cardiac resynchronization therapy.** *J Cardiovasc Transl Res.* 6(4):616-622 I.F.: 3.062

26. Egea G, C. Serra-Peinado, L. Salcedo-Sicilia and E. Gutiérrez-Martínez. **Actin acting at the Golgi.** *Histochem Cell Biol* 140(3):347-360 I.F.: 2.613

27. Partemi S, Batlle M, Berne P, Berruezo A, Campos B, Mont L, Riuró H, Roig E, Pérez-Villa F, Ortiz J, Pascali VL, Oliva A, Brugada R, Brugada J. **Analysis of the arrhythmogenic substrate in human heart failure.** *Cardiovasc Pathol.* 22(2):133-140 I.F.: 2.352

28. Kitada R, Fukuda S, Watanabe H, Oe H, Abe Y, Yoshiyama M, Song JM, Sitges M, Shiota T, Ito H, Yoshikawa J. **Diagnostic accuracy and cost-effectiveness of a pocket-sized transthoracic echocardiographic imaging device.** *Clin Cardiol*36(10):603-10 I.F.: 1.834

29. Campuzano O, Alcalde M, Berne P, Zorio E, Iglesias A, Navarro-Manchón J, Brugada J, Brugada R. **Role of novel DSP_p.Q986X genetic variation in arrhythmogenic right ventricular cardiomyopathy.** *Eur J Med Genet.* 56(10):541-545 I.F.: 1.685

30. Perez-Villa F, Farrero M, Cardona M, Castel MA, Tatjer I, Penela D, Vallejos I. **Bosentan in heart transplantation candidates with severe pulmonary hypertension: efficacy, safety and outcome after transplantation.** *Clin Transplant.* 27(1):25-31 I.F.: 1.634

31. Femenía F, Arce M, Van Grieken J, Trucco E, Mont L, Abello M, Merino JL, Rivero Ayerza M, Gorenek B, Rodriguez C, Hopman WM, Baranchuk A; **Fragmented QRS in Hypertrophic Obstructive Cardiomyopathy (FHOCM) Study Investigators. Fragmented QRS as a predictor of arrhythmic events in patients with hypertrophic obstructive cardiomyopathy.** *J Interv Card Electr.* 38(3):159-165 I.F.: 1.386

32. Cevallos J, Andrea R, Falces C,

Martin-Yuste V, Freixa X, Vidal B, Brugaletta S, Castellá M, Masotti M, Sabaté M. **Transcatheter aortic valve implantation in patients with left main percutaneous coronary intervention.** *J Heart Valve Dis.* 22(6):874-877 (I.F.: 1.071

33. Andrea R, Falces C, Sanchis L, Sitges M, Heras M, Brugada J. **[Diagnosis of heart failure with preserved or reduced ejection fraction in a one-stop clinic].** *Aten Primaria.* 45(4):184-192 I.F.: 0.957

34. Sarquella-Brugada G, Campuzano O, Iglesias A, Sánchez-Malagón J, Guerra-Balic M, Brugada J, Brugada R. **Genetics of sudden cardiac death in children and young athletes.** *Cardiol Young.* 23(2):159-173 I.F.: 0.948

35. Fernández-Armenta J, Berruezo A, Andreu D, Camara O, Silva E, Serra L, Barbarito V, Carotenutto L, Evertz R, Ortiz-Pérez JT, De Caralt TM, Perea RJ, Sitges M, Mont L, Frangi A, Brugada J. **hree-dimensional architecture of scar and conducting channels based on high resolution ce-CMR: insights for ventricular tachycardia ablation.** *Circ Arrhythm Electrophysiol.* 6(3):528-537 I.F.: 0.871

Reviews / I.F.: 19.800

1. Campuzano O, Alcalde M, Allegue C, Iglesias A, García-Pavía P, Partemi S, Oliva A, Pascali VL, Berne P, Sarquella-Brugada G, Brugada J, Brugada P, Brugada R. **Genetics of arrhythmogenic right ventricular cardiomyopathy.** *J Med Genet.* 50(5):280-289 I.F.: 5.703

2. Brugada P, Brugada J, Roy D. **Brugada syndrome 1992-2012: 20 years of scientific excitement, and more.** *Eur Heart J.* 34(47):3610-3615 I.F.: 14.097

Editorials / I.F.: 36.528

1. Fernández-Lozano I, Brugada J. **Right bundle branch block: are we looking in the right direction?** *Eur Heart J.* 34(2):86-88 I.F.: 14.097

2. Bosch X, Sitges M, Rovira M, Ortiz-Pérez JT, Esteve J. Reply: **Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies.** *J Am Coll Cardiol.* 62(25):2452 I.F.: 14.086

3. Gay-Jordi G, Guash E, Benito B, Brugada J, Nattel S, Mont L, Serrano-Mollar A. **Losartan prevents heart fibrosis induced by long-term intensive exercise in an animal model.** *PLoS One.* 2013;8(2):e55427 I.F.: 3.730

4. Evertz R, Mont L. **Differential diagnosis between dual ventricular response and bigeminy arising from the bundle of his.** *Rev Esp Cardiol.* 66(6):515-516 I.F.: 3.204

5. Evertz R, Arbelo E, Mont L. **Rapid palpitations: three of a kind?** *Neth Heart J.* 21(10):472 I.F.: 1.411

Clinical Guidelines / I.F. 30.641

1. Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, Blom N, Brugada J, Chiang CE, Huikuri H, Kannankeril P, Krahn A, Leenhardt A, Moss A, Schwartz PJ, Shimizu W, Tomaselli G, Tracy C. **HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes:document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013.** *Heart Rhythm.* 10(12):1932-1963 I.F.: 5.045

2. Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, Janousek J, Abrams D, Bauersfeld U, Brugada R, Drago F, de Groot N, Happonen JM, Hebe J, Yen Ho S, Marijon E, Paul T, Pfammatter JP, Rosenthal E; European Heart Rhythm Association; Association for European Paediatric and Congenital Cardiology. **Pharmacological and non-pharmacological therapy for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement.** *Europace.* 15(9):1337-1382 I.F.: 2.765

3. Blomström Lundqvist C, Auricchio A, Brugada J, Boriani G, Bremerich J, Cabrera JA, Frank H, Gutberlet M, Heidbuchel H, Kuck KH, Lancellotti P, Rademakers F, Winkels G, Wolpert C, Vardas PE; European Association of Cardiovascular Imaging; Council of Cardiovascular Imaging; European Society of Cardiac Radiology. **The use of imaging for electrophysiological and devices procedures: a report from the first European Heart Rhythm Association Policy Conference, jointly organized with the European Association of Cardiovascular Imaging (EACVI), the Council of Cardiovascular Imaging and the European Society of Cardiac Radiology.** Europace. 15(7):927-36 I.F.: 2.765

4. Kirchhof P, Breithardt G, Aliot E, Al Khatib S, Apostolakis S, Auricchio A, Bailleul C, Bax J, Benninger G, Blomstrom-Lundqvist C, Boersma L, Boriani G, Brandes A, Brown H, Brueckmann M, Calkins H, Casadei B, Clemens A, Crijns H, Derwand R, Dobrev D, Ezekowitz M, Fetsch T, Gerth A, Gillis A, Gulizia M, Hack G, Haegeli L, Hatem S, Georg Häusler K, Heidbüchel H, Hernandez-Brichis J, Jais P, Kappenberger L, Kautzner J, Kim S, Kuck KH, Lane D, Leute A, Lewalter T, Meyer R, Mont L, Moses G, Mueller M, Münzel F, Näbauer M, Nielsen JC, Oeff M, Oto A, Pieske B, Pisters R, Potpara T, Rasmussen L, Ravens U, Reiffel J, Richard-Lordereau I, Schäfer H, Schotten U, Stegink W, Stein K, Steinbeck G, Szumowski L, Tavazzi L, Themistoclakis S, Thomitzek K, Van Gelder IC, von Stritzky B, Vincent A, Werring D, Willems S, Lip GY, Camm AJ. **Personalized management of atrial fibrillation: Proceedings from the fourth Atrial Fibrillation competence NETwork/European Heart Rhythm Association consensus conference.** *Europace.* 15(11):1540-1556 I.F.: 2.765

5. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, Cleland J, Deharo JC, Delgado V, Elliott PM, Gorenek B, Israel CW, Leclercq C, Linde C, Mont L, Padeletti L, Sutton R, Vardas PE; ESC Committee for Practice Guidelines (CPG), Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, Kirchhof P, Blomstrom-Lundqvist C, Badano LP, Aliyev F, Bänsch D, Baumgartner H, Bsata W, Buser P, Charron P, Daubert JC, Dobreanu D, Faerestrand S, Hasdai D, Hoes AW, Le Heuzey JY, Mavrakis H, McDonagh T, Merino JL, Nawar MM, Nielsen JC, Pieske B, Poposka L, Ruschitzka F, Tendera M, Van Gelder IC, Wilson CM. **2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J**.34(29):2281-2329 I.F.: 14.097

6. Autores/miembros del Grupo de Trabajo, Camm AJ, Lip GY, Caterina RD, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P; Comité de la ESC de Guías para la Práctica Clínica (CGPC), Bax JJ, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Popescu BA, Reiner Z, Sechtem U, Anton Sirnes P, Tendera M, Torbicki A, Vahanian A, Windecker S; Revisores del documento, Vardas P, Al-Attar N, Alfieri O, Angelini A, Blömstrom-Lundqvist C, Colonna P, De Sutter J, Ernst S, Goette A, Gorenek B, Hatala R, Heidbüchel H, Heldal M, Dalby Kristensen S, Kolh P, Le Heuzey JY, Mavrakis H, Mont L, Perrone Filardi P, Ponikowski P, Prendergast B, Rutten FH, Schotten U, Van Gelder IC, Verheugt FW. **Actualización de las guías de la Sociedad Europea de Cardiología (ESC) para el manejo de la fibrilación auricular de 2010 Elaborada en colaboración con la Asociación Europea del Ritmo Cardiaco.** *Rev Esp Cardiol.* 66(1):54.e1-54.e24 I.F.: 3.204

Multicenter / I.F.: 18.887

1. Lalani T, Chu VH, Park LP, Cecchi E, Corey GR, Durante-Mangoni E, Fowler VG Jr, Gordon D, Grossi P, Hannan M, Hoen B, Muñoz P, Rizk H, Kanj SS, Selton-Suty C, Sexton DJ, Spelman D, Ravasio V, Tripodi MF, Wang A; **International Collaboration on Endocarditis–Prospective Cohort Study Investigators. In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis.** *JAMA Intern Med.* 173(16):1495-1504 I.F.: 10.579

2. Chirouze C, Athan E, Alla F, Chu VH, Ralph Corey G, Selton-Suty C, Erpelding ML, Miro JM, Olaison L, Hoen B; International Collaboration on Endocarditis Study Group. **Enterococcal endocarditis in the beginning of the 21st century: analysis from the International Collaboration on Endocarditis-Prospective Cohort Study.** *Clin Microbiol Infect.* 19(12):1140-1147 I.F.:4.578

3. Chambers ST, Murdoch D, Morris A, Holland D, Pappas P, Almela M, Fernández-Hidalgo N, Almirante B, Bouza E, Forno D, del Rio A, Hannan MM, Harkness J, Kanafani ZA, Lalani T, Lang S, Raymond N, Read K, Vinogradova T, Woods CW, Wray D, Corey GR, Chu VH; International Collaboration on Endocarditis Prospective Cohort Study Investigators. **HACEK infective endocarditis: characteristics and outcomes from a large, multi-national cohort.** *PLoS One.* 8(5):e63181 I.F.: 3.730

GRANTS FOR RESEARCH IN PROGRESS

Berruezo A. **Identificación, análisis y eliminación de canales de conducción para tratar arritmias ventriculares.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/02049. Duration: 01/01/2012-31/12/2014

Brugada J. **cvREMOD: Convergencia de tecnologías médicas para la gestión integral del remodelado vascular.** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI). 09/370. Duration: 09/09/2009-31/12/9998

Brugada J. **Comparative Effectiveness Research to Assess the Use of Primary ProphylacTic Implantable Cardioverter Defibrillators in EUrope.** Sponsored by: European Commission. 602299-2. Duration: 01/10/2013-30/09/2017

Brugada J. **Red Cardiovascular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0042/0044. Duration: 01/01/2013-31/12/2016

Brugada J. **REDINSCOR - Red de Investigación en Insuficiencia Cardíaca en España.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0003/0008. Duration: 01/01/2007-30/06/2014

Brugada J. **Arítmies i estimulació cardiaca.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1104. Duration: 05/08/2009-30/04/2014

Brugada J. **An Intelligent Platform for Personalized Remote Monitoring of the Cardiac Patients with Electronic Implant Devices.** Sponsored by: European Commission. 248240. Duration: 01/02/2010-31/01/2014

Brugada J. **Sudden cardiac death: definig clinical algorithms for a thorough investigation.** Sponsored by: CNIC. CNIC-03-2008. Duration: 21/11/2008-31/12/2013

Brugada J. **Integración de las diferentes técnicas de imagen médica en una única imagen multimodal. Desarrollo de distintos modelos de aplicación. Estudios electrofisiológicos y de imagen cardiaca.** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI). CDTEAM1.
Duration: 11/01/2006-11/01/2013

Castel M.A. **Optimización de la terapia de resincronización cardiaca mediante el QRS: valoración del efecto agudo y la respuesta a medio plazo.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01569.
Duration: 01/01/2011-31/03/2014

Mont L. **Estudi de la teràpia de resincronització a Catalunya.**
Sponsored by: Agència d'Avaluació de Tecnologia Medica (AATM). 154/4/2008.
Duration: 01/12/2009-31/12/2014

Mont L. **Estudio del remodelado miocárdico en un modelo animal crónico de síndrome de apnea-hipopnea del sueño.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00834.
Duration: 01/01/2011-31/12/2013

Sitges M. **cvREMOD: Convergencia de tecnologías médicas para la gestión integral del remodelado vascular.**
Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI). 09/370.
Duration: 09/09/2009-31/12/9998

Sitges M. **Efecto del entrenamiento crónico sobre el ventrículo derecho:análisis por imagen de la deformación miocárdica en humanos e histopatología en modelos experimentales murinos.** Sponsored by: Ministerio de Economía y Competitividad. DEP2010-20565.
Duration: 01/01/2011-31/12/2014

Vidal B. **Factores anatómicos y tisulares predictores de éxito en la ablación de la fibrilación auricular.**
Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/02003.
Duration: 01/01/2012-31/12/2014

DOCTORAL THESES

Berruezo A., Mont L. **Utilidad de la resonancia magnética con realce tardío en la ablación de arritmias ventriculares. PhD student: Andreu Caballero David Egea G. Función de la fosfatasa de fosfolípidos 3 (LPP3) en las etapas tempranas de la vía secretora.**
PhD student: Enrique Gutiérrez Martínez

Mont L. **Análisis sistemático de las diferentes estrategias de tratamiento en la práctica clínica habitual e impacto de la instauración de protocolos de actuación para el tratamiento de la fibrilación auricular.**
PhD student: Naiara Calvo Galiano

2.3 Nephro-urological diseases and kidney transplantation

LOCATION
CELLEX building

KEYWORDS
1. **Chronic allograft dysfunction**
2. **Dialysis**
3. **Immunosupression**
4. **Posttransplant cancer**
5. **Renal regeneration**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	63.97	20	7	6
2012	84.61	25	13	5
2013	107.72	22	16	4

TEAM INVOLVED IN
REDinREN

TEAM LEADER
Josep Mª Campistol (HCB)
T. 93 227 54 00 (Ext.: 3395)
jmcampis@clinic.cat

GROUP LEADER
Ignacio Revuelta (HCB - IDIBAPS)

RESEARCHERS
Aleix Cases (HCB)
Fritz Diekmann (HCB - IDIBAPS)
Georgina Hotter (IIBB-CSIC)
Federico Oppenheimer (HCB)
Esteban Poch (HCB)
Luis F. Quintana (HCB)

POST-DOCTORAL RESEARCHERS
Elisenda Banón-Maneus (FCRB)
María José Ramírez-Bajo (IDIBAPS)
Jordi Rovira (FCRB - IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Marta Arias (HCB)
Sebastián Azorín (HCB)
Miquel Blasco (HCB)
Marta Lazo (FCRB)
Joan Nistal (FCRB)
Marina Ventayol (IIBB-CSIC)

TECHNICIANS
Natalia Hierro (IDIBAPS)
Daniel Moya-Rull (FCRB)

COLLABORATORS
Pilar Arrizabalaga (HCB)
Celia Bádenas (FCRB)
Albert Botey (HCB)
Federico Cofán (HCB)
Guadalupe Ercilla (HCB)
Nuria Esforzado (HCB)
Nestor Fontseré (HCB)
Francesc Maduell (HCB)
Jaume Martorell (HCB)
Eduard Mirapeix (HCB)
Maria J. Ricart (HCB)
Anna M Sola (IIBB-CSIC)
Vicenç Torregrosa (HCB)
Manel Vera (HCB)
José Luis Viñas (IIBB-CSIC)

STRATEGIC OBJECTIVES

The multidisciplinary nature of our research group stems from well-balanced collaboration between clinicians and medical researchers, biologists, biochemists, veterinarians and specialist technicians. The LENIT performs translational research to broaden the knowledge of various renal diseases, which sometimes require replacement therapies such as dialysis or kidney transplantation, in addition to side effects caused by the treatments themselves. This knowledge will enable us to personalize and improve current therapies and to discover new ways of action. Scientific objectives of LENIT are focused on the following areas of research: i) chronic graft dysfunction: etiopathogenic factors and biomarkers in urine; II) mTOR signaling: immunosuppression, proteinuria, cardiovascular disease and side effects of the application of mTOR inhibitors; III) The role of immunosuppression and immunosuppressive medications in posttransplantation oncogenesis; IV) Identification of new uremic toxins; immunology of transplantation (V); cell therapy and renal regeneration (VI) and primary glomerular diseases (VII).

MAIN LINES OF RESEARCH

i) Chronic allograft dysfunction (CAD): etiopathogenic factors and biomarkers in urine
The main goal has been the search for urinary biomarkers that allow early diagnosis of CAD. One of the proteins identified was Wnt1 one of the ligands of the Wnt signaling/β-catenin. This line was developed through four FIS projects already completed and Dr. Campistol got new one in which it is intended to modulate Wnt/β-catenin signaling in preventing the progression of CAD in animal models and its potential clinical application in humans.

ii) mTOR signaling: immunosuppression, proteinuria, cardiovascular disease and side effects of the application of mTOR inhibitors
The objective is to evaluate the pathogenic mechanisms of proteinuria associated with treatment of mTOR inhibitors due to a possible malfunction of the glomerular endothelium using various experimental models of chronic renal failure and renal transplant. The inhibition of mTOR pathway may provide an alternative to calcineurin inhibitor-based therapies, which is associated with increased nephrotoxicity, incidence of cardiovascular disease and cancer in transplant patients. Moreover, the regulation of the mTOR pathway represents a cornerstone in the development of cardiovascular disease.

iii) The role of immunosuppression and immunosuppressive medications in posttransplantation oncogenesis
The main objective is to study the impact of exosomes from tumor cells on proliferation, angiogenesis and development of premethastatic niche and their involvement in tumor progression, migration and metastasis of malignant tumors in patients undergoing different immunosuppressive regimens after kidney transplantation.

iv) Identification of new uremic toxins
The main objective is the detection of new uremic toxins using proteomic techniques. Assess the different purification capacity of the dialysis techniques.

v) Immunology of transplantation
The objective is to study the role of T and B cell subsets during acute and chronic humoral rejection in kidney transplant patients. Characterization and monitoring of B cell subsets in kidney transplant patients which are treated for an acute antibody-mediated rejection.

vi) Cell therapy and renal regeneration
The main objective is to analyze the role of mesenchymal stem cells and their microvesicles on in vitro and in vivo models that reproduce the kidney damage by nephrotoxicity or during graft rejection. Moreover, the study of nephrogenesis by the generation of ureteric bud structures and the correction of monogenic kidney diseases in vitro.

vii) Primary glomerular diseases
The goal is the search for biomarkers plasma and/or urine that allow early diagnosis and non-invasive to improve the management of these patients.

50/50 PROGRAM

TRANSLATIONAL RESEARCH IN POSTTRASPLANT NEOPLASIA

GROUP LEADER
Ignacio Revuelta (HCB-IDIBAPS)

The effect of the immunosuppressive therapy in tumour immune escape and in several oncogenic pathways lead to tumoral progression, angiogenesis and pre-metastatic niche formation. Exosomes released from cancer cells (CaEx) are crucial for intercellular communication between primary tumour, microenvironment and host organs. CaEx role in posttransplant neoplasms is unknown. He aims to characterize CaEx under different immunosuppressive treatments and the relationship with immune, stromal and pre-metastatic cells. Understanding how CaExs work will give us tools for future interventions in posttransplant malignancies without losing effectiveness of immunotherapy, improving patient survival.

PUBLICATIONS

Originals / I.F.: 107.722

1. Xia Y, Nivet E, Sancho-Martinez I, Gallegos T, Suzuki K, Okamura D, Wu MZ, Dubova I, Esteban CR, Montserrat N, Campistol JM, Izpisua Belmonte JC. **Directed differentiation of human pluripotent cells to ureteric bud kidney progenitor-like cells.** *Nat Cell Biol.* 15(12):1507-1515 I.F.: 20.761

2. Borges FT, Melo SA, Ozdemir BC, Kato N, Revuelta I, Miller CA, Gattone VH 2nd, Lebleu VS, Kalluri R. **TGF-β1-Containing Exosomes from Injured Epithelial Cells Activate Fibroblasts to Initiate Tissue Regenerative Responses and Fibrosis.** *J Am Soc Nephrol* 24(3): 385-392 I.F.: 8.987

3. Maduell F, Moreso F, Pons M, Ramos R, Mora-Macià J, Carreras J, Soler J, Torres F, Campistol JM, Martinez-Castelao A; **ESHOL Study Group. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients.** J *Am Soc Nephrol.* 24(3):487-497 I.F.: 8.987

4. Lopez-Hellin J, Cantarell C, Jimeno L, Sanchez-Fructuoso A, Puig-Gay N, Guirado L, Vilariño N, Gonzalez-Roncero FM, Mazuecos A, Lauzurica R, Burgos D, Plumed JS, Jacobs-Cacha C, Jimenez C, Fernandez A, Fernandez-Alvarez P, Torregrosa V, Nieto JL, Meseguer A, Alonso A; GREAT Study Group. **A form of apolipoprotein a-I is found specifically in relapses of focal segmental glomerulosclerosis following transplantation.** *Am J Transplant.* 13(2):493-500 I.F.: 6.192

5. Tedesco-Silva H, Kho MM, Hartmann A, Vitko S, Russ G, Rostaing L, Budde K, Campistol JM, Eris J, Krishnan I, Gopalakrishnan U, Klupp J. **Sotrastaurin in calcineurin inhibitor-free regimen using everolimus in de novo kidney transplant recipients.** *Am J Transplant.* 13(7):1757-1768 I.F.: 6.192

6. Eggenhofer E, Rovira J, Sabet-Baktach M, Groell A, Scherer MN, Dahlke MH, Farkas SA, Loss M, Koehl GE, Lang SA, Melter M, Schlitt HJ, Geissler EK, Kroemer A. **Unconventional RORγt+ T cells drive hepatic ischemia reperfusion injury.** *J Immunol.* 191(1):480-7 I.F.: 5.520

7. Sabet-Baktach M, Eggenhofer E, Rovira J, Renner P, Lantow M, Farkas SA, Malaisé M, Edtinger K, Shaotang Z, Koehl GE, Dahlke MH, Schlitt HJ, Geissler EK, Kroemer A. **Double deficiency for RORγt and T-bet drives Th2-mediated allograft rejection in mice.** *J Immunol.* 191(8):4440-4446 I.F.: 5.520

8. Moissl U, Arias-Guillén M, Wabel P, Fontseré N, Carrera M, Campistol JM, Maduell F. **Bioimpedance-guided fluid management in hemodialysis patients.** *Clin J Am Soc Nephrol.* 8(9):1575-1582 I.F.: 5.068

9. Diekmann F, Campistol JM, Rovira J, Budde K, Neumayer HH, Oppenheimer F, Flechner SM. **Treatment with sirolimus is associated with less weight gain after kidney transplantation.** *Transplantation* 96(5):480-486 (I.F.: 3.781)

10. Flechner SM, Gurkan A, Hartmann A, Legendre CM, Russ GR, Campistol JM, Schena FP, Hahn CM, Li H, Korth-Bradley JM, Tai SS, Schulman SL. **A randomized, open-label study of sirolimus versus cyclosporine in primary de novo renal allograft recipients.** *Transplantation* 95(10):1233-1241 I.F.: 3.781

11. Musquera M, Pérez M, Peri L, Esforzado N, Sebastià MC, Paredes D, Ribal MJ, Oppenheimer F, Campistol JM, Alcaraz A. **Kidneys from donors with incidental renal tumors: should they be considered acceptable option for transplantation?** *Transplantation* 95(9):1129-1133 I.F.: 3.781

12. Pascual J, Jiménez C, Franco A, Gil M, Obrador-Mulet AR, Gentil MA, Romero R, Grinyó JM, Hernández D, Morales JM, Pallardó LM, Serón D, Arias M, Campistol JM; ANEMIART Study Group. **Early-onset anemia after kidney transplantation is an independent factor for graft loss: a multicenter, observational cohort study.** *Transplantation* 96(8):717-725 I.F.: 3.781

13. Rovira J, Sabet-Baktach M, Eggenhofer E, Lantow M, Koehl GE, Schlitt HJ, Campistol JM, Geissler EK, Kroemer A. **A color-coded reporter model to study the effect of immunosuppressants on CD8+ T-cell memory in antitumor and alloimmune responses.** *Transplantation* 95(1):54-62 I.F.: 3.781

14. Viñas JL, Ventayol M, Brüne B, Jung M, Sola A, Pi F, Mastora C, Hotter G. **miRNA let-7e modulates the Wnt pathway and early nephrogenic markers in mouse embryonic stem cell differentiation.** *PLoS One* 8(4):e60937 I.F.: 3.730

15. Maduell F, Ramos R, Palomares I, Martín-Malo A, Molina M, Bustamante J, Pérez-García R, Grassmann A, Merello JI; ORD Group. **Impact of targeting Kt instead of Kt/V.** *Nephrol Dial Transplant.* 2013 Oct; 28(10):2595-2603 I.F.: 3.371

16. Gatica R, Bertinat R, Silva P, Carpio D, Ramírez MJ, Slebe JC, San Martín R, Nualart F, Campistol JM, Caelles C, Yáñez AJ. **Altered expression and localization of insulin receptor in proximal tubule cells from human and rat diabetic kidney.** *J Cell Biochem* 114(3):639-649 I.F.: 3.062

17. Fuster D, Depetris M, Torregrosa JV, Squarcia M, Paschoalin RP, Mayoral M, Granados U, Colletti PM, Rubello D, Pons F. **Advantages of pinhole collimator double-phase scintigraphy with 99mTc-MIBI in secondary hyperparathyroidism.** *Clin Nucl Med* 38(11):878-881 I.F.: 2.955

18. Martí J, Fuster J, Solà AM, Hotter G, Molina R, Pelegrina A, Ferrer J, Deulofeu R, Fondevila C, García-Valdecasas JC. **Prognostic value of serum neutrophil gelatinase-associated lipocalin in metastatic and nonmetastatic colorectal cancer.** *World J Surg* 37(5):1103-1109 I.F.: 2.228

19. Maduell F, Arias M, Massó E, Fontseré N, Carrera M, Vera M, Cases A, Campistol JM. **Sensitivity of blood volume monitoring for fluid status assessment in hemodialysis patients.** *Blood Purif* 35(1-3):202-208 I.F.: 2.062

20. Marco H, Mirapeix E, Arcos E, Comas J, Ara J, Gil-Vernet S, Puig J, Vinyas O, Perello M, Oppenheimer F, Poveda R, Ibernón M, Díaz M, Ballarin J; Catalan Study Group of Glomerular Diseases (GLOMCAT). **Long-term outcome of antineutrophil cytoplasmic antibody-associated small vessel vasculitis after renal transplantation.** *Clin Transplant* 27(3):338-347 I.F.: 1.634

21. Fontseré N, Mestres G, Barrufet M, Burrel M, Vera M, Arias M, Masso E, Cases A, Maduell F, Campistol JM. **Practical utility of thermodilution versus doppler ultrasound to measure hemodialysis blood access flow.** *Nefrologia* 33(3):325-332 I.F.: 1.274

22. Herrero JA, López-Gómez JM, Maduell F, Martín-de Francisco ÁL, Martín-Malo A, Martínez-Castelao A, Navarro-González JF, Pérez-Fontán M, Pérez J, Selgas R, Solozabal C. **Activation of vitamin D receptors in the optimization of hyperparathyroidism secondary to dialysis.** *Nefrologia* 33(4):571-584 I.F.: 1.274

Reviews / I.F.: 2.548

1. Torregrosa JV, Barros X. Management of hypercalcemia after renal transplantation. Nefrologia 33(6):751-7 I.F.: 1.274

2. Campistol JM, Arias M, Ariceta G, Blasco M, Espinosa M, Grinyó JM, Praga M, Torra R, Vilalta R, Rodríguez de Córdoba S. **An update for atypical haemolytic uraemic syndrome: diagnosis and treatment. A consensus document.** *Nefrologia* 33(1):27-45 I.F.: 1.274

GRANTS FOR RESEARCH IN PROGRESS

Campistol J.M. **LENIT (Laboratori Experimental de Nefrologia i Transplantament).** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1125. Duration: 20/07/2009-30/04/2014

Campistol J.M. **Análisis de biomarcadores urinarios en la disfunción crónica del injerto: estudio de validación e implicación de la vía WNT/BETA-CATENINA.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/0281. Duration: 01/01/2010-30/06/2013

Campistol J.M. **Red de investigación renal.** Sponsored by: Instituto de Salud Carlos III. RD12/0021/0028. Duration: 01/01/2013-31/12/2016

Campistol J.M. **Proteomic analysis of transthyretin post-translational modifications as a disease activity marker in TTR-hereditary amyloidosis: a case-control study.** Sponsored by: Fundació La Marató de TV3. 101430. Duration: 03/02/2011-02/02/2015

Campistol JM, **Análisis proteómico de modificaciones post-traduccionales de la transtiretina como marcador de actividad en pacientes con amiloidosis hereditaria por mutación de la TTR: un estudio caso-control.** Sponsored by: Fundació La Marató - TV3 (101430). Duration: 2011-2013

Campistol J.M. **Remodelación tisular en el rechazo crónico.** Sponsored by: Fundacion de Investigacion Medica Mutua Madrileña. AP92582011. Duration: 26/11/2011-25/11/2014

Campistol J.M. **Caracterización de la transición epitelio-mesenquimal (TEM) mediada por TGF-B y la relación con Wnt/B-catenina en DCI en in vitro.** Sponsored by: Sociedad Española Trasplante (SET). SET_ASTELLAS_01. Duration: 21/12/2013-20/12/2014

Diekmann F. **Inhibición de JAK3, de PKC, de proteasas y de mTOR en el rechazo humoral.** Sponsored by: Instituto de Salud Carlos III. PI11/01112. Duration: 01/01/2012-31/12/2014.

Quintana Porras LF. **Generation of induced pluripotent stem cells (iPS) lines from patients with genetic renal involvement: targeting and modeling renal diseases in vitro.** Sponsored by: Fundació Marató TV3 (121331). Duration: 01/01/2013-31/12/2015

Hotter G. **Bioregeneració i micromonitorització hipóxica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1074. Duration: 29/07/2009-30/04/2014

DOCTORAL THESES

Hotter G, Viñas JL.. **Paper del miRNA en la diferenciació de les cèl·lules mare.** PhD student: Marina Ventayol Espinazo.

2.4 Hypertension, lipids and cardiovascular risk

LOCATION
CELLEX building

KEYWORDS
1. **Nutrition**
2. **Mediterranean diet**
3. **Cardiovascular disease**
4. **Cardiovascular risk factors**
5. **Cognition**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	78.21	22	9	10
2012	131.94	33	20	12
2013	186.04	30	28	2

TEAM INVOLVED IN
CIBEROBN

AWARDS
2013 Dr. Carles Martí Hennenberg Award for Scientific Career in Nutrition.
Institution: Instituto Danone
Awardee/s: Emilio Ros

TEAM LEADER
Emili Ros (HCB)
T. 93 227 93 83
eros@clinic.cat

RESEARCHERS
Antonio Coca (HCB)
Ramón Estruch (HCB)
Ferran Masanes (HCB)
Emilio Sacanella (HCB)
Cristina Sierra (HCB)
Daniel Zambón (HCB)

POST-DOCTORAL RESEARCHERS
Sara Arranz (ISCIII)
Gemma Chiva (FBG-UB)
Montserrat Cofán (ISCIII)
Aleix Sala-Vila (ISCIII)

PRE-DOCTORAL RESEARCHERS
Rosa Casas (ISCIII)
Mònica Doménech (ISCIII/FCRB)
Palmira Valderas (UB)
Cinta Valls (FCRB)

NURSING STAFF
Laia de Lama (FCRB)
Anna López (FCRB)

DIETITIANS
Ana Mª Pérez-Heras (FCRB)
Irene Roth (FCRB)
Mercè Serra (FCRB)
Conxa Viñas (ISCIII)

STATISTICIAN
Emili Corbella (IDIBELL)

COLLABORATORS
Núria Bargalló (HCB)
Maria Teresa de Caralt (HCB)
Miquel Camafort (HCB)
Rosa Gilabert (HCB)
Isabel Núñez (HCB)

STRATEGIC OBJECTIVES

Our general aim is to gain in-depth knowledge of the nutritional determinants of arterial hypertension, dyslipidemia, obesity, diabetes, cardiovascular diseases and age-related cognitive decline.
The group's main research lines are:

1. Dietary factors, in particular the Mediterranean diet and its components, as determinants of healthy aging and reduced risk of chronic diseases, such as cardiovascular diseases, diabetes, cognitive impairment and dementia, and their intermediate biomarkers
2. Genetic characterization of hypertension and dyslipidemia.
3. Vascular imaging for detection of preclinical atherosclerosis.
4. Intestinal absorption and synthesis of cholesterol.
5. Fatty acid profiles in blood cell membranes and their associations with diet and cardiovascular risk phenotypes.
6. Health effects of moderate consumption of wine and beer.
7. The PREDIMED-PLUS study, a large, 6-year randomized trial of lifestyle intervention for primary cardiovascular prevention through weight loss with Mediterranean diet and physical activity in subjects with metabolic syndrome, launched in 2013 (launched 2013).

MAIN LINES OF RESEARCH

1. Assessment of carotid artery IMT and plaque by sonography in: a) subjects at high cardiovascular risk, b) pre-diabetes; c) healthy older persons. Associations with conventional and emergent risk factors and dietary biomarkers, including blood unsaturated fatty acids and phytosterols. Influence of diet on carotid atheroma plaque vulnerability evaluated by sequential MRI.

2. Circadian patterns, arterial pressure variability and target organ damage. Sensitivity to salt, inflammation, and atrial fibrillation in hypertension.

3. Study of candidate genes for: a) autosomal dominant hypercholesterolemia without known genetic defects, b) risk of stroke in hypertension, c) risk of heart failure in hypertensive patients.

4. Age-associated cognitive impairment in participants in the PREDIMED study after 5 years of intervention with Mediterranean diets or a control diet.

5. Effect of hypercholesterolemia of different origin and severity on cognitive function as assessed by neuropsychological tests and functional brain MRI.

6. Cholesterol absorption and synthesis evaluated by determination of plasma non-cholesterol sterol levels using gas chromatography: measurement, genetic conditioning factors, influence on cardiovascular risk, and relationship with lipid response to phytosterols, ezetimibe and statins.

7. Influence of plant and marine omega-3 fatty acids on progression of carotid atherosclerosis by B-mode ultrasound and carotid plaque vulnerability by MRI in subjects at high vascular risk; and on 6-months post-ischemic myocardial recovery by MRI-assessed changes in infarct size in myocardial infarction survivors.

8. Study of a) pathologic progression of Alzheimer's disease (AD) in relation to the proportion of omega-3 fatty acids in phospholipids of different areas of post-mortem brain samples of AD patients, b) fatty acid profile in circulating lipids and/or cerebrospinal fluid (CSF) as predictor of the evolution of cognitive decline and development of AD.

9. Membrane omega-3 fatty acid enrichment as a factor influencing the organization of membrane microdomains, ensuing changes on virus infectivity and development of cardiometabolic diseases.

10. Effect of diet supplementation with walnuts for 2 years on cognitive function, the integrity of the retina, telomere length, and markers of inflammation, oxidation and cardiovascular risk in old people (WAHA Study).

11. Coordination of a randomized trial of lifestyle intervention for primary cardiovascular prevention through weight loss with Mediterranean diet and physical activity in subjects with metabolic syndrome (PREDIMED -PLUS study).

12. Study of the effects of moderate wine and beer consumption and other polyphenol-rich products such as tomatoes on the primary prevention of cardiovascular disease and other degenerative disorders.

PUBLICATIONS

Originals:/ I.F.: 186.04

1. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Martínez-González MA, for the PREDIMED Study Investigators. **Primary prevention of cardiovascular disease with a Mediterranean diet.** *N Engl J Med.* 368(14):1279-90. I.F.: 51.658

2. Corella D, Carrasco P, Sorlí JV, Estruch R, Rico-Sanz J, Martínez-González MA, Salas-Salvadó J, Covas MI, Coltell O, Arós F, Lapetra J, Serra-Majem L, Ruíz-Guiterrez V, Warnberg J, Fiol M, Pintó X, Ortega-Azorín C, Muñoz MA, Martínez JA, Gómez-Gracia E, González JI, Ros E, Ordovás JM. **Mediterranean Diet Reduces the Adverse Effect of the TCF7L2-rs7903146 Polymorphism on Cardiovascular Risk Factors and Stroke Incidence: A randomized controlled trial in a high-cardiovascular-risk population.** *Diabetes Care* 36(11):3803-3811 I.F.: 7.735

3. Gea A, Beunza JJ, Estruch R, Sánchez-Villegas A, Salas-Salvadó J, Buil-Cosiales P, Gómez-Gracia E, Covas MI, Corella D, Fiol M, Arós F, Lapetra J, Lamuela-Raventós RM, Wärnberg J, Pintó X, Serra-Majem L, Martínez-González MA; PREDIMED GROUP. **Alcohol intake, wine consumption and the development of depression: the PREDIMED study.** *BMC Med* 11:192 I.F.: 6.679

4. Guasch-Ferré M, Bulló M, Martínez-González MA, Ros E, Corella D, Estruch R, Fitó M, Arós F, Wärnberg J, Fiol M, Lapetra J, Vinyoles E, Lamuela-Raventós RM, Serra-Majem L, Pintó X, Ruiz-Gutiérrez V, Basora J, Salas-Salvadó J. **Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial.** *BMC Med* 11:164 I.F.: 6.679

5. Sánchez-Villegas A, Martínez-González MA, Estruch R, Salas-Salvadó J, Corella D, Covas MI, Arós F, Romaguera D, Gómez-Gracia E, Lapetra J, Pintó X, Martínez JA, Lamuela-Raventós RM, Ros E, Gea A, Wärnberg J, Serra-Majem L. **Mediterranean dietary pattern and depression: the PREDIMED randomized trial.** *BMC Med* 11(1):208 I.F.: 6.679

6. Toledo E, Hu FB, Estruch R, Buil-Cosiales P, Corella D, Salas-Salvadó J, Covas MI, Arós F, Gómez-Gracia E, Fiol M, Lapetra J, Serra-Majem L, Pinto X, Lamuela-Raventós RM, Saez G, Bulló M, Ruiz-Gutiérrez V, Ros E, Sorli JV, Martinez-Gonzalez MA. **Effect of the Mediterranean diet on blood pressure in the PREDIMED trial: results from a randomized controlled trial.** *BMC Med* 11(1):207 I.F.: 6.679

7. Flores-Mateo G, Rojas-Rueda D, Basora J, Ros E, Salas-Salvadó J. **Nut intake and adiposity: meta-analysis of clinical trials.** *Am J Clin Nutr* 97(6):1346-1355 I.F.: 6.504

8. Díaz-López A, Bulló M, Juanola-Falgarona M, Martínez-González MA, Estruch R, Covas MI, Arós F, Salas-Salvadó J. **Reduced serum concentrations of carboxylated and undercarboxylated osteocalcin are associated with risk of developing type 2 diabetes mellitus in a high cardiovascular risk population: a nested case-control study.** *J Clin Endocrinol Metab* 98(11):4524-4531 I.F.: 6.430

9. Díaz-López A, Chacón MR, Bulló M, Maymó-Masip E, Martínez-González MA, Estruch R, Vendrell J, Basora J, Díez-Espino J, Covas MI, Salas-Salvadó J. **Serum sTWEAK concentrations and risk of developing type 2 diabetes in a high cardiovascular risk population: a nested case-control study.** *J Clin Endocrinol Metab* 98(8):3482-3490 I.F.: 6.430

10. Fernández-Real JM, Corella D, Goumidi L, Mercader J, Valdés S, Rojo-Martínez G, Ortega F, Martinez-Larrad M, Gómez-Zumaquero JM, Salas-Salvadó J, Martinez-González MA, Covas MI, Botas P, Delgado E, Cottel D, Ferrieres J, Amouyel P, Ricart W, Ros E, Meirhaeghe A, Serrano-Rios M, Soriguer F, Estruch R. **Thyroid hormone receptor alpha gene variants increase the risk of developing obesity and show gene-diet interactions.** *Int J Obesity* 37(11):1499-1505 I.F.: 5.221

11. Martínez-Lapiscina EH, Clavero P, Toledo E, Estruch R, Salas-Salvadó J, San Julián B, Sánchez-Tainta A, Ros E, Valls-Pedret C, Martínez-González MA. **Mediterranean diet improves cognition: the PREDIMED-NAVARRA randomized trial.** *J Neurol Neurosurg Psychiatry* 84(12):1318-1325 I.F.: 4.924

12. Llaverias G, Escolà-Gil JC, Lerma E, Julve J, Pons C, Cabré A, Cofán M, Ros E, Sánchez-Quesada JL, Blanco-Vaca F. **Phytosterols inhibit the tumor growth and lipoprotein oxidizability induced by a high-fat diet in mice with inherited breast cancer.** *J Nutr Biochem* 24(1):39-48 I.F.: 4.552

13. Sala-Vila A, Cofán M, Mateo-Gallego R, Cenarro A, Civeira F, Ros E. **Eicosapentaenoic acid in serum phosphatidylcholine is associated with a less atherogenic lipoprotein profile in Spanish subjects with familial hypercholesterolemia.** *J Nutr Biochem* 24(9):1604-1608 I.F.: 4.552

14. Guasch-Ferré M, Bulló M, Babio N, Martínez-González MA, Estruch R, Covas MI, Wärnberg J, Arós F, Lapetra J, Serra-Majem L, Basora J, Salas-Salvadó J. **Mediterranean diet and risk of hyperuricemia in elderly participants at high cardiovascular risk.** *J Gerontol A Biol Sci Med Sci.* 68(10):1263-1270 I.F.: 4.314

15. Juanola-Falgarona M, Salas-Salvadó J, Estruch R, Portillo MP, Casas R, Miranda J, Martínez-González MA, Bulló M. **Association between dietary phylloquinone intake and peripheral metabolic risk markers related to insulin resistance and diabetes in elderly subjects at high cardiovascular risk.** *Cardiovasc Diabetol* 8;12:7 I.F.: 4.209

16. Bulló M, Casas R, Portillo MP, Basora J, Estruch R, García-Arellano A, Lasa A, Juanola-Falgarona M, Arós F, Salas-Salvadó J. **Dietary glycemic index/load and peripheral adipokines and inflammatory markers in elderly subjects at high cardiovascular risk.** *Nutr Metab Cardiovasc Dis* 23(5):443-450 I.F.: 3.978

17. Medina-Remón A, Vallverdú-Queralt A, Arranz-Martinez S, Sacanella E, Martínez-González MA, Covas MI, Corella D, Salas-Salvadó J, Gómez-Gracia E, Ruiz-Gutiérrez V, Lapetra J, Fiol M, Arós F, Saez GT, Ros E, Serra-Majem L, Pinto X, Estruch R, Lamuela-Raventos RM, on behalf of the PREDIMED Study Investigators. **Gazpacho consumption is associated with lower blood pressure and reduced hypertension in a high cardiovascular risk cohort. Cross-sectional study within the PREDIMED trial.** *Nutr Metab Cardiovasc Dis.* 23(10):944-952 I.F.: 3.978

18. Tresserra-Rimbau A, Medina-Remón A, Pérez-Jiménez J, Martínez-González MA, Covas MI, Corella D, Salas-Salvadó J, Gómez-Gracia E, Lapetra J, Arós F, Fiol M, Ros E, Serra-Majem L, Pintó X, Muñoz MA, Saez GT, Ruiz-Gutiérrez V, Warnberg V, Estruch R, Lamuela-Raventós

RM, on behalf of the PREDIMED Study Investigators. **Dietary intake and major food sources of polyphenols in a Spanish population at high cardiovascular risk: the PREDIMED study.** *Nutr Metab Cardiovasc Dis.* 23(10):953-959 I.F.: 3.978

19. Zamora-Ros R, Serafini M, Estruch R, Lamuela-Raventós RM, Martínez-González MA, Salas-Salvadó J, Fiol M, Lapetra J, Arós F, Covas MI, Andres-Lacueva C; PREDIMED Study Investigators. **Mediterranean diet and non enzymatic antioxidant capacity in the PREDIMED study: evidence for a mechanism of antioxidant tuning.** *Nutr Metab Cardiovasc Dis* 23(12):1167-1174 I.F.: 3.978

20. Babio N, Ibarrola-Jurado N, Bulló M, Martínez-González MÁ, Wärnberg J, Salaverría I, Ortega-Calvo M, Estruch R, Serra-Majem L, Covas MI, Sorli JV, Salas-Salvadó J; PREDIMED Study Investigators. **White Blood Cell Counts as Risk Markers of Developing Metabolic Syndrome and Its Components in the Predimed Study** *PLoS One.* 8(3):e58354 I.F.: 3.730

21. Hu EA, Toledo E, Diez-Espino J, Estruch R, Corella D, Salas-Salvado J, Vinyoles E, Gomez-Gracia E, Aros F, Fiol M, Lapetra J, Serra-Majem L, Pinto X, Portillo MP, Lamuela-Raventos RM, Ros E, Sorli JV, Martinez-Gonzalez MA**. Lifestyles and risk factors associated with adherence to the Mediterranean diet: a baseline assessment of the PREDIMED trial.** *PLoS One.* 8(4):e60166 I.F.: 3.730

22. Ibarrola-Jurado N, Bulló M, Guasch-Ferré M, Ros E, Martínez-González MA, Corella D, Fiol M, Wärnberg J, Estruch R, Lapetra J, Arós F, Muñoz MA, Serra-Majem L, Pintó X, Covas MI, Basora J, Salas-Salvadó J; on behalf of the PREDIMED Study Investigators. **Cross-sectional assessment of nut consumption and obesity, metabolic syndrome and other cardiometabolic risk factors. The PREDIMED study.** *PLoS One.* 8(2);e57367 I.F.: 3.730

23. Juanola-Falgarona M, Cándido-Fernández J, Salas-Salvadó J, Martínez-González MA, Estruch R, Fiol M, Arija-Val V; Mònica Bulló; PREDIMED Study Investigators. **Association between serum ferritin and osteocalcin as a potential mechanism explaining the iron-induced insulin resistance.** *PLoS One.* 8(10):e76433 I.F.: 3.730

24. Damasceno NRT, Sala-Vila A, Cofán M, Pérez-Heras AM, Fitó M, Ruiz-Gutiérrez V, Martínez-González MA, Corella D, Arós F, Estruch R, Ros E. **Mediterranean diet supplemented with nuts reduces waist circumference and shifts lipoprotein subfractions to a less atherogenic pattern in subjects at high cardiovascular risk.** *Atherosclerosis.* 230(2):347-353 I.F.: 3.706

25. Bautista-Castaño I, Sánchez-Villegas A, Estruch R, Martínez- González MA, Corella D, Salas-Salvadó J, Covas MI, Schroder H, Alvarez-Pérez J, Quilez J, Lamuela-Raventós RM, Ros E, Arós F, Fiol M, Lapetra J, Muñoz MA, Gómez-Gracia E, Tur J, Pintó X, Ruiz-Gutierrez V, Portillo-Baquedano MP, Serra-Majem L. **Changes in bread consumption and 4-year changes in adiposity in Spanish men and women at high cardiovascular risk. The PREDIMED study.** *Br J Nutr.* 110:337–346 I.F.: 3.302

26. Chiva-Blanch G, Urpi-Sarda M, Ros E, Valderas-Martinez P, Casas R, Arranz S, Guillén M, Lamuela-Raventós RM, Llorach R, Andres-Lacueva C, Estruch R. **Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: a randomized clinical trial.** *Clin Nutr.* 32(2):200-206 I.F.: 3.298

27. Díaz-López A, Bulló M, Basora J, Martínez-González MA, Guasch-Ferré M, Estruch R, Wärnberg J, Serra-Majem L, Arós F, Lapetra J, Ros E, Pintó X, Covas MI, Salas-Salvadó J**. Cross-sectional associations between nutrient intake and chronic kidney disease in a population at high cardiovascular risk.** *Clin Nutr* 32:606-612 I.F.: 3.298

28. Mitjavila MT, Fandos M, Salas-Salvadó J, Covas MI, Borrego S, Estruch R, Lamuela-Raventós R, Corella D, Martínez-Gonzalez MÁ, Sánchez JM, Bulló M, Fitó M, Tormos C, Cerdá C, Casillas R, Moreno JJ, Iradi A, Zaragoza C, Chaves J, Sáez GT. **The Mediterranean diet improves the systemic lipid and DNA oxidative damage in metabolic syndrome individuals. A randomized, controlled, trial.** *Clin Nutr.* 32(2):172-178 I.F.: 3.298

29. Mejía-Lancheros C, Estruch R, Martínez-González MA, Salas-Salvadó J, Corella D, Gómez-Gracia E, Fiol M, Lapetra J, Covas MI, Arós F, Serra-Majem L, Pintó X, Basora J, Sorlí JV, Muñoz MA; en nombre de los investigadores del estudio PREDIMED. **Socioeconomic Status and Health Inequalities for Cardiovascular Prevention Among Elderly Spaniards.** *Rev Esp Cardiol.* 66(10):803-811 I.F.: 3.204

30. Baila-Rueda L, Cenarro A, Cofán M, Orera I, Pocoví M, Ros E, Civeira F, Nerín C, Domeño C. **New fast method for quantification of non-cholesterol sterols by high performance liquid chromatography coupled to mass spectrometry.** *Anal Methods.* 5:2249–2257 I.F.: 1.855

Reviews / I.F.: 15.202

1. Ros E, Hu FB. **Consumption of plant seeds and cardiovascular health: epidemiologic and clinical trial evidence.** *Circulation.* 128(5):553-65 I.F.: 15.202

Editorials / I.F.: 24.777

1. Estruch R, Ros E. **Eat a healthy diet and drink wisely to postpone dying if you survived a myocardial infarction?: yes, but randomized clinical trials are needed.** *JAMA Intern Med.*173(19):1819-1820 I.F.: 10.579

2. Estruch R, Salas-Salvadó J. **Towards an even healthier Mediterranean diet.** *Nutr Metab Cardiovasc Dis.* 23(12):1163-6 I.F.: 3.978

3. Arós F, Estruch R. **Mediterranean diet and cardiovascular prevention.** *Rev Esp Cardiol (Engl Ed)* 66(10):771-774 I.F.: 3.204

4. Arós F, Corella D, Covas MI, Estruch R, Fiol M, Lapetra J, Gómez-Gracia E, Lamuela-Raventos RM, Martínez A, Martínez-González MA, Pintó X, Portillo Mdel P, Ros E, Ruiz-Gutiérrez V, Saez G, Salas-Salvadó J, Serra-Majem L, Tur J; los investigadores PREDIMED. **How to publish in The New England Journal of Medicine and not to die while trying it; the PREDIMED experience.** *Nutr Hosp.* 28(4):977-979 I.F.: 1.305

5. Valls-Pedret C, Ros E. **Mediterranean diet and cognitive outcomes. Epidemiological evidence suggestive, randomized trials needed.** *Epidemiology* 24(4):503-506 I.F.: 5.738

Multicenter / I.F.: 6.504

1. Castañer O, Corella D, Covas MI, Sorlí JV, Subirana I, Flores-Mateo G, Nonell L, Bulló M, de la Torre R, Portolés O, Fitó M; PREDIMED study investigators. **In vivo transcriptomic profile after a Mediterranean diet in high-cardiovascular risk patients: a randomized controlled trial.** *Am J Clin Nutr* 98(3):845-853 I.F.: 6.504

GRANTS FOR RESEARCH IN PROGRESS

Estruch R. **Alimentación saludable en la prevención primaria de enfermedades crónicas: la Red PREDIMED.**
Sponsoredby: Instituto de Salud Carlos III (ISCIII) RD06/0045/1003.
Duration: 29/02/2008-31/12/2013.

Ros E. **Bases genéticas de las Hipercolesterolemias Hereditarias no dependientes del receptor LDL ni apolipoproteína B. Subproyecto 3. Biomarcadores de la homeostasis del colesterol.**Sponsoredby: Instituto de Salud Carlos III (ISCIII). PI12/01321.
Duration: 01/01/2013-31/12/2015

Ros E. **Contribución de la variabilidad en el promotor del gen del receptor LDL a la hipercolesterolemia poligénica. Subproyecto 5: Análisis de biomarcadores de absorción y síntesis de colesterol.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1292.
Duration: 01/01/2010-31/03/2013

Sacanella E. **Evaluación del efecto antihipertensivo y antiinflamatorio de los polifenoles, carotenos y vitamina C del tomate, según la ración dietética ingerida.** Sponsoredby: Ministerio de Ciencia e Innovación, AGL201022319-C03-02.
Duration: 01/01/2011-31/12/2013.

Sacanella E. **Efecto del consumo crónico de tomate sobre presión arterial y la función endotelial de sujetos con alto riesgo vascular.** Sponsoredby: Ministerio de Economía y Competitividad AGL2010-22319-C03-02.
Duration: 01/01/2011-31/12/2013.

Zambon D. **Evaluación y caracterización de la ateroesclerosis coronaria subclínica mediante Angio-TAC en la hipercolesterolemia familiar.**
Sponsoredby: Instituto de Salud Carlos III (ISCIII). PI12/01299.
Duration: 01/01/2013-31/12/2015

DOCTORAL THESES

Estruch R. **Balanç benefici/risc del contingut en polifenols i alcohol del vi: bases científiques dels efectes del consum moderat de vi sobre el sistema cardiovascular.**
PhD student: Gemma Chiva Blanch.

2.5

Respiratory biophysics and bioengineering

LOCATION
UB School of Medicine

FOR FURTHER INFORMATION
www.ub.edu/biofisica

KEYWORDS
1. **Respiratory mechanics**
2. **Lung bioengineering**
3. **Neuroimaging in refractory epilepsy**
4. **Neuroimaging in Parkinson's disease**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	56.27	11	8	2
2012	65.76	14	11	2
2013	47.23	11	8	-

TEAM INVOLVED IN
CIBERES
CIBER-BBN

TEAM LEADER
Ramon Farré (UB)
t. 93 402 45 15
rfarre@ub.edu

RESEARCHERS
Javier Pavía (HCB)
Domènec Ros (UB)

POST-DOCTORAL RESEARCHERS
Elena Garreta (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Noelia Campillo (IBEC)
Valentina Isetta (UE)
Berta Martí (IBEC)
Esther Melo (MEC)
Aida Niñerola (CIBER-BBN)
Paula Nonaka (FAPES-Brasil)
Renata K. da Palma (FAPES-Brasil)
Foteini Popota (IDIBAPS)
Juan José Uriarte (UB)

TECHNICIANS
Rocío Nieto (CIBERES)
Miguel Rodríguez (UB)

COLLABORATORS
Jordi Alcaraz (UB)
Albert Cot (UB-CIBER-BBN)
Carles Falcón (IDIBAPS)
Daniel Navajas (UB-IBEC)
Pere Roca-Cusachs (UB-IBEC)
Xavier Trepat (UB-IBEC)
Raúl Tudela (CIBER-BBN)

STRATEGIC OBJECTIVES

The general objectives of the group are the study of the biophysical mechanisms determining respiratory function, and the development of models and methods for the processing of biomedical images and signals. The work of the group is based on an interdisciplinary approach, with integration between basic and clinical research. In parallel to the scientific objectives, our group pro-motes transfer to the industrial setting of the technological advances derived from the research work.

MAIN LINES OF RESEARCH

1. **Respiratory mechanics.**
The aim of research in respiratory mechanics is to investigate the viscoelastic properties of the airways and lung tissues. At present, the work fundamentally focuses on the study of upper airway collapsibility in obstructive apnea-hypopnea during sleep and in the monitoring of noninvasive mechanical ventilation during respiratory failure. The clinical aim of this research is to obtain improved noninvasive diagnostic techniques, and to optimize the treatment methods based on ventilation assist measures.

2. **Molecular and cellular nanomechanics.**
The introduction of nanotechnologies allowing the manipulation of materials on the nanometric and pico-Newton scale has opened up new perspectives for the investigation of individual biomolecules and cells. Our group uses atomic force microscopy, magnetic microspheres and traction force microscopy to study cell adhesion and the mechanical properties of lung cells and leukocytes. Studies are also made of the mechanical properties of embryonic and adult stem cells during the differentiation process, and of the way in which mechanical stimuli can enhance differentiation towards the alveolar epithelial phenotype. One of our projects in this setting focuses on organ regeneration. Specifically, work is done on the bioartificial production of functional rat lungs by means of the re-cellularization of the extracellular matrix of the organ with stem cells, and recreation of the mechanical pulmonary micro-nano environment, to optimize cell differentiation.

3. **Biomedical imaging analysis.**
Research in imaging analysis currently focuses on the processing of photon emission tomography (SPECT) and positron emission tomography (PET) images, with the purpose of securing more precise quantification of gammagraphic (scintigraphic) studies. With this objective in mind, iterative algorithms are being developed for the three-dimensional reconstruction of images and for the fusion of SPECT and magnetic resonance imaging (MRI) images.

PUBLICATIONS

Originals / I.F.: 47.227

1. Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, Duran-Cantolla J, de la Pena M, Masdeu MJ, Gonzalez M, del Campo F, Gallego I, Marin JM, Barbe F, Montserrat JM, Farre R. **Association between Obstructive Sleep Apnea and Cancer Incidence in a large multicenter Spanish Cohort.** *Am J Respir Crit Med* 187: 99-105 I.F.: 11.041

2. Li Bassi G, Tavares O, Marti JD, Giunta V, Luque N, Isetta V, Ferrer M, Farre R, Leite G, Torres A. **An in-vitro study to assess determinant features associated with fluid sealing in the design of endotracheal tube cuffs and exerted tracheal pressures.** *Critical Care Med* 41: 518-526 I.F.: 6.124

3. Quintero M, Gonzalez-Martin MC, Vega-Agapito V, Gonzalez C, Obeso A, Farré R, Agapito T, Yubero S. **The effects of intermittent hypoxia on redox status, NFkB activation, and plasma lipid levels is dependent on the lowest oxygen saturation.** *Free Radical Biology Medicine* 2013; 65C: 1142-1154 I.F.: 5.271

4. Luque T, Melo E, Garreta E, Cortiella J, Nichols J, Farré R, Navajas D. **Local micromechanical properties of decellularized lung scaffolds measured with atomic force microscopy**. *Acta Biomaterialia* 9 (2013) 6852–6859 I.F.: 5.093

5. Isetta V, López-Agustina C, López-Bernal E, Amat M, Vila M, Valls C, Navajas D, Farré R. **Cost-Effectiveness of a New Internet-based Monitoring Tool for Neonatal Post-Discharge Home Care.** *J Med Internet Res* 15(2): e38 I.F.: 3.768

Puig F, Fuster G, Adda M, Blanch L, Farré R, Navajas D, Artigas A. **Barrier-protective effects of activated protein C in human alveolar epithelial cells.** *PLoS ONE* 8(2): e56965 I.F.: 3.730

6. Fuster, BM, Esteban O, Planes X, Aguiar P, Crespo C, Falcon C, Wollny G, Sureda SR, Setoain X, Frangi AF, Ledesma MJ, Santos A, Pavia J, Ros D FocusDET, **A New Toolbox for SISCOM Analysis. Evaluation of the Registration Accuracy Using Monte Carlo Simulation.** *Neuroinformatics* 11(1):77-89 I.F.: 3.136

7. Falcon C, Tsoumpas C, Livieratos L, Aguiar P, Cot A, Ros D, Thielemans K. **Integration of advanced 3D SPECT modeling into the open-source STIR framework.** *Med Phys* 40(9):092502 I.F.: 2.911

8. Almendros I, Montserrat JM, Torres M, Dalmases M, Cabañas ML, Campos-Rodríguez F, Navajas D, Farré R. **Intermittent hypoxia increases melanoma metastasis to the lung in a mouse model of sleep apnea.** *Respir Physiol Neurbiol* 186:303– 307 I.F.: 2.051

9. Peñuelas O, Melo E, Sánchez E, Sánchez I, Quinn K, Ferruelo A, Pérez-Vizcaíno F, Esteban A, Navajas D, Nin N, Lorente JA, Farré R. **Antioxidant effect of human adult adipose-derived stromal stem cells in alveolar epithelial cells undergoing stretch.** *Respir Physiol Neurobiol* 188:1– 8 I.F.: 2.051

10. Torres M, Montserrat JM, Pavía J, Dalmases M, Ros D, Fernandez Y, Barbé F, Navajas D, Farré R. **Chronic intermittent hypoxia preserves bone density in a mouse model of sleep apnea.** *Respir Physiol Neurobiol* 189(3):646-648 I.F.: 2.051

Reviews / I.F.: 3.781

1. Franquesa M, Hoogduijn MJ, Reinders ME, Eggenhofer E, Engela AU, Mensah FK, Torras J, Pileggi A, van Kooten C, Mahon B, Detry O, Popp FC, Benseler V, Casiraghi

F, Johnson C, Ancans J, Fillenberg B, Delarosa O, Aran JM, Roemeling-Vanrhijn M, Pinxteren J, Perico N, Gotti E, Christ B, Reading J, Introna M, Deans R, Shagidulin M, Farré R, Rambaldi A, Sanchez-Fueyo A, Obermajer N, Pulin A, Dor FJ, Portero-Sanchez I, Baan CC, Rabelink TJ, Remuzzi G, Betjes MG, Dahlke MH, Grinyó JM; the MiSOT Study Group. **Mesenchymal Stem Cells in Solid Organ Transplantation (MiSOT) Fourth Meeting: Lessons learned from First Clinical Trials.** *Transplantation* 96: 234-238 I.F.: 3.781

Editorials / I.F.: 22.496

1. Kheirandish-Gozal L, Farré R. **The Injury theory, endothelial progenitors and sleep apnea.** *Am J Respir Crit Care Med* 187: 5-7 I.F.: 11.041

2. Calverley PMA, Farré R. **Putting non-invasive lung mechanics into context.** *Eur Respir* J 42: 1435–1437 I.F.: 6.355

3. Farré R, Navajas D, Montserrat JM. **"Is there an optimal nasal pressure for treating obstructive sleep apnea – and if so, what is it?** *SLEEP* 36: 463-464 I.F.: 5.100

GRANTS FOR RESEARCH IN PROGRESS

Farré R. **Biongeniería del pulmón mediante cultivo de células madre en la matriz descelularizada del órgano: efecto de los estímulos biofísicos en la optimización del bioreactor.**
Sponsored by: Ministerio de Economía y Competitividad. SAF2011-22576.
Duration: 01/01/2012-31/12/2014.

Farré R. **Clinical tRials fOr elderly patients with MultiplE Disease (CHROMED)**
Sponsored by: European Commission COOPERATION 306093-2
Duration: 01/01/2012-31/12/2015.

Ros D. **Cuantificacion de estudios de SPECT de neurotransmision del sistema dopaminergico nigroestriatal. Optimizacion para la utilizacion en la rutina clinica (PI12/00390)**.
Sponsored by: Ministerio de Economía y Competitividad.
Duration: 01/01/2013-31/12/2015

DOCTORAL THESES

Farré R. **Advances in the application of information and communication technologies in healthcare at the patient's home.**
PhD student: Valentina Isetta

Pavía J. **Image processing of emission tomography studies in refractory epilepsy.**
PhD student: Berta Martí Fuster.

2.6 Applied research in infectious respiratory diseases, critically ill patients and lung cancer

LOCATION
CELLEX building

FOR FURTHER INFORMATION
www.idibapsrespiratoryresearch.org

KEYWORDS
1. **Respiratory Infections**
2. **Mechanical Ventilation**
3. **Pneumonia**
4. **COPD, bronchiectasis**
5. **Breathing disturbances in sleep**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	160.67	33	31	10
2012	256.68	49	31	10
2013	253.81	36	28	3

TEAM INVOLVED IN
CIBERES

AWARDS

Premio a la "Excelencia Profesional"
Institution: Col·legi Oficial de Metges de Barcelona
Awardee: Dr. Antoni Torres

ICREA Academia 2013
Institution: Institució Catalana de Recerca i Estudis Avançats
Awardee: Dr. Antoni Torres

Young Investigator Award
Institution: Annual Congress ESICM LIVE 2013
Awardee: Dr. Gianluigi Li Bassi

TEAM LEADER
Antoni Torres (HCB)
T. 93 227 55 49
atorres@clinic.cat

GROUP LEADER
Josep Mª Montserrat (HCB)

RESEARCHERS
Carles Agustí (HCB)
Joan Ramon Badia (HCB)
Miquel Ferrer (HCB)
Néstor Soler (HCB)
Dolors Soy (HCB)

POST-DOCTORAL RESEARCHERS
Laura Guerrero (IDIBAPS)
Gianluigi Li Bassi (IDIBAPS)
Eva Polverino (HCB)
Jacob Sellarés (HCB)

PRE-DOCTORAL RESEARCHERS
Elisabet Aguilera Xiol (CIBERES)
Victoria Alcaraz (FCRB)
Rosanel Amaro (HCB)
Marco Carbonara (Italy)
Catia Cillóniz (FCRB)
Talitha Comaru (Hospital São Lucas de Porto Alegre, Brasil)
Mireia Dalmases (Socap)
Laia Fernàndez (CIBERES)
Leonardo di Francesco (Universitá degli Studi di Roma, Italy)
Arnoldo Guerrero (HCB)
Mònica Guerrero (FCRB)
Arturo Huerta (HCB)
Hugo Loureiro ((HCB)
Carmen Lucena (HCB)
Sandra Manca (Universitá degli Studi di Sassari)
Joan Daniel Martí (CIBERES)
Rogelio Peralta (Burgos)
Mariano Rinaudo (FCRB)
Francesca da Rosa (Italy)
Marta Torres López (CIBERES)
Silvia Terraneo (Universitá degli Studi di Milano)

NURSING STAFF
Rebeca Domingo (FCRB)
Patrícia Fernández (FCRB)
Encarnación Moreno (FCRB)
Montserrat Sola (FCRB)

ADMINISTRATIVE STAFF
Elisabet Sancho (Ciberes)

STATISTICIAN
Albert Gabarrús Barri (FCRB)

COLLABORATORS
Néstor Luque (Sagrat Cor)
Montserrat Rigol (IDIBAPS)

STRATEGIC OBJECTIVES

- Study of community-acquired respiratory infections, nosocomial infections and infections in immune depressed patients.
- Study of invasive and noninasive mechanical ventilation in acute respiratory failure, particularly in weaning from artificial ventilation
- Study of the exacerbation of chronic obstructive pulmonary disease (COPD) and the implication of bacterial, viral and fungal infectious agents.
- Physiopathological and treatment studies in an animal model of ventilation associated pneumonia
- Epidemiology, diagnosis and treatment of adult bronchiectasia not associated with cystic fibrosis: Study of inflammatory response, new treatment modalities and immunoglobulin replacement therapy.
- Randomized clinical trial in respiratory infections and or mechanical ventilation
- Human and animal model research in sleep apnea syndrome. Telemedicine and multcientre studies.
- Multicenter studies in relation to sleep respiratory pathology and cardiovascular disease.

MAIN LINES OF RESEARCH

1. Epidemiology, prevention and new treatments of pneumonias associated with artificial ventilation and new methods of fast diagnosis. Resistances of microorganisms. Study of biofilms in endotracheal tubes. Local and systemic inflammatory response.

2. Epidemiology and diagnosis of community-acquired pneumonia. Multicenter studies in the setting of community-acquired pneumonia. New methods for fast diagnosis. New treatments. Resistances of microorganisms. Local and systemic inflammatory response. S. pneumoniae in the context of new vaccines.

3. Study of the risk factors, microbiology and prognosis of Health Care Associated Pneumonia (HCAP).

4. Etiopathogenesis, bronchial infection and inflammation in the patient with chronic obstructive pulmonary disease (COPD). Role of infections in exacerbation of the disease. Study of bronchial and associated systemic response. Analysis of the risk and prognostic factors in acute episodes. Smoking. Epidemiology and diagnosis of alpha-1-antitrypsin deficiency.

5. Chronic pulmonary infections: bronchiectasia not associated with cystic fibrosis, immune deficiencies and cystic fibrosis in the adult. Control of bronchial colonization. Study of bronchial inflammatory and associated systemic response. New treatment modalities (nebulizer antibiotic treatment). Replacement therapy with immunoglobulins.

6. Infectious lung complications in immune depressed patients. Evaluation of the etiological factors. Optimization of the diagnostic techniques. Study of bronchial inflammatory and associated systemic response. Analysis of prognostic factors.

7. Invasive and noninvasive mechanical ventilation: epidemiology, cost-effectiveness and physiopathology. New techniques. Weaning from mechanical ventilation: role of the inflammatory response and respiratory failure following extubation.

8. Study of the pharmacokinetics of antibiotics and other drugs in the ventilated and non-ventilated patient.

9. Porcine model of acute pulmonary damage due to methicillinresistant P. aeruginosa, S. aureus and S. pneumoniae: study of new coadjuvant drugs in the treatment of pneumonia, study of new antibiotics, prevention of ventilator-associated pneumonia (VAP), and new forms of mechanical ventilation.

10. European studies of respiratory infections. Participation in the GRACE, MOSAR and THERAEDGE projects, which respectively investigate community-acquired respiratory infections, in-hospital respiratory infections and new diagnostic methods.

11. Chronic sleep apnea models.

12. Multicenter Study to assess the effect of CPAP on cardiovascular diseases in patients with sleep apnea.

13. Telematic control of CPAP treatment in sleep apnea syndrome.

RESEARCH GROUP
BREATHING DISTURBANCES IN SLEEP

GROUP LEADER
Josep M. Montserrat (HCB)

The main research line of this group is the analysis of respiratory disturbances in sleep. Specifically, the two most important lines are the following: the study of diagnostic methods and effects of treatment in a population of apneic patients in which the indication is not clear; and the study of animal models for exploring the mechanisms underlying the origin and consequences of the disorder. Both lines are carried out in the context of national multicenter clinical trials.

PUBLICATIONS

Originals / I.F.: 253.806

1. Little P, Stuart B, Francis N, Douglas E, Tonkin-Crine S, Anthierens S, Cals JW, Melbye H, Santer M, Moore M, Coenen S, Butler C, Hood K, Kelly M, Godycki-Cwirko M, Mierzecki A, Torres A, Llor C, Davies M, Mullee M, O'Reilly G, van der Velden A, Geraghty AW, Goossens H, Verheij T, Yardley L; GRACE consortium. **Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial.** *Lancet* 382(9899):1175-1182 I.F.: 39.060

2. Martínez-García MA, Capote F, Campos-Rodríguez F, Lloberes P, Díaz de Atauri MJ, Somoza M, Masa JF, González M, Sacristán L, Barbé F, Durán-Cantolla J, Aizpuru F, Mañas E, Barreiro B, Mosteiro M, Cebrián JJ, de la Peña M, García-Río F, Maimó A, Zapater J, Hernández C, Grau SanMarti N, Montserrat JM; Spanish Sleep Network. **Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial.** *JAMA -J AM MED ASSOC* 310(22):2407-2415 I.F.: 29.978

3. Little P, Stuart B, Moore M, Coenen S, Butler CC, Godycki-Cwirko M, Mierzecki A, Chlabicz S, Torres A, Almirall J, Davies M, Schaberg T, Mölstad S, Blasi F, De Sutter A, Kersnik J, Hupkova H, Touboul P, Hood K, Mullee M, O'Reilly G, Brugman C, Goossens H, Verheij T; GRACE consortium. **Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial.** *Lancet Infect Dis* 13(2):123-129 I.F.:19,966

4. Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, Duran-Cantolla J, Peña Mde L, Masdeu MJ, Gonzalez M, Campo Fd, Gallego I, Marin JM, Barbe F, Montserrat JM, Farre R; Spanish Sleep Network. **Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort.** *Am J Respir Crit Care Med* 187(1):99-105 I.F.: 11.041

5. Sellares J, López-Giraldo A, Lucena C, Cilloniz C, Amaro R, Polverino E, Ferrer M, Menéndez R, Mensa J, Torres A. **Influence of Previous Use of Inhaled Corticoids on the Development of Pleural Effusion in Community-Acquired Pneumonia.** *Am J Respir Crit Care Med* 187(11):1241-1248 I.F.: 11.041

6. Polverino E, Torres A, Menendez R, Cillóniz C, Valles JM, Capelastegui A, Marcos MA, Alfageme I, Zalacain R, Almirall J, Molinos L, Bello S, Rodríguez F, Blanquer J, Dorado A, Llevat N, Rello J; HCAP Study investigators. **Microbial aetiology of healthcare associated pneumonia in Spain: a prospective, multicentre, case-control study.** *Thorax* 68(11):1007-1014 I.F.: 8.376

7. Aliberti S, Cilloniz C, Chalmers JD, Zanaboni AM, Cosentini R, Tarsia P, Pesci A, Blasi F, Torres A. **Multidrug-resistant pathogens in hospitalised patients coming from the community with pneumonia: a European perspective.** *Thorax* 68(11):997-999 I.F.: 8.376

8. Chamorro N, Sellarés J, Millán G, Cano E, Soler N, Embid C, Montserrat JM. **An integrated model involving sleep units and primary care for the diagnosis of sleep apnoea.** *Eur Respir J* 42(4):1151-1154 I.F.: 6.355

9. Masa JF, Corral J, Pereira R, Duran-Cantolla J, Cabello M, Hernández-Blasco L, Monasterio C, Alonso-Fernandez A, Chiner E, Vázquez-Polo FJ, Montserrat JM; Spanish Sleep Group. **Effectiveness of sequential automatic-manual home respiratory polygraphy scoring.** *Eur Respir J* 41(4):879-887 I.F.: 6.355

10. Esperatti M, Ferrer M, Giunta V, Ranzani OT, Saucedo LM, Li Bassi G, Blasi F, Rello J, Niederman MS, Torres A. **Validation of predictors of adverse outcomes in hospital-acquired pneumonia in the ICU.** *Crit Care Med* 41(9):2151-2161 I.F.: 6.124

11. Giunta V, Ferrer M, Esperatti M, Ranzani OT, Saucedo LM, Li Bassi G, Blasi F, Torres A. **ICU-acquired pneumonia with or without etiologic diagnosis: a comparison of outcomes.** *Crit Care Med* 41(9):2133-2143 I.F.: 6.124

12. Martí JD, Li Bassi G, Rigol M, Saucedo L, Ranzani OT, Esperatti M, LuqueN, Ferrer M, Vilaro J, Kolobow T, Torres A. **Effects of Manual Rib Cage Compressions on Expiratory Flow and Mucus Clearance During Mechanical Ventilation.** *Crit Care Med* 41(3):850-856 I.F.: 6.124

13. Vallés J, Palomar M, Alvárez-Lerma F, Rello J, Blanco A, Garnacho-Montero J, Martín-Loeches I; GTEI/SEMICYUC Working Group on Bacteremia. **Evolution over a 15-year period of clinical characteristics and outcomes of critically ill patients with community-acquired bacteremia.** *Crit Care Med* 41(1):76-83 I.F.: 6.124

14. Cillóniz C, Polverino E, Ewig S, Aliberti S, Gabarrús A, Menéndez R, Mensa J, Blasi F, Torres A. **Impact of Age and Comorbidity on Etiology and Outcome in Community-Acquired Pneumonia.** *Chest* 144(3):999-1007 I.F.: 5.854

15. Crisafulli E, Menéndez R, Huerta A, Martinez R, Montull B, Clini E, Torres A. **Systemic inflammatory pattern of patients with community-acquired pneumonia with and without COPD.** *Chest* 143(4):1009-1017 I.F.: 5.854

16. Huerta A, Crisafulli E, Menéndez R, Martinez R, Soler N, Guerrero M, Montull B, Torres A. **Pneumonic and non-pneumonic exacerbations of copd: systemic inflammatory response and clinical characteristics.** *Chest* 144(4):1134-1142 I.F.: 5.854

17. Prina E, Ferrer M, Ranzani OT, Polverino E, Cillóniz C, Moreno E, Mensa J, Montull B, Menéndez R, Cosentini R, Torres A. **Thrombocytosis is a marker of poor**

outcome in community-acquired pneumonia. *Chest* 143(3):767-775 I.F.: 5.854

18. Di Pasquale M, Esperatti M, Crisafulli E, Ferrer M, Bassi GL, Rinaudo M, Escorsell A, Fernandez J, Mas A, Blasi F, Torres A. **Impact of chronic liver disease in intensive care unit acquired pneumonia: a prospective study.** *Intensive Care Med* 39(10):1776-1784 I.F.: 5.258

19. Martín-Loeches I, Bermejo-Martin JF, Vallés J, Granada R, Vidaur L, Vergara-Serrano JC, Martín M, Figueira JC, Sirvent JM, Blanquer J, Suarez D, Artigas A, Torres A, Diaz E, Rodriguez A; SEMICYUC/REIPI/CIBERES H1N1 Working Group. **Macrolide-based regimens in absence of bacterial co-infection in critically ill H1N1 patients with primary viral pneumonia.** *Intensive Care Med* 39(4):693-702 I.F.: 5.258

20. Martin-Loeches I, Deja M, Koulenti D, Dimopoulos G, Marsh B, Torres A, Niederman MS, Rello J; EU-VAP Study Investigators. **Potentially resistant microorganisms in intubated patients with hospital-acquired pneumonia: the interaction of ecology, shock and risk factors.** *Intensive Care Med* 39(4):672-681 I.F.: 5.258

21. Masa JF, Corral J, Sanchez de Cos J, Duran-Cantolla J, Cabello M, Hernández-Blasco L, Monasterio C, Alonso A, Chiner E, Aizpuru F, Vázquez-Polo FJ, Zamorano J, Montserrat JM; Collaborating group:, Garcia-Ledesma E, Pereira R, Cancelo L, Martinez A, Sacristan L, Salord N, Carrera M, Sancho-Chust JN, Negrín MA, Embid C. **Effectiveness of three sleep apnea management alternatives.** *Sleep* 36(12):1799-1807 I.F.: 5.100

22. Masa JF, Corral J, Gomez de Terreros J, Duran-Cantolla J, Cabello M, Hernández-Blasco L, Monasterio C, Alonso A, Chiner E, Aizpuru F, Zamorano J, Cano R, Montserrat JM, Collaborating group, Garcia-Ledesma E, Pereira R, Cancelo L, Martinez A, Sacristan L, Salord N, Carrera M, Sancho-Chust JN, Embid C. **Significance of including a surrogate arousal for sleep apnea-hypopnea syndrome diagnosis by respiratory polygraphy**. *Sleep* 36(2):249-257 I.F.: 5.100

23. Pinazo MJ, Guerrero L, Posada E, De Lazzari E, Soy D, Gascón J. **Adverse effects of benznidazole and its relationship with serum drug concentrations in patients with chronic Chagas disease.** *Antimicrob Agents Chemother* 57(1):390-395 I.F.: 4.565

24. García-de-la-Mària C, Pericas JM, del Río A, Castañeda X, Vila-Farrés X, Armero Y, Espinal PA, Cervera C, Soy D, Falces C, Ninot S, Almela M, Mestres CA, Gatell JM, Vila J, Moreno A, Marco F, Miró JM, and the Hospital Clinic **Experimental Endocarditis Study Group. Early In Vitro and In Vivo Development of High-Level Daptomycin Resistance is Common in Mitis-Group S treptococci after Exposure to Daptomycin.** *Antimicrob Agents Chemother* 57(5): 2319-2325 I.F.: 4.565

25. Rey-Jurado E, Tudó G, Soy D, González-Martín J. **Activity and interactions of Levofloxacin, Linezolid, Ethambutol and Amikacin in three-drug combinations against M. tuberculosis isolates in a human macrophage model (cell line THP-1).** *Int J Antimicrob Ag* 42: 524-530. I.F.: 4.415

26. Gasa M, Salord N, Fortuna AM, Mayos M, Embid C, Vilarrasa N, Montserrat JM, Monasterio C. **Optimizing screening of severe obstructive sleep apnea in patients undergoing bariatric surgery.** *Surg Obes Relat Dis* 9(4):539-546 I.F.: 4.121

27. Almirall J, Bolíbar I, Serra-Prat M, Palomera E, Roig J, Hospital I, Carandell E, Agustí M, Ayuso P, Estela A, Torres A. **Relationship between the Use of Inhaled Steroids for Chronic Respiratory Diseases and Early Outcomes in Community-Acquired Pneumonia. Community-Acquired Pneumonia in Catalan Countries (PACAP).** *PLoS One* 8(9):e73271 I.F.: 3.730

28. Polverino E, Cillóniz C, Dambrava P, Gabarrús A, Ferrer M, Agustí C, Prina E, Montull B, Menendez R, Niederman MS, Torres A. **Systemic corticosteroids for Community Acquired Pneumonia: reasons for use and lack of benefit on outcome.** Respirology 18(2):263-271 I.F.: 2.781

29. Farré E, Villarón P, López-Cabezas MC, Guerrero L, Soy D, Ribas J. **Physical compatibility of highly concentrated midazolam infusions with other drugs commonly used in intensive care units.** *Eur J Clin Pharm* 15(5) 336-338. I.F.: 2.741

30. de la Torre MC, Bolíbar I, Vendrell M, de Gracia J, Vendrell E, Rodrigo MJ, Boquet X, Torrebadella P, Yébenes JC, Serra-Prat M, Rello J, Torres A, Almirall J. **Serum immunoglobulins in the infected and convalescent phases in community-acquired pneumonia.** *Respir Med* 107 (12) :2038-2045 I.F.: 2.585

31. Gómez FP, Amado VM, Roca J, Torres A, Nicolas JM, Rodriguez-Roisin R, Barberà **Effect of nitric oxide inhalation on gas exchange in acute severe pneumonia.** *Respir Physiol Neurobiol* 187(2):157-163I.F.: 2.051

32. Torres M, Montserrat JM, Pavía J, Dalmases M, Ros D, Fernandez Y, Barbé F,Navajas D, Farré R. **Chronic intermittent hypoxia preserves bone density in a mouse model of sleep apnea.** *Respir Physiol Neurobiol* 189(3):646-648 I.F.: 2.051

33. Almendros I, Montserrat JM, Torres M, Dalmases M, Cabañas ML, Campos-Rodríguez F, Navajas D, Farré R. **Intermittent hypoxia increases melanoma metastasis to the lung in a mouse model of sleep apnea.** Respir *Physiol Neurobiol* 186(3):303-307. I.F.: 2.051

34. Sirvent JM, Carmen de la Torre M, Lorencio C, Taché A, Ferri C, Garcia-Gil J, Torres A. **Predictive factors of mortality in severe community-acquired pneumonia: A model with data on the first 24h of ICU admission.** *Med Intensiva* 37(5):308-315 I.F.: 1.323

35. Guerrero L, Carcelero E, Ribas J, Soy D. **A fast and accurate high performance liquid chromatography assay to quantify plasma ceftazidime concentrations for clinical routine.** *J Liq Chromatogr R T* 36(13):1777–1787 I.F.: 0.565

Reviews / I.F.: 20.923

1. Torres A. **Peetermans WE, Viegi G, Blasi F. Risk factors for community-acquired pneumonia in adults in Europe: a literature review.** *Thorax* 68(11):1057-1065 I.F.: 8.376

2. Durando P, Faust SN, Fletcher M, Krizova P, Torres A, Welte T. **Experience with pneumococcal polysaccharide conjugate vaccine (conjugated to CRM197 carrier protein) in children and adults.** *Clin Microbiol Infect* 19 Suppl 1:1-9 I.F.: 4.578

3. Liapikou A, Torres A. **Current treatment of community-acquired pneumonia.** Expert Opin Pharmacother 14(10):1319-1332 I.F.: 2.860

4. Sialer S, Liapikou A, Torres A. **What is the best approach to the nonresponding patient with community-acquired pneumonia?** *Infect Dis Clin North Am* 27(1):189-203 I.F.: 2.626

5. Liapikou A, Torres A. **Emerging drugs on methicillin-resistant Staphylococcus aureus.** *Expert Opin Emerg Drugs* 18(3):291-305 I.F.: 2.483

Editorials / I.F.: 9.818

1. Masa JF, Corral J, Sanchez de Cos Farré R, Navajas D, Montserrat JM. **Is there an optimal nasal pressure for treating obstructive sleep apnea-and if so, what is it?** Sleep 36(4):463-464 I.F.: 5.100

Martin-Loeches I, Torres A. **A week seems to be weak: tailoring duration of antibiotic treatment in Gram-negative ventilator-associated pneumonia.** *Crit Care* 17(1):106 I.F.: 4.718

Clinical Guidelines / I.F.: 1.399

1. Torres A, Barberán J, Falguera M, Menéndez R, Molina J, Olaechea P, Rodríguez A; en nombre del Grupo de la Guía Multidisciplinar para el Manejo de la Neumonía Adquirida en la Comunidad. **Multidisciplinary guidelines for the management of community-acquired pneumonia.** *Med Clin (Barc)* 140(5):223.e1-223.e19 I.F.: 1.399

Multicenter / I.F.: 5.901

1. Masclans JR, Pérez M, Almirall J, Lorente L, Marqués A, Socias L, Vidaur L, Rello J; H1N1 GTEI/SEMICYUC Investigators. **Early non-invasive ventilation treatment for severe influenza pneumonia.** *Clin Microbiol Infect* 19(3):249-256 I.F.: 4.578

2. Rello J, Gattarello S, Souto J, Sole-Violan J, Valles J, Peredo R, Zaragoza R, Vidaur L, Parra A, Roig J; Community-Acquired Pneumonia in Unidad de Cuidados Intensivos 2 CAPUCI 2 Study Investigators. **Community-acquired Legionella Pneumonia in the intensive care unit: Impact on survival of combined antibiotic therapy.** *Med Intensiva* 37(5):320-326 I.F.: 1.323

GRANTS FOR RESEARCH IN PROGRESS

Agusti C. **Complicaciones pulmonares en pacientes receptores de trasplante de progenitores hematopoyéticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00507. Duration: 01/01/2011-31/12/2014

Marrades R. **Detección del CTC y microRNAs en la sangre venosa pulmonar tumoral como indicadores de enfermedad residual o generación de M1 en pacientes intervenidos de cáncer de pulmón.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00405. Duration: 01/01/2013-31/12/2015

Montserrat J.M. **Consecuencias y tratamiento de la apnea obstructiva del sueño en la edad avanzada.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01892. Duration: 01/01/2012-31/12/2014

Soler N. **Impacto de la infección vírica en las agudizaciones de la enfermedad pulmonar obstructiva crónica (AEPOC): caracterización clínica, gravedad y factores pronósticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01504. Duration: 01/01/2011-31/12/2014

Soler N. Utilidad del tratamiento antibiótico en las agudizaciones de la enfermedad pulmonar obstructiva crónica (EPOC) sin purulencia en el esputo: ensayo clinico aleatorizado, controlado y doble ciego de eficacia y seguridad. Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00061. Duration: 01/01/2009-31/12/2013

Soy D. **Estudio farmacocinético y farmacodinámico de los antibióticos de amplio espectro de utilización más frecuente en la unidad de cuidados intensivos (piperacilina/tazobactam, meropenem, ceftriaxona) en pacientes con shock séptico sometidos a depuración renal de alto flujo.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-159. Duration: 01/01/2012-31/12/2014

Torres A. **Beneficios potenciales de la posición Lateral en Trendelemburg en la prevención de la neumonía asociada a la ventilación mecánico.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-33744. Duration: 01/01/2013-31/12/2015

Torres A. **Fisiopatologia i tractament de les malalties respiratòries.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_911. Duration: 15/09/2009-30/04/2014

DOCTORAL THESES

Montserrat JM. **Nuevas estrategias para el diagnóstico y tratamiento del Síndrome de apnea-hipopnea del Sueño.** PhD student: Cristina Embid López.

Torres A. **Estudio del biofilm en un modelo porcino de neumonía asociada al ventilador: papel de la antibioterapia sistémica en su microbiología y morfología microscópica.** PhD student: Laia Fernández Barat.

Torres A. **New insights into the role of the semirecumbent position in the pathogenesis of ventilator-associated pneumonia and potential preventive measures.** PhD student: Gianluigi Li Bassi.

Torres A. **Efficacy and safety assessment of ventilatory strategies and respiratory therapy techniques to improve mucociliary clearance during invasive mechanical ventilation.** PhD student: Joan-Daniel Martí Romeu.

2.7 Physiopathological mechanisms of respiratory illnesses

LOCATION
CELLEX building

KEYWORDS
1. **Pulmonary Hypertension**
2. **COPD**
3. **Systems Medicine**
4. **Endothelium**
5. **Stem Cells**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	91.96	21	10	3
2012	62.04	16	10	3
2013	63.29	16	10	1

TEAM INVOLVED IN
CIBERES

AWARDS
Reference Sites Award
Institution: European Union
Awardees: NEXES Project (Supporting Healthier and Independent Living for Chronic Patients and Elderly). Josep Roca (HCB), Albert Alonso (HCB), Felip Burgos (HCB), Carme Hernández (HCB), Anael Barberan (IDIBAPS), Isaac Cano (IDIBAPS)

Congress Chairs Award
Institution: European Respiratory Society
Awardee: Josep Roca (HCB)

TEAM LEADER
Joan Albert Barberà (HCB)
T. 93 227 57 47
jbarbera@clinic.cat

GROUP LEADER
Isabel Blanco (HCB-IDIBAPS)

RESEARCHERS
Felip Burgos (HCB)
Graciela Martínez-Pallí (HCB)
Josep Roca (HCB)
Robert Rodríguez-Roisín (HCB)
Elizabeth Zavala (HCB)

POST-DOCTORAL RESEARCHERS
Melina Musri (IDIBAPS)
Olga Tura-Ceide (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Gemma Argemí (FCRB)
Ebymar Arismendi (FCRB)
Anael Barberan (IDIBAPS)
Isaac Cano (IDIBAPS)
Núria Chamorro (FCRB)
Núria Coll (FCRB)
Maria Lorena Coronel (FCRB)
David Domínguez (FCRB)
Jéssica Garcia (FCRB)
Roberto del Pozo (FCRB)

TECHNICIANS
Núria Aventín (FCRB)
Cristina Bonjoch (FCRB)
Susana Maqueda (FCRB)

NURSING STAFF
Xavier Alsina (HCB)
Conchi Gistau (HCB)
Maria Palomo (FCRB)
Yolanda Torralba (CIBERES)
Laura Villa (FCRB)

ADMINISTRATIVE STAFF
Mirjam Hillenius (IDIBAPS)
Julio Más (FCRB)
Mª Dolores Sanz (FCRB)

PHYSIOTHERAPISTS
Beatriz Valeiro (IDIBAPS)

COLLABORATORS
Albert Alonso (FCRB)
Mª José Arguis (HCB)
Xavier Borrat (HCB)
Marta Cascante (UB)
Carme Hernández (HCB)
Victor I. Peinado (CIBERES)
Eva Rivas (HCB)
Jordi Vilaró (FCRB)

STRATEGIC OBJECTIVES

- Increase the understanding of the cellular and molecular mechanisms involved in the development of pulmonary vascular diseases
- Identification of new biomarkers and therapeutic targets for pulmonary hypertension
- Characterization of factors involved in the development of extrapulmonary disorders in chronic obstructive pulmonary disease (COPD)
- Determination of intra-and extrapulmonary manifestations of severe obesity
- Evaluation of the role of stem cells in lung injury and repair mechanisms.
- Get personalized medical care for chronic respiratory diseases from a systems medicine strategy.

MAIN LINES OF RESEARCH

- Clinical research in pulmonary hypertension: biomarkers and new therapies
- Endothelial dysfunction and vascular remodeling.
- Experimental models of COPD and pulmonary hypertension.
- Stem and progenitor cells.
- Interaction between airway, lung and systemic inflammation in COPD and severe obesity.
- Pathophysiology of pulmonary gas exchange.
- Systems medicine

50/50 PROGRAM

TRANSLATIONAL RESEARCH IN PULMONARY VASCULAR DISEASES: CELL PROLIFERATION AND APOPTOTIC MECHANISMS IN PULMONARY ARTERIAL HYPERTENSION

GROUP LEADER

Isabel Blanco (HCB-IDIBAPS)

Pulmonary arterial hypertension (PAH) is a disease of small pulmonary arteries, characterized by gradual obliteration of the arterial lumen due to the enlargement of the vessel wall. It results in a progressive increase of pulmonary vascular resistance (PVR) and, finally, right ventricular failure and death. While vasoconstriction contributes, especially in earlier stages, the obstructive vascular remodelling is the major cause of the elevated PVR and ultimately the right heart failure. Recent therapeutic advances increase survival and improve quality of life of patients with PAH. However, currently available drugs act primarily as vasodilators and do not alter the disease process or the structural lesions in the pulmonary arteries. There is a need to identify new signaling pathways in the pathogenesis of PAH, which may represent different more appropriate therapeutic targets. We propose going from the bench to the bed side studying with cells, tissue samples, animal models and also human samples potential biomarkers of the disease activity and progression; as well as potential new drugs to reverse the proliferative remodelling phenotype in PAH.

PUBLICATIONS

Originals / I.F.: 63.293

1. Blanco I, Santos S, Gea J, Güell R, Torres F, Gimeno-Santos E, Rodriguez DA, Vilaró J, Gómez B, Roca J, Barberà JA. **Sildenafil to improve respiratory rehabilitation outcomes in COPD: a controlled trial.** *Eur Respir J* 42: 982-992 I.F.: 6.355

2. Donaire-Gonzalez D, Gimeno-Santos E, Balcells E, Rodríguez DA, Farrero E, Batlle JD, Benet M, Ferrer A, Barberà JA, Gea J, Rodriguez-Roisin R, Antó JM, Garcia-Aymerich J. **Physical activity in COPD patients: patterns and bouts.** *Eur Respir J* 42: 993-1002 I.F.: 6.355

3. Freixa X, Portillo K, Paré C, Garcia-Aymerich J, Gomez FP, Benet M, Roca J, Farrero E, Ferrer J, Fernandez-Palomeque C, M Antó J, Barberà JA; on behalf of the PAC-COPD Study Investigators. **Echocardiographic abnormalities in patients with copd at their first hospital admission.** *Eur Respir* J 41: 784-791 I.F.: 6.355

4. Meyer S, McLaughlin VV, Seyfarth HJ, Bull TM, Vizza CD, Gomberg-Maitland M, Preston IR, Barberà JA, Hassoun PM, Halank M, Jaïs X, Nickel N, Hoeper MM, Humbert M. **Outcome of non-cardiac, non-obstetric surgery in patients with pulmonary arterial hypertension: results from an international prospective survey.** *Eur Respir* J 41: 1302-1307 I.F.: 6.355

5. Lang IM, Simonneau G, Pepke-Zaba JW, Mayer E, Ambrož D, Blanco I, Torbicki A, Mellemkjaer S, Yaici A, Delcroix M. **Factors associated with diagnosis and operability of chronic thromboembolic pulmonary hypertension. A case-control study.** *Thromb Haemost* 110 (1):83-91 I.F.: 6.094

6. Córdova H, San José Estépar R, Rodríguez-D'Jesús A, Martínez-Pallí G, Arguis P, Rodríguez de Miguel C, Navarro-Ripoll R, Perdomo JM, Cuatrecasas M, Llach J, Vosburgh KG, Fernández-Esparrach G. **Comparative study of NOTES alone**

versus NOTES guided by a new image registration system for navigation in the mediastinum: a study in a porcine model. *Gastrointest Endosc* 77: 102-107 I.F.: 5.210

7. Peinado VI, Gómez FP, Barberà JA, Roman A, Angels Montero M, Ramírez J, Roca J, Rodriguez-Roisin R. **Pulmonary vascular abnormalities in chronic obstructive pulmonary disease undergoing lung transplant.** *J Heart Lung Transplant* 32: 1262-1269 I.F.: 5.112

8. Balderramo D, Sendino O, Miquel R, de Miguel CR, Bordas JM, Martinez-Palli G, Leoz ML, Rimola A, Navasa M, Llach J, Cardenas A. **Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract.** *Liver Transpl* 19: 199-206 I.F.: 3.944

9. Monyarch G, de Castro Reis F, Zock JP, Giraldo J, Pozo-Rodríguez F, Espinosa A, Rodríguez-Trigo G, Verea H, Castaño-Vinyals G, Gómez FP, Antó JM, Coll MD, Barberà JA, Fuster C. **Chromosomal bands affected by acute oil exposure and DNA repair errors.** *PLoS One* 8: e81276 I.F.: 3.730

10. de Lacy AM, Rattner DW, Adelsdorfer C, Tasende MM, Fernández M, Delgado S, Sylla P, Martínez-Palli G. **Transanal natural orifice transluminal endoscopic surgery (NOTES) rectal resection: "down-to-up" total mesorectal excision (TME)-short-term outcomes in the first 20 cases.** *Surg Endosc* 27: 3165-3172 I.F.: 3.427

11. Vizcaya D, Mirabelli MC, Orriols R, Antó JM, Barreiro E, Burgos F, Arjona L, Gomez F, Zock JP. **Functional and biological characteristics of asthma in cleaning workers.** *Respir Med* 107: 673-683 I.F.: 2.585

12. Cano I, Mickael M, Gomez-Cabrero D, Tegnér J, Roca J, Wagner PD. **Importance of mitochondrial PO2 in maximal O2 transport and utilization: A theoretical analysis.** *Respir Physiol Neurobiol* 189: 477-483 I.F.: 2.051

13. Gómez FP, Amado VM, Roca J, Torres A, Nicolas JM, Rodriguez-Roisin R, Barberà JA. **Effect of nitric oxide inhalation on gas exchange in acute severe pneumonia.** *Respir Physiol Neurobiol* 187: 157-163 I.F.: 2.051

14. Roger N, Burgos F, Giner J, Rosas A, Tresserras R, Escarrabill J; el grupo de trabajo de Función Pulmonar del Plan Director de las Enfermedades del Aparato Respiratorio (PDMAR). **Encuesta de utilización de la función pulmonar en los hospitales públicos de Cataluña en 2009.** *Arch Bronconeumol* 49: 371-377 I.F.: 1.372

15. Roman A, Barbera JA, Castillo MJ, Muñoz R, Escribano P. **Calidad de vida relacionada con la salud en una cohorte nacional de pacientes con hipertensión arterial pulmonar o hipertensión pulmonar tromboembólica crónica.** *Arch Bronconeumol* 49: 181-188 I.F.: 1.372

16. Córdova H, Martinez-Pallí G, Fernández-Esparrach G. **Feasibility of systematic transesophageal endoscopic mediastinoscopy.** *Thorac Cardiovasc Surg* 61: 486-488 I.F.: 0.925

Reviews / I.F.: 31.921

1. Agusti A, Barberà JA, Wouters EF, Peinado VI, Jeffery PK. **Lungs, bone marrow and adipose tissue: A network approach to the pathobiology of chronic obstructive pulmonary disease.** *Am J Respir Crit Care Med* 188: 1396-1406 I.F.: 11.041

2. Rodriguez-Roisin R, Llufriu S, Fabbri LM. **Changes in your breathing can change your brain.** *Am J Respir Crit Care Med* 188: 763-764 I.F.: 11.041

3. Agusti A, Hurd S, Jones P, Fabbri L, Martinez F, Vogelmeier C, Vestbo J, Rodriguez-Roisin R. **Frequently asked questions (FAQs) about the GOLD 2011 assessment proposal of COPD.** *Eur Respir J* 42: 1391-1401 I.F.: 6.355

4. Gea J, Agustí A, Roca J. **Pathophysiology of muscle dysfunction in COPD.** *J Appl Physiol* 114: 1222-1234 I.F.: 3.484

Editorials / I.F.: 11.041

1. Barberà JA. **Chronic obstructive pulmonary disease: a disease of the endothelium?** *Am J Respir Crit Care Med* 188: 5-7 I.F.: 11.041

Clinical Guidelines / I.F.: 40.585

1. Seeger W, Adir Y, Barberà JA, Champion H, Coghlan JG, Cottin V, De Marco T, Galiè N, Ghio S, Gibbs S, Martinez FJ, Semigran MJ, Simonneau G, Wells AU, Vachiéry JL. **Pulmonary hypertension in chronic lung diseases.** *J Am Coll Cardiol* 62: D109-116 I.F.: 14.086

2. Vachiéry JL, Adir Y, Barberà JA, Champion H, Coghlan JG, Cottin V, De Marco T, Galiè N, Ghio S, Gibbs JS, Martinez F, Semigran M, Simonneau G, Wells A, Seeger W. **Pulmonary hypertension due to left heart diseases.** *J Am Coll Cardiol* 62: D100-108 I.F.: 14.086

3. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA, Sin DD, Rodriguez-Roisin R. **Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, GOLD Executive Summary.** *Am J Respir Crit Care Med* 187: 347-365 I.F.: 11.041

4. García-Río F, Calle M, Burgos F, Casan P, Del Campo F, Galdiz JB, Giner J, González-Mangado N, Ortega F, Puente Maestu L. **Normativa SEPAR. Espirometría.** *Arch Bronconeumol* 49: 388-401 I.F.: 1.372

Multicenter / I.F.: 168.770

1. Ghofrani HA, D'Armini AM, Grimminger F, Hoeper MM, Jansa P, Kim NH, Mayer

E, Simonneau G, Wilkins MR, Fritsch A, Neuser D, Weimann G, Wang C; CHEST-1 Study Group (Barberà JA). **Riociguat for the treatment of chronic thromboembolic pulmonary hypertension.** *N Engl J Med* 369: 319-329 I.F.: 51.658

2. Ghofrani HA, Galiè N, Grimminger F, Grünig E, Humbert M, Jing ZC, Keogh AM, Langleben D, Kilama MO, Fritsch A, Neuser D, Rubin LJ; PATENT-1 Study Group (Barberà JA). **Riociguat for the treatment of pulmonary arterial hypertension.** *N Engl J Med* 369: 330-340 I.F.: 51.658

3. Pulido T, Adzerikho I, Channick RN, Delcroix M, Galiè N, Ghofrani HA, Jansa P, Jing ZC, Le Brun FO, Mehta S, Mittelholzer CM, Perchenet L, Sastry BK, Sitbon O, Souza R, Torbicki A, Zeng X, Rubin LJ, Simonneau G; SERAPHIN Investigators (Barberà JA). **Macitentan and morbidity and mortality in pulmonary arterial hypertension.** *N Engl J Med* 369: 809-818 I.F.: 51.658

4. Villar J, Pérez-Méndez L, Blanco J, Añón JM, Blanch L, Belda J, Santos-Bouza A, Fernández RL, Kacmarek RM; Spanish Initiative for Epidemiology, Stratification, and Therapies for ARDS (SIESTA) Network (Zavala E). **A universal definition of ARDS: the PaO2/FiO2 ratio under a standard ventilatory setting--a prospective, multicenter validation study.** *Intensive Care Med* 39: 583-592 I.F.: 5.258

5. Perez-Padilla R, Wehrmeister FC, Celli BR, Lopez-Varela MV, Montes de Oca M, Muiño A, Talamo C, Jardim JR, Valdivia G, Lisboa C, Menezes AM; PLATINO Team (Rodríguez-Roisin R). **Reliability of FEV1/FEV6 to diagnose airflow obstruction compared with FEV1/FVC: the PLATINO longitudinal study.** *PLoS One 8*: e67960 I.F.: 3.730

6. Herrera-Gutiérrez ME, Seller-Pérez G, Sánchez-Izquierdo-Riera JA, Maynar-Moliner J; COFRADE investigators group (Zavala E). Prevalence of acute kidney injury in intensive care units: the "COrte de prevalencia de disFunción RenAl y DEpuración en críticos" point-prevalence multicenter study. J Crit Care 28: 687-694 I.F.: 2.498

7. Faner R, Nuñez B, Sauleda J, Garcia-Aymerich J, Pons J, Crespí C, Milà J, González JR, Maria Antó J, Agusti A; PAC-COPD Study Group (Barberà JA, Roca J, Rodriguez-Roisin R). **HLA distribution in COPD patients.** *COPD* 10: 138-146 I.F.: 2.310

GRANTS FOR RESEARCH IN PROGRESS

Barberà J.A. **Biomarcadores endoteliales en la hipertensión arterial pulmonar: relación con la heterogeneidad clínica y la respuesta terapéutica.** Sponsored by Instituto de Salud Carlos III (ISCIII). PI12/00510.
Duration: 01/01/2013-31/12/2015

Barberà J.A. **Redes temática de investigación cooperativa en salud (RETICS) de Biobancos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD09/0076/00038.
Duration: 01/01/2010-31/12/2014

Roca J. **Regions of Europe Working together for Health (RENEWING HEALTH).** Sponsored by: European Commission. 250487. IP-ICT-PSP-2009-3.
Duration: 01/02/2012-31/01/2014.

Roca J. **Advancing Care Coordination & TeleHealth Deployment Programme.** Sponsored by: European Commission. 20121209.
Duration: 15/02/2013-14/10/2015

Roca J. **Modelling and simulation environment for systems medicine (Chronic Obstructive pulmonary disease -COPD- as a use case).** Sponsored by: European Commission. 270086.
Duration: 01/02/2011-30/04/2014

Roca J. PITES-ISA: **Escalabilidad regional de los servicios de atención integrada y ayuda a la decisión clínica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01241.
Duration: 01/01/2013-31/12/2015

Roca J. **Servicios innovadores de atención integrada para pacientes crónicos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/90634.
Duration: 01/01/2010-30/06/2013

Roca J. **Despliegue de nuevos servicios sanitarios soportados por tecnologías de la información y comunicación (DENSSA-TIC).** Sponsored by: Ministerio de Economía y Competitividad. IPT-2011-1333-900000.
Duration: 05/05/2011-31/12/2014

Roca J. **Desarrollo de un sistema de rehabilitación física domiciliario.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2011-1193-900000.
Duration: 04/05/2011-30/06/2014

Barberà J.A. **Marcadores biológicos de integridad y función endotelial en la evaluación y seguimiento de los pacientes con hipertensión arterial pulmonar.** Sponsored by: Fundación Contra la Hipertensión Pulmonar (FCHP). FCHP_12_001.
Duration: 22/04/2013-21/04/2014

DOCTORAL THESES

Roca J. **Impact of Information and Communication Technologies on Remote Testing, Forced Spirometry as a Use Case.**
PhD student: Felipe Burgos Rincón.

Roca J. **Effects of training in patients with chronic obstructive pulmonary disease: a systems approach.**
PhD student: Diego Agustín Rodríguez.

2.8 Clinical and Experimental Respiratory Immunoallergy

LOCATION
CELLEX building

KEYWORDS
1. **Chronic rhinosinusitis and nasal polyps.**
2. **Aspirin Sensitive Asthma**
3. **Drug & Food allergy**
4. **Olfactory disorders**
5. **Idiopathic Pulmonary Fibrosis**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	81.17	28	9	11
2012	79.70	24	13	6
2013	90.15	31	16	6

AWARDS

Award to the best Oral Presentation on "Markers of chronic rhinosinusitis".
Institution: European Academy of Allergology and Clinical Immunology (EAACI) & World Allergy Oragnization (WAO). Milan (Italy), June 22-26th, 2013.
Awardees: Callejas FB, Martínez-Antón A, Fuentes M, Roca-Ferrer J, Picado C, Mullol J.

Award to the best Oral Presentation on "Immunology of the nose and the eye".
Institution: European Academy of Allergology and Clinical Immunology (EAACI) & World Allergy Organization (WAO). Milan (Italy), June 22-26th, 2013.
Awardees: Pujols L, Fernández-Bertolín L, Mullol J, Fuentes-Prado M, Alobid I, Roca-Ferrer J, Picado C.

Award to the best research clinical study published in an international journal in 2012.
Institution: Sociedad Española de Otorrinolaringología y Patología Cérvicofacial (SEORL-PCF). Madrid, October 26th, 2013.
Awardees: Mullol J, I Alobid, F Mariño-Sánchez, M Bernal-Sprekelsen, A Valero, C Picado, C Marin.

TEAM LEADER
Joaquim Mullol i Miret (IDIBAPS)
T. 93 227 98 72
jmullol@clinic.cat

RESEARCHERS
Isam Alobid (HCB)
Joan Bartra Tomàs (HCB)
Concepció Marin i Agustin (IDIBAPS)
Margarita Martin Andorra (UB)
César Picado Vallés (HCB)
Laura Pujols i Tarrés (IDIBAPS)
Antonio Valero Santiago (HCB)
Antoni Xaubet Mir (HCB)

POST-DOCTORAL RESEARCHERS:
Manuel Bernal Sprekelsen (HCB)
Joaquim Ensenyat Nora (HCB)
Josep Maria Guilemany (HCB)
Mariona Pascal Capdevila (HCB)
Jordi Roca i Ferrer (UB)
Jaume Sánchez López (FCRB)
Eva Serrano Candelas (FCRB)

PRE-DOCTORAL RESEARCHERS:
Erola Ainsua Enrich (FCRB)
Francisco de Borja Callejas Díaz (IDIBAPS)
Liliana Carvalho (FCRB)
Laura Fernández Bertolin (IDIBAPS)
Marta Gabasa Fernández (CIBERES)
Francisco Garcia Garcia (FCRB)
Alba Garcia Moral (FCRB)
Fernanda Hernàndez (HCB)
Suha Jabr (Ministeri Assumptes Exteriors i Cooperació)
Francesca Jaume Monroig (HCB)
Cristobal Langdon Montero (HCB)
Eduardo Lehrer Coriat (HCB)
Mauricio López Chacón (HCB)
Franklin Mariño Sánchez (HCB)
Alexandra Moreno García (UB)
Maria Rueda Garcia (FCRB)
Inés Tejero Royes (IDIBAPS)
Meritxell Valls Mateus (HCB)

TECHNICIANS:
Mercè Bonastre Garcia (IDIBAPS)
Mireia Fuentes Prado (IDIBAPS)
María Pérez González (FCRB)

NURSING STAFF:
Sílvia Centellas (HCB)
Rosa Cortés Aguilar (HCB)
Rossó de Lluís (FCRB)
Gemma López Sáiz (FCRB)

ADMINISTRATIVE STAFF:
Elena Arrufat (FCRB)

COLLABORATORS:
Pedro Benítez Silva (Hospital Moisés Broggi)
José Antonio Castillo Vizuete (Hospital Dexeus-Quirón)
Marta Ferrer Puga (Clínica Universitaria de Navarra)
Carolea Logun (CCMD, NIH, USA)
Asunción Martínez Antón (CCMD, NIH, USA)
Maria Molina Molina (Hospital de Bellvitge)
Fernando de Mora Pérez (UAB)
Rosa Maria Muñoz Cano (NIAID, NIH, USA)
José Obeso Indausti (CIMA, Universidad de Navarra)
María Cruz Rodríguez Oroz (Biodonostia, San Sebastian)
Anthony Schapira (UCL, London, UK)
James Shelhamer (CCMD, NIH, USA)
Rosa Torres Blanch (UAB)
María del Carmen Vennera (CIBERES)

STRATEGIC OBJECTIVES

1. Investigation of the mechanisms regulating inflammatory response and remodelling in bronchial asthma, allergic and non-allergic rhinitis, chronic rhinosinusitis and nasal polyposis, and pulmonary interstitial diseases.
2. Investigation of the mechanisms underlying food and drug allergies.
3. Investigation of the mechanisms involved in anaphylaxis of complex etiopathogenesis and mast cell physiology.
4. Investigation of the mechanisms involved in sudden and progressive loss of smell from different ethiologies: acute and chronic sinonasal inflammation, allergies, Traumatic Brain Injury, Parkinson Disease, iatrogenic, or idiopatic.

MAIN LINES OF RESEARCH

1. **Inflammation of the upper and lower airway mucosa.** Investigation of the pathophysiological mechanisms involved in sinonasal inflamation and remodelling (MUC and mucins, metaloproteinases, microRNA), and association with broncho-pulmonary diseases (asthma, bronchiectasis, COPD).
2. **The sense of smell in health and disease.** Investigation of the pathophysiological mechanisms involved in olfactory dysfunctions such as sinonasal inflammation, united airway diseases, allergies, Traumatic Brain Injury, Parkinson Disease.
3. **Food and drug allergy.** Investigation of genetic, immunological, and biochemical mechanisms involved in respiratory allergy, food allergy, drug allergy, and NSAID hypersensitivity reactions.
4. **Glucocorticoid resistance in respiratory diseases.** Investigation of molecular mechanisms involved in glucocorticoid resistance in respiratory and non-respiratory diseases, seeking for biomarkers of therapeutic response.
5. **Aspirin and non-steroidal antiinflammatory drug (nsaid) intolerance.** Investigation of the mechanisms of action involved in NSAID intolerance: association of allergy and cofactors, cyclooxygenase regulation, leukotriene and prostaglandin regulation, PGE2 receptor agonists and PGE2 relationship with geneticabnormalitis in cystic fibrosis and severe asthma.
6. **Idiopatic pulmonary fibrosis.** Investigation of the mechanisms of action of Idiopathic Pulmonary Fibrosis: expression of PGE2, IL-1β, and their receptors and clinical efficacy of intrabronchial installation of type II alveolar cells.
7. **Pathophysiology of mast cells.** Study of the mechanisms of anaphylactic reactions of multiple origin (indolent mastocytosis, predisposing genetic alterations) and Identification and characterization of adapter molecules in the signaling of IgE high affinity receptor and KIT receptor.

RESEARCH GROUP
NASOSINUSAL INFLAMMATORY AND OLFACTORY RESEARCH GROUP (INGENIO)

GROUP LEADER
Joaquim Mullol (IDIBAPS)

1. Investigation of different aspects of inflammatory sinonasal disorders (allergic and non-allergic rhinitis, chronic rhinosinusitis, nasal polyposis):
   - The physiopathological mechanisms of nasosinusal mucosal hypersecretion and regulation of mucins and MUC genes.
   - The physiopathological and clinical association of upper and lower airway inflammatory diseases and their impact upon patient quality of life.
2. Evaluation olfactory alterations and their mechanisms of action as diagnosis and severity markers. We have validated an olfactometric test (BAST-24) and performed a smell epidemiological study (OLFACAT) in the Catalan population.
3. Development and use of a human in vitro model of eosinophilic inflammation for test and compare the antiinflammatory action of different drugs used in airway inflammation (corticosteroids, antihistamines, antileukotrienes).

PUBLICATIONS

Originals / .F.: 90.145

1. Fernández-Bertolín L, J Mullol, M Fuentes-Prado, I Alobid, J Roca-Ferrer, C Picado, L Pujols. **Deficient glucocorticoid induction of anti-inflammatory genes in nasal polyp fibroblasts of asthmatic patients with and without aspirin intolerance.** *J Allergy Clin Immunol* 132(5):1243-1246.e12 I.F.: 12.050

2. Quiroga-Varela A, Walters JR, Brazhnik E, Marin C, Obeso JA. **What basal ganglia changes underlie the parkinsonian state? The significance of neuronal oscillatory activity.** *Neurobiol Dis* 58:242-248 I.F.: 5.624

3. Mullol J, J Bartra, A del Cuvillo, I Izquierdo, R Muñoz-Cano, A Valero. **Validation of the modified ARIA classification: specialist free-choice treatment reduces the severity of allergic rhinitis.** *Clin Exp Allergy* 43:723-729 I.F.: 5.624

4. Marin C, Rodríguez-Oroz MC, Mengod G, Cortés R, Bonastre M, Obeso JA. **Subthalamic 6-OHDA-induced lesion attenuates levodopa-induced dyskinesias in ther at model of Parkinson's disease.** *Exp Neurol* 250:304-312 I.F.: 4.789

5. Torres R, Herrerias A, Serra-Pagès M, Marco A, Plaza J, Costa-Farré C, Montoya M, Picado C, de Mora F. **Locally administered prostaglandin E2 prevents aeroallergen-induced airway sensitization in mice through immunomodulatory mechanisms.** *Pharmacol Res* 70(1):50-59 I.F.: 4.346

6. Liu T, Ullenbruch M, Young Choi Y, Yu H, Ding L, Xaubet A, Pereda J, Feghali-Bostwick CA, Bitterman PB, Henke CA, Pardo A, Selman M, Phan SH. **Telomerase and telomere length in pulmonary fibrosis.** *Am J Respir Cell Mol Biol* 49(2):260-268 I.F.: 4.148

7. Ros C, A Tercero, I Alobid, J Balasch, J Santamaria, J Mullol*, C Castelo-Branco*. **Hearing loss in adult women with Turner's Syndrome and other congenital hypogonadisms.** *Gynecol Endocrinol* 30(2):111-116 I.F.: 3.877

8. Gabasa M, Royo D, Molina-Molina M, Roca-Ferrer J, Pujols L, Picado C, Xaubet A, Pereda J. **Lung myofibroblasts are characterized by down-regulated cyclooxygenase-2 and its main metabolite, prostaglandin E2.** *PLoS One* 8(6):e65445 I.F.: 3.730

9. Labrador-Horrillo M, Valero A, Velasco M, Jáuregui I, Sastre J, Bartra J, Silvestre JF, Ortiz de Frutos J, Gimenez-Arnau A, Ferrer M. **Efficacy of omalizumab in chronic spontaneous urticaria refractory to conventional therapy: analysis of 110 patients in real-life practice.** *Expert Opin Biol Ther* 13(9):1225-1228 I.F.: 3.345

10. Roca-Ferrer J, M Perez-Gonzalez, FJ Garcia-Garcia, J Pereda, L Pujols, I Alobid, J Mullol*, C Picado*. **Low prostaglandin E2 and cyclooxygenase expression in nasal mucosa fibroblasts of aspirin-intolerant asthmathics.** *Respirology* 18:711-717 I.F.: 2.781

11. Jabr S, Gartner S, Milne GL, Roca-Ferrer J, Casas J, Moreno A, Gelpí E, Picado C. **Quantification of major urinary metabolites of PGE2 and PGD2 in cystic fibrosis: correlation with disease severity.** *Prostaglandins Leukot Essent Fatty Acids* 89(2-3):121-126 I.F.: 2.732

12. Vilaseca I, Ballesteros F, Martínez-Vidal BM, Lehrer E, Bernal-Sprekelsen M, Blanch JL. **Quality of life after transoral laser microresection of laryngeal cancer: a longitudinal study.** *J Surg Oncol* 108(1):52-56 I.F.: 2.644

13. Alobid I, J Ensenyat, F Mariño-Sánchez, M de Notaris, S Centellas, J Mullol*, M Bernal-Sprekelsen*. **Impairment of olfaction and mucociliary clearance after expanded endonasal approach using vascularised septal flap reconstruction for skull base tumors.** *Neurosurgery* 72:540-546 I.F.: 2.532

14. Alobid I, Rioja E, Enseñat J, de Notaris M, Mullol J, Bernal-Sprekelsen M. **In Reply: Avoiding Olfactory Impairment After Endoscopic Endonasal Expanded Approaches.** *Neurosurgery* 73(3):E563-564 I.F.: 2.532

15. Gago B, Marin C, Rodríguez-Oroz MC, Obeso JA. **L-dopa-induced dyskinesias in unilateral 6-hydroxydopamine-lesioned rats are not modified by excitotoxic lesion of the entopeduncular nucleus and substantia nigra pars reticulata.** *Synapse* 67:407-414 I.F.: 2.310

16. Meltzer EO, P Ratner, C Bachert, W Carr, W Berger, GW Canonica, J Hadley, P Lieberman, J Mullol, U Munzel, D Price, G Scadding, C Virchow, U Wahn, J Bousquet. **Characterizing the efficacy of MP29-02 vs firstline rhinitis therapy – post hoc assessment of a randomized trial.** *Int Arch Allergy Immunol* 161 (4): 369-377 I.F.: 2.248

17. Muñoz-Cano R, Bartra J, Sanchez-Lopez J, Picado C, Bissinger I, Valero A. **Acoustic rhinometry and aspirin nasal challenge in the diagnosis of aspirin-intolerant asthma: clinical finding and safety aspects.** *Int Arch Allergy Immunol* ;160(3):307-312 I.F.: 2.248

18. Mullol J, C Crespo, C Carré, M Brosa. **Pharmacoeconomics of Cyclamen europaeum in the management of acute rhinosinusitis.** *Laryngoscope* 123(11):2620-2625 I.F.: 1.979

19. Delgado J, Dávila ID, Domínguez-Ortega J, Quirce S, Martí-Guadaño E, Valero A. **Quality of life in patients with respiratory allergy is influenced by the causative allergen.** *J Investig Allergol Clin Immunol* 23(5):309-314 I.F.: 1.887

20. Sala-Cunill A, Bartra J, Dalmau G, Tella R, Botey E, Raga E, Valero A; Comitè de Al-lergia Respiratòria de Catalunya, Spain. **Prevalence of asthma and severity of allergic rhinitis comparing 2 perennial allergens: house dust mites and Parietaria judaica pollen.** *J Investig Allergol Clin Immunol* 23(3):145-151 I.F.: 1.887

21. Valero A, I Izquierdo, J Sastre, AM Navarro, E Baró, E Martí-Guadaño, M Ferrer, I Dávila, A del Cuvillo, C Colás, I Antépara, J Alonso, J Mullol. ESPRINT-15 **Questionnaire (Spanish version): Reference values according to disease severity using both original and modified ARIA classifications.** *J Investig Allergol Clin Immunol* 23(1):14-19 I.F.: 1.887

22. De Llano LP, Vennera MdelC, Álvarez FJ, Medina JF, Borderías L, Pellicer C, González H, Gullón JA, Martínez-Moragón E, Sabadell C, Zamarro S, Picado C; Spanish Registry. **Effects of omalizumab in non-atopic asthma: results from a Spanish multicenter registry.** *J Asthma* 50(3):296-301 I.F.: 1.848

23. de Notaris M, Topczewski T, de Angelis M, Enseñat J, Alobid I, Gondolbleu AM, Soria G, Gonzalez JB, Ferrer E, Prats-Galino A. **Anatomic skull base education using advanced neuroimaging techniques.** *World Neurosurg* 79(2 Suppl):S16.e9-13 I.F.: 1.765

24. Alobid I, J Enseñat, F Mariño-Sánchez, E Rioja, M de Notaris, J Mullol*, M Bernal-Sprekelsen*. **Expanded endonasal approach using vascularised septal flap reconstruction for skull base tumors has a negative impact on sinonasal symptoms and quality of life.** *Am J Rhinol Allergy* ;27(5):426-431 I.F.: 1.744

25. Callejas FB, C Picado, A Martínez-Antón, I Alobid, L Pujols, A Valero, J Roca-Ferrer, J Mullol. **Differential expression of matrix of remodelling markers by tissue structure in nasal polyposis.** *Am J Rhinol Allergy* ;27(3):e69-e74 I.F.: 1.744

26. Muñoz-Cano, J Bartra, J Mullol, C Picado, A Valero. **Platelet-activating factor nasal challenge induces nasal congestion and reduces nasal volume in both healthy volunteers and allergic rhinitis patients.** *Am J Rhinol Allergy* 27(2):e48-e52 I.F.: 1.744

27. Enseñat J, de Notaris M, Sanchez M, Fernandez C, Ferrer E, Bernal-Sprekelsen M, Alobid I. **Endoscopic endonasal surgery for skull base tumours: technique and preliminary results in a consecutive case series report.** *Rhinology* 51(1):37-46 I.F.: 1.720

28. Bernal-Sprekelsen M, Blanch JL, Caballero-Borrego M, Vilaseca I. **The learning curve in transoral laser microsurgery for malignant tumors of the larynx and hypopharynx: parameters for a levelled surgical approach.** *Eur Arch Otorhinolaryngol* 270(2):623-628 I.F.: 1.458

29. Roger A, Vázquez R, Almonacid C, Padilla A, Serrano J, García-Salmones M, Molina F, Pinedo C, Torrejón M, Picado C, López-Viña A, Plaza V; Grupo Emergente Asma. Área Asma de SEPAR. **Knowledge of their own allergic sensitizations in asthmatic patients and its impact on the level of asthma control.** *Arch Bronconeumol* 49(7):289-296 I.F.: 1.372

30. Ros C, I Alobid, Juan Balasch, J Mullol*, C Castelo-Branco*. **Turner's syndrome and other congenital hypogonadisms impair quality of life and sexual function.** *Am J Obstet Gynecol* 286(6):484.e1-6 I.F.: 1.303

31. Yepes-Nuñez JJ, J Bartra, R Muñoz-Cano, J Sánchez-López, C Serrano, J Mullol, I Alobid, J Sastre, C Picado, A Valero. **Assessment of nasal obstruction: Correlation between subjective and objective techniques.** *Allergol Immunopath* (Madr.) 41(6):397-401 I.F.: 1.229

Reviews / I.F.: 24.893

1. Hellings PW, Fokkens WJ, Akdis C, Bachert C, Cingi C, Dietz de Loos D, Gevaert P, Hox V, Kalogjera L, Lund V, Mullol J, Papadopoulos NG, Passalacqua G, Rondón C, Scadding G, Timmermans M, Toskala E, Zhang N, Bousquet J. **Uncontrolled allergic rhinitis and chronic rhinosinusitis: where do we stand today?** *Allergy* 68: 1-7 I.F.: 5.883

2. Jáuregui I, M Ferrer, J Bartra, A del Cuvillo, I Dávila, J Montoro, J Mullol, J Sastre, A Valero. **Bilastine for the treatment of urticaria.** *Exp Opin Pharmacother* 14(11):1537-1544 I.F.: 2.860

3. González-Núñez V, Valero A, Mullol J. **Impact of Sleep as a Specific Marker for Quality of Life in Allergic Rhinitis**. *Curr Allergy Asthma Rep* 13:131-141 I.F.: 2.746

4. Izquierdo A, A Valero, J Mullol. **Comparative analysis of Allergic Rhinitis in Children and Adults.** *Curr Allergy Asthma Rep* 13:142-151 I.F.: 2.746

5. González-Núñez V, Valero A, Mullol J. **Safety evaluation of desloratadine in allergic rhinitis.** *Exp Opin Drug Saf* 12(3):445-453 I.F.: 2.621

6. Mullol J, C Picado. **Rhinosinusitis and Nasal Polyps in Aspirin-Exacerbated Respiratory Disease**. **Immunol Allergy Clin N Am** 33:163-176 I.F.: 2.376

7. Dávila I, del Cuvillo A, Mullol J, Jáuregui I, Bartra J, Ferrer M, Montoro J, Sastre J, Valero A. **Use of second generation H1 antihistamines in special situations.** *J Investig Allergol Clin Immunol* 23 (Suppl 1):1-16 I.F.: 1.887

8. Jáuregui I, Ferrer M, Montoro J, Dávila I, Bartra J, del Cuvillo A, Mullol J, Sastre J, Valero A. **Antihistamines in drivers, aircrew and occupations of risk.** *J Investig Allergol Clin Immunol* 23 (Suppl 1):27-34 I.F.: 1.887

9. Montoro J, Bartra J, Sastre J, Dávila I, Ferrer M, Mullol J, del Cuvillo A, Jáuregui I, Valero A. **H1 antihistamines and benzodiazepines. Pharmacological interactions and their impact on cerebral function.** *J Investig Allergol Clin Immunol* 23(Suppl 1):17-26 I.F.: 1.887

Clinical Guidelines / I.F.: 2.248

1. Bousquet J, Antó J, Sunyer J, Nieuwenhuijsen M, Vrijheid M, Keil Tand collaborators: Bousquet J, Antó JM, Akdis M, Auffray C, Keil T, Postma DS, Valenta R, Haahtela T, Cambon-Thomsen A, Lambrecht BN, Sunyer J, Akdis CA, Annesi-Maesano I, Arno A, Bachert C, Ballester F, Basagana X, Baumgartner U, Bindslev-Jensen C, Brunekreef B, Carlsen KH, Chatzi L, Eller E, Forastiere F, Garcia-Aymerich J, Guerra S, Gehring U, Hammad H, Heinrich J, Hohmann C, Kauffmann F, Kerkhof M, Kogevinas M, Koppelman GH, Kowalski ML,

Kull I, Lau S, Lodrup-Carlsen KC, Lupinek C, Maier D, Makela MJ, Martínez FD, Momas I, Nawijn MC, Neubauer A, Oddie S, Palkonen S, Reitamo S, Rial-Sebbag E, Salapatas M, Siroux V, Smagghe D, Smit HA, Torrent M, Toskala E, van Oosterhout AJ, Varaso R, von Hertzen L, Wickman M, Wijmenga C, Wright J, Vrijheid M, Chatzi L, Duijts L, Jaddoe V, Kogevinas M, Lawlor D, Lucas P, Magnus P, Merletti F, Nieuwenhuijsen M, Nybo Andersen AM, Raat H, Stoltenberg C, Sunyer J, Nieuwenhuijsen M, Vrijheid M, Casas M, Bergström A, Carmichael A, Chen C-, Cordier S, Eggesbø M, Eller E, Fantini MP, Fernández MF, Fernández-Somoano A, Gehring U, Grazuleviciene R, Heinrich J, Hohmann C, Karvonen AM, Keil T, Kogevinas M, Koppen G, Krämer U, Kuehni CE, Magnus P, Majewska R, Nybo Andersen AM, Patelarou E, Petersen M, Pierik FH, Polanska K, Porta D, Richiardi L, Santos AC, Slama R, Sram RJ, Thijs C, Tischer C, Toft G, Trnovec T, Vandentorren S, Vardavas C, Vrijkotte TG, Wilhelm M, Wright J, Zuberbier T, Bousquet J, Burney PG, Van Cauwenberge P, Akdis CA, Bindslev-Jensen C, Bonini S, Fokkens WJ, Kauffmann F, Keil T, Kowalski ML, Kramer U, Kull I, Lau S, Lodrup-Carlsen K, Mullol J, Nizankowska-Mogilnicka E, Papadopoulos N, Toskala E, Wickman M, Anto J, Alm B, Alm J, Arshad SH, Bachert C, Bousquet PJ, Bravi F, Brunekreef B, Canonica GW, Carlsen KH, Custovic A, Dubakiene R, Eller E, Fantini MP, Forastiere F, Gjomarkaj M, Halken S, Host A, Heinrich J, Howarth P, Kuehni C, Lotvall J, Momas I, Mommers M, Porta D, Radon K, Ring J, Roberts G, Salapatas M, Schünemann HJ, Simpson A, Smit HA, Sunyer J, Szczecklik A, Thijs C, Todo-Bom A, Torrent M, Valenta R, Valovirta E, van Steen K, Von Berg A, von Mutius E, Wahn U, Wennergren G, Wijga AH, Zock JP. **Pooling birth cohorts in allergy and asthma: European Union-funded initiatives - a MeDALL, CHICOS, ENRIECO, and GA²LEN joint paper.** *Int Arch Allergy Immunol* 161(1):1-10 I.F.: 2.248

Multicenter / I.F.: 6.355

1. Raghu G, Million-Rousseau R, Morganti A, Perchenet L, Behr J; MUSIC Study Group. **Macitentan for the treatment of idiopathic pulmonary fibrosis: the randomised controlled MUSIC trial.** *Eur Respir J* ;42(6):1622-1632 I.F.: 6.355

GRANTS FOR RESEARCH IN PROGRESS

Bartra J. **Red de Investigación de Reacciones Adversas a Alérgenos y Fármacos (RIRAAF).** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD07/0064/0006.
Duration: 29/02/2008-31/12/2013.

Bartra J. **Red de Investigación de Reacciones Adversas a Alérgenos y Fármacos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0013/0012.
Duration: 01/01/2013-31/12/2016.

Bartra J. **Anafilaxia por alergia alimentaria inducida por AINEs y ejercicio (AAAIA/E): Mecanismos de acción y efecto protector de PGE2.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01326.
Duration: 01/01/2012-31/12/2014.

Marin C. **Neurogénesis en la enfermedad de Parkinson y su modulación con el tratamiento farmacológico: un estudio comportamental, molecular y de neuroimagen en el parkinsonismo experimental.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01267.
Duration: 01/01/2012-31/12/2014.

Martin-Andorra M. **Modulación de la función del receptor KIT por receptores de la familia CD150, CD300 y moléculas adaptadoras asociadas en mastocitos y estudio en patologías donde KIT está mutado.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00332.
Duration: 01/01/2013-31/12/2015.

Mullol J. **Estudio del papel de la inflamación neurógena no alérgica en la expresión de mucinas y en el proceso de remodelado de la mucosa respiratoria nasosinusal.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI08/0188.
Duration: 01/01/2009-30/06/2013.

Mullol J. **Impact of acute Traumatic Brain Injury on the sense of smell: The role of smell training ang neuroprotection in post-trauma smell recovery.** Sponsored by: Fundació La Marató de TV3. 110610.
Duration: 03/01/2012-02/01/2015.

Mullol J. **Papel de los microRNA en la diferenciación de la mucosa respiratoria humana. Comparación entre células epiteliales nasales y bronquiales.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01129.
Duration: 01/01/2013-31/12/2015.

Picado C. **Inflamació i tractament de les malalties respiratòries.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_954.
Duration: 15/09/2009-30/04/2014.

Picado C. **Estudio de la regulación epigenética del gen de l Cox-2 en el asma con intolerancia a los antiinflamatorios no esteroideos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI08/0249.
Duration: 01/01/2009-30/06/2013.

Picado C. **Estudio de los mecanismos involucrados en el desarrollo de obstrucción bronquial irreversible en el asma bronquial.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00254.
Duration: 01/01/2013-31/12/2015.

Valero A. **Efecto clínico e inflamatorio nasal tras la aplicación del factor de agregación plaquetaria (PAF).** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1202.
Duration: 01/01/2010-31/12/2013.

Xaubet A. **Implicación del sistema de la angiotensina en la etiopatogenia de la fibrosis pulmonar idiopática.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/0672.
Duration: 01/01/2010-30/03/2013.

Xaubet A. **Trasplante de células alveolares tipo II en el tratamiento de la fibrosis pulmonar idiopática.**
Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01122.
Duration: 01/01/2013-31/12/2015.

DOCTORAL THESES

Bernal-Sprekelsen M. **Sordera súbita neurosensorial idiopática. Análisis de los factores de riesgo vascular clásicos y genéticos.**
PhD student: Ferran Ballesteros.

Marin C. **Caracterización de un modelo progresivo y bilateral de enfermedad de Parkinson con administración intraventricular de 6-OHDA en la rata.**
PhD student: Rosa Anna Quiroga Varela.

Picado C. **Contribution to the study of the role of arachidonic acid metabolism in inflammatory airway diseases (nasal polyps, asthma and cystic fibrosis).**
PhD student: Suha Jabr.

Picado C, Pujols L. **Mecanismes involucrats en la resposta als glucocorticoides en malalties inflamatòries de les vies aèries.**
PhD student: Laura Fernández Bertolín.

Picado C, Roca-Ferrer J. **Regulació del metabolisme de l'àcid araquidònic i senyalització cel·lular en un model d'asma i intolerància als aines.**
PhD student: Francesc Josep García García.

Mullol J, Valero A. **Efecte de la inhibició del factor d'activació de plaquetes (PAF) sobre la resposta al·lèrgica: model in vivo i in vitro.**
PhD student: Rosa Maria Muñoz Cano.

2.9 Inflammation and repair in respiratory illnesses

LOCATION
CELLEX building

KEYWORDS
1. **COPD**
2. **Emphysema**
3. **Inflammation**
4. **Networks**
5. **Systems biology**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	115.32	20	9	2
2012	136.99	7	15	0
2013	43.933	8	4	2

TEAM INVOLVED IN
CIBERES

TEAM LEADER
Alvar Agustí García-Navarro (HCB)
T. 93 227 17 01
aagusti@clinic.cat

RESEARCHERS
Eugeni Ballester (HCB)
Abel Gomez-Caro (HCB)
Ramon Marrades (HCB)

COLLABORATORS
Teresa Caserres (IDIBAPS)
Ignacio Coca (IDIBAPS)
Tamara Cruz (FCRB)
Rosa Faner (FCRB)
Susana Kalko (IDIBAPS)
Alejandra López (FCRB)
Gemma Sunyer (CIBERES)

STRATEGIC OBJECTIVES

The general objective of the group is to investigate the inflammatory and tissue repair mechanisms in chronic obstructive pulmonary disease (COPD), their clinical-functional correlation, the diagnostic, prognostic and therapeutic implications of such knowledge, and particularly their relevance in relation to pulmonary oncogenesis. COPD is presently the fourth most common cause of death in the world, and will rank third within a decade. Lung cancer is the most common malignant tumor in males (and soon also will be the most common malignancy in females), and involves one of the poorest prognosis with the currently available treatment options. To investigate these objectives the group uses systems network methods.

MAIN LINES OF RESEARCH

1. Mechanism of abnormal repair in COPD related to the inflammation present in COPD patients (in collaboration with Dr. Ernest Sala, of the Hospital Son Espases, Mallorca).
2. Mechanisms of oncogenesis in COPD (in collaboration with investigators of the Fundació Caubet-Cimera in Mallorca and the CIBER of respiratory diseases (CIBERES): SINECAN project).

3. Application of the methodology of systems biology ("omic" platforms and bioinformatics) to COPD, with a view to integrate the cellular and molecular alterations with clinical data. This line is developed in the setting of the CIBER of respiratory diseases (www.ciberes.org), involving a strategic alliance with the Institute for Systems Biology (Seattle, USA), Harvard University (USA) and the pharmaceutical industry with an interest in COPD.

PUBLICATIONS

Originals / I.F.: 43.933

1. Cheng DT, Kim DK, Cockayne DA, Belousov A, Bitter H, Cho MH, Duvoix A, Edwards LD, Lomas DA, Miller BE, Reynaert N, Tal-Singer R, Wouters EF, Agustí A, Fabbri LM, Rames A, Visvanathan S, Rennard SI, Jones P, Parmar H, MacNee W, Wolff G, Silverman EK, Mayer RJ, Pillai SG; TESRA and ECLIPSE Investigators. **Systemic soluble receptor for advanced glycation endproducts is a biomarker of emphysema and associated with ager genetic variants in patients with chronic obstructive pulmonary disease.** *Am J Respir Crit Care Med* 188:948-957 I.F.: 11.041

2. Polkey MI, Spruit MA, Edwards LD, Watkins ML, Pinto-Plata V, Vestbo J, Calverley PM, Tal-Singer R, Agustí A, Bakke PS, Coxson HO, Lomas DA, MacNee W, Rennard S, Silverman EK, Miller BE, Crim C, Yates J, Wouters EF, Celli B; **Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Study Investigators. Six Minute Walk Test in COPD: Minimal Clinically Important Difference for Death or Hospitalization.** *Am J Respir Crit Care Med* 187 (4): 382-386 I.F.: 11.041

3. Agusti A, Edwards LD, Celli B, Macnee W, Calverley PM, Müllerova H, Lomas DA, Wouters E, Bakke P, Rennard S, Crim C, Miller BE, Coxson HO, Yates JC, Tal-Singer R, Vestbo J; ECLIPSE Investigators. **Characteristics, stability and outcomes of the 2011 gold copd groups in the eclipse cohort.** *Eur Respir J* 42:636-646 I.F.: 6.355

4. Campayo M, Navarro A, Viñolas N, Diaz T, Tejero R, Gimferrer JM, Molins L, Cabanas ML, Ramirez J, Monzo M, Marrades R. **Low miR-145 and high miR-367 are associated with unfavourable prognosis in resected nonsmall cell lung cancer.** *Eur Respir* J. 41:1172-8. I.F.: 6.355

5. Kerwin EM, Scott-Wilson C, Sanford L, Rennard S, Agusti A, Barnes N, Crim C. **A randomised trial of fluticasone furoate/vilanterol (50/25 µg; 100/25 µg) on lung function in COPD.** *Respir Med* 107:560-569 I.F.: 2.585

6. Scrimini S, Pons J, Agustí A, Soriano JB, Cosio BG, Torrecilla JA, Núñez B, Córdova R, Iglesias A, Jahn A, Crespi C, Sauleda J. **Differential effects of smoking and copd upon circulating myeloid derived suppressor cells.** *Respir Med* 107:1895-1903 I.F.: 2.585

7. Faner R, Nuñez B, Sauleda J, Garcia-Aymerich J, Pons J, Crespí C, Milà J, González JR, Maria Antó J, Agusti A; PAC-COPD Study Group. **HLA Distribution in COPD Patients.** *COPD* 10:1-9 I.F.: 2.310

8. Rutten EP, Calverley PM, Casaburi R, Agusti A, Bakke P, Celli B, Coxson HO, Crim C, Lomas DA, Macnee W, Miller BE, Rennard SI, Scanlon PD, Silverman EK, Tal-Singer R, Vestbo J, Watkins ML, Wouters EF. **Changes in body composition in patients with chronic obstructive pulmonary disease: Do they influence patient-related outcomes?** *Ann Nutr Metab* 63:239-247 I.F.: 1.661

Reviews / I.F.: 45.058

1. Agusti A, Barbera JA, Wouters EF, Peinado VI, Jeffery PK. **Lungs, bone marrow, and adipose tissue. A network approach to the pathobiology of chronic obstructive pulmonary disease.** *Am J Respir Crit Care Med* 188:1396-1406 I.F.: 11.041

2. Agusti A, MacNee W. T**he copd control panel: Towards personalised medicine in COPD.** *Thorax* 68:687-690 I.F.: 8.376

3. Agusti A, Hurd S, Jones P, Fabbri LM, Martinez F, Vogelmeier C, Vestbo J, Rodriguez-Roisin R. **Faqs about the gold 2011 assessment proposal of copd: A comparative analysis of four different cohorts.** *Eur Respir* J 42:1391-1401 I.F.: 6.355

4. Müllerova H, Agusti A, Erqou S, Mapel DW. **Cardiovascular Comorbidity in Chronic Obstructive Pulmonary Disease: Systematic Literature Review.** *Chest* 144(4): 1163-1178 I.F.: 5.854

5. Molins L, Agusti A. **Chronic obstructive pulmonary disease and risk of lung cancer: The importance of smoking and timing of diagnosis.** *J Thorac Oncol* 2013;8:e34 I.F.: 4.473

6. Gea J, Agustí A, Roca J. **Pathophysiology of muscle dysfunction in COPD.** J *Appl Physiol* 114:1222-1234 I.F.: 3.484

7. Faner R1, Cruz T, Agusti A**. Inmune response in Chronic obstructive pulmonary disease.** *Expert Rev Clin. Immu* 9(9), 821-833 I.F.: 2.890

8. Dekhuijzen PN, Vincken W, Virchow JC, Roche N, Agusti A, Lavorini F, van Aalderen WM, Price D. **Prescription of inhalers in asthma and copd: Towards a rational, rapid and effective approach.** *Respir Med* 107:1817-1821 I.F.: 2.585

GRANTS FOR RESEARCH IN PROGRESS

Agusti A. **Capacidad regenerativa pulmonar en pacientes con EPOC. Análisis integrado de la funcionalidad de las células madre y el microambiente inflamatorio.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01117. Duration: 01/01/2013-31/12/2015

Agusti A. **Envelliment pulmonar prematur i MPOC.** Sponsored by: Associació Catalana d'Universitats Púnliques (ACUP).

2012ACUP00001.
Duration: 01/01/2013-31/12/2014

Agusti A. **Riboleucograma en la Enfermedad Pulmonar Obstructiva Crónica.** Sponsored by: Fundación Mútua Madrileña AP103772012.
Duration: 22/06/2012 - 21/06/2013.

Agusti A. **Epigenética e Inflamación Sistémica persistente en la EPOC.** Sponsored by: Sociedad Española de Neumología y Cirugía Torácica (SEPAR). 065/2013
Duration: 01/01/2013-31/12/2013.

2.10 Genetic and urological tumours

LOCATION
CELLEX building

KEYWORDS
1. **Bladder cancer**
2. **Prostate cancer**
3. **Gene expression**
4. **Real time quantitative PCR**
5. **Non invasive diagnostic methods**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	28.86	7	3	3
2012	71.26	19	11	5
2013	52.54	14	9	4

TEAM INVOLVED IN
RIRAF

TEAM LEADER
Antonio Alcaraz (HCB)
T. 93 227 55 45
aalcaraz@clinic.cat

RESEARCHERS
Laura Izquierdo (HCB)
Lourdes Mengual (FCRB)
Mireia Musquera (HCB)
Maria José Ribal (HCB)

PRE-DOCTORAL RESEARCHERS
Alexandru Ciudin (HCB)
Meritxell Pérez (HCB)

TECHNICIANS
Mercedes Ingelmo-Torres (IDIBAPS)

ADMINISTRATIVE STAFF
Maite Dalet (FCRB)

COLLABORATOR
Juan José Lozano (CIBEREHD)
Antoine G. Van Der Heijden (Radboud University Nijmegen Medical Center)

STRATEGIC OBJECTIVES

At present, the research group in urological oncology is conducting two main lines of research, based on the two most frequent urological tumors: urothelial and prostate cancer. The objectives are summarized below:

1. Identification of noninvasive molecular markers for the diagnosis and prognosis of bladder and prostate cancer.
2. Study of molecular markers to identify dsseminated tumour cells and the response to chemotherapy in patients with muscle invasive bladder cancer.
3. Determination of molecular prognostic factors in upper urinary tract tumors.

MAIN LINES OF RESEARCH

Noninvasive diagnosis and prognosis of bladder tumors.
- Development of a gene/miRNA expression signature in urine samples
- Identification of DNA aneuploidies in urine samples by FISH
- Determination of methylation profiles of urine samples

Biomarkers in muscle invasive bladder cancer patients
- Markers of disseminated tumour disease in lymph nodes and peripheral blood.
- Markers of response to neoadjuvant chemotherapy
- Prognostic factors in upper urinary tract tumors.

Noninvasive diagnosis and prognosis of prostate tumours.
- Development of a gene/miRNA expression signature in post-prostatic massage urine samples

PUBLICATIONS

Originals / I.F.: 52.544

1. Schröder F, Bangma C, Angulo JC, Alcaraz A, Colombel M, McNicholas R, Tammela TL; Nandy I, Castro R.

Dutasteride treatment over 2 years delays prostate-specific antigen progresión in patients with biochemical failure alter radical therapy for prostate cancer: results from the randomised, placebo-controlled Avodart after radical therapy for prostate cancer study (ARTS). *Eur Urol* 63:779-787 I.F.: 10.476

2. Mengual L, Lozano JJ, Ingelmo-Torres M, Gazquez C, Ribal MJ, Alcaraz A. **Using microRNA profiling in urine samples to develop a non-invasive test for bladder cancer.** *Int J Cancer.* 133(11):2631-2641 I.F.: 6.198

3. Alcaraz A, González-López R, Morote J, de la Piedra C, Meseguer C, Esteban E, Climent M, González-Gragera B, Alvarez-Ossorio JL, Chirivella I, Mellado B, Lara PC, Vázquez F, Contreras JA, Carles J, Murias A, Calderero V, Comet-Batlle J, González-Del Alba A, León-Mateos L, Mañas A, Segarra J, Lassa A, González-Enguita C, Méndez MJ, Samper P, Unda M, Mahillo-Fernández I, Bellmunt J; TUGAMO GROUP. **Biochemical markers of bone turnover and clinical outcome in patients with renal cell and bladder carcinoma with bone metastases following treatment with zoledronic acid: the TUGAMO study.** *Brit J Cancer* 109(1):121-130 I.F.: 5.082

4. de la Piedra C, Alcaraz A, Bellmunt J, Meseguer C, Gómez-Caamano A, Ribal MJ, Vázquez F, Anido U, Samper P, Esteban E, Alvarez-Ossorio JL, Lara PC, San José LA, Contreras JA, Del Alba AG, González-Gragera B, Tabernero AJ, González-Enguita C, Fernández JM, García-Escudero A, Gómez-Veiga F, Méndez MJ, Segarra J, Virizuela JA, Carles J, Lassa A, Calderero V, Constela M, Delgado D, Mañas A, Murias A, Reynes G, Rodriguez B, Rubio G, Sánchez E, Unda M, Solsona E, Martínez-Javaloyas JM, Comet-Batlle J, Quicios C, Martín-Fernández M, Mahillo-Fernández I, Morote J. **Usefulness of bone turnover markers as predictors of mortality risk, disease progression and skeletal-related events appearance in patients with prostate cancer with bone metastases following treatment with zoledronic acid: TUGAMO study.** *Brit J Cancer* 108(12):2565-2572 I.F.: 5.082

5. Musquera M, Perez M, Peri L, Esforzado N, Sebastiá MC, Paredes D, Ribal MJ, Oppenheimer F, Campistol JM, Alcaraz A. **Kidneys from donors with incidental renal tumors: should they be considered aceptable option for transplantaiton?** Transplantation 95(9):1129-1133 I.F.: 3.781

6. Ciudin A, Diaconu MG, Gosalbez D, Peri L, García-Cruz E, Franco A, Alcaraz A. **Air cystoscopy is superior to water cystoscopy for the diagnosis of active hematuria.** *J Urology* 190(6):2097-2101 I.F.: 3.696

7. Rosser CJ, Ross S, Chang M, Dai Y, Mengual L, Zhang G, Kim J, Urquidi V, Alcaraz A, Goodison S. **Multiprex protein signature for the detection of bladder cancer in voided urine samples.** *J Urology* 190(6):2257-2262 I.F.: 3.696

8. García-Cruz E, Leibar-Tamayo A, Romero J, Piqueras M, Luque P, Cardeñosa O, Alcaraz A. **Metabolic syndrome in men with low testosterone levels: relationship with cardiovascular risk factors and comorbidities and with erectile dysfunction.** *J Sex Med* 10(10):2529-2538 I.F.: 3.513

9. Ribal MJ, Huguet J, Alcaraz A. **Oncologic outcomes obtained after laparoscopic, robotic and/or single port nephroureterectomy for upper urinary tract tumours.** *World J Urol* 31(1):93-107 I.F.: 2.888

10. Ciudin A, Luque MP, Salvador R, Diaconu MG, Franco A, Constantin V, Alvarez-Vijande R, Nicolau C, Alcaraz A. **Validation of Randall's plaque theory using unenhanced abdominal computed tomography.** *Urology* 81:246-250 I.F.: 2.424

11. Ciudin A, Luque MP, Salvador R, Diaconu MG, Franco A, Constantin V, Alvarez-Vijande R, Nicolau C, Alcaraz A. **The abdominal CT – a new tool for predicting recurrent stone disease.** *J Endourol* 27(8):965-969 I.F.: 2.074

12. Miyake M, Ross S, Lawton A, Chang M, Dai Y, Mengual L, Alcaraz A, Giacoia EG, Goodison S, Rosser CJ. **Investigation of CCL18 and A1AT as potentital urinary biomarkers for bladder cancer detection.** *BMC Urology* 13:42 I.F.: 1.694

13. García-Cruz E, Carrion A, Garcia A, Sallent A, Castañeda R, Piqueras M, Ribal MJ, Leibar A, Romero J, Alcaraz A. **Higher sex hormone-binding globulin and lower bioavailable testosterone are related to prostate cancer detection on prostate biopsy.** *Scand J Urol Nephrol* 47(4):282-289 I.F.: 1.007

14. Lombraña M, Izquierdo L, Gomez A, Alcaraz A. **Impact of a nurse-run clinic on prevalence of urinary incontinence and everyday life in men undergoing radical prostatectomy.** *J Wound Ostomy Continence Nurs* 2013 40(3):309-12 I.F.: 0.933

Review / **I.F.: 2.982**

1. Izquierdo L, Peri L, García-Cruz E, Musquera M, Piqueras M, Gosálbez D, Alcaraz A. **Recent advances of natural orifice transluminal endoscopic surgery in urological surgery.** *Int J Urol* 20(5):462-466 I.F.: 1.734

2. Izquierdo L, Bolton D, Lawrentschuk N. **Radical cystectomy and orthotopic bladder substitution: surgical Tricks and Management of complications.** *Minerva Urol Nefrol* 65(4):225-234 I.F.: 0.634

3. Joniau S, Pfister D, de la Taille A, Gaboardi F, Thompson A, Ribal MJ. **Controversies on individualized prostate cancer care: gaps in current practice.** *Ther Adv Urol* 5(5):233-244 I.F.: 0.614

Guidelines / **I.F.: 10.476**

1. Gakis G, Witjes JA, Compérat E, Cowan NC, De Santis M, Lebret T, Ribal MJ, Sherif

AM. **EAU Guidelines on primary urethral carcinoma.** *Eur Urol* 64(5):823-830 I.F.: 10.476

GRANTS FOR RESEARCH IN PROGRESS

Alcaraz A. **Prostate Predict. Desarrollo de una prueba de pronóstico para predecir la probabilidad de enfermedad agresiva después de la cirugía.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2012-1311-300000.
Duration: 01/01/2013-31/12/2015

Alcaraz A. **miRNAs para el diagnóstico no invasivo del carcinoma urotelial.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01145.
Duration: 01/01/2011-31/12/2013

Musquera, Mireia. **Identificación de un apanel de microRNAs para el diagnóstico no invasivo del cáncer de próstata.** Sponsored by: Fundación de Investigación en Urología (FIU) "Beca de Ayuda a la Investigación "Pedro Cifuentes Díaz".
Duration: 01/01/2011 – 31/12/2013.

Izquierdo, Laura. **Validación de un perfil de microRNA pronóstico en tumores de tracto urinario superior.** Sponsored by: Fundación de Investigación en Urología (FIU) "Beca de Ayuda a la Investigación "Pedro Cifuentes Díaz".
Duration: 01/07/2011 – 30/06/2013.

DOCTORAL THESES

Alcaraz A. **Afectación extravesical en varones con carcinoma urotelial de vejiga sometidos a cistectomía radical.**
PhD student: Jorge Huguet Pérez

Alcaraz A, Izquierdo L. **Impacto de la prostatectomía radical en la incontinencia urinaria y disfunción eréctil. Influencia de un programa de intervención para la educación sanitaria.**
PhD student: María Lombraña Mencía.

Ribal MJ, Mengual L. **Biomarcadores de estadiaje molecular y de respuesta terapéutica en pacientes con cáncer de vejiga músculo invasivo.**
PhD student: Cristina Baylo Gazquez.

AREA 3

Liver, digestive system and metabolism

3.1 **Gynecological endocrinology and human reproduction** 136
Juan Balasch

3.2 **Fetal and perinatal medicine** 139
Eduard Gratacós

3.3 **Viral hepatitis in the immunocompetent host and in liver transplant patients** 145
Xavier Forns

3.4 **Pathophysiology and treatment of ascites and altered renal function in liver cirrhosis.** 148
Vicente Arroyo

3.5 **Hepatic oncology** 152
Jordi Bruix

3.6 **Liver hemodynamics and portal hypertension Digestive bleeding secondary to ruptured esophageal varicose veins.** 156
Jaume Bosch

3.7 **Inflammatory bowel disease.** 161
Julià Panés

3.8 **Cholestasis and bone pathology** 165
Albert Parés / Núria Guañabens

3.9 **Mitochondrial regulation of cell death and steatohepatitis** 168
José Carlos Fernández-Checa

3.10 **Liver transplantation and graft viability** 171
Antoni Rimola

3.11 **Gastrointestinal and pancreatic oncology** 175
Antoni Castells

3.12 **Inherited metabolic diseases** 182
Antonia Ribes

3.13 **Genomic Programming of Beta Cells and Diabetes** 185
Jorge Ferrer

3.14 **Diabetes: metabolic and molecular networks** 187
Josep Vidal

3.15 **Pathogenesis and prevention of diabetes** 192
Anna Novials

3.1 Gynecological endocrinology and human reproduction

LOCATION
HCB building

KEYWORDS
1. **Human papillomavirus**
2. **Endometrial cancer**
3. **Assisted reproductive technologies**
4. **Recurrent miscarriage**
5. **Gynecological laparoscopy**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	76.25	21	15	2
2012	49.19	14	8	5
2013	67.55	17	10	4

TEAM LEADER
Juan Balasch (HCB)
T. 93 227 54 36
jbalasch@ub.edu

RESEARCHERS
Francisco Carmona (HCB)
Camil Castelo-Branco (HCB)
Montserrat Creus (HCB)
Francisco Fábregues (HCB)
Dolors Manau Trullás (FCRB)
Mª Angels Martínez-Zamora (HCB)
Jaume Pahisa (HCB)
Bienvenido Puerto (HCB)
Aureli Torné (HCB)

COLLABORATORS
José Luís Ballescá (HCB)
Gemma Casals (HCB)
Roser Casamitjana (HCB)
Salvadora Cívico (HCB)
Marta Guimerà (HCB)
Jaume Ordi (HCB)
Joana Peñarrubia Alonso (FCRB)
Marta del Pino (HCB)
Elena Suárez Cisneros (IDIBAPS)

STRATEGIC OBJECTIVES

The global aim of this research group for the coming years is to advance in the knowledge of different aspects relating to the physiopathology of human reproduction: from endocrinological considerations to the most important benign and malignant pathological processes of the female reproductive system, as well as the investigation and treatment of human reproduction failure. More specifically, the main objectives of our research group are to advance in the existing lines of work, with the purpose of:

1. Determining the most relevant mechanisms in the pathogenesis of reproductive failure (sterility, repeated miscarriages, repeated implant failure after in vitro fertilization) and of the principal female reproductive disease processes (endometriosis, uterine myoma, genital cancer).

2. Optimizing and innovating as far as possible the preventive or therapeutic potential in the aforementioned situations.

MAIN LINES OF RESEARCH

1. **Reproductive failure markers**
   Analysis of the possible role of new markers of hemostasis alterations as a new pathogenic mechanism of thrombotic disease in early and advanced pregnancy, in patients with or without antiphospholipid syndrome. Study is also made of the usefulness of immunohistochemical and quantitative and qualitative proteomic parameters in the human endometrium as markers of endometrial receptiveness. In-depth research of the pathogenic mechanisms involved in the block of pre-implantation embryonic development in vitro.

2. **Ovarian dysfunction and stimulation/hyperstimulation**
   Investigation of the possibilities of ultrasound, hormonal, endocrinemetabolic and genetic markers in relation to the prediction of ovarian response. Study of the role of LH and the androgens as ovarian sensitizing factors in relation to ulterior stimulation with FSH. Investigation of the possible role of the ovarian follicular cells (granulosum, macrophages) in the pathogenesis of ovarian hyperstimulation syndrome, with the exploration of new ovarian stimulation or endometrial preparation protocols allowing improved results in assisted reproduction techniques.

3. **Optimization of the surgical management of diseases of the reproductive apparatus**
   Designed to analyze the role of the surgical variables allowing improvement of the results and reduction of the morbidity in the surgical treatment of benign and malignant disorders of the female reproductive apparatus. This also implies defining the prognostic value of HPV (human papillomavirus) detection and viral typing as prognostic and progression markers of precancerous lesions of the cervix, vagina and vulva.

PUBLICATIONS

Originals / I.F.: 67.550

1. Valenzuela-Alcaraz B, Crispi F, Bijnens B, Cruz-Lemini M, Creus M, Sitges M, Bartrons J, Civico S, Balasch J, Gratacós E. **Assisted reproductive technologies are associated with cardiovascular remodeling in utero that persists postnatally.** *Circulation* 128:1442-1450 I.F.: 15.202

2. Vegliante MC, Palomero J, Pérez-Galán P, Roué G, Castellano G, Navarro A, Clot G, Moros A, Suárez-Cisneros H, Beà S, Hernández L, Enjuanes A, Jares P, Villamor N, Colomer D, Martín-Subero JI, Campo E, Amador V. **SOX11 regulates PAX5 expression and blocks terminal B-cell differentiation in aggressive mantle cell lymphoma.** *Blood* 121:2175-2185 I.F.: 9.060

3. Szarewski A, Skinner SR, Garland SM, Romanowski B, Schwarz TF, Apter D, Chow SN, Paavonen J, Del Rosario-Raymundo MR, Teixeira JC, De Carvalho NS,Castro-Sanchez M, Castellsagué X, Poppe WA, De Sutter P, Huh W, Chatterjee A, Tjalma WA, Ackerman RT, Martens M, Papp KA, Bajo-Arenas J, Harper DM, Torné A, David MP, Struyf F, Lehtinen M, Dubin G. **Efficacy of the HPV-16/18 AS04-adjuvanted vaccine against low-risk HPV types (PATRICIA randomized trial): an unexpected observation.** *J Infect Dis* 208:1391-1396 I.F.: 5.848

4. Perissinotti A, Paredes P, Vidal-Sicart S, Torné A, Albela S, Navales I, Martínez-Román S, Pahisa J, Pons F. **Use of SPECT/CT for improved sentinel lymph node localization in endometrial cancer.** *Gynecol Oncol* 129:42–48 I.F.: 3.929

5. Rodriguez-Manfredi A, Alonso I, del Pino M, Fusté P, Torné A, Ordi J. **Predictors of absence of cervical intraepithelial neoplasia in the conization specimen.** *Gynecol Oncol* 128:271-276 I.F.: 3.929

6. Torné A, Pahisa J, Vidal-Sicart S, Martínez-Roman S, Paredes P, Puerto B, Albela S, Fusté P, Perisinotti A, Ordi J. **Transvaginal ultrasound-guided myometrial injection of radiotracer (TUMIR): a new method for sentinel lymph node detection in endometrial cancer.** *Gynecol Oncol.* 128:88-94 I.F.: 3.929

7. Ros C, Alobid, Balasch J, Mullol J, Castelo-Branco C. **Turner's syndrome and other congenital hypogonadisms impair quality of life and sexual function.** *Am J Obstet Gynecol* 208:484.e1-6 I.F.: 3.877

8. Torné A, Fusté P, Rodríguez-Carunchio L, Alonso I, del Pino M, Nonell R, Cardona M, Rodríguez A, Castillo P, Pahisa J, Balasch J, Ramírez J, Ordi J. **Intraoperative post-conisation human papillomavirus (IOP-HPV) testing for early detection of treatment failure in patients with cervical intraepithelial neoplasia: a pilot study.** *Br J Obstet Gynaecol* 120:392-399 I.F.: 3.760

9. Garcia-Posada R, Eixarch E, Sanz M, Puerto B, Figueras F, Borrell A. **Cisterna magna width at 11-13 weeks in the detection of posterior fossa anomalies.** *Ultrasound Obstet Gynecol* 41:515-520 I.F.: 3.557

10. Creus M, Deulofeu R, Peñarrubia J, Carmona F, Balasch J. **Plasma homocysteine and vitamin B12 serum levels, red blood cell folate concentrations, C677T methylenetetrahydrofolate reductase gene mutation and risk of recurrent miscarriage: a case-control study in Spain.** *Clin Chem Lab Med.* 51:693-699 I.F.: 3.009

11. Del Pino M, Fusté P, Pahisa J, Rovirosa A, Martínez-Serrano MJ, Martínez-Román S, Alonso I, Vidal L, Ordi J, Torné A. **Laparoscopic lymphadenectomy in advanced cervical cancer: prognostic and therapeutic value.** *Int J Gynecol Cancer* 23:1675-1683 I.F.: 1.941

12. Martínez JM, Prat J, Gómez O, Crispi F, Bennasar M, Puerto B, Castañón M, Gratacós E. **Decompression through tracheobronchial endoscopy of bronchial atresia presenting as massive**

pulmonary tumor: a new indication for fetoscopic surgery. *Fetal Diagn Ther* 33:69-74 I.F.: 1.902

13. Martínez JM, Castañón M, Gómez O, Prat J, Eixarch E, Bennasar M, Puerto B, Gratacós E. **Evaluation of Fetal Vocal Cords to Select Candidates for Successful Fetoscopic Treatment of Congenital High Airway Obstruction Syndrome: Preliminary Case Series.** *Fetal Diagn Ther* 34:77-84 I.F.: 1.902

14. Casals G, Fábregues F, Pavesi M, Arroyo V, Balasch J. **Conservative medical treatment of ovarian hyperstimulation syndrome: a single center series and cost analysis study.** *Acta Obstet Gynecol Scand.*92:686-691 I.F.: 1.850

15. Fábregues F, Creus M, Casals G, Carmona F, Balasch J .**Outcome from consecutive ICSI cycles in patients treated with recombinant human LH and those supplemented with urinary hCG-based LH activity during controlled ovarian stimulation in the long GnRH-agonist protocol.** *Gynecol Endocrinol.* 29:430-435 I.F.: 1.303

16. Rovirosa A, Valduvieco I, Ascaso C, Herreros A, Bautista C, Romera I, Arenas M, Pahisa J, Biete A. **Daily schedule for high-dose-rate brachytherapy in postoperative treatment of endometrial carcinoma.** *Clin Transl Oncol* 15:111-116 I.F.: 1.276

17. Valduvieco I, Rovirosa A, Herreros A, Romera I, Ríos I, Ascaso C, Sánchez-Reyes A, Arenas M, Pahisa J, Biete A. **Three or four fractions per week in postoperative high-dose-rate brachytherapy for endometrial carcinoma. The long-term results on vaginal relapses and toxicity.** *Clin Transl Oncol.* 15:602–607 I.F.: 1.276

Reviews / I.F.: 4.174

1. Meldrum DR, Chang J, Giudice LC, Balasch J, Barbieri RL. Role of decreased androgens in the ovarian response to stimulation in older women. *Fertil Steril.* 99:5-11. I.F.: 4.174

GRANTS FOR RESEARCH IN PROGRESS

Balasch J. **Investigación de las micropartículas procoagulantes como mecanismo patogénico en la patología gestacional precoz y avanzada. Relación con los anticuerpos antifosfolipídicos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01560.
Duration: 01/01/2012-31/12/2014

Balasch J. **Fisiopatologia de la Reproducció Humana.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1099.
Duration: 23/07/2009-30/04/2014

Ordi J. **Expresión del oncogén E7 del VPH y de la metilación de los promotores de CADM1 y MAL como biomarcadores de progresión/regresión en lesiones precursoras del cáncer de cérvix.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01165.
Duration: 01/01/2013-31/12/2015

Ordi J. **Patrones de expresión de miRNA en la progresión y la transformación maligna de las lesiones precursoras del cáncer de cérvix uterino.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1084.
Duration: 01/01/2010-31/12/2013

Torne A. **Detección intraoperatoria del VPH en el cervix residual tras la conización como marcador precoz de fracaso terapéutico en la neoplasia cervical intraepitelial.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01231.
Duration: 01/01/2013-31/12/2015

Torne A. **Valor clínico de la infección múltiple por virus del papiloma humano (VPH) en pacientes con lesiones premalignas y cáncer de cuello uterino.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1524.
Duration: 01/01/2010-30/06/2013

DOCTORAL THESES

Puerto B. **Cribado de aneuploidías de primer trimestre en las gestaciones gemelares.**
PhD student: Pilar Prats Rodriguez

3.2 Fetal and perinatal medicine

LOCATION
MATERNITAT building

KEYWORDS
1. **Prenatal diseases**
2. **Intrauterine growth restriction**
3. **Fetal cardiovascular programming**
4. **Fetal brain damage**
5. **Prematurity**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	116.03	43	21	11
2012	108.65	34	18	9
2013	163.97	44	33	6

TEAM INVOLVED IN
CIBERER

AWARDS

Award of Research Excellence of Society for Fetal-Maternal Medicine
Institution Society for Maternal Fetal-Medicine
Awardee/s: Montse Palacio, on behalf of the PROMISE Collaborative Group

Supratentorial pathologies of the brain Section Award
Institution: MRI Vienna 2013 Congress (Ultrasound meets Magnetic Ressonance Imaging)
Awardee: Míriam Illa (poster)

Mejores Ideas 2013 - Investigación y Farmacología
Institution: Diario Médico
Awardee: Eduard Gratacós

Premi Àmbit infància
Institution: Fundació Agrupació Mútua
Awardee: Fàtima Crispi

TEAM LEADER
Eduard Gratacós (HCB)
T. 93 227 99 46
gratacos@clinic.cat

RESEARCHERS
Antoni Borrell (HCB)
Francesc Botet (HCB)
Vicenç Cararach (HCB)
Xavier Carbonell (HCB)
Elena Casals (HCB)
Fátima Crispi (HCB-IDIBAPS)
Francesc Figueras (HCB)
Josep Figueras (HCB)
Josep Maria Martinez-Crespo (HCB)
Montserrat Palacio (HCB)

POST-DOCTORAL RESEARCHERS
Emilia Ruthy Acosta-Rojas (FCRB-CIBERER)
Rubén Cardenas (FCRB)
Tere Cobo (FCRB)
Elena Demicheva (FCRB)
Elisenda Eixarch (IDIBAPS)
Emma Muñoz (FCRB)
Nelly Padilla (IDIBAPS)
Magdalena Sanz (IDIBAPS)
Rui V Simoes (FCRB)
Erwin Van Vliet (FCRB)

PRE-DOCTORAL RESEARCHERS
Dafnis Batallé (CIBERER)
Mónica Cruz-Lemini (IDIBAPS)
Gabriela Egaña (FCRB)
Patricia Garcia (FCRB)
Anna González (IDIBAPS)
Miriam Illa (IDIBAPS)
Miguel Parra (FCRB)
Stefan Savchev (FCRB)
Elena Scazocchio (INSTITUT DEXEUS)
Violeta Tenorio (FCRB)
Brenda Valenzuela (IDIBAPS)

TECHNICIANS
Àngels Kateb (FCRB)
Imma Mercade (FCRB)
Mireia Parés (FCRB)
Ana Belén Sánchez (IDIBAPS)

NURSING STAFF
Ángela Arranz (FCRB)
Alba Camacho (FCRB)
Marta García (FCRB)

ADMINISTRATIVE STAFF
Maite Aguilera (FCRB)
Estefanía Callado (FCRB)
Luis Enciso (IDIBAPS)
Gemma Fornons (FCRB)
Balma Gil (FCRB)
Héctor Gómez (FCRB)
Pere Lorente (FCRB)
Belén Sánchez (FCRB)

COLLABORATORS
Jordi Bellart (HCB)
Mar Benassar (HCB)
Bart Bijnens (UPF)
Olga Gómez (HCB)
Anna Gonce (HCB)
Maribel Grande (FCRB)
Xavier Miracle (HCB)
Mª Dolors Salvía (HCB)

VISITING SCIENTISTS
Hagai Avnet (The Lady Davis Carmel Medical Center, Haifa, Israel)
Nuruddin Badruddin (Aga Khan University, Pakistan)
Carolina Bazán (Hospital Carlos Van Buren de Valparaíso, Chile)
Nadine Hahner (Universitätsklinikum, Eppendorf, Hamburg)
Luís Claudio Erick Hernández (Hospital General Regional 200, México)
Silvia Lobmaier (Klinikum rechts der Isar, Munich, Germany)
Hilde Logghe (Lucas Hospital, Bruges, Belgium)
Rozina Nuruddin (Aga Khan University, Pakistan)
Javier Ortiz (Klinikum rechts der Isar, Munich, Germany)
Mauro Parra (Hospital Clínico, Chile)
Mariana Pina (Careggi's Hospital, Florence, Italy)
Jessica Scremin (Stanford Hospital, USA)
Álvaro Sepúlveda (Hospital Clínico, Chile)
Serena Simoeone (Università degli Studi di Firenze, Italy)
Iosefine Stergitou (Topiki autodioikisi Kykladon)
Kai Lit Tan (Singapore health Services, Singapore)
Stefania Triunfo (Gemelli Hospital, Rome, Italy)
Maria Zarlenga (University of Rome,Italy)

STRATEGIC OBJECTIVES

The principal strategic objective is to search for solutions to prenatal diseases, identifying the mechanisms involved in fetal brain and cardiac reprogramming, and consolidating our existing lines of work in different fields, such as perinatal infections, HIV and neonatal infection, fetal therapy and surgery, screening strategies and prediction of fetal and maternal pathology in large populations, preeclampsia and prematurity.

We work on several cross-disciplinary projects so as to come up with real solutions to fetal problems by:

- Improving identification of those fetuses at risk and provide new clinical definitions to diagnose fetal growth restriction problems.
- Developing new imaging technologies for research purposes and non-invasive early diagnosis procedures.
- Identifying new biomarker signatures for several pathologies that can be used in clinical practice, as well as new molecular signaling ways and therapeutic targets.
- Consolidating our models for characterization and follow-up of the molecular mechanisms associated with fetal heart and brain reprogramming

MAIN LINES OF RESEARCH

1. **Prematurity:** The main objective of the Prematurity line is to gain a better insight into the causes of preterm birth, the most frequent cause of perinatal morbimortality. The research combines clinical practice and lab work: the team looks for better detection methods of patients at real risk of preterm delivery, and works to optimize the management and care of neonatal patients, This way, the team expects to find biomarkers to distinguish at-risk patients from patients with a good prognosis, minimizing needless surgeries and management of time and resources in clinical care to achieve the best possible results.

2. **Metabolomics and Microstructure.** The metabolomics and microstructure research line wants to find and define metabolic differences in the brain of fetuses and children who are diagnosed with growth restriction and that can be considered at risk of neurodevelopmental problems. In this line, doctors, biologists, psychologists, and engineers work together in order to identify subtle changes in brain microstructure, using the latest technologies, mainly based on MRI techniques. Knowing what changes occur in the brain at a metabolic level will be of great value while diagnosing and treating these children at risk, improving their prognosis.

3. **Diagnosis and Therapy in IUGR.** The Diagnosis and Therapy in IUGR research line aim is to identify before birth those babies with growth problems that, unlike small-for-gestational-age babies, will present an abnormal neurodevelopment. Despite not being severe, these subtle neurodevelopmental alterations are being increasingly taken into account because of its family and social implications. Therefore, using the right definition for IUGR and correctly identifying at-risk babies is especially important in order to establish preventive measures during pregnancy and childbirth, as well as therapies during early childhood.

4. **Brain Connectivity.** The main objective of the brain connectivity line is to develop quantitative imaging biomarkers for early diagnosis of neurodevelopmental disorders based on the analysis of the connections in the brain by magnetic resonance imaging (MRI), a methodology known as connectomics. Having these biomarkers available would make early identification of neurodevelopmental disorders possible, as well as the implementation of specific programs of early stimulation and education to improve the development of these children.

5. **Fetal Cardiovascular Programming**. The fetal cardiovascular programming research line focuses on those prenatal circumstances that may induce a higher postnatal cardiovascular risk, such as intrauterine growth restriction, pregnancies obtained via

assisted reproduction techniques, and prematurity. The main objectives of the line include getting a better understanding of the pathophysiologic mechanisms of fetal cardiovascular programming, the development of biomarkers that allow early detection and monitoring of cardiovascular remodeling and putting into practice therapies that can improve the cardiovascular prognosis of these children.

PUBLICATIONS

Originals / I.F.: 163.970

1. Valenzuela-Alcaraz B, Crispi F, Bijnens B, Cruz-Lemini M, Creus M, Sitges M, Bartrons J, Civico S, Balasch J, Gratacós E. **Assisted reproductive technologies are associated with cardiovascular remodeling in utero that persists postnatally.** *Circulation* 128:1442–1450 I.F.: 15.202

2. Wang K, Ahmad S, Cai M, Rennie J, Fujisawa T, Crispi F, Baily J, Miller MR, Cudmore M, Hadoke PWF, Wang R, Gratacós E, Buhimschi IA, Buhimschi CS, Ahmed A. **Dysregulation of hydrogen sulfide producing enzyme cystathionine γ-lyase contributes to maternal hypertension and placental abnormalities in preeclampsia.** *Circulation* 127:2514–2522 I.F.: 15.202

3. Dadvand P, Figueras F, Basagana X, Beelen R, Martinez D, Cirach M, Schembari A, Hoek G, Brunekreef B, Nieuwenhuijsen MJ. **Ambient air pollution and preeclampsia: a spatiotemporal analysis.** *Environ Health Perspect* 121:1365–1371 I.F.: 7.260

4. Batalle D, Muñoz-Moreno E, Figueras F, Bargalló N, Eixarch E, Gratacós E. **Normalization of similarity-based individual brain networks from gray matter MRI and its association with neurodevelopment in infants with intrauterine growth restriction.** *Neuroimage* 83:901–911 I.F.: 7.260

5. Ahlin K, Himmelmann K, Hagberg G, Kacerovsky M, Cobo T, Wennerholm U-B, Jacobsson B. **Cerebral palsy and perinatal infection in children born at term.** *Obstet Gynecol* 122:41–49 I.F.: 4.798

6. Egaña-Ugrinovic G, Sanz-Cortés M, Figueras F, Bargalló N, Gratacós E. **Differences in cortical development assessed by fetal MRI in late-onset intrauterine growth restriction.** *Am J Obstet Gynecol* 209:126.e1–8 I.F.: 3.877

7. Scazzocchio E, Figueras F, Crispi F, Meler E, Masoller N, Mula R, Gratacós E. **Performance of a first-trimester screening of preeclampsia in a routine care low-risk setting.** *Am J Obstet* Gynecol 208:203.e1–203.e10 I.F.: 3.877

8. Stergiotou I, Crispi F, Valenzuela-Alcaraz B, Bijnens B, Gratacós E. **Patterns of maternal vascular remodeling and responsiveness in early- versus late-onset preeclampsia.** *Am J Obstet Gynecol* 209:558.e1–558.e14 I.F.: 3.877

9. Brix N, Secher N, McCormack C, Helmig R, Hein M, Weber T, Mittal S, Kurdi W, Palacio M, Henriksen T. **Randomised trial of cervical cerclage, with and without occlusion, for the prevention of preterm birth in women suspected for cervical insufficiency.** *BJOG An Int J Obstet Gynaecol* 120:613–620 I.F.: 3.760

10. Ahlin K, Himmelmann K, Hagberg G, Kacerovsky M, Cobo T, Wennerholm U-B, Jacobsson B. **Non-infectious risk factors for different types of cerebral palsy in term-born babies: a population-based, case-control study.** *BJOG An Int J Obstet Gynaecol* 120:724–731 I.F.: 3.760

11. Cobo T, Kacerovsky M, Andrys C, Drahosova M, Musilova I, Hornychova H, Jacobsson B. **Umbilical cord blood IL-6 as predictor of early-onset neonatal sepsis in women with preterm prelabour rupture of membranes.** *PLoS One* 8:e69341 I.F.: 3.730

12. Illa M, Eixarch E, Batalle D, Arbat-Plana A, Muñoz-Moreno E, Figueras F, Gratacós E. **Long-term functional outcomes and correlation with regional brain connectivity by MRI diffusion tractography metrics in a near-term rabbit model of intrauterine growth restriction.** *PLoS One* 8:e76453 I.F.: 3.730

13. Kacerovsky M, Celec P, Vlkova B, Skogstrand K, Hougaard DM, Cobo T, Jacobsson B. **Amniotic fluid protein profiles of intraamniotic inflammatory response to Ureaplasma spp. and other bacteria.** *PLoS One* 8:e60399 I.F.: 3.730

14. Muñoz-Moreno E, Arbat-Plana A, Batalle D, Soria G, Illa M, Prats-Galino A, Eixarch E, Gratacós E. **A magnetic resonance image based atlas of the rabbit brain for automatic parcellation.** *PLoS One* 8:e67418 I.F.: 3.730

15. Sanz-Cortés M, Carbajo RJ, Crispi F, Figueras F, Pineda-Lucena A, Gratacós E. **Metabolomic profile of umbilical cord blood plasma from early and late intrauterine growth restricted (IUGR) neonates with and without signs of brain vasodilation.** *PLoS One* 8:e80121 I.F.: 3.730

16. Sanz-Cortés M, Rattá GA, Figueras F, Bonet-Carne E, Padilla N, Arranz A, Bargalló N, Gratacós E. **Automatic quantitative MRI texture analysis in small-for-gestational-age fetuses discriminates abnormal neonatal neurobehavior.** *PLoS One* 8:e69595 I.F.: 3.730

17. Soria G, Tudela R, Márquez-Martín A, Camón L, Batalle D, Muñoz-Moreno E, Eixarch E, Puig J, Pedraza S, Vila E, Prats-Galino A, Planas AM. **The ins and outs of the BCCAo model for chronic hypoperfusion: a multimodal and longitudinal MRI approach.** *PLoS One* 8:e74631 I.F.: 3.730

18. Van Vliet E, Eixarch E, Illa M, Arbat-Plana A, Gonzalez-Tendero A, Hogberg HT, Zhao L, Hartung T, Gratacós E. **Metabolomics reveals metabolic alterations by intrauterine growth restriction in the fetal rabbit brain.** *PLoS One* 8:e64545 I.F.: 3.730

19. Gonzalez-Tendero A, Torre I, Garcia-Canadilla P, Crispi F, García-García F, Dopazo J, Bijnens B, Gratacós E. **Intrauterine growth restriction is associated with cardiac ultrastructural and gene expression changes related to the energetic metabolism in a rabbit model.** *Am J Physiol Heart Circ Physiol* 305:H1752–1760 I.F.: 3.629

20. Borrell A, Grande M, Bennasar M, Borobio V, Jimenez JM, Stergiotou I, Martínez-Crespo JM, Cuckle H. **First-trimester detection of major cardiac defects with the use of ductus venosus blood flow.** *Ultrasound Obstet Gynecol* 42:51–57 I.F.: 3.557

21. Cruz-Lemini M, Crispi F, Valenzuela-Alcaraz B, Figueras F, Sitges M, Gómez O, Bijnens B, Gratacós E. **Value of annular M-mode displacement vs tissue Doppler velocities to assess cardiac function in intrauterine growth restriction.** *Ultrasound Obstet Gynecol* 42:175–181 I.F.: 3.557

22. Cruz-Martinez R, Castañon M, Moreno-Alvarez O, Acosta-Rojas R, Martínez-Crespo JM, Gratacós E. **Usefulness of lung-to-head ratio and intrapulmonary arterial Doppler in predicting neonatal morbidity in fetuses with congenital diaphragmatic hernia treated with fetoscopic tracheal occlusion.** *Ultrasound Obstet Gynecol* 41:59–65 I.F.: 3.557

23. Doné E, Gratacós E, Nicolaides K, Allegaert K, Valencia CM, Castañon M, Martínez-Crespo JM, Jani J, Van Mieghem T, Greenough A, Gomez O, Lewi P, Deprest J. **Predictors of neonatal morbidity in fetuses with severe isolated congenital diaphragmatic hernia undergoing fetoscopic tracheal occlusion.** *Ultrasound Obstet Gynecol* 42:77–83 I.F.: 3.557

24. Garcia-Posada R, Eixarch E, Sanz-Cortés M, Puerto B, Figueras F, Borrell A. **Cisterna magna width at 11-13 weeks in the detection of posterior fossa anomalies.** *Ultrasound Obstet Gynecol* 41:515–520 I.F.: 3.557

25. Mademont-Soler I, Morales C, Soler A, Martínez-Crespo JM, Shen Y, Margarit E, Clusellas N, Obón M, Wu BL, Sánchez A. **Prenatal diagnosis of chromosomal abnormalities in fetuses with abnormal cardiac ultrasound findings: evaluation of chromosomal microarray-based analysis.** *Ultrasound Obstet Gynecol* 41:375–382 I.F.: 3.557

26. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Parra G, Sanz-Cortés M, Gratacós E, Figueras F. **Added value of umbilical vein flow as a predictor of perinatal outcome in term small-for-gestational-age fetuses.** *Ultrasound Obstet Gynecol* 42:189–195 I.F.: 3.557

27. Savchev S, Sanz-Cortés M, Cruz-Martinez R, Arranz A, Botet F, Gratacós E, Figueras F. **Neurodevelopmental outcome of full-term small-for-gestational-age infants with normal placental function.** *Ultrasound Obstet Gynecol* 42:201–206 I.F.: 3.557

28. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, Parra G, Gratacós E, Figueras F. **Placental findings in late-onset SGA births without Doppler signs of placental insufficiency.** *Placenta* 34:1136–1141 I.F.: 3.117

29. Engels AC, Dekoninck P, van der Merwe JL, Van Mieghem T, Stevens P, Power B, Nicolaides K, Gratacós E, Deprest J. **Does website-based information add any value in counseling mothers expecting a baby with severe congenital diaphragmatic hernia?** *Prenat Diagn* 33:1027–1032 I.F.: 2.683

30. Eixarch E, Valsky D V, Deprest J, Baschat A, Lewi L, Ortiz JU, Martínez-Crespo JM, Gratacós E. **Preoperative prediction of the individualized risk of early fetal death after laser therapy in twin-to-twin transfusion syndrome.** *Prenat Diagn* 2013:1–6 I.F.: 2.683

31. Grande M, Ordoñez E, Cirigliano V, Cid J, Grau E, Pericot A, Teixido I, Marin JL, Borrell A. **Clinical application of midtrimester non-invasive fetal RHD genotyping and identification of RHD variants in a mixed-ethnic population.** *Prenat Diagn* 33:173–178 I.F.: 2.683

32. Grande M, Cararach V, Casals E, Borrell A. **First-trimester Down syndrome screening in renal-transplanted pregnant women: a model for adjusting the false-positives rates.** *Prenat Diagn* 33:467–470 I.F.: 2.683

33. Sabria J, Comas C, Barceló-Vidal C, Illa M, Echevarria M, Gomez-Roig MD, Borrell A. **Cumulative sum plots and retrospective parameters in first-trimester ductus venosus quality assurance.** *Prenat Diagn* 33:384–390 I.F.: 2.683

34. Illa M, Mula R, Arigita M, Grande M, Goncé A, Borobio V, Borrell A. **Likelihood ratios to apply for nasal bone, ductus venosus and tricuspid flow at the 11-13 weeks' scan in down syndrome screening.** *Fetal Diagn Ther* 34:116–120 I.F.: 1.902

35. Martínez-Crespo JM, Castañon M, Gómez O, Prat J, Eixarch E, Bennasar M, Puerto B, Gratacós E. **Evaluation of fetal vocal cords to select candidates for successful fetoscopic treatment of congenital high airway obstruction syndrome: preliminary case series.** *Fetal Diagn Ther* 34:77–84 I.F.: 1.902

36. Martínez-Crespo JM, Prat J, Gómez O, Crispi F, Bennasar M, Puerto B, Castañon M, Gratacós E. **Decompression through Tracheobronchial Endoscopy of Bronchial Atresia Presenting as Massive Pulmonary Tumor: A New Indication for Fetoscopic Surgery.** *Fetal Diagn Ther* 33:69–74 I.F.: 1.902

37. Mula R, Savchev S, Parra-Saavedra M, Arranz A, Botet F, Costas-Moragas C, Gratacós E, Figueras F. **Increased fetal brain perfusion and neonatal neurobehavioral performance in normally grown fetuses.** *Fetal Diagn Ther* 33:182–188 I.F.: 1.902

38. Sanz-Cortés M, Figueras F, Bonet-Carne E, Padilla N, Tenorio V, Bargalló N, Amat-Roldan I, Gratacós E. **Fetal brain MRI texture analysis identifies different microstructural patterns in adequate and small for gestational age fetuses at term.** *Fetal Diagn Ther* 33:122–129 I.F.: 1.902

39. Cobo T, Tsiartas P, Kacerovsky M, Holst R-M, Hougaard DM, Skogstrand K, Wennerholm U-B, Hagberg H, Jacobsson B. **Maternal inflammatory response to microbial invasion of the amniotic cavity: analyses of multiple proteins in the maternal serum.** *Acta Obstet Gynecol Scand* 92:61–68 I.F.: 1.850

40. Carbonell-Estrany X, Fullarton JR, Gooch KL, Vo PG, Figueras-Aloy J, Lanari M, Gouyon J-B, Liese JG. **Effects of parental and household smoking on the risk of respiratory syncytial virus (RSV) hospitalisation in late-preterm infants and the potential impact of RSV prophylaxis.** *J Matern Fetal Neonatal Med* 26:926–931 I.F.: 1.518

41. Kacerovsky M, Cobo T, Andrys C, Musilova I, Drahosova M, Hornychova H, Janku P, Jacobsson B. **The fetal inflammatory response in subgroups of women with preterm prelabor rupture of the membranes.** *J Matern Fetal Neonatal Med* 26:795–801 I.F.: 1.518

42. Tsiartas P, Kacerovsky M, Musilova I, Hornychova H, Cobo T, Sävman K, Jacobsson B. **The association between histological chorioamnionitis, funisitis and neonatal outcome in women with preterm prelabor rupture of membranes.** *J Matern Fetal Neonatal Med* 26:1332–1336 I.F.: 1.518

43. Álvarez Domínguez E, Figueras Aloy J, Botet Mussons F, Marcos Maeso MA, Pérez Fernández JM. **Screening for cytomegalovirus infection in very low birth weight infants.** *An Pediatr* (Barc) 79:3–9 I.F.: 0.867

44. Botet F, Figueras Aloy J, Echaniz Urcelay I, Rite S, Moreno J, Fernández Lorenzo JR, Herranz Carrillo G, Salguero E, Sánchez Luna M. **Recommendations for the computerisation of** *neonatology services.* An Pediatr (Barc). 78:336.e1-4. I.F.: 0.867

Reviews / I.F.: 10.733

1. Borrell A, Stergiotou I. **Miscarriage in contemporary maternal-fetal medicine: targeting clinical dilemmas.** *Ultrasound Obstet Gynecol* 42:491–497 I.F.: 3.557

2. Crovetto F, Somigliana E, Peguero A, Figueras F. **Stroke during pregnancy and pre-eclampsia.** *Curr Opin Obstet Gynecol* 25:425–432 I.F.: 2.637

3. Hernández-Andrade E, Stampalija T, Figueras F. **Cerebral blood flow studies in the diagnosis and management of intrauterine growth restriction.** *Curr Opin Obstet Gynecol* 25:138–144 I.F.: 2.637

4. Gratacós E. **Towards an integrated third-trimester screening in pregnancy.** *Fetal Diagn Ther* 33:141–142 I.F.: 1.902

Editorials / I.F.: 2.683

1. Benn P, Borrell A, Chiu R, Cuckle H, Dugoff L, Faas B, Gross S, Johnson J, Maymon R, Norton M, Odibo A, Schielen P, Spencer K, Huang T, Wright D, Yaron Y. **Response to "On gestational weeks and maths".** *Prenat Diagn* 33:1218–1219 I.F.: 2.683

Clinical Guidelines

1. Parra-Saavedra M, Cruz-Lemini M, Borobio V, Bennasar M, Goncé A, Martínez-Crespo JM, Borrell A. **Amniocentesis: guía práctica.** *Diagnóstico Prenat* 2013:8.

GRANTS FOR RESEARCH IN PROGRESS

Borrell A. **Papel de la hormona antimuleriana como marcador de edad ovárica en el cribado prenatal de síndrome de down.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00685. Duration: 01/01/2012-31/12/2014

Botet F. **Prevención de la Nefrocalcinosis del prematuro extremo mediante suplementos de citrato de potasio oral.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-161. Duration: 01/01/2012-31/12/2014

Crispi F. **Efecto de la terapia antihipertensiva prenatal sobre el remodelado cardiovascular en la restricción de crecimiento intrauterino.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00051. Duration: 01/01/2012-31/12/2014

Figueras F. **Prevención de la lesión neurológica por hipoxia crónica perinatal en un modelo animal de coneja gestante.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00851. Duration: 01/01/2013-31/12/2015

Figueras F. **Ácido acetil salicílico para la mejora de la invasión trofoblástica en gestantes con Doppler patológico de las uterinas a las 11-14 semanas de gestación.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-169. Duration: 01/01/2012-31/12/2014

Gratacós E. **EVERREST - Does vascular endothelial growth factor gene therapy safely improve outcome in severe early-onset fetal growth restriction?** Sponsored by: European Commission. 305823. Duration: 01/01/2013-31/12/2018

Gratacós E. **Identificación de biomarcadores de remodelado subcelular en la programación fetal de disfunción cardiovascular por retraso de crecimiento intrauterino.** Sponsored by: Ministerio de Economía y Competitividad.

SAF2012-37196.
Duration: 01/01/2013-31/12/2015

Gratacós E. **Evaluación de la función cardiovascular en gemelos supervivientes a una transfusión feto-fetal severa tratada por cirugía fetal.** Sponsored by: Fundacion de Investigacion Medica Mutua Madrileña. AP116192013.
Duration: 22/06/2013-21/06/2015

Gratacós E. **eVV- endoVascularVision: new endoscopic tools for real time vascular assisted vision.** Sponsored by: European Commission. 251356.
Duration: 01/09/2010-30/08/2014

Gratacós E. **A multidisciplinary research programme for the evaluation of diagnostic techniques and intervention measures for prenatal brain damage using growth restriction as a model.** Sponsored by: CEREBRA. CEREBRA_06_001.
Duration: 29/18/2007-31/12/2013

Martinez J.M. **Evaluación de la función cardiovascular en gemelos supervivientes a una transfusión feto-fetal tratada por cirugía fetal.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/02230.
Duration: 01/01/2013-31/12/2015

Palacio M. **Evaluación del valor predictivo de mal resultado perinatal del perfil proteómico y metabolómico cérvico-vaginal en pacientes con amenaza de parto prematuro y rotura prematura de membranas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01308.
Duration: 01/01/2011-31/12/2014

Palacio M. **Evaluación de la utilidad de la indometacina como tratamiento de soporte en pacientes con amenaza de parto pretérmino y alto riesgo d inflamación intraamniótica: EUDRA-CT: INDOGEST 2010-022998-33.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC10-065.
Duration: 01/01/2011-30/09/2013

Palacio M. **Progesterona vaginal como tratamiento de mantenimiento de gestantes con amenaza de parto pretérmino (Promesa).** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC07/90023.
Duration: 29/10/2007-30/06/2013

DOCTORAL THESES

Gratacós E, Crispi F. **Fetal cardiovascular dysfunction in intrauterine growth restriction as a predictive marker of perinatal outcome and cardiovascular disease in childhood.**
PhD student: Mónica Cruz-Lemini.

Gratacós E, Figueras F. **Development of biomarkers to predict adverse outcomes in fetal growth restriction.**
PhD student: Stefan Iliev Savchev.

Botet F, Costas C, Fornieles A. **Anàlisi de la relació entre variables fisiològiques i conductuals del nadó prematur.**
PhD student: Quer Palomas, S.

3.3 Viral hepatitis in the immunocompetent host and in liver transplant patients

LOCATION
CEK building

KEYWORDS
1. **HCV imaging**
2. **Ultra-deep pyrosequencing**
3. **cell culture**
4. **liver transplantation**
5. **direct acting antivirals**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	77.73	15	8	2
2012	81.79	18	13	1
2013	64.17	11	9	-

TEAM INVOLVED IN
CIBEREHD

TEAM LEADER
Xavier Forns (HCB)
T. 93 227 54 99
xforns@clinic.cat

RESEARCHERS
Josep Maria Barrera (HCB)
Josep Costa (HCB)
Gonzalo Crespo (HCB)
Maria Carlota Londoño (HCB)
Miquel Navasa (HCB)
Jose M Sánchez-Tapias (HCB)

PRE-DOCTORAL RESEARCHERS
Noelia Caro (FCRB)
Mairene Coto (FCRB)
Carlos Fernández (FCRB)
Martina Gambato (University of Padua)
Sabela Lens (HCB)
Zoe Mariño (CIBEREHD)
Laura Mensa (IDIBAPS)

TECHNICIANS
Patricia González (CIBEREHD)

NURSING STAFF
Concepció Bartrés (HCB)
Javier Pérez (FCRB)

COLLABORATORS
Marta Montero (FCRB)
Sofia Pérez del Pulgar (CIBEREHD)

STRATEGIC OBJECTIVES

- Impact of antiviral treatment in patients with hepatitis C recurrence after liver transplantation and in the natural history of chronic hepatitis C.
- Evaluation of new hepatitis C treatments.
- Study of host factors in relation to the natural history and treatment response among patients with chronic hepatitis C.
- Validation of non-invasive diagnostic methods of liver fibrosis in chronic hepatitis C and liver transplantation.
- Identification of serum markers of liver fibrosis using metabolomic tools.
- Evaluation of early histological markers of fibrosis progression in liver transplant recipients with hepatitis C recurrence.
- Genetic evolution of hepatitis C virus in the liver transplantation setting using ultra-deep pyrosequencing.
- Characterization of hepatitis C virus life cycle using in vitro cell culture models.

- Development of diagnostic tools for the detection of hepatitis C antigens in liver tissue.

MAIN LINES OF RESEARCH

Detection of HCV antigens in liver biopsies: We have established an immunohistochemical assay to detect HCV antigens in liver tissue from HCV-infected liver transplant patients in formalin-fixed paraffin paraffin-embedded liver biopsies. The system has been validated by assessing HCV antigens using confocal microscopy and we have been able to confirm our results in samples provided by other transplant centers. This method might be helpful for the diagnosis of severe hepatitis C recurrence after liver transplantation in cases where the histopahtological findings are not conclusive. We will follow-on with this project and try to analyse interactions of HCV antigens with host proteins, as well as analyse its potential application in different clinical situations.

HCV massive sequencing: We have consolidated an active collaboration with our CIBERehd partners in Institut de Recerca de l'Hospital Vall d'Hebron (Barcelona) to study HCV genetic evolution in the liver transplantation setting by ultra-deep pyrosequencing (UDPS). In particular, we have performed a very detailed analysis of HCV quasispecies dynamics and the competition of hepatitis C viral strains in HCV-infected patients who underwent liver transplantation and received a liver from an HCV-infected donor. In the following years we wil try to use this method to analyze changes in quasispecies in patients undergoing interferon-free treatments.

R & D competitive projects: In January 2013 began the implementation of the European project entitled " Human monoclonal antibody therapy to prevent hepatitis C virus reinfection of liver transplants: advancing lead monoclonal antibodies into clinical trial" (Ref. 305500, HepaMAb).

The main objectives of this project are: 1) the preclinical development of two monoclonal antibodies capable of blocking HCV entry into hepatocytes and 2) the development of a proof of concept clinical trial for the prevention of graft infection after liver transplantation. We intend to continue this multicenter collaboration, which is very useful to assess the mechanisms of HCV entry in hepatocytes and try to find out potential adjuvant treatments to prevent liver graft infection.

Treatment of chronic hepatitis C: 1) Participation in clinical trials for the evaluation of the efficacy and safety of new antiviral molecules in immunocompetent patients and 2) leadership, coordination and design of clinical studies using new direct acting antivirals in special populations: decompensated cirrhotics, cirrhotics awaiting liver transplantation and liver transplant recipients.

PUBLICATIONS

Originals / I.F.: 64.116

1. Pedersen J, Carlsen TH, Prentoe J, Ramirez S, Jensen TB, Forns X, Alter H, Foung SK, Law M, Gottwein J, Weis N, Bukh J. **Neutralization resistance of hepatitis C virus can be overcome by recombinant human monoclonal antibodies.** *Hepatology* 58(5):1587-1597 I.F.: 12.003

2. Reichenbach V, Muñoz-Luque J, Ros J, Casals G, Navasa M, Fernández-Varo G, Morales-Ruiz M, Jiménez W. **Bacterial lipopolyshaccaride inhibits CB2 receptor expression in human monocytic cells.** *Gut* 62(7):1089-91 I.F.: 10.732

3. Mariño Z, Crespo G, D'Amato M, Brambilla N, Giacovelli G, Rovati L, Costa J, Navasa M, Forns X. **Intravenous silibinin monotherapy shows significant antiviral activity in HCV-infected patients in the peri-transplantation period.** *J Hepatol* 58(3):415-20 I.F.: 9.858

4. Mensa L, Pérez-Del-Pulgar S, Crespo G, Koutsoudakis G, Fernández-Carrillo C, Coto-Llerena M, Miquel R, Allende H, Castells L, Navasa M, Forns X. **Imaging of hepatitis C virus infection in liver grafts after liver transplantation.** *J Hepatol* 59(2):271-278 I.F.: 9.858

5. Retamozo S, Díaz-Lagares C, Bosch X, Bové A, Brito-Zerón P, Gómez ME, Yagüe J, Forns X, Cid MC, Ramos-Casals M. **Life-Threatening Cryoglobulinemic Patients With Hepatitis C Clinical Description and Outcome of 279 Patients.** *Medicine* 92: 273-284. I.F.: 4.233

6. Balderramo D, Sendino O, Miquel R, de Miguel CR, Bordas JM, Martinez-Palli G, Leoz ML, Rimola A, Navasa M, Llach J, Cardenas A. **Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract.** *Liver Transplant* 19(2):199-206 I.F.: 3.944

7. Schepis F, Vukotic R, Berzigotti A, Carrión JA, Forns X, Abraldes JG, García-Valdecasas JC, Navasa M, García-Pagán JC, Bosch J. **Hemodynamic response to propranolol in patients with recurrent hepatitis C virus-related cirrhosis after liver.** *Liver Transplant* 19(4):450-456 I.F.: 3.944

8. Crespo G, Carrión JA, Coto-Llerena M, Mariño Z, Lens S, Pérez-Del-Pulgar S, García-Retortillo M, Miquel R, Bosch J, Navasa M, Forns X. **Combinations of simple baseline variables accurately predict sustained virological response in patients with recurrent hepatitis C after liver transplantation.** *J Gastroenterol* 48(6):762-769 I.F.: 3.788

9. Darwich E, To-Figueras J, Molina-López RA, Deulofeu R, Olbina G, Westerman M, Sánchez-Tápias JM, Muñoz-Santos C, Herrero C. **Increased serum hepcidin levels in patients with porphyria cutanea tarda.** *J Eur Acad Dermatol* 27(1):e68-74 I.F.: 2.694

10. Monegal A, Navasa M, Peris P, Colmenero J, Cuervo A, Muxí A, Gifre L,

Guañabens N. **Bone disease in patients awaiting liver transplantation. Has the situation improved in the last two decades?** *Calcified Tissue Int* 93(6):571-576 I.F.: 2.495

11. Carnero E, Díez J, Fortes P, Gastaminza P, Majano P, Martínez MA, Pérez-del-Pulgar S, Quer J, López-Labrador FX, Grupo de Estudio de Hepatitis Víricas de la Sociedad Española de Virología. **Meeting Report: 20 years after the First International Symposium on hepatitis C virus and related viruses.** *Gastroent Hepat* 36 (10):641-646 I.F.: 0.567

Reviews / I.F.: 5.317

1. Londoño MC, Crespo G, Forns X. **Pretransplant and posttransplant treatment of hepatitis C virus infection with protease inhibitors.** *Curr Opin Organ Transplant* 18(3):271-278 I.F.: 3.272

2. Solà R, Forns X. **Telaprevir in HCV-monoinfected patients with failure to prior treatment.** *Enferm Infecc Microbiol* Clin 31(3):14-18 I.F.: 1.478

3. Koutsoudakis G, Forns X, Pérez-Del-Pulgar S. **The molecular biology of hepatitis C virus.** *Gastroenterol Hepatol* 36(4):280-93 I.F.: 0.567

Editorials / I.F.: 11.336

1. Londoño MC, Lens S, Forns X. **Interferon free regimens for the "difficult-to-treat": Are we there?** *J Hepatol* 58(4):643-645 I.F.: 9.858

2. Lens S, Forns X. **Usefulness of liver stiffness measurement after antiviral response in chronic hepatitis C.** *Enferm Infecc Microbiol Clin* 31(7):421-423 I.F.: 1.478

GRANTS FOR RESEARCH IN PROGRESS

Forns X. **Human monoclonal antibody therapy to prevent hepatitis C virus reinfection of liver transplants: advancing lead monoclonal antibodies into clinical trial.** Sponsored by: European Commission. 305600
Duration: 01/01/2013-31/12/2017

Forns X. **Cultivo de virus de la hepatitis C (genotipos 1 y 3) a partir de suero de pacientes trasplantados hepáticos (TH). Estudio del efecto del TH en la cuasispecie viral mediante pirosecuenciación.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01907
Duration: 01/01/2012-31/12/2015

Forns X. **Early identification of severe hepatitis C recurrence after liver transplantation.** Sponsored by: Roche Organ Transplantation Research Foundation. INT_ROTRF_11_01.
Duration: 01/10/2011-31/12/2014

Forns X. **Estudio longitudinal para evaluar la utilidad de la elastografía de transición y los marcadores serológicos de fibrosis en la progresión de la hepatitis crónica C.** Sponsored by: Gilead Sciences, S.L. GLD13-00080.
Duration: 31/07/2013-30/07/2014

Forns X. **Hepatitis víriques a l'hoste immunocompetent i al trasplantat hepàtic.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1503.
Duration: 23/09/2009-30/04/2014

Forns X, Perez del Pulgar S, Gambatto M, Caro N. **Estudios de quasiespecies de los virus de la hepatitis B y C (VHB y VHC) y de polimorfismos genómicos asociados a la respuesta al tratamiento antiviral por pirosecuenciación.** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI). MINECO. CDTI IDI-20110115.
Duration: 01/03/2010- 03/12/2013.

Navasa N. **Infección del injerto por el virus de la hepatitis C (VHC) en el trasplante hepático: cinética viral precoz, mecanismos de entrada e histopatología y diagnóstico no invasivo de la fibrosis.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01551.
Duration: 01/01/2011-31/12/2013

DOCTORAL THESES

Pérez del Pulgar S, Forns X. **Polimorfismos del gen de la IL28B en la respuesta al tratamiento contra el virus de la hepatitis c en receptores de trasplante hepático.** PhD student: Mairene Coto Llerena

3.4

Pathophysiology and treatment of ascites and altered renal function in liver cirrhosis

LOCATION
CEK building

KEYWORDS
1. **Cirrhosis**
2. **Non-alcoholic steatohepatitis**
3. **Liver Stem cells**
4. **Kidney Failure**
5. **Chronic liver diseases**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	94.79	12	10	2
2012	178.78	24	21	2
2013	166.75	20	16	2

TEAM INVOLVED IN
CIBEREHD

AWARDS

Lucie Bolte Prize 2013
Institution: Lucie Bolte Foundation, Germany
Awardee/s: Pere Ginès

TEAM LEADER
Vicente Arroyo (HCB)
T. 93 227 1724
varroyo@clinic.cat

RESEARCHERS
Joan Claria (HCB)
Ramon Bataller (IDIBAPS)
Javier Fernandez-Gómez (HCB)
Pere Ginès (HCB)
Monica Guevara (IDIBAPS)
Wladimiro Jimenez (HCB)
Manuel Morales (HCB)
Pau Sancho (IDIBAPS)

POST-DOCTORAL RESEARCHERS:
Gregori Casals (FCRB)
Mar Coll (IDIBAPS)
Guillermo Fernandez Varó (CIBEREHD)
Montserrat Pauta (FCRB)
Vedrana Reichemback (FCRB)
Jordi Ribera (CIBEREHD)
Juan Rodriguez Vita (IDIBAPS)
Esther Titos (CIBEREHD)

PRE-DOCTORAL RESEARCHERS
Silvia Affò (IDIBAPS)
Xavier Ariza (FCRB)
Rogelio Barreto (FCRB)
Delia Blaya (IDIBAPS)
Chiara Elia (EASL)
Verónica García Alonso (FCRB)
Isabel Graupera (IDIBAPS)
Cristina López Vicario (IDIBAPS)
Oriol Morales (CIBEREHD)
Denisse Oro Bozzini (FCRB)
Bibiana Rius Boadas (FCRB)
Daniel Rodrigo Torres (FCRB)
Ezequiel Rodriguez (FCRB)
Valeria Tubita (FCRB)

TECHNICIANS
Montse Bernat (HCB)
Carmen Cano (HCB)
Cristina Díez (HCB)
Cristina Millán (IDIBAPS)

NURSING STAFF
Miriam Castro (CIBEREHD)
Raquel Cela (HCB)
Rebeca Moreira (FCRB)

COLLABORATORS
Jordi Colmenero (HCB)
Nuria Fabrellas (UB)
Marco Pavesi (CIBERehd)
Elsa Solà- Verges (HCB)

STRATEGIC OBJECTIVES

This is an interdisciplinary group that investigates the mechanisms of progression and treatment of liver fibrotic inflammation leading to cirrhosis, as well as the pathogenesis and treatment of the multiorgan complications derived from the existence of established liver cirrhosis.

MAIN LINES OF RESEARCH

1. Molecular determinants of liver inflammation. Role of lipid mediators and macrophages
2. Acute bacterial infections in cirrhosis
3. Pathophysiology and treatment of hepatorenal syndrome and renal failure associated with bacterial infections
4. Evaluation of biomarkers in cirrhosis.
5. Pathogenesis, clinical implications and treatment of hyponatremia
6. Evaluation of different brain MRI techniques in cirrhotic patients. Relationship to hepatic encephalopathy
7. Pathogenesis, clinical implications and treatment of adrenal dysfunction
8. Role of endogenous cannabinoids in the physiopathology of arterial vasodilatation
9. Application of genomics and gene therapy to liver dysfunction
10. Angiogenesis, endothelial dysfunction, edema and vascular remodeling in liver cirrhosis
11. Pathogenesis of liver fibrosis: cellular bases and identification of new therapeutic strategies
12. Pathophysiology and treatment of arterial vasodilatation
13. Pathophysiology and treatment of ascites
14. Artificial liver support systems
15. Mechanisms of systemic inflammation in cirrhosis.
16. Identification of new therapeutic targets in alcoholic hepatitis
17. Role of liver progenitor/stem cells in liver disease and regeneration
18. Physiopathology and treatment of acute-on-chronic liver failure

PUBLICATIONS

Originals / I.F.: 166.750

1. Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. **Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies: the OVERCOME trial (preventiOn of left Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive ChemOtherapy for the treatment of Malignant hEmopathies).** *J Am Coll Cardiol* 61(23):2355-2362 I.F.: 14.086

2. Moreau R, Jalan R, Gines P, Pavesi M, Angeli P, Cordoba J, Durand F, Gustot T, Saliba F, Domenicali M, Gerbes A, Wendon J, Alessandria C, Laleman W, Zeuzem S, Trebicka J, Bernardi M, Arroyo V; CANONIC Study Investigators of the EASL–CLIF Consortium. **Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis.** *Gastroenterology* 144(7):1426-37 I.F.: 12.821

3. Acevedo J, Fernández J, Prado V, Silva A, Castro M, Pavesi M, Roca D, Jimenez W, Ginès P, Arroyo V. **Relative adrenal insufficiency in decompensated cirrhosis: Relationship to short-term risk of severe sepsis, hepatorenal syndrome, and death.** *Hepatology* 58(5):1757-1765 I.F.: 12.003

4. Bañares R, Nevens F, Larsen FS, Jalan R, Albillos A, Dollinger M, Saliba F, Sauerbruch T, Klammt S, Ockenga J, Pares A, Wendon J, Brünnler T, Kramer L, Mathurin P, de la Mata M, Gasbarrini A, Müllhaupt B, Wilmer A, Laleman W, Eefsen M, Sen S, Zipprich A, Tenorio T, Pavesi M, Schmidt HH, Mitzner S, Williams R, Arroyo V; RELIEF study group. **Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: the RELIEF trial.** *Hepatology* 57(3):1153-1162 I.F.: 12.003

5. Morales-Ibanez O, Domínguez M, Ki SH, Marcos M, Chaves JF, Nguyen-Khac E, Houchi H, Affò S, Sancho-Bru P, Altamirano J, Michelena J, García-Pagán JC, Abraldes JG, Arroyo V, Caballería J, Laso FJ, Gao B, Bataller R. **Human and experimental evidence supporting a role for osteopontin in alcoholic hepatitis.** *Hepatology* 58(5):1742-1756 I.F.: 12.003

6. Affò S, Dominguez M, Lozano JJ, Sancho-Bru P, Rodrigo-Torres D, Morales-Ibanez O, Moreno M, Millán C, Loaeza-del-Castillo A, Altamirano J, García-Pagán JC, Arroyo V, Ginès P, Caballería J, Schwabe RF, Bataller R. **Transcriptome analysis identifies TNF superfamily receptors as potential therapeutic targets in alcoholic hepatitis.** *Gut* 62(3):452-460 I.F.: 10.732

7. Reichenbach V, Muñoz-Luque J, Ros J, Casals G, Navasa M, Fernández-Varo G, Morales-Ruiz M, Jiménez W. **Bacterial lipopolyshaccaride**

inhibits CB2 receptor expression in human monocytic cells. *Gut* 62(7):1089-1091 I.F.: 10.732

8. Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF, Soria G, Tudela R, Planas AM, Fernández-Hernando C, Arroyo V, Jiménez W, Morales-Ruiz M. **Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats.** *Gut* 62(1):138-145 I.F.: 10.732

9. Fagundes C, Barreto R, Guevara M, Garcia E, Solà E, Rodríguez E, Graupera I, Ariza X, Pereira G, Alfaro I, Cárdenas A, Fernández J, Poch E, Ginès P. **A modified acute kidney injury classification for diagnosis and risk stratification of impairment of kidney function in cirrhosis.** *J Hepatol* 59(3):474-481 I.F.: 9.858

10. Morán-Salvador E, Titos E, Rius B, González-Périz A, García-Alonso V, López-Vicario C, Miquel R, Barak Y, Arroyo V, Clària J. **Cell-specific PPARγ deficiency establishes anti-inflammatory and anti-fibrogenic properties for this nuclear receptor in non-parenchymal liver cells.** *J Hepatol* 59(5):1045-1053 I.F.: 9.858

11. Nazar A, Guevara M, Sitges M, Terra C, Solà E, Guigou C, Arroyo V, Ginès P. **LEFT ventricular function assessed by echocardiography in cirrhosis: relationship to systemic hemodynamics and renal dysfunction.** *J Hepatol* 58(1):51-57 I.F.: 9.858

12. Pauta M, Rotllan N, Vales F, Fernandez-Hernando A, Allen RM, Ford DA, Marí M, Jiménez W, Baldán A, Morales-Ruiz M, Fernández-Hernando C. **Impaired liver regeneration in Ldlr-/- mice is associated with an altered hepatic profile of cytokines, growth factors, and lipids.** *J Hepatol* 59(4):731-737 I.F.: 9.858

13. Simón-Talero M, García-Martínez R, Torrens M, Augustin S, Gómez S, Pereira G, Guevara M, Ginés P, Soriano G, Román E, Sánchez-Delgado J, Ferrer R, Nieto JC, Sunyé P, Fuentes I, Esteban R, Córdoba J. **Effects of intravenous albumin in patients with cirrhosis and episodic hepatic encephalopathy: a randomized double-blind study.** *J Hepatol* 59(6):1184-1192 I.F.: 9.858

14. García-Alonso V, López-Vicario C, Titos E, Morán-Salvador E, González-Périz A, Rius B, Párrizas M, Werz O, Arroyo V, Clària J. **Coordinate functional regulation between microsomal prostaglandin E synthase-1 (mPGES-1) and peroxisome proliferator-activated receptor γ (PPARγ) in the conversion of white-to-brown adipocytes.** *J Biol Chem* 288(39):28230-28242 I.F.: 4.651

15. Leeming DJ, Byrjalsen I, Jiménez W, Christiansen C, Karsdal MA. **Protein fingerprinting of the extracellular matrix remodelling in a rat model of liver fibrosis--a serological evaluation.** *Liver Int* ;33(3):439-447 I.F.: 3.870

16. Clària J, Nguyen BT, Madenci AL, Ozaki CK, Serhan CN. **Diversity of lipid mediators in human adipose tissue depots.** *Am J Physiol Cell Physiol* 304(12):C1141-1149 I.F.: 3.711

17. Casals G, Fernández-Varo G, Melgar-Lesmes P, Marfà S, Reichenbach V, Morales-Ruiz M, Jiménez W. **Factors involved in extracellular matrix turnover in human derived cardiomyocytes.** *Cell Physiol Biochem* 32(5):1125-1136 I.F.: 3.415

18. Filella X, Foj L, Milà M, Augé JM, Molina R, Jiménez W. **PCA3 in the detection and management of early prostate cancer.** *Tumour Biol* 34(3):1337-1347 I.F.: 2.518

19. Watson H, Jepsen P, Wong F, Ginès P, Córdoba J, Vilstrup H. **Satavaptan treatment for ascites in patients with cirrhosis: a meta-analysis of effect on hepatic encephalopathy development.** *Metab Brain Dis* 28(2):301-5 I.F.: 2.333

20. Casals G, Fábregues F, Pavesi M, Arroyo V, Balasch J. **Conservative medical treatment of ovarian hyperstimulation syndrome: a single center series and cost analysis study.** *Acta Obstet Gynecol Scand* 92(6):686-91 I.F.: 1.850

Reviews / I.F.: 17.697

1. Garcia-Martinez R, Caraceni P, Bernardi M, Gines P, Arroyo V, Jalan R. **Albumin: pathophysiologic basis of its role in the treatment of cirrhosis and its complications.** *Hepatology* 58(5):1836-1846 I.F.: 12.003

2. Solà E, Cárdenas A, Ginès P. **Results of pretransplant treatment of hepatorenal syndrome with terlipressin.** *Curr Opin Organ Transplant* 18(3):265-270 I.F.: 3.272

3. Titos E, Clària J. **Omega-3-derived mediators counteract obesity-induced adipose tissue inflammation.** *Prostaglandins Other Lipid Mediat* 107:77-84 I.F.: 2.422

Editorials / I.F.: 21.861

1. Rodriguez-Vita J, Morales-Ruiz M. **Down the liver sinusoidal endothelial cell (LSEC) hole. Is there a role for lipid rafts in LSEC fenestration?** *Hepatology* 57(3):1272-1274 I.F.: 12.003

2. Arroyo V. **Acute kidney injury (AKI) in cirrhosis: should we change current definition and diagnostic criteria of renal failure in cirrhosis?** *J Hepatol* 59(3):415-417 I.F.: 9.858

GRANTS FOR RESEARCH IN PROGRESS

Arroyo V. **Identificación de los mecanismos moleculares y factores responsables de la progresión de la cirrosis humana.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01274. Duration: 01/01/2013-31/12/2015

Arroyo V. **Investigacióhepàtica: recerca bàsica i experimental.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i

de Recerca (AGAUR). 2009_SGR_1484.
Duration: 15/09/2009-30/04/2014

Bataller R. **Enfermedad heptica en pacientes con consumo de riesgo de alcohol: Identificación de los factores genéticos y ambientales y de nuevas dianas terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01990.
Duration: 01/01/2012-31/12/2014

Bataller R, Sancho P. **MIF in progression and treatment of ALD.** Sponsored by: National Institute of Health (NIH). 1U01AA020821-01A1.
Duration: 01/09/2012-31/08/2014

Claria J. **Resolución de la inflamación en el tejido adiposo obeso. Mecanismos y mediadores.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-32789.
Duration: 01/01/2013-31/12/2015

Claria J. **Papel de los mediadores lipídicos en la inflamación del tejido adiposo y su influencia sobre la respuesta esteatogénica del higado en la obesidad.** Sponsored by: Ministerio de Economía y Competitividad. SAF2009_08767.
Duration: 01/01/2010-30/06/2013

Fernandez J. **Polimorfismos genéticos del sistema inmune innato (MBL/MASP-2 y TLR2/4) y riesgo de infecciones bacterianas en la cirrosis avanzada.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01373.
Duration: 01/01/2011-30/06/2014

Ginés P. **Insuficiencia hepática crónica agudizada y disfunción multiorgánica: Mecanismos moleculares y evaluación de nuevos métodos diagnósticos y terapéuticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00330.
Duration: 01/01/2013-31/12/2016

Ginés P. **Efecto de la administración prolongada de albúminaymidodrina en la prevención de complicaciones en pacientes en lista de espera de transplante hepático.** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC07/90077.
Duration: 29/10/2007-31/12/2014

Ginés P. **Disfunción renal en la cirrosis hepática. Investigación de nuevos métodos diagnósticos y terapéuticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI080126.
Duration: 01/01/2009-31/12/2014

Ginés P. **Grup de recerca en hepatologiaclinica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1401.
Duration: 23/09/2009-30/04/2014

DOCTORAL THESES

Clària J. **Papel del receptor nuclear PPARg en la inflamación y la esteatosis hepática.**
PhD student: Eva Morán Salvador.

Ginés P. **Estudis sobre la insuficiència renal en la cirrosi hepàtica: anàlisi del pronòstic i investigació en el tractament farmacològic de la síndrome hepatorenal.**
PhD student: Marta Martín Llahí.

Ginés P. **Contribució a l´estudi de la hiponatrèmia a la cirrosi hepàtica: descripció d´una nova causa i implicacions sobre la qualitat de vida dels pacients.**
PhD student: Elsa Solà Vergés.

Jiménez W. **Mecanismes moleculars de secreció miocardíaca: remodelat ventricular i secreció de pèptid natriurètictipus B.**
PhD student: Gregori Casals Mercada

Morales M. **Nuevos mecanismos de regulación hepática mediados por miR-33 y el receptor de las lipoproteinas de baja densidad.**
PhD student: Montserrat Pauta Puig.

3.5

Hepatic oncology

LOCATION
HCB
CEK building

FOR FURTHER INFORMATION
www.bclc.cat

KEYWORDS
1. **Hepatocellular Carcinoma**
2. **Intrahepatic cholangiocarcinoma**
3. **Biomarker profiling**
4. **Treatment**
5. **Outcomes research**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	81.94	10	8	1
2012	149.73	16	15	1
2013	115.95	11	11	-

TEAM INVOLVED IN
CIBEREHD

AWARDS
Scientific Recognition Award
Institution: Colombian Liver Association
Awardee/s: Jordi Bruix

TEAM LEADER
Jordi Bruix (HCB)
T. 93 227 98 03
jbruix@clinic.cat

GROUP LEADER
Josep M. Llovet (ICREA-IDIBAPS)

RESEARCHERS
M. Carmen Ayuso (HCB)
Concepció Bru (HCB)
Josep Fuster (HCB)
Ramon Vilana (HCB)

PRE-DOCTORAL RESEARCHERS
Clara Alsinet (FCRB)
Helena Cornella (IDIBAPS)
Iris Martínez (CIBEREHD)
María Reig (CIBEREHD)

TECHNICIANS
Juan M. López (FCRB)
Judit Peix (CIBEREHD)
Ingrid Rengel (CIBEREHD)
Anna Carolina Rhodes (FCRB)

NURSING STAFF
Neus Llarch (HCB)

ADMINISTRATIVE STAFF
Ariadna Farré (IDIBAPS)
Núria Pérez (CIBEREHD)

COLLABORATORS
Lluís Bianchi (HCB)
Loreto Boix (CIBEREHD)
Marta Burrel (HCB)
Anna Darnell (HCB)
Alejandro Forner (HCB)
M. Angeles García-Criado (HCB)
Rosa Miquel (HCB)
Agrin Moeini (IDIBAPS)
Roser Pinyol (IDIBAPS)
Jordi Rimola (HCB)
Manel Solé (HCB)
Victoria Tovar (IDIBAPS)

STRATEGIC OBJECTIVES

It is a multidisciplinary team, known internationally as "Barcelona Clinic Liver Cancer (BCLC) group", which develops an intense clinical and translational research in liver cancer. The aim of the team is to investigate the efficacy of clinical and therapeutic interventions as well as the mechanisms regulating the disease progression.

MAIN LINES OF RESEARCH

At clinical level, work is done in the definition of new diagnostic tools and, with a view to evaluating treatment efficacy, the optimum criteria for indicating radical treatment are refined (surgical resection, transplantation, percutaneous approach with ablation) – with the aim of ensuring maximum efficacy in terms of both survival and associated morbidity. In the treatment setting, evaluations are made of the options for improving the efficacy of non-curative therapies which have been shown to improve survival (arterial chemical embolization, sorafenib). In this sense, phase 1, 2 and 3 studies are carried out and led at international level together with the Biomedical Industry, with a view to determining the efficacy of new molecular agents. At the same time, evaluations are being made of the efficacy of antiangiogenic treatment to prevent relapse after surgical treatment or ablation. Likewise, cancer prevention studies are being conducted in patients with liver cirrhosis. In relation to translational research, studies are being made of the pathogenesis of hepatocellular carcinoma, together with the analysis of new signaling pathways and genomic aberrations implicated in the development of the tumor, as well as the identification of novel therapeutic targets. An international genomic research consortium has been created in hepatocellular carcinoma, in collaboration with the Mount Sinai Medical School, Harvard University and the Instituto di Tumori in Milan, which has consolidated a tissue bank of paramount importance.

RESEARCH GROUP
TRANSLATIONAL RESEARCH IN HEPATIC ONCOLOGY

GROUP LEADER

Josep M. Llovet (ICREA-IDIBAPS)

The group was created in the year 2006 with the purpose of conducting genomic studies in hepatocellular carcinoma and of identifying therapeutic targets and new molecular treatments. We have established two lines of research in the context of an international consortium (HCC Genomic Project), organized by Dr. Llovet, and involving the participation of the BCLC-Clínic-IDIBAPS, the Mount Sinai School of Medicine (NY), the Dana-Farber Cancer Institute and the Broad Institute (Boston), and the National Tumor Institute (Milan):

1. Genomics. Identification of the genomic alterations in hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) and clarification of their implications in relation to diagnosis and treatment. Integral analysis of the transcriptome (oligonucleotide microarrays) and of the genomic aberrations (SNP arrays). Identification of markers for the early diagnosis of HCC.

2. Signaling pathways and molecular therapies. Identification of the role of the signal transduction pathways in the pathogenesis of HCC, and identification of new therapeutic targets and new molecular treatments. We are currently studying the signaling pathways corresponding to Akt/ mTOR, EGFR-Ras-MAPK, IGF and Wnt, in human samples, cell lines and experimental animals.

PUBLICATIONS

Originals / I.F.: 115.952

1. Llovet JM, Decaens T, Raoul JL, Boucher E, Kudo M, Chang C, Kang YK, Assenat E, Lim HY, Boige V, Mathurin P, Fartoux L, Lin DY, Bruix J, Poon RT, Sherman M, Blanc JF, Finn RS, Tak WY, Chao Y, Ezzeddine R, Liu D, Walters I, Park JW. **Brivanib in patients with advanced hepatocellular carcinoma who where intolerant to sorafenib or for whom sorafenib failed: results from the randomized Phase III BRISK-PS Study** *J. Clin. Oncol* 31:3509-3516 I.F.: 18.038

2. Sia D, Hoshida Y, Villanueva A, Roayaie S, Ferrer J, Tabak B, Peix J, Sole M, Tovar V, Alsinet C, Cornella H, Klotzle B, Fan JB, Cotsoglou C, Thung SN, Fuster J, Waxman S, Garcia-Valdecasas JC, Bruix J, Schwartz ME, Beroukhim R, Mazzaferro V, Llovet JM. **Integrative molecular analysis of intrahepatic cholangiocarcinoma reveals 2 classes that have different outcomes.** *Gastroenterology* 144:829-840 I.F.: 12.821

3. Revill K, Wang T, Lachenmayer A, Kojima K, Harrington A, Li J, Hoshida Y, Llovet JM, Powers S. **Genome-wide methylation analysis and epigenetic unmasking identify tumor suppressor genes in hepatocellular carcinoma.** *Gastroenterology* 145(6):1424-1435 I.F.: 12.821

4. Nault JC, De Reyniès A, Villanueva A, Calderaro J, Rebouissou S, Couchy G, Decaens T, Franco D, Imbeaud S, Rousseau F, Azoulay D, Saric J, Blanc JF, Balabaud C, Bioulac-Sage P, Laurent A, Laurent-Puig P, Llovet JM, Zucman-Rossi J. **A hepatocellular carcinoma 5-gene score associated with survival of patients after liver resection.** *Gastroenterology* 145(1):176-187 I.F.: 12.821

5. Hoshida Y, Villanueva A, Sangiovanni A, Sole M, Hur C, Andersson KL, Chung RT, Gould J, Kojima K, Gupta S, Taylor B, Crenshaw A, Gabriel S, Minguez B, Iavarone M, Friedman SL, Colombo M, Llovet JM, Golub TR. **Prognostic gene**

expression signature for patients with hepatitis C-related early-stage cirrhosis. *Gastroenterology* 144(5):1024-1030 I.F.: 12.821

6. Reig M, Rimola J, Torres F, Darnell A, Lope CR, Forner A, Llarch N, Ríos J, Ayuso C, Bruix. **Post progression survival of patients with advanced hepatocellular carcinoma. Rationale for second line trial design.** *Hepatology* 58(6):2023-2031 I.F.: 12.003

7. Finn RS, Poon RT, Yau T, Klümpen HJ, Chen LT, Kang YK, Kim TY, Gomez-Martin C, Rodriguez-Lope C, Kunz T, Paquet T, Brandt U, Sellami D, Bruix J. **Phase I Study investigating Everolimus combined with Sorafenib in patients with advanced hepatocellular carcinoma.** *J. Hepatol* SO168-8278 I.F.: 9.858

8. Poynard T, Bruix J, Schiff ER, Diago M, Berg T, Moreno-Otero R, Lyra AC, Carrilho F, Griffel LH, Boparai N, Jiang R, Burroughs M, Brass CA, Albercht JK. **Improved inflammatory activity with peginterferon alfa-2b maintenance therapy in non-cirrhotic prior non-responders: a randomized study.** J. *Hepatol* 58(3):452-459 I.F.: 9.858

9. Santoro A, Simonelli M, Rodriguez-Lope C, Zucali P, Camacho LH, Granito A, Senzer N, Rimassa L, Abbadessa G, Schwartz B, Lamar M, Savage RE, .Bruix J. **A Phase-1b study of tivatinib (ARQ 197) in adult patients with hepatocellular carcinoma and cirrhosis Brit.** *J. Cancer* 108(1):21-24 I.F.: 5.082

10. Huidobro C, Toraño EG, Fernández AF, Urdinguio RG, Rodríguez RM, Ferrero C, Martínez-Camblor P, Boix L, Bruix J, García-Rodríguez JL, Varela-Rey M, Mato JM, Martínez-Chantar ML, Fraga MF. **A DNA methylation signature associated with the epigenetic repression of glycine N-methyltransferase in human hepatocellular carcinoma.** *J Mol Med (Berl)* 91:939-950 I.F.: 5.061

11. Bruix J, Tak WY, Gasbarrini A, Santoro A, Colombo M, Lim HY, Mazzaferro V, Wiest R, Reig M, Wagner A, Bolondi L. **Regorafenib as second-line therapy for intermediate or advanced hepatocellular carcinoma: Multicentre, open-label, phase II safety study.** *Eur. J. Cancer* 16:3412-3419 I.F.: 4.768

Reviews / I.F.: 29.242

1. Hernandez-Gea V, Toffanin S, Friedman SL, Llovet JM. **Role of the microenvironment in the pathogenesis and treatment of hepatocellular carcinoma.** *Gastroenterology* 144(3):512-527 I.F.: 12.821

2. Sia D, Tovar V, Moeini A, Llovet JM. **Intrahepatic cholangiocarcinoma: pathogenesis and rationale for molecular therapies.** *Oncogene* 32(41):4861-4870 I.F.: 7.357

3. Wald C, Russo MW, Heimbach JK, Hussain HK, Pomfret EA, Bruix J. **New OPTN/UNOS policy for liver transplant allocation: standardization of liver imaging, diagnosis, classification, and reporting of hepatocellular carcinoma.** *Radiology* 266(2):376-382 I.F.: 6.339

4. Forner A, Bruix J. **The size of the problema: Clinical algorithms.** *Digest Dis* 31:95-103 I.F.: 2.725

Editorials / I.F.: 5.872

1. Reig M, Berzigotti A, Bruix J. **If portal hipertension predicts outcome in cirrosis, why should this not be the case alter surgical resection?** *Liver Int* 33:1454-1456 I.F.: 3.870

2. Reig M, Burrel M, Bruix J. **Treatment of hepatocellular carcinoma with radioembolization: gathering assumptions for trial design.** *J Vasc Interv Radiol* 24:1197-1199 I.F.: 2.002

GRANTS FOR RESEARCH IN PROGRESS

Bruix J. **Antiangiogénesis en el carcinoma hepatocelular (CHC). Seguridad a largo plazo, nuevos criterios de respuesta y mecanismos moleculares de evasión al tratamiento.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01830. Duration: 01/01/2012-31/12/2014

Bruix J. **Oncologia Hepàtica- Barcelona Clinic Liver Cancer (BCLC).** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1100. Duration: 15/09/2009-30/04/2014

Llovet JM. **HEPTROMIC - Genomic predictors and oncogenic drivers in hepatocellular carcinoma.** Sponsored by: European Commission CE-FP7-HEALTH-2ST-10259744 Duration: 01/11/2010 - 30/10/2014

Llovet J.M. **Integrative Genomic Analysis of Human Intrahepatic Cholangiocarcinoma.** Sponsored by: Asociación Española Contra el Cáncer (AECC). GCA110347LLOV. Duration: 01/09/2011-28/02/2015

Llovet J.M. **Predictores genómicos pronósticos y nuevas dianas moleculares en el carcinoma hepatocelular.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-16055. Duration: 01/01/2011-30/06/2014

Llovet J.M. **Recerca translacional en oncología hepàtica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1186. Duration: 22/07/2009-30/04/2014

DOCTORAL THESES

Bruix J. **Tratamiento del carcinoma hepatocelular con sorafenib: Perfil de seguridad, evaluación de marcadores de respuesta e impacto hemodinámico en la circulación sistémica y portal.**

Correlación de los eventos secundarios, tiempo a progresión y supervivencia de esta cohorte de pacientes para definir criterios de respuesta al tratamiento.
PhD student: María Elisa Reig Monzón.

Fuster J. **Análisis de los resultados y factores pronósticos en el retrasplante hepático.**
PhD student: Josep Martí Sánchez.

Llovet J.M. **Characterization of driver pathways in hepatocellular carcinoma through genomic profiling and animal models.**
PhD student: Clara Alsinet Armengol.

3.6

Liver hemodynamics and portal hypertension. Digestive bleeding secondary to ruptured esophageal varicose veins

LOCATION
CEK building

KEYWORDS
1. **Portal Hypertension**
2. **Cirrhosis of the liver**
3. **Angiogenesis**
4. **Hepatic sinusoidal endothelial cells**
5. **Vascular liver diseases**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	161.36	22	17	3
2012	170.26	33	24	5
2013	197.42	25	23	1

TEAM INVOLVED IN
CIBEREHD

AWARDS
Premio Lilly de Investigación Biomédica (Investigación Clínica)
Institution: Fundación Lilly
Awardee/s: Jaume Bosch

Premio Extraordinario de Doctorado
Institution: Universidad de Barcelona.
Awardee/s: Annalisa Berzigotti

TEAM LEADER
Jaume Bosch (HCB)
T. 93 227 57 90
jbosch@clinic.cat

GROUP LEADERS
Mercedes Fernández Lobato (IDIBAPS)
Joan C. García-Pagán (HCB)

RESEARCHERS
Ramon Deulofeu (HCB)
Àngels Escorsell (HCB)
Mª Rosa Gilabert (HCB)
Juan González-Abraldes (HCB)
Jordi Gracia-Sancho (IDIBAPS)
Virginia Hernández-Gea (HCB)
Carles Nicolau (HCB)

POST-DOCTORAL RESEARCHERS
Annalisa Berzigotti (CIBEREHD)
Marc Mejías (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Federica Cerini (EASL)
Laura Coch (IDIBAPS)
Javier Gallego (CIBEREHD)
Sergi Guixé (UB)
Diana Hide (FPU)
Erica Lafoz (UB)
Raquel Maeso (UB)
Dinesh Mani Tripathi (ACI-COLABORA)
Giusi Marrone (IDIBAPS)
Cintia de Meireles (MRLD)
Martí Ortega (UB)
Enric Reverter (CIBEREHD)
Susana Seijó (FCRB)
Sith Siramolpiwat (HCB)
Fanny Turon (HCB)
Marina Vilaseca (CIBEREHD)

TECHNICIANS
Ester García (CIBEREHD)
Héctor García (CIBEREHD)
Montse Monclús (IDIBAPS)
Sergi Vila (CIBEREHD)

NURSING STAFF
Lara Orts (CIBEREHD)
Rosa Sáez (CIBEREHD)

STRATEGIC OBJECTIVES

Translational research aimed at advancing in the Knowledge of the pathophysiology of portal hypertension the main complication of chronic liver diseases, discovery of new therapeutic targets, introduction of new treatments for this syndrome, and development of new noninvasive

techniques for its clinical evaluation. In addition, the group is active in the fields of vascular liver diseases, angiogenesis abnormalities in liver disease and on organ preservation.

MAIN LINES OF RESEARCH

1. Factors regulating liver microcirculation under normal conditions and in cirrhosis, based on isolated liver perfusion studies and studies in isolated liver sinusoid endothelial cells.
2. Regulation of the transcription of liver sinusoid endothelial cell protecting genes: relevance in the physiopathology of portal hypertension, in ex vivo liver preservation and in the complications of cirrhosis.
3. Angiogenesis and portal hypertension: contribution to the regulation of the development of collateral circulation, hyperdynamic circulation and liver fibrogenesis.
4. New noninvasive methods for evaluating cirrhosis.
5. Randomized clinical studies of novel treatments for portal hypertension.
6. Hepatic vascular diseases.
7. Prevention of decompensation of cirrhosis.
8. Discovery of diagnostic biomarkers for idiophatic portal hypertension and for risk-stratification.
9. Role of sinusoidal endothelium in ischemia-reperfusion hepatic injury
10. Liver protection from external injury in healthy and cirrhotic livers.

RESEARCH GROUP

REGULATION OF LIVER MICROCIRCULATION IN CIRRHOSIS AND HEPATIC VASCULAR DISEASES

GROUP LEADER

Juan Carlos García-Pagán (HCB)

One of the mechanisms responsible for the development of portal hypertension and its serious consequences is the increase in portal resistance observed within the cirrhotic liver. Improved knowledge based on experimental models in animals of the cellular, biochemical and molecular mechanisms regulating the mechanisms involved in the increased intrahepatic resistance in cirrhosis and the potential mechanisms to modulate them will allow us to design new strategies for the treatment of these disorders.

Liver vascular disorders, particularly Budd-Chiari syndrome and non-cirrhotic portal thrombosis, are infrequent causes of portal hypertension. This complicates progress in our knowledge of these illnesses, their prognosis and treatments. This circumstance is of particular relevance, since these diseases mainly affect young patients with a potentially long life expectancy. For a number of years, our group has served as a reference center for these illnesses – thus allowing us to propose new treatment options and to advance in furthering our knowledge.

RESEARCH GROUP

ANGIOGENESIS IN LIVER DISEASES

GROUP LEADER

Mercedes Fernández Lobato (IDIBAPS)

Our research group investigates the role of angiogenesis, that is, the formation of new blood vessels, in the pathophysiology of chronic liver diseases, which affect millions of human beings all over the world. In the course of our research, we have demonstrated that angiogenesis is a crucial pathological hallmark of chronic liver disease, which contributes to the development and maintainance of portal hypertension, hyperdynamic splanchnic circulation, and postosystemic collateralization, and is also closely linked to fibrogenesis and inflammation in the cirrhotic liver. Much of our work is now devoted to understanding the molecular and cellular mechanisms that regulate the angiogenic process. This is essential to fully elucidate the pathological functions of angiogenesis, and to facilitate the identification of new and more effective therapeutic strategies, which, by inhibiting or attenuating angiogenesis, could be potentially useful to reduce the morbility and mortality of patients suffering from chronic liver diseases. This is of particular significance since the incidence of chronic liver disease is increasing in the world's population and the therapeutic options are limited. Our approach is multidisciplinary and employs a variety of animal models of liver diseases in rat and mouse, genetically engineered mouse models, established mammalian cell lines, samples of liver tissue from patients with liver disease, in vivo hemodynamic studies in animals, in vitro cell culture studies, tissue histology and immunohistochemistry, and biochemical, cellular and molecular biology strategies.

PUBLICATIONS

Originals / I.F.: 197.417

1. Berzigotti A, Seijo S, Arena U, Abraldes JG, Vizzutti F, García-Pagán JC, Pinzani M, Bosch J. **Elastography, Spleen Size, and Platelet Count Identify Portal Hypertension in Patients with Compensated Cirrhosis.** *Gastroenterology* 144(1):102-111.e1 I.F.: 12.821

2. La Mura V, Pasarín M, Meireles CZ, Miquel R, Rodriguez-Vilarrupla A, Hide D, Gracia-Sancho J, García-Pagán JC, Bosch J, Abraldes JG. **Effects of simvastatin administration on rats with LPS induced liver microvascular dysfunction.** *Hepatology* 57(3):1172-81 I.F.: 12.003

3. Laleman W, Simon-Talero M, Maleux G, Perez M, Ameloot K, Soriano G, Villalba J, García-Pagán JC, Barrufet M, Jalan R, Brookes J, Thalassinos E, Burroughs AK, Cordoba J, Nevens F; EASL-CLIF-Consortium. **Embolization of Large Spontaneous Portosystemic Shunts for Refractory Hepatic Encephalopathy: A Multicenter Survey on Safety and Efficacy.** *Hepatology* 57(6): 2448-2457 I.F.: 12.003

4. Ripoll C, Genescà J, Araujo IK, Graupera I, Augustin S, Tejedor M, Cirera I, Aracil C, Sala M, Hernandez-Guerra M, Llop E, Escorsell A, Catalina MV, Cañete N, Albillos A, Villanueva C, Abraldes JG, Bañares R, Bosch J. **Rebleeding prophylaxis improves outcomes in patients with hepatocellular carcinoma. A multicenter case-control study.** *Hepatology* 58(6):2079-2088 I.F.: 12.003

5. Rosado E, Rodríguez-Vilarrupla A, Gracia-Sancho J, Tripathi D, García-Calderó H, Bosch J, García-Pagán JC. Terutroban, A. **TP-receptor antagonist, reduces portal pressure in cirrhotic rats.** *Hepatology* 58(4):1424-1435 I.F.: 12.003

6. Affò S, Dominguez M, Lozano JJ, Sancho-Bru P, Rodrigo-Torres D, Morales-Ibanez O, Moreno M, Millán C, Loaeza-del-Castillo A, Altamirano J, García-Pagán JC, Arroyo V, Ginès P, Caballería J, Schwabe RF, Bataller R. **Transcriptome Analysis Identifies TNF Superfamily Receptors as Potential Therapeutic Targets in Alcoholic Hepatitis.** *Gut* 62(3):452-460 I.F.: 10.732

7. Berzigotti A, Reverter E, García-Criado A, Abraldes JG, Cerini F, García-Pagán JC, Bosch J. **Reliability of the estimation of total hepatic blood flow by doppler ultrasound in patients with cirrhotic portal hypertension.** *J Hepatol* 59(4):717-722 I.F.: 9.858

8. Garcia-Pagán JC, Di Pascoli M, Caca K, Laleman W, Bureau C, Appenrodt B, Luca A, Zipprich A, Abraldes JG, Nevens F, Vinel JP, Sauerbruch T, Bosch J. **Use of Early-TIPS for High-Risk Variceal Bleeding. Results of a post-RCT Surveillance Study.** *J Hepato* 58(1):45-50 I.F.: 9.858

9. Gracia-Sancho J, García-Calderó H, Hide D, Marrone G, Guixé-Muntet S, Peralta C, García-Pagán JC, Abraldes JG, Bosch J. **Simvastatin Maintains Function and Viability of Steatotic Rat Livers Procured for Transplantation.** *J Hepatol* 58(6):1140-1146 I.F.: 9.858

10. Guillaume M, Rodriguez-Vilarrupla A, Gracia-Sancho J, Rosado E, Mancini A, Bosch J, Garcia-Pagán JC. **Recombinant Human Manganese Superoxide Dismutase Reduces Liver Fibrosis and Portal Pressure in CCL(4)-Cirrhotic Rats.** *J Hepatol* 58(2):240-246 I.F.: 9.858

11. Jiménez-Castro MB, Casillas-Ramírez A, Mendes-Braz M, Massip-Salcedo M, Gracia-Sancho J, Elias-Miró M, Rodés J, Peralta C. **Adiponectin and Resistin Protect Steatotic Livers Undergoing Transplantation.** *J Hepatol* 59(6):1208-1124 I.F.: 9.858

12. Marrone G, Russo L, Rosado E, Hide D, García-Cardeña G, García-Pagán JC, Bosch J, Gracia-Sancho J. **The transcription factor KLF2 mediates hepatic endothelial protection and paracrine endothelial-stellate cell deactivation induced by statins.** *J Hepatol* 58(1):98-103 I.F.: 9.858

13. Pascoli MD, Diví M, Rodríguez-Vilarrupla A, Rosado E, Gracia-Sancho J, Vilaseca M, Bosch J, García-Pagán JC. **Resveratrol Improves Intrahepatic Endothelial Dysfunction and Reduces Hepatic Fibrosis and Portal Pressure in Cirrhotic Rats.** *J Hepatol* 58(5):904-910 I.F.: 9.858

14. Peralta C, Jiménez-Castro MB, Gracia-Sancho J. **Hepatic ischemia and reperfusion injury: Effects on the liver sinusoidal milieu.** *J Hepatol* 59(5):1094-1106 I.F.: 9.858

15. Berzigotti A, Erice E, Gilabert R, Reverter E, Abraldes JG, García-Pagan JC, Bosch J. **Cardiovascular risk factors and systemic endothelial function in patients with cirrhosis.** *Am J Gastroenterol* 108(1):75-82 I.F.: 7.553

16. Seijo S, Lozano JJ, Alonso C, Reverter E, Miquel R, Abraldes JG, Martinez-Chantar ML, Garcia-Criado A, Berzigotti A, Castro A, Mato JM, Bosch J, Garcia-Pagan JC. **Metabolomics Discloses Potential Biomarkers for the Noninvasive Diagnosis of Idiopathic Portal Hypertension.** *Am J Gastroenterol* 108(6):926-932 I.F.: 7.553

17. Smalberg JH, Koehler E, Murad SD, Plessier A, Seijo S, Trebicka J, Primignani M, Rijken DC, de Maat MP, García-Pagán JC, Valla DC, Janssen HL, Leebeek FW; European Network for Vascular Disorders of the Liver (EN-Vie). **Fibrinogen γ' and variation in fibrinogen gamma genes in the etiology of portal vein thrombosis.** *Thromb Haemost* 109(3):558-560 I.F.: 6.094

18. Di Pasquales, Crisafulli E, Ferrer M, Esperatti M, Li Bassi G, Escorsell A, Blasi F, Torres A. **Intensive care unit acquired pneumonia in patients with chronic liver disease: etiology and outcomes.** *Intensive Care Med* 39(10):1776-1784 I.F.: 5.258

19. Schepis F, Vukotic R, Berzigotti A, Carrión JA, Forns X, G Abraldes J, García-Valdecasas JC, Navasa M, García-Pagán JC, Bosch J. **Hemodynamic response to propranolol in patients with recurrent HCV-related cirrhosis after liver transplantation: A case-control study.** *Liver Transpl* 19(4):450-456 I.F.: 3.944

20. Berzigotti A, De Gottardi A, Vukotic R, Siramolpiwat S, Abraldes JG, García-Pagan JC, Bosch J. **Effect of meal ingestion on liver stiffness in patients with cirrhosis and portal hypertension.** *PLoS One* 8(3):e58742 I.F.: 3.730

21. Delgado MG, Gracia-Sancho J, Marrone G, Rodriguez-Vilarrupla A, Deulofeu R, Abraldes JG, Bosch J, Garcia-Pagan JC. **Leptin receptor blockade reduces intrahepatic vascular resistance and portal pressure in an experimental model of rat liver cirrhosis**. *Am J Physiol Gastrointest Liver Physiol* 305(7):G496-G502 I.F.: 3.649

22. Creus M, Deulofeu R, Peñarrubia J, Carmona F, Balasch J. **Plasma homocysteine and vitamin B12 serum levels, red blood cell folate concentrations, C677T methylenetetrahydrofolate reductase gene mutation and risk of recurrent miscarriage: a case-control study in Spain.** *Clin Chem Lab Med* 51(3):693-699 I.F.: 3.009

23. Darwich E, To-Figueras J, Molina-López RA, Deulofeu R, Olbina G, Westerman M, Sánchez-Tápias JM, Muñoz-Santos C, Herrero C. **Increased serum hepcidin levels in patients with porphyria cutanea tarda.** *J Eur Acad Dermatol Venereol* 27(1):e68-74 I.F.: 2.694

24. Martí J, Fuster J, Solà AM, Hotter G, Molina R, Pelegrina A, Ferrer J, Deulofeu R, Fondevila C, García-Valdecasas JC. **Prognostic value of serum neutrophil gelatinase-associated lipocalin in metastatic and nonmetastatic colorectal cancer.** *World J Surg* 37(5):1103-1109. I.F.: 2.228

25. Martí J, Fuster J, Estanyol JM, Fernández F, Deulofeu R, Ferrer J, Pelegrina A, Reyes A, Fondevila C, García-Valdecasas JC. **Clinical and prognostic usefulness of serum proteomic profile in hepatic colorectal metastases: a pilot prospective study.** *Clin Transl Oncol* 15(9):691-697 I.F.: 1.276

Reviews / I.F: 2.788

1. Berzigotti A, Seijo S, Reverter E, Bosch J. **Assessing portal hypertension in liver diseases.** *Expert Rev Gastroenterol Hepatol* 7(2):141-55 I.F.: 2.221

2. Berzigotti A, Abraldes JG. **Impact of obesity and insulin-resistance on cirrhosis and portal hypertension.** *Gastroenterol Hepatol* 36(8):527-533 I.F.: 0.567

Editorials / I.F.: 44.596

1. Abraldes JG, Reverter E, Berzigotti A. **Spleen stiffness: toward a noninvasive portal sphygmomanometer?** *Hepatology* 57(3):1278-1280 I.F.: 12.003

2. Bosch J. **Carvedilol for Preventing Recurrent Variceal Bleeding: Waiting for convincing evidence.** *Hepatology* 57(4):1665-1667 I.F.: 12.003

3. Bosch J. Carvedilol: **the β-blocker of choice for portal hypertension?** *Gut* 62(11):1529-1530 I.F.: 10.732

4. Bosch J. **EASL Recognition Awardee 2013: Dr. Andrew Kenneth Burroughs.** *J Hepatol* 59(3):411-412 I.F.: 9.858

GRANTS FOR RESEARCH IN PROGRESS

Bosch J. **Contrast-enhanced uLtrasound for livEr-disease eValuation: development and validation of a novel E-Health-software for Risk-stratification.** Sponsored by: European Commission. 612273. Duration: 01/10/2013-30/09/2017

Bosch J. **Hepatic hemodynamics and portal hypertension in cirrhosis. Advances in the pathophysiology, non-invasive evaluation and therapy. (Clinical & experimental studies).** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1261. Duration: 01/01/2010-30/06/2014

Bosch J. **Hemodinamica hepatica i hipertensió portal. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1108.** Duration: 15/09/2009-30/04/2014

Bosch J. **A randomized, controlled multicenter clinical trial comparing endoscopic band ligation versus oral carvedilol in the primary prophylaxis of esophageal variceal bleeding in patients with cirrhosis.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-234. Duration: 12/09/2012-31/12/2013

Bosch J. **Estudio multicéntrico, aleatorizado, doble-ciego, controlado con placebo, sobre la eficacia del tratamiento con beta-bloqueantes para la prevención de la descompensación de la cirrosis con hipertensión portal.** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00091. Duration: 01/01/2009-30/06/2013

Bosch J. **Mecanismos celulares y moleculares en la hipertensión portal no-cirrótica.** Sponsored by: Ministerio de Educación, Cultura y Deporte. ACI2009-0938. Duration: 01/12/2009-30/03/2013

Bosch J. **"Desarrollo de biomarcadores del grado de fibrosis hepática y del pronóstico de pacientes con enfermedades hepáticas avanzadas mediante el uso de herramientas metabolómicas" (LIVERBIOMARK).** Sponsored by: Ministerio de Economía y Competitividad. INNPACTO 2010 Duration: 01/01/2010-31/12/2013.

Fernández Lobato M. **Mecanismos reguladores moleculares y celulares de la angiogenesis en la hipertensión portal y la cirrosis hepatica: base racional para nuevas estrategias terapeuticas.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-29491. Duration: 01/01/2012-31/12/2014

Fernández Lobato M. **Regulation of angiogenesis in portal hypertension. Evaluation of new therapeutic strategies.** Sponsored by: Fundació La Marató de TV3. 081210. Duration: 02/02/2009-01/02/2013

García-Pagán J.C. **Caracterización y Manipulación de Nuevas Dianas Terapéuticas Involucradas en la Fisiopatología de la Hipertensión Portal en la Cirrosis.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-17043. Duration: 01/01/2011-30/06/2014

García-Pagán J.C. **Estudio aleatorizado, doble ciego, controlado con placebo, sobre los efectos de sapropterina en la hemodinámica hepática y sistémica en pacientes con cirrosis hepática e hipertensión portal.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC10-069. Duration: 01/01/2011-31/12/2013

González Abraldes, J. **Disfunción hepática asociada a la hemorragia por varices en la cirrosis: mecanismos y nuevas perspectivas terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/00883. Duration: 1/1/2012-31/12/2014

Gracia J. **Protección endotelial durante la preservación de órganos para trasplante: Mecanismos implicados y nuevas dianas terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00235. Duration: 01/02/2012-31/12/2014

DOCTORAL THESES

García-Pagán J.C, Bosch J. **Mecanismes involucrats en la regularització del to vascular hepatic en la cirrosi: paper dels antioxidants en la biodisponibilitat de l'òxid nítric.** PhD student: Marta Diví Oriol.

García-Pagán J.C, Bosch J. **Mecanismes involucrats en la regulació del to vascular heoàtic en la cirrosi: paper dels prostanoids vasoconstrictors i biodisponibilitat d'òxid nítric.** PhD student: Eugenio Rosado Mateo.

García-Pagán J.C, Bosch J. **Avances en el diagnóstico, etiopatogenia y pronóstico de la hipertensión portal no cirrótica.** PhD student: Susana Seijo Ríos.

3.7 Inflammatory bowel disease

LOCATION
CEK building

KEYWORDS
1. **Inflammatory bowel diseases**
2. **Crohn's disease**
3. **Ulcerative colitis**
4. **Cell therapy**
5. **Cross-sectional imaging**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	110.31	19	8	6
2012	197.00	24	12	8
2013	117.77	19	14	5

TEAM INVOLVED IN
CIBEREHD

AWARDS
International Award and Visiting professor in Inflammatory Bowel Disease at the Mount Sinai School of Medicine
Institution: Icahn School of Medicine at Mount Sinai.
Awardee: Julián Panés.

Best oral communication
Institution: SEDIA- Sociedad Española de Diagnóstico por imagen del abdomen.
Awardees: Jordi Rimola, Sonia Rodríguez, Orlando Garcia, Ordàs I, Ricart E.

TEAM LEADER
Julián Panés (HCB)
T. 93 227 54 18
jpanes@clinic.cat

RESEARCHERS
Salvadora Delgado (HCB)
Faust Feu (HCB)
Glòria Lacima (HCB)
Josep Llach (HCB)
Josep M. Piqué (HCB)
Elena Ricart (HCB)
Azucena Salas (IDIBAPS)

POST-DOCTORAL RESEARCHERS
Elisabeth Calderón (IDIBAPS)
Isabella Dotti (IDIBAPS)
Raquel Franco Leal ()

PRE-DOCTORAL RESEARCHERS
Raquel Cabezón (FCRB)
Maria del Carme Masamunt (FCRB)
Rut Mora (IDIBAPS)
Núria Planell (CIBERhed)

TECHNICIANS
Carolina España (Ciberhed)
Miriam Esteller (CIBERehd)

NURSING STAFF
Marta Gallego (HCB)
Susana Pinó (FCRB)
Anna Ramírez (CIBERehd)

COLLABORATORS
Daniel Benítez (CIBEREHD)
Arantza Jauregui-Amezaga (HCB)
Ingrid Ordás (HCB)

STRATEGIC OBJECTIVES

This IDIBAPS research team has a translational orientation, aimed at generating knowledge in the area of inflammatory bowel diseases to provide a direct benefit to patients suffering from Crohn's disease or ulcerative colitis in the near future. The team's research plan includes three main strategic objectives:

- The development of new treatments for Crohn's disease and ulcerative colitis, focused on celltherapy and the identification of new therapeutic targets susceptible to pharmacological modulation.
- Further in-depth knowledge of the genetic and environmental factors

responsible for susceptibility and the course of the disease, with a view to designing personalized therapies.
- Optimization of the radiological and biochemical diagnostic techniques with the aim of adapting treatment to the needs of each individual patient.

MAIN LINES OF RESEARCH

1. Hematopoietic stem cell autotransplantation in refractory Crohn's disease. Characterization of host and intestinal microbiota related factors in the therapeutic response.

2. Evaluation of the efficacy and safety of treatment with autologous tolerogenic dendritic cells derived from peripheral blood monocytes in refractory Crohn's disease.

3. Development and optimization of intestinal epithelial stem cells production. Evaluation of the therapeutic potential of intestinal stem cell transplantation in severe Crohn's disease and ulcerative colitis

4. Optimization of cross sectional imaging techniques, for evaluation of the extent, severity and prognosis of the inflammatory lesions in Crohn's disease and ulcerative colitis.

5. Advanced endoscopic techniques for diagnosis and treatment of IBD

PUBLICATIONS

Originals / I.F.: 117.772

1. Panés J, López-Sanromán A, Bermejo F, García-Sánchez V, Esteve M, Torres Y, Domènech E, Piqueras M, Gomez-García M, Gutiérrez A, Taxonera C, Sans M, AZTEC Study Group. **Early azathioprine therapy is no more effective than placebo for newly diagnosed Crohn's Disease.** *Gastroenterology* 145(4): 766-774. e1 I.F.: 12.821

2. Cleynen I, González JR, Figueroa C, Franke A, McGovern D, Bortlík M, Crusius BJ, Vecchi M, Artieda M, Szczypiorska M, Bethge J, Arteta D, Ayala E, Danese S, van Hogezand RA, Panés J, Peña SA, Lukas M, Jewell DP, Schreiber S, Vermeire S, Sans M. **Genetic factors conferring an increased susceptibility to develop Crohn's disease also influence disease phenotype: results from the IBDchip European Project.** *Gut* 62(11): 1556-1565 I.F.: 10.732

3. Julià A, Domènech E, Ricart E, Tortosa R, García-Sánchez V, Gisbert JP, Nos Mateu P, Gutiérrez A, Gomollón F, Mendoza JL, Garcia-Planella E, Barreiro-de Acosta M, Muñoz F, Vera M, Saro C, Esteve M, Andreu M, Alonso A, López-Lasanta M, Codó L, Gelpí JL, García-Montero AC, Bertranpetit J, Absher D, Panés J, Marsal S. **A genome-wide association study on a southern European population identifies a new Crohn's disease susceptibility locus at RBX1-EP300.** *Gut* 62(10): 1440-1445 I.F.: 10.732

4. Ordás I, Rimola J, García-Bosch O, Rodríguez S, Gallego M, Etchevers MJ, Pellisé M, Feu F, González-Suárez B, Ayuso C, Ricart E, Panés J. **Diagnostic accuracy of magnetic resonance colonography for the evaluation of disease activity and severity in ulcerative colitis: a prospective study.** *Gut* 62(11): 1566-1572 I.F.: 10.732

5. Planell N, Lozano JJ, Mora-Buch R, Masamunt MC, Jimeno M, Ordás I, Esteller M, Ricart E, Piqué JM, Panés J, Salas A. **Transcriptional analysis of the intestinal mucosa of patients with ulcerative colitis in remission reveals lasting epithelial cell alterations.** *Gut* 62(7):967-976 I.F.: 10.732

6. Jin S, Chin J, Seeber S, Niewoehner J, Weiser B, Beaucamp N, Woods J, Murphy C, Fanning A, Shanahan F, Nally K, Kajekar R, Salas A, Planell N, Lozano J, Panes J, Parmar H, DeMartino J, Narula S, Thomas-Karyat DA. **TL1A/TNFSF15 directly induces proinflammatory cytokines, including TNF, from CD3+CD161+ T cells to exacerbate gut inflammation.** *Mucosal Immunol* 6(5): 886-899 I.F.: 7.000

7. Jiménez A, Casamitjana R, Flores L, Delgado S, Lacy A, Vidal J. **GLP-1 and the long-term outcome of type 2 diabetes mellitus after Roux-en-Y gastric bypass surgery in morbidly obese subjects.** *Ann Surg* 257(5): 894-899 I.F.: 6.329

8. Córdova H, San José Estépar R, Rodríguez-D'Jesús A, Martínez-Pallí G, Arguis P, Rodríguez de Miguel C, Navarro-Ripoll R, Perdomo JM, Cuatrecasas M, Llach J, Vosburgh KG, Fernández-Esparrach G. **Comparative study of NOTES alone versus NOTES guided by a new image registration system for navigation in the mediastinum: a study in a porcine model.** *Gastrointest Endosc* 77(1): 102-107 I.F.: 5.210

9. Fernández-Bañares F, de Sousa MR, Salas A, Beltrán B, Piqueras M, Iglesias E, Gisbert JP, Lobo B, Puig-Diví V, García-Planella E, Ordás I, Andreu M, Calvo M, Montoro M, Esteve M, Viver JM; RECOMINA Project, GETECCU Grupo Español de Enfermedades de Crohn y Colitis Ulcerosa. **Epidemiological risk factors in microscopic colitis: a prospective case-control study.** *Inflamm Bowel Dis* 19(2):411-417 I.F.: 5.119

10. Mañosa M, Cabré E, Bernal I, Esteve M, Garcia-Planella E, Ricart E, Peñalva M, Cortes X, Boix J, Piñol M, Gassull MA, Domènech E. **Addition of metronidazole to azathioprine for the prevention of postoperative recurrence of Crohn's disease: a randomized, double-blind, placebo-controlled trial.** *Inflamm Bowel Dis* 19(9):1889-1895 I.F.: 5.119

11. Román J, Planell N, Lozano JJ, Aceituno M, Esteller M, Pontes C, Balsa D, Merlos M, Panés J, Salas A. **Evaluation of responsive gene expression as a sensitive and specific biomarker in patients with ulcerative colitis.** *Inflamm Bowel Dis* 19(2):221-229 I.F.: 5.119

12. Nunes T, Etchevers MJ, Domènech E, García-Sánchez V, Ber Y, Peñalva M, Merino O, Nos P, Garcia-Planella E, Casbas AG, Esteve M, Taxonera Samsó C, Montoro

Huguet M, Gisbert JP, Martín Arranz MD, García-Sepulcre MF, Barreiro-de Acosta M, Beltrán B, Alcaide Suárez N, Saro Gismera C, Cabriada JL, Cañas-Ventura A, Gomollón F, Panés J; Tobacco-Eneida Study Group of GETECCU. **Smoking does influence disease behaviour and impacts the need for therapy in Crohn's disease in the biologic era.** *Aliment Pharm Ther* 38(7):752-760 I.F.: 4.548

13. Balderramo D, Sendino O, Miquel R, de Miguel CR, Bordas JM, Martinez-Palli G, Leoz ML, Rimola A, Navasa M, Llach J, Cardenas A. **Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract.** *Liver Transplant* 19(2): 199-206 I.F.: 3.944

14. Zabala W, Cruz R, Barreiro-de Acosta M, Chaparro M, Panes J, Echarri A, Esteve M, Carpio D, Andreu M, García-Planella E, Domenech E, Carracedo A, Gisbert JP, Barros F, EIGA & ENEIDA investigators. **New genetic associations in thiopurine-related bone marrow toxicity among inflammatory bowel disease patients.** *Pharmacogenomics* 14(6): 631-640 I.F.: 3.857

15. Saibeni S, Etchevers MJ, Tassies D, Panés J, Reverter JC, Danese S, Piqué JM, Bruno S, Vecchi M, Gasbarrini A, Sans M. **Assessment of anti-prothrombin antibodies in thrombosis complicating inflammatory bowel diseases.** *Int J Colorectal Dis* 28(9): 1281-1286 I.F.: 2.238

16. Sandborn WJ, Colombel JF, Panés J, Castillo M, Robinson AM, Zhou Q, Yang M, Thakkar R. **Exploring the use of adalimumab for patients with moderate Crohn's disease: subanalyses from induction and maintenance trials.** *J Crohns Colitis.* 15;7(12):958-67. I.F.: 3.385

17. García-Bosch O, Gisbert JP, Cañas-Ventura A, Merino O, Cabriada JL, García-Sánchez V, Gutiérrez A, Nos P, Peñalva M, Hinojosa J, García-Planella E, Muñoz F, Calvet X, Panés J. **Observational study on the efficacy of adalimumab for the treatment of ulcerative colitis and predictors of outcome.** *J Crohns Colitis.* 7(9):717-22. I.F.: 3.385

18. Schreiber S, Panés J, Louis E, Holley D, Buch M, Paridaens K. **National differences in ulcerative colitis experience and management among patients from five European countries and Canada: an online survey.** *J Crohns Colitis.* 7(6):497-509. I.F.: 3.385

19. Jauregui-Amezaga A, Turon F, Ordás I, Gallego M, Feu F, Ricart E, Panés J. **Risk of developing tuberculosis under anti-TNF treatment despite latent infection screening.** *J Crohns Colitis.*7(3):208-12. I.F.: 3.385

Reviews / I.F.: 7.233

1. Ricart E, Jauregui-Amezaga A, Ordás I, Pinó S, Ramírez AM, Panés J. **Cell therapies for IBD: what works?** *Curr Drug Targets* 14(12):1453-1459. I.F.: 3.848

2. Van Assche G, Dignass A, Bokemeyer B, Danese S, Gionchetti P, Moser G, Beaugerie L, Gomollón F, Häuser W, Herrlinger K, Oldenburg B, Panes J, Portela F, Rogler G, Stein J, Tilg H, Travis S, Lindsay JO; European Crohn's and Colitis Organisation. **Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 3: special situations.** *J Crohns Colitis.*7(1):1-33. I.F.: 3.385

3. Papay P, Ignjatovic A, Karmiris K, Amarante H, Milheller P, Feagan B, D'Haens G, Marteau P, Reinisch W, Sturm A, Steinwurz F, Egan L, Panés J, Louis E, Colombel JF, Panaccione R. **Optimising monitoring in the management of Crohn's disease: a physician's perspective.** *J Crohn Colitis* 7(8): 653-656 I.F.: 3.385

Editorials / I.F.: 12.131

1. Salas A. **The IL-33/ST2 axis: yet another therapeutic target in inflammatory bowel disease?** *Gut* 62(10): 1392-1393 I.F.: 10.732

2. Piqué JM. **[Health care system: where is now and where it goes?].** *Med Clin* 140(11): 514-519 I.F.: 1.399

Clinical Guidelines / I.F.: 7.337

1. Panes J, Bouhnik Y, Reinisch W, Stoker J, Taylor SA, Baumgart DC, Danese S, Halligan S, Marincek B, Matos C, Peyrin-Biroulet L, Rimola J, Rogler G, van Assche G, Ardizzone S, Ba-Ssalamah A, Bali MA, Bellini D, Biancone L, Castiglione F, Ehehalt R, Grassi R, Kucharzik T, Maccioni F, Maconi G, Magro F, Martín-Comín J, Morana G, Pendsé D, Sebastian S, Signore A, Tolan D, Tielbeek JA, Weishaupt D, Wiarda B, Laghi A. **Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines.** *J Crohn Colitis* 7(7): 556-585 I.F.: 3.385

2. Cabriada JL, Vera I, Domènech E, Barreiro-de Acosta M, Esteve M, Gisbert JP, Panés J, Gomollón F, Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa (GETECCU). **[Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis on the use of anti-tumor necrosis factor drugs in inflammatory bowel disease].** *Gastroent Hepat* (3): 127-146 I.F.: 0.567

Multicenter / I.F.: 8.517

1. Beaudoin M, Goyette P, Boucher G, Lo KS, Rivas MA, Stevens C, Alikashani A, Ladouceur M, Ellinghaus D, Törkvist L, Goel G, Lagacé C, Annese V, Bitton A, Begun J, Brant SR, Bresso F, Cho JH, Duerr RH, Halfvarson J, McGovern DP, Radford-Smith G, Schreiber S, Schumm PL, Sharma Y, Silverberg MS, Weersma

RK, Quebec IBD Genetics Consortium, NIDDK IBD Genetics Consortium, International IBD Genetics Consortium, D'Amato M, Vermeire S, Franke A, Lettre G, Xavier RJ, Daly MJ, Rioux JD. **Deep resequencing of GWAS loci identifies rare variants in CARD9, IL23R and RNF186 that are associated with ulcerative colitis.** *PLoS Genet* 9(9): e1003723
I.F.: 8.517

GRANTS FOR RESEARCH IN PROGRESS

Lacima G. **Eficacia de la neuromodulación sacra en el tratamiento del estreñimiento crónico de tránsito lento: estudio cruzado, randomizado y doble ciego.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00405.
Duration: 01/01/2012-31/12/2014.

Panes J. **Desarrollo de un kit diagnóstico para las enfermedades inflamatorias mediadas por mecanismos inmunes (IMID-Kit). Subproyecto 1: Estudio de asociación de genoma completo en las enfermedades inflamatorias mediadas por mecanismos inmunes (IMID Immune Mediated Inflammatory Diseases) ("WGAS-IMID"). Sobproyecto 4: Estudio de asociación de genoma completo en nuevas IMID.** Sponsored by: Ministerio de Economía y Competitividad. PSE-010000-2008-9.
Duration: 01/01/2009-31/01/2014

Panes J. **Transplante autólogo de células madre hematopoyéticas en la enfermedad de Crohn: factores genéticos, inmunes y microbiológicos implicados en el control de la enfermedad.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-33560.
Duration: 01/01/2013-31/12/2015.

Panes J. **Characterization of regulatory B cells in human inflammatory bowel disease. Sponsored by: International Organization for the Study of Inflammatory Bowel Diseases.** IOIBD_GRANTS2011_01.
Duration: 01/01/2012-31/12/2014.

Panes J. **Malaltia Inflamatòria Intestinal.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1206.
Duration: 15/09/2009-30/04/2014.

Salas A. **Exploring the therapeutic potential of intestinal stem cell transplantation in inflammatory bowel diseases.** Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 122931.
Duration: 11/01/2013-10/01/2016.

Salas A. **Papel de las células epiteliales intestinales y sus progenitores en la patogénesis de la enfermedad inflamatoria intestinal.** Sponsored by: Ministerio de Economía y Competitividad. BFU2012-35999.
Duration: 01/01/2013-31/12/2015.

Salas A. **Delivering nanopharmaceuticals through Blological BArriers.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/02998(NANO-MED).
Duration: 01/01/2011-31/01/2015.

Salas A. **Delivering nanopharmaceuticals through Blological BArriers.** Sponsored by: European Commission. ERA-NET_NANOMED10_02.
Duration: 01/03/2011-28/02/2014.

DOCTORAL THESES

Llach J. **La utilidad del Narrow Band Imaging para el estudio de las enfermedades con alto riesgo de cáncer digestivo.**
PhD student: María López-Cerón Pinilla.

3.8 Cholestasis and Bone pathology

LOCATION
HCB building

KEYWORDS
1. **Primary biliary cirrhosis**
2. **Osteoporosis**
3. **Pruritus**
4. **Bone metabolism**
5. **Albumin dialysis**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	36.73	8	5	1
2012	42.91	9	3	4
2013	107.14	15	9	4

TEAM INVOLVED IN
CIBEREHD

TEAM LEADER
Albert Parés (HCB)
T. 93 227 57 53
apares@clinic.cat

TEAM LEADER
Núria Guañabens (HCB)
T. 93 227 54 00 ext 2235
nguana@clinic.cat

GROUP LEADERS
Núria Guañabens (HCB)
Albert Parés (HCB)

RESEARCHERS
M. Lluisa Álvarez (HCB)
Antoni Mas (HCB)
Ana Monegal Brancós (HCB)
Pilar Peris (HCB)

PRE-DOCTORAL RESEARCHERS
Laia Gifre (HCB)

TECHNICIANS
Marta Dubreuil (CIBEREHD)

NURSING STAFF
Pilar Sesé (FCRB)

COLLABORATORS
Mª Jesús Martinez de Osaba (HCB)
Silvia Ruiz-Gaspá (CIBEREHD)

STRATEGIC OBJECTIVES

1. Study of the epidemiology, pathogenesis, diagnosis and treatment of adult chronic cholestatic disorders and autoimmune hepatitis.
2. Knowledge of the pathogenic

mechanisms underlying pruritus and osteoporosis in primary biliary cirrhosis.
3. Investigation of the pathogenic and therapeutic aspects of metabolic bone diseases.
4. Definition of the therapeutic potential of different artificial liver support procedures in liver failure.

MAIN LINES OF RESEARCH

The research lines of this team are divided into two associated groups.

RESEARCH GROUP **CHOLESTASIS**

GROUP LEADER

Albert Parés (HCB)

1. Epidemiology, natural history and therapeutic response of chronic cholestatic disorders in adults.
2. Evaluation of the factors conditioning treatment response, and proposition of new treatment regimens in patients showing suboptimum response to ursodeoxycholic acid.
3. Pruritus in chronic cholestasis and treatment response to albumin dialysis.
4. Pathogenesis of osteoporosis and fracture development in primary biliary cirrhosis and other chronic cholestatic disorders.
5. Evaluation of the safety and efficacy of different bioartificial liver and hepatic support systems in treating acute liver failure and exacerbated chronic liver failure.

RESEARCH GROUP **BONE METABOLIC DISEASE**

GROUP LEADER

Núria Guanyabens (HCB)

1. Osteoporosis in premenopausal women and in males. Study of the clinical characteristics and mechanisms involved in the development of the disorder.
2. Osteoporosis in primary biliary cirrhosis. Clinical and "in vitro" analysis. Evaluation of the key factors in the development of low bone mass and fractures, and proposal of new therapeutic protocols.
3. Osteoporosis in liver transplantation.
4. Evaluation of vertebroplasty as treatment for osteoporotic vertebral fractures.
5. Evaluation of bone remodeling regulators on the pathogenesis of osteoporosis.

PUBLICATIONS

Originals / **I.F.: 107.144**

1. Liu JZ, Hov JR, Folseraas T, Ellinghaus E, Rushbrook SM, Doncheva NT, Andreassen OA, Weersma RK, Weismüller TJ, Eksteen B, Invernizzi P, Hirschfield GM, Gotthardt DN, Pares A, Ellinghaus D, Shah T, Juran BD, Milkiewicz P, Rust C, Schramm C, Müller T, Srivastava B, Dalekos G, Nöthen MM, Herms S, Winkelmann J,Mitrovic M, Braun F, Ponsioen CY, Croucher PJ, Sterneck M, Teufel A, Mason AL, Saarela J, Leppa V, Dorfman R, Alvaro D, Floreani A, Onengut-Gumuscu S, Rich SS, Thompson WK, Schork AJ, Næss S, Thomsen I, Mayr G, König IR, Hveem K, Cleynen I, Gutierrez-Achury J, Ricaño-Ponce I, van Heel D, Björnsson E, Sandford RN, Durie PR, Melum E, Vatn MH, Silverberg MS, Duerr RH, Padyukov L, Brand S, Sans M, Annese V, Achkar JP, Boberg KM, Marschall HU, Chazouillères O, Bowlus CL, Wijmenga C, Schrumpf E, Vermeire S, Albrecht M; UK-PSCSC Consortium; International IBD Genetics Consortium, Rioux JD, Alexander G, Bergquist A, Cho J, Schreiber S, Manns MP, Färkkilä M, Dale AM, Chapman RW, Lazaridis KN; International PSC Study Group, Franke A, Anderson CA, Karlsen TH. **Dense genotyping of immune-related disease regions identifies nine new risk loci for primary sclerosing cholangitis.** *Nat Genet* 45(6):670-675 I.F.: 35.209

2. Guañabens N, Monegal A, Cerdá D, Muxí Á, Gifre L, Peris P, Parés A. **Randomized trial comparing monthly ibandronate and weekly alendronate for osteoporosis in patients with primary biliary cirrhosis.** *Hepatology* 58(6):2070-2078 I.F.: 12.003

3. Bañares R, Nevens F, Larsen FS, Jalan R, Albillos A, Dollinger M, Saliba F, Sauerbruch T, Klammt S, Ockenga J, Pares A, Wendon J, Brünnler T, Kramer L, Mathurin P, de la Mata M, Gasbarrini A, Müllhaupt B, Wilmer A, Laleman W, Eefsen M, Sen S, Zipprich A, Tenorio T, Pavesi M, Schmidt HH, Mitzner S, Williams R, Arroyo V; RELIEF study group. **Extracorporeal albumin dialysis with the molecular adsorbent recirculating system in acute-on-chronic liver failure: the RELIEF trial.** *Hepatology* 57(3):1153-1162 I.F.: 12.003

4. Martinez-Ferrer A, Blasco J, Carrasco JL, Macho JM, Román LS, López A, Monegal A, Guañabens N, Peris P. **Risk factors for the development of vertebral fractures after percutaneous vertebroplasty.** *J Bone Miner Res* 28(8):1821-1829 I.F.: 6.128

5. Glüer CC, Marin F, Ringe JD, Hawkins F, Möricke R, Papaioannu N, Farahmand P, Minisola S, Martínez G, Nolla JM, Niedhart C, Guañabens N, Nuti R, Martín-Mola E, Thomasius F, Kapetanos G, Peña J, Graeff C, Petto H, Sanz B, Reisinger A, Zysset PK. **Comparative effects of teriparatide and risedronate in glucocorticoid-induced osteoporosis in men: 18-month results of the EuroGIOPs trial.** *J Bone Miner Res* 28(6):1355-1368 I.F.: 6.128

6. Peris P, Atkinson EJ, Gössl M, Kane TL, McCready LK, Lerman A, Khosla S, McGregor UI. **Effects of bisphosphonate treatment on circulating osteogenic endothelial progenitor cells in postmenopausal women.** *Mayo Clin Proc* 88(1):46-55 I.F.: 5.790

7. Di Pasquale M, Esperatti M, Crisafulli E, Ferrer M, Bassi GL, Rinaudo M, Escorsell A, Fernandez J, Mas A, Blasi F, Torres A. **Impact of chronic liver disease in intensive care unit acquired pneumonia: a prospective study.** *Intens Care Med* 39(10):1776-1784 I.F.: 5.258

8. Gómez-Puerta JA, Peris P, Reverter JC, Espinosa G, Martinez-Ferrer A, Monegal A, Monteagudo J, Tàssies D, Guañabens N. **High prevalence of prothrombotic abnormalities in multifocal osteonecrosis: description of a series and review of the literature.** *Medicine (Baltimore)* 92(6):295-304 I.F.: 4.233

9. Farahmand P, Marin F, Hawkins F, Möricke R, Ringe JD, Glüer CC, Papaioannou N, Minisola S, Martínez G, Nolla JM, Niedhart C, Guañabens N, Nuti R, Martín-Mola E, Thomasius F, Peña J, Graeff C, Kapetanos G, Petto H, Gentzel A, Reisinger A, Zysset PK. **Early changes in biochemical markers of bone formation during teriparatide therapy correlate with improvements in vertebral strength in men with glucocorticoid-induced osteoporosis.** *Osteoporos Int* 24(12):2971-2981 I.F.: 4.039

10. Dubreuil M, Ruiz-Gaspà S, Guañabens N, Peris P, Alvarez L, Monegal A, Combalia A, Parés A. **Ursodeoxycholic acid increases differentiation and mineralization and neutralizes the damaging effects of bilirubin on osteoblastic cells.** *Liver Int* 33(7):1029-1038 I.F.: 3.870

11. Gifre L, Ruiz-Gaspà S, Monegal A, Nomdedeu B, Filella X, Guañabens N, Peris P. **Effect of glucocorticoid treatment on Wnt signalling antagonists (sclerostin and Dkk-1) and their relationship with bone turnover.** *Bone* 57(1):272-276 I.F.: 3.823

12. Cerda C, Bruguera M, Parés A. **Hepatotoxicity associated with glucosamine and chondroitin sulfate in patients with chronic liver disease.** *World J Gastroenterol* 19(32):5381-5384 I.F.: 2.547

13. Monegal A, Navasa M, Peris P, Colmenero J, Cuervo A, Muxí A, Gifre L, Guañabens N. **Bone disease in patients awaiting liver transplantation. Has the situation improved in the last two decades?** *Calcif Tissue Int* 93(6):571-576 I.F.: 2.495

14. Kanterewicz E, Peris P, Puigoriol E, Yáñez A, Rosique P, Del Rio L; FRODOS Research Group. **Distribution of serum βCTX in a population-based study of postmenopausal women taking into account different anti-osteoporotic therapies (the FRODOS Cohort).** *J Bone Miner Metab* 31(2):231-239 I.F.: 2.219

15. Martínez-Ferrer A, Blasco J, Guañabens N, Pomés J, Peris P. **[Effectiveness of vertebroplasty in painful chronic osteoporotic vertebral fractures].** *Med Clin (Barc)* 140(3):115-118 I.F.: 1.399

GRANTS FOR RESEARCH IN PROGRESS

Guañabens N. **Ácido ursodeoxicólico y osteoporosis en la colestasis crónica. Estudio "in vitro" en células óseas y repercusión clínica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00281.
Duration: 01/01/2012-31/12/2014

Pares A. **Prurito de la colestasis. Análisis metabólico.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01448.
Duration: 01/01/2013-31/12/2015

Peris P. **Prospective study of bone loss after spinal cord injury, risk factors and role of osteocyte markers.** Sponsored by: Fundació La Marató de TV3. 110710.
Duration: 31/01/2012-30/01/2015

3.9

Mitochondrial regulation of cell death and steatohepatitis

LOCATION
CEK building

KEYWORDS
1. **Cholesterol/sphingolipids**
2. **Mitochondrial death**
3. **Oxidative stress**
4. **Alcoholic and non-alcoholic steatohepatitis (ASH/NASH)**
5. **Lipid therapies**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	46.82	6	5	-
2012	57.66	9	7	1
2013	62.15	6	6	-

TEAM INVOLVED IN
CIBEREHD

TEAM LEADER
José Carlos Fernández-Checa
(IIBB-CSIC)
T. 93 227 57 09
checa229@yahoo.com

RESEARCHERS
Joan Caballeria (HCB)
Anna Colell (IIBB-CSIC
Carmen García Ruíz (IIBB-CSIC)
Montserrat Marí (IIBB-CSIC)
Albert Morales (IIBB-CSIC)

POST-DOCTORAL RESEARCHERS
Laura Conde de la Rosa (IIBB-CSIC)
Nuria Matias (IDIBAPS)
Vicente Ribas Serra (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Elisabeth Barbero (IIBB-CSIC)
Cristina Bárcena (IDIBAPS)
Anna Baulies (IIBB-CSIC)
Raquel Fucho (CIBEREHD)
Laura Martínez (IIBB-CSIC)
Guillermo Antonio Martínez Nieto (IIBB-CSIC)
Álvaro de Mingo Pulido (IIBB-CSIC)
Milica Stefanovic (CSIC)
Sandra Torres (IIBB-CSIC)
Anna Tutusaus (IIBB-CSIC)

TECHNICIANS
Susana Núñez Pozuelo (CIBEREHD)

STRATEGIC OBJECTIVES

The overall aim is to examine the cell biology of lipids and cholesterol trafficking in liver diseases and neurodegeneration. This includes the role of mitochondrial cholesterol and sphingolipids in steatohepatitis, liver cancer, liver fibrogenesis, hepatic ischemia/reperfusion injury, Alzheimer's disease and lysosomal storage disorders.

MAIN LINES OF RESEARCH

1. Sphingolipid and mitochondrial oxidative-stress regulation of cell death (Dr Fernández-Checa).
2. Mechanisms responsible for cholesterol transport to the mitochondria (Dr Fernández-Checa).
3. Role of cholesterol in hepatocellular

carcinoma response to chemotherapy (Dr Fernández-Checa).
4. Functional relationship between methionine metabolites, acid sphingomyelinase and phosphatidylcholine in steatohepatitis (Dr. Fernandez-Checa).
5. Contribution of acid sphingomyelinase in acetaminophen induced acute liver failure (Dr. García-Ruiz)
6. Regulation of cholesterol homeostasis in patients and experimental models of non-alcoholic steatohepatitis and ischemia-reperfusion injury (Dr C. García-Ruiz).
7. Contribution of sphingolipids and autophagy to lipid metabolism and non-alcoholic steatohepatitis (Dr C. García-Ruiz).
8. Development of non-invasive diagnostic methods for diagnosis and prognosis in alcohol-induced liver disease (Dr J. Caballería).
9. Parenchyma-stroma interaction in cancer and ischemia/reperfusion-induced liver damage: lipid therapies (Dr A. Morales)
10. Role of cholesterol and the mitochondria in Alzheimer's Disease (Dr A. Colell)
11. Contribution of cathepsins to fibrosis and inflammation of the liver (Dr M. Marí).

PUBLICATIONS

Originals / I.F.: 62.146

1. Morales-Ibanez O, Domínguez M, Ki SH, Marcos M, Chaves JF, Nguyen-Khac E, Houchi H, Affò S, Sancho-Bru P, Altamirano J, Michelena J, García-Pagán JC, Abraldes JG, Arroyo V, Caballería J, Laso FJ, Gao B, Bataller R. **Human and experimental evidence supporting a role for osteopontin in alcoholic hepatitis.** *Hepatology* 58(5):1742-1756 I.F.: 12.003

2. Vazquez-Chantada M, Gonzalez-Lahera A, Martinez-Arranz I, Garcia-Monzon C, Regueiro MM, Garcia-Rodriguez JL, Schlangen KA, Mendibil I, Rodriguez-Ezpeleta N, Lozano JJ, Banasik K, Justesen JM, Joergensen T, Witte DR, Lauritzen T, Hansen T, Pedersen O, Veyrie N, Clement K, Tordjman J, Tran A, Le Marchand-Brustel Y, Buque X, Aspichueta P, Echevarria-Uraga JJ, Martin-Duce A, Caballeria J, Gual P, Castro A, Mato JM, Martinez-Chantar ML, Aransay AM. **Solute carrier family 2 member 1 is involved in the development of nonalcoholic fatty liver disease.** *Hepatology* 57(2):505-514 I.F.: 12.003

3. Affò S, Dominguez M, Lozano JJ, Sancho-Bru P, Rodrigo-Torres D, Morales-Ibanez O, Moreno M, Millán C, Loaeza-del-Castillo A, Altamirano J, García-Pagán JC, Arroyo V, Ginès P, Caballería J, Schwabe RF, Bataller R. **Transcriptome analysis identifies TNF superfamily receptors as potential therapeutic targets in alcoholic hepatitis.** *Gut* 62(3):452-460 I.F.: 10.732

4. Fernandez A, Matias N, Fucho R, Ribas V, Von Montfort C, Nuño N, Baulies A, Martinez L, Tarrats N, Mari M, Colell A, Morales A, Dubuquoy L, Mathurin P, Bataller R, Caballeria J, Elena M, Balsinde J, Kaplowitz N, Garcia-Ruiz C, Fernandez-Checa JC. **ASMase is required for chronic alcohol induced hepatic endoplasmic reticulum stress and mitochondrial cholesterol loading.** *J Hepatol* 59(4):805-813 I.F.: 9.858

5. Pauta M, Rotllan N, Vales F, Fernandez-Hernando A, Allen RM, Ford DA, Marí M, Jiménez W, Baldán A, Morales-Ruiz M, Fernández-Hernando C. **Impaired liver regeneration in Ldlr-/- mice is associated with an altered hepatic profile of cytokines, growth factors, and lipids.** *J Hepatol* 59(4):731-737 I.F.: 9.858

6. Barbero-Camps E, Fernández A, Martínez L, Fernández-Checa JC, Colell A. **APP/PS1 mice overexpressing SREBP-2 exhibit combined Aβ accumulation and tau pathology underlying Alzheimer's disease.** *Hum Mol Genet* 22(17):3460-3476 I.F.: 7.692

Reviews / I.F.: 8.779

1. Marí M, Morales A, Colell A, García-Ruiz C, Kaplowitz N, Fernández-Checa JC. **Mitochondrial glutathione: features, regulation and role in disease.** *Biochim Biophys Acta* 1830(5):3317-3328 I.F.: 3.848

2. García-Ruiz C, Baulies A, Mari M, García-Rovés PM, Fernandez-Checa JC. **Mitochondrial dysfunction in non-alcoholic fatty liver disease and insulin resistance: cause or consequence?** *Free Radic Res* 47(11):854-868 I.F.: 3.279

3. Caballeria J. **Establishing prognosis in alcoholic hepatitis.** *Rev Esp Enferm Dig* 105(9):509-512 I.F.: 1.652

Editorials / I.F.: 12.003

1. Garcia-Ruiz C, Fernandez-Checa JC. **To binge or not to binge: binge drinking disrupts glucose homeostasis by impairing hypothalamic but not liver insulin signaling.** Hepatology 57(6):2535-2538 I.F.: 12.00

GRANTS FOR RESEARCH IN PROGRESS

Caballeria J. **Análisis de la disfunción endotelial y miRNAs en el pronóstico de la hepatitis alcohólica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01265.
Duration: 01/01/2013-31/12/2015

Caballeria J. **Molecular subtypes for targeted therapies in alcoholic hepatitis.** Sponsored by: National Institute of Health (NIH). 5-33490.
Duration: 01/06/2013-31/05/2014

Colell A. **Regulacion mitocondrial de la citotoxicidad inducida por beta-amiloide.** Sponsored by: Ministerio Ciencia e Innovación, SAF2010-15760.
Duration: 01/01/2011-31/12/2013.

Fernandez-Checa J.C. **USC-UCLA Research Center for Alcoholic Liver and Pancreatic Injury Research Project#1.** Sponsored by: National Institute of Health (NIH). 5P50AA011999.
Duration: 01/01/2013-31/12/2014

Fernandez-Checa J.C. **From gut-derived inflammation to obesity-related liver disease.** Sponsored by: European Commission. JTC_META_2011_001. Duration: 07/04/2011-06/04/2014

Fernandez-Checa JC. **Colesterol y glicoesfingolípidos en la mitocondria hepática y del cerebro y la alteración del metabolismo contribuye a la patología de la enfermedad de Niemann Pick tipo C y caveolinopatías.** Sponsored by: Fundació La Marató de TV3, 050506110015. Duration: 03/02/2011-31/12/2014.

Fernandez-Checa JC. **Relación funcional y metabólica entre los metabolitos de la metionina, esfingomielinasa acida y fosfatidilcolina: impacto en esteatohepatitis.** Sponsored by: Ministerio de Ciencia e Innovación, SAF2011-34831. Duration: 01/01/2013-31/12/2015.

Garcia-Ruiz C. **Análisis lipídico del injerto hepático para discriminar su viabilidad en el trasplante de hígado.** Sponsored by: Fundacion de Investigacion Médica Mutua Madrileña. AP103502012. Duration: 11/07/2012-10/07/2015

Garcia-Ruiz, C. **Esfingomielinasa ácida y autofagia: regulación del metabolismo lipídico y esteatohepatitis.** Sponsored by: Ministerio de Ciencia e Innovación, SAF2011-23031. Duration: 01/01/2012-31/12/2014.

Marí M. **Catepsinas en la Fibrosis Hepática e Inflamación: Regulación por TNF.** Sponsored by: Instituto de Salud Carlos III (ISCIII), PI10/02114. Duration: 01/01/2011-31/12/2013.

Morales A. **Terapia lipídica en daño hepatocelular y cáncer: bases moleculares y modelos experimentales.** Sponsored by: Instituto de Salud Carlos III (ISCIII), PI12/00110. Duration: 01/01/2013-31/12/2015.

DOCTORAL THESES

García-Ruiz C.; Fernández-Checa J.C. **Role of acid sphingomyelinase in steatohepatitis.** PhD student: Raquel Fucho Salvador.

3.10 Liver transplantation and graft viability

LOCATION
CEK building

KEYWORDS
1. **Liver transplantation**
2. **Graft viability**
3. **Immunosuppression**
4. **Allograft tolerance**
5. **Hepatic ischemia-reperfusion injury**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	69.84	16	10	2
2012	90.99	23	13	2
2013	127.80	27	15	4

TEAM INVOLVED IN
CIBEREHD

TEAM LEADER
Antoni Rimola (HCB)
T. 93 227 57 53
arimola@clinic.cat

GROUP LEADER
Carmen Peralta (IDIBAPS)

RESEARCHERS
Annabel Blasi (HCB)
Mercedes Brunet (HCB)
Jordi Colmenero (HCB)
Constantino Fondevila (HCB)
Juan C. García-Valdecasas (HCB)
Martí Manyalich (HCB)
Miquel Navasa (HCB)
Joan Rosselló-Catafau (IIBB-CSIC)
Albert Sánchez Fueyo (HCB)

POST-DOCTORAL RESEARCHERS
Araní Casillas (IDIBAPS)
Mª Carlota Londoño (CIBEREHED)
Marta Massip (CIBEREHD)
Olga Millán (CIBEREHD)

PRE-DOCTORAL RESEARCHERS
Mohamed Bejaoui (CSIC)
Mónica Jiménez (IDIBAPS)
Mariana Mendes Braz (IDIBAPS)
Ana Teresa Menjívar (FCRB)
Maria Elias Miro (IDIBAPS)
Xavier Muñoz (CIBERehd)
Eirini Pantazi (CSIC)

TECHNICIANS
Marta Martínez (IDIBAPS)
Anna Rodríguez (IDIBAPS)

NURSING STAFF
Pilar Sesé (IDIBAPS)

COLLABORATORS
Chloë Ballesté (UB)
David Calatayud (HCB)
Andrés Cárdenas (HCB)
Emma Folch (IIBB-CSIC)
Jose Fuster (HCB)
Joan Oliva (Harbor UCLA Medical Center, USA)
Oscar Vidal (HCB)

STRATEGIC OBJECTIVES

Investigation of clinical, mechanistic and therapeutic aspects of liver transplantation.

MAIN LINES OF RESEARCH

1. Hepatic ischemia-reperfusion damage and liver graft viability in different models: experimental liver transplantation in the pig with whole or partial grafts, or grafts obtained from donors in asystolia; and liver transplantation in humans. The main objective of this line of research is to define the mechanisms of damage and to design beneficial strategies in the clinical setting.
2. Immunosuppression, with special interest in three fields: immune tolerance of the allograft, biomarkers of the effects of immunosuppressive drugs, and identification of populations with different risks of rejection. The main objective of this line of research is to suit the immunosuppression after liver transplantation to the real needs of each individual patient.

RESEARCH GROUP

PROTECTIVE STRATEGIES AGAINST HEPATIC ISCHEMIA-REPERFUSION INJURY

GROUP LEADER

Carmen Peralta (IDIBAPS)

The investigations led by Carmen Peralta are pioneers in the study of experimental surgical and pharmacological strategies (in vivo pharmacological treatments, improvements in preservation solutions and ischemic preconditioning) that protect livers against damage induced by ischemia-reperfusion and increase the tolerance of steatotic livers and reduced-size liver grafts against the risk that show these liver types to damage and regenerative failure when they are submitted to transplantation or hepatic resections.

PUBLICATIONS

Originals / I.F.: 127.799

1. Sia D, Hoshida Y, Villanueva A, Roayaie S, Ferrer J, Tabak B, Peix J, Sole M, Tovar V, Alsinet C, Cornella H, Klotzle B, Fan JB, Cotsoglou C, Thung SN, Fuster J, Waxman S, Garcia-Valdecasas JC, Bruix J, Schwartz ME, Beroukhim R, Mazzaferro V, Llovet JM. **Integrative molecular analysis of intrahepatic cholangiocarcinoma reveals 2 classes that have different outcomes.** *Gastroenterology* 144(4):829-840 I.F.: 12.821

2. Benítez C, Londoño MC, Miquel R, Manzia TM, Abraldes JG, Lozano JJ, Martínez-Llordella M, López M, Angelico R, Bohne F, Sese P, Daoud F, Larcier P, Roelen DL, Claas F, Whitehouse G, Lerut J, Pirenne J, Rimola A, Tisone G, Sánchez-Fueyo A. **Prospective multicenter clinical trial of immunosuppressive drug withdrawal in stable adult liver transplant recipients.** *Hepatology* 58(5):1824-35 I.F.: 12.003

3. Gracia-Sancho J, García-Calderó H, Hide D, Marrone G, Guixé-Muntet S, Peralta C, García-Pagán JC, Abraldes JG, Bosch J. **Simvastatin maintains function and viability of steatotic rat livers procured for transplantation.** J Hepatol 58(6):1140-1146 I.F.: 9.858

4. Jiménez-Castro MB, Casillas-Ramírez A, Mendes-Braz M, Massip-Salcedo M, Gracia-Sancho J, Elias-Miró M, Rodés J, Peralta C. **Adiponectin and resistin protect steatotic livers undergoing transplantation.** *J Hepatol* 59(6):1208-1214 I.F.: 9.858

5. Mariño Z, Crespo G, D'Amato M, Brambilla N, Giacovelli G, Rovati L, Costa J, Navasa M, Forns X. **Intravenous silibinin monotherapy shows significant antiviral activity in HCV-infected patients in the peri-transplantation period.** *J Hepatol* 58(3):415-420 I.F.: 9.858

6. Mensa L, Pérez-del-Pulgar S, Crespo G, Koutsoudakis G, Fernández-Carrillo C, Coto-Llerena M, Miquel R, Allende H, Castells L, Navasa M, Forns X. **Imaging of hepatitis C virus infection in liver grafts after liver transplantation.** *J Hepatol* 59(2):271-278 I.F.: 9.858

7. Gironella M, Calvo C, Fernández A, Closa D, Iovanna JL, Rosello-Catafau J, Folch-Puy E. **Reg3β deficiency impairs pancreatic tumor growth by skewing macrophage polarization.** *Cancer Res* 73(18):5682-5694 I.F.: 8.650

8. Zaouali MA, Boncompagni E, Reiter RJ, Bejaoui M, Freitas I, Pantazi E, Folch-Puy E, Abdennebi HB, Garcia-Gil FA, Rosello-Catafau J. **AMPK involvement in endoplasmic reticulum stress and autophagy modulation after fatty liver graft preservation: a role for melatonin and trimetazidine cocktail.** *J Pineal Res* 55(1):65-78 I.F.: 7.304

9. Morata L, Cuesta M, Rojas JF, Rodriguez S, Brunet M, Casals G, Cobos N, Hernandez C, Martínez JA, Mensa J, Soriano A. **Risk factors for a low linezolid trough plasma concentration in acute infections.** *Antimicrob Agents Chemother* 57(4):1913-1917 I.F.: 4.565

10. Orlando G, Adam R, Mirza D, Soderdahl G, Porte RJ, Paul A, Burroughs AK, Seiler CA, Colledan M, Graziadei I, Garcia-Valdecasas JC, Pruvot FR, Karam V, Lerut J. **Hepatic hemangiosarcoma: an absolute contraindication to liver transplantation--the European Liver Transplant Registry experience.** *Transplantation* 95(6):872-877 I.F.: 3.781

11. Balderramo D, Sendino O, Miquel R, de Miguel CR, Bordas JM, Martinez-Palli G, Leoz ML, Rimola A, Navasa M, Llach J, Cardenas A. **Prospective evaluation of single-operator peroral cholangioscopy in liver transplant recipients requiring an evaluation of the biliary tract.** *Liver Transpl* 19(2):199-206 I.F.: 3.870

12. Sánchez-Cabús S, Fondevila C, Calatayud D, Ferrer J, Taurá P, Fuster J, García-Valdecasas JC. **Importance of the temporary portocaval shunt during adult living donor liver transplantation.** *Liver Transpl* 19(2):174-183 I.F.: 3.870

13. Schepis F, Vukotic R, Berzigotti A, Carrión JA, Forns X, Abraldes JG, García-Valdecasas JC, Navasa M, García-Pagán JC, Bosch J. **Hemodynamic response to propranolol in patients with recurrent hepatitis C virus-related cirrhosis after liver transplantation: a case-control study.** *Liver Transpl* 19(4):450-456 I.F.: 3.870

14. Crespo G, Carrión JA, Coto-Llerena M, Mariño Z, Lens S, Pérez-Del-Pulgar S, García-Retortillo M, Miquel R, Bosch J, Navasa M, Forns X. **Combinations of simple baseline variables accurately predict sustained virological response in patients with recurrent hepatitis C after liver transplantation.** *J Gastroenterol* 48(6):762-769 I.F.: 3.788

15. Manyalich M, Guasch X, Paez G, Valero R, Istrate M. **ETPOD (European Training Program on Organ Donation): a successful training program to improve organ donation.** *Transpl Int* 26(4):373-384 I.F.: 3.155

16. Gómez-Bravo MA, Salcedo M, Fondevila C, Suarez F, Castellote J, Rufian S, Pons JA, Alamo JM, Millán O, Brunet M. **Impact of donor and recipient CYP3A5 and ABCB1 genetic polymorphisms on tacrolimus dosage requirements and rejection in Caucasian Spanish liver transplant patients.** *J Clin Pharmacol* 53(11):1146-1154 I.F.: 2.963

17. Millán O, Rafael-Valdivia L, Torrademé E, López A, Fortuna V, Sánchez-Cabus S, López-Púa Y, Rimola A, Brunet M. **Intracellular IFN-γ and IL-2 expression monitoring as surrogate markers of the risk of acute rejection and personal drug response in de novo liver transplant recipients.** *Cytokine* 61(2):556-564 I.F.: 2.518

18. Monegal A, Navasa M, Peris P, Colmenero J, Cuervo A, Muxí A, Gifre L, Guañabens N. **Bone disease in patients awaiting liver transplantation. Has the situation improved in the last two decades?** *Calcif Tissue Int* 93(6):571-576 I.F.: 2.495

19. Martínez-Rebollar M, Muñoz A, Pérez I, Hidalgo S, Brunet M, Laguno M, González A, Calvo M, Loncà M, Blanco JL, Martínez E, Gatell JM, Mallolas J. **Pharmacokinetic study of dual therapy with raltegravir 400 mg twice daily and Darunavir/Ritonavir 800/100 mg once daily in HIV-1-infected patients.** *Ther Drug Monit* 35(4):552-556 I.F.: 2.234

20. Martí J, Fuster J, Solà AM, Hotter G, Molina R, Pelegrina A, Ferrer J, Deulofeu R, Fondevila C, García-Valdecasas JC. **Prognostic value of serum neutrophil gelatinase-associated lipocalin in metastatic and nonmetastatic colorectal cancer.** *World J Surg* 37(5):1103-1109 I.F.: 2.228

21. Zaouali MA, Bardag-Gorce F, Carbonell T, Oliva J, Pantazi E, Bejaoui M, Ben Abdennebi H, Rimola A, Rosello-Catafau J. **Proteasome inhibitors protect the steatotic and non-steatotic liver graft against cold ischemia reperfusion injury.** *Exp Mol Pathol* 94(2):352-359 I.F.: 2.128

22. Bartoletti M, Cervera C, Hoyo I, Linares L, Sanclemente G, Bosch J, Marco F, Cofán F, Ricart MJ, Navasa M, Moreno A. **Incidence and outcome of early Candida peritonitis after liver and pancreas transplantation.** *Mycoses* 56(2):162-167 I.F.: 1.278

23. Martí J, Fuster J, Estanyol JM, Fernández F, Deulofeu R, Ferrer J, Pelegrina A, Reyes A, Fondevila C, García-Valdecasas JC. **Clinical and prognostic usefulness of serum proteomic profile in hepatic colorectal metastases: a pilot prospective study.** *Clin Transl Oncol* 15(9):691-7 I.F.: 1.276

24. Manyalich M, Guasch X, Gomez MP, Páez G, Teixeira L; ODEQUS Consortium. **Organ Donation European Quality System: ODEQUS project methodology.** *Transplant Proc* 45(10):3462-3465 I.F.: 0.952

25. Ginestà C, Saavedra-Perez D, Valentini M, Vidal O, Benarroch G, García-Valdecasas JC. **Total extraperitoneal (TEP) hernioplasty with intestinal resection assisted by laparoscopy for a strangulated Richter femoral hernia. Surg Laparosc Endosc Percutan.** *Tech* 23(3):334-336 I.F.: 0.876

26. Sánchez Cabús S, Calatayud D, García-Roca R, Ferrer J, Martí J, Navasa M, Rimola A, Fondevila C, Fuster J, García-Valdecasas JC. **Las complicaciones biliares en el trasplante hepático de donante vivo no afectan los resultados a largo plazo.** *Cir Esp* 91(1):17-24 I.F.: 0.871

27. Sánchez Cabús S, Calatayud D, Fondevila C, Ferrer J, Fuster J, García-Valdecasas JC. **Protocolo de monitorización hemodinámica hepática en el trasplante hepático de donante vivo en adultos.** *Cir Esp* 91(3):169-176 I.F.: 0.871

Reviews / I.F.: 30.823

1. Londoño MC, Rimola A, O'Grady J, Sanchez-Fueyo A. **Immunosuppression minimization vs. complete drug withdrawal in liver transplantation.** *J Hepatol* 59(4):872-879 I.F.: 9.858

2. Peralta C, Jiménez-Castro MB, Gracia-Sancho J. **Hepatic ischemia and reperfusion injury: effects on the liver sinusoidal milieu.** *J Hepatol* 59(5):1094-1106 I.F.: 9.858

3. Franquesa M, Hoogduijn MJ, Reinders ME, Eggenhofer E, Engela AU, Mensah FK, Torras J, Pileggi A, van Kooten C, Mahon B, Detry O, Popp FC, Benseler V, Casiraghi F, Johnson C, Ancans J, Fillenberg B, delaRosa O, Aran JM, Roemeling-van Rhijn M, Pinxteren J, Perico N, Gotti E, Christ B, Reading J, Introna M, Deans R, Shagidulin M, Farré R, Rambaldi A, Sanchez-Fueyo A, Obermajer N, Pulin A, Dor FJ, Portero-

Sanchez I, Baan CC, Rabelink TJ, Remuzzi G, Betjes MG, Dahlke MH, Grinyó JM; MiSOT Study Group. **Mesenchymal Stem Cells in Solid Organ Transplantation (MiSOT) Fourth Meeting: lessons learned from first clinical trials.** *Transplantation* 96(3):234-238 I.F.: 3.781

4. Elias-Miró M, Jiménez-Castro MB, Rodés J, Peralta C. **Current knowledge on oxidative stress in hepatic ischemia/reperfusion.** *Free Radic Res* 47(8):555-568 I.F.: 3.279

5. Pantazi E, Zaouali MA, Bejaoui M, Folch-Puy E, Ben Abdennebi H, Rosello-Catafau J. **Role of sirtuins in ischemia-reperfusion injury.** *World J Gastroenterol* 19(43):7594-7602 I.F.: 2.547

6. Cantarovich M, Birk P, Ekbeg H, Delmonico F, Schoenberg R, Garcia C, Manyalich M, Wall W, Arbogast H, Sherry W, Young-Kipp S, Cantarovich F. **First global forum on education on organ donation and transplantation for schools.** *Pediatr Transplant* 17(1):12-18 I.F.: 1.500

Multicenter / I.F.: 6.192

1. Saliba F, De Simone P, Nevens F, De Carlis L, Metselaar HJ, Beckebaum S, Jonas S, Sudan D, Fischer L, Duvoux C, Chavin KD, Koneru B, Huang MA, Chapman WC, Foltys D, Dong G, Lopez PM, Fung J, Junge G; H2304 Study Group (among them: Navasa M). **Renal function at two years in liver transplant patients receiving everolimus: results of a randomized, multicenter study.** *Am J Transplant* 13(7):1734-1745 I.F.: 6.192

GRANTS FOR RESEARCH IN PROGRESS

Fondevila C. **Métodos para incrementar la aplicabilidad clínica del trasplante procedente de los donantes a corazón parado tipo 2 de la clasificación de Maastrich.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01979.
Duration: 01/01/2012-31/12/2014

Manyalich M. **Impacto psicosocial del proceso de donación en el donante vivo de órganos para trasplante.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00949.
Duration: 01/01/2011-30/06/2014

Manyalich M. **European Living Donor Psychosocial Follow-up.** Sponsored by: European Commission. 20081104.
Duration: 01/12/2009-31/01/2013

Peralta C. **El efecto de la muerte cerebral en los injertos hepáticos esteatósicos y no esteatósicos sometidos a trasplante.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-31238.
Duration: 01/01/2013-31/12/2015

Peralta C. **Preservació de l'empelt hepatic.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_952.
Duration: 22/07/2009-30/04/2014

Sanchez-Fueyo A. **Immunosuppression Withdrawal for Stable Pediatric Liver Transplant Recipient. NIDDK Multi-Center Clinical Study Implementation Planning Grants (U34).** Sponsored by: National Institute of Health (NIH). 5813SC.
Duration: 30/09/2009-31/12/9998

Sanchez-Fueyo A. **Influencia de la regulación del metabolismo del hierro sobre el desarrollo de tolerancia inmunológica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01881.
Duration: 01/01/2012-31/12/2014

Sanchez-Fueyo A. **Estudio piloto de retirada de la medicación inmunosupresora en pacientes que exhiben marcadores transcripcionales de alta probabilidad de tolerancia.** Sponsored by: FUNDACION DE INVESTIGACION MEDICA MUTUA MADRILEÑA. AP93762011.
Duration: 16/09/2011-15/09/2013

Blasi A: **Glicemia en el trasplante hepatico: factores implicados e impacto sobre el funcionalismo del injerto.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/0059.
Duration: 01/01/2010-30/06/2013

Roselló-Catafau J. **Papel de la carboanhidrasa II en la preservación hepática.** Sponsored by: Instituto de Salud Carlos III (ISCIII).
Duration: 01/01/2013-31/12/2014

DOCTORAL THESES

García-Valdecasas J.C. **Importancia de la monitorización hemodinámica en el trasplante hepático de donante vivo.**
PhD student: Santiago Sánchez Cabús.

Fondevila C, Gomar C. **Repercusión de la capacidad de respuesta cardiovascular en la estabilidad hemodinámica y en la aparición de complicaciones en el trasplante hepático.**
PhD student: Bibiana J. Escobar Suárez

3.11 Gastrointestinal and pancreatic oncology

LOCATION
CEK building

KEYWORDS
1. **Colorectal cancer**
2. **Pancreatic cancer**
3. **Genetics**
4. **Inherited disorders**
5. **Susceptibility to cancer**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	206.49	33	12	10
2012	224.81	33	18	7
2013	236.20	39	36	1

TEAM INVOLVED IN
CIBEREHD
CIBERER

AWARDS
Premios Fundación Pfizer de Investigación. XIV Premio de Investigación clínica
Institution; Fundación Pfizer
Awardee: Castells A

XIII Premi Biennal d'Investigació Ramon Trias Fargas
Institution: Fundació Catalana Síndrome de Down
Awardees: Cristina Fillat, Xavier Bofill de Ros, Eneko Villanueva

TEAM LEADER
Antoni Castells Garangou (HCB)
T. 93 227 57 39
castells@clinic.cat

GROUP LEADER
Cristina Fillat Fonts (IDIBAPS)

RESEARCHERS
Juan Ramon Ayuso (HCB)
Francesc Balaguer Prunés (HCB)
Sergi Castellví Bel (IDIBAPS)
José Ignacio Elizalde (HCB)
Laureano Fernández-Cruz (HCB)
Mª Glòria Fernández-Esparrach (HCB)
Mª Àngels Ginès Gibert (HCB)
Antonio Mª de Lacy Fortuny (HCB)
Salvador Navarro Colás (HCB)
Maria Pellisè Urquiza (HCB)
Eva Cristina Vaquero Raya (HCB)
Oscar Vidal Pérez (HCB)

POST-DOCTORAL RESEARCHERS
Jordi Camps Pólo (FCRB)
Henry Nelson Córdova Guevara (HCB)
Pere Gambús Cerillo (HCB)
Mª Dolores Giráldez Jiménez (HCB)
Anabel José Segarra-Martínez (IDIBAPS)
María López-Cerón Pinilla (FCRB)
Jeroni Luna Conradó (IDIBAPS)
Maria Victoria Maliandi (IDIBAPS)
Leticia Moreira Ruiz (HCB) ´
Oriol Sendino Garcia (HCB)

PRE-DOCTORAL RESEARCHERS
Xavier Bofill de Ros (IDIBAPS)
Xavier Borrat Frigola (HCB)
Saray Durán Sanchón (CIBEREHD)
Clara Esteban Jurado (CIBEREHD)
Maria Liz Leoz Allegreth (HCB)
Isabel Quintanilla Leo (FCRB)
Ana Mato Berciano (IDIBAPS)
Maria Rovira Rigau (IDIBAPS)
Erwin Sanabria Velásquez (CIBEREHD)
Hugo Uchima Koecklin (CIBEREHD)
Elena Vila Navarro (CIBEREHD)
Eneko Villanueva Verdejo (IDIBAPS)
Sergio Villazala Merino (FCRB)
Laura Visa Turmo (HCB)

TECHNICIANS
Ana Boullosa Goberna (IDIBAPS)
Jennifer Múñoz Sancho (CIBEREHD)
Esther Samper Lirola (CIBEREHD)
Irene Sangrador Escrig (FCRB)

NURSING STAFF
Teresa Ocaña Bombardo (HCB)
Àngels Pozo Fernández (HCB)
Cristina Rodríguez de Miguel (FCRB)
Anna Serradesanferm Fabregas (HCB)

ADMINISTRATIVE STAFF
Diana Vargas Ríos (HCB)

COLLABORATORS
Imma Garrell Lluis (CAPSE)
Meritxell Gironella Cos (CIBEREHD)

STRATEGIC OBJECTIVES

The gaining of in-depth knowledge of the mechanisms underlying the development and progression of gastrointestinal and pancreatic premalignant and malignant lesions, with a view to defining new diagnostic, therapeutic and/or preventive strategies.

MAIN LINES OF RESEARCH

The activity of the research group in Gastrointestinal and Pancreatic Oncology is divided into four areas, and these in turn correspond to different lines of investigation:

1. **Physiopathology of colorectal cancer:**
- Hereditary forms of colorectal cancer, screening and surveillance.
- Genetic susceptibility in colorectal cancer.
- Epigenetics of colorectal cancer.

2. **Physiopathology of pancreatic cancer:**
- Implication of microRNAs in pancreatic cancer.
- Epithelial-mesenchymal transition in the local and metastatic spread of pancreatic cancer.

3. **Research and innovation in endoscopy:**
- Endoscopic ultrasound.
- Advanced diagnostic techniques.
- Endoscopic therapies.

4. **Research and innovation in surgery:**
- Surgery for colorectal cancer.
- Surgery for pancreatic cancer.

RESEARCH GROUP
GENE THERAPY AND CANCER GROUP

GROUP LEADER
Cristina Fillat Fonts (IDIBAPS)

The research of the group focuses on the study of the molecular and cellular basis of pancreatic ductal adenocarcinoma and the development of novel experimental therapies based on gene transfer and virotherapy.

The main research lines are:

1. Identify specific cellular pathways and molecular determinants altered in pancreatic tumors.
2. Development of antitumoral therapies based on oncolytic adenovirus. Main interest is devoted to the search for sensitizers of adenoviral oncolysis and to study their mechanisms of synergie. Special emphasis is also applied to engineer tumor-selective oncolytic adenoviruses.
3. Explore novel non-viral experimental therapies for pancreatic tumors. Preclinical testing of the newly developed therapies is studied in genetically-modified mouse models and in orthotopic xenografts. Some of the animal models are specially designed to allow for the non-invasive imaging of tumor progression and metastatic processes.
4. Development of gene therapy strategies to study rare genetic diseases.

PUBLICATIONS

Originals / I.F.: 236.203

1. van der Pas MH, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC, Bonjer HJ; COlorectal cancer Laparoscopic or Open Resection II (COLOR II) Study Group. **Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial.** *Lancet Oncol* 14(3):210-218 I.F.: 25.117

2. Castells A, Bessa X, Quintero E, Bujanda L, Cubiella J, Salas D, Lanas A, Carballo F, Morillas JD, Hernández C, Jover R, Montalvo I, Arenas J, Cosme A, Hernández V, Iglesias B, Castro I, Cid L, Sala T, Ponce M, Andrés M, Teruel G, Peris A, Roncales MP, González-Rubio F, Seoane-Urgorri A, Grau J, Serradesanferm A, Pellisé M, Ono A, Cruzado J, Pérez-Riquelme F, Alonso-Abreu I, Carrillo-Palau M, de la Vega-Prieto M, Iglesias R, Amador J, Blanco JM, Sastre R, Ferrándiz J, González-Hernández MJ, Andreu M; COLONPREV study investigators. **Risk of advanced proximal neoplasms according to distal colorectal findings: comparison of sigmoidoscopy-based strategies.** *J Natl Cancer Inst* 105(12):878-886 I.F.: 14.336

3. Rodríguez-Soler M, Pérez-Carbonell L, Guarinos C, Zapater P, Castillejo A, Barberá VM, Juárez M, Bessa X, Xicola RM, Clofent J, Bujanda L, Balaguer F, Reñé JM, de-Castro L, Marín-Gabriel JC, Lanas A, Cubiella J, Nicolás-Pérez D, Brea-Fernández A, Castellví-Bel S, Alenda C, Ruiz-Ponte C, Carracedo A, Castells A, Andreu M, Llor X, Soto JL, Payá A, Jover R. **Risk of cancer in cases of suspected lynch syndrome without germline mutation.** *Gastroenterology* 144(5):926-932 I.F.: 12.821

4. Rohof WO, Salvador R, Annese V, Bruley des Varannes S, Chaussade S, Costantini M, Elizalde JI, Gaudric M, Smout AJ, Tack J, Busch OR, Zaninotto G, Boeckxstaens GE. **Outcomes of treatment for achalasia depend on manometric subtype.** *Gastroenterology* 144(4):718-725 I.F.: 12.821

5. Dunlop MG, Tenesa A, Farrington SM, Ballereau S, Brewster DH, Koessler T, Pharoah P, Schafmayer C, Hampe J, Völzke H, Chang-Claude J, Hoffmeister M, Brenner H, von Holst S, Picelli S, Lindblom A, Jenkins MA, Hopper JL, Casey G, Duggan D, Newcomb PA, Abulí A, Bessa X, Ruiz-Ponte C, Castellví-Bel S, Niittymäki I, Tuupanen S, Karhu A, Aaltonen L, Zanke B, Hudson T, Gallinger S, Barclay E, Martin L, Gorman M, Carvajal-Carmona L, Walther A, Kerr D, Lubbe S, Broderick P, Chandler I, Pittman A, Penegar S, Campbell H, Tomlinson I, Houlston RS. **Cumulative impact of common genetic variants and other risk factors on colorectal cancer risk in 42,103 individuals.** *Gut* 62(6):871-881 I.F.: 10.732

6. Ordás I, Rimola J, García-Bosch O, Rodríguez S, Gallego M, Etchevers MJ, Pellisé M, Feu F, González-Suárez B, Ayuso C, Ricart E, Panés J. **Diagnostic accuracy of magnetic resonance colonography for the evaluation of disease activity and severity in ulcerative colitis: a prospective study.** *Gut* 62(11):1566-1572 I.F.: 10.732

7. Sánchez-Tilló E, de Barrios O, Siles L, Amendola PG, Darling DS, Cuatrecasas M, Castells A, Postigo A. **ZEB1 Promotes invasiveness of colorectal carcinoma cells through the opposing regulation of uPA and PAI-1.** *Clin Cancer Res* 19(5):1071-1082 I.F.: 7.837

8. Guarinos C, Sánchez-Fortún C, Rodríguez-Soler M, Pérez-Carbonell L, Egoavil C, Juárez M, Serradesanferm A, Bujanda L, Fernández-Bañares F, Cubiella J, de-Castro L, Guerra A, Aguirre E, Herreros-de-Tejada A, Bessa X, Herráiz M, Marín-Gabriel JC, Balmaña J, Cuatrecasas M, Balaguer F, Castells A, Soto JL, Alenda C, Payá A, Jover R. **Clinical subtypes and molecular characteristics of serrated polyposis syndrome.** *Clin Gastroenterol Hepatol* 11(6):705-711 I.F.: 6.648

9. Giráldez MD, Lozano JJ, Ramírez G, Hijona E, Bujanda L, Castells A, Gironella M. **Circulating microRNAs as biomarkers of colorectal cancer: results from a genome-wide profiling and validation study.** *Clin Gastroenterol Hepatol* 11(6):681-688 I.F.: 6.648

10. José A, Sobrevals L, Camacho-Sánchez JM, Huch M, Andreu N, Ayuso E, Navarro P, Alemany R, Fillat C. **Intraductal delivery of adenoviruses targets pancreatic tumors in transgenic Ela-myc mice and orthotopic xenografts.** *Oncotarget* 4:94-105 I.F.: 6.636

11. Jiménez Fonts A, Casamitjana R, Flores L, Delgado S, Lacy A, Vidal J. **GLP-1 and the long-term outcome of type 2 diabetes mellitus after Roux-en-Y gastric bypass surgery in morbidly obese subjects.** *Ann Surg* 257(5):894-899 I.F.: 6.329

12. Giráldez MD, Lozano JJ, Cuatrecasas M, Alonso-Espinaco V, Maurel J, Mármol M, Hörndler C, Ortego J, Alonso V, Escudero P, Ramírez G, Petry C, Lasalvia L, Bohmann K, Wirtz R, Mira A, Castells A. **Gene-expression signature of tumor recurrence in patients with stage II and III colon cancer treated with 5'fluoruracil-based adjuvant chemotherapy.** *Int J Cancer* 132(5):1090-1097 I.F.: 6.198

13. Bujanda L, Lanas Á, Quintero E, Castells A, Sarasqueta C, Cubiella J, Hernandez V, Morillas JD, Perez-Fernández T, Salas D, Andreu M, Carballo F, Bessa X, Cosme A, Jover R; COLONPREV Study Investigators. **Effect of aspirin and antiplatelet drugs on the outcome of the fecal immunochemical test.** *Mayo Clin Proc* 88(7):683-9 I.F.: 5.790

14. Abulí A, Lozano JJ, Rodríguez-Soler M, Jover R, Bessa X, Muñoz J, Esteban-Jurado C, Fernández-Rozadilla C, Carracedo A, Ruiz-Ponte C, Cubiella J, Balaguer F, Bujanda L, Reñé JM, Clofent J, Morillas JD, Nicolás-Pérez D, Xicola RM, Llor X, Piqué JM, Andreu M, Castells A, Castellví-Bel S; Gastrointestinal Oncology Group of Spanish Gastroenterological Association. **Genetic susceptibility variants associated with colorectal cancer prognosis.** *Carcinogenesis* 34(10):2286-2291 I.F.: 5.635

15. Fernandez-Rozadilla C, Palles C, Carvajal-Carmona L, Peterlongo P, Nici C, Veneroni S, Pinheiro M, Teixeira MR, Moreno V, Lamas MJ, Baiget M, Lopez-Fernandez LA, Gonzalez D, Brea-Fernandez A, Clofent J, Bujanda L, Bessa X, Andreu M, Xicola R, Llor X, Jover R; EPICOLON Consortium, Castells A, Castellvi-Bel S, Carracedo A, Tomlinson I, Ruiz-Ponte C. **BMP2/BMP4 colorectal cancer susceptibility loci in northern and southern European populations.** *Carcinogenesis* (2):314-318 I.F.: 5.635

16. Altafaj X, Martin E, Ortiz-Abalia J, Valderrama A, Lao-Peregrin C, Dierssen M, Fillat C. **Normalization of Dyrk1A expression by AAV2/1-shDyrk1A-mediated delivery attenuates hippocampal-dependent defects in the trisomic Ts65Dn mouse model of Down syndrome.** *Neurobiol. Dis* 52:117-127 I.F.: 5.624

17. Álvarez C, Andreu M, Castells A, Quintero E, Bujanda L, Cubiella J, Salas D, Lanas Á, Carballo F, Morillas JD, Hernández C, Jover R, Sarasqueta C, Enriquéz-Navascués JM, Hernández V, Estévez P, Macenlle R, Sala T, Balaguer F, Pellisé M, Moreira L, Gil I, Peris A, González-Rubio F, Ferrández A, Poves C, Ponce M, Grau J, Serradesanferm A, Ono A, Cruzado J, Pérez-Riquelme F, Alonso-Abreu I, Carrillo-Palau M, Santander C, Díaz Tasende J, Herreros A, Cacho G, Barranco LE, Bessa X; ColonPrev study investigators. **Relationship of colonoscopy-detected serrated polyps with synchronous advanced neoplasia in average-risk individuals.** *Gastrointest Endosc* 78(2):333-341 I.F.: 5.210

18. Córdova H, San José Estépar R, Rodríguez-D'Jesús A, Martínez-Pallí G, Arguis P, Rodríguez de Miguel C, Navarro-Ripoll R, Perdomo JM, Cuatrecasas M, Llach J, Vosburgh KG, Fernández-Esparrach G. **Comparative study of NOTES alone versus NOTES guided**

by a new image registration system for navigation in the mediastinum: a study in a porcine model. *Gastrointest Endosc* 77(1):102-7 I.F.: 5.210

19. Hazewinkel Y, López-Cerón M, East JE, Rastogi A, Pellisé M, Nakajima T, van Eeden S, Tytgat KM, Fockens P, Dekker E. **Endoscopic features of sessile serrated adenomas: validation by international experts using high-resolution white-light endoscopy and narrow-band imaging.** *Gastrointest Endosc* 77(6):916-24 I.F.: 5.210

20. Jover R, Zapater P, Polanía E, Bujanda L, Lanas A, Hermo JA, Cubiella J, Ono A, González-Méndez Y, Peris A, Pellisé M, Seoane A, Herreros-de-Tejada A, Ponce M, Marín-Gabriel JC, Chaparro M, Cacho G, Fernández-Díez S, Arenas J, Sopeña F, de-Castro L, Vega-Villaamil P, Rodríguez-Soler M, Carballo F, Salas D, Morillas JD, Andreu M, Quintero E, Castells A; COLONPREV study investigators. **Modifiable endoscopic factors that influence the adenoma detection rate in colorectal cancer screening colonoscopies.** *Gastrointest Endosc* 77(3):381-389 I.F.: 5.210

21. Borrat X, Trocóniz IF, Valencia JF, Rivadulla S, Sendino O, Llach J, Muñoz J, Castellví-Bel S, Jospin M, Jensen EW, Castells A, Gambús PL. **Modeling the influence of the A118G polymorphism in the OPRM1 gene and of noxious stimulation on the synergistic relation between propofol and remifentanil: sedation and analgesia in endoscopic procedures.** *Anesthesiology* 118(6):1395-1407 I.F.: 5.163

22. Fernandez-Rozadilla C, Cazier JB, Moreno V, Crous-Bou M, Guinó E, Durán G, Lamas MJ, López R, Candamio S, Gallardo E, Paré L, Baiget M, Páez D, López-Fernández LA, Cortejoso L, García MI, Bujanda L, González D, Gonzalo V, Rodrigo L, Reñé JM, Jover R, Brea-Fernández A, Andreu M, Bessa X, Llor X, Xicola R, Palles C, Tomlinson I, Castellví-Bel S, Castells A, Ruiz-Ponte C, Carracedo A; EPICOLON Consortium. **Pharmacogenomics in colorectal cancer: a genome-wide association study to predict toxicity after 5-fluorouracil or FOLFOX administration.** *Pharmacogenomics* J 13(3):209-217 I.F.: 5.134

23. Hijazi M, Fillat C, Medina JM, Velasco A. **Overexpression of Dyrk1A inhibits choline acetyltransferase induction by oleic acid in cellular models of Down syndrome.** *Exp. Neurol* 239:229-234 I.F.: 4.645

24. Fernandez-Rozadilla C, Cazier JB, Tomlinson IP, Carvajal-Carmona LG, Palles C, Lamas MJ, Baiget M, López-Fernández LA, Brea-Fernández A, Abulí A, Bujanda L, Clofent J, Gonzalez D, Xicola R, Andreu M, Bessa X, Jover R, Llor X; EPICOLON Consortium, Moreno V, Castells A, Carracedo Á, Castellvi-Bel S, Ruiz-Ponte C. **A colorectal cancer genome-wide association study in a Spanish cohort identifies two variants associated with colorectal cancer risk at 1p33 and 8p12.** *BMC Genomics* 14:55 I.F.: 4.397

25. Fernandez-Rozadilla C, Brea-Fernández A, Bessa X, Alvarez-Urturi C, Abulí A, Clofent J, Payá A; EPICOLON Consortium, Jover R, Xicola R, Llor X, Andreu M, Castells A, Carracedo A, Castellví-Bel S, Ruiz-Ponte C. **BMPR1A mutations in early-onset colorectal cancer with mismatch repair proficiency.** *Clin Genet* 84(1):94-96 I.F.: 4.247

26. Jean-Philippe Adam, Alexandre Jacquin, Christophe Laurent, Denis Collet, Masson B, Fernández-Cruz L, Sa-Cunha A. **Laparoscopic spleen-preserving distal pancreatectomy: splenic vessel preservation compared with the Warshaw technique.** *JAMA Surg* 148(3):246-252 I.F.: 4.100

27. Bujanda L, Sarasqueta C, Cosme A, Hijona E, Enríquez-Navascués JM, Placer C, Villarreal E, Herreros-Villanueva M, Giraldez MD, Gironella M, Balaguer F, Castells A. **Evaluation of alpha 1-antitrypsin and the levels of mRNA expression of matrix metalloproteinase 7, urokinase type plasminogen activator receptor and COX-2 for the diagnosis of colorectal cancer.** *PLoS One* 8(1):e51810 I.F.: 3.730

28. Link A, Balaguer F, Shen Y, Lozano JJ, Leung HC, Boland CR, Goel A. **Curcumin modulates DNA methylation in colorectal cancer cells.** *PLoS One* 8(2):e57709 I.F.: 3.730

29. Picelli S, Lorenzo Bermejo J, Chang-Claude J, Hoffmeister M, Fernández-Rozadilla C, Carracedo A, Castells A, Castellví-Bel S; Memebers of EPICOLON Consortium-Gastrointestinal Oncology Group of the Spanish Gastroenterological Association, Naccarati A, Pardini B, Vodickova L, Müller H, Talseth-Palmer BA, Stibbard G, Peterlongo P, Nici C, Veneroni S, Li L, Casey G, Tenesa A, Farrington SM, Tomlinson I, Moreno V, van Wezel T, Wijnen J, Dunlop M, Radice P, Scott RJ, Vodicka P, Ruiz-Ponte C, Brenner H, Buch S, Völzke H, Hampe J, Schafmayer C, Lindblom A. **Meta-analysis of mismatch repair polymorphisms within the cogent consortium for colorectal cancer susceptibility.** *PLoS One* 8(9):e72091 I.F.: 3.730

30. Sylla P, Bordeianou LG, Berger D, Han KS, Lauwers GY, Sahani DV, Sbeih MA, Lacy AM, Rattner DW. **A pilot study of natural orifice transanal endoscopic total mesorectal excision with laparoscopic assistance for rectal cancer.** *Surg Endosc* 27(9):3396-3405 I.F.: 3.427

31. Lacy AM, Rattner DW, Adelsdorfer C, Tasende MM, Fernández M, Delgado S, Sylla P, Martínez-Palli G. **Transanal natural orifice transluminal endoscopic surgery (NOTES) rectal resection: "down-to-up" total mesorectal excision (TME)--short-term outcomes in the first 20 cases.** *Surg Endosc* 27(9):3165-3172 I.F.: 3.427

32. Amor A, Jiménez A, Moizé V, Ibarzabal A, Flores L, Lacy AM, Vidal J. **Weight loss independently predicts urinary albumin excretion normalization in morbidly obese type 2 diabetic patients undergoing bariatric surgery.** *Surg Endosc* 27(6):2046-2051 I.F.: 3.427

33. Lacy AM, Adelsdorfer C, Delgado S, Sylla P, Rattner DW. **Minilaparoscopy-assisted transrectal low anterior resection (LAR): a preliminary study.** *Surg Endosc* 27(1):339-346 I.F.: 3.427

34. Moizé V, Andreu A, Rodríguez L, Flores L, Ibarzabal A, Lacy A, Jiménez A, Vidal J. **Protein intake and lean tissue mass retention following bariatric surgery.** *Clin Nutr* 32(4):550-555 I.F.: 3.298

35. Jiménez A, Perea V, Corcelles R, Moizé V, Lacy A, Vidal J. **Metabolic effects of bariatric surgery in insulin-sensitive morbidly obese subjects.** *Obes Surg* 23(4):494-500 I.F.: 3.102

36. Mathus-Vliegen E, Pellisé M, Heresbach D, Fischbach W, Dixon T, Belsey J, Parente F, Rio-Tinto R, Brown A, Toth E, Crosta C, Layer P, Epstein O, Boustiere C. **Consensus guidelines for the use of bowel preparation prior to colonic diagnostic procedures: colonoscopy and small bowel video capsule endoscopy.** *Curr Med Res Opin* 29(8):931-945 I.F.: 2.263

37. Fernández-Cruz L, Jiménez Chavarría E, Taurà P, Closa D, Boado MA, Ferrer J. **Prospective randomized trial of the effect of octreotide on pancreatic juice output after pancreaticoduodenectomy in relation to histological diagnosis, duct size and leakage.** *HPB (Oxford)* 15(5):392-399 I.F.: 1.939

38. Auge JM, Rodriguez C, Pellise M, Bernal A, Grau J, Castells A, Filella X, Molina R. **Analytical and Clinical Performance of Kroma iT, A Compact Fully-automated Immunochemistry Analyzer for Fecal Occult Hemoglobin.** *Anticancer Res* 33(12):5633-5637 I.F.: 1.713

39. Córdova H, Martinez-Pallí G, Fernández-Esparrach G. **Feasibility of systematic transesophageal endoscopic mediastinoscopy.** *Thorac Cardiovasc Surg* 61(6):486- 488 I.F.: 0.925

Reviews / I.F.: 21.499

1. Meining A, Spaun G, Fernández-Esparrach G, Arezzo A, Wilhelm D, Martinek J, Spicak J, Feussner H, Fuchs KH, Hucl T, Meisner S, Neuhaus H. **NOTES in Europe: summary of the working group reports of the 2012 EURO-NOTES meeting.** *Endoscopy* 45(3):214-7 I.F.: 5.735

2. Van Cutsem E, Borràs JM, Castells A, Ciardiello F, Ducreux M, Haq A, Schmoll HJ, Tabernero J. **Improving outcomes in colorectal cancer: Where do we go from here?** *Eur J Cancer* 49(11):2476-2485 I.F.: 5.061

3. Fuchs KH, Meining A, von Renteln D, Fernandez-Esparrach G, Breithaupt W, Zornig C, Lacy A. **Euro-NOTES Status Paper: from the concept to clinical practice.** *Surg Endosc* 27(5):1456-1467 I.F.: 3.427

4. Herreros-Villanueva M, Gironella M, Castells A, Bujanda L. **Molecular markers in pancreatic cancer diagnosis.** *Clin Chim Acta* 418:22-29 I.F.: 2.850

5. Pellisé M. **Overcoming challenges in IBD management: management of colonic dysplastic lesions.** *Dig Dis* 31(2):244-247 I.F.: 2.725

6. Balaguer F. **Genetics of colorectal cancer.** *Gastroenterol Hepatol 36 Suppl* 2:73-279 I.F.: 0.567

7. Castells A. **Colorectal cancer screening.** *Gastroenterol Hepatol* 36:66-72 I.F.: 0.567

8. Galletto P, Leoz ML, Castells A, Balaguer F. **Intraabdominal desmoid tumors in familial adenomatous polyposis.** *Gastroenterol Hepatol* 36(9):580-586. I.F.: 0.567

Editorials / I.F.: 25.642

1. Camps J, Ried T, Castells A. **Intratumor heterogeneity: finding the needle in a haystack for cancer treatment.** *Gastroenterology* 145(1):242-244 I.F.: 12.821

2. Castells A, Giardiello FM. **Familial colorectal cancer screening: so close, so far.** *Gastroenterology* 144(3):492-494 I.F.: 12.821

Clinical Guidelines / I.F.: 13.689

1. Balmaña J, Balaguer F, Cervantes A, Arnold D; ESMO Guidelines Working Group. **Familial risk-colorectal cancer: ESMO Clinical Practice Guidelines.** *Ann Oncol 24 Suppl* 6:vi73-80 I.F.: 7.384

2. Martínez J, Abad-González A, Aparicio JR, Aparisi L, Boadas J, Boix E, de Las Heras G, Domínguez-Muñoz E, Farré A, Fernández-Cruz L, Gómez L, Iglesias-García J, García-Malpartida K, Guarner L, Lariño-Noia J, Lluís F, López A, Molero X, Moreno-Pérez O, Navarro S, Palazón JM, Pérez-Mateo M, Sabater L, Sastre Y, Vaquero E, de-Madaria E. **The Spanish Pancreatic Club recommendations for the diagnosis and treatment of chronic pancreatitis: part 1 (diagnosis).** *Pancreatology* 13(1):8-17 I.F.: 2.043

3. de-Madaria E, Abad-González A, Aparicio JR, Aparisi L, Boadas J, Boix E, de-Las-Heras G, Domínguez-Muñoz E, Farré A, Fernández-Cruz L, Gómez L, Iglesias-García J, García-Malpartida K, Guarner L, Lariño-Noia J, Lluís F, López A, Molero X, Moreno-Pérez O, Navarro S, Palazón JM, Pérez-Mateo M, Sabater L, Sastre Y, Vaquero EC, Martínez J. **The Spanish Pancreatic Club's recommendations for the diagnosis and treatment of chronic pancreatitis: part 2 (treatment).** *Pancreatology* 13(1):18-28 I.F.: 2.043

4. Vázquez-Sequeiros E, González-Panizo-Tamargo F, Barturen A, Calderón A, Esteban JM, Fernández-Esparrach G, Gimeno-García A, Ginés A, Lariño J, Pérez-Carreras M, Romero R, Súbtil JC, Vila J. **The role of endoscopic ultrasound guided fine needle aspiration (EUS-FNA) in non small cell lung cancer (NSCLC)**

patients: SEED-SEPD-AEG Joint Guideline. *Rev Esp Enferm Dig* 105(4):215-224 I.F.: 1.652

5. Gisbert JP, Calvet X, Bermejo F, Boixeda D, Bory F, Bujanda L, Castro-Fernández M, Dominguez-Muñoz E, Elizalde JI, Forné M, Gené E, Gomollón F, Lanas Á, Martín de Argila C, McNicholl AG, Mearin F, Molina-Infante J, Montoro M, Pajares JM, Pérez-Aisa A, Pérez-Trallero E, Sánchez-Delgado J. **III Spanish Consensus Conference on Helicobacter pylori infection.** *Gastroenterol Hepatol* 36(5):340-74 I.F.: 0.567

GRANTS FOR RESEARCH IN PROGRESS

Balaguer F. **Implicación del metiloma en la patogénesis y diagnóstico del cáncer colorrectal.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00384. Duration: 01/01/2011-31/12/2014

Balaguer F. **Síndrome de Poliposis Serrada: caracterización clínico-patológica y molecular.** Sponsored by: Asociación Española de Gastroenterologia. Beca Gonzalo Miño 2013. IP040268. Duration 01/03/2013-28/02/2014

Camps J. **Implications of copy number variants of the genome in the etiology and progression of colorectal cancer.** Sponsored by; Europena Commission. CE-FP7-PPLE-2012-CIG. Duration: 01/12/2013-30/11/2017.

Castells A. **Identificación de nuevos biomarcadores para la prevención del cáncer colorrectal. Sponsored by: Asociación Española Contra el Cáncer (AECC).** GCB13131592CAST. Duration: 01/10/2013-30/09/2016

Castells A. **Caracterización genómica del síndrome de Lynch mediante secuenciación de nueva generación (NGS): correlación con el perfil transcriptómico y epigenómico.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-19273. Duration: 01/01/2011-31/12/2014

Castells A. **Grup de recerca en oncologia gastrointestinal i pancreàtica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_849. Duration: 29/07/2009-30/04/2014

Castellvi S. **Genetic Study of Common Hereditary Bowel Cancers in Hispania and the Americas.** Sponsored by: European Commission. 223678. Duration: 01/06/2009-16/12/2013

Castellví S. **Identificación de nuevos genes de predisposición al cáncer colorrectal mediante secuenciación del exoma.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00219. Duration: 01/01/2012-31/12/2014

Elizalde J.I. **Identificación de factores genéticos, ambientales y de expresión fenotípica asociados a la progresión de lesiones precursoras del cáncer gástrico: estudio coordinado español de seguimiento.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01031. Duration: 01/01/2011-30/06/2014

Fernandez-Esparrach G. **Utilidad de un biomarcador serológico para evaluar el riesgo de transformación maligna de los pacientes con esófago de Barrett y correlación con marcadores histológicos. Estudio prospectivo.** Sponsored by: Fundación de Investigación Médica Mutua Madrileña. AP100262012. Duration: 22/06/2012-21/06/2015

Fernandez-Esparrach G. **Mediastinoscopia transesofágica guiada por un sistema de registro de la imagen versus mediastinoscopia convencional. Estudio comparativo en un modelo porcino.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-15635. Duration: 01/01/2011-30/06/2014

Fernandez-Cruz L. **Modelo experimental animal de trasplante de páncreas: papel del JNK-inhibitor como estrategia terapéutica para la prevención de los fenómenos de isquemia-reperfusión.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01940. Duration: 01/01/2012-31/12/2014

Fillat C. **Grup de Recerca Singular en Teràpia Gènica.** Sponsored by: AGAUR 2009_SGR_1527. Duration: 29/7/2009-31/12/2013

Fillat C. **Caracterización de microRNAs sensibilizadores de la oncolisis adenoviral frente al cáncer de páncreas.** Sponsored by: Ministerio de Economía y Competitividad. BIO2011-30299-C02-02. Duration: 01/01/2012-31/12/2014

Gambus P. **Descripción y validación prospectiva de un sistema de control de la respuesta al estímulo nociceptivo durante la anestesia, basado en el análisis de señales neurofisiológicas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1209. Duration: 01/01/2010-30/06/2013

Ginès M.A. **Determinación de SPARC, Phospho IGF-1R y CXCL12 a partir del material obtenido por punción aspirativa con aguja fina guiada por ecoendoscopia (USE-PAAF) de los tumores pancreáticos. Correlación con la respuesta al tratamiento con quimioterapia.** Sponsored by: Asociación Española de Gastroenterologia. Beca Miguel Pérez Mateo 2013. Duration 01/03/2013-28/02/2014

Pellise M. **Impacto de las técnicas de endoscopia avanzada y de los miRNAs en el diagnóstico y manejo de la neoplasia colorrectal asociada a la enfermedad inflamatoria intestinal de larga evolución.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01481. Duration: 01/01/2013-31/12/2015

Pellise M. **Implicación de los focos de criptas aberrantes en la carcinogénesis colorrectal: estudio morfológico con técnicas de endoscopia avanzada y caracterización molecular.** Sponsored

by: Instituto de Salud Carlos III (ISCIII).
PI09/0669.
Duration: 01/01/2010-31/12/2013

Vaquero E.C. **Regulación mediada por ZEB1 del estroma tumoral: Implicaciones en el desarrollo y la quioresistencia en el cáncer de páncreas.** Sponsored by: Instituto de Salud Carlos III (ISCIII).
PI12/01430.
Duration: 01/01/2013-31/12/2015

Vidal O. **Papel terapeutico de las anhidrasas carbonicas ix y ii en la prevencion de la lesion por isquemia reperfusion asociada al trasplante hepatico.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01407
Duration: 01/01/2013-31/12/2015

DOCTORAL THESES

Balaguer F. **Nueva caracterización clínica y molecular del síndrome de Lynch.** PhD student: Leticia Moreira Ruiz.

Pellisé Mª. **Utilidad del Narrow Band Imaging para el estudio de las enfermedades con alto riesgo de cáncer de cáncer digestivo.** PhD student Maria López-Ceron Pinilla.

Fernández-Esparrach, Mª G. **Utilidad de un sistema de navegación endoscópica basado en la tomografía computarizada para la cirugía endoscópica transluminal a través de orificios naturales (NOTES).** PhD student Henry Nelson Córdova Guevara.

3.12 Inherited metabolic diseases

LOCATION
HCB building

KEYWORDS
1. **Mitochondrial diseases**
2. **Mitochondrial cofactors**
3. **Lysosomal diseases**
4. **Inherited metabolic diseases**
5. **Inborn errors of metabolism**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	38.49	8	4	3
2012	44.77	13	2	7
2013	54.11	16	7	9

TEAM INVOLVED IN
CIBERER

AWARDS
12th International Congress of Inborn Errors of Metabolism. Best oral communication presented in the session of "hot topics and late breaking news"
Institution: Society for the Studies of Inborn Errors of Metabolism (SSIEM)
Awardee/s: Frederic Tort

TEAM LEADER
Antonia Ribes (HCB)
T. 93 227 54 00 (9340)
aribes@clinic.cat

RESEARCHERS
Paz Briones (CSIC)
Mª Josep Coll (HCB)
Laura Gort (HCB)
Rosa Mª López (HCB)
Teresa Pàmpols (HCB)

POST-DOCTORAL RESEARCHERS
Angela Arias (CIBERER)
Judit Macías (Fundació Niemann Pick)
Frederic Tort (CIBERER)

PRE-DOCTORAL RESEARCHERS
Nuria Bujan (FIS)
Xènia Ferrer (IDIBAPS)
Leslie Matalonga (FCRB)
Sonia Pajares (FCRB)

COLLABORATORS
Judit Garcia-Villoria (HCB)
Marisa Girós (HCB)
José Luis Marin (HCB)
Aleix Navarro-Sastre (HCB)

STRATEGIC OBJECTIVES

The strategic objective of our group is to investigate the genetic and biochemical bases, as well as the physiopathological mechanisms, of a group of rare diseases called "inherited metabolic diseases or inborn errors of metabolism". The ultimate aim is to develop new diagnostic and therapeutic strategies. On the other hand, we conduct translational research, stimulating the transfer of knowledge from basic research to the clinical practice, and vice versa.

MAIN LINES OF RESEARCH

Within the general line of inherited metabolic diseases, our specific research lines are based on the following:

1. Identification of genes responsible for Mendelian disorders in patients preselected on the basis of their clinical and biochemical characteristics;

within this line we have used exome sequencing to identify genes in patients with mitochondrial respiratory chain deficiencies, organic acidurias and congenital defects of glycosylation (CDG). Recently, our group has been focused in the identification of genes involved in the biosynthesis and transport of cofactors of the mitochondrial energy metabolism (lipoic acid, thiamine, CoQ10, riboflavin and iron sulfur clusters). We aim to identify new defects to generate knowledge that could be implemented to the diagnosis and to the design therapeutic options

2. In vitro therapeutic approaches. This line of research involves the testing of chemical and peptide libraries. Selection has been made of disease-causing stop and missense mutations previously identified by our group in a wide range of diseases. We make use of fibroblasts, pluripotent induced stem (IPS) cells and neuronal cell cultures obtained from IPS.

3. Cerebral creatine deficiency. Our group has been a pioneer in the identification of patients with cerebral creatine deficiency. Actually, we are focused on the evaluation of different creatine derivatives with the purpose of establishing a treatment for creatine transport deficiency. These creatine uptake studies are carried out in neurons derived from IPS cells as well as in HUVEC and HBMEC cells silenced with RNA interference.

4. Niemann-Pick type C disease. The study of this disorder has been carried out in a knock-in murine model in order to gain further knowledge of the underlying physiopathological mechanisms involved in this disease and to test different drugs with potential therapeutic activity that act in the proteosomal degradation pathways.

PUBLICATIONS

Originals / I.F.: 54.112

1. Tiscornia G, Vivas EL, Matalonga L, Berniakovich I, Barragán Monasterio M, Eguizábal C, Gort L, González F, Ortiz Mellet C, García Fernández JM, Ribes A, Veiga A, Izpisua Belmonte JC. **Neuronopathic Gaucher's disease: induced pluripotent stem cells for disease modelling and testing chaperone activity of small compounds.** *Hum Mol Genet* 22(4):633-645 I.F.: 7.692

2. van de Kamp JM, Betsalel OT, Mercimek-Mahmutoglu S, Abulhoul L, Grünewald S, Anselm I, Azzouz H, Bratkovic D, de Brouwer A, Hamel B, Kleefstra T, Yntema H, Campistol J, Vilaseca MA, Cheillan D, D'Hooghe M, Diogo L, Garcia P, Valongo C, Fonseca M, Frints S, Wilcken B, von der Haar S, Meijers-Heijboer HE, Hofstede F, Johnson D, Kant SG, Lion-Francois L, Pitelet G, Longo N, Maat-Kievit JA, Monteiro JP, Munnich A, Muntau AC, Nassogne MC, Osaka H, Ounap K, Pinard JM, Quijano-Roy S, Poggenburg I, Poplawski N, Abdul-Rahman O, Ribes A, Arias A, Yaplito-Lee J, Schulze A, Schwartz CE, Schwenger S, Soares G, Sznajer Y, Valayannopoulos V, Van Esch H, Waltz S, Wamelink MM, Pouwels PJ, Errami A, van der Knaap MS, Jakobs C, Mancini GM, Salomons GS. **Phenotype and genotype in 101 males with X-linked creatine transporter deficiency.** *J Med Genet* 50(7):463-472 I.F.: 5.703

3. Delgadillo V, O'Callaghan Mdel M, Gort L, Coll MJ, Pineda M. **Natural history of Sanfilippo syndrome in Spain.** *Orphanet J Rare Dis* 8:189 I.F.: 4.315

4. Couce ML, Sánchez-Pintos P, Diogo L, Leão-Teles E, Martins E, Santos H, Bueno MA, Delgado-Pecellín C, Castiñeiras DE, Cocho JA, García-Villoria J, Ribes A, Fraga JM, Rocha H. **Newborn screening for medium-chain acyl-CoA dehydrogenase deficiency: regional experience and high incidence of carnitine deficiency.** *Orphanet J Rare* Dis 8:102 I.F.: 4.315

5. Ferrer-Cortès X, Font A, Bujan N, Navarro-Sastre A, Matalonga L, Arranz JA, Riudor E, del Toro M, Garcia-Cazorla A, Campistol J, Briones P, Ribes A, Tort F. **Protein expression profiles in patients carrying NFU1 mutations. Contribution to the pathophysiology of the disease.** *J Inherit Metab Dis* 36(5):841-847 I.F.: 4.070

6. Montero R, Grazina M, López-Gallardo E, Montoya J, Briones P, Navarro-Sastre A, Land JM, Hargreaves IP, Artuch R; Coenzyme Q10 Deficiency Study Group. **Coenzyme Q10 deficiency in mitochondrial DNA depletion syndromes.** *Mitochondrion* 13(4):337-41 I.F.: 4.025

7. Jesús S, Cáceres-Redondo MT, Carrillo F, Cordones I, Escudero M, Macías-Vidal J, Coll MJ, Bautista J, Mir P. **Adult form of Niemann-Pick type C with the variant biochemical phenotype on treatment with Miglustat.** *Parkinsonism Relat Disord* 19(10):916-7 I.F.: 3.274

8. Matos IV, Castejón E, Meavilla S, O'Callaghan M, Garcia-Villoria J, López-Sala A, Ribes A, Artuch R, Garcia-Cazorla A. **Clinical and biochemical outcome after hydroxocobalamin dose escalation in a series of patients with cobalamin C deficiency.** *Mol Genet Metab* 109(4):360-365 I.F.: 2.834

9. Pajares S, Arias A, García-Villoria J, Briones P, Ribes A. **Role of creatine as biomarker of mitochondrial diseases.** *Mol Genet Metab* 108(2):119-124 I.F.: 2.834

10. Puisac B, Teresa-Rodrigo ME, Arnedo M, Gil-Rodríguez MC, Pérez-Cerdá C, Ribes A, Pié A, Bueno G, Gómez-Puertas P, Pié J. **Analysis of aberrant splicing and nonsense-mediated decay of the stop codon mutations c.109G>T and c.504_505delCT in 7 patients with HMG-CoA lyase deficiency.** *Mol Genet Metab* 108(4):232-40 I.F.: 2.834

11. Tort F, García-Silva MT, Ferrer-Cortès X, Navarro-Sastre A, Garcia-Villoria J, Coll MJ, Vidal E, Jiménez-Almazán J, Dopazo J, Briones P, Elpeleg O, Ribes A.

Exome sequencing identifies a new mutation in SERAC1 in a patient with 3-methylglutaconic aciduria. *Mol Genet Metab* 110(1-2):73-77 I.F.: 2.834

12. García-Villoria J, Hernández-Pérez JM, Arias A, Ribes A. **Improvement of the cystine measurement in granulocytes by liquid chromatograhy-tandem mass spectrometry.** *Clin Biochem* 46(3):271-4 I.F.: 2.450

13. Couce ML, López-Suárez O, Bóveda MD, Castiñeiras DE, Cocho JA, García-Villoria J, Castro-Gago M, Fraga JM, Ribes A. **Glutaric aciduria type I: outcome of patients with early- versus late-diagnosis.** *Eur J Paediatr Neurol* 17(4):383-389 I.F.: 1.982

14. Scalais E, Chafai R, Van Coster R, Bindl L, Nuttin C, Panagiotaraki C, Seneca S, Lissens W, Ribes A, Geers C, Smet J, De Meirleir L. **Early myoclonic epilepsy, hypertrophic cardiomyopathy and subsequently a nephrotic syndrome in a patient with CoQ10 deficiency caused by mutations in para-hydroxybenzoate-polyprenyl transferase (COQ2).** *Eur J Paediatr Neurol* 17(6):625-630 I.F.: 1.982

15. Fernández-Ayala DJ, Guerra I, Jiménez-Gancedo S, Cascajo MV, Gavilán A, Dimauro S, Hirano M, Briones P, Artuch R, De Cabo R, Salviati L, Navas P. **Survival transcriptome in the coenzyme Q10 deficiency syndrome is acquired by epigenetic modifications: a modelling study for human coenzyme Q10 deficiencies.** *BMJ Open* 3(3)pii: e002524 I.F.: 1.583

16. Pérez-Poyato MS, Marfa MP, Abizanda IF, Rodriguez-Revenga L, Sánchez VC, González MJ, Puñal JE, Pérez AV, González MM, Bermejo AM, Hernández EM, Coll Rosell MJ, Gort L, Milá M. **Late infantile neuronal ceroid lipofuscinosis: mutations in the CLN2 gene and clinical course in Spanish patients.** *J Child Neurol* 28(4):470-478 I.F.: 1.385

GRANTS FOR RESEARCH IN PROGRESS

Briones P. **Caracterizacion bioquimica y genetica de nuevos pacientes y tipos de defectos congenitos de glicosilación.** Sponsored by: Instituto de Salud Carlos III (ISCIII). Ref: PI11/01096. Duration: 01/01/2012 - 31/12/2014

Coll MJ. **Análisis de los mecanismos implicados en la enfermedad de Niemann-Pick tipo C: generación de un modelo murino de la enfermedad y valoración de una nueva aproximación terapéutica mutación dependiente.** Sponsored by: Instituto de Salud Carlos III, PI10/00936. Duration: 01/01/2011-31/12/2013.

Coll MJ. **An EU rare disease registry for Niemann-Pick disease type A, B and C.** Sponsored by: European Commission DG-SANCO. 308901. Duration: 01/01/2013-31-12-2016

Ribes A. **Identificación de pacientes con mutaciones en genes implicados en la biosíntesis y transporte de cofactores del metabolismo energético mitocondrial.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01138. Duration: 01/01/2013-31/12/2015

Ribes A. **European registry and network for Intoxication type Metabolic Diseases (E-IMD).** Sponsored by: European Comission DG-SANCO. A/100886-E-IMD. Duration: 01/01/2011-31/12/2013

Ribes A. **European Network and registry for Homocystinurias and Methylation Defects.** Sponsored by: European Comission DG-SANCO. E-HOD. Duration: 01/01/2013-31/12/2016.

3.13 Genomic Programming of Beta Cells and Diabetes

LOCATION
CEK building

FOR FURTHER INFORMATION
http://betacellregulation.net

KEYWORDS
1. **Epigenetics**
2. **Mouse Genetic Analysis of Beta Cells Regulation**
3. **Genomic Regulation of Pancreatic Beta Cells**
4. **Pancreas Regeneration**
5. **Type 2 Diabetes Molecular Pathophysiology**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	46.59	3	3	-
2012	27.87	3	3	-
2013	41.04	4	4	-

TEAM INVOLVED IN
CIBERDEM

AWARDS
Premio de Investigación Senior Alberto Sols
Institution: Sociedad Española de Diabetes
Awardee/s: Jorge Ferrer

TEAM LEADER
Jorge Ferrer (IDIBAPS/IMPERIAL COLLEGE LONDON)
T. 93 227 54 00
jferrer@clinic.cat

RESEARCHERS
Ildem Akerman (IDIBAPS)

POST-DOCTORAL RESEARCHERS
Anthony Beucher (CIBERDEM)
Inês Cebola (IDIBAPS)
Miguel Angel Maestro (CIBERDEM)
Loris Mularoni (FCRB)
Lorenzo Pasquali (FCRB)
Meritxell Rovira (BIOTRACK)

PRE-DOCTORAL RESEARCHERS
Mar Armengol (IDIBAPS)
Miguel Angel Correa (IDIBAPS)
Ignasi Moran (FCRB)
Nikolina Nakic (IDIBAPS)

TECHNICIANS
Natalia Castro (IDIBAPS)
Xavier Garcia (CIBERDEM)
Vanessa Grau (CIBERDEM)

ADMINISTRATIVE STAFF
Carme Sanahuja (CIBERDEM)

STRATEGIC OBJECTIVES

1. Use of genomic tools for establishing the genetic and epigenetic mechanisms that modify the risk of developing diabetes.
2. Identification of pathogenic mechanisms and new therapeutic options for monogenic forms of diabetes.
3. Discovery of new pancreatic regeneration pathways.

Our lab is interested in understanding the transcriptional mechanisms that control the differentiation and function of pancreatic insulin-producing ß-cells. We use this information to gain new insights into the molecular defects that cause different forms of diabetes. This knowledge is also very relevant for the generation of new insulin-producing cells for replacement therapies in Type 1 diabetes.

MAIN LINES OF RESEARCH

1. Pancreatic regeneration and programming.
2. Epigenomic regulation of beta cells and diabetes.
3. Monogenic diabetes.

PUBLICATIONS

Originals / I.F.: 41.038

1. Al-Hasani K, Pfeifer A, Courtney M, Ben-Othman N, Gjernes E, Vieira A, Druelle N, Avolio F, Ravassard P, Leuckx G, Lacas-Gervais S, Ambrosetti D, Benizri E,Hecksher-Sorensen J, Gounon P, Ferrer J, Gradwohl G, Heimberg H, Mansouri A, Collombat P. **Adult duct-lining cells can reprogram into β-like cells able to counter repeated cycles of toxin-induced diabetes.** *Dev Cell* 26(1):86-100 I.F.: 12.861

2. van Arensbergen J, García-Hurtado J, Maestro MA, Correa-Tapia M, Rutter GA, Vidal M, Ferrer J. **Ring1b bookmarks genes in pancreatic embryonic progenitors for repression in adult β cells.** *Gene Dev* 27(1):52-63 I.F.: 12.444

3. Jeliazkova P, Jörs S, Lee M, Zimber-Strobl U, Ferrer J, Schmid RM, Siveke JT, Geisler F. **Canonical Notch2 signaling determines biliary cell fates of embryonic hepatoblasts and adult hepatocytes independent of Hes1.** *Hepatology* 57(6):2469-2479 I.F.: 12.003

4. van de Bunt M, Gaulton KJ, Parts L, Moran I, Johnson PR, Lindgren CM, Ferrer J, Gloyn AL, McCarthy MI. **The miRNA profile of human pancreatic islets and beta-cells and relationship to type 2 diabetes pathogenesis.** *PLoS One* 8(1):e55272 I.F.: 3.730

GRANTS FOR RESEARCH IN PROGRESS

Ferrer J. **DIabetes REsearCh on patients Tratification.** Sponsored by: Innovative Medicines Initiative (IMI). IMI/115317. Duration: 01/02/2012-31/01/2017

Ferrer J. **Epigenetic mechanisms underlying predisposition to metabolic syndrome-associated diseases.** Sponsored by: European Commission. JTC_META_2011_002. Duration: 01/01/2012-31/12/2014

Ferrer J. **Regulación epigenética de las células beta y diabetes.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-27086. Duration: 01/01/2012-31/12/2014

Ferrer J. **Beta Cell Biology Consortium.** Sponsored by: National Institute of Health (NIH). 2U01DK072473-06L. Duration: 01/03/2011-31/07/2014

Ferrer J. **Biology of Liver and Pancreatic Development and Disease (BOLD)** Sponsored by: European Commission PF7. Marie Curie Integrated Training Network 238821 Duration: 01/09/2009-31/08/2013

Pasquali, L. **Mapping the human pancreatic islet-cell cis regulome.** Sponsored by: European Foundation for the Study of Diabetes. EFSD/LILLY_11_1_001 Duration: 01/01/2013-31/12/2014

3.14 Diabetes: metabolic and molecular networks

LOCATION
CEK building

KEYWORDS
1. **Type 1 Diabetes**
2. **Type 2 diabetes**
3. **Obesity**
4. **Autoimmunity**
5. **Pancreatic islets**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	71.18	18	10	2
2012	122.59	27	21	3
2013	197.55	35	29	5

TEAM INVOLVED IN
CIBERDEM

TEAM LEADER
Josep Vidal (HCB)
T. 93 227 98 46
jovidal@clinic.cat

GROUP LEADERS
Ramon Gomis (HCB)
Alexandra Felicia Hanzu (HCB-IDIBAPS)
Pere Santamaria (IDIBAPS)
Josep Vidal (HCB)

RESEARCHERS
Roser Casamitjana (HCB)
Marc Claret (IDIBAPS)
Ignacio Conget (HCB)
Enric Esmatjes (HCB)
Rosa Gasa (IDIBAPS)
Emilio Ortega (HCB)
Pau Serra (IDIBAPS)

POST-DOCTORAL RESEARCHERS
Paola Casini (IDIBAPS)
Sara Cervantes (IDIBAPS)
Eduardo Fernández (IDIBAPS)
Rebeca Fernández (CIBERDEM)
Elena González (CIBERDEM)
Rita Malpique (IDIBAPS)
Mercè Martin (IDIBAPS)
Laura Martinez (IDIBAPS)
Maria Laura Perez (Marie Curie)
Sandra Rebuffat (CIBERDEM)
Maud Soty (CIBERDEM)
Elaine Vieira (CIBERDEM)

PRE-DOCTORAL RESEARCHERS
Hugo Alves (FCRB)
Mariona Balfego (FCRB)
Silvia Canivell (IDIBAPS)
Ana Lucía Castillo (CONACYT, México)
Joana Duarte (FCRB)
Miriam Ejarque (IDIBAPS)
Alba González (FCRB)
Katerina Papageorgiou (IDIBAPS)
Marta Pradas (FCRB)
Andrea Ruiz Tarrago (IDIBAPS)
Marc Schneeberger (UB)
Montse Visa (FCRB)

TECHNICIANS
Yaiza Esteban (CIBERDEM)
Cesar Fandos (IDIBAPS)
Ainhoa García (CIBERDEM)
Elena Lopez (IDIBAPS)

NURSING STAFF
Judith Viaplana (IDIBAPS)

COLLABORATORS
Antonio Jesús Blanco (HCB)
Laura Brugnara (CIBERDEM)
María José Coves (CIBERDEM)
Lilliam Flores (HCB)
Marga Gimenez (HCB)
Irene Halperin (HCB)
Pere Leyes (HCB)
Mireia Mora (HCB)
Belén Nadal (UB)

STRATEGIC OBJECTIVES

1. Understanding the molecular mechanisms regulating plasticity of the pancreatic islets in type 2 diabetes and obesity.
2. Evaluation of molecular, genetic, and environmental contributors to the pancreatic beta cell dysfunction in type 2 diabetes.
3. Understanding the role of the gastrointestinal tract in the regulation of glucose homeostasis and energy balance
4. Depicting the cross-talk between central and peripheral determinants of energy balance
5. Unravelling the Molecular and genetic factors in the development and function of the immune system
6. Translating knowledge into therapeutic modulation of autoimmunity in type 1 diabetes and other human autoimmune disorders

MAIN LINES OF RESEARCH

1. Analysis of the transcriptional circuits regulating the beta-cell population and its function.
2. Description of the modulating effects of the transcription factors neuroD1 and neurogenin 3 in the embryonic development of the pancreas.
3. Description of the molecular pathways involved in the antiobesity and antidiabetic effects of sodium tungstate in experimental animals.
4. Impact of normal blood glucose upon endothelial dysfunction: use of treatments with insulin pumps.
5. Determination of the role of the hypothalamus in the control of energy homeostasis in obesity.
6. Analysis of the epigenetic regulation of adipogenesis.
7. GLP-1 as key factor in the resolution of type 2 diabetes after bariatric surgery
9. Genes and molecules in the development and functioning of the immune system.
9. Immunological approach to the treatment of autoimmune diseases.
10. Bariatric surgery and the resolution of metabolic comorbidities in obesity.

RESEARCH GROUP
OBESITY: FROM EXCESS BODY FAT TO METABOLIC COMPLICATIONS

GROUP LEADER
Josep Vidal (HCB)

Our group's main line of research seeks to deepen our understanding of the mechanisms that associate obesity with the onset of metabolic disorders. Bridging clinical and basic research, we look for answers to the question of why certain overweight individuals appear to have a greater protection from developing metabolic disorders than orders, as well as what determines inter-individual variability in metabolic response to therapeutic strategies associated with weight loss.

RESEARCH GROUP
PANCREATIC ISLETS: BIOMARKERS AND FUNCTION

GROUP LEADER
Ramon Gomis (IDIBAPS)

The group headed by Dr. Ramon Gomis investigates the physiology of pancreatic islets and adipose tissue, and the causes leading to dysfunction of these tissues. A central aspect of these studies is the determination of the molecular mechanisms implicated in cell mass balance at both embryonic development level and as refers to adult age – with special emphasis on cell regeneration and apoptotic processes.

RESEARCH GROUP
PATHOGENESIS AND TREATMENT OF AUTOIMMUNITY

GROUP LEADER
Pere Santamaria (IDIBAPS)

Our laboratory has two distinct components: one for purely basic biomedical research which studies the role of particular genes and molecules in the development and functioning of the immune system; and another, more applied, based on the study of the immunological effects of a new therapeutic platform we have developed for the treatment of autoimmune diseases, which include type 1 diabetes, lupus and autoimmune diseases of the central nervous system. This treatment, based on nanotechnology, works by way of an immunological mechanism for protection against autoimmunity designed by mother nature, which we have learned to manipulate by using a new type of drug, also discovered

by us. One of our main objectives is to start using this therapeutic platform with patients through the conducting of clinical trials.

50/50 PROGRAM

ENDOCRINE DISORDERS: CROSSTALK BETWEEN MOLECULAR AND METABOLIC DETERMINANTS

GROUP LEADER
Felicia Hanzu (HCB-IDIBAPS)

Our group studies the crosstalk between molecular and metabolic determinants in endocrine pathologies, respectively the molecular determinants underlying physiopathological mechanisms of endocrine tumours and gender dysphoria. The aim is to translate knowledge from the basic research into the clinical practice by focusing on the development of new treatment strategies.

PUBLICATIONS

Originals / I.F.: 197.548

1. Schneeberger M, Dietrich MO, Sebastián D, Imbernón M, Castaño C, Garcia A, Esteban Y, Gonzalez-Franquesa A, Rodríguez IC, Bortolozzi A, Garcia-Roves PM, Gomis R, Nogueiras R, Horvath TL, Zorzano A, Claret M. **Mitofusin 2 in POMC neurons connects ER stress with leptin resistance and energy imbalance.** *Cell* 155(1):172-187 I.F.: 31.957

2. Tsai S, Serra P, Clemente-Casares X, Yamanouchi J, Thiessen S, Slattery RM, Elliott JF, Santamaria P. **Antidiabetogenic MHC class II promotes the differentiation of MHC-promiscuous autoreactive T cells into FOXP3+ regulatory T cells.** *Proc Natl Acad Sci U S A* 110(9):3471-3476 I.F.: 9.737

3. Alkemade GM, Clemente-Casares X, Yu Z, Xu BY, Wang J, Tsai S, Wright JR Jr, Roep BO, Santamaria P. **Local autoantigen expression as essential gatekeeper of memory T-cell recruitment to islet grafts in diabetic hosts.** *Diabetes* 62(3):905-911 I.F.: 7.895

4. Lanuza-Masdeu J, Arévalo MI, Vila C, Barberà A, Gomis R, Caelles C. **In vivo JNK activation in pancreatic β-cells leads to glucose intolerance caused by insulin resistance in pancreas.** *Diabetes* 62(7):2308-2317 I.F.: 7.895

5. Ceriello A, Novials A, Ortega E, Canivell S, La Sala L, Pujadas G, Bucciarelli L, Rondinelli M, Genovese S. **Vitamin C further improves the protective effect of glucagon-like peptide-1 on acute hypoglycemia-induced oxidative stress, inflammation, and endothelial dysfunction in type 1 diabetes.** *Diabetes Care* 36(12):4104-4108 I.F.: 7.735

6. Ceriello A, Novials A, Ortega E, Canivell S, La Sala L, Pujadas G, Esposito K, Giugliano D, Genovese S. **Glucagon-like peptide 1 reduces endothelial dysfunction, inflammation, and oxidative stress induced by both hyperglycemia and hypoglycemia in type 1 diabetes.** *Diabetes Care* 36(8):2346-2350 I.F.: 7.735

7. Jiménez A, Casamitjana R, Viaplana-Masclans J, Lacy A, Vidal J. **GLP-1 action and glucose tolerance in subjects with remission of type 2 diabetes after gastric bypass surgery.** *Diabetes Care* 36(7):2062-2069 I.F.: 7.735

8. Sinkeler SJ, Kwakernaak AJ, Bakker SJ, Shahinfar S, Esmatjes E, de Zeeuw D, Navis G, Lambers Heerspink HJ. **Creatinine excretion rate and mortality in type 2 diabetes and nephropathy.** *Diabetes Care* 36(6):1489-1494 I.F.: 7.735

9. Rebuffat SA, Oliveira JM, Altirriba J, Palau N, Garcia A, Esteban Y, Nadal B, Gomis R. **Downregulation of Sfrp5 promotes beta cell proliferation during obesity in the rat.** *Diabetologia* 56(11):2446-2455 I.F.: 6.487

10. Ziegler AI, Le Page MA, Maxwell MJ, Stolp J, Guo H, Jayasimhan A, Hibbs ML, Santamaria P, Miller JF, Plebanski M, Silveira PA, Slattery RM. **The CD19 signalling molecule is elevated in NOD mice and controls type 1 diabetes development.** *Diabetologia* 56(12):2659-2668 I.F.: 6.487

11. Jiménez A, Casamitjana R, Flores L, Delgado S, Lacy A, Vidal J. **GLP-1 and the long-term outcome of type 2 diabetes mellitus after Roux-en-Y gastric bypass surgery in morbidly obese subjects.** *Ann Surg* 257(5):894-899 I.F.: 6.329

12. Tsai S, Serra P, Clemente-Casares X, Slattery RM, Santamaria P. **Dendritic cell-dependent in vivo generation of autoregulatory T cells by antidiabetogenic MHC class II.** *J Immunol* 191(1):70-82 I.F.: 5.520

13. Ejarque M, Altirriba J, Gomis R, Gasa R. **Characterization of the transcriptional activity of the basic helix-loop-helix (bHLH) transcription factor Atoh8.** *Biochim Biophys Acta* 1829(11):1175-1183 I.F.: 5.456

14. Shameli A, Yamanouchi J, Tsai S, Yang Y, Clemente-Casares X, Moore A, Serra P, Santamaria P. **IL-2 promotes the function of memory-like autoregulatory CD8+ T cells but suppresses their development via FoxP3+ Treg cells.** *Eur J Immunol* 43(2):394-403 I.F.: 4.970

15. Gutiérrez-Repiso C, Rojo-Martínez G, Soriguer F, García-Fuentes E, Vendrell J, Vázquez JA, Valdés S, Urrutia I, Serrano-Rios M, Pascual-Manich G, Ortega E, Mora-Peces I, Menéndez E, Martínez-Larrad MT, López-Alba A, Gutiérrez G, Gomis R, Goday A, Girbés J, Gaztambide S, Franch J, Delgado E, Catalá M, Castell C, Castaño L, Casamitjana R, Carmena R, Calle-Pascual A, Bordiú E, Bosch-Comas A. **Factors affecting levels of urinary albumin excretion in the general population of Spain: the Di@bet.es study.** *Clin Sci (Lond)* 124(4):269-277 I.F.: 4.859

16. Gonzalez A, Merino B, Marroquí L, Ñeco P, Alonso-Magdalena P, Caballero-Garrido E, Vieira E, Soriano S, Gomis R, Nadal A,

Quesada I. **Insulin hypersecretion in islets from diet-induced hyperinsulinemic obese female mice is associated with several functional adaptations in individual β-cells.** *Endocrinology* 154(10):3515-3524 I.F.: 4.717

17. Ejarque M, Cervantes S, Pujadas G, Tutusaus A, Sanchez L, Gasa R. **Neurogenin3 cooperates with Foxa2 to autoactivate its own expression.** *J Biol Chem* 288(17):11705-11717 I.F.: 4.651

18. Marcuello C, Calle-Pascual AL, Fuentes M, Runkle I, Rubio MA, Montañez C, Rojo-Martinez G, Soriguer F, Bordiu E, Goday A, Bosch-Comas A, Carmena R, Casamitjana R, Castaño L, Castell C, Catalá M, Delgado E, Franch J, Gaztambide S, Girbés J, Gomis R, Urrutia I, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Serrano-Rios M, Valdés S, Vázquez JA, Vendrell J. **Prevalence of the metabolic syndrome in Spain using regional cutoff points for waist circumference: the di@bet.es study.** *Acta Diabetol* 50(4):615-623 I.F.: 4.631

19. Perea V, Jiménez A, Flores L, Ortega E, Coves MJ, Vidal J. **Anthropometric indexes outperform bioelectrical impedance analysis-derived estimates of body composition in identification of metabolic abnormalities in morbid obesity.** *Surg Obes Relat Dis* 9(5):648-652 I.F.: 4.121

20. Sugarman J, Tsai S, Santamaria P, Khadra A. **Quantifying the importance of pMHC valency, total pMHC dose and frequency on nanoparticle therapeutic efficacy.** *Immunol Cell Biol* 91(5):350-359 I.F.: 3.935

21. Hanzu FA, Musri MM, Sánchez-Herrero A, Claret M, Esteban Y, Kaliman P, Gomis R, Párrizas M. **Histone demethylase KDM1A represses inflammatory gene expression in preadipocytes.** *Obesity* 21(12):E616-625 I.F.: 3.922

22. Canivell S, Ruano EG, Sisó-Almirall A, Kostov B, González-de Paz L, Fernandez-Rebollo E, Hanzu F, Párrizas M, Novials A, Gomis R. **Gastric inhibitory polypeptide receptor methylation in newly diagnosed, drug-naïve patients with type 2 diabetes: a case-control study.** *PLoS One* 8(9):e75474 I.F.: 3.730

23. Vieira E, Marroquí L, Figueroa AL, Merino B, Fernandez-Ruiz R, Nadal A, Burris TP, Gomis R, Quesada I. **Involvement of the clock gene Rev-erb alpha in the regulation of glucagon secretion in pancreatic alpha-cells.** *PLoS One* 8(7):e69939 I.F.: 3.730

24. Amor A, Jiménez A, Moizé V, Ibarzabal A, Flores L, Lacy AM, Vidal J. **Weight loss independently predicts urinary albumin excretion normalization in morbidly obese type 2 diabetic patients undergoing bariatric surgery.** *Surg Endosc* 27(6):2046-2051 I.F.: 3.427

25. Comas J, Arcos E, Castell C, Cases A, Martínez-Castelao A, Doñate T, Esmatjes E. **Evolution of the incidence of chronic kidney disease Stage 5 requiring renal replacement therapy in the diabetic population of Catalonia.** *Nephrol Dial Transplant* 28(5):1191-1198 I.F.: 3.371

26. Rojo-Martínez G, Soriguer F, Colomo N, Calle A, Goday A, Bordiú E, Delgado E, Menéndez E, Ortega E, Urrutia I, Girbés J, Castaño L, Catalá M, Gaztambide S, Valdés S; di@bet.es study group. **Factors determining high-sensitivity C-reactive protein values in the Spanish population. Di@bet.es study**. *Eur J Clin Invest* 43(1):1-10 I.F.: 3.365

27. Moizé V, Andreu A, Rodríguez L, Flores L, Ibarzabal A, Lacy A, Jiménez A, Vidal J. **Protein intake and lean tissue mass retention following bariatric surgery.** *Clin Nutr* 32(4):550-555 I.F.: 3.298

28. Rojo-Martínez G, Valdés S, Colomo N, Lucena MI, Gaztambide S, Gomis R, Casamitjana R, Carmena R, Catalá M, Martínez-Larrad MT, Serrano-Ríos M, Castaño L, Vendrell J, Girbés J, Franch J, Vázquez JA, Mora-Peces I, Urrutia I, Pascual-Manich G, Ortega E, Menéndez E, Delgado E, Bordiú E, Castell C, López-Alba A, Goday A, Calle A, Bosch-Comas A, Soriguer F. **Use of Drugs Related to the Treatment of Diabetes Mellitus and Other Cardiovascular Risk Factors in the Spanish Population. The Di@bet.es Study.** *Rev Esp Cardiol* 66(11):854-863 I.F.: 3.204

29. Mukherjee G, Geliebter A, Babad J, Santamaria P, Serreze DV, Freeman GJ, Tarbell KV, Sharpe A, DiLorenzo TP. **DEC-205-mediated antigen targeting to steady-state dendritic cells induces deletion of diabetogenic CD8⁺ T cells independently of PD-1 and PD-L1.** *Int Immunol* 25(11):651-660 I.F.: 3.135

30. Caixàs A, Lecube A, Morales MJ, Calañas A, Moreiro J, Cordido F, Díaz MJ, Masmiquel L, Moreno B, Vidal J, Goday A, Arrizabalaga JJ, García-Luna PP, Iglesias P, Burguera B, Rubio MA, Monereo S; Group for the Study of Obesity of the Spanish Endocrinology and Nutrition Society (SEEN), Crosby RD, Kolotkin RL. **Weight-related quality of life in Spanish obese subjects suitable for bariatric surgery is lower than in their North American counterparts: a case-control study.** *Obes Surg* 23(4):509-514 I.F.: 3.102

31. Jiménez A, Perea V, Corcelles R, Moizé V, Lacy A, Vidal J. **Metabolic effects of bariatric surgery in insulin-sensitive morbidly obese subjects.** *Obes Surg* 23(4):494-500 I.F.: 3.102

32. Soriguer F, Rojo-Martínez G, Goday A, Bosch-Comas A, Bordiú E, Caballero-Díaz F, Calle-Pascual A, Carmena R, Casamitjana R, Castaño L, Castell C, Catalá M, Delgado E, Franch J, Gaztambide S, Girbés J, Gomis R, Gutiérrez G, López-Alba A, Teresa Martínez-Larrad M, Menéndez E, Mora-Peces I, Ortega E, Pascual-Manich G, Serrano-Rios M, Urrutia I, Valdés S, Antonio Vázquez J, Vendrell J. **Olive oil has a beneficial effect on impaired glucose regulation and other cardiometabolic risk factors. Di@bet.es study.** *Eur J Clin Nutr* 67(9):911-916 I.F.: 2.756

33. Flores L, Janka M, Canivell S, Jiménez A, Vidal J. **Glucose abnormalities associated with impaired nocturnal fall in blood pressure in normotensive severely**

obese patients. *Diabetes Res Clin Pract* 101(2):153-158 I.F.: 2.741

34. Mathieu C, Barnett AH, Brath H, Conget I, de Castro JJ, Göke R, Márquez Rodriguez E, Nilsson PM, Pagkalos E, Penfornis A, Schaper NC, Wangnoo SK, Kothny W, Bader G. **Effectiveness and tolerability of second-line therapy with vildagliptin vs. other oral agents in type 2 diabetes: a real-life worldwide observational study (EDGE).** *Int J Clin Pract* 67(10):947-56 I.F.: 2.427

35. Ortega E, Franch J, Castell C, Goday A, Ribas-Barba L, Soriguer F, Vendrell J, Casamitjana R, Bosch-Comas A, Bordiú E, Calle-Pascual A, Carmena R, Castaño L, Catalá M, Delgado E, Gaztambide S, Girbés J, López-Alba A, Martínez-Larrad MT, Menéndez E, Mora-Peces I, Pascual-Manich G, Rojo-Martínez G, Serrano-Rios M, Urrutía I, Valdés S, Vázquez JA, Gomis R. **Mediterranean diet adherence in individuals with prediabetes and unknown diabetes: the Di@bet.es Study.** *Ann Nutr Metab* 62(4):339-46 I.F.: 1.661

Reviews / I.F.: 2.923

1. Vidal J, Jiménez A. **Diabetes remission following metabolic surgery: is GLP-1 the culprit?** *Curr Atheroscler Rep* 15(10):357 I.F.: 2.923

Multicenter / I.F.: 62.237

1. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, Ohman P, Frederich R, Wiviott SD, Hoffman EB, Cavender MA, Udell JA, Desai NR, Mosenzon O, McGuire DK, Ray KK, Leiter LA, Raz I; SAVOR-TIMI 53 Steering Committee and Investigators. **Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus.** *N Engl J Med* 369(14):1317-26 I.F.: 51.658

2. Dunkler D, Dehghan M, Teo KK, Heinze G, Gao P, Kohl M, Clase CM, Mann JF, Yusuf S, Oberbauer R; ONTARGET Investigators. **Diet and kidney disease in high-risk individuals with type 2 diabetes mellitus.** *JAMA Intern Med* 173(18):1682-92 I.F.: 10.579

GRANTS FOR RESEARCH IN PROGRESS

Claret M. **MicroRNAs hipotalámicos y regulación del metabolismo energético: posibles dianas terapéuticas para el tratamiento de la obesidad y la diabetes.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01074.
Duration: 01/01/2011-30/06/2015

Claret M. **Mitochondrial fusion protein Mitofusin 1 in POMC neurons: potential regulator of energy homeostasis.** Sponsored by: EUROPEAN FOUNDATION FOR THE STUDY OF DIABETES. EFSD/LILLY_12_1_002.
Duration: 09/07/2012-31/05/2014

Claret M. **Role of hypothalamic mitochondrial fusion in appetite and body weight control: potential therapeutic target for the treatment of obesity.** Sponsored by: Associació Catalana d'Universitats Púnliques (ACUP). 2010ACUP_00275.
Duration: 01/12/2010-01/12/2013

Gasa R. **Development of novel strategies to generate insulin-producing cells from somatic and induced pluripotent stem cells.** Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 120830.
Duration: 21/01/2013-20/01/2016

Gomis R. **Diabetis experimental. Investigació cel·lular i molecular en models de diabetis experimental.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1426.
Duration: 07/08/2009-30/04/2014

Gomis R. **Determinantes moleculares de la plasticidad de la célula beta en diabetes: efectos del tungstato sódico.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-19527.
Duration: 01/01/2011-31/12/2013

Gomis R. **Supporting healthy lifestiles in the mediterranean area.** Sponsored by: European Commission. 230848.
Duration: 01/03/2009-28/02/2013

Lerin C. **Unraveling Novel Molecular Mechanisms Underlying the Development of Insulin Resistance.** Sponsored by: EUROPEAN FOUNDATION FOR THE STUDY OF DIABETES. EFSD/LILLY_11_2_001.
Duration: 01/01/2012-15/07/2013

Lerin C. **Efectos Metabólicos y Bioquímicos de la Betaína sobre la Sensibilidad a Insulina y el Ejercicio Físico.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-28502.
Duration: 01/01/2012-08/07/2013

Serra P. **New nanomedicines for the treatment of type 1 diabetes: modulating antiantidiabetogeniC T- and B-regulatory networks.** Sponsored by: EUROPEAN FOUNDATION FOR THE STUDY OF DIABETES. EFSD/JDRF/NN_01.
Duration: 01/01/2013-31/12/2015

Vidal J. **GLP-1 y resolución a largo plazo de diabetes mellitus tipo 2 tras cirugía bariátrica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00892.
Duration: 01/01/2012-31/12/2014

Vidal J. **Estudi aleatoritzat prospectiu sobre els efectes del tractament mèdic intensiu amb o sense bypass gàstric en Y de Roux, sobre el gruix de la íntima mitja carotídea en malalts amb obesitat grau I.** Sponsored by: Agència d'Avaluació de Tecnologia Medica (AATM) . 401/17/2008.
Duration: 01/12/2009-30/11/2013

DOCTORAL THESES

Gomis R. **Targeting B-cell death in type 2 diabetes: the effect of sodium tungstate in IRS2 knockout mice.** PhD student: Joana Raquel Moitinho de Oliveira

Gomis R. **Impact of adipose tissue on endothelial cells: effect of metabolic disorders.** PhD student: Aikaterini Papageorgiou.

3.15 Pathogenesis and prevention of diabetes

LOCATION
CEK building

FOR FURTHER INFORMATION
www.diabetes-obesity-research.org

KEYWORDS
1. **Islet amyloid polypeptide/amylin**
2. **Beta-cell dysfuntion**
3. **Lifestyle**
4. **Endothelial dysfunction**
5. **Epigenetics**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	-	-	-	-
2012	-	-	-	-
2013	108.92	17	12	4

TEAM INVOLVED IN
CIBERDEM

TEAM LEADER
Anna Novials (IDIBAPS)
T. (+34) 93 227 5400 x.4153
anovials@clinic.cat

RESEARCHERS
Antonio Ceriello (IDIBAPS)
Pablo Miguel García-Roves (IDIBAPS)
Marcelina Párrizas (FCRB)
Joan Marc Servitja (IDIBAPS)

POST-DOCTORAL RESEARCHERS
Gema Alcarraz (CIBERDEM)
Elizabeth Gordillo (HCB)
Lucia La Sala (IDIBAPS)
Joel Montané (IDIBAPS)
Gemma Pujades (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Laura Brugnara (CIBERDEM)
Lisa Cadavez (FCRB)
Alba Gonzalez-Franquesa (IDIBAPS)
Alba Moreno (IDIBAPS)
Valeria de Nigris (IDIBAPS)
Montserrat Visa (FCRB)

TECHNICIANS
Carlos Castaño (CIBERDEM)
Mercè Obach (IDIBAPS)

DIETITIANS
Serafín Murillo (CIBERDEM)

COLLABORATORS
Ana Isabel García (HCB)

STRATEGIC OBJECTIVES

1. **To study metabolic and molecular responses to exercise and nutrition in diabetes.**

1A. To investigate metabolomic and lipidomic profiles in patients with type 1 and type 2 diabetes in response to different patterns of exercise.

1B. To understand the mechanisms that control energy metabolism and cellular plasticity of the tissues involved in the control and regulation of glucose homeostasis.

2. **To investigate epigenetic alterations as potential biomarkers of certain pathophysiological mechanisms in diabetes.**

2A. To identify the changes in patterns of circulating microRNAs in the prediabetic and diabetic populations.
2B. To unravel the role that microRNAs play in intercellular communication in the context of diabetes.

3. To investigate the mechanisms of endothelial dysfunction in diabetes.
3A. To analyse the therapeutic action of GLP-1 on endothelial cells under conditions of hyperglycaemia and its relationship with oxidative stress.
3B. To investigate the role of different microRNAs in modulating the intracellular antioxidant response of endothelial cells exposed to glucose oscillations.

4. To investigate the mechanisms of beta-cell dysfunction in the search for new therapeutic targets.
4A. To study the effect of human IAPP on ER stress response and apoptosis in pancreatic beta-cells.
4B. To develop new approaches to treating inflammation of the pancreatic islet
4C. To analyse transcriptional networks under stressful situations such as hypoglycaemia or treatment with inflammatory cytokines in pancreatic beta-cells.

MAIN LINES OF RESEARCH

Bridging basic and clinical research, the team performs studies in both animal models and humans to improve our understanding of diabetes, with the mission of innovating treatment and prevention methods. Our main lines of research are focused on several fields related to diabetes:

- Prevention and control of diabetes through lifestyle interventions;
- Epigenetic markers to help predict the development of diabetes and vascular complications;
- Mechanisms of endothelial dysfunction related to diabetes and vascular complications; and finally,
- Molecular mechanisms that lead to deterioration of pancreatic beta-cells during the progression of the disease, with the end goal of finding new therapeutic targets.

PUBLICATIONS

Original / I.F.: 108.924

1. Schneeberger M, Dietrich MO, Sebastián D, Imbernón M, Castaño C, Garcia A, Esteban Y, Gonzalez-Franquesa A, Rodríguez IC, Bortolozzi A, Garcia-Roves PM, Gomis R, Nogueiras R, Horvath TL, Zorzano A, Claret M. **Mitofusin 2 in POMC neurons connects ER stress with leptin resistance and energy imbalance.** *Cell* 155(1):172-187 I.F.: 31.957

2. Bosi E, Scavini M, Ceriello A, Cucinotta D, Tiengo A, Marino R, Bonizzoni E, Giorgino F; PRISMA Study Group. **Intensive structured self-monitoring of blood glucose and glycemic control in noninsulin-treated type 2 diabetes: the PRISMA randomized trial.** *Diabetes Care* 36(10):2887-2894 I.F.: 7.735

3. Ceriello A, Novials A, Ortega E, Canivell S, La Sala L, Pujadas G, Bucciarelli L, Rondinelli M, Genovese S. **Vitamin C further improves the protective effect of glucagon-like peptide-1 on acute hypoglycemia-inducedoxidative stress, inflammation, and endothelial dysfunction in type 1 diabetes.** *Diabetes Care* 36(12):4104-4108 I.F.: 7.735

4. Ceriello A, Novials A, Ortega E, Canivell S, La Sala L, Pujadas G, Esposito K, Giugliano D, Genovese S. **Glucagon-Like Peptide 1 Reduces Endothelial Dysfunction, Inflammation, and Oxidative Stress Induced by Both Hyperglycemia and Hypoglycemia in Type 1 Diabetes.** *Diabetes Care* 36(8):2346-2350 I.F.: 7.735

5. Moreno-Asso A, Castaño C, Grilli A, Novials A, Servitja JM. **Glucose regulation of a cell cycle gene module is selectively lost in mouse pancreatic islets during ageing.** *Diabetologia* 56(8):1761-1772 I.F.: 6.487

6. Garagnani P, Giuliani C, Pirazzini C, Olivieri F, Bacalini MG, Ostan R, Mari D, Passarino G, Monti D, Bonfigli AR, Boemi M, Ceriello A, Genovese S, Sevini F, Luiselli D, Tieri P, Capri M, Salvioli S, Vijg J, Suh Y, Delledonne M, Testa R, Franceschi C. **Centenarians as super-controls to assess the biological relevance of genetic risk factors for common age-related diseases: a proof of principle on type 2 diabetes.** *Aging* 5(5):373-385 I.F.: 4.696

7. García-Alonso V, López-Vicario C, Titos E, Morán-Salvador E, González-Périz A, Rius B, Párrizas M, Werz O, Arroyo V, Clària J. **Coordinate functional regulation between microsomal prostaglandin E synthase-1 (mPGES-1) and peroxisome proliferator-activated receptor γ (PPARγ) in the conversion of white-to-brown adipocytes.** *J Biol Chem* 288(39):28230-28242 I.F.: 4.651

8. Bonfigli AR, Sirolla C, Testa R, Cucchi M, Spazzafumo L, Salvioli S, Ceriello A, Olivieri F, Festa R, Procopio AD, Brandoni G, Boemi M, Marra M, Franceschi C. **The p53 codon 72 (Arg72Pro) polymorphism is associated with the degree of insulin resistance in type 2 diabetic subjects: a cross-sectional study.** *Acta Diabetol* 50(3):429-436 I.F.: 4.631

9. Scavini M, Bosi E, Ceriello A, Giorgino F, Porta M, Tiengo A, Vespasiani G, Bottalico D, Marino R, Parkin C, Bonizzoni E, Cucinotta D. **Prospective, randomized trial on intensive SMBG management added value in non-insulin-treated T2DM patients (PRISMA): a study to determine the effect of a structured SMBG intervention.** *Acta Diabetol* 50(5):663-672 I.F.: 4.631

10. Ceriello A, Novials A, Ortega E, Canivell S, Pujadas G, La Sala L, Bucciarelli L, Rondinelli M, Genovese S. **Vitamin C further improves the protective effect of GLP-1 on the ischemia-reperfusion-**

like effect induced by hyperglycemia post-hypoglycemia in type 1 diabetes. *Cardiovasc Diabetol* 12(1):97 I.F.: 4.209

11. Alvarez-López MJ, Castro-Freire M, Cosín-Tomás M, Sanchez-Roige S, Lalanza JF, Del Valle J, Párrizas M, Camins A, Pallás M, Escorihuela RM, Kaliman P. **Long-term exercise modulates hippocampal gene expression in senescent female mice.** *J Alzheimers Dis* 33(4):1177-1190 I.F.: 4.174

12. Gutiérrez-Rojas I, Lozano D, Nuche-Berenguer B, Moreno P, Acitores A, Ramos-Álvarez I, Rovira A, Novials A, Martín-Crespo E, Villanueva-Peñacarrillo ML, Esbrit P. **Amylin exerts osteogenic actions with different efficacy depending on the diabetic status.** *Mol Cell Endocrinol* 365(2):309-315 I.F.: 4.039

13. Hanzu FA, Musri MM, Sánchez-Herrero A, Claret M, Esteban Y, Kaliman P, Gomis R, Párrizas M. **Histone demethylase KDM1A represses inflammatory gene expression in preadipocytes.** *Obesit* 21(12):E616-25 I.F.: 3.922

14. Canivell S, Ruano EG, Sisó-Almirall A, Kostov B, González-de Paz L, Fernandez-Rebollo E, Hanzu F, Párrizas M, Novials A, Gomis R. **Gastric inhibitory polypeptide receptor methylation in newly diagnosed, drug-naïve patients with type 2 diabetes: a case-control study.** *PLoS One*; 8(9):e75474 I.F.: 3.730

15. Marra M, Marchegiani F, Ceriello A, Sirolla C, Boemi M, Franceschi C, Spazzafumo L, Testa I, Bonfigli AR, Cucchi M, Testa R. **Chronic renal impairment and DDAH2-1151 A/C polymorphism determine ADMA levels in type 2 diabetic subjects.** *Nephrol Dial Transplant* 28(4):964-71 I.F.: 3.371

16. Holmström MH, Tom RZ, Björnholm M, Garcia-Roves PM, Zierath JR. **Effect of leptin treatment on mitochondrial function in obese leptin-deficient ob/ob mice.** *Metabolism* 62(9):1258-67 I.F.: 3.096

17. Genovese S, De Berardis G, Nicolucci A, Mannucci E, Evangelista V, Totani L, Pellegrini F, Ceriello A. **Effect of pioglitazone versus metformin on cardiovascular risk markers in type 2 diabetes.** *Adv Ther* 30(2):190-202 I.F.: 2.125

Reviews / I.F.: 16.830

1. Ceriello A, Kilpatrick ES. **Glycemic variability: both sides of the story.** *Diabetes Care* 36 Suppl 2:S272-5 I.F.: 7.735

2. Frontoni S, Di Bartolo P, Avogaro A, Bosi E, Paolisso G, Ceriello A. **Glucose variability: An emerging target for the treatment of diabetes mellitus.** *Diabetes Res Clin Pract* 102(2):86-95 I.F.: 2.741

3. Schnell O, Cappuccio F, Genovese S, Standl E, Valensi P, Ceriello A. **Type 1 diabetes and cardiovascular disease.** *Cardiovasc Diabetol* 12(1):156 I.F.: 4.209

4. von Bibra H, St John Sutton M, Schuster T, Ceriello A, Siegmund T, Schumm-Draeger PM. **Oxidative stress after a carbohydrate meal contributes to the deterioration of diastolic cardiac function in nonhypertensive insulin-treated patients with moderately well controlled type 2 diabetes.** *Horm Metab Res* 45(6):449-55 I.F.: 2.145

Editorials / I.F.: 6.459

1. Esposito K, Gentile S, Candido R, De Micheli A, Gallo M, Medea G, Ceriello A, Associazione Medici Diabetologi. **Management of hyperglycemia in type 2 diabetes: evidence and uncertainty.** *Cardiovasc Diabetol* 12:81 I.F.: 4.209

2. Esposito K, Ceriello A, Giugliano D. *Does personalized diabetology overcome clinical uncertainty and therapeutic inertia in type 2 diabetes? Endocrine* 44(2):343-5 I.F.: 2.250

Clinical Guidelines / I.F.: 14.097

1. Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, Danchin N, Deaton C, Escaned J, Hammes HP, Huikuri H, Marre M, Marx N, Mellbin L, Ostergren J, Patrono C, Seferovic P, Uva MS, Taskinen MR, Tendera M, Tuomilehto J, Valensi P, Zamorano JL; ESC Committee for Practice Guidelines (CPG), Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S; Document Reviewers, De Backer G, Sirnes PA, Ezquerra EA, Avogaro A, Badimon L, Baranova E, Baumgartner H, Betteridge J, Ceriello A, Fagard R, Funck-Brentano C, Gulba DC, Hasdai D, Hoes AW, Kjekshus JK, Knuuti J, Kolh P, Lev E, Mueller C, Neyses L, Nilsson PM, Perk J, Ponikowski P, Reiner Z, Sattar N, Schächinger V, Scheen A, Schirmer H, Strömberg A, Sudzhaeva S, Tamargo JL, Viigimaa M, Vlachopoulos C, Xuereb RG. **ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD).** *Eur Heart J*; 34(39):3035-3087 I.F.: 14.097

GRANTS FOR RESEARCH IN PROGRESS

Ceriello A. **Respuesta antioxidativa alterada en células endoteliales expuestas a gluocsa oscilatoria: papel de Nrf2.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01256. Duration: 01/01/2011-31/12/2013.

Garcia-Roves P. **Descifrando la respuesta integral capaz de restituir la normoglucemia en ratones con diabetes**

tipo 2 debido a cambios en su estilo de vida (dieta y/o ejercicio). Sponsored by: Ministerio de Economía y Competitividad. BFU2011-24679. Duration: 01/01/2012-31/12/2014

Novials A. **Implicación del enzima BACE2 en el mecanismo por el cual el péptido pancreático humano IAPP induce alteraciones de la célula beta-pancreática en la diabetes del tipo2.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00679. Duration: 01/01/2012-31/12/2014

Párrizas M. **Papel de la demetilasa de histonas LSD1 en la adipogénesis.** Sponsored by: Ministerio de Ciencia e Innovación. BFU2009-09988/BMC. Duration: 01/01/2010-31/12/2013.

Servitja JM. **Epigenetic control of gene expression in pancreatic islets.** Sponsored by: European Foundation for the Study of Diabetes (EFSD) /Lilly Fellowship Programme. Duration: 01/07/2010-30/06/2013.

Servitja JM. **Regulación y función de microRNAs en islotes pancreáticos.** Sponsored by: Ministerio de Ciencia e Innovación. BFU2010-17639. Duration: 01/01/2011-31/12/2013.

AREA 4

Clinical and experimental neuroscience

4.1 **Neuropharmacology and experimental neuropathology** 198
Guadalupe Mengod

4.2 **Brain ischemia: Clinical and experimental studies** 203
Ángel Chamorro

4.3 **Neurodegenerative diseases: Clinical and experimental research** 207
Eduardo Tolosa

4.4 **Neurophysiology and functional studies of the nervous system** 213
Josep Valls

4.5 **Muscle research and mitochondrial function** 217
Josep Maria Grau

4.6 **Pathophysiology and treatment of neurodegenerative disorders** 220
Jordi Alberch

4.7 **Biological bases of psychiatric disorders and nuclear psychiatry** 223
Miquel Bernardo

4.8 **Neuropsychology** 234
Carme Junqué

4.9 **Systems neuroscience** 238
Maria Victoria Sánchez Vives

4.10 **Clinical and experimental neuroimmunology** 242
Francesc Graus

4.11 **Neurobiology Unit** 248
Ramon Trullàs

4.1 Neuropharmacology and experimental neuropathology

LOCATION
IIBB-CSIC labs
UB School of Medicine

KEYWORDS
1. **Neuropsychopharmacology**
2. **Brain aging and Neurotoxicity**
3. **Neurodegeneration**
4. **Neuroinflammation**
5. **Medulloblastoma**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	68.14	15	9	2
2012	138.08	27	22	4
2013	98.18	16	12	1

TEAM INVOLVED IN
CIBERNED
CIBERSAM
CIBERESP

AWARDS
26th ECNP Congress Poster Award
Institution: European College of Neuropsychopharmachology
Awardees: A. Ferrés-Coy, F. Pilar-Cuellar, R. Vidal, M. Galofré, V. Paz, L. Campa, Á. Pazos, A. Montefeltro, E.M. Valdizán, F. Artigas, A. Bortolozzi

TEAM LEADER
Guadalupe Mengod (IIBB-CSIC)
T. 93 363 83 23
gmlnqr@iibb.csic.es

GROUP LEADERS
Francesc Artigas (IIBB-CSIC)
Guadalupe Mengod (IIBB-CSIC)
Sebastià Pons (IIBB-CSIC)
Josep Saura (UB)
Cristina Suñol (IIBB-CSIC)

RESEARCHERS
Albert Adell (IIBB-CSIC)
Analia Bortolozzi (IDIBAPS)
Anna Castañé (IIBB-CSIC)
Pau Celada (IDIBAPS)
Roser Cortés (IIBB-CSIC)
Rosa Cristòfol (IIBB-CSIC)
Eduard Rodriguez Farré (IIBB-CSIC)
Coral Sanfeliu (IIBB-CSIC)
Joan Serratosa (IIBB-CSIC)
Carme Solà (IIBB-CSIC)
Josep Maria Tusell (IIBB-CSIC)
Mª Teresa Vilaró (IIBB-CSIC)

PRE-DOCTORAL RESEARCHERS
Diana Alarcón Arís (IIBB-CSIC)
Alessandra Antunes dos Santos (CNPq, Brasil)
Cristina Belles (IIBB-CSIC)
Lidia Cantacorps (IIBB-CSIC)
Rubén Corpas (IIBB-CSIC)
Guido Dentesano (IDIBAPS)
Albert Ferrés (IIBB-CSIC)
Anna García-Miralles (IDIBAPS)
Júlia Gasull (IIBB-CSIC)
Antonio Herrera-Camacho (IDIBAPS)
Laura Jiménez (IDIBAPS)
Giuseppe Mocci (IIBB-CSIC)
Núria Paúl Fernández (IIBB-CSIC)
Marta Pulido (IIBB-CSIC)
Neus Rabaneda (IIBB-CSIC)
Susana Revilla (IIBB-CSIC)
Maurizio Riga (IDIBAPS)
Blanca Torroba (IIBB-CSIC)
Eva Troyano (IIBB-CSIC)
Dana Tupa (Universitat Basel)
Sara Sarroca (IIBB-CSIC)
Cristina Villacampa (IIBB-CSIC)
Laura Vuolo (IIBB-CSIC)

TECHNICIANS
Leticia Campa (IIBB-CSIC)
Mireia Galofré (IDIBAPS)
Noemí Jurado (IIBB-CSIC)
Rocío Martín-Álvarez (CIBERNED)
Anghara Menéndez (IDIBAPS)
Mercedes Nuñez (IIBB-CSIC)
Albert Parull (IIBB-CSIC)
Verónica Paz (CIBERSAM)

Irene Porcar (IIBB-CSIC)
Rosario Ruiz (UB)
Silvia Serrano (CIBERNED)
Esther Ruíz (IDIBAPS)

ADMINISTRATIVE STAFF
María Jaramillo (CIBERSAM)

COLLABORATORS
Perla Kaliman (IIBB-CSIC)
Mathieu Lichtenstein (IIBB-CSIC)
Laia Lladó (IIBB-CSIC)
Nair Olguin (IIBB-CSIC)
Noemí Santana (CIBERSAM)
Tony Valente (IIBB-CSIC)

STRATEGIC OBJECTIVES

Furthering of knowledge of the physiopathological mechanisms of neurological and psychiatric diseases and neurotoxic and aging processes of the central nervous system, with a view to identifying new cellular and functional targets and proposing new treatments.

MAIN LINES OF RESEARCH

The Systems Neuropharmacology group studies the brain circuits and neuronal elements involved in the physiopathology and treatment of depression and schizophrenia. Special emphasis is placed on the prefrontal cortex and anatomically and functionally related areas. It also explores chemical neurotransmission processes and physiology in genetic and pharmacological models of psychiatric diseases, with a view to identifying new therapeutic targets.

The Neurotoxicity and Neurodegeneration Mechanisms group carries out studies on nerve cell death, oxidative stress, synaptic functions, genomics and proteomics, for the determination of altered targets in toxicity and aging processes of the central nervous system in vivo and in vitro. It also focuses on neuroprotective strategies and the development of in vitro methods for predicting neurotoxicity. Studies of age-related cognitive loss focus in the preventive therapies of physical exercise and healthy diet and the signaling mechanisms involved.

The Molecular Neuropharmacology group is focussed in neurotransmission and its anatomical, cellular and molecular aspects implicated in neurodegenerative disorders with an inflammatory component: 1) Modulation by cAMP regulation of cytokines and cells involved in neuroinflammation in the CNS of multiple sclerosis mice model EAE; 2) Proteomic identification and validation of proteins differentially altered in the brain of Alzheimer's disease and argyrophilic grain disease patients; 3) Use of agonists for serotonin 5-HT4 receptors as a treatment for Alzheimer's disease. Study in animal models.

The study of novel targets to modulate neuroinflammation. The Cellular Neurobiology group is focused on the role of transcription factors of the C/EBP family and of neuronal-microglial communication molecules (CD200, CD200R, TREM2) in microglial activation and in microglial-induced neurotoxicity. They use primary cell cultures (mixed glial, astroglial and microglial-enriched, neuronal, mixed neuron-glial), cell lines and in vivo models of neuroinflammation (systemic LPS) and neurodegeneration (EAE, ME7 prion, G93A-SOD1 mice).

Wingless (Wnt) and Hedgehog (Hh) signalling pathways are chief during embryonic development. However, their abnormal regulation causes growth malformations and different neoplastic pathologies. The Neuronal Proliferation Control group, is currently studying whether the polarity anomalies caused by oncogenic forms of β-Catenin, the main effector of Wnt pathway, are at the origin of Wnt subtype of Medulloblastomas. In addition, in another independent but related project we are trying to unravel the complex regulation of Adenylyl Cyclases induced by Sonic Hedgehog signalling pathway.

RESEARCH GROUP
SYSTEMS NEUROPHARMACOLOGY GROUP

GROUP LEADER
Francesc Artigas (IIBB-CSIC)

The group studies the brain networks involved in the physiopathology and treatment of depression and schizophrenia.

RESEARCH GROUP
NEUROTOXICITY AND NEURODEGENERATION MECHANISMS GROUP

GROUP LEADER
Cristina Suñol (IIBB-CSIC)

The group studies neuronal targets in toxicity and aging processes by using in vivo and in vitro models. It also focuses on neuroprotection and on preventive therapies of physical exercise and healthy diet strategies for age-related cognitive loss.

RESEARCH GROUP
MOLECULAR NEUROPHARMACOLOGY GROUP

GROUP LEADER
Guadalupe Mengod (IIBB-CSIC)

Neurodegenerative diseases such as multiple sclerosis, Alzheimer's disease and argyrophilic grain disease, both in animal models and human post-mortem brain tissue.

RESEARCH GROUP
CELLULAR NEUROBIOLOGY GROUP

GROUP LEADER
Josep Saura (UB)

The Cellular Neurobiology group is focused on the study of neuroinflammation.

RESEARCH GROUP
NEURONAL PROLIFERATION CONTROL GROUP

GROUP LEADER
Sebastián Pons (IIBB-CSIC)

Mechanisms controlling the proliferation of neuronal precursors during both normal development and in neoplastic growth with especial focus on the molecular and cellular anomalies that contribute to Medulloblastoma.

PUBLICATIONS

Originals / I.F.: 98.179

1. Schneeberger M, Dietrich MO, Sebastián D, Imbernón M, Castaño C, Garcia A, Esteban Y, Gonzalez-Franquesa A, Castrillón Rodríguez I, Bortolozzi A, Garcia-Roves PM, Gomis R, Nogueiras R, Horvath TL, Zorzano A, Claret M. **Mitofusin 2 in POMC neurons connects ER Stress with leptin resistance and energy imbalance.** *Cell* 155:172-187 I.F.: 31.957

2. Valente T, Straccia M, Gresa-Arribas N, Dentesano G, Tusell JM, Serratosa J, Mancera P, Solà C, Saura J. **CCAAT/enhancer binding protein δ regulates glial proinflammatory gene expression.** *Neurobiol Aging* 34:2110-2124 I.F.: 6.166

3. Rojas S, Herance JR, Gispert JD, Abad S, Torrent E, Jiménez X, Pareto D, Perpiña U, Sarroca S, Rodríguez E, Ortega-Aznar A, Sanfeliu C. **In vivo evaluation of amyloid deposition and brain glucose metabolism of 5XFAD mice using Positron Emission Tomography.** *Neurobiol Aging* 34:1790-1798 I.F.: 6.166

4. Miguez D, Gil-Guiñon E, Pons S and Marti E. **Smad2 and Smad3 cooperate and antagonize simultaneously in vertebrate neurogenesis.** *J Cell Sci* 126(23):5335-5343 I.F.: 5.877

5. Santana N, Mengod G, Artigas F. **Expression of alpha1-adrenergic receptors in rat prefrontal cortex: cellular co-localization with 5-HT2A receptors.** *Int.J. Neuropsychopharmacol* 16:1139-1151 I.F.: 5.641

6. Slavikova B, Bujons Ja, Matyas L, Vidal M, Babot Z, Kristofikova S, Suñol C, Kasal A. **Allopregnanolone and pregnanolone analogues modified in the C ring: synthesis and activity.** *J Med Chem* 56:2323-2336 I.F.: 5.614

7. Berenguer J, Herrera A, Vuolo L, Torroba B, Llorens F, Sumoy L and Pons S. **Mir-22 regulates cell-cycle length in Cerebellar Granular Neuron Precursors.** *Mol Cell Biol* 33(14):2706-2717 I.F.: 5.614

8. Straccia M, Dentesano G, Valente T, Pulido-Salgado M, Solà C, Saura J. **CCAAT/enhancer binding protein β regulates prostaglandin E synthase expression and prostaglandin E2 production in activated microglial cells.** *Glia* 61:1607-1619 I.F.: 5.066

9. Marin C, Bonastre M, Mengod G, Cortes R, Rodriguez-Oroz MC, Obeso JA. **Subthalamic 6-OHDA-induced lesion attenuates levodopa-induced dyskinesias in the rat model of Parkinson's disease.** *Exp Neurol* 250:304-312 I.F.: 4.645

10. Ferrés-Coy A, Pilar-Cuellar F, Vidal R, Paz V, Masana M, Cortés R, Carmona MC, Campa L, Pazos A, Montefeltro A, Valdizán EM, Artigas F, Bortolozzi A. **RNAi-mediated serotonin transporter suppression rapidly increases serotonergic neurotransmission and hippocampal neurogenesis.** *Transl Psychiatry*; 3:e211. I.F.: 4.360

11. Ferrés-Coy A, Santana N, Castañé A, Cortés R, Carmona MC, Toth M, Montefeltro A, Artigas F, Bortolozzi A. **Acute 5-HT(1A) autoreceptor knockdown increases antidepressant responses and serotonin release in stressful conditions.** *Psychopharmacology* 225:61-74 I.F.: 4.061

12. Moral-Vico J, Carretero NM, Perez E, Suñol C, Lichtenstein M, Casañ-Pastor N. **Dynamic electrodeposition of aminoacid-polypyrrole on aminoacid-PEDOT substrates:Conducting polymer bilayers as electrodes in neural systems**. *Electrochim. Acta* 111: 250-260 I.F.: 3.777

13. Montes de Oca L, Moreno M, Cardona D, Campa L, Suñol C, Galofré M, Flores P, Sánchez-Santed F. **Long term compulsivity on the 5-choice serial reaction time task after acute Chlorpyrifos exposure.** *Toxicol Lett* 216:73-85 I.F.: 3.145

14. Sanabra C, Johansson EM, Mengod G. **Critical role for PDE4 subfamilies in the development of experimental autoimmune encephalomyelitis.** *J Chem Neuroanat* 47:96-105 I.F.: 2.475

15. Lopez-Gimenez JF, Vilaro MT, Palacios JM, Mengod G. **Multiple conformations of 5-HT and 5-HT receptors in rat brain: an autoradiographic study with [I](+/-)DOI.** *Exp Brain Res* 230:395-406 I.F.: 2.221

16. Reiner GN, Delgado-Marín L, Olguín N, Sánchez-Redondo S, Sánchez-Borzone M, Rodríguez-Farré E, Suñol C, García DA. **Gabaergic Pharmacological Activity of Propofol Related Compounds as Possible Enhancers of General**

Anesthetics and Interaction with Membranes. *Cell Biochem Biophys* 67:515-525 I.F.: 1.912

Reviews / I.F.: 25.442

1. Artigas F. **Serotonin receptors involved in antidepressant effects.** *Pharmacol Ther* 137:119-131 I.F.: 7.793

2. Celada P, Llado-Pelfort L , Santana N, Kargieman L, Troyano-Rodriguez E, Riga MS, Artigas F. **Disruption of thalamocortical activity in schizophrenia models: relevance to antipsychotic drug action.** *Int J Neuropsychopharmacol* 16:2145-2163 I.F.: 5.641

3. Celada P, Bortolozzi A, Artigas F. **Serotonin 5-HT1A receptors as targets for agents to treat psychiatric disorders: rationale and Current Status of research.** *CNS Drugs* 27:703-716 I.F.: 4.826

4. Artigas F. **Future directions for serotonin and antidepressants.** *ACS Chem Neurosci* 4:5-8 I.F.: 3.871

5. Pallàs M, Porquet D, Vicente A, Sanfeliu C. **Resveratrol: new avenues for a natural compound in neuroprotection.** *Curr Pharm Des* 19:6726-6731 I.F.: 3.311

Editorials / I.F.: 5.641

1. Frazer A, Artigas F. **Preclinical models of schizophrenia.** Int J Neuropsychopharmacol 16:2129 I.F.: 5.641

GRANTS FOR RESEARCH IN PROGRESS

Adell A. **Papel de la corteza prefrontal en la fisiopatología y tratamiento de la depresión y esquizofrenia. Estudio con modelos animales.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI10/01103.
Duration: 01/01/2011-31/12/2013.

Artigas F. **Grup de Recerca Consolidat, Neuroquímica i Neurofarmacologia.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009SGR220.
Duration: 01/01/2009-31/12/2013.

Artigas F. **Novel Methods leading to New Medications in Depression and Schizophrenia (NEWMEDS).** Sponsored by: Innovative Medicines Initiative (IMI) 115008.
Duration: 01/09/2009-31/08/2014.

Artigas F. **Papel de la corteza infralímbica en depresión: conectividad funcional y desarrollo de un modelo animal.** Sponsored by: Ministerio de Economia y Competitividad. SAF2012-35183.
Duration: 01/01/2013-31/12/2015

Bortolozzi A, Artigas F. **DENDRIA -Modulación de los genes asociados al sistema serotonérgico con moléculas RNA antisentido (siRNA) y su efecto en modelos de depresión.** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI) 10/166.
Duration: 01/07/2010-31/12/2013.

Bortolozzi A. **K2P Potassium Channels: A New Therapeutic Target for Mood and Cognitive Disorders.** Sponsored by: Brain and Behavior Research Foundation. NARSAD13_IIG_01.
Duration: 15/09/2013-14/09/2015

Bortolozzi A. **Papel de los canales de K en el mecanismo de acción de los fármacos antidepresivos. Relevancia del canal TREK-1 y su relación con el receptor de serotonina1A.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00290.
Duration: 01/01/2011-30/06/2014

Bortolozzi A. **Supresión de la expresión de alfa-sinucleina y de la actividad de PDE10 como estrategia terapéutica combinada para el tratamiento de parkinson y mejora de las disfunciones cognitivas derivadas.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2012-1208-300000.
Duration: 01/01/2013-31/03/2015

Celada M.P. **Actividad cortical y alucinaciones. Nuevo modelo experimental para la identificación de dianas terapéuticas en esquizofrenia.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI09/1245.
Duration: 01/01/2010-30/06/2013

Celada M.P. **Actividad de la corteza prefrontal en nuevas estrategias antidepresivas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/00156.
Duration: 01/01/2013-31/12/2015

Celada M.P. **Apoyo tecnológico referente al proyecto: "Caracterizar la actividad oscilatoria cortical en ratones transgénicos PKEHUM0801 y su afectación por el antipsicótico clozapina".** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI) 10/156.
Duration: 18/05/2010-31/12/2013

Cortés R. **Expresión de marcadores neuronales en demencias: enfermedad de los granos argirófilos y Alzheimer.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PS09/01087.
Duration: 01/01/2010-31/12/2013.

Mengod G. **El papel de las fosfodiesterasas del AMPc en la evolución y tratamiento de la esclerosis múltiple en el modelo de EAE en ratón. Nuevas aproximaciones terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI10/01874.
Duration: 01/01/2011-30/06/2015

Pons S. **Mecanismos de control de la proliferación y la diferenciación celular durante el desarrollo del sistema nervioso.** Sponsored by: Ministerio de Economía y Competitividad. BFU2011-24099.
Duration: 01/01/2012-31/12/2014

Rodríguez Farré E. **Grup de Recerca Consolidat, Farmacologia i Toxicologia.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 2009SGR214.
Duration: 01/01/2009-31/12/2013

Sanfeliu C. **Disfunción cerebral durante el envejecimiento: relevancia para la enfermedad de Alzheimer (BrainAge).** Sponsored by: Ministerio de Economía y Competitividad. CSD2010-00045. Duration: 27/12/2010-26/12/2015.

Sanfeliu C. **Interplay Sirtuin 1-AMPK-mTOR on mitochondrial frailty processes as a target for the prevention of neurodegeneration: Implications for Alzheimer's disease.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-39852-C02-02. Duration: 1/01/2013-31/12/2015

Saura J. **Efecto antiinflamatorio y neuroprotector de la inhibición de C/EBPβ y C/EBPδ en un modelo animal de esclerosis múltiple.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI10/378. Duration: 01/01/2011-31/12/2013.

Solà, C. **Modulació de l'activitat dels receptors immunitaris: nova estratègia terapèutica per al dany agut al SNC.** Sponsored by: Fundació la Marató deTV3. Duration: 01/01/2012-31/12/2014.

Solà, C. **El receptor inmune inhibitorio CD200R1 en el control de la neuroinflamación: implicaciones terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/709. Duration: 01/01/2013-31/12/2015.

Suñol C. **Estudio de mecanismos de neurotoxicidad crónica de contaminantes tóxicos: papel de los receptores GABA-A, de glutamato y de estrógenos. Posibles intervenciones terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PS10/00453. Duration: 01/01/2011-31/12/2013.

Suñol C. **Nano-structured Electroactive Materials for Electrodes in Central Nervous System (CNS) stimulation and repair.** Sponsored by: Fundació la Marató de TV3, 110131. Duration: 01/01/2012 – 31/12/2014

Vilaró MT. **Efecto de la activación de receptores 5-HT4 de serotonina sobre la deposición del péptido amiloide Aß, en un ratón triple transgénico de la enfermedad de Alzheimer.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PS09/00468. Duration: 01/01/2010-31/12/2013.

DOCTORAL THESES

Artigas F. **Alteració dels Circuits Talamocorticals en el Model NMDA d'Esquizofrènia. Reversió per Antipsicòtics.**
PhD student: Eva Troyano Rodríguez.

Vilaró MT. **Efecto de la activación de receptores de serotonina 5-HT4 sobre la patología amiloide y el deterioro cognitivo en el modelo triple transgénico 3xTg-AD de la enfermedad de alzehimer.**
PhD student: Ana García Miralles.

Adell A. **Papel de la corteza prefrontal en la fisiopatología y tratamiento de la depresión. Estudios en modelos animales.**
PhD student: Laura Jiménez Sánchez.

Sanfeliu C, Cristofol RM. **Neuroprotection by Physical Exercise and GDNF Transfection Therapies in the 3xTg-AD Mouse and MC65 Cell Models of Alzheimer's Disease.**
PhD student: Susana Revilla Ortueta.

4.2 Brain ischemia: Clinical and experimental studies

LOCATION
CELLEX building
IIBB-CSIC labs

KEYWORDS
1. **Brain**
2. **Stroke**
3. **Cerebrovascular diseases**
4. **Neuroinflamamtion**
5. **Oxidative stress**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	103.37	14	10	2
2012	51.04	10	10	-
2013	86.09	17	14	2

TEAM LEADER
Ángel Chamorro (HCB)
T. 93 363 83 27
achamorro@clinic.cat

RESEARCHERS
Sergi Amaro (HCB)
Lluïsa Camón (IIBB-CSIC)
Álvaro Cervera (HCB)
Carles Justicia (IIBB-CSIC)
Emili Martínez (IIBB-CSIC)
Valérie Petegnief (IIBB-CSIC)
Anna M. Planas (IIBB-CSIC)
Esther Pozas (IDIBAPS)
Tomàs Santalucia (IDIBAPS)
Xabier Urra (HCB)
Núria de Vera (IIBB-CSIC)

PRE-DOCTORAL RESEARCHERS
Ester Bonfill (IIBB-CSIC)
Javier Codas (HCB)
Maura Ferrer (IDIBAPS)
Isabel Pérez de Puig (IDIBAPS)
Xavier de la Rosa Siles (CSIC)
Angélica Salas (IDIBAPS)

TECHNICIANS
Ana Guerrero (IDIBAPS)
Carlos Laredo (HCB)
Leonardo J. Márquez (IIBB-CSIC)
Francisca Ruiz (IDIBAPS)

NURSING STAFF
Elisabet González (HCB)

COLLABORATORS
Vanessa Brait (IDIBAPS)
Laura Llull (HCB)
Francesc Miró (IDIBAPS)
Víctor Obach (HCB)
Martha Vargas (FCRB)

STRATEGIC OBJECTIVES

Study of cerebrovascular pathology from the clinical and basic perspective, with special emphasis on inflammation and immune response, and oxidative stress, as well as on the use of neuroimaging techniques.
The ultimate aim is to develop therapeutic strategies in application to stroke.

MAIN LINES OF RESEARCH

Inflammation and immunity in stroke

- Immunological mechanisms implicated in the progression of ischemic stroke and in the appearance of infectious complications. Study of inflammatory and innate immune responses in stroke. Genetic aspects of immune response. Studies of the lectin pathway.
- Study of brain-derived antigens in secondary lymphoid organs and its involvement in brain damage after stroke
- Relevance of adaptive immune responses in stroke outcome

Multimodal neuroimaging in Stroke

- Neuroimaging in brain ischemia: application of magnetic resonance (MR), CT or optical imaging techniques for the in vivo noninvasive monitorization of patients and experimental animals in relation to anatomical and functional parameters of brain damage – including immune response. Application in the vascular dementia model and the studies of functional recovery after stroke.

Neuroprotection

- Identification of new antioxidant treatments in stroke. Preclinical studies of the protective effects of these treatments and of the mechanisms involved. Design and conduction of a phase III study involving the administration of uric acid in stroke patients treated with rtPA.
- Use of intraarterial rescue treatments with rtPA in patients previously treated with intravenous rtPA and selected by multimodal imaging techniques.
- Neurological repair and neurogenesis in brain ischemia: effect of inflammation upon neurogenesis; experimental functional MRI.

Clinical trials

- Combination of thrombolysis with antioxidants (uric acid).

PUBLICATIONS

Originals / I.F.: 86.085

1. Ribera J, Pauta M, Melgar-Lesmes P, Tugues S, Fernández-Varo G, Held KF, Soria G, Tudela R, Planas AM, Fernández-Hernando C, Arroyo V, Jiménez W, Morales-Ruiz M. **Increased nitric oxide production in lymphatic endothelial cells causes impairment of lymphatic drainage in cirrhotic rats.** *Gut* 62(1):138-45 I.F.: 10.732

2. Ringelstein EB, Thijs V, Norrving B, Chamorro A, Aichner F, Grond M, Saver J, Laage R, Schneider A, Rathgeb F, Vogt G, Charissé G, Fiebach JB, Schwab S, Schäbitz WR, Kollmar R, Fisher M, Brozman M, Skoloudik D, Gruber F, Serena Leal J, Veltkamp R, Köhrmann M, Berrouschot J; AXIS 2 Investigators. **Granulocyte colony-stimulating factor in patients with acute ischemic stroke: results of the AX200 for Ischemic Stroke trial.** *Stroke* 44(10):2681-2687 I.F.: 6.158

3. Strbian D, Ringleb P, Michel P, Breuer L, Ollikainen J, Murao K, Seiffge DJ, Jung S, Obach V, Weder B, Eskandari A, Gensicke H, Chamorro A, Mattle HP, Engelter S, Leys D, Numminen H, Köhrmann M, Hacke W, Tatlisumak T. **Ultra-early intravenous stroke thrombolysis: do all patients benefit similarly?** *Stroke* 44(10):2913-2916 I.F.: 6.158

4. Strbian D, Seiffge DJ, Breuer L, Numminen H, Michel P, Meretoja A, Coote S, Bordet R, Obach V, Weder B, Jung S, Caso V, Curtze S, Ollikainen J, Lyrer PA, Eskandari A, Mattle HP, Chamorro A, Leys D, Bladin C, Davis SM, Köhrmann M, Engelter ST, Tatlisumak T. **Validation of the DRAGON score in 12 stroke centers in anterior and posterior circulation.** *Stroke* 44(10):2718-2721 I.F.: 6.158

5. Strbian D, Michel P, Ringleb P, Numminen H, Breuer L, Bodenant M, Seiffge DJ, Jung S, Obach V, Weder B, Tiainen M, Eskandari A, Gumbinger C, Gensicke H, Chamorro A, Mattle HP, Engelter ST, Leys D, Köhrmann M, Parkkila AK, Hacke W, Tatlisumak T. **Relationship between onset-to-door time and door-to-thrombolysis time: a pooled analysis of 10 dedicated stroke centers.** *Stroke* 44(10):2808-2813 I.F.: 6.158

6. Perez-Asensio FJ, Perpiñá U, Planas AM, Pozas E. **Interleukin-10 regulates progenitor differentiation and modulates neurogenesis on adult brain.** *J Cell Sci* 126:4208-4219 I.F.: 5.877

7. Fox K, Bousser MG, Amarenco P, Chamorro A, Fisher M, Ford I, Hennerici MG, Mattle HP, Rothwell PM; PERFORM Study Investigators. **Heart rate is a prognostic risk factor for myocardial infarction: a post hoc analysis in the PERFORM (Prevention of cerebrovascular and cardiovascular Events of ischemic origin with teRutroban in patients with a history oF ischemic strOke or tRansient ischeMic attack) study population.** *Int J Cardiol* 168(4):3500-3505 I.F.: 5.509

8. Pérez-de Puig I, Miró F, Salas-Pérdomo A, Bonfill-Teixidor E, Ferrer-Ferrer M, Márquez-Kisinousky L, Planas AM. **IL-10 deficiency exacerbates the brain inflammatory response to permanent ischemia without preventing resolution of the lesion.** *J Cereb Blood Flow Metab* 33(12):1955-1966 I.F.: 5.398

9. de la Rosa X, Santalucia T, Fortin P-Y, Purroy J, Calvo M, Salas-Perdomo A, Justicia C, Couillaud F, Planas AM. **In vivo imaging induction of heat-shock protein-70 gene expression with fluorescence reflectance imaging and intravital confocal microscopy following brain ischemia in reporter mica.** *Eur J Nucl Med Mol Imag* 40(3):426-438 I.F.: 5.114

10. Medina-Pulido L, Molina-Arcas M, Justicia C, Soriano E, Burgaya F, Planas A, Pastor- Anglada M. **Role of hypoxia and P1 receptor activation on the high affinity concentrative adenosine transporter CNT2 in PC12 cells.** *Biochem J* 454(3):437-445 I.F.: 4.654

11. Amaro S, Llull L, Urra X, Obach V, Cervera Á, Chamorro Á. **Risks and benefits of**

early antithrombotic therapy after thrombolytic treatment in patients with acute stroke. *PLoS One* 8(8):e71132 I.F.: 3.730

12. Soria G, Tudela R, Márquez-Martín A, Camón L, Batallé D, Muñoz-Moreno E, Eixarch E, Puig J, Pedraza S, Vila E, Prats-Galino A, Planas AM. **The ins and outs of the BCCAo model for chronic hypoperfusion: a multimodal and longitudinal MRI approach.** *PLoS One* 8(9):e74631 I.F.: 3.730

13. Urra X, Ariño H, Llull L, Amaro S, Obach V, Cervera Á, Chamorro Á. **The outcome of patients with mild stroke improves after treatment with systemic thrombolysis.** *PLoS One* 8(3):e59420 I.F.: 3.730

14. Psilodimitrakopoulos S, Petegnief V, de Vera N, Hernández O, Artigas D, Planas AM, Loza-Alvarez P. **Quantitative imaging of microtubule alteration as an early marker of axonal degeneration after ischemia in neurons.** *Biophys J* 104(5):968-975 I.F.: 3.668

15. Tajes M, Ill-Raga G, Palomer E, Ramos-Fernámdez E, Guix FX, Bosch-Morató M, Guivernau B, Jiménez-Conde J, Ois A, Pérez-Asensio F, Rayes-Navarro M, Caballo C, Galán AM, Alameda F, Escolar G, Opazo C, Planas A, Roquer J, Valverde MA, Muñoz FJ. **Nitro-Oxidative Stress after Neuronal Ischemia Induces Protein Nitrotyrosination and Cell Death.** *Oxid Med Cell Longev* 2013:826143 I.F.: 3.393

16. Perez-de-Puig I, Martin A, Gorina R, de la Rosa X, Martinez E, Planas AM. **Induction of hemeoxygenase (HO)-1 expression after inhibition of HO activity promotes inflammation and worsens ischemic brain damage in mice.** *Neuroscience* 243:22-32 I.F.: 3.122

17. Buj R, Iglesias N, Planas AM, Santalucia T. **A plasmid toolkit for cloning chimeric cDNAs encoding customized fusion proteins into any Gateway destination expression vector BMC.** *Mol Biol* 14(1):18 I.F.: 2.796

Reviews / I.F.: 11.675

1. Ringelstein EB, Chamorro A, Kaste M, Langhorne P, Leys D, Lyrer P, Thijs V, Thomassen L, Toni D; ESO Stroke Unit Certification Committee. **European Stroke Organisation recommendations to establish a stroke unit and stroke center.** *Stroke* 44(3):828-840 I.F.: 6.158

2. Urra X, Chamorro A. **Emerging issues in acute ischemic stroke.** *J Neurol.* 2013 Jun;260(6):1687-92 I.F.: 3.578

3. Petegnief V, Planas AM. **SIRT1 regulation modulates stroke outcome.** *Transl Stroke Res* 4(6):663-71 I.F.: 1.939

Editorials / I.F.: 12.316

1. Planas AM. **Advances in Translational Medicine 2012.** *Stroke* 44(2):318-319 I.F.: 6.158

2. Dirnagl U, Hakim A, Macleod M, Fisher M, Howells D, Alan SM, Steinberg G, Planas A, Boltze J, Savitz S, Iadecola C, Meairs S. **A Concerted Appeal for International Cooperation in Preclinical Stroke Research.** *Stroke* 44(6):1754-1760 I.F.: 6.158

Multicenter / I.F.: 75.575

1. Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, Lindley R, Robinson T, Lavados P, Neal B, Hata J, Arima H, Parsons M, Li Y, Wang J, Heritier S, Li Q, Woodward M, Simes RJ, Davis SM, Chalmers J; INTERACT2 Investigators. **Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage.** *N Engl J Med* 368(25):2355-2365 I.F.: 51.658

2. Ederle J, Davagnanam I, van der Worp HB, Venables GS, Lyrer PA, Featherstone RL, Brown MM, Jäger HR; ICSS investigators. **Effect of white-matter lesions on the risk of periprocedural stroke after carotid artery stenting versus endarterectomy in the International Carotid Stenting Study (ICSS): a prespecified analysis of data from a randomised trial.** *Lancet Neurol* 12(9):866-872 I.F.: 23.917

GRANTS FOR RESEARCH IN PROGRESS

Cervera A. **Activación del complemento por la vía de la lectinas: relevancia clínica y utilidad de su inhibición para la mejoría pronóstica.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI10/01898. Duration: 01/01/2011-31/12/2013.

Chamorro A. **Enfermedades vasculares cerebrales (Ictus)**. Sponsored by: Instituto de Salud Carlos III (ISCIII) RD12/0014/0011. Duration: 01/01/2013-31/12/2016

Chamorro A. **Estudio de marcadores inmunológicos circulantes y tisulares (tejido linfoide y cerebro) y de su relación pronóstica en el paciente con ictus isquémico.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI09/1313. Duration: 01/01/2010-30/09/2013.

Chamorro A. **La respuesta inmune en el ictus: Papel de la especificidad antigénica.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/01437. Duration: 01/01/2013-31/12/2015

Chamorro A. **Uricoictus-fase III. Estudio doble ciego, aleatorizado frente a vehículo de la eficacia clínica del tratamiento combinado con ácido úrico y RTPA administrados por via intravenosa en pacientes con ictus isquémico de menos de 3 horas de evolución.** Sponsored by: Ministerio Sanidad y Consumo. EC07/90276. Duration: 29/10/2007-30/12/2013.

Petegnief V. **Boosting endogenous mechanisms for neural protection and repair after acute damage to the nervous system.** Sponsored by: Fundació la Marató de TV3. 110431. Duration: 01/01/2012 – 31/12/2014

Planas AM. **Affording recovery in Stroke**

(ARISE). Sponsored by: European Commission.
FP7- HEALTH-2007-2.2.1-1 – 201024.
Duration: 01/04/2008-01/03/2013.

Planas AM. **Imaging of Neuroinflammation in Neurodegenerative Diseases.** Sponsored by: European Commission 278850.
Duration: 01/03/2012-28/02/2017

Planas AM. **Estudios de neuroimagen.** Sponsored by: Ministerio de Economía y Competitividad, CENIT10 10/157.
Duration: 18/05/2010-31/12/2014.

Planas AM. **Múltiples facetas de la inflamación en el ictus: modulación de señales como estrategia terapéutica.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-30492-C02-01).
Duration: 01/01/2012 – 31/12/2014

Planas AM. **Role of danger signals in stroke and therapeutic targeting by nanobodies.** Sponsored by: Ministerio de Economía y Competitividad. PRI-PIMNEU-2011-1342.
Duration: 01/01/2012-31/12/2014

Planas A.M. **Grup d'investigació cerebrovascular (GICV).** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_890.
Duration: 28/09/2009-30/04/2014

Pozas E. **Neuroinflammation and adult neurogenesis after acute brain injury. Perspectives for neuronal recovery after brain damage.** Sponsored by: Fundació la Marató de TV3.
Duration: 31/01/2012-30/01/2015.

Pozas E. **Papel de las citocinas inflamatorias en la producción de nuevas neuronas y en la recuperación funcional ante una lesión cerebral aguda.** Sponsored by: Fundación MAPFRE. SA/11/AYU/115.
Duration: 01/01/2012-31/05/2013

4.3 Neurodegenerative diseases: Clinical and experimental research

LOCATION
CELLEX building

KEYWORDS
1. **Parkinson Disease**
2. **Alzheimer Disease**
3. **Degenerative neurological deiseases**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	237.08	44	24	10
2012	127.01	32	20	8
2013	242.04	40	31	7

TEAM INVOLVED IN
CIBERNED

TEAM LEADER
Eduardo Tolosa (HCB)
T. 93 227 57 85
etolosa@clinic.cat

RESEARCHERS
Mario Ezquerra (FCRB)
Albert Lladó (HCB)
Maria Josep Martí (HCB)
José Luís Molinuevo (HCB)
Esteban Muñoz (HCB)
Lorena Rami (FCRB)
Raquel Sánchez del Valle (HCB)
Francesc Valldeoriola (HCB)

POST-DOCTORAL RESEARCHERS
Anna Antonell (IDIBAPS)
Mircea Balasa (HCB)
Beatriz Bosch (IDIBAPS)
Yaroslau Compta (HCB)
Rubén Fernández-Santiago (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Maria Teresa Buongiorno (FCRB)
Magda Castellví (HCB)
Judith Navarro (IDIBAPS)
Jaume Olives (FCRB)
Claustre Pont (FCRB)
Dolores Vilas (FCRB)

TECHNICIANS
Esther Aguilar (FCRB)
Mercè Bonastre (FCRB)
Adrià Dangla (FCRB
Manel Fernández (FCRB)
Cristina Muñoz (IDIBAPS)

NURSING STAFF
Rosa Maria Álvarez (FCRB)
Ana Cámara (HCB)
Guadalupe Fernández (FCRB)

STRATEGIC OBJECTIVES

1. Development of research projects which yield results that hopefully have short term application, with a view to improving the diagnosis and treatment of neurodegenerative diseases. Many of the research lines are linked to clinical research protocols of the Neurology Service at the Hospital clinic Universitari.
2. Investigations on clinical, molecular and imaging biomarkers that characterize the preclinical phase of Parkinson and Alzheimer disease
3. Investigation of biological pathways involved in the pathogenesis of Alzheimer's disease and detection of new cognitive, biochemical and neuroimaging markers in preclinical and prodromal patients

MAIN LINES OF RESEARCH

1. LRRK2 associated Parkinson disease. Clinical, imaging and genetic characterizarion of the prodromic phase

2. Neurochemichal, genetic and imaging biomarkers of cognitive deterioration in Parkinson disease

3. Generation of IPSC-derived dopaminergic neurons by reprogramming of idiopathic and genetic Parkinson's disease patient skin fibroblasts. Molecular characterization and elucidation of underlying pathophysiologic mechanisms.

4. Whole-transcriptomic analysis of human postmortem brain tissues in Parkinson's disease and identification of associated pathogenic molecular processes.

5. Genetic and diagnostic and predictive marker studies in Alzheimer's disease and other dementias. Experimental functional neuroimaging studies in healthy and in pathological aging.

6. Study of the biological and molecular bases of Alzheimer's disease and Parkinson's disease in preclinical stages: mild cognitive impairment and pre-motor Parkinson's disease.

7. Study of genetically determined Alzheimer's disease and fronto temporal lobar degeneration: clinical, biochemical and neuroimaging characterization

RESEARCH GROUP
PARKINSON'S DISEASE AND MOVEMENT DISORDERS

GROUP LEADER
Eduardo Tolosa (HCB)

1. We have created a repository of biological material of subjects with LRRK2 associated Parkinson disease and their asymptomatic relatives. We have describe for the first time alpha-synuclein aggregates in epicardial fat tissue in living subjects without parkinsonism. a probable preclinical marker of Parkinson disease. A novel LRRK2 mutation that causes familiar Parkinson disease has been identified and brain transcriptomic profiling in idiopathic and LRRK2-associated Parkinson's disease performed.

2. We have consolidated a line of research on cerebrospinal fluid biomarkers in Parkinson dementia and established a correlation between neurochemical Alzheimer and imaging markers in Parkinson disease. Work has been initiated in Parkinson patients to characterize in vivo brain amyloid pathology with PET technology

PUBLICATIONS

Originals / I.F.: 242.044

1. Iranzo A, Tolosa E, Gelpi E, Molinuevo JL, Valldeoriola F, Serradell M, Sanchez-Valle R, Vilaseca I, Lomeña F, Vilas D, Lladó A, Gaig C, Santamaria J. **Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study.** *Lancet Neurol* (5):443-453 I.F.: 23.917

2. Wenning GK, Geser F, Krismer F, Seppi K, Duerr S, Boesch S, Köllensperger M, Goebel G, Pfeiffer KP, Barone P, Pellecchia MT, Quinn NP, Koukouni V, Fowler CJ, Schrag A, Mathias CJ, Giladi N, Gurevich T, Dupont E, Ostergaard K, Nilsson CF, Widner H, Oertel W, Eggert KM, Albanese A, del Sorbo F, Tolosa E, Cardozo A, Deuschl G, Hellriegel H, Klockgether T, Dodel R, Sampaio C, Coelho M, Djaldetti R, Melamed E, Gasser T, Kamm C, Meco G, Colosimo C, Rascol O, Meissner WG, Tison F, Poewe W; European Multiple System Atrophy Study Group. **The natural history of multiple system atrophy: a prospective European cohort study.** *Lancet Neurol* 12(3):264-274 I.F.: 23.917

3. Gauthier S, Molinuevo JL. **Benefits of combined cholinesterase inhibitor andmemantine treatment in moderate-severe Alzheimer's disease.** *Alzheimers Dement* 9(3):326-331 I.F.: 14.483

4. Mattsson N, Andreasson U, Persson S, Carrillo MC, Collins S, Chalbot S, Cutler N, Dufour Rainfray D, Fagan AM, Heegaard NH, Robin Hsiung GY, Hyman B, Iqbal K, Lachno DR, Lleó A, Lewczuk P, Molinuevo JL, Parchi P, Regeniter A, Rissman R, Rosenmann H, Sancesario G, Schröder J, Shaw LM, Teunissen CE, Trojanowski JQ, Vanderstichele H, Vandijck M, Verbeek MM, Zetterberg H, Blennow K, Käser SA; Alzheimer's Association QC Program Work Group. **CSF biomarker variability in the Alzheimer's Association quality control program.** *Alzheimers Dement* 9(3):251-261 I.F.: 14.483

5. Podlesniy P, Figueiro-Silva J, Llado A, Antonell A, Sanchez-Valle R, Alcolea D, Lleo A, Molinuevo JL, Serra N, Trullas R. **Low cerebrospinal fluid concentration of mitochondrial DNA in preclinical Alzheimer disease.** *Ann Neurol* 74(5):655-668 I.F.: 11.193

6. Pera M, Alcolea D, Sánchez-Valle R, Guardia-Laguarta C, Colom-Cadena M, Badiola N, Suárez-Calvet M, Lladó A, Barrera-Ocampo AA, Sepulveda-Falla D, Blesa R, Molinuevo JL, Clarimón J, Ferrer I, Gelpi E, Lleó A. **Distinct patterns of APP processing in the CNS in autosomal dominant and sporadic Alzheimer disease.** *Acta Neuropathol* 125(2):201-213 I.F.: 9.734

7. Armstrong MJ, Litvan I, Lang AE, Bak TH, Bhatia KP, Borroni B, Boxer AL, Dickson DW, Grossman M, Hallett M, Josephs KA, Kertesz A, Lee SE, Miller BL, Reich SG, Riley DE, Tolosa E, Tröster AI, Vidailhet M, Weiner WJ. **Criteria for the diagnosis of corticobasal degeneration.** *Neurology* 80(5):496-503 I.F.: 8.249

8. Jovicich J, Marizzoni M, Sala-Llonch R, Bosch B, Bartrés-Faz D, Arnold J, Benninghoff J, Wiltfang J, Roccatagliata L, Nobili F, Hensch T, Tränkner A, Schönknecht P, Leroy M, Lopes R, Bordet R, Chanoine V, Ranjeva JP, Didic M, Gros-Dagnac H, Payoux P, Zoccatelli G, Alessandrini F, Beltramello A, Bargalló N, Blin O, Frisoni GB; PharmaCog Consortium. **Brain morphometry reproducibility in multi-center 3T MRI studies: a comparison of cross-sectional and longitudinal segmentations.** *Neuroimage* 83:472-484 I.F.: 6.252

9. Antonell A, Lladó A, Altirriba J, Botta-Orfila T, Balasa M, Fernández M, Ferrer I, Sánchez-Valle R, Molinuevo JL. **A preliminary study of the whole-genome expression profile of sporadic and monogenic early-onset Alzheimer's disease.** *Neurobiol Aging* 34(7):1772-1778 I.F.: 6.166

10. Colom-Cadena M, Gelpi E, Martí MJ, Charif S, Dols-Icardo O, Blesa R, Clarimón J, Lleó A. **MAPT H1 haplotype is associated with enhanced α-synuclein deposition in dementia with Lewy bodies.** *Neurobiol Aging* 34(3):936-942 I.F.: 6.166

11. Moreno F, Sala-Llonch R, Barandiaran M, Sánchez-Valle R, Estanga A, Bartrés-Faz D, Sistiaga A, Alzualde A, Fernández E, Martí Massó JF, López de Munain A, Indakoetxea B. **Distinctive age-related temporal cortical thinning in asymptomatic granulin gene mutation carriers.** *Neurobiol Aging* 34(5):1462-1468 I.F.: 6.166

12. Ortega-Cubero S, Lorenzo-Betancor O, Lorenzo E, Alonso E, Coria F, Pastor MA, Fernández-Santiago R, Martí MJ, Ezquerra M, Valldeoriola F, Compta Y, Tolosa E, Agundez JA, Jiménez-Jiménez FJ, Gironell A, Clarimon J, de Castro P, García-Martín E, Alonso-Navarro H, Pastor P. **Fused in Sarcoma (FUS) gene mutations are not a frequent cause of essential tremor in Europeans.** *Neurobiol Aging* 34(10):2441.e9-2441.e11 I.F.: 6.166

13. Pereira JB, Junqué C, Bartrés-Faz D, Ramírez-Ruiz B, Marti MJ, Tolosa E. **Regional vulnerability of hippocampal subfields and memory deficits in Parkinson's disease.** *Hippocampus* 23(8):720-728 I.F.: 5.492

14. van der Zee J, Gijselinck I, Dillen L, Van Langenhove T, Theuns J, Engelborghs S, Philtjens S, Vandenbulcke M, Sleegers K, Sieben A, Bäumer V, Maes G, Corsmit E, Borroni B, Padovani A, Archetti S, Perneczky R, Diehl-Schmid J, de Mendonça A, Miltenberger-Miltenyi G, Pereira S, Pimentel J, Nacmias B, Bagnoli S, Sorbi S, Graff C, Chiang HH, Westerlund M, Sanchez-Valle R, Llado A, Gelpi E, Santana I, Almeida MR, Santiago B, Frisoni G, Zanetti O, Bonvicini C, Synofzik M, Maetzler W, Vom Hagen JM, Schöls L, Heneka MT, Jessen F, Matej R, Parobkova E, Kovacs GG, Ströbel T, Sarafov S, Tournev I, Jordanova A, Danek A, Arzberger T, Fabrizi GM, Testi S, Salmon E, Santens P, Martin JJ, Cras P, Vandenberghe R, De Deyn PP, Cruts M, Van Broeckhoven C; European Early-Onset Dementia Consortium. **A pan-European study of the C9orf72 repeat associated with FTLD: geographic prevalence, genomic instability, and intermediate repeats.** *Hum Mutat* 34(2):363-373 I.F.: 5.213

15. Boeve BF, Silber MH, Ferman TJ, Lin SC, Benarroch EE, Schmeichel AM, Ahlskog JE, Caselli RJ, Jacobson S, Sabbagh M, Adler C, Woodruff B, Beach TG, Iranzo A, Gelpi E, Santamaria J, Tolosa E, Singer C, Mash DC, Luca C, Arnulf I, Duyckaerts C, Schenck CH, Mahowald MW, Dauvilliers Y, Zarei M, Ibarretxe-Bilbao N, Compta Y, Hough M, Junque C, Bargallo N, Tolosa E, Martí MJ. **Cortical thinning is associated with disease stages and dementia in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(8):875-881 I.F.: 4.924

16. Segura B, Ibarretxe-Bilbao N, Sala-Llonch R, Baggio HC, Martí MJ, Valldeoriola F, Vendrell P, Bargalló N, Tolosa E, Junqué C. **Progressive changes in a recognition memory network in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(4):370-378 I.F.: 4.924

17. Compta Y, Revesz T, Lees AJ. **The more cortical amyloid-β, the more postural instability in Parkinson's disease: more grist to the mill for a link between walking, falling, and remembering?** *Movement Disord* 28(3):263-264 I.F.: 4.558

18. Stocchi F, Rascol O, Destee A, Hattori N, Hauser RA, Lang AE, Poewe W, Stacy M, Tolosa E, Gao H, Nagel J, Merschhemke M, Graf A, Kenney C, Trenkwalder C. **AFQ056 in Parkinson patients with levodopa-induced dyskinesia: 13-week, randomized, dose-finding study.** *Movement Disord* 28(13):1838-1846 I.F.: 4.558

19. Pereira JB, Junqué C, Bartrés-Faz D, Martí MJ, Sala-Llonch R, Compta Y, Falcón C, Vendrell P, Pascual-Leone A, Valls-Solé J, Tolosa E. **Modulation of verbal fluency networks by transcranial direct current stimulation (tDCS) in Parkinson's disease.** *Brain Stimul* 6(1):16-24 I.F.: 4.558

20. Atri A, Molinuevo JL, Lemming O, Wirth Y, Pulte I, Wilkinson D. **Memantine in patients with Alzheimer's disease receiving donepezil: new analyses of efficacy and safety for combination therapy.** *Alzheimers ResTher* 5(1):6 I.F.: 4.390

21. Colom-Cadena M, Gelpi E, Charif S, Belbin O, Blesa R, Martí MJ, Clarimón J, Lleó A. **Confluence of α-synuclein, tau, and β-amyloid pathologies in dementia with Lewy bodies.** *J Neuropathol Exp Neuro* 72(12):1203-1212 I.F.: 4.345

22. Arenaza-Urquijo EM, Molinuevo JL, Sala-Llonch R, Solé-Padullés C, Balasa M, Bosch B, Olives J, Antonell A, Lladó A, Sánchez-Valle R, Rami L, Bartrés-Faz D. **Cognitive reserve proxies relate to gray matter loss in cognitively healthy elderly with abnormal cerebrospinal fluid amyloid-β levels.** *J Alzheimers Dis* 35(4):715-726 I.F.: 4.174

23. Dal-Ré R, Fauria K, Gramunt N, Molinuevo JL. **Clinical observational research on Alzheimer's disease: what clinical trial registries can tell.** *J Alzheimers Dis* 34(1):183-190 I.F.: 4.174

24. Molinuevo JL, Gispert JD, Dubois B, Heneka MT, Lleo A, Engelborghs S, Pujol J, de Souza LC, Alcolea D, Jessen F, Sarazin M, Lamari F, Balasa M, Antonell A, Rami L. **The AD-CSF-index discriminates Alzheimer's disease patients from healthy controls: a validation study.** *J Alzheimers Dis* 36(1):67-77 I.F.: 4.174

25. Sala-Llonch R, Fortea J, Bartrés-Faz D, Bosch B, Lladó A, Peña-Gómez C, Antonell A, Castellanos-Pinedo F, Bargalló N, Molinuevo JL, Sánchez-Valle R. **Evolving brain functional abnormalities in PSEN1 mutation carriers: a resting and visual encoding fMRI study.** *J Alzheimers Dis* 36(1):165-175 I.F.: 4.174

26. López-Bosque MJ, Tejeda-Montes E, Cazorla M, Linacero J, Atienza Y, Smith KH, Lladó A, Colombelli J, Engel E, Mata A. **Fabrication of hierarchical micro nanotopographies for cell attachment studies.** *Nanotechnology* 24(25):255305 I.F.: 3.842

27. Rubio-Moscardo F, Setó-Salvia N, Pera M, Bosch-Morató M, Plata C, Belbin O,Gené G, Dols Icardo O, Ingelsson M, Helisalmi S, Soininen H, Hiltunen M, Giedraitis V, Lannfelt L, Frank A, Bullido MJ, Combarros O, Sánchez-Juan P, Boada M, Tárraga L, Pastor P, Pérez-Tur J, Baquero M, Molinuevo JL, Sánchez-Valle R, Fuentes-Prior P, Fortea J, Blesa R, Muñoz FJ, Lleó A, Valverde MA, Clarimón J. **Rare variants in calcium homeostasis modulator 1 (CALHM1) found in early onset Alzheimer's disease patients alter calcium homeostasis.** *PLoS One* 8(9):e74203 I.F.: 3.730

28. Eggington S, Valldeoriola F, Chaudhuri KR, Ashkan K, Annoni E, Deuschl G. **The cost-effectiveness of deep brain stimulation in combination with best medical therapy, versus best medical therapy alone, in advanced Parkinson's disease.** *J Neurol* 261(1):106-116 I.F.: 3.578

29. Grau-Rivera O, Gelpi E, Rey MJ, Valldeoriola F, Tolosa E, Compta Y, Martí MJ. **Prominent psychiatric symptoms in patients with Parkinson's disease and concomitant argyrophilic grain disease.** *J Neurol* 260(12):3002-3009 I.F.: 3.578

30. Volkmann J, Albanese A, Antonini A, Chaudhuri KR, Clarke CE, de Bie RM, Deuschl G, Eggert K, Houeto JL, Kulisevsky J, Nyholm D, Odin P, Østergaard K, Poewe W, Pollak P, Rabey JM, Rascol O, Ruzicka E, Samuel M, Speelman H, Sydow O, Valldeoriola F, van der Linden C, Oertel W. **Selecting deep brain stimulation or infusion therapies in advanced Parkinson's disease: an evidence-based review.** *J Neurol* 260(11):2701-2714 I.F.: 3.578

31. Solé-Padullés C, Bartrés-Faz D, Lladó A, Bosch B, Peña-Gómez C, Castellví M, Rami L, Bargalló N, Sánchez-Valle R, Molinuevo JL. **Donepezil treatment stabilizes functional connectivity during resting state and brain activity during memory encoding in Alzheimer's disease.** *J Clin Psychopharmacol* 33(2):199-205 I.F.: 3.513

32. Compta Y, Pereira JB, Ríos J, Ibarretxe-Bilbao N, Junqué C, Bargalló N, Cámara A, Buongiorno M, Fernández M, Pont-Sunyer C, Martí MJ. **Combined dementia-risk biomarkers in Parkinson's disease: a prospective longitudinal study.** *Parkinsonism Relat Disord* 19(8):717-724 I.F.: 3.274

33. Iranzo A, Serradell M, Vilaseca I, Valldeoriola F, Salamero M, Molina C, Santamaria J, Tolosa E. **Longitudinal assessment of olfactory function in idiopathic REM sleep behavior disorder.** *Parkinsonism Relat Disord* 19(6):600-604 I.F.: 3.274

34. Navarro-Otano J, Gelpi E, Mestres CA, Quintana E, Rauek S, Ribalta T, Santiago V, Tolosa E. **Alpha-synuclein aggregates in epicardial fat tissue in living subjects without parkinsonism.** *Parkinsonism Relat Disord* 19(1):27-31 I.F.: 3.274

35. Siri C, Duerr S, Canesi M, Delazer M, Esselink R, Bloem BR, Gurevich T, Balas M, Giladi N, Santacruz P, Marti F, Tolosa E, Rubino A, Meco G, Poewe W, Pezzoli G, Wenning G, Antonini A. **A cross-sectional multicenter study of cognitive and behavioural features in multiple system atrophy patients of the parkinsonian and cerebellar type.** *J Neural Transm* 120(4):613-8 I.F.: 3.052

36. Gil-Navarro S, Lladó A, Rami L, Castellví M, Bosch B, Bargalló N, Lomeña F, Reñé R, Montagut N, Antonell A, Molinuevo JL, Sánchez-Valle R. **Neuroimaging and biochemical markers in the three variants of primary progressive aphasia.** *Dement Geriatr Cogn Disord* 35(1-2):106-117 I.F.: 2.787

37. Cummings JL, Dubois B, Molinuevo JL, Scheltens P. **International Work Group criteria for the diagnosis of Alzheimer disease.** *Med Clin North Am* 97(3):363-368 I.F.: 2.607

38. Casals-Coll M, Sánchez-Benavides G, Meza-Cavazos S, Manero RM, Aguilar M, Badenes D, Molinuevo JL, Robles A, Barquero MS, Antúnez C, Martínez-Parra C, Frank-García A, Fernández M, Blesa R, Peña-Casanova J; NEURONORMA Study Team. **Spanish multicenter normative studies (NEURONORMA project): normative data andequivalence of four BNT short-form versions.** *Arch Clin Neuropsychol* 29(1):60-74 I.F.: 2.000

39. Gelpi E, Soler Insa JM, Parchi P, Saverioni D, Yagüe J, Nos C, Martínez-Saez E, Ribalta T, Ferrer I, Sanchez-Valle R. **Atypical neuropathological sCJD-MM henotype with abundant white matter Kuru-type plaques sparing the cerebellar cortex.** *Neuropathology* 33(2):204-208 I.F.: 1.909

40. Grossberg G, Cummings J, Frölich L, Bellelli G, Molinuevo JL, Krahnke T, Strohmaier C. **Efficacy of higher dose 13.3 mg/24 h rivastigmine patch on instrumental activities of daily living in patients with mild-to-moderate Alzheimer's disease.** *Am J Alzheimers Dis Other Demen* 28(6):583-591 I.F.: 1.518

Review / **I.F.: 11.126**

1. Ferreira JJ, Katzenschlager R, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Schüpbach M, Tolosa E, Trenkwalder C, Schapira A, Berardelli A, Oertel WH. **Summary of the recommendations of the EFNS/MDS-ES review on therapeutic management of Parkinson's disease.** *Eur J Neurol* 20(1):5-15 I.F.: 4.162

2. Müller T, van Laar T, Cornblath DR, Odin P, Klostermann F, Grandas FJ, Ebersbach G, Urban PP, Valldeoriola F, Antonini A. **Peripheral neuropathy in Parkinson's disease: levodopa exposure and implications for duodenal delivery.** *Parkinsonism Relat Disord* 19(5):501-507 I.F.: 3.274

3. Molinuevo JL, Rami L. **Applying the IWG research criteria in clinical practice: feasibility and ethical issues.** *Med Clin N Am* 97(3):477-84 I.F.: 2.607

4. Salat D, Tolosa E. **Levodopa in the treatment of Parkinson's disease: current status and new developments.** *J Parkinsons Dis* 3(3):255-269 I.F.: 1.083

Clinical guidelines / **I.F.: 15.518**

1. Martí MJ, Tolosa E. **Parkinson disease: New guidelines for diagnosis of Parkinson disease.** *Nat Rev Neurol* 9(4):190-191 I.F.: 15.518

Multicenter / **I.F.: 8.265**

1. Quadri M, Fang M, Picillo M, Olgiati S, Breedveld GJ, Graafland J, Wu B, Xu F, Erro R, Amboni M, Pappatà S, Quarantelli M, Annesi G, Quattrone A, Chien HF, Barbosa ER; International Parkinsonism Genetics Network, Oostra BA, Barone P, Wang J, Bonifati V. **Mutation in the SYNJ1 gene associated with autosomal recessive, early-onset Parkinsonism.** *Hum Mutat* 34(9):1208-1215 I.F.: 5.213

2. LeWitt PA, Boroojerdi B, Surmann E, Poewe W; SP716 Study Group; SP715 Study Group. **Rotigotine transdermal system for long-term treatment of patients with advanced Parkinson's disease: results of two open-label extension studies, CLEOPATRA-PD and PREFER.** *J Neural Transm* 120(7):1069-1081 I.F.: 3.052

GRANTS FOR RESEARCH IN PROGRESS

Llado A. **Caracterización clínico-biológica de la emfermedad de Alzheimer de inicio precoz: desde las fases predemencia a los hallazgos neuropatológicos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00234. Duration: 01/01/2012-31/12/2014

Marti M.J. **PET-FDDNP y diagnóstico in vivo de taupatíaen el parkinsonismo inclasificable.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/02031. Duration: 01/01/2012-31/12/2014

Molinuevo J.L. **Disfunción cerebral durante el envejecimiento: relevancia para la enfermedad de Alzheimer.** Sponsored by: Ministerio de Economía y Competitividad. CSD2010-00045. Duration: 27/12/2010-26/12/2015

Molinuevo J.L. **Biomarkers for Alzheimer's Disease and Parkinson's Disease.** Sponsored by: European Commission. JPND_JTC_11_002. Duration: 01/01/2012-31/12/2014

Molinuevo J.L. **BIOMARKAPD: Biomarkers for Alzheimer's disease and Parkinson's disease.** Sponsoredby: Instituto de Salud Carlos III (ISCIII). PI11/03023 (JPND). Duration: 01/01/2012-31/12/2014

Molinuevo J. **Characterization of subjects with objective or subjective memory impairment with Alzheimer's disease biomarkers. Analysis of the cerebrospinal fluid and magnetic resonance imaging as predictors of their cognitive evolution** Sponsored by:. ISCIII (programa Miguel Servet) CP08/00147. Duration: 7/1/2009-6/1/2015

Rami L. **Cambios cognitivos y de resonancia magnética en sujetos con cognición normal y evidencia biológica de enfermedad de Alzheimer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01071. Duration: 01/01/2012-31/12/2014

Rami L. **Estudio, promoción y difusión del impacto de factores relacionados con el envejecimiento saludable en la cognición de sujetos sanos con biomarcador positivo para la enfermedad de Alzheimer y promoción de un envejecimiento saludable.** Sponsored by: Fundación MAPFRE. SA/12/AYU/S01. Duration: 14/02/2013-14/03/2014

Sanchez-Valle R. **Estudio de portadores de mutaciones determinantes de enfermedad de Alzheimer genética en fases preclínicas cognición, neuroimagen estructural y funcional y marcadores bioquímicos.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/00013.
Duration: 01/01/2013-31/12/2015

Tolosa E. **Fox Trial Finder Spain.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2013_01.
Duration: 01/01/2013-30/06/2014

Tolosa E. **Neuropathological tissue collection in LRRK2 mutation carriers with and without Parkinson's disease.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2013_02.
Duration: 16/02/2012-31/12/2014

Tolosa E. **Penetrance of LRRK2 in the MJ Fox LRRK Cohort Consortium.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2013_03.
Duration: 18/09/2013-17/09/2014

Tolosa E. **LRRK2 Cohort Consortium Writing Grant - Publishing on Prodromal LRRK2 Parkinsonism**. Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2013_4.
Duration: 19/06/2013-18/06/2014

Tolosa E. **LRRK2 Mutations and Cancer Risk.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2012_01.
Duration: 18/09/2012-17/09/2014

Tolosa E. **Gait and motor symptoms in healthy asymptomatic relatives of Patients with PD carriers of mutations in the LRRK2 gene.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2011_01.
Duration: 21/05/2012-20/05/2014

Tolosa E. **Autonomic dysfunction in LRRK2 mutation carriers: Characterization of autonomic profiles of patients with PD, carriers of mutations in the LRRK2 gene and no-manifesting first degree relatives.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2011_02.
Duration: 18/05/2012-17/05/2014

Tolosa E. **Analytic Models in Biomarker Development.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJFF_2011_BIMC.
Duration: 01/03/2013-30/01/2014

Tolosa E. **Expansion of the ASAP study: ASymptomatic G2019S/ R1441G LRRK2 Mutation carriers and Assessment of Factors influencing LRRK2-related PD Expression Study.** Sponsored by: Michael J. Fox Foundation for Parkinson's Research. MJF_LRRK2_10_001.
Duration: 04/10/2011-31/12/2013

Tolosa E. **European Project on Mendelian Forms of Parkinson's Disease.** Sponsored by: European Commission CE-FP7-HEALTH-1ST-09 (coordinated by Eberhard-Karls Universitaet Tuebingen) 241791.
Duration: 01/04/2010-30/09/2013.

Tolosa E. **Síntomas no-motores e integridad de la vía nigroestriatal en portadores "asintomáticos" de mutaciones en el gen LRRK2.** Sponsoredby: Instituto de Salud Carlos III (ISCIII). PI08/0155.
Duration: 01/01/2009-31/07/2013

Tolosa E. **Grup de recerca de malalties neurològiques.** Sponsored by: Agència de Gestió d'Ajuts Universitaris de Recerca (AGAUR). 2009_SGR_1019.
Duration: 15/09/2009-30/04/2014

Compta Y. **Endofenotipos clínicos según el perfil de biomarcadores de beta-amíloide y TAU como posibles predicotres de demencia en la enfermedad de Parkinson.** Sponsored by: Federación Española de Parkinson. FEP_Premios11.
Duration: 25/10/2011-01/06/2013

DOCTORAL THESES

Martí M.J. **Cerebrospinal fluid biomarkers in parkinson's disease dementia: clinico-pathological rationale and clinical correlates.**
PhDstudent: YaroslauCompta Hirnyj.

Sánchez-Valle R, Lladó A. **Afasias primarias progresivas: caracterización clínica y marcadores biológicos.**
PhD student: Silvia Gil Navarro

Sánchez-Valle R, Lladó A. **Enfermedad de alzheimer de inicio presenil esporádica: caracterización clínico-biológica y diagnóstico precoz**.
PhD student: Mircea Balasa

4.4 Neurophysiology and functional studies of the nervous system

LOCATION
HCB building

FOR FURTHER INFORMATION
www.ub.edu/neurofisiologia

KEYWORDS
1. **Neurophysiology**
2. **Motor Control and Sensorimotor Integration**
3. **Neuropathic Pain**
4. **Sleep**
5. **Epilepsy**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	128.70	26	12	7
2012	89.25	21	17	1
2013	92.93	20	14	4

TEAM INVOLVED IN
OFTARED

TEAM LEADER
Josep Valls Solé (HCB)
T. 93 227 54 13
jvalls@clinic.cat

GROUP LEADER
Xavier Gasull (UB)

RESEARCHERS
Mar Carreño (HCB)
Arcadi Gual (UB)
Alejandro Iranzo (HCB)
Joan Santamaria (HCB)

PRE-DOCTORAL RESEARCHERS
Christopher Cabib (FCRB)
Gerard Callejo Martin (UB)
Aida Castellanos (UB)
Merche Morales (IDIBAPS)
Marc Güaita (IDIBAPS)
Monica Serradell (FCRB)
Astrid Tulleuda (UB)

COLLABORATORS
Javier Aparicio (HCB)
Antonio Donaire (HCB)
Carles Gaig (HCB)
Jonathan Giblin (UB)
Jordi Palés (UB)
Xavier Sala Blanch (HCB)

VISITING SCIENTISTS
Pablo Arias (Universidad de La Coruña)
Juan M. Castellote (ISCIII)
Markus Kofler (HochzirlNeurorehabilitation Hospital, Zirl, Austria)

STRATEGIC OBJECTIVES

Expansion of scientific knowledge on functional aspects of the nervous system, with maximum integration of basic and clinical aspects, fundamentally using neurophysiological techniques. From the clinical perspective, the principal objectives are the characterization of the neurophysiological aspects of motor control and perception, and the physiopathological aspects of neuromuscular diseases, sleep disturbances, epilepsy, and conditions characterized by neuropathic pain. In basic research, the principal objective is to understand the way that sensory neurons change their excitability in response to

injury, inflammation or other abnormalities, as well as the role of different ion channels in the generation of inflammatory and neuropathic pain. The ocular research lines study the cellular processes involved in dry eye and glaucoma pathophysiology.

MAIN LINES OF RESEARCH

1. The participation of subcortical motor systems in the execution of movements, postural maintenance and reflex control. Study of the alarm circuits based on auditory or somatosensory stimuli. Prepulsephenomena.

2. Physiology and physiopathology of neuropathic pain. Study of nociceptive evoked potentials. Reflex reactions of the autonomous nervous system in response to nociceptive stimulation. Conscious sensory perception.

3. Study of sleep and its disturbances in different disorders. "Narcolepsy" "Excessive daytime sleepiness " i "REM sleep behavior disorder Sleep multiple latency testing. Restless legs syndrome. Periodic leg movements during sleep.

4. Epileptic phenomena and their treatment. Status epilepticus. Monitoring of epileptic seizures. Video-EEG and epidural recording. Epileptic crisis recordings with functional magnetic resonance imaging.

5. Characterization of ion channels involved in neuronal excitability in the sensory nervous system. Study of their role in sensory transduction and the generation of inflammatory and neuropathic pain.

6. Physiology of aqueous humor drainage and physiopathology of glaucoma. Ocular pathology in aging. Physiology of the cells of the ocular trabecular meshwork. Physiopathology of dry eye.

RESEARCH GROUP
NEUROPHYSIOLOGY

GROUP LEADER
Xavier Gasull (UB)

Within the field of neurophysiology, the group is interested in establishing the role of different ion channels implicated in shaping the excitability of sensory neurons of the dorsal root and trigeminal ganglia, and determining which alterations occur during inflammatory and neuropathic pain states. We are especially interested on ocular pain after inflammation, injury or dry eye disease. On the other hand, in trabecular cells that regulate aqueous humor flow in the eye and intraocular pressure, we are exploring the role of ion channels that regulate contraction, shape and cell volume and how this is related to the physiopathology of glaucoma.

PUBLICATIONS

Originals / I.F.: 92.934

1. Iranzo A, Tolosa E, Gelpi E, Molinuevo JL, Valldeoriola F, Serradell M, Sanchez-Valle R, Vilaseca I, Lomeña F, Vilas D, Lladó A, Gaig C, Santamaria J. **Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study.** *Lancet Neurol* 12(5):443-453 I.F.: 23.917

2. Capdevila-Nortes X, López-Hernández T, Apaja PM, López de Heredia M, Sirisi S, Callejo G, Arnedo T, Nunes V, Lukacs GL, Gasull X, Estévez R. **Insights into MLC pathogenesis: GlialCAM is an MLC1 chaperone required for proper activation of volume-regulated anion currents.** *Hum Mol Genet* 22(21):4405-4416 I.F.: 7.692

3. Medici C, Barraza G, Castillo CD, Morales M, Schestatsky P, Casanova-Mollà J, Valls-Sole J. **Disturbed sensory perception of changes in thermoalgesic stimuli in patients with small fiber neuropathies.** *Pain* 154(10):2100-2107 I.F.: 5.644

4. Navarro-Otano J, Valls-Sole J, Guaita M, Santamaria J, Cardellach F, Muñoz E. **Chewing-induced segmental myoclonus in a patient with Leigh syndrome.** *Movement Disord* 28(12):1756-1757 I.F.: 4.558

5. Pereira JB, Junqué C, Bartrés-Faz D, Martí MJ, Sala-Llonch R, Compta Y, Falcón C, Vendrell P, Pascual-Leone A, Valls-Sole J, Tolosa E. **Modulation of verbal fluency networks by transcranial direct current stimulation (tDCS) in Parkinson's disease.** *Brain Stimul* 6(1):16-24 I.F.: 4.538

6. Serranová T, Sieger T, Dušek P, Růžička F, Urgošík D, Růžička E, Valls-Sole J, Jech R. **Sex, food and threat: startling changes after subthalamic stimulation in Parkinson's disease.** *Brain Stimul* 6(5):740-745 I.F.: 4.538

7. Kumru H, Benito J, Murillo N, Valls-Sole J, Valles M, Lopez-Blazquez R, Costa U, Tormos JM, Pascual-Leone A, Vidal J. **Effects of high-frequency repetitive transcranial magnetic stimulation on motor and gait improvement in incomplete spinal cord injury patients.** *Neurorehabil Neural Repair* 27(5):421-429 I.F.: 4.278

8. Gil-Navarro S, Lomeña F, Cot A, Lladó A, Montagut N, Castellví M, Bosch B, Rami L, Antonell A, Balasa M, Pavia J, Iranzo A, Molinuevo JL, Sánchez-Valle R. **Decreased striatal dopamine transporter uptake in the non-fluent/agrammatic variant of primary progressive aphasia.** *Eur J Neurol* 20(11):1459-e126 I.F.: 4.162

9. Donaire A, Capdevila A, Carreño M, Setoain X, Rumià J, Aparicio J, Campistol J, Padilla N, Sanmartí F, Vernet O, Pintor L, Boget T, Ortells J, Bargalló N. **Identifying the cortical substrates of interictal epileptI.F.orm activity in patients with extratemporal epilepsy: An EEG-fMRI**

sequential analysis and FDG-PET study. *Epilepsia* 54(4):678-690 I.F.: 3.909

10. Sierra-Marcos A, Maestro I, Falcón C, Donaire A, Setoain J, Aparicio J, Rumià J, Pintor L, Boget T, Carreño M, Bargalló N. **Ictal EEG-fMRI in localization of epileptogenic area in patients with refractory neocortical focal epilepsy.** *Epilepsia* 54(9):1688-1698 I.F.: 3.909

11. Callejo G, Giblin JP, Gasull X. **Modulation of TRESK background K+ channel by membrane stretch.** *PLoS One* 8(5):e64471 I.F.: 3.730

12. Iranzo A, Serradell M, Vilaseca I, Valldeoriola F, Salamero M, Molina C, Santamaria J, Tolosa E. **Longitudinal assessment of olfactory function in idiopathic REM sleep behavior disorder.** *Parkinsonism Relat Disord* 19(6):600-604 I.F.: 3.274

13. Kumru H, Portell E, Marti M, Albu S, Tormos JM, Vidal J, Valls-Sole J. **Mechanical and thermal hyperalgesia in patients with poliomyelitis.** *Clin Neurophysiol* 124(7):1431-1438 I.F.: 3.144

14. Kumru H, Soler D, Vidal J, Navarro X, Tormos JM, Pascual-Leone A, Valls-Sole J. **The effects of transcranial direct current stimulation with visual illusion in neuropathic pain due to spinal cord injury: an evoked potentials and quantitative thermal testing study.** *Eur J Pain* 7(1):55-66 I.F.: 3.067

15. Brito-Zerón P, Akasbi M, Bosch X, Bové A, Pérez-De-Lis M, Diaz-Lagares C, Retamozo S, Gandía M, Pérez-Alvarez R, Soto-Cárdenas MJ, Sisó A, Valls-Sole J, Graus F, Ramos-Casals M. **Classification and characterisation of peripheral neuropathies in 102 patients with primary Sjögren's syndrome.** *Clin Exp Rheumatol* 31(1):103-110 I.F.: 2.655

16. Rumià J, Marmol F, Sanchez J, Giménez-Crouseilles J, Carreño M, Bargalló N, Boget T, Pintor L, Setoain X, Donaire A, Saez GT, Ribalta T, Ferrer E, Puig-Parellada P. **Oxidative stress markers in the neocortex of drug-resistant epilepsy patients submitted to epilepsy surgery.** *Epilepsy Res* 107(1-2):75-81 I.F.: 2.241

17. Llobera J, González-Franco M, Perez-Marcos D, Valls-Sole J, Slater M, Sanchez-Vives MV. **Virtual reality for assessment of patients suffering chronic pain: a case study.** *Exp Brain Res* 225(1):105-117 I.F.: 2.221

18. Fernandez-Del-Olmo M, Bello O, Lopez-Alonso V, Marquez G, Sanchez JA, Morenilla L, Valls-Sole J. **The effects of startle and non-startle auditory stimuli on wrist flexion movement in Parkinson's disease.** *Neurosci Lett* 548:56-60 I.F.: 2.026

19. Luis L, Costa J, Vaz Garcia F, Valls-Sole J, Brandt T, Schneider E. **Spontaneous plugging of the horizontal semicircular canal with reversible canal dysfunction and recovery of vestibular evoked myogenic potentials.** *Otol Neurotol* 34(4):743-747 I.F.: 2.014

20. Cortes M, Elder J, Rykman A, Murray L, Avedissian M, Stampa A, Thickbroom GW, Pascual-Leone A, Krebs HI, Valls-Sole J, Edwards DJ. **Improved motor performance in chronic spinal cord injury following upper-limb robotic training.** *NeuroRehabilitation* 33(1):57-65 I.F.: 1.417

Reviews / I.F.: 5.105

1. Iranzo A. **Parkinson disease and sleep: sleep-wake changes in the premotor stage of Parkinson disease; impaired olfaction and other prodromal features.** *Curr Neurol Neurosci Rep* 13(9):373 I.F.: 3.783

2. Fernández V, Valls-Sole J, Relova JL, Raguer N, Miralles F, Dinca L, Taramundi S, Costa-Frossard L, Ferrandiz M, Ramió-Torrentà L, Villoslada P, Saiz A, Calles C, Antigüedad A, Alvarez-Cermeño JC, Prieto JM, Izquierdo G, Montalbán X, Fernández O. **[Recommendations for the clinical use of motor evoked potentials in multiple sclerosis].** *Neurologia* 28(7):408-16 I.F.: 1.322

GRANTS FOR RESEARCH IN PROGRESS

Gasull X. **Inflamación y dolor ocular: implicación de los canales ASIC (acid-sensing ion channels) como dianas farmacológicas.** Sponsored by: Ministerio de Ciencia e Innovación, PI11/01601. Duration: 31/12/2011-31/12/2014.

Gasull X. **Desarrollo de un proyecto llamado "Soluciones innovadoras para acelerar la identificación y desarrollo de fármacos para patologías del Sistema Nervioso".** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI). 10/158. Duration: 01/01/2011-31/12/2014

Gual A. **Lab. Neurofisiologia. Grup consolidat Generalitat de Catalunya.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) SGR09_869. Duration: 01/01/2009-31/12/2013.

Iranzo de Riquer, A. **El trastorno de conducta durante el sueño REM y el SPECT cerebral del transportador de la dopamina (123i-FP-CIT) como marcadores diferenciales del deterioro cognitivo leve.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/01732. Duration: 01/01/2012-31/12/2014.

Valls Sole J. **Neurofisiologia del dolor, epilèpsia, son i control motor (NEDESC).** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) SGR09_1253. Duration: 15/09/2009-31/12/2014.

Valls Sole, J. **Nuevas estrategias para optimizar la adquisición y consolidación de habilidades motoras.** Sponsored by: Ministerio de Economía y Competitividad BFU2011-15462-E. Duration: 26/10/2011-25/10/2013.

Valls Sole, J. **Non-invasive early neurophysiological interventions in brain and spinal cord injury patients.** Sponsored by: Fundació la Marató

de TV3 110930.
Duration: 31/01/2012-30/01/2015.

Valls Sole J. **Estudio de respuestas preconscientes y conscientes al dolor evocado en sujetos sanos y en pacientes con polineuropatía de fibra fina.**
Sponsored by Fondo de Investigaciones Sanitarias del Instituto de Salud Carlos III.
PI13 0526.
Duración 01/11/2013 – 30/10/2016.

DOCTORAL THESES

Valls-Sole J. **Entrenamiento de la marcha en el lesionado medular. Uso de sistemas electromecánicos y estimulación transcraneal no invasiva.**
PhD Student: Jesús Benito Penalva.

4.5 Muscle research and mitochondrial function

LOCATION
CELLEX building

KEYWORDS
1. **Muscle**
2. **Mitochondria**
3. **Alcoholic Cardiomyopathy**
4. **Chronic fatigue syndrome**
5. **Septic shock**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	-	-	-	-
2012	47.50	11	6	3
2013	36.09	10	4	4

TEAM INVOLVED IN
CIBERER
CIBEROBN

AWARDS
Premio Final Residencia 2013
Institution: Hospital Clínic de Barcelona.
Awardee/s: Pedro Castro

IV Jornades de l'Institut de recerca de Sant Pau (Best original article on Genetic, metabolic and inflammatory diseases)
Institution: Hospital de Sant Pau
Awardees: Garrabou G, Morén C, Lopez S, Tobias E, Cardellach F, Miró Ò, Casademont J.

TEAM LEADER
Josep M. Grau Junyent (HCB)
T. 93 227 55 39
jmgrau@clinic.cat

RESEARCHERS
Francesc Cardellach (HCB)
Joaquim Fernández (HCB)
José Maria Nicolas (HCB)

POST-DOCTORAL RESEARCHERS
Glòria Garrabou (CIBERER)
Constanza Morén (CIBERER-FIPSE)

PRE-DOCTORAL RESEARCHERS
Maria Bañó (CIBERER)
Pedro Castro (HCB)
Marc Catalán (Fundació Cellex)
Mariona Guitart (Fundació Cellex)
Anna Sandra Hernàndez (HCB)

TECHNICIANS
Esther Tobias (UB)

COLLABORATORS
Emilia Antunez (UB)
Xavier Bosch (HCB)

STRATEGIC OBJECTIVES

1. Muscular pathology of mitochondrial, inflammatory and autoimmune origin.
2. Mitochondrial basis of rare diseases such as inclusion body myositis, Parkinson disease, X-fragile syndrome, inborn errors of metabolism and intrauterine growth restriction.
3. Mitotoxicity.
4. Mitochondrial involvement in physiologic and pathologic processes.
5. Cardiomyopathy in chronic alcoholic patients.
6. Chronic fatigue syndrome.
7. Septic shock and organ failure in critically-ill patients
8. Journalology: research of editorial and ethical policies of biomedical journals.

MAIN LINES OF RESEARCH

1. Research in inborn errors of metabolism, muscle and primary mitochondrial diseases of patients attended by the Group of Medical Care of Adult Patients with Rare Diseases (HCB)

2. Research in other rare diseases with potential mitochondrial basis, such as inclusion body myositis, Parkinson disease (associated to mutations in Parkin and LRRK2 genes), X-fragile syndrome, obstetric problems (especially intrauterine growth restriction) and inflammatory and autoimmune muscle diseases.

3. Secondary mitochondrial pathology due to contact with toxic agents: gases as CO and NO, abuse drugs as tobacco, chemical products as methylene chloride, biological agents as HIV and pharmacological drugs as antibiotics, antipsychotics, antiretrovirals and hypolipemiant agents.

4. Mitochondrial dysfunction secondary to other medical problems (such as lipodystrophy, hyperlactatemia, peripheral neuropathy, sepsis, schizophrenia or infertility) and physiological processes (cell division, aging or inflammation)

5. Study of the pathological mechanisms of alcohol upon the organ cells and its pathological effects at neurological and cardiocirculatory level: (i) Prognosis of alcoholic myocardiopathy and its best management options; (ii) Study of muscle and myocardial apoptosis in subjects presenting chronic alcohol abuse; (iii) Study of myocardial regeneration in alcoholic cardiomyopathy; (iv) Study of factors influencing in myocyte hypertrophy (myostatin, IGF-1).

6. Clinical and functional repercussions of chronic fatigue syndrome (CFS). (i) Evaluation of long-term effects of multidisciplinary treatment, (ii) Role and significance of co-morbid diseases in CFS, (iii) Influence of chemical and environmental factors in the pathogenesis of CFS.

7. Clinical and translational research on septic shock and multiorgan failure. Research on antibiotic policies in critically-ill patients.

8. Journalology of biomedical journals: research of editorial and ethical policies.

Our future challenges are:

1. Deeply exploring mitochondrial basis of rare diseases with muscle and central nervous system involvement as well as secondary mitochondrial implication in toxicities, or physiological processes.
2. Cardiomyopathy and chronic fatigue. Improving knowledge in physiopathological mechanisms leading to disease in alcoholic cardiomyopathy and also in chronic fatigue syndrome in order to prevent or delay development of disease and apply potential treatment strategies.
3. To understand the pathophysiology in the development of organ failure in patients with severe sepsis and septic shock, as well as is to identify biological targets for prevention of organ damage.
4. Medical publishing: Study of the open-access movement. Comprehensive comparison of the editorial and ethical policies of open-access vs. non open-access journals through a case-control study.

PUBLICATIONS

Originals / I.F.: 36.089

1. Espígol-Frigolé G, Corbera-Bellalta M, Planas-Rigol E, Lozano E, Segarra M, García-Martínez A, Prieto-González S, Hernández-Rodríguez J, Grau JM, Rahman MU, Cid MC. **Increased IL-17A expression in temporal artery lesions is a predictor of sustained response to glucocorticoid treatment in patients with giant-cell arteritis.** *Ann Rheum Dis* 72(9):1481-1487 I.F.: 9.111

2. Doti P, Castro P, Martínez MJ, Zboromyrska Y, Aldasoro E, Inciarte A, Requena A, Milisenda J, Fernández S, Nicolás JM, Muñoz J. **A case of Japanese encephalitis in a 20 year-old Spanish sportsman.** *Euro Surveill* 18(35):20573 I.F.: 5.491

3. Navarro-Otano J, Valls-Solé J, Guaita M, Santamaria J, Cardellach F, Muñoz E. **Chewing-induced segmental myoclonus in a patient with Leigh syndrome.** *Mov Disord* 28(12):1756-1757 I.F.: 4.558

4. Llorente-Folch I, Sahún I, Contreras L, Casarejos MJ, Grau JM, Saheki T, Mena MA, Satrústegui J, Dierssen M, Pardo B. **AGC1-malate aspartate shuttle activity is critical for dopamine handling in the nigrostriatal pathway.** *J Neurochem* 124(3):347-362 I.F.: 3.973

5. Rinaudo M, Cobos-Trigueros N, Solé M, Castro P, Hernández C, Nicolas JM, Vila J, Morata L, Pumarol J, Soriano A, Mensa J, Martínez JA. **Comparison of acquisition of resistant microorganisms and infections in critically-ill patients with and without malignancies.** *Minerva Anestesiol* 79(11):1217-1228 I.F.: 2.818

6. Castro P, Plana M, González R, López A, Vilella A, Nicolas JM, Gallart T, Pumarola T, Bayas JM, Gatell JM, García F. **Influence of episodes of intermittent viremia ("blips") on immune responses and viral load rebound in successfully treated HIV-infected patients.** *AIDS Res Hum Retroviruses* 29(1):68-76 I.F.: 2.705

7. Herrera-Gutiérrez ME[1], Seller-Pérez G, Sánchez-Izquierdo-Riera JA, Maynar-Moliner J; COFRADE investigators group. **Prevalence of acute kidney injury in intensive care units: the "COrte de prevalencia de disFunción RenAl y DEpuración en críticos" point-prevalence multicenter study.** *J Crit Care* 28(5):687-94 I.F.: 2.498

8. Gómez FP, Amado VM, Roca J, Torres A, Nicolas JM, Rodriguez-Roisin R, Barberà JA. **Effect of nitric oxide inhalation on gas exchange in acute severe pneumonia.** *Resp Physiol Neurobi* 187(2):157-163 I.F.: 2.051

9. Vives-Corrons JL, Koralkova P, Grau JM, Mañú Pereira Mdel M, Van Wijk R. **First description of phosphofructokinase deficiency in Spain: identification of a novel homozygous missense mutation in the PFKM gene.** *Front Physiol* 4:393 I.F.: 1.591

10. Morén C, Garrabou G, Noguera-Julian A, Rovira N, Catalán M, Hernández S, Tobías E, Cardellach F, Fortuny C, Miró Ò. **Study of oxidative, enzymatic mitochondrial respiratory chain function and apoptosis in perinatally HIV-infected pediatric patients**. *Drug Chem Toxicol* 36(4):496-500 I.F.: 1.293

Reviews / I.F.: 2.822

1. Fernández-Solà J. **Management of extrahepatic manifestations of Alcoholic Liver Diseases. Clinical Liver Diseases.** *Wiley-Blackwell* 2(2):89-93 I.F.: 2.822

GRANTS FOR RESEARCH IN PROGRESS

Cardellach F. **Implicación mitocondrial en el crecimiento intrauterino restringido y la remodelación cardiovascular asociada.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01199.
Duration: 01/01/2013-31/12/2015

Fernandez-Solà J. **Cell Death in Alcoholic Heart and Muscle.** Sponsored by: National Institute of Health (NIH). 1 U01 AA021122.
Duration: 01/05/2012-30/04/2014

Grau J.M. **Grup de recerca muscular.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1158.
Duration: 23/09/2009-30/04/2014

4.6 Pathophysiology and treatment of neurodegenerative disorders

LOCATION
CELLEX building

KEYWORDS
1. **Huntington's disease**
2. **Motor and cognitive function**
3. **Neuroprotection**
4. **Trophic factors**
5. **Stem cells**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	74.18	12	9	-
2012	39.22	8	5	1
2013	72.45	10	10	-

TEAM INVOLVED IN
CIBERNED
Red Terapia Celular

TEAM LEADER
Jordi Alberch (UB)
T. 93 403 52 85
alberch@ub.edu

RESEARCHERS
Josep M. Canals (UB)
Silvia Ginés (UB)
Esther Pérez (UB)

POST-DOCTORAL RESEARCHERS
Verónica Brito (IDIBAPS)
Albert Giralt (UB)
Andrés Míguez (IDIBAPS)
Ana Saavedra (UB)
Philip Sanders (IDIBAPS)
Marco Straccia (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Rafael Alcalá (UB)
Marta Anglada (UB)
Marta Cherubini (CIBERNED)
Gerardo García (UB)
Andreas Mezger (UB)
Mónica Pardo (UB)
Mar Puigdellívol (IDIBAPS)
Laura Rué (UB)
Shiraz Tyebji (UB)

TECHNICIANS
Laetitia Casano (IDIBAPS)
Cristina Herranz (IDIBAPS)
Ana López (CIBERNED)
Maite Muñoz (UB)

COLLABORATORS
Raquel Martín-Ibáñez (CIBERNED-UB)
Xavier Xifro (UdG)

STRATEGIC OBJECTIVES

1. Study of the cellular and molecular bases involved in neuronal dysfunction and death associated with basal ganglia neurodegenerative disorders, mainly Huntington's disease. Our aim is to identify intracellular pathways – both neuroprotective and apoptotic – that are selectively altered in the affected neuron populations, with the ultimate purpose of identifying new therapeutic targets in the management of these neurodegenerative diseases.

2. Identification of the mechanisms participating in the cognitive defects seen in Huntington's disease. Knowledge of these mechanisms will make it possible to develop new treatments for avoiding the cognitive disorders induced by the mutated huntingtin gene.
3. Characterization of the mechanisms of neuron differentiation of stem cells from different organs. Our aim is to identify different extrinsic and intrinsic factors contributing to neuron differentiation, with the aim of employing stem cells in cell substitution therapies against neurodegenerative diseases.

MAIN LINES OF RESEARCH

1. Study of the implication of neurotrophic factors in the physiopathology and treatment of neurodegenerative diseases of the basal ganglia.

2. Study of the intracellular signaling cascades implicated in the degeneration of striatal and hippocampal neurons in Huntington's disease.

3. Study of the mechanisms underlying the differentiation of stem cells into neurons, for application to cellular therapy in neurodegenerative diseases such as Huntington's chorea.

4. Characterization of extrinsic factors and new transcription factors of the development of human and mouse striatum.

PUBLICATIONS

Originals / I.F.: 72.451

1. Marco S, Giralt A, Petrovic MM, Pouladi MA, Martínez-Turrillas R, Martínez-Hernández J, Kaltenbach LS, Torres-Peraza J, Graham RK, Watanabe M, Luján R, Nakanishi N, Lipton SA, Lo DC, Hayden MR, Alberch J, Wesseling JF, Pérez-Otaño I. **Suppressing aberrant GluN3A expression rescues synaptic and behavioral impairments in Huntington's disease models.** *Nat Med* 19(8):1030-1038 I.F.: 24.300

2. Damiano M, Diguet E, Malgorn C, D'Aurelio M, Galvan L, Petit F, Benhaim L, Guillermier M, Houitte D, Dufour N, Hantraye P, Canals JM, Alberch J, Delzescaux T, Déglon N, Beal MF, Brouillet E. **A role of mitochondrial complex II defects in genetic models of Huntington's disease expressing N-terminal fragments of mutant huntingtin.** *Hum Mol Genet* 22(19):3869-3882 I.F.: 7.692

3. Brito V, Puigdellívol M, Giralt A, del Toro D, Alberch J, Ginés S. **Imbalance of p75(NTR)/TrkB protein expression in Huntington's disease: implication for neuroprotective therapies.** *Cell Death Dis* 4:e595 I.F.: 6.044

4. Rué L, Lopez-Soop G, Gelpí E, Martínez-Vicente M, Alberch J, Pérez-Navarro E. **Brain region- and age-dependent dysregulation of p62 and NBR1 in a mouse model of Huntington's disease.** *Neurobiol Dis* 52:219-228 I.F.: 5.624

5. Pascual-García M, Rué L, León T, Julve J, Carbó JM, Matalonga J, Auer H, Celada A, Escolà-Gil JC, Steffensen KR, Pérez-Navarro E, Valledor AF. **Reciprocal negative cross-talk between liver X receptors (LXRs) and STAT1: effects on IFN-γ-induced inflammatory responses and LXR-dependent gene expression.** *J Immunol* 190:6520-6532 I.F.: 5.520

6. Giralt A, Saavedra A, Carretón O, Arumí H, Tyebji S, Alberch J, Pérez-Navarro E. **PDE10 inhibition increases GluA1 and CREB phosphorylation and improves spatial and recognition memories in a Huntington's disease mouse model.** *Hippocampus* 23:684-695 I.F.: 5.492

7. Barroso E, del Valle J, Porquet D, Vieira Santos AM, Salvadó L, Rodríguez-Rodríguez R, Gutiérrez P, Anglada-Huguet M, Alberch J, Camins A, Palomer X, Pallàs M, Michalik L, Wahli W, Vázquez-Carrera M. **Tau hyperphosphorylation and increased BACE1 and RAGE levels in the cortex of PPARb/g-null mice.** *Biochim Biophys Acta* 1832(8):1241-1248 I.F.: 4.910

8. Giralt A, Sanchis D, Cherubini M, Ginés S, Cañas X, Comella JX, Alberch J. **Neurobehavioral characterization of Endonuclease G knockout mice reveals a new putative molecular player in the regulation of anxiety.** *Exp Neurol* 247:122-129 I.F.: 4.645

9. Villar-Menéndez I, Blanch M, Tyebji S, Pereira-Veiga T, Albasanz JL, Martín M, Ferrer I, Pérez-Navarro E, Barrachina M. **Increased 5-methylcytosine and decreased 5-hydroxymethylcytosine levels are associated with reduced striatal A2AR levels in Huntington's disease.** *Neuromolecular Med* 15:295-309 I.F.: 4.492

10. Saavedra A, Giralt A, Arumí H, Alberch J, Pérez-Navarro E. **Regulation of hippocampal cGMP levels as a candidate to treat cognitive deficits in Huntington's disease.** *PLoS One* 8:e73664 I.F.: 3.730

GRANTS FOR RESEARCH IN PROGRESS

Alberch J. **Regulación de la plasticidad sináptica y la disfunción neuronal por nuevos métodos de liberación de BDNF en modelos de enfermedad de Huntington.** Sponsored by: Ministerio de Ciencia e Innovación, SAF2011-29507. Duration: 01/01/2012-31/12/2014.

Canals J.M. **Red de terapia celular.** Sponsored by: Instituto de Salud Carlos III (ISCIII) RD12/0019/0002. Duration: 01/01/2013-31/12/2016

Canals J.M. **Red de Terapia Celular.** Sponsored by: Instituto de Salud Carlos III (ISCIII) RD06/0010/0006. Duration: 01/01/2007-31/12/2014

Canals J.M. **Stem cell Differentiation JSC-**

Joint Collaborative effort between the IDIBAPS, Univ of Milano and Univ of Cardiff. Sponsored by: CHDI Foundation. A-4530.
Duration: 01/01/2012-31/12/2015

Ginés S. **Role of Cdk5 in Striatal and Hippocamapl Pathology in Huntington's Disease.** Sponsored by: CHDI Foundation. A-3880.
Duration: 01/11/2010-31/10/2014

Ginés S. Complete Characterization of p75 Knockdown in Q111 Mouse.
Sponsored by: CHDI Foundation. A6965.
Duration: 01/09/2013-31/08/2014

Ginés S. **Role of p75 Neurotrophin Receptor in Huntington's Disease. Sponsored by: CHDI Foundation.**
A-3468.
Duration: 01/05/2010-31/05/2013

Ginés S. **Cdk5: una diana terapéutica para el tratamiento de los déficits motores y cognitivos en la Enfermedad de Huntington.** Sponsored by: Fundación Ramón Areces.
Duration: 01/07/2012-30/06/2015

Pérez E. **Regulación de la vía PKA como estrategia terapéutica para la enfermedad de Huntington.**
Sponsored by: Instituto de Salud Carlos III (ISCIII) PI10/0172.
Duration: 10/12/2010-10/12/2013.

DOCTORAL THESES

Alberch J. **Characterization of mechanisms underlying neuronal survival and plasticity in Huntington's disease.**
PhD Student: Marta Anglada Huguet.

4.7 Biological bases of psychiatric disorders and nuclear psychiatry

LOCATION
HCB building

KEYWORDS
1. **Schizophrenia**
2. **Bipolar disorders**
3. **Psychiatry**
4. **Alcohol**
5. **Child and Adolescent Psychiatry and Psychology**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	286.57	68	46	10
2012	339.62	88	63	13
2013	314.08	78	60	12

TEAM INVOLVED IN
CIBERSAM

AWARDS

Awarded Best Doctoral Thesis
Institution: Sociedad Española de Psiquiatría Biológica
Awardee/s: Clemente García-Rizo

Awarded Best Poster in Neuropsicopharmacology
Institution: Sociedad Española de Psiquiatría Biológica
Awardee/s: Grande I, Magalhães PVS, Chendo I, Stertz L, Fries GR, Udina M, Martín-Santos R, Kapczinski F, Vieta E,

Best Poster Presentation at the 13th International Forum on Mood and Anxiety Disorders congress, Monte Carlo, 2013
Institution: 13th International Forum on Mood and Anxiety Disorders
Awardee/s: Popovic D., Torrent C., Vieta E

TEAM LEADER
Miquel Bernardo (HCB)
T. 93 227 54 00 (Ext 3142)
bernardo@clinic.cat

GROUP LEADERS
Miquel Bernardo (HCB)
Josefina Castro (HCB)
Cristobal Gastó (HCB)
Gisela Sugranyes (HCB-IDIBAPS)
Eduard Vieta (HCB)

RESEARCHERS
Susana Andrés (HCB)
Inmaculada Baeza (HCB)
Antonio Benabarre (HCB)
Rosa Catalán (HCB)
Francesc Colom (IDIBAPS)
Lluïsa Garcia-Esteve (HCB)
Jose Manuel Goikolea (HCB)
Antoni Gual (HCB)
Fernando Gutierrez (HCB)
Amalia Lafuente (TU)
Luisa Lázaro (HCB)
Francisco J. Lomeña (HCB)
Rocío Martín-Santos (HCB)
Anabel Martínez-Arán (HCB)
Guillem Masana (HCB)
Astrid Morer Liñán (HCB)
Eduard Parellada (HCB)
Rafel Penadés (HCB)
Luis Pintor (HCB)
Mercè Torra (HCB)
Manuel Valdés (HCB)

POST-DOCTORAL RESEARCHERS
Miquel Bioque (CIBERSAM)
Caterina del Mar Bonnin (IDIBAPS)
Rosa Calvo (HCB)
Clemente Garcia-Rizo (HCB)
Patricia Gasso (UB)
Iria Grande (IDIBAPS)
Andrea Murru (IDIBAPS)
Isabella Pachiarotti (CIBERSAM)
Nuria Pujol (HCB)
Vanessa Sánchez (HCB)
Elena de la Serna (CIBERSAM)
Juan Undurraga (HCB)
Marc Valentí (CIBERSAM)

PRE-DOCTORAL RESEARCHERS
Bibiana Cabrera (FCRB)
Javier Goti (HCB)
M Luisa Imaz (HCB)
Esther Jimenez (IDIBAPS)
Gisela Mezquida (FCRB)
Maria Teresa Plana (HCB)
Olga Puig (HCB)

Alessandra Nivoli (FCRB)
Soledad Romero (HCB)
José Sánchez-Moreno (CIBERSAM)
Brisa Solé (IDIBAPS)
Anna Torres (HCB)
Imma Torres (IDIBAPS)

TECHNICIANS
M Alicia Durán (FCRB)
Rosa Maria Palaus (FCRB)

NURSING STAFF
Ana Meseguer (CIBERSAM)

ADMINISTRATIVE STAFF
Anna Folch (FCRB)

COLLABORATORS
Jordi Blanch (HCB)
Enric Buisan (HCB)
Mercè Comes (HCB)
Rosa Díaz (HCB)
Ester Gómez (HCB)
Joana Guarch (HCB)
Sergi Mas Herrero (UB)
Victor Navarro (HCB)
Cristina V. Oliveira (FCRB)
Maria Reinares (IDIBAPS)
Carla Torrent (CIBERSAM)

STRATEGIC OBJECTIVES

Our group studies severe psychiatric disorders from the neurobiological, psychological and therapeutic perspectives, based on the following 6 research lines: bipolar disorders, schizophrenia and depression-anxiety, child and adolescens pediatric psychiatry and psychology,liaison psychiatry psychiatric and alcoholism.

MAIN LINES OF RESEARCH

- The bipolar disorders program mainly investigates the neurobiological and anatomofunctional mechanisms involved in the development of the disease (genetics, neuromodulators, hormone factors and neuroimaging) and its relapses, the clinical course and neuropsychological consequences, the efficacy of drug treatments and novel therapies, and psychological interventions for the early detection and prevention of recurrences .

- The schizophrenia program focuses research on first episodes and on resistant and comorbid schizophrenia. The main lines include neuroimaging, neurobiology and molecular psychiatry; neurocognition, neuropsychology and psychoeducation; pharmacogenetics of antipsychotic drugs; physical health; high-risk population, A program has been developed for characterizing and preventing second psychotic episodes.

- The main research lines of the Alcohol Unit are: prospectives longitudinal follow-up of alcohol dependent patients; development of screening instruments and techniques for early detection and brief interventions in risk drinkers.; evaluation and prognosis of alcoholic patients candidates for liver transplantation; treatment of smoking in alcoholic patients; evaluation of te European alcohol policies and their public health impact; and research on anticraving drugs.

- The line relating to depression aims to implement new psychopathological and biological endophenotypic methods applied to major depression, with the development of mechanisms for the analysis of the mechanism of action of antidepressant drugs based on the platelet model of depression; investigation of neurotrophic factors (BDNF) in depressive patients; and the exploration of factors conditioning the residual symptoms of major depression.

- The main research lines of the pediatric psychiatry and psychology research group are: children and adolescent with a first psychotic episode, cognitive rehabilitation of subjects at high-risk of developing a psychotic or affective disorder..Alterations in anorexia and bulimia nervosa and new management approaches. Alterations in obsessive-compulsive disorder and autoimmune alterations in obsessive behaviors. Addictive behaviors in children and adolescents, efficacy and safety of psychoactive drugs, autistic spectrum disorders, the development and validation of clinical scales, and the study of children diagnosed with attention deficit hyperactivity disorder (ADHD).

- The line of liasison psychiatry has focused research on psychiatric and psychological aspects in the main neurological diseases: dementia, multiple sclerosis, epilepsy, Parkinson's disease and Huntington's disease. and also on those associated with medical-surgical hospital processes (transplantation, delirium, suicide). In outpatients setting the research has focused on clinical and biological markers related with gender identity disorder (transsexual population).

- Investigations likewise have been conducted into personality disorders: the structure of the diagnostic systems, their relationship to adjustment to the environment and the validation of new models and instruments.

RESEARCH GROUP
BIPOLAR DISORDERS

GROUP LEADER
Eduard Vieta (HCB)

The bipolar disorder program has been recognized as a consolidated research group (2009 SGR 1022) by the Agència de Gestió d'Ajuts Universitaris i de Recerca, AGAUR. The program, characterizad by a multidisciplinary approach, investigates the neurobiological and anatomofunctional mechanisms involved in the development and clinical course of the disease,

comorbidity, implicatd neurocognitive mechanisms, and the search for new pharmacological,biophysical and psychosocial treatments. As a result, the main international diagnostic and treatment guides document these contributions and recommend their application. We have active collaboration (multicenter studies in translational and innovative investigation) with other IDIBAPS, CIBERSAM, and research groups.

RESEARCH GROUP
SCHIZOPHRENIA

GROUP LEADER
Miquel Bernardo (HCB)

The Clinical Schizophrenia Group (GEC) has been recognized as a consolidated research group (2005SGR00223; 2009SGR1295) by the Agència de Gestió d'Ajuts Universitaris i de Recerca, AGAUR. This interdisciplinary group focuses on schizophrenia and related disorders in clinical care, research and teaching. The research is centered on the study of first episodes, childhood and adolescent-onset, resistant and comorbid schizophrenia.. We have active collaboration (multicenter studies in translational and innovative investigation) with other IDIBAPS, CIBERSAM, and international research groups. We collaborate with a European network of research in schizophrenia and maintain close relationship to American research networks.

RESEARCH GROUP
RESEARCH GROUP IN PEDIATRIC PSYCHIATRY AND PSYCHOLOGY

GROUP LEADER
Josefina Castro (HCB)

This research group is part of the Department of Childhood and Adolescent Psychiatry of the Hospital Clinic. Our aim is to facilitate both clinical research and collaboration with groups specialized in genetics, neuroimaging and neurobiology. The group forms part of the CIBERSAM (Centro de Investigación Biomédica en Red de Salud Mental) and it has established important collaborations with the Department of Adult Psychiatry of the Hospital Clinic as well as with other centers at international level, such as the Childhood Psychiatry Group of the European College of Neuopsychopharmacology, the University of Pittsburgh (United States), and the Child and Adolescent Psychiatry Center of Yale, New Haven (United States).

EMERGENT GROUP
CLINICAL DEPRESSION GROUP

GROUP LEADER
Cristobal Gastó (HCB)

Our group investigates the neurobiological bases and clinical indicators associated with treatment response and the course of depression. Depression is currently one of the most important health problems, due to its slow and sometimes incomplete resolution, the interference with the normal functions of patients and relatives, and its high suicide risk. Our group is actively involved in the early detection and treatment of this disease, and its comorbidities. The genetic and neuroendocrine markers we are investigating have contributed to better understanding the physiopathological mechanisms of depression. We also work on the design of new pharmacological and psychotherapeutic management strategies.

50/50 PROGRAM
MULTIMODAL NEUROIMAGING IN HIGH RISK AND EARLY PSYCHOSIS

GROUP LEADER
Gisela Sugranyes (HCB-IDIBAPS)

This programme seeks to understand the neural mechanisms underlying the development of psychotic disorders in children and adolescents. Specifically, it aims to identify structural and functional neural correlates which characterize youth at high risk for psychosis and during the early phase of the disorder. It also aims to explore the relationship between neuroimaging measures and clinical and neuropsychological phenotypes, in addition to the interaction with specific genotypes. Particular focus is given to the interaction between illness-related changes and processes associated to normative child and adolescent neurodevelopment, given the age range of this sample. On a translational level, priority is given to the identification of factors predicting transition to psychosis and functional outcomes, in addition to identification of treatment targets.

PUBLICATIONS

Originals / I.F.: 314.076

1. Torrent C, Bonnin Cdel M, Martínez-Arán A, Valle J, Amann BL, González-Pinto A, Crespo JM, Ibáñez Á, Garcia-Portilla MP, Tabarés-Seisdedos R, Arango C, Colom F, Solé B, Pacchiarotti I, Rosa AR, Ayuso-Mateos JL, Anaya C, Fernández P, Landín-Romero R, Alonso-Lana S, Ortiz-Gil J, Segura B, Barbeito S, Vega P, Fernández M, Ugarte A, Subirà M, Cerrillo E, Custal N, Menchón JM, Saiz-Ruiz J, Rodao JM, Isella S, Alegría A, Al-Halabi S, Bobes J, Galván G, Saiz PA, Balanzá Martínez V, Selva G, Fuentes-Durá I, Correa P, Mayoral M, Chiclana G, Merchan-Naranjo J, Rapado-Castro M, Salamero M, Vieta E. **Efficacy of functional remediation in bipolar disorder: a multicenter randomized controlled study.** *Am J Psychiatry* 170(8):852-859 I.F.: 14.721

2. Carrión JA, Gonzalez-Colominas E, García-Retortillo M, Cañete N, Cirera I, Coll S, Giménez MD, Márquez C, Martin-Escudero V, Castellví P, Navinés R, Castaño JR, Galeras JA, Salas E, Bory F, Martín-Santos R, Solà R. **A multidisciplinary support programme increases the efficiency of pegylated interferon alfa-2a and ribavirin in hepatitis C.** *J Hepatol* 59(5):926-933 I.F.: 9.858

3. Penadés R, Pujol N, Catalán R, Massana G, Rametti G, García-Rizo C, Bargalló N, Gastó C, Bernardo M, Junqué C. **Brain effects of cognitive remediation therapy in schizophrenia: a structural and functional neuroimaging study.** *Biol Psychiatry* 73(10):1015-1023 I.F.: 9.247

4. Bioque M, García-Bueno B, Mac-Dowell KS, Meseguer A, Saiz PA, Parellada M, González-Pinto A, Rodriguez-Jimenez R, Lobo A, Leza JC, Bernardo M. **Peripheral endocannabinoid system dysregulation in first episodes of psychosis.** *Neuropsychopharmacology* 38(13):2568-2577 I.F.: 8.678

5. Alemán-Gómez Y, Janssen J, Schnack H, Balaban E, Pina-Camacho L, Alfaro-Almagro F, Castro-Fornieles J, Otero S, Baeza I, Moreno D, Bargalló N, Parellada M, Arango C, Desco M. **The human cerebral cortex flattens during adolescence.** *J Neurosci* 33(38):15004-15010 I.F.: 6.908

6. Sanchez-Gistau V, Baeza I, Arango C, González-Pinto A, de la Serna E, Parellada M, Graell M, Paya B, Llorente C, Castro-Fornieles J. **Predictors of suicide attempt in early-onset, first-episode psychoses: a longitudinal 24-month follow-up study.** *J Clin Psychiat* 74(1):59-66 I.F.: 5.812

7. Grande I, de Arce R, Jiménez-Arriero MÁ, Lorenzo FG, Valverde JI, Balanzá-Martínez V, Zaragoza S, Cobaleda S, Vieta E; SIN-DEPRES Group. **Patterns of pharmacological maintenance treatment in a community mental health services bipolar disorder cohort study (SIN-DEPRES).** *Int J Neuropsychopharmacol* 16(3):513-523 I.F.: 5.641

8. Vieta E, Langosch JM, Figueira ML, Souery D, Blasco-Colmenares E, Medina E, Moreno-Manzanaro M, Gonzalez MA, Bellivier F. **Clinical management and burden of bipolar disorder: results from a multinational longitudinal study (WAVE-bd).** *Int J Neuropsychopharmacol* 16(8):1719-1732 I.F.: 5.641

9. Garcia-Rizo C, Fernandez-Egea E, Miller BJ, Justicia A, Heaphy CM, Griffith JK, Bernardo M, Kirkpatrick B. **Abnormal Glucose Tolerance and Decreased Telomere Length in Newly Diagnosed, Antidepressant-Naïve Patients with Depression**. *Brain Behav Immun* 28:49-53 I.F.: 5.612

10. Atakan Z, Bhattacharyya S, Allen P, Martín-Santos R, Crippa JA, Borgwardt SJ, Fusar-Poli P, Seal M, Sallis H, Stahl D, Zuardi AW, Rubia K, McGuire P. **Cannabis affects people differently: inter-subject variation in the psychotogenic effects of Δ9-tetrahydrocannabinol: a functional magnetic resonance imaging study with healthy volunteers.** *Psychol Med* 43(6):1255-1267 I.F.: 5.587

11. Bombin I, Mayoral M, Castro-Fornieles J, Gonzalez-Pinto A, de la Serna E, Rapado-Castro M, Barbeito S, Parellada M, Baeza I, Graell M, Payá B, Arango C. **Neuropsychological evidence for abnormal neurodevelopment associated with early-onset psychoses.** *Psychol Med* 43(4):757-768 I.F.: 5.587

12. Mora E, Portella MJ, Forcada I, Vieta E, Mur M. **Persistence of cognitive impairment and its negative impact on psychosocial functioning in lithium-treated, euthymic bipolar patients: a 6-year follow-up study.** *Psychol Med* 43(6):1187-1196 I.F.: 5.587

13. Madre M, Pomarol-Clotet E, McKenna P, Radua J, Ortiz-Gil J, Panicali F, Goikolea JM, Vieta E, Sarró S, Salvador R, Amann BL. **Brain functional abnormality in schizo-affective disorder: an fMRI study.** *Psychol Med* 43(1):143-153 I.F.: 5.587

14. Pujol J, Giménez M, Ortiz H, Soriano-Mas C, López-Solà M, Farré M, Deus J, Merlo-Pich E, Harrison BJ, Cardoner N, Navinés R, Martín-Santos R. **Neural response to the observable self in social anxiety disorder.** *Psychol Med* 43(4):721-731 I.F.: 5.587

15. Udina M, Moreno-España J, Navinés R, Giménez D, Langohr K, Gratacòs M, Capuron L, de la Torre R, Solà R, Martín-Santos R. **Serotonin and interleukin-6: the role of genetic polymorphisms in IFN-induced neuropsychiatric symptoms.** *Psychoneuroendocrinology* 38(9):1803-1813 I.F.: 5.137

16. Bourne C, Aydemir Ö, Balanzá-Martínez V, Bora E, Brissos S, Cavanagh JT, Clark L, Cubukcuoglu Z, Dias VV, Dittmann S, Ferrier IN, Fleck DE, Frangou S, Gallagher P, Jones L, Kieseppä T, Martínez-Arán A, Melle I, Moore PB, Mur M, Pfennig A, Raust A, Senturk V, Simonsen C, Smith DJ, Bio DS, Soeiro-de-Souza MG, Stoddart SD, Sundet K, Szöke A, Thompson JM, Torrent C, Zalla T, Craddock N, Andreassen OA, Leboyer M, Vieta E, Bauer M, Worhunsky PD, Tzagarakis C, Rogers RD, Geddes

JR, Goodwin GM. **Neuropsychological testing of cognitive impairment in euthymic bipolar disorder: an individual patient data meta-analysis.** *Acta Psychiatr Scand* 128(3):149-162 I.F.: 4.857

17. De Barros Pellegrinelli K, de O Costa LF, Silval KI, Dias VV, Roso MC, Bandeira M, Colom F, Moreno RA. **Efficacy of psychoeducation on symptomatic and functional recovery in bipolar disorder.** *Acta Psychiatr Scand* 127(2):153-158 I.F.: 4.857

18. Grande I, Goikolea JM, de Dios C, González-Pinto A, Montes JM, Saiz-Ruiz J, Prieto E, Vieta E; PREBIS group. **Occupational disability in bipolar disorder: analysis of predictors of being on severe disablement benefit (PREBIS study data).** *Acta Psychiatr Scand* 127(5):403-411 I.F.: 4.857

19. Perugi G, Angst J, Azorin JM, Bowden C, Vieta E, Young AH; BRIDGE Study Group. **The bipolar-borderline personality disorders connection in major depressive patients.** *Acta Psychiatr Scand* 128(5):376-383 I.F.: 4.857

20. Soeiro-de-Souza MG, Bio DS, Dias VV, Vieta E, Machado-Vieira R, Moreno RA. **The CACNA1C risk allele selectively impacts on executive function in bipolar type I disorder.** *Acta Psychiatr Scand* 128(5):362-369 I.F.: 4.857

21. Strejilevich SA, Martino DJ, Murru A, Teitelbaum J, Fassi G, Marengo E, Igoa A, Colom F. **Mood instability and functional recovery in bipolar disorders.** *Acta Psychiatr Scand* 128(3):194-202 I.F.: 4.857

22. Gamma A, Angst J, Azorin JM, Bowden CL, Perugi G, Vieta E, Young AH. **Transcultural validity of the Hypomania Checklist-32 (HCL-32) in patients with major depressive episodes.** *Bipolar Disord* 15(6):701-712 I.F.: 4.621

23. Moreno C, Hasin DS, Arango C, Oquendo MA, Vieta E, Liu S, Grant BF, Blanco C. **The bipolar-depressive continuum in the National Epidemiologic Survey on Alcohol and Related Conditions.** *Bipolar Disord* 15(1):112-113 I.F.: 4.621

24. Suppes T, Vieta E, Gustafsson U, Ekholm B. **Maintenance treatment with quetiapine when combined with either lithium or divalproex in bipolar I disorder: analysis of two large randomized, placebo-controlled trials.** *Depress Anxiety* 30(11):1089-1098 I.F.: 4.610

25. Goikolea JM, Colom F, Capapey J, Torres I, Valenti M, Grande I, Undurraga J, Vieta E. **Faster onset of antimanic action with haloperidol compared to second-generation antipsychotics. A meta-analysis of randomized clinical trials in acute mania.** *Eur Neuropsychopharmacol* 23(4):305-316 I.F.: 4.595

26. Jiménez E, Arias B, Mitjans M, Goikolea JM, Roda E, Sáiz PA, García-Portilla MP, Burón P, Bobes J, Oquendo MA, Vieta E, Benabarre A. **Genetic variability at IMPA2, INPP1 and GSK3β increases the risk of suicidal behavior in bipolar patients.** *Eur Neuropsychopharmacol* 23(11):1452-1462 I.F.: 4.595

27. Mas S, Gassó P, Bernardo M, Lafuente A. **Functional analysis of gene expression in risperidone treated cells provide new insights in molecular mechanism and new candidategenes for pharmacogenetic studies.** *Eur Neuropsychopharmacol* 23(4):329-337 I.F.: 4.595

28. Nivoli AM, Colom F, Pacchiarotti I, Murru A, Scott J, Valentí M, Mazzarini L, Del Mar Bonnin C, Sánchez-Moreno J, Serretti A, Vieta E. **Treatment strategies according to clinical features in a naturalistic cohort study of bipolar patients: a principal component analysis of lifetime pharmacological and biophysic treatment options.** *Eur Neuropsychopharmacol* 23(4):263-275 I.F.: 4.595

29. Batalla A, Garcia-Rizo C, Castellví P, Fernandez-Egea E, Yücel M, Parellada E, Kirkpatrick B, Martin-Santos R, Bernardo M. **Screening for substance use disorders in first-episode psychosis: implications for readmission.** *Schizophr Res* 146:125-131 I.F.: 4.590

30. Puig O, Penadés R, Baeza I, De la Serna E, Sánchez-Gistau V, Lázaro L, Bernardo M, Castro-Fornieles J. **Assessment of real-world daily-living skills in early-onset schizophrenia trough the Life Skills Profile scale.** *Schizophr Res* 145(1-3):95-100 I.F.: 4.590

31. Garrido G, Barrios M, Penadés R, Enríquez M, Garolera M, Aragay N, Pajares M, Vallès V, Delgado L, Alberni J, Faixa C, Vendrell JM. **Computer-assisted cognitive remediation therapy: cognition, self-esteem and quality of life in schizophrenia.** *Schizophr Res* 150(2-3):563-569 I.F.: 4.590

32. Payá B, Rodríguez-Sánchez JM, Otero S, Muñoz P, Castro-Fornieles J, Parellada M, Gonzalez-Pinto A, Soutullo C, Baeza I, Rapado-Castro M, Sáenz-Herrero M, Moreno D, Arango C. **Premorbid impairments in early-onset psychosis: differences between patients with schizophrenia and bipolar disorder.** *Schizophr Res* 146(1-3):103-110 I.F.: 4.590

33. De la Serna E, Andrés-Perpiñá S, Puig O, Baeza I, Bombin I, Bartrés-Faz D, Arango C, Gonzalez-Pinto A, Parellada M, Mayoral M, Graell M, Otero S, Guardia J, Castro-Fornieles J. **Cognitive reserve as a predictor of two year neuropsychological performance in early onset first-episode schizophrenia.** *Schizophr Res* 143(1):125-131 I.F.: 4.590

34. Glodberg X, Fatjó-Vilas M, Alemany S, Nanedic I, Gastó C, Fañanas L. **Gene-enviroment interaction on cognition: atwin study of childhood maltreatment and COMT variability.** *J Psychiatr Res* 47(7):989-994 I.F.: 4.066

35. Mas S, Plana MT, Castro-Fornieles J, Gassó P, Lafuente A, Moreno E, Martinez E, Milà M, Lázaro L. **Common genetic**

background in anorexia nervosa and obsessive compulsive disorder: preliminary results from an association study. *J Psychiat Res* 47(6):747-754 I.F.: 4.066

36. Mitjans M, Serretti A, Fabbri C, Gastó C, Catalán R, Fañanas L, Arias B. **Screening genetic variability at the CNR1 gene in both major depression etiology and clinical response to citalopram treatment.** *Psychophramacology* 227(3):509-519 I.F.: 3.857

37. Gutiérrez F, Gárriz M, Peri JM, Ferraz L, Sol D, Navarro JB, Barbadilla A, Valdés M. **Fitness costs and benefits of personality disorder traits.** *Evol Hum Behav* 34:41-48 I.F.: 3.946

38. Donaire A, Capdevila A, Carreño M, Setoain X, Rumià J, Aparicio J, Campistol J, Padilla N, Sanmartí F, Vernet O, Pintor L, Boget T, Ortells J, Bargalló N. **Identifying the cortical substrates of interictal epileptiform activity in patients with extratemporal epilepsy: An EEG-fMRI sequential analysis and FDG-PET study.** *Epilepsia* 54(4):678-690 I.F.: 3.909

39. Sierra-Marcos A, Maestro I, Falcón C, Donaire A, Setoain J, Aparicio J, Rumià J, Pintor L, Boget T, Carreño M, Bargalló N. **Ictal EEG-fMRI in localization of epileptogenic area in patients with refractory neocortical focal epilepsy.** *Epilepsia* 54(9):1688-1698 I.F.: 3.909

40. Gassó P, Papagianni K, Mas S, Fernández de Bobadilla R, Arnaiz JÁ, Bernardo M, Lafuente A. **Relationship betwee CYP2D6 genotype and haloperidol pharmacokinetics and extrapiramidal symptoms in healthy volunteers.** *Pharmacogenomics* 14(13):1551-1563 I.F.: 3.857

41. Nardi AE, Machado S, Almada LF, Paes F, Silva AC, Marques RJ, Amrein R, Freire RC, Martin-Santos R, Cosci F, Hallak JE, Crippa JA, Arias-Carrión O. **Clonazepam for the treatment of panic disorder.** *Curr Drug Targets* 14(3):353-364 I.F.: 3.848

42. Noguera A, Ballesta P, Baeza I, Arango C, de la Serna E, González-Pinto A, Parellada M, Graell M, Moreno C, Otero S, Castro-Fornieles J. **Twenty-four months of antipsychotic treatment in children and adolescents with first psychotic episode: discontinuation and tolerability.** *J Clin Psychopharm* 33(4):463-471 I.F.: 3.513

43. Fernández-Corcuera P, Salvador R, Monté GC, Salvador Sarró S, Goikolea JM, Amann B, Moro N, Sans-Sansa B, Ortiz-Gil J, Vieta E, Maristany T, McKenna PJ, Pomarol-Clotet E. **Bipolar depressed patients show both failure to activate and failure to de-activate during performance of a working memory task.** *J Affect Disord* 148(2-3):170-178 I.F.: 3.295

44. M'bailara K, Cosnefroy O, Vieta E, Scott J, Henry C. **Group-based trajectory modeling: a novel approach to examining symptom trajectories in acute bipolar episodes.** *J Affect Disord* 145(1):36-41 I.F.: 3.295

45. Murru A, Pacchiarotti I, Amann BL, Nivoli AM, Vieta E, Colom F. **Treatment adherence in bipolar I and schizoaffective disorder, bipolar type.** *J Affect Disord* 151(3):1003-1008 I.F.: 3.295

46. Navarro V, Gonzalez A, Guarch J, Penadés R, Torra M, Fañanas I, Arias B, Serra M, Pintor L, Gastó C. **Association between symptomatic profile and remission following antidepressant treatment in unipolar major depression.** *J Affect Disord* 150(2):209-215 I.F.: 3.295

47. Pacchiarotti I, Nivoli AM, Mazzarini L, Kotzalidis GD, Sani G, Koukopoulos A, Scott J, Strejilevich S, Sánchez-Moreno J, Murru A, Valentí M, Girardi P, Vieta E, Colom F. **The symptom structure of bipolar acute episodes: in search for the mixing link.** *J Affect Disord* 149(1-3):56-66 I.F.: 3.295

48. Perugi G, Angst J, Azorin JM, Bowden C, Vieta E, Young AH; BRIDGE Study Group. **Is comorbid borderline personality disorder in patients with major depressive episode and bipolarity a developmental subtype? Findings from the international BRIDGE study.** *J Affect Disord* 144(1-2):72-78 I.F.: 3.295

49. Reinares M, Papachristou E, Harvey P, Mar Bonnín C, Sánchez-Moreno J, Torrent C, Ayuso-Mateos JL, Ploubidis GB, Vieta E, Frangou S. **Towards a clinical staging for bipolar disorder: defining patient subtypes based on functional outcome.** *J Affect Disord* 144(1-2):65-71 I.F.: 3.295

50. Roca A, Imaz ML, Torres A, Plaza A, Subirà S, Valdés M, Martin-Santos R, Garcia-Esteve L. **Unplanned pregnancy and discontinuation of SSRIs in pregnant women with previously treated affective disorder.** *J Affect Disord* 150(3):807-813 I.F.: 3.295

51. Rosa AR, Mercadé C, Sánchez-Moreno J, Solé B, Mar Bonnin CD, Torrent C, Grande I, Sugranyes G, Popovic D, Salamero M, Kapczinski F, Vieta E, Martinez-Aran A. **Validity and reliability of a rating scale on subjective cognitive deficits in bipolar disorder (COBRA).** *J Affect Disord* 150(1):29-36 I.F.: 3.295

52. Undurraga J, Tondo L, Schalkwijk S, Vieta E, Baldessarini RJ. **Re-analysis of the earliest controlled trials of imipramine.** *J Affect Disord* 147(1-3):451-454 I.F.: 3.295

53. Vieta E, Bauer M, Montgomery S, McIntyre RS, Szamosi J, Earley WR, Eriksson H. **Pooled analysis of sustained response rates for extended release quetiapine fumarate as monotherapy or adjunct to antidepressant therapy in patients with major depressive disorder.** *J Affect Disord* 150(2):639-643 I.F.: 3.295

54. Alemany S, Goldberg X, van Winkel R, Gastó C, Peralta V, fañanas L. **Childhood adversity and psychosis: examining whether the association is due to genetic confounding using monozygotic twin differences approach.** *Eur Psychiatry* 28(4):207-212 I.F.: 3.285

55. Garcia-Amador M, de la Serna E, Vila M, Romero S, Valenti M, Sánchez-Gistau

V, Benabarre A, Vieta E, Castro-Fornieles J. **Parents with bipolar disorder: are disease characteristics good predictors of psychopathology in offspring?** *Eur Psychiatry* 28(4):240-246 I.F.: 3.285

56. Angst J, Gamma A, Bowden CL, Azorin JM, Perugi G, Vieta E, Young AH. **Evidence-based definitions of bipolar-I and bipolar-II disorders among 5,635 patients with major depressive episodes in the Bridge Study: validity and comorbidity.** *Eur Arch Psychiatry Clin Neurosci* 263(8):663-673 I.F.: 3.200

57. Torres X, Baillès E, Gutiérrez F, Peri JM, Collado A, Arias A, Gómez E. **Personality does not distinguish people with fibromyalgia but identifies subgroups of patients.** *Gen Hosp Psychiat* 35:640-648 I.F.: 2.977

58. Lázaro L, Andrés S, Calvo A, Cullell C, Moreno E, Plana MT, Falcón C, Bargalló N, Castro-Fornieles J. **Normal gray and white matter volume after weight restoration in adolescents with anorexia nervosa.** *Int J Eat Disorder* 46(8):841-848 I.F.: 2.877

59. Baeza I, Correll CU, Saito E, Amanbekova D, Ramani M, Kapoor S, Chekuri R, De Hert M, Carbon M. **Frequency, characteristics and management of adolescent inpatient aggression.** *J Child Adol Psychop* 23(4):271-81 I.F.: 2.773

60. Barrio P, Batalla A, Castellví P, Hidalgo D, García M, Ortiz A, Grande I, Pons A, Parellada E. **Effectiveness of long-acting injectable risperidone versus oral antipsychotics in the treatment of recent-onset schizophrenia: a case-control study.** *Int Clin Psychopharm* 28(4):164-170 I.F.: 2.705

61. Ferraz L, Portella M, Vállez M, Gutiérrez F, Martín-Blanco A, Martín-Santos R, Subirà S. **Hostility and childhood sexual abuse as predictors of suicidal behavior in Borderline Personality Disorder.** *Psychiat Res* 210:980-985 I.F.: 2.456

62. Gómez-Gil E, Gutiérrez F, Cañizares S, Zubiaurre-Elorza L, Monràs M, Esteva de Antonio I, Salamero M, Guillamón A. **Temperament and character in transsexuals.** *Psychiat Res* 210:969-974 I.F.: 2.456

63. Pujol N, Penadés R, Rametti G, Catalán R, Vidal-Piñeiro D, Palacios E, Bargallo N, Bernardo M, Junqué C. **Inferior frontal and insular cortical thinning is related to dysfunctional brain activation/ deactivation during working memory task in schizophrenic patients.** *Psychiat Res* 214(2):94-101 I.F.: 2.456

64. Magallón-Neri EM, Forns M, Canalda G, De La Fuente JE, García R, González E, Lara A, Castro-Fornieles J. **Usefulness of the International Personality Disorder Examination Screening Questionnaire for borderline and impulsive personality pathology in adolescents.** *Compr Psychiat* 54(3):301-308 I.F.: 2.376

65. Arias B, Fabbri C, Gressier F, Serretti A, Mitjans M, Gastó C, Catalán R, De Ronchi D, Fañanas L. **TPH1, MAOA, serotonin receptor 2A and 2C genes in citalopram response: possible effect in melancholic and psychotic depression.** *Neuropsycholbiology* 67(1):41-47 I.F.: 2.371

66. Rumià J, Marmol F, Sanchez J, Giménez-Crouseilles J, Carreño M, Bargalló N, Boget T, Pintor L, Setoain X, Donaire A, Saez GT, Ribalta T, Ferrer E, Puig-Parellada P. **Oxidative stress markers in the neocortex of drug-resistant epilepsy patients submitted to epilepsy surgery.** *Epilepsy Res* 107(1-2):75-81 I.F.: 2.241

67. Cieza A, Bostan C, Ayuso-Mateos JL, Oberhauser C, Bickenbach J, Raggi A, Leonardi M, Vieta E, Chatterji S. **The psychosocial difficulties in brain disorders that explain short term changes in health outcomes.** *BMC Psychiatry* 13(1):78 I.F.: 2.233

68. Gómez-Benito J, Guilera G, Pino O, Rojo E, Tabarés-Seisdedos R, Safont G, Martínez-Arán A, Franco M, Cuesta MJ, Crespo-Facorro B, Bernardo M, Vieta E, Purdon SE, Mesa F, Rejas J. **The screen for cognitive impairment in psychiatry: diagnostic-specific standardization in psychiatric ill patients.** *BMC Psychiatry* 13(1):127 I.F.: 2.233

69. Serrano E, Ezpeleta L, Castro-Fornieles J. **Comorbidity and phenomenology of bipolar disorder in children with ADHD.** *J Atten Disord* 17(4):330-338 I.F.: 2.163

70. Narvaez JC, Magalhães PV, Fries GR, Colpo GD, Czepielewski LS, Vianna P, Chies JA, Rosa AR, Von Diemen L, Vieta E, Pechansky F, Kapczinski F. **Peripheral toxicity in crack cocaine use disorders.** *Neurosci Lett* 544:80-84 I.F.: 2.026

71. Bravo F, Gual A, Lligoña A, Colom J. **Gender differences in the long-term outcome of alcohol dependence treatments: An analysis of twenty-year prospective follow up.** *Drug Alcohol Rev* 32(4):381-388 I.F.: 2.017

72. Ayuso-Mateos JL, Avila CC, Anaya C, Cieza A, Vieta E; Bipolar Disorders Core Sets Expert Group. **Development of the International Classification of Functioning, Disability and Health core sets for bipolar disorders: results of an international consensus process.** *Disabil Rehabil* 35(25):2138-2146 I.F.: 1.541

73. Navines R, Gutierrez F, Arranz B, Moreno-España J, Imaz ML, Soler V, Vazquez M, Pascual JC, Martin-Santos R. **Long-term and bizarre self-injurious behaviour: An approach to the underlying psychological mechanisms and management.** *J Psychiatr Pract* 19:65-71 I.F.: 1.288

74. Pintor L, Torres X, Bailles E, Navarro V, de Osaba MJ, Belmonte A, Gastó C. **CRF test in melancholic depressive patients with partial versus complete relapses: a 2-year follow-up study.** *Nord J Psychiatry* 67(3):177-184 I.F.: 1.221

75. Calvo N, Gutiérrez F, Casas M (2013) **Diagnostic agreement between the**

Personality Diagnostic Questionnaire-4+ (PDQ-4+) and its Clinical Significance Scale. *Psicothema* 25:427-32 I.F.: 0.961

76. Bernardo M, Bioque M, Parellada M, Saiz Ruiz J, Cuesta MJ, Llerena A, Sanjuán J, Castro-Fornieles J, Arango C, Cabrera B; PEPs Group. **Assessing clinical and functional outcomes in a gene-environment interaction study in first episode of psychosis (PEPs).** *Rev Psiquiatr Salud* 6(1):4-16 I.F.: 0.667

77. Castro-Fornieles J. **Child and adolescent psychiatry: the need for training and development.** *Rev Psiquiatr Salud* 6(2):57-59 I.F.: 0.667

78. Pons A, Torres A, Goti J, Fernandez-Egea E, Carne X, Bernardo M. **Should obesity be a limiting factor for clozapine treatment?** *Rev Psiquiatr Salud* 6(2):75-79 I.F.: 0.667

Reviews / I.F.: 75.742

1. Pacchiarotti I, Bond DJ, Baldessarini RJ, Nolen WA, Grunze H, Licht RW, Post RM, Berk M, Goodwin GM, Sachs GS, Tondo L, Findling RL, Youngstrom EA, Tohen M, Undurraga J, González-Pinto A, Goldberg JF, Yildiz A, Altshuler LL, Calabrese JR, Mitchell PB, Thase ME, Koukopoulos A, Colom F, Frye MA, Malhi GS, Fountoulakis KN, Vázquez G, Perlis RH, Ketter TA, Cassidy F, Akiskal H, Azorin JM, Valentí M, Mazzei DH, Lafer B, Kato T, Mazzarini L, Martínez-Arán A, Parker G, Souery D, Ozerdem A, McElroy SL, Girardi P, Bauer M, Yatham LN, Zarate CA, Nierenberg AA, Birmaher B, Kanba S, El-Mallakh RS, Serretti A, Rihmer Z, Young AH, Kotzalidis GD, MacQueen GM, Bowden CL, Ghaemi SN, Lopez-Jaramillo C, Rybakowski J, Ha K, Perugi G, Kasper S, Amsterdam JD, Hirschfeld RM, Kapczinski F, Vieta E. **The International Society for Bipolar Disorders (ISBD) task force report on antidepressant use in bipolar disorders.** *Am J Psychiatry* 170(11):1249-1262 I.F.: 14.721

2. Lim CS, Baldessarini RJ, Vieta E, Yucel M, Bora E, Sim K. **Longitudinal neuroimaging and neuropsychological changes in bipolar disorder patients: review of the evidence.** *Neurosci Biobehav Rev* 37(3):418-435 I.F.: 9.440

3. Miret M, Ayuso-Mateos JL, Sanchez-Moreno J, Vieta E. **Depressive disorders and suicide: Epidemiology, risk factors, and burden.** *Neurosci Biobehav Rev* 37(10):2372-2374 I.F.: 9.440

4. Popovic D, Reinares M, Scott J, Nivoli A, Murru A, Pacchiarotti I, Vieta E, Colom F. **Polarity index of psychological interventions in maintenance treatment of bipolar disorder.** *Psychother Psychosom* 82(5):292-8 I.F.: 7.230

5. Roerke M, Gual A, Rehm J. **Reduction of alcohol consumption and subsequent mortality in alcohol use disorders: systematic review and meta-analyses.** *J Clin Psychiatry* 74(12):e1181-e1189 I.F.: 5.812

6. Reinares M, Rosa AR, Franco C, Goikolea JM, Fountoulakis K, Siamouli M, Gonda X, Frangou S, Vieta E. **A systematic review on the role of anticonvulsants in the treatment of acute bipolar depression.** *Int J Neuropsychopharmacol* 16(2):485-96 I.F.:5.641

7. Vieta E, Valentí M. **Pharmacological management of bipolar depression: acute treatment, maintenance, and prophylaxis.** *CNS Drugs* 27(7):515-529 I.F.: 4.826

8. Batalla A, Bhattacharyya S, Yücel M, Fusar-Poli P, Crippa JA, Nogué S, Torrens M, Pujol J, Farré M, Martin-Santos R. **Structural and functional imaging studies in chronic cannabis users: a systematic review of adolescent and adult findings.** *PLoS One* 8(2):e55821 I.F.: 3.730

9. Goikolea JM, Colom F, Torres I, Capapey J, Valentí M, Undurraga J, Grande I, Sanchez-Moreno J, Vieta E. **Lower rate of depressive switch following antimanic treatment with second-generation antipsychotics versus haloperidol.** *J Affect Disord* 144(3):191-8 I.F.: 3.295

10. Vargas C, López-Jaramillo C, Vieta E. **A systematic literature review of resting state network--functional MRI in bipolar disorder.** *J Affect Disord* 150(3):727-35 I.F.: 3.295

11. Vieta E, Valentí M. **Mixed states in DSM-5: implications for clinical care, education, and research.** *J Affect Disord* 148(1):28-36 I.F.: 3.295

12. Vieta E, Popovic D, Rosa AR, Solé B, Grande I, Frey BN, Martinez-Aran A, Sanchez-Moreno J, Balanzá-Martínez V, Tabarés-Seisdedos R, Kapczinski F. **The clinical implications of cognitive impairment and allostatic load in bipolar disorder.** *Eur Psychiatry* 28(1):21-29 I.F.: 3.285

13. Udina M, Foulon H, Valdés M, Bhattacharyya S, Martín-Santos R. **Dhat syndrome: a systematic review.** *Psychosomatics* 54(3):212-218 I.F.: 1.732

Editorials / I.F.: 49.688

1. Scott J, Fowler D, McGorry P, Birchwood M, Killackey E, Christensen H, Glozier N, Yung A, Power P, Nordentoft M, Singh S, Brietzke E, Davidson S, Conus P, Bellivier F, Delorme R, Macmillan I, Buchanan J, Colom F, Vieta E, Bauer M, McGuire P, Merikangas K, Hickie I. **Adolescents and young adults who are not in employment, education, or training.** *Brit Med J* 347:f5270 I.F.: 17.215

2. Freedman R, Lewis DA, Michels R, Pine DS, Schultz SK, Tamminga CA, Gabbard GO, Gau SS, Javitt DC, Oquendo MA, Shrout PE, Vieta E, Yager J. **The initial field trials of DSM-5: new blooms and old thorns.** *Am J Psychiatry* 170(1):1-5 I.F.: 14.721

3. Vieta E. **Pros and cons of specialised care in bipolar disorder: an international perspective.** *Brit J Psychiatry* 202(3):170-171 I.F.: 6.606

4. Catalá-López F, Gènova-Maleras R, Vieta E, Tabarés-Seisdedos R. **The increasing burden of mental and neurological disorders.** *Eur Neuropsychopharmacol* 23(11):1337-1339 I.F.: 4.595

5. Nutt D, Gispen-de Wied CC, Arango C, Keefe RS, Penadés R, Murphy DG, Robbins TW, Sahakian BJ. **Cognition in schizophrenia: summary Nice Consultation Meeting 2012.** *Eur Neuropsychopharmacol* 23(8):769-778 I.F.: 4.595

6. Rehm J, Marmet S, Anderson P, Gual A, Kraus L, Nutt DJ, Room R, Samokhvalov AV, Scafato E, Trapencieris M, Wiers RW, Gmel G. **Defining Substance Use Disorders: Do We Really Need More Than Heavy Use?** *Alcohol Alcohol* 48(6):633-40 I.F.: 1.956

Clinical Guidelines / I.F.: 7.142

1. Bauer M, Pfennig A, Severus E, Whybrow PC, Angst J, Möller HJ; World Federation of Societies of Biological Psychiatry. **Task Force on Unipolar Depressive Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of unipolar depressive disorders, part 1: update 2013 on the acute and continuation treatment of unipolar depressive disorders.** *World J Biol Psychiatry* 14(5):334-85 I.F.: 3.571

2. Grunze H, Vieta E, Goodwin GM, Bowden C, Licht RW, Möller HJ, Kasper S; WFSBP Task Force on Treatment Guidelines for Bipolar Disorders. **The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of bipolar disorders: update 2012 on the long-term treatment of bipolar disorder.** *World J Biol Psychiatry* 14(3):154-219 I.F.: 3.571

Multicenter / I.F.: 2.233

1. Kluge M, Hegerl U, Sander C, Dietzel J, Mergl R, Bitter I, Demyttenaere K, Gusmão R, Gonzalez-Pinto A, Perez-Sola V, Vieta E, Juckel G, Zimmermann US, Bauer M, Sienaert P, Quintão S, Edel MA, Bolyos C, Ayuso-Mateos JL, López-García P. **Methylphenidate in mania project (MEMAP): study protocol of an international randomised double-blind placebo-controlled study on the initial treatment of acute mania with methylphenidate.** *BMC Psychiatry* 13:71 I.F.: 2.233

GRANTS FOR RESEARCH IN PROGRESS

Andrés S. **Trastornos de la conducta alimentria, veinte años después. Estudio de estado psicopatológico y físico y su relación con el funcionamiento general. System number: 23409.** Sponsored by: Instituto de la mujer-Ministerio de igualdad. Duration: 01/01/2010-30/06-2013

Baeza I. **Estudio multicéntrico longitudinal sobre características clínicas, cognitivas y de neuroimagen en niños y adolescentes con Síndrome de Riesgo de Psicosis.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01349. Duration: 01/01/2012-31/12/2014

Baeza I. **"Predictor variables of clinical and functional outcome in children and adolescents with first-episode of psychosis".** Sponsored by: Fundación Alicia Koplowitz. Duration: 01/01/2013-31/12/2015

Benabarre A. **Identificación de variables predictoras clínicas, neurocognitivas y genéticas en la emergencia y recurrencia de la conducta suicida en el trastorno bipolar.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00906. Duration: 01/01/2013-31/12/2015

Bernardo M. **Antipsicóticos típicos vs. Atípicos; impacto de la farmacogenética en la farmacocinética, la ocupación de receptores estriatales y la aparición sintomatología extrapiramidal.** Sponsored by: Instituto de Salud Carlos III (ISCIII) TRA-065. Duration: 01/01/2010-30/06/2013

Bernardo M. **S02078- Diabetes in Neuropsychiatric Disorders. (subaward nº 07-20846A1.** Sponsored by: National Institute of Health (NIH). 1R01DK069265-01A1. Duration: 01/04/2005-31/12/2013

Bernardo M. **Determinantes clínicos y neurobiológicos de segundos episodios de esquizofrenia. Estudio longitudinal de primeros episodios psicóticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/00325. Duration: 01/01/2012-31/12/2014

Bernardo M. **Grup esquizofrènia clinic.** Sponsoredby: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1295. Duration: 15/09/2009-30/04/2014

Bernardo M. **Interacción genotipo-fenotipo y ambiente. Aplicación a un modelo predictivo en primeros episodios psicóticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI08/0208. Duration: 01/01/2009-30/06/2013

Castro J. **Aggression subtyping for improved insight and treatment innovation in psychiatric disorders.** Sponsored by: European Commission. 602805-2. Duration: 01/11/2013-31/10/2018

Castro J. **Paediatric European Risperidone Studies.** Sponsored by: European Commission. 241959. Duration: 01/05/2010-30/04/2015

Castro J. **Estudio de seguimiento tras cuatro años de la primera evaluación de niños y adolescentes hijos de pacientes con esquizofrenia o trastorno bipolar.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00683. Duration: 01/01/2012-31/12/2014

Castro J. **Grup de recerca en Psiquiatria i Psicologia Infantil Clínic (GRUPPIC).** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR).

2009_SGR_1119.
Duration: 29/07/2009-30/04/2014

Castro J. **Two year follow-up study of children and adolescent offspring of subjects with schizophrenia or bipolar disorders.** Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 091630.
Duration: 29/01/2010-31/03/2014

Castro J. **Suicidality: Treatment Occurring in Paediatrics.** Sponsored by: European Commission. 261411.
Duration: 01/11/2010-30/04/2015

Catalan R. **Evaluación del coste/ efectividad de la intervención farmacogenética en la optimización del tratamiento con antipsicóticos en pacientes con esquizofrenia.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/02006.
Duration: 01/01/2012-31/12/2014

Catalan R. **Identificación de predictores clínicos, neurohormonales, farmacogenéticos en la respuesta terapéutica a clozapina en pacientes diagnosticados de esquizofrenia refractaria.** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00184.
Duration: 01/01/2009-30/06/2013

Colom F. **Bioequivalencia, aplicabilidad clínica y utilidad terapéutica de la monitorización salivar de litio y valproato en pacientes bipolares.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00910.
Duration: 01/01/2013-31/12/2015

Colom F. **e-Enseñanza y desarrollo de un programa psicoeducativo basado en la evidencia en primeros episodios psicóticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/02209.
Duration: 01/01/2011-30/06/2015

Colom F. **Factores neurobiológicos, cognitivos y clínicos asociados al pronóstico clínico y funcional a un año de seguimiento de la psicoeducación en el trastorno bipolar.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1044.
Duration: 01/01/2010-30/06/2014

Garcia-Esteve M.L. **Violencia sexual, estrés agudo y calidad de vida: estudio de los factores de riesgo en las mujeres atendidas en urgencias tras una agresión sexual.** Sponsored by: INSTITUTO DE LA MUJER. 235/09.
Duration: 03/02/2010-21/12/2013

Garcia-Esteve M.L. **Estudio farmacogenético y de seguridad clínica en hijos de madres tratadas con antidepresivos ISRS durante el embarazo: Evaluación del funcionamiento cognitivo-conductual a los 5 años.** Sponsored by: Instituto de Salud Carlos III (ISCIII). EC08/00170.
Duration: 01/01/2009-31/07/2013

Goikolea Alberdi, JM. **Alteraciones Cerebrales de los primeros Episodios Psicóticos y Maníacos: Un estudio de neuroimagen multimodal.** Sponsored by: Insituto de Salud Carlos III (PS09/01927).
Duration: 01/01/2010-31/06/2013

Gual A. **Red de Trastornos Adictivos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0028/0016.
Duration: 01/01/2013-31/12/2016

Gual A. **Addictions and Lifestyles In Contemporary Europe - Reframing Addictions Project.** Sponsored by: European Commission. 266813.
Duration: 01/04/2011-31/03/2016

Gual A. **Good practice on brief interventions to address alcohol use disorders in primary health care, workplace health services, emergency care and social services.** Sponsored by: European Commission. 29908.
Duration: 01/05/2012-30/04/2015

Gual A. **STREP: Alcohol Measures for Public Health Research Alliance.** Sponsored by: European Commission. 223059.
Duration: 01/01/2009-31/12/2014

Gual A. **European Workplace and Alcohol.** Sponsored by: European Commission. CE_SANCO_09_01.
Duration: 01/01/2011-31/12/2014

Gual A. **Optimizing delivery of health care interventions.** Sponsored by: European Commission. 259268.
Duration: 01/01/2011-31/12/2014

Gual A. **Conferencies i taules rodones transdisciplinars sobre l'impacte de les addiccions en el benestar de la població europea.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2012 ARCS1 00083.
Duration: 23/04/2013-30/11/2013

Lazaro L. **Analysis of polimorphisms in candidate genes in early onset obsessive-compulsive disorder. Relationship with cerebral abnormalities and symptom dimensions.** Sponsored by: FUNDACIÓ LA MARATÓ DE TV3. 091710.
Duration: 29/01/2010-30/03/2014

Lázaro L. **Identificacion de predictores farmacogeneticos en la respuesta terapeutica a fluoxetina en pacientes diagnosticados de trastorno obsesivo compulsivo de inicio en la infancia y la adolescencia.** Sponsored by: Fundación Alicia Koplowitz.
Duration: 01/06/2011-31/12/2014

Lazaro L. **Identificación de predictores farmacogenéticos en la respuesta terapéutica a Fluoxetina en niños y adolescentes.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01965.
Duration: 01/01/2011-30/06/2014

Martin-Santos R. **Bases neurobiológicas de la depresión inducida por interferón en la hepatitis C crónica. Estudio PSICOCIT. Subproyecto I.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/02206.
Duration: 01/01/2011-31/12/2014

Martin-Santos R. **Repercusión del inicio precoz del consumo continuado (crónico) de substancias de abuso sobre la red atencional: estudio de conectividad**

funcional cerebral y modulación genética. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. 2011/050.
Duration: 08/11/2011-07/11/2014

Martin-Santos R. **Grup de recerca en: "Vulnerabilitat, psicopatologia i gènere".** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1435.
Duration: 26/11/2009-30/04/2014

Martinez-Aran A. **Eficacia comparativa de una estrategia de rehabilitación neurocognitiva en pacientes con trastorno bipolar tipo I tras un primer episodio maníaco versus pacientes con múltiples episodios.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00637
Duration: 01/01/2012-31/12/2014

Martinez-Aran A. **Efficacy of Functional Remediation in bipolar euthymic patients and effects on Brain Derived Neurotrophic Factor (BDNF): The BIpolar FUnctional REmediation study.** Sponsored by: Brain & Behavior Research Foundation (2013 NARSAD Independent Investigator Grantees).
Duration: 2013-2015

Morer A. **European Multicentre Tics in Children Studies.** Sponsored by: European Commission. 278367.
Duration: 01/12/2011-31/05/2017

Morer A. **Inflamación, autoinmunidad y psicopatología: estudio en niños y adolescentes con patología psiquiátrica aguda y en hijos de madres afectadas de lupus eritematoso sistémico.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1347
Duration: 01/01/2010-30/06/2014

Moya J. **"Correlatos cerebrales de las alteraciones de flexibilidad cognitiva en Anorexia Nerviosa, un estudio con resonancia magnética funcional pre y post tratamiento, comparando mejoría exclusivamente ponderal y mejoría ponderal más cognitiva de los pacientes."** Sponsored by. Fundación Alicia Koplowitz.
Duration: 01/01/2012-31/12/2014

Parellada E. **Apoptosis y cambios neuroestructurales progresivos en pacientes con un primer episodio de esquizofrenia: estudio longitudinal y multimodal de neuroimagen y biología molecular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI08/0055.
Duration: 01/01/2009-30/06/2013

Penadès R. **El BDNF (Brain-derived neurotrophic factor) como posible biomarcador del tratamiento de rehabilitación neurocognitiva en la esquizofrenia de predominio negativo.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI 11/01958.
Duration 2012-2014.

Sugranyes G. **Conectividad Funcional en una muestra de niños y adolescentes de riesgo para psicosis.** Sponsored by. Fundación Alicia Koplowitz.
Duration: 01/01/2013-31/12/2015

Sugranyes G. **Estudio longitudinal de primeros episodios psicóticos en la infancia y adolescencia. Seguimiento a 10 años. System number: PI13/0064.** Sponsored by: Instituto de Salud Carlos III (ISCIII).
Duration: 01/01/2013-31/12/2015

Vieta E. **Especificidad de los síntomas prodrómicos en el trastorno bipolar y predicción del curso clínico de la enfermedad.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00912.
Duration: 01/01/2013-31/12/2015

Vieta E. **Metilfenidato en el tratamiento inicial de mania aguda.** Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC10-064.
Duration: 01/01/2011-31/12/2014

Vieta E. **Trastorn bipolar.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1022.
Duration: 15/09/2009-30/04/2014

Vieta E. **The neural correlates of euthymic cognitive impairment in bipolar disorder.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1893.
Duration: 01/01/2010-03/07/2013

Vieta E. **Impacte d'un programa d'intervenció multidisciplinar sobre l'estil de vida en la millora del funcionament psicosocial i la qualitat de vida dels pacients bipolars d'inici precoç.** Sponsored by: COL·LEGI OFIC INFERM BCN-DOCENCIA. PR-5385-11.
Duration: 01/01/2012-31/12/2013

DOCTORAL THESES

Bernardo, M; Leza JC. **Neuroinflammation in first episodes of psychosis.**
PhD student: Miquel Bioque Alcázar.

Vieta, E. **Desenvolupament i validaciód'unmodeld'estadificació en el trastorn bipolar: variables clíniques, funcionals i biomarcadorsperifèrics.**
PhD student: Iria Grande Fullana

Vieta, E, Colom F. **Treatment adherence in schizoaffective disorder.**
PhD student: Andrea Murru

Vieta, E. **Uso de antidepresivos suicidio en el trastorno bipolar.**
PhD student: Juan Pablo Undurraga Fourcade.

Marín-Santos, R. **Estudi de la incidència, factors de risc (sociodemogràfics, clínics i genètics), i resposta al tractamentprofilàcticambantidepressius de la depressió induïda per interferó alfa en la hepatitis C crònica.**
PhD student: Marc Udina Bonet

Penadés R. **Functional and structural correlates of cognitive impairments in schizophrenia disorder and brain effects of cognitive remediation therapy.**
PhD student: Nuria Pujol Giménez

García-Esteve L, Valdés M. **Efecto de las adversidades en la infancia en la patología depresiva y tiroidea en el posparto.**
PhD student: Anna Plaza Estradé

4.8 Neuropsychology

LOCATION
UB School of Medicine

FOR FURTHER INFORMATION
www.ub.edu/neuropsychology/html/portada.html

KEYWORDS
1. **Magnetic Resonance Imaging**
2. **Structural and functional connectivity**
3. **Aging and degenerative illness**
4. **Transcranial Magnetic Stimulation**
5. **Brain Plasticity**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	125.07	29	17	4
2012	142.75	30	22	7
2013	148.62	29	24	5

TEAM LEADER
Carme Junqué (UB)
T. 93 403 92 98
cjunque@ub.edu

RESEARCHERS
Núria Bargalló (HCB)
David Bartrés-Faz (UB)
Teresa Boget (HCB)
Manuel Salamero (HCB)
Josep M. Serra (UB)
Pere Vendrell (UB)

POST-DOCTORAL RESEARCHERS
Bárbara Segura (UB)

PRE-DOCTORAL RESEARCHERS
Hugo Cesar Baggio (UB)
Juan Pablo Martin Trias (IDIBAPS)
Eider Martinez de Arenaza (UB)
Eva M. Palacios (IDIBAPS)
Joana B. Pereira (UB)
Nuria Pujol (HCB)
Roser Sala (UB)
Didac Vidal (UB)
Leire Zubiaurre (UB)

STRATEGIC OBJECTIVES

Study of the consequences of cerebral lesions and dysfunctions in behavior and cognition. The technique preferentially used in our studies is magnetic resonance imaging in its structural and functional applications. We are equipped with a neuroimaging laboratory with several high-performance workstations as well as with a neuronavigated transcranial magnetic stimulation (TMS) equipment. We are using a multimodal approach to study connectivity changes associated to aging and degenerative illness as well as the mechanisms of brain reorganization after traumatic brain injury-

MAIN LINES OF RESEARCH

1. **Neuropsychology and neuroimaging in normal aging and in degenerative diseases:** Neuroanatomical and neurofunctional bases of cognitive impairment in normal aging, Pakinson's disease and Alzheimer's disease. This line makes use

of combined structural and functional magnetic resonance imaging to detect early alterations in brain connectivity prior to clear cerebral atrophy caused by neuronal death. Identification of the symptoms prior to actual clinical manifestations in degenerative diseases is a challenge for treatment intervention aimed to slow the neurodegenerative processes. As a subline, mention should be made of the study of the contribution of the so-called 'cognitive or brain reserve' variables as modulators of the relationships between brain damage and its clinical and cognitive expression associated with age and dementia, as well as of the neuroanatomical and neurophysiological bases of this phenomenon.

2. **Cerebral plasticity:** Long-term consequences of brain damage. In the field of cerebral plasticity we investigate the changes in brain structure and function detectable by magnetic resonance imaging that are induced by transcranial electric stimulation. This technique can be used to simulate reversible lesions or to investigate the changes in brain connectivity in normal subjects and also in degenerative processes. Another line of interest in which work is being done is the study of cerebral language response in patients who as a result of head injuries are in a chronic vegetative state or minimally responsive state. Brain response in the absence of motor response can have clear consequences in the differential diagnosis of these two conditions. Likewise in head injury patients, we study the relationship between the long-term cognitive sequelae and the white matter alterations identified by diffusion tensor imaging (DTI), and also analyze the changes in the cortical thickness related to alterations attributable to diffuse axonal damage.

3. **Development of imaging techniques to study the areas of the brain implicated in the higher function alterations in epileptic patients, based on functional magnetic resonance imaging.** The aim of this line of research is to develop cognitive paradigms such as those relating to speech, perception or memory, based on functional magnetic resonance imaging techniques - validating and applying them to clinical practice with a view to predicting neuropsychological sequelae and investigating cerebral plasticity mechanisms.

PUBLICATIONS

Originals / I.F.: 148.621

1. Torrent C, Bonnin Cdel M, Martínez-Arán A, Valle J, Amann BL, González-Pinto A, Crespo JM, Ibáñez Á, Garcia-Portilla MP, Tabarés-Seisdedos R, Arango C, Colom F, Solé B, Pacchiarotti I, Rosa AR, Ayuso-Mateos JL, Anaya C, Fernández P, Landín-Romero R, Alonso-Lana S, Ortiz-Gil J, Segura B, Barbeito S, Vega P, Fernández M, Ugarte A, Subirà M, Cerrillo E, Custal N, Menchón JM, Saiz-Ruiz J, Rodao JM, Isella S, Alegría A, Al-Halabi S, Bobes J, Galván G, Saiz PA, Balanzá-Martínez V, Selva G, Fuentes-Durá I, Correa P, Mayoral M, Chiclana G, Merchan-Naranjo J, Rapado-Castro M, Salamero M, Vieta E. **Efficacy of functional remediation in bipolar disorder: a multicenter randomized controlled study.** *Am J Psychiatry* 170(8):852-859 I.F.: 14.720

2. Penadés R, Pujol N, Catalán R, Massana G, Rametti G, García-Rizo C, Bargalló N, Gastó C, Bernardo M, Junqué C. **Brain Effects of Cognitive Remediation Therapy in Schizophrenia: A Structural and Functional Neuroimaging Study.** *Biol Psychiatry* 73(10):1015-1023 I.F.: 9.247

3. Palacios EM, Sala-Llonch R, Junque C, Roig T, Tormos JM, Bargallo N, Vendrell P. **Resting-state functional magnetic resonance imaging activity and connectivity and cognitive outcome in traumatic brain injury.** *JAMA Neurol* 70(7):845-851 I.F.: 7.685

4. Alemán-Gómez Y, Janssen J, Schnack H, Balaban E, Pina-Camacho L, Alfaro-Almagro F, Castro-Fornieles J, Otero S, Baeza I, Moreno D, Bargalló N, Parellada M, Arango C, Desco M. **The human cerebral cortex flattens during adolescence.** *J Neurosci* 33(38):15004-15010 I.F.: 6.908

5. Zubiaurre-Elorza L, Junque C, Gómez-Gil E, Segovia S, Carrillo B, Rametti G Guillamon A. **Cortical Thickness in Untreated Transsexuals.** *Cereb Cortex* 23(12):2855-2862 I.F.: 6.828

6. Arenaza-Urquijo EM, Landeau B, La Joie R, Mevel K, Mézenge F, Perrotin A, Desgranges B, Bartrés-Faz D, Eustache F, Chételat G. **Relationships between years of education and gray matter volume, metabolism and functional connectivity in healthy elders.** *Neuroimage* 83C:450-457 I.F.: 6.252

7. Batalle D, Muñoz-Moreno E, Figueras F, Bargallo N, Eixarch E, Gratacos E. **Normalization of similarity-based individual brain networks from gray matter MRI and its association with neurodevelopment in infants with intrauterine growth restriction.** *Neuroimage* 83:901-11 I.F.: 6.252

8. Jovicich J, Marizzoni M, Sala-Llonch R, Bosch B, Bartrés-Faz D, Arnold J, Benninghoff J, Wiltfang J, Roccatagliata L, Nobili F, Hensch T, Tränkner A, Schönknecht P, Leroy M, Lopes R, Bordet R, Chanoine V, Ranjeva JP, Didic M, Gros-Dagnac H, Payoux P, Zoccatelli G, Alessandrini F, Beltramello A, Bargalló N, Blin O, Frisoni GB; The PharmaCog Consortium. **Brain morphometry reproducibility in multi-center 3T MRI studies: A comparison of cross-sectional and longitudinal segmentations.** *Neuroimage* 83C:472-484 I.F.: 6.252

9. Moreno F, Sala-Llonch R, Barandiaran M, Sánchez-Valle R, Estanga A, Bartrés-Faz D, Sistiaga A, Alzualde A, Fernández E, Martí Massó JF, López de Munain A, Indakoetxea B. **Distinctive age-related temporal cortical thinning in asymptomatic**

granulin gene mutation carriers. *Neurobiol Aging* 34(5):1462-1468 I.F.: 6.166

10. Palacios EM, Sala-Llonch R, Junque C, Fernandez-Espejo D, Roig T, Tormos JM, Bargallo N, Vendrell P. **Long-term declarative memory deficits in diffuse TBI: Correlations with cortical thickness, white matter integrity and hippocampal volume.** *Cortex* 49(3):646-657 I.F.: 6.161

11. Pereira JB, Junqué C, Bartrés-Faz D, Ramírez-Ruiz B, Marti MJ, Tolosa E. **Regional vulnerability of hippocampal subfields and memory deficits in parkinson's disease.** *Hippocampus* 23(8):720-728 I.F.: 5.492

12. Segura B, Ibarretxe-Bilbao N, Sala-Llonch R, Baggio HC, Martí MJ, Valldeoriola F, Vendrell P, Bargalló N, Tolosa E, Junqué C. **Progressive changes in a recognition memory network in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(4):370-378 I.F.: 4.924

13. Zarei M, Ibarretxe-Bilbao N, Compta Y, Hough M, Junque C, Bargallo N, Tolosa E, Martí MJ. **Cortical thinning is associated with disease stages and dementia in Parkinson's disease.** *J Neurol Neurosurg Psychiatry* 84(8):875-882 I.F.: 4.924

14. de la Serna E, Andrés-Perpiñá S, Puig O, Baeza I, Bombin I, Bartrés-Faz D, Arango C, Gonzalez-Pinto A, Parellada M, Mayoral M, Graell M, Otero S, Guardia J, Castro-Fornieles J. **Cognitive reserve as a predictor of two year neuropsychological performance in early onset first-episode schizophrenia.** *Schizophr Res* 143(1):125-131 I.F.: 4.590

15. Pereira JB, Junqué C, Bartrés-Faz D, Martí MJ, Sala-Llonch R, Compta Y, Falcón C, Vendrell P, Pascual-Leone A, Valls-Solé J, Tolosa E. **Modulation of verbal fluency networks by transcranial direct current stimulation (tDCS) in Parkinson's disease.** *Brain Stimul* 6(1):16-24 I.F.: 4.538

16. Palacios EM, Sala-Llonch R, Junque C, Roig-Rovira T, Tormos JM, Bargallo N, Vendrell P. **White Matter/Gray Matter Contrast Changes in Chronic and Diffuse Traumatic brain Injury.** *J Neurotrauma* 30(23):1991-1994 I.F.: 4.295

17. Arenaza-Urquijo EM, Molinuevo JL, Sala-Llonch R, Solé-Padullés C, Balasa M Bosch B, Olives J, Antonell A, Lladó A, Sánchez-Valle R, Rami L, Bartrés-Faz D. **Cognitive reserve proxies relate to gray matter loss in cognitively healthy elderly with abnormal cerebrospinal fluid amyloid-β levels.** *J Alzheimers Dis* 35(4):715-726 I.F.: 4.174

18. Sala-Llonch R, Fortea J, Bartrés-Faz D, Bosch B, Lladó A, Peña-Gómez C, Antonell A, Castellanos-Pinedo F, Bargalló N, Molinuevo JL, Sánchez-Valle R. **Evolving brain functional abnormalities in PSEN1 mutation carriers: a resting and visual encoding fMRI study.** *J Alzheimers Dis* 36(1):165-175 I.F.: 4.174

19. Donaire A, Capdevila A, Carreño M, Setoain X, Rumià J, Aparicio J, Campistol J, Padilla N, Sanmartí F, Vernet O, Pintor L, Boget T, Ortells J, Bargalló N. **Identifying the cortical substrates of interictal epileptiform activity in patients with extratemporal epilepsy: An EEG-fMRI sequential analysis and FDG-PET study.** *Epilepsia* 54(4):678-690 I.F.: 3.909

20. Sierra-Marcos A, Maestro I, Falcón C, Donaire A, Setoain J, Aparicio J, Rumià J, Pintor L, Boget T, Carreño M, Bargalló N. **Ictal EEG-fMRI in localization of epileptogenic area in patients with refractory neocortical focal epilepsy**. *Epilepsia* 54(9):1688-1698 I.F.: 3.909

21. Sanz-Cortes M, Ratta GA, Figueras F, Bonet-Carne E, Padilla N, Arranz A, Bargallo N, Gratacos E. **Automatic quantitative MRI texture analysis in small-for-gestational-age fetuses discriminates abnormal neonatal neurobehavior.** *PLoS One* 8(7):e69595 I.F.: 3.730

22. Segura B, Baggio HC, Solana E, Palacios EM, Vendrell P, Bargalló N, Junqué C. **Neuroanatomical correlates of olfactory loss in normal aged subjects.** *Behav Brain Res* 246C:148-153 I.F.: 3.327

23. Rosa AR, Mercadé C, Sánchez-Moreno J, Solé B, Mar Bonnin CD, Torrent C, Grande I, Sugranyes G, Popovic D, Salamero M, Kapczinski F, Vieta E, Martinez-Aran A. **Validity and reliability of a rating scale on subjective cognitive deficits in bipolar disorder (COBRA).** *J Affect Disord* 150(1):29-36 I.F.: 3.295

24. Compta Y, Pereira JB, Ríos J, Ibarretxe-Bilbao N, Junqué C, Bargalló N, Cámara A, Buongiorno M, Fernández M, Pont-Sunyer C, Martí MJ. **Combined dementia-riskbiomarkers in Parkinson's disease: A prospective longitudinal study.** *Parkinsonism Relat Disord* 19(8):717-724 I.F.: 3.274

25. Iranzo A, Serradell M, Vilaseca I, Valldeoriola F, Salamero M, Molina C, Santamaria J, Tolosa E. **Longitudinal assessment of olfactory function in idiopathic REM sleep behavior disorder.** *Parkinsonism Relat Disord* 19(6):600-604 I.F.: 3.274

26. González-Ortiz S, Oleaga L, Pujol T, Medrano S, Rumiá J, Caral L, Boget T, Capellades J, Bargalló N. **Simple fMRI postprocessing suffices for normal clinical practice.** *Am J Neuroradiol* 34(6):1188-1193 I.F.: 3.167

27. Marqués-Iturria I, Pueyo R, Garolera M, Segura B, Junqué C, García-García I, José Sender-Palacios M, Vernet-Vernet M, Narberhaus A, Ariza M, Jurado MA. **Frontal cortical thinning and subcortical volume reductions in early adulthood obesity.** *Psychiat Res* 214(2):109-115 I.F.: 2.456

28. Pujol N, Penadés R, Rametti G, Catalán R, Vidal-Piñeiro D, Palacios E, Bargallo N, Bernardo M, Junqué C. **Inferior frontal and insular cortical thinning is related to dysfunctional brain activation/deactivation during working memory task in schizophrenic patients.** *Psychiat Res* 214(2):94-101 I.F.: 2.456

29. Rumià J, Marmol F, Sanchez J, Giménez-Crouseilles J, Carreño M, Bargalló N, Boget T, Pintor L, Setoain X, Donaire A, Saez GT, Ribalta T, Ferrer E, Puig-Parellada P. Oxidative st**ress markers in the neocortex of drug-resistant epilepsy patients submitted to epilepsy surgery.** *Epilepsy Res* 107(1-2):75-81
I.F.: 2.241

Editorials / I.F.: 1.399

1. Bartrés-Faz D. **[Cognitive and brain reserve in traumatic brain injury: Implications and opportunities].** *Med Clin* (Barc) 140(12):542-543
I.F.: 1.399

GRANTS FOR RESEARCH IN PROGRESS

Bargallo N. **Utilidad de los estudios de perfusión cerebral obtenidos mediante ASL en pacientes con epiplepsia refractaria.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00465.
Duration: 01/01/2013-31/12/2015

Bartres D. **Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in early clinical development.** Sponsored by: Innovative Medicines Initiative (IMI). IMI/115009_ROCHE.
Duration: 09/06/2010-31/12/2014

Bartres D. **Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in early clinical development.** Sponsored by: Innovative Medicines Initiative (IMI). AIXIMI/115009.
Duration: 01/01/2010-31/12/2014

Bartrés D. **Estilos de vida y variantes genéticas como predictores de diferencias individuales del estado y funcionalidad cerebrales en el envejecimiento sano. Estudio mediante resonancia magnética funcional y estructural.** Sponsored by: Instituto de Mayores y Servicios Sociales (IMSERSO).
Duration 01/01/2012-31/03/2013.

Junqué C. **Ajuts de Suport als grups de Recerca.** Sponsored by: AGAUR, 2009SGR941.
Duration: 01/01/2009-31/12/2013.

Junqué C. **Alteraciones en la conectividad cerebral estructural y funcional relacionadas con el deterioro cognitivo leve en la enfermedad de Parkinson.**
Sponsored by: Ministerio de Ciencia e Innovación, PSI2010-16174.
Duration: 01/01/2011-31/12/2013.

DOCTORAL THESES

Bargalló N. **Identificación de las estructuras corticales implicadas en la generación de la actividad epiléptica crítica e intercrítica en pacientes con Post o predoctoral?epilepsia fármacorresistente: un estudio de resonancia magnética funcional con EEG simultáneo.**
PhD student: Antonio Jesús Donaire Pedraza

Bartrés D. **Structural and functional brain correlates of education and cognitive activities in healthy aging and elders at higher risk for Alzheimer's disease.**
PhD student: Eider Martínez de Arenaza Urquijo.

Junqué C. **Long-term brain MRI morphological patterns and cognitive performance in subjects born pretemp at low and high risk for neurodevelopmental deficits.**
PhD student: Leire Zubiaurre Elorza.

Junqué C. **Functional and structural correlates of cognitive impairments in schizophrenia disorder and brain effects of cognitive remediation therapy.**
PhD student: Nuria Pujol Giménez

Junqué C. **Structural and functional connectivity alterations and their relationship with cognitive impairment in traumatic brain injury**.
PhD student: Eva M. Palacios Martinez

4.9 Systems neuroscience

LOCATION
CEK building
Còrsega labs

FOR FURTHER INFORMATION
www.sanchez-vives.org
complab.fcrb.es

KEYWORDS
1. **Cerebral cortex**
2. **Computational neuroscience**
3. **Oscillations**
4. **Virtual reality**
5. **Body representation**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	16.04	3	3	1
2012	54.40	8	3	2
2013	29.51	8	3	3

TEAM LEADER
Maria Victoria Sánchez Vives
(ICREA-IDIBAPS)
T. 93 227 5400 (Ext. 4301)
msanche3@clinic.cat

GROUP LEADER
Albert Compte (IDIBAPS)

RESEARCHERS
Jaime de la Rocha (IDIBAPS)
David Robbe (IDIBAPS)

POST-DOCTORAL RESEARCHERS:
Ilias Bergstrom (IDIBAPS)
Pierre Bourdin (IDIBAPS)
Matteo Martini (IDIBAPS)
Gabriela Mochol
Maria Pérez Zabalza (IDIBAPS)
Marc Ramon-Bohigas (IDIBAPS)
Alexander Roxin (IDIBAPS)
Marcel Ruiz Mejias (IDIBAPS)
Klaus Wimmer (Deutsche Forschungsgemeinschaft)

PRE-DOCTORAL RESEARCHERS
Mattia D'Andola (IDIBAPS)
Maria Cano Colino (IDIBAPS)
Patricia Castaño Prat (IDIBAPS)
Ainhoa Hermoso Mendizabal (IDIBAPS)
Daniel Jercog (IDIBAPS)
Diego López Pigozzi (IDIBAPS)
Marta Matamala (IDIBAPS)
Birgit Nierula (IDIBAPS)
Juan Pablo Ramírez Mahaluf (IDIBAPS)
Beatriz Rebollo (IDIBAPS)
Sofia Seinfeld (IDIBAPS)
Nuria Tort (IDIBAPS)
Julia Weinert (IDIBAPS)

COLLABORATORS
Vanessa Fernandez Descalzo (IDIBAPS)
Thomas Gener (CRG)
Lorena Pérez Méndez (IDIBAPS)
Guillermo Uriretagoyena (IDIBAPS)
Luis Zapata (IDIBAPS)

VISITING SCIENTISTS
Maurizio Mattia
(Istituto Superiore di Sanità, Roma)

STRATEGIC OBJECTIVES

The growing knowledge of synaptic physiology and brain circuits, together with the development of new instruments with which to register, analyze and model the activity of a large number of neurons has made possible to address one of the great pending challenges in neuroscience: to understand the relationship between the activity of the neuron population and behavioral performance. The objective of the systems neuroscience group is to address this challenge combining experimental studies in cerebral cortex networks with a combined experimental and theorical approach.

MAIN LINES OF RESEARCH

- Electrical activity generation and control mechanisms in neuronal networks – specifically, in the cerebral cortex.
- Mechanisms of neuronal activity synchronization in cortical networks.
- Distributed cortical network mechanisms implicated in selective attention, working memory, perceptual decision-making and executive control.
- Use of virtual reality in neuroscience.

1. **Cortical networks and EVENT Lab (Virtual Environments in Neuroscience and Technology). Headed by Dr. Maria Victoria Sánchez (IDIBAPS)**
   Neuronal connectivity and cellular and synaptic properties determine and shape the emergent population activity (spontaneous or invoked) generated by the neuronal networks. Such activity has effects upon the network, with the regulation of relevant mechanisms such as synaptic plasticity. We are interested in different aspects of the activity generated: the mechanisms that regulate it, the information it encodes, and the consequences of this activity upon the network.

   Changes in the functional structure of the cerebral cortex results into altered patterns of the emergent activity. We are studying this in transgenic mice that are models of different neurological disorders. The understanding of these changes gives us hints mechanisms underlying these processes and their possible reversion with treatment.

   Lastly, integration of the cortical information giving rise to body representation and the combination of brain-computer interfaces and virtual reality for understanding these processes, is another research line of our group, as part of the EVENT Lab (http://www.event-lab.org).

2. **Theoretical neurobiology of cortical networks. Headed by Dr. Albert Compte (IDIBAPS)**
   We investigate the mechanisms that support working memory and memory-guided discriminations in neuronal networks of the cerebral cortex. We study the role of microcircuit connectivity, long-range intracortical feedback loops, and synaptic dynamics in maintaining active memories over short periods of time. We formulate our hypothesis quantitatively in computational network models, we test their behavioral predictions in psychophysical experiments, and we analyze neural data from collaborating laboratories to validate or refute the proposed mechanisms.

3. **Cortical Circuit Dynamics. Headed by Dr. Jaime de la Rocha (IDIBAPS)**
   We study of the neuronal mechanisms underlying perception and decision making. In particular we are interested in the neural basis of auditory representation, its dependence on brain state and expectation. We investigate the generation and spatio-temporal structure of ongoing cortical activity and its impact on perception. We are particularly interested in the variability observed in cortical activity, the underlying mechanisms and its impact on behavior. Our techniques include cortical recordings in rats, quantitative analysis and computational modeling.

RESEARCH GROUP
THEORETICAL NEUROBIOLOGY OF CORTICAL CIRCUITS

GROUP LEADER
Albert Compte (IDIBAPS)

Our research is aimed at clarifying the mechanisms that operate in the cortical microcircuit, with a view to conducting computations of relevance to behavior. The tools we use are computer-implemented cortical network models seeking biological plausibility, and technically sophisticated data-analysis tools. We work in parallel at two levels. On the one hand, we model the activity of the cortical microcircuit in order to understand and quantify the mechanisms underlying the generation of population activity in the circuit. On the other hand, we study the physiological bases of cognitive capacities such as working memory and selective attention, and their dysfunction in psychiatric disorders.

PUBLICATIONS

Originals / I.F.: 29.507

1. Gener T, Perez-Mendez L, Sanchez-Vives MV. **Tactile modulation of hippocampal place fields.** *Hippocampus* 23(12):1453-1462 I.F.: 5.492

2. Llobera J, Sánchez-Vives MV., Slater M. **The relationship between virtual body ownership and temperature sensitivity.** *J R Soc Interface* 10(85):20130300 I.F.: 4.907

3. Roggeman C, Klingberg T, Feenstra H, Compte A, Almeida R. **Trade-off between capacity and precision in visuospatial working memory.** *J Cognitive Neurosci* 26:211–222 I.F.: 4.493

4. Abolafia JM, Martinez-Garcia M,

Deco G, Sanchez-Vives MV. **Variability and information content in auditory cortex spike trains during an interval-discrimination task.** *J Neurophysiol* 110(9):2163-2174 I.F.: 3.301

5. Weinert J, Perez-Mendez L, Perez-Zabalza M, Sanchez-Vives M. **P16. Modulating emerging cortical activity with electric fields in brain slices.** *Clin Neurophysiol* 124:e72. I.F.: 3.144

6. Arnold MM, Szczepanski J, Montejo N, Amigo JM, Wajnryb E, Sanchez-Vives MV. **Information content in cortical spike trains during brain state transitions.** *J Sleep Res* 22:13-21 I.F.: 3.043

7. Martini M, Perez-Marcos D, Sanchez-Vives MV. **What color is my arm? Changes in skin color of an embodied virtual arm modulates pain threshold.** *Front Hum Neurosci* 7:438 I.F.: 2.906

8. Llobera J, Gonzalez-Franco M, Perez-Marcos D, Valls-Sole J, Slater M, Sanchez-Vives MV. **Virtual reality for assessment of patients suffering chronic pain: a case study.** *Exp Brain Res* 225(1):105-117 I.F.: 2.221

GRANTS FOR RESEARCH IN PROGRESS

Compte A. **Investigating the neural mechanisms of feature-based and spatial attention in a network model of two coupled brain areas.** Sponsored by: European Commission. 275800.
Duration: 01/06/2011-31/05/2013

Compte A. **Mecanismos de red de la memoria de trabajo espacial y sus disfunciones en transtornos del estado ánimo.** Sponsored by: Ministerio de Economía y Competitividad. BFU2012-34838.
Duration: 01/01/2013-31/12/2015

Compte A. **Mecanismos de redes distribuidas en memoria de trabajo y atención selectiva.** Sponsored by: Ministerio de Economía y Competitividad. BFU2009_09537.
Duration: 01/01/2010-31/12/2013

Compte A. **Noise in decision making: theory meets experiment.** Sponsored by: EUROPEAN SCIENCE FOUNDATION. EW12-019.
Duration: 01/02/2013-31/12/2013

De la Rocha J. **Dinámica estocástica de los circuitos corticales y codificación de información sensorial.** Sponsored by: Ministerio de Economía y Competitividad. SAF2010-15730.
Duration: 01/01/2011-31/08/2014

De La Rocha J. **Network dynamics of auditory cortex and the impact of correlations on the encoding of sensory information.** Sponsored by: European Commission, FP7PEOPLE-IRG-10_01.
Duration: 01/09/2010-31/08/2014.

De la Rocha J. **Noise in decision making: theory meets experiment.** Sponsored by: EUROPEAN SCIENCE FOUNDATION. EW12-019.
Duration: 01/02/2013-31/12/2013

Sanchez-Vives M.V. **Beaming through augmented media for natural networked gatherings.** Sponsored by: European Commission. 248620.
Duration: 01/01/2010-30/06/2014

Sanchez-Vives M.V. **Computations and Organization of Retes Through the Interaction of Computational, Optical and Neurophysiological Investigations of the Cerebral cortex.** Sponsored by: European Commission. 600806.
Duration: 01/01/2013-31/12/2015

Sanchez-Vives M.V. **Dinámica y modulación de ritmos de la red cortical en diferentes estados cerebrales.** Sponsored by: Ministerio de Economía y Competitividad. BFU2011-27094.
Duration: 01/01/2012-31/12/2014

Sanchez-Vives M.V. **Optimización de la respuesra terapéutica a la modulación de estímulos auditivos.** Sponsored by: Ministerio de Economía y Competitividad. IPT-300000-2010-0010.
Duration: 22/06/2010-30/09/2013

Sanchez-Vives M.V. **Systems neuroscience.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1363.
Duration: 16/09/2009-30/04/2014

Sanchez-Vives M.V. **Understanding brain network alteration leading to cognitive impairment in Down Syndrome and indentification of new therapeutic targets.** Sponsored by: FONDATION JEROME LEJEUNE. INT_FLEJEUNE_2011_01.
Duration: 21/02/2012-06/03/2014

Sanchez-Vives M.V. **Virtual Embodiment and Robotic Re-Embodiment.** Sponsored by: European Commission. 257695.
Duration: 01/06/2010-31/12/2015

DOCTORAL THESES

Compte A. **Serotonergic neuromodulation and schizophrenia dysfunctions in a spatial working memory model.**
PhD student: María Cano Colino.

Compte A., De la Rocha J., Sánchez-Vives MV **Dynamics of spontaneous activity in the cerebral cortex across brain states.**
PhD student: Daniel Alejandro Jercog.

Sánchez-Vives M.V. **Synaptic and intrinsic mechanisms involved in the generation of cortical slow rhythms.**
PhD student: María Pérez Zabala.

Sánchez-Vives M.V. **Oscillations in the cerebral cortex: mechanisms of control and alterations in a transgenic model of down syndrome.**
PhD student: Marcel Ruiz Mejías.

Sánchez-Vives M.V. **Brain mechanisms underlying the tracking and localization of dynamic cues.**
PhD student: Diego López Pigozzi.

Sánchez-Vives M.V., Slater M. **Uso de la realidad virtual en violencia de género: tecnología al servicio de la rehabilitación de conductas violentas.**
PhD student: Luis E Zapata Raboso.

4.10 Clinical and experimental neuroimmunology

LOCATION
CELLEX building

FOR FURTHER INFORMATION
www.neuroimmunologybcn.org

KEYWORDS
1. **Autoimmunity**
2. **Paraneoplastic**
3. **Encephalitis**
4. **Autoantibodies**
5. **Cancer**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	139.97	24	12	5
2012	131.10	25	19	6
2013	200.57	36	23	6

TEAM INVOLVED IN
REEM

AWARDS

European School of Neuroimmunology (ESNI) Career Award
Institution: European School of Neuroimmunology
Awardee: Josep Dalmau

Spanish Society of Neurology, Conference "Lluis Barraquer Ferré"
Institution: Spanish Society of Neurology
Awardee: Josep Dalmau

Catalan Society of Neurology, Career Trajectory Award
Institution: Catalan Society of Neurology
Awardee: Josep Dalmau

TEAM LEADER
Francesc Graus (HCB)
T. 93 227 57 85
fgraus@clinic.cat

GROUP LEADERS
Josep Dalmau (ICREA-IDIBAPS)
Núria de la Iglesia (IDIBAPS)
Pablo Villoslada (IDIBAPS)

RESEARCHERS
Yolanda Blanco (HCB)
Beatriz Moreno (IDIBAPS)
Myrna Rosenfeld (IDIBAPS)
Lidia Sabater (FCRB)
Albert Saiz (HCB)

POST-DOCTORAL RESEARCHERS
Nuria Gresa (IDIBAPS)
Romana Höftberger (IDIBAPS)
Ekaterina Kotelnikova (IDIBAPS)
Frank Leypold (IDIBAPS)
Eugenia Martínez (IDIBAPS)
Jesus Pladagumà (IDIBAPS)
Vesna Prchkovska (IDIBAPS)
Maarten Titulaer (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Helena Ariño (HCB)
Thais Armangué (IDIBAPS)
Oihana Errea (IDIBAPS)
Iñigo Gabilondo (IDIBAPS)
Elena Hernandez (IDIBAPS)
Sara Llufriu (IDIBAPS)
Francesco Mannara (FCRB)
Marta Moreno (FPI)
Inna Pertsovskaya (IDIBAPS)
Mar Petit (IDIBAPS)

TECHNICIANS
Esther Aguilar (IDIBAPS)
Mercè Albà (FCRB)
Magi Andorra (IDIBAPS)
Eva Caballero (FCRB)
Begoña Fernández (IDIBAPS)
Elena Fraga (IDIBAPS)
Raquel Vazquez (IDIBAPS)

NURSING STAFF
Montserrat Artola (IDIBAPS)

ADMINISTRATIVE STAFF
Gemma Castillo (FCRB)
Laura Planas (IDIBAPS)
Maria Rodés (IDIBAPS)
Eva Valero (IDIBAPS)

COLLABORATORS
Santiago Ortiz (HCB)
Bernardo Sanchez-Dalmau (HCB)

STRATEGIC OBJECTIVES

1. The principal objective of the neuroimmunology group is the study of inflammation of the central nervous system, and of the mechanisms that are involved in this inflammatory response, and their implication in neurological disorders - fundamentally multiple sclerosis, autoimmune encephalitis and paraneoplastic neurological disorders.
2. Identification and characterization of factors implicated in the pathogenesis of gliomas, based on the study of proteins that control the maintenance, differentiation and migration of normal neural stem cells.

MAIN LINES OF RESEARCH

1. Study of autoimmune mechanisms in paraneoplastic neurological disorders.
2. Synaptic autoimmunity study in encephalitis and other autoimmune diseases of the central nervous system.
3. Development of biomarkers and new therapies in application to multiple sclerosis and other neurological diseases.
4. Functional imaging in neuroimmunology.
5. Study of the molecular bases of glioma pathogenesis: Identification and functional characterization of new factors implicated in the maintenance, differentiation and/ or migration of neural stem cells, and study of the role of these factors in the initiation and invasion of gliomas.

RESEARCH GROUP
PATHOGENESIS AND NEW TREATMENTS IN MULTIPLE SCLEROSIS

GROUP LEADER
Pablo Villoslada (IDIBAPS)

The great challenge for our research team is to apply our discoveries to the clinical management of patients with multiple sclerosis. Our team is pioneering the application of Systems Medicine to the study of MS and development new tools for personalized medicine. As a result, we are developing new therapies for this disease such as the trophic factor like drug BN201 or the metabolite MTA, which are going to enter clinical phases next year. Also, we have developed new diagnostic tools such as molecular imaging of the retina, which are going to help in the monitoring of patient progression. As the coordinating team of the RETICS REEM (Spanish Multiple Sclerosis Network), another of our strategic objectives is the transverse diffusion of knowledge and optimum use of synergies, with a view to transferring the advances in research to the clinical practice setting and to patients. Lastly, the group has a constant commitment to innovation, both in terms of the generation of patents and as regards the creation of spin-off companies.

RESEARCH GROUP
PATHOGENESIS OF AUTOIMMUNE NEURONAL DISORDERS

GROUP LEADER
Josep Dalmau (ICREA-IDIBAPS)

Our research is focused on a group of disorders at the intersection of autoimmunity, cancer and synaptic proteins. This includes the description of novel syndromes and associated immune-mechanisms, isolation of the target antigens and development of diagnostic tests and treatment strategies. These studies have identified 17 auto-antigens and have generated a number of diagnostic tests, some of which are used worldwide. In the last 5 years, we have discovered a new category of autoimmune disorders which affect memory, behavioural and cognitive functions and can cause psychosis.
In 2013 we have characterized a new antibody against DPPX, a protein involved in modulation of somatodendritic signaling, In patients with encephalitis and symptoms of brain hyperexcitability. In addition, we recently started developing animal models of these disorders. Results of these studies have had an impact on many different medical and neuroscience disciplines, providing a link between immunological processes and neuronal functions involved in memory, behaviour, psychosis, epilepsy and neuronal degeneration.

EMERGENT GROUP
GLIOMA AND NEURAL STEM CELL GROUP

GROUP LEADER
Nuria de la Iglesia (IDIBAPS)

Our research group is devoted to applying developmental neurobiology knowledge to the study of gliomas, some of the most aggressive human tumors. Gliomas arise from a rare subpopulation of cells which have stem-like properties such as self-renewal, multipotency and the ability to initiate a tumor upon serial transplantation. These so-called glioma initiating cells (GIC) share specific properties with neural stem cells (NSC), including the localization to specialized microenvironments within the brain that support their maintenance. This suggests that factors involved in either NSC

maintenance or differentiation are likely to contribute to the pathogenesis of gliomas.

Our main lines of research are:
1) Identification and characterization of new factors involved in NSC maintenance and differentiation, with a special emphasis on factors that mediate the localization of NSC to their niches. **2)** Functional characterization of the factors identified above in the initiation, maintenance and invasiveness of gliomas and **3)** Design of new, alternative therapies for gliomas.

PUBLICATIONS

Originals / I.F.: 200.570

1. Titulaer MJ, McCracken L, Gabilondo I, Armangue T, Glaser C, Iizuka T, Honig LS, Benseler S, Kawachi I, Martinez-Hernandez E, Aguilar E, Gresa-Arribas N, Ryan-Florance N, Torrents A, Saiz A, Rosenfeld MR, Balice-Gordon R, Graus F, Dalmau J. **Treatment and prognostic factors for long-term outcome in patients with anti-N-Methyl-D-Aspartate (NMDA) receptor encephalitis: a cohort study.** *Lancet Neurol* 12(2):157-165 I.F.: 23.917

2. Boronat A, Gelfand JM, Gresa-Arribas N, Jeong H-Y, Walsh M, Roberts K, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R, Graus F, Rudy B, Dalmau J. **Encephalitis and antibodies to DPPX, a subunit of Kv4.2 potassium channels.** *Ann Neurol* 73(1):120-128 I.F.: 11.193

3. Höftberger R, Titulaer MJ, Sabater L, Dome B, Rózsás A, Hegedus B, Hoda MA, Laszlo V, Ankersmit HJ, Harms L, Boyero S, de Felipe A, Saiz A, Dalmau J, Graus F. **Encephalitis and GABAB receptor antibodies: novel findings in a new case series of 20 patients.** *Neurology* 81(17):1500-1506 I.F.: 8.249

4. Leypoldt F, Titulaer MJ, Aguilar E, Walther J, Bönstrup M, Havemeister S, Teegen B, Lütgehetmann M, Rosenkranz M, Magnus T, Dalmau J. **Herpes simplex virus-1 encephalitis can trigger anti-NMDA receptor encephalitis – A case report.** *Neurology* 81(22):1637-1639 I.F.: 8.249

5. Mat A, Adler H, Merwick A, Chadwick G, Gullo G, Dalmau J, Tubridy N. **Ophelia Syndrome with metabotropic glutamate receptor 5 antibodies in CSF.** *Neurology* 80(14):1349-1350 I.F.: 8.249

6. Ortiz-Pérez S, Martínez-Lapiscina EH, Gabilondo I, Fraga-Pumar E, Martínez-Heras E, Saiz A, Sanchez-Dalmau B, Villoslada P. **Retinal periphlebitis is associated with multiple sclerosis severity.** *Neurology* 81(10):877-881 I.F.: 8.249

7. Titulaer MJ, McCracken L, Gabilondo I, Iizuka T, Kawachi I, Bataller L, Torrents A, Rosenfeld MR, Balice-Gordon R, Graus F, Dalmau J. **Late-onset anti-N-methyl-D-aspartate receptor encephalitis.** *Neurology* 2013;81:1058-1063 I.F.: 8.249

8. Fleisher F, Richie M, Price R, Scherer S, Dalmau J, Lancaster E. **Acquired neuromyotonia heralding recurrent thymoma in myasthenia gravis.** *JAMA Neurol* 70(10):1311-1314 I.F.: 7.685

9. Höftberger R, Sabater L, Ortega A, Dalmau J, Graus F. **Patient with Homer 3 antibodies and cerebellitis.** *JAMA Neurol* 70(4):506-509 I.F.: 7.685

10. Hansen H-C, Klingbeil C, Dalmau J, Li W, Weißbrich B, Wandinger K-P. **Persistent intrathecal antibody synthesis 15 years after recovering from anti-NMDAR encephalitis.** *JAMA Neurol* 70(1):117-119 I.F.: 7.685

11. Kayser MS, Titulaer MJ, Gresa-Arribas N, Dalmau J. **Frequency and characteristics of isolated psychiatric episodes in anti-N-methyl-d-aspartate receptor encephalitis.** *JAMA Neurol* 70(9):1133-1139 I.F.: 7.685

12. McKeon A, Martinez-Hernandez E, Lancaster E, Matsumoto JY, Harvey RJ, McEvoy KM, Pittock SJ, Lennon VA, Dalmau J. **Glycine receptor autoimmunity in Stiff-Man syndrome phenotypes.** *JAMA Neurol* 70(12):44-50 I.F.: 7.685

13. Thomas A, Rauschkolb P, Gresa-Arribas N, Schned A, Dalmau J, Fadul CE. **Anti- N-methyl-D-aspartate receptor encephalitis: a patient with refractory illness after 25 months of intensive immunotherapy.** *JAMA Neurol* 70(12):1566-1568 I.F.: 7.685

14. Graus F, Bruna J, Pardo J, Escudero D, Vilas D, Barceló I, Brell M, Pascual C, Crespo JA, Erro E, García-Romero JC, Estela J, Martino J, García-Castaño A, Mata E, Lema M, Gelabert M, Fuentes R, Pérez P, Manzano A, Aguas J, Belenguer A, Simón A, Henríquez I, Murcia M, Vivanco R, Rojas-Marcos I, Muñoz-Carmona D, Navas I, de Andrés P, Mas G, Gil M, Verger E. **Patterns of care and outcome for patients with glioblastoma diagnosed during 2008-2010 in Spain.** *Neuro Oncol* 15(6):797-805 I.F.: 6.180

15. Alcina A, Fedetz M, Fernández O, Saiz A, Izquierdo G, Lucas M, Leyva L, García-León JA, Abad-Grau Mdel M, Alloza I, Antigüedad A, Garcia-Barcina MJ, Vandenbroeck K, Varadé J, de la Hera B, Arroyo R, Comabella M, Montalban X, Petit-Marty N, Navarro A, Otaegui D, Olascoaga J, Blanco Y, Urcelay E, Matesanz F. **Identification of a functional variant in the KIF5A-CYP27B1-METTL1-FAM119B locus associated with multiple sclerosis.** *J Med Genet* 50(1):25-33 I.F.: 5.703

16. Gabilondo I, Sepúlveda M, Ortiz-Perez S, Fraga-Pumar E, Martínez-Lapiscina EH, Llufriu S, Solá N, Saiz A, Sanchez-Dalmau B, Villoslada P. **Retrograde retinal damage after acute optic tract lesion in MS.** *J Neurol Neurosurg Psychiatry* 84(7):824-826 I.F.: 4.924

17. Labate A, Quattrone A, Dalmau J, Gambardella A. **Anti-N-methyl-D-aspartate-glutamate-receptor encephalitis presenting as paroxysmal exercise-induced foot weakness.** *Movement Disord* 28(6):820-822 I.F.: 4.558

18. Sepúlveda M, Blanco Y, Rovira A, Rio J, Mendibe M, Llufriu S, Gabilondo I, Villoslada P, Castilló J, Corral J, Ayuso T, Iñiguez C, Santos S, Guijarro C, Ramió-Torrentà L, Sempere AP, Olascoaga J, Graus F, Montalban X, Saiz A. **Analysis of prognostic factors associated with longitudinally extensive transverse myelitis.** *Mult Scler J* 19(6):742-748 I.F.: 4.472

19. Armangue T, Titulaer MJ, Málaga I, Bataller L, Gabilondo I, Graus F, Dalmau J. **Pediatric Anti-NMDAR encephalitis-Clinical analysis and novel findings in a series of 20 patients.** *J Pediatrics* 162(4):850-856 I.F.: 4.035

20. Di Penta A, Chiba A, Alloza I, Wyssenbach A, Yamamura T, Villoslada P, Miyake S, Vandenbroeck K. **A trifluoromethyl analogue of celecoxib exerts beneficial effects in neuroinflammation.** *PLoS One* 8(12):e83119 I.F.: 3.730

21. Di Penta A, Moreno B, Reix S, Fernandez-Diez B, Villanueva M, Errea O, Escala N, Vandenbroeck K, Comella JX, Villoslada P. **Oxidative stress and proinflammatorycytokines contribute to demyelination and axonal damage in a cerebellar culturemodel of neuroinflammation.** *PLoS One* 8(2):e54722 I.F.: 3.730

22. Höftberger R, Sabater L, Marignier R, Aboul-Enein F, Bernard-Valnet R, Rauschka H, Ruiz A, Blanco Y, Graus F, Dalmau J, Saiz A. **An optimized immunohistochemistry technique improves NMO-IgG detection: study comparison with cell-based assays.** *PLoS One* 8(11):e79083 I.F.: 3.730

23. Mowry EM, Carey RF, Blasco MR, Pelletier J, Duquette P, Villoslada P, Malikova I, Roger E, Kinkel RP, McDonald J, Bacchetti P, Waubant E. **Association of multiple sclerosis susceptibility variants and early attack location in the CNS.** *PLoS One* 8(10):e75565 I.F.: 3.730

24. Mowry EM, Carey RF, Blasco MR, Pelletier J, Duquette P, Villoslada P, Malikova I, Roger E, Kinkel RP, McDonald J, Bacchetti P, Waubant E. **Multiple sclerosis susceptibility genes: associations with relapse severity and recovery.** *PLoS One* 8(10):e75416 I.F.: 3.730

25. Sabater L, Höftberger R, Boronat A, Saiz A, Dalmau J, Graus F. **Antibody repertoire in paraneoplastic cerebellar degeneration and small cell lung cancer.** *PLoS One* 8(3):e60438 I.F.: 3.730

26. Velez de Mendizabal N, Hutmacher MM, Troconiz IF, Goñi J, Villoslada P, Bagnato F, Bies RR. **Predicting relapsing-remitting dynamics in multiple sclerosis using discrete distribution models: a population approach.** *PLoS One* 8(9):e73361 I.F.: 3.730

27. Höftberger R, Kovacs GG, Sabater L, Nagy P, Racz G, Miquel R, Dalmau J, Graus F. **Protein kinase C gamma antibodies and paraneoplastic cerebellar degeneration.** *J Neuroimmunol* 256(1-2):91-93 I.F.: 3.033

28. Martin-Garcia H, Mannara F, Gutierrez-Cuesta J, Sabater L, Dalmau J, Maldonado R, Graus F. **Intrathecal injection of P/Q type voltaje-gated calcium cannel antibodies from paraneoplastic cerebellar degeneration cause ataxia in mice.** *J Neuroimmunol* 15(1-2):53-59 I.F.: 3.033

29. Martinez-Pasamar S, Abad E, Moreno B, Velez de Mendizabal N, Martinez-Forerol, Garcia-Ojalvo J, Villoslada P. **Dynamic cross-regulation of antigen-specificeffector and regulatory T cell subpopulations and microglia in brainautoimmunity.** *BMC Syst Biol* 7:34 I.F.: 2.982

30. Pertsovskaya I, Abad E, Domedel-Puig N, Garcia-Ojalvo J, Villoslada P. **Transient oscillatory dynamics of interferon beta signaling in macrophages.** *BMC Syst Biol* 7(1):59 I.F.: 2.982

31. Brito-Zerón P1, Akasbi M, Bosch X, Bové A, Pérez-De-Lis M, Diaz-Lagares C, Retamozo S, Gandía M, Pérez-Alvarez R, Soto-Cárdenas MJ, Sisó A, Valls-Solé J, Graus F, Ramos-Casals M. **Classification and characterisation of peripheral neuropathies in 102 patients with primary Sjögren's syndrome.** *Clin Exp Rheumatol* 31(1):103-110 I.F.: 2.655

32. Merwick A, Dalmau J, Delanty N. **Insights into antibody-associated encephalitis: Bickerstaff's 1950's papers revisted.** *J Neurol Sci* 334(1-2):167-168 I.F.: 2.243

33. Dalmau J, Berenguer J, Saiz A. **Clinical-pathological conference, case 149-2012: A 40-years old woman with headache and diplopia.** *Med Clin* 141:543-549 I.F.: 1.399

34. Höftberger R, Armangue T, Leypoldt F, Graus F, Dalmau J. **Clinical neuropathology practice guide 4-2013: post-herpes simplex encephalitis: N-methyl-D-aspartate receptor antibodies are part of the problem.** *Clin Neuropathol* 32(4):251-254 I.F.: 1.341

35. Valduvieco I, Verger E, Bruna J, Caral L, Pujol T, Ribalta T, Boget T, Oleaga L, Pineda E, Graus F. **Impact of radiotherapy delay on survival in glioblastoma.** *Clin Transl Oncol* 15(4):278-282 I.F.: 1.276

36. Bravo-Oro A, Abud-Mendoza C, Quezada-Corona A, Dalmau J, Campos-Guevara V. **[Encephalitis associated with antibodies against the NMDA receptor: experience with 6 pediatric patients; potential efficacy of Methotrexate].** *Rev Neurologia* 57:405-410 I.F.: 1.179

Reviews / I.F.: 26.754

1. Clardy SL, Lennon VA, Dalmau J, Pittock SJ, Royden Jones H, Renaud DL, Harper CM, Matsumoto JY, McKeon A. **Childhood onset** *of stiff-man syndrome.* JAMA Neurol 70:1531-1536 I.F.: 13.685

2. Graus F, Dalmau J. **Paraneoplastic Neuropathies.** *Curr Opin Neurol* 26:489-495 I.F.: 5.416

3. Davis R, Dalmau J. **Autoimmunity, seizures and status epilepticus.** *Epilepsia* 54 Suppl 6:46-49 I.F.: 3.909

4. Rosenfeld MR, Dalmau J. **Diagnosis and management of paraneoplastic neurologic disorders.** *Curr Treat Opt Oncol* 14:528-538 I.F.: 2.422

5. Fernández V, Valls-Sole J, Relova JL, Raguer N, Miralles F, Dinca L, TaramundiS, Costa-Frossard L, Ferrandiz M, Ramió-Torrentà L, Villoslada P, Saiz A, Calles C, Antigüedad A, Alvarez-Cermeño JC, Prieto JM, Izquierdo G, Montalbán X, Fernández O. **Recommendations for the clinical use of motor evoked potentials in multiple sclerosis.** *Neurologia* 28(7):408-162012 I.F.: 1.322

GRANTS FOR RESEARCH IN PROGRESS

Dalmau J. **Paraneoplasic Disorders of CNS: Autoantigen.** Sponsored by: National Institutes of Health (NIH), NINDS 9RO1NS077851-05A2 (previously RO1CA107192).
Duration: 01/04/2004-31/07/2016.

Dalmau J. **Immunity to brain Ma proteins: A remote effect of cancer.** Sponsored by: National Institutes of Health (NIH), NCI, 2RO1CA89054-06A2.
Duration: 01/12/2000-31/05/2013.

Dalmau J. **Caspr2, Igi-1 and novel antigen autoimmunity in neuropsychiatric dysfunction.** Sponsored by: NIMH, Eureka, 1RO1MH094741.
Duration: 01/08/2011-30/04/2015.

Dalmau J. **Cellular, synaptic, and circuit mechanisms of autoimmune anti-glutamate receptor disorders of memory and cognition.** Sponsored by: MCKNIGHT FOUNDATION.
Duration: 01/02/2010-31/01/2013.

Dalmau J. **Treatment of anti-NMDA receptor encephalitis.**
Sponsored by NIH Extramural-intramural, bedside-to-bench project .
Duration: 01/01/2012-31/12/2014

Dalmau J. **Immune-mediated disorders of memory, behavior, cognition and psychosis.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/01780.
Duration: 01/01/2012-31/12/2014

Dalmau J. **Clinical spectrum and celular and synaptic mechanisms of autoinmune synaptic encephalitides.** Sponsored by: Fundació La Marató de TV3. 101530.
Duration: 01/12/2011-31/08/2014

Graus F. **Anticuerpos contra antígenos de membrana neuronal en el síndrome opsoclonus mioclonus.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00611.
Duration: 01/01/2013-31/12/2015

Graus F. **REEM: Red española de esclerosis múltiple.** Sponsored by: Instituto de Salud Carlos III (ISCIII) RD07/0060/0012.
Duration: 29/02/2008-04/03/2014

Villoslada P. **Red Española de Esclerosis Múltiple.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0032/0001.
Duration: 01/01/2013-31/12/2016

Villoslada P. **Mecanismos de daño axonal en neuroinflamación: nuevas estrategias de neuroprotección.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01823.
Duration: 01/01/2013-31/12/2015

Villoslada P. **A novel drug discovery method based on systems biology: combination therapy and biomarkers for Multiple Sclerosis.** Sponsored by: European Commission. 305397.
Duration: 01/01/2013-31/12/2014

Villoslada P. **Systems biology of T-cell activation in health and disease.** Sponsored by: European Commission. 201106.
Duration: 01/03/2011-31/03/2013

Villoslada P. **Red Española de Esclerosis Múltiple.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD07/0060/0000.
Duration: 10/02/2009-31/12/2014

Villoslada P. **Estudio del daño axonal en esclerosis múltiple mediante estudios de neuroimagen de la vía óptica.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/0259.
Duration: 01/01/2010-30/06/2013

Villoslada P. **Desarrollo de terapias neuroprotectoras para Esclerosis Múltiple.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2011-1312-900000.
Duration: 04/05/2011-30/06/2014

Villoslada P. **STOP-ELA: Aproximación multi-tecnológica para el desarrollo de nuevas terapias y sistemas.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2011-1091-900000.
Duration: 04/05/2011-30/06/2014

Villoslada P. **Nuevas aproximaciones terapéuticas para la Esclerosis Múltiple y la Esclerosis Lateral Amiotrófica: efectos modificadores de la enfermedad y neuroprotección.** Sponsored by: Ministerio de Economía y Competitividad. IPT-010000-2010-0035.
Duration: 25/06/2010-30/06/2013

Villoslada P. **Development of a Raman Spectrofotometer Camera for molecular imaging of the retina in patients with retina and brain diseases.** Sponsored by: Institució CERCA. PROVAT-2011-007-BES.
Duration: 01/01/2012-31/12/2013

Villoslada P. **Studying the relapsing dynamics of major depression through network analysis of fMRI connectivity maps: implications for therapy.** Sponsored by: Fundació La Marató de TV3. 091430.
Duration: 29/01/2010-01/04/2013

DOCTORAL THESES

Villoslada P. **Dinámica del linfocitos T en autoinmunidad.**
PhD student: Sara Martínez Pasamar.

Blanco Y., Saiz A. **Estudios de resonancia magnética y técnicas electrofisiológicas para evaluar y predecir la discapacidad en pacientes con esclerosis múltiple.**
PhD student: Sara Llufriu Duran.

4.11 Neurobiology Unit

LOCATION
IIBB-CSIC labs

KEYWORDS
1. **Neurodegeneration**
2. **Alzheimer's Disease**
3. **Microglia**
4. **Neuronal Pentraxin**
5. **Neuronal Death**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	11.11	2	1	-
2012	34.98	6	6	-
2013	29.42	5	4	1

TEAM INVOLVED IN
CIBERNED

TEAM LEADER
Ramon Trullàs (IIBB-CSIC)
T. 93 363 83 03
ramon.trullas@iibb.csic.es

RESEARCHERS
Nicole Mahy (UB)
Manuel Rodríguez (UB)

PRE-DOCTORAL RESEARCHERS
Iván Cester (IDIBAPS)
Javier Gimeno-Bayón (UB)
Alan López (IDIBAPS)
Margot Martínez (IDIBAPS)

TECHNICIANS
Carmen Andrade (UB)
Monica Romo (IIBB-CSIC)
Nuria Serra (CIBERNED)

COLLABORATORS
Marco Pugliese (UB)
Petar Podlesniy (CIBERNED)
José Manuel Vidal-Taboada (UB)

STRATEGIC OBJECTIVES

The Neurobiology Unit investigates molecular mechanisms of excitotoxic and apoptotic neuron death with the objective of identifying new therapeutic targets for the management of neurodegenerative diseases. Another objective is to gain knowledge of the mechanisms regulating neurogenesis in the adult brain.

MAIN LINES OF RESEARCH

1. Identify new biomarkers for early detection of Alzheimer's disease in the preclinical phase, using a new method of differential proteomic analysis.
2. Investigation of the function of neuronal pentraxin 1 (NP1) during programmed neuron death, with the hypothesis that inhibition of the expression of this protein may constitute a new treatment for chronic neurodegenerative disorders.
3. Study of the mechanism by which the KATP channel modulates microglial activation, thereby allowing the in vivo and in vitro characterization of the neuroprotective and neurotoxic effect of microglia in various neurological disorders, through the activation and blockade of this channel.

4. Investigation of the role of the glia in the neurogenesis mechanisms associated with chronic neurodegeneration in the hippocampus of the adult brain.

5. Investigation of the efficacy and safety of anti-A beta immunotherapy as treatment for Alzheimer's disease.

Throughout the past year we have confirmed that a decrease in the content of cell free circulating mitochondrial DNA (mtDNA) in cerebrospinal fluid (CSF) is associated with both sporadic and familial forms of Alzheimer's Disease (AD), but not with Fronto-temporal Lobe Degeneration. The drop in mtDNA content in CSF occurs in asymptomatic carriers of pathogenic AD mutations at least one decade before the expected emergence of clinical signs of dementia and well before any alteration in currently known AD biomarkers, indicating that mtDNA depletion is an early event in the neurodegenerative process of AD. Because neurons are highly dependent on aerobic energy provided by mitochondria, a drop in the amount of mtDNA of the magnitude found in CSF is likely to cause neurodegeneration by cellular energy deprivation.

Based on these findings, we hypothesize that mtDNA depletion is a fundamental pathophysiological mechanism of AD and that restoring mtDNA copy number to normal levels should have a therapeutic effect in preventing neurodegeneration and cognitive disorders associated with AD. Regarding the study of the KATP channel role in the modulation of microglial activity, we found that the channel activation with diazoxide decreases the pathological symptoms in a mouse model of multiple sclerosis. We also demonstrated that acute KATP channel blockade with glibenclamide has long term neuroprotective effects, increases neurogenesis and improves motor and learning abilities after transient focal cerebral ischaemia in rats. Finally, we found that anti-Abeta immunotherapy improves cognitive dysfunction in aged dogs without any significant side effects.

PUBLICATIONS

Originals / I.F.: 29.418

1. Podlesniy P, Figueiro-Silva J, Llado A, Antonell A, Sanchez-Valle R, Alcolea D, Lleo A, Molinuevo JL, Serra N, Trullas R. **Low cerebrospinal fluid concentration of mitochondrial DNA in preclinical Alzheimer disease.** *Ann Neurol* 74(5):655-668 I.F.: 11.193

2. Ortega FJ, Jolkkonen J, Mahy N, and Rodríguez MJ. **Glibenclamide enhances neurogenesis and improves long-term functional recovery after transient focal cerebral ischemia.** *J Cerebr Blood* F Met 33:356-364 I.F.: 5.398

3. Ortega FJ, Jolkkonen J, and Rodríguez MJ. **Microglia is an active player in how glibenclamide improves stroke outcome.** *J Cerebr Blood* F Met 33:1138-1139 I.F.: 5.398

4. Redondo-Castro E, Hernández J, Mahy N, Navarro X. **Phagocytic microglial phenotype induced by glibenclamide improves functional recovery but worsens hyperalgesia after spinal cord injury in adult rats.** *Eur J Neurosci* 38:3786-3798 I.F.: 3.753

5. Bosch MN, Gimeno-Bayón J, Rodríguez MJ, Pugliese M, and Mahy N. **Rapid improvement of canine cognitive dysfunction with immunotherapy designed for Alzheimer's disease.** *Curr Alzheimer Res* 10:482-493 I.F.: 3.676

Reviews / I.F.: 3.393

1. Rodríguez MJ, Martínez-Moreno M, Ortega FJ, and Mahy N. **Targeting microglial KATP channels to treat neurodegenerative diseases: a mitochondrial issue.** *Oxid Med Cell Long* 2013:194546 I.F.: 3.393

GRANTS FOR RESEARCH IN PROGRESS

Mahy N. **STOP-ELA: Aproximación multi-tecnológica para el desarrollo de nuevas terapias y sistemas.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2011-1091-900000. Duration: 04/05/2011-30/06/2014

Mahy N. **Grup de neuroquímica FM.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 2009_SGR_1380. Duration: 29/09/2009-30/04/2014

Mahy N. **Nuevas aproximaciones terapéuticas para la Esclerosis Múltiple y la Esclerosis Lateral Amiotrófica: efectos modificadores de la enfermedad y neuroprotección.** Sponsored by: Ministerio de Economía y Competitividad. IPT-010000-2010-0035. Duration: 25/06/2010-30/06/2013

Rodríguez MJ. **Nuevas aproximaciones terapéuticas basadas en derivados de ácidos grasos esenciales dirigidos a enfermedades oncológicas y neurológicas no cubiertas.** Sponsored by: Ministerio de Economia y Competitividad. IPT-2012-0614-010000. Duration: 01/10/2012 - 31/12/2015.

Trullas R. **Mecanismos de eliminación de sinapsis y dinámica mitocondrial durante la neurodegeneración: función de la pentraxina neuronal 1.** Sponsored by. Ministerio de Economia y competitividad. SAF2011-23550. Duration 01/01/2012- 31/12/2014

DOCTORAL THESES

Rodríguez MJ. **Efecte de l'activació del canal KATP al perfil d'expressió microglial durant la neurodegeneració a l'hipocamp de la rata.** PhD student: Margot Martínez Moreno.

Trullàs R **Regulation of synapse density and mitochondrial dynamics by Neuronal Pentraxin 1.** PhD student: Joana Figueiro Silva.

AREA 5

Oncology and haematology

5.1 **Biological markers in oncology** 252
Rafael Molina

5.2 **Human and experimental functional oncomorphology** 254
Elías Campo

5.3 **Diagnosis and therapy in oncology** 262
Francesca Pons

5.4 **Molecular genetics** 265
Cristóbal Mezquita

5.5 **Genetics** 267
Montserrat Milà

5.6 **Melanoma: imaging, genetics and immunology** 270
Susana Puig

5.7 **Hematopoietic progenitor cell transplantation** 274
Álvaro Urbano-Ispizua

5.8 **Hematological oncology** 277
Francisco Cervantes

5.9 **Physiopathology and molecular bases in hematology** 285
Dolors Colomer

5.10 **Hemotherapy - hemostasis** 289
Ginés Escolar

5.11 **Molecular and translational oncology** 292
Pere Gascón

5.12 **Cell proliferation and signaling** 297
Oriol Bachs

5.1 Biological markers in oncology

LOCATION
HCB building

KEYWORDS
1. **Tumor markers**
2. **HE-4**
3. **ProGRP**
4. **Histological diagnosis**
5. **PCA-3**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	26.71	6	4	2
2012	14.31	5	2	-
2013	18.32	5	3	1

TEAM LEADER
Rafael Molina (HCB - UB)
T. 93.227.54.00
rmolina@clinic.cat

RESEARCHERS
Xavier Filella (HCB)

PRE-DOCTORAL RESEARCHER
José María Auge Fradera (FCRB)

TECHNICIAN
Alba Roset (FCRB)

COLLABORATORS
Amàlia Lafuente (UB)
M. Portas (HCB)
S. Román (HCB)

STRATEGIC OBJECTIVES

The group focuses mainly on applied clinical research and works in collaboration with different clinical groups both within and outside Hospital Clínic de Barcelona.

MAIN LINES OF RESEARCH

1. Circulating tumor markers. Development of new techniques for the study of biological markers, which are the peripheral expression of the presence of malignant tumors. Study of the usefulness of proPSA in the diagnosis of prostate cancer. Evaluation of new tumor markers such as: epididymal protein HE4, of great interest in ovarian cancer; and PCA3 in urine in prostate cancers.

2. Consolidation of diagnostic guides to the clinical use of tumor markers. Collaboration with European and North American groups for establishing consensus and publishing clinical guides. Diffusion of these guides at national level through the Cancer Biological Markers Commission, created by members of the group, within the scientific committee of the Spanish Society of Biochemistry and Molecular Pathology.

3. Introduction of a technique for the detection of the PCA3 antigen by detection of mRNA in urine. Evaluation of the clinical interest in this methodology and its application in the diagnosis of prostate cancer and in the reduction in the number of unnecessary prostate biopsies. Introduction of a new assay, HE-4 useful in the diagnosis and differential diagnosis of ovarian masses

4. Collaboration in the colon and rectal cancer population screening program through the detection of occult blood in stools. During the last year over 15,000 asymptomatic individuals have been analyzed.

5. Evaluating two different protocols to use tumor markers as screening tools in lung cancer and ovarian cancer in combination with different deparments in the Hospital Clinic.

6. Evaluation and confirmation of the efficacy of a computer program for establishing risk in patients with symptoms suggestive of lung cancer which assesses risk on the basis of 6 tumour markers and points to the histological type (small cell or non-small-cell). An added feature has been introduced to enable sub-classification of non-small-cell carcinomas into adenocarcinomas and squamous-cell carcinomas. The process of obtaining a licence for distribution of the program is presently underway.

7. Evaluation of a computer program for establishing risk in patients with symptoms suggestive of cancer (paraneoplastic syndromes), which assesses risk on the basis of 9 tumour markers and points to the origin.

8. Evaluation and study of a population screening programme for ovarian cancer through the determination of HE-4 and CA125 in high-risk women: BRCA-1, BRCA-2 mutations, previous medical history of breast and/or ovarian cancer.

PUBLICATIONS

Originals / I.F.: 18.323

1. Tovar N, de Larrea CF, Aróstegui JI, Cibeira MT, Rosiñol L, Rovira M, Elena M, Filella X, Yagüe J, Bladé J. **Natural history and prognostic impact of oligoclonal humoral response in patients with multiple myeloma after autologous stem cell transplantation: long-term results from a single institution.** *Haematologica* 98(7):1142-1146 I.F.: 5.935

2. Codony-Servat J, Marín-Aguilera M, Visa L, García-Albéniz X, Pineda E, Fernández PL, Filella X, Gascón P, Mellado B. **Nuclear factor-kappa B and interleukin-6 related docetaxel resistance in castration-resistant prostate cancer.** *Prostate* 73(5):512-521 I.F.: 3.843

3. Gifre L, Ruiz-Gaspà S, Monegal A, Nomdedeu B, Filella X, Guañabens N, Peris P. **Effect of glucocorticoid treatment on Wnt signalling antagonists (sclerostin and Dkk-1) and their relationship with bone turnover.** *Bone* 57(1):272-26 I.F.: 3.823

4. Filella X, Giménez N. **Evaluation of [-2] proPSA and Prostate Health Index (phi) for the detection of prostate cancer: a systematic review and meta-analysis.** *Clin Chem Lab Med* 51(4):729-739 I.F.: 3.009

5. Auge JM, Rodriguez C , Pellise M, Bernal A, Grau J, Castells A, Filella X, Molina R. **Analytical and clinical performance of Kroma iT, a compact fully-automated immunochemistry analyzer for fecal occult hemoglobin**. *Anticancer Res* 33(12):5633-5637 I.F.: 1.713

Reviews / I.F.: 2.518

1. Filella X, Foj L, Milà M, Augé JM, Molina R, Jiménez W. **PCA3 in the detection and management of early prostate cancer.** *Tumour Biol* 34(3):1337-1347 I.F.: 2.518

5.2 Human and experimental functional oncomorphology

LOCATION
CEK building
CELLEX building

KEYWORDS
1. **Lymphoid neoplasms**
2. **Mantle cell lymphoma**
3. **Chronic Lymphatic Leukemia**
4. **Next generation sequencing**
5. **Molecular Pathology**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	322.81	50	31	9
2012	472.98	75	51	16
2013	386.28	46	40	4

TEAM INVOLVED IN
RTICC

AWARDS

ICREA Academia
Institution: Institució Catalana de Recerca i Estudis Avançats
Awardee/s: Elias Campo

Premi Nacional de Recerca
Institution: Fundació Catalana per la Recerca i la Innovació. Generalitat de Catalunya
Awardee/s: Elias Campo

Julián Sanz del Río 2013 para jóvenes investigadores de España y Alemania
Institution: Fundación para la proyección internacional de las universidades españolas – Universidad.es y el Servicio Alemán de Intercambio Académico – DAAD
Awardee/s: Itziar Salaverria

TEAM LEADER
Elías Campo (HCB)
T. 93 227 54 50
ecampo@clinic.cat

GROUP LEADERS
Pedro Luis Fernández (HCB)
Antonio Postigo (ICREA - IDIBAPS)

RESEARCHERS
Llúcia Alós (HCB)
Virginia Amador (IDIBAPS)
Sílvia M. Beà (IDIBAPS)
Josep Antoni Bombí (HCB)
Lluis Colomo (HCB)
Lluis Hernández Pous (IDIBAPS)
Pedro Jares (HCB)
Carme Mallofré (HCB)
José Ignacio Martín-Subero (UB)
Antonio Martínez Pozo (HCB)
Alfons Nadal (HCB)
José Francisco Ramírez (HCB)
Teresa Ribalta (HCB)
Manel Solé (HCB)

POST-DOCTORAL RESEARCHER:
Renée Beekman (IDIBAPS)
Giancarlo Castellano (IDIBAPS)
Adriana García Herrera (HCB)
Kenosuke Karube (IDIBAPS)
Yeny Martinez de la Torre (IDIBAPS)
Alba Navarro López (IDIBAPS)
Cristina Royo Moreno (IDIBAPS)
Itziar Salaverria (FCRB)
Ester Sánchez Tilló (IDIBAPS)
Ester Valls Jordana (IDIBAPS)

PRE-DOCTORAL RESEARCHERS:
Robert Albero (FCRB)
Oriol de Barrios Barri (FCRB)
Marlies Cortes Hinojosa (IDIBAPS)
Alvaro Equileor (FCRB)
Lucia Fanlo Escudero (IDIBAPS)
Blanca Gonzalez (HCB)
David Martín-García (FCRB)
Daniel Martínez (HCB)
Jara Palomero Gorrindo (MCyT)
Lourdes Sánchez Cid (IDIBAPS)
Laura Siles Mena (IDIBAPS)
Carla Solé Cañadas (FCRB)
Alexandra Valera (IDIBAPS)

Maria Carmela Vegliante (FCRB)

TECHNICIANS
Cristina Capdevila Lózar (FCRB)
Eva Fernández López (FCRB - HCB)
Noelia García Martínez (FCRB)
Sara Guijarro Gallardo (FCRB)
Silvia Martín Román (FCRB)
Concepción Muñoz Lozano (IDIBAPS)
Miriam Prieto Beato (IDIBAPS)
Marta Leonor Rodríguez (IDIBAPS)
Nuria Russiñol (IDIBAPS)

ADMINISTRATIVE STAFF
Carmen Muro (FCRB)
Judith Safont (FCRB)
Nathalie Villahoz (FCRB)

STATISTICIAN
Guillem Clot Razquin (FCRB)

COLLABORATORS
Raquel Bermudo Gascón (IDIBAPS)
Miriam Cuatrecasas Freixas (HCB)
Ana Enjuanes Guardiola (IDIBAPS)
Rosa Miquel Morera (HCB)
Magdalena Pinyol Martínez (IDIBAPS)

STRATEGIC OBJECTIVES

Identification of genetic and molecular mechanisms implicated in the development and progression of human neoplasms.

Development of strategies for transferring to clinical practice the knowledge generated by basic research on human tumors.

Identification of parameters allowing the improved diagnosis and prognosis of neoplastic disease, and the identification of possible therapeutic targets.

MAIN LINES OF RESEARCH

Molecular Pathology of Lymphoid Neoplasms

a) To understand the genetic and molecular mechanisms involved in the development and progression of lymphoid neoplasms and to identify parameters that may improve the diagnosis of these disease, stratify patients according to biological risk, and define possible therapeutic targets.

b) To define the complete catalogue of somatic genomic alterations in several lymphoid neoplasm and their clinical and functional relevance

c) To develop strategies for transferring the knowledge generated in the basic studies of these neoplasms into the clinics

Molecular Pathology of Solid neoplasms

a) To study the molecular mechanisms of invasion and metastasis, transcriptional expression profiles implicated in the development and progression of different human tumors in relation to development, biological aggressivity and therapeutic options. We focus mainly on breast and prostate tumors as neoplasms under hormone influence, and urological tumors and airway neoplasms – including head and neck tumors.

a) Study of the possible criteria of treatment response and prognosis in neurological tumors.

RESEARCH GROUP MOLECULAR PATHOLOGY OF LYMPHOID NEOPLASMS

GROUP LEADER
Elías Campo (HCB)

Lymphoid neoplasias are a very heterogeneous group of tumors with remarkable variability in their biological behavior and clinical manifestations. Our group is concentrated in understanding the genetic, epigenetic, and molecular mechanisms underlying the biological diversity of these tumors and how they may influence the different clinical evolution of the patients. The use of Next generation sequencing technologies in cancer samples is able to provide a full catalogue of the somatic alterations (both structural variants and mutations) of the tumor genomes. We are using these technologies to sequence the genome, exome and transcriptome of several lymphoid neoplasms, particularly chronic lymphocytic leukemia, mantle cell lymphoma and diffuse large B-cell lymphoma. We complement these studies with different methodological approaches that include DNA and methylation arrays and several biological cell and animal models. We validate the functional and clinical relevance of these somatic alterations in a large series of patients.

RESEARCH GROUP MOLECULAR PATHOLOGY OF SOLID TUMORS

GROUP LEADER
Pedro Luis Fernández (HCB)

The study of solid tumours has encompassed a variety of neoplasms from urological, ginecological, head and neck and neurological sites. We have continued to deepen in the role of microRNA in the progression of mammary carcinomas from primary sites to distant metastasis and are testing the hypothesis of the possible usefulness of miRNA detection in blood of cancer patients as a method to help in their staging. We have demonstrated the importance of GATA3 expression in the evolution of luminal breast cancers and collaborated in the study of the role of Sustance P in the progression of mammary cancer cells and aggressiveness and responsiveness of prostate cancer.

We analyzed the IDH1 mutations in gliomas of different histological types and grades from children and adults. We studied BRAF alterations in Pilocytic Astrocytoma (PA) and other gliomas and we found the BRAF gene fusion in a fraction of PA and in a few diffuse low grade gliomas from adult patients and also identified a 49-gene signature of meningioma aggressivity.

RESEARCH GROUP

TRANSCRIPTIONAL REGULATION OF GENE EXPRESSION

GROUP LEADER

A. Postigo (ICREA-IDIBAPS)

The group investigates the molecular mechanisms involved in the regulation of gene expression during normal cell differentiation and cancer by the ZEB family of proteins and a wide array of in vitro and in vivo approaches. ZEB1 (also known as delta-EF1, zfhx1a) and ZEB2 (SIP1, zfhx1b) are transcription factors that regulate key genes involved in cell determination and differentiation, "stemness" in normal and cancer stem cells, oncogenic transformation and tumor invasion and metastasis. The group uses cell-based approaches, transgenic mice and human samples to study normal cell differentiation and cancer in epithelial (colon, breast, lung), muscle and hematopoietic systems. The group is funded by grants from the Spanish Ministry of Economy and Competitiveness, the European Union, the Spainish Association Against Cancer (AECC), Fundació La Caixa, Fundació Olga Torres and Avon Cosmetics SAU, Academy of Health and Medical Sciences of Catalonia and the Balearic Islands and the Leukemia Research Campaign.

PUBLICATIONS

Originals / I.F.: 386.280

1. Alexandrov LB, Nik-Zainal S, Wedge DC, Aparicio SA, Behjati S, Biankin AV, Bignell GR, Bolli N, Borg A, Børresen-Dale AL, Boyault S, Burkhardt B, Butler AP, Caldas C, Davies HR, Desmedt C, Eils R, Eyfjörd JE, Foekens JA, Greaves M, Hosoda F, Hutter B, Ilicic T, Imbeaud S, Imielinsk M, Jäger N, Jones DT, Jones D, Knappskog S, Kool M, Lakhani SR, López-Otín C, Martin S, Munshi NC, Nakamura H, Northcott PA, Pajic M, Papaemmanuil E, Paradiso A, Pearson JV, Puente XS, Raine K, Ramakrishna M, Richardson AL, Richter J, Rosenstiel P, Schlesner M, Schumacher TN, Span PN, Teague JW, Totoki Y, Tutt AN, Valdés-Mas R, van Buuren MM, van 't Veer L, Vincent-Salomon A, Waddell N, Yates LR; Australian Pancreatic Cancer Genome Initiative; ICGC Breast Cancer Consortium; ICGC MMML-Seq Consortium; ICGC PedBrain, Zucman-Rossi J, Futreal PA, McDermott U, Lichter P, Meyerson M, Grimmond SM, Siebert R, Campo E, Shibata T, Pfister SM, Campbell PJ, Stratton MR. **Signatures of mutational processes in human cancer.** *Nature* 500(7463):415-421 I.F.: 38.597

2. Berndt SI, Skibola CF, Joseph V, Camp NJ, Nieters A, Wang Z, Cozen W, Monnereau A, Wang SS, Kelly RS, Lan Q, Teras LR, Chatterjee N, Chung CC, Yeager M, Brooks-Wilson AR, Hartge P, Purdue MP, Birmann BM, Armstrong BK, Cocco P, Zhang Y, Severi G, Zeleniuch-Jacquotte A, Lawrence C, Burdette L, Yuenger J, Hutchinson A, Jacobs KB, Call TG, Shanafelt TD, Novak AJ, Kay NE, Liebow M, Wang AH, Smedby KE, Adami HO, Melbye M, Glimelius B, Chang ET, Glenn M, Curtin K, Cannon-Albright LA, Jones B, Diver WR, Link BK, Weiner GJ, Conde L, Bracci PM, Riby J, Holly EA, Smith MT, Jackson RD, Tinker LF, Benavente Y, Becker N, Boffetta P, Brennan P, Foretova L, Maynadie M, McKay J, Staines A, Rabe KG, Achenbach SJ, Vachon CM, Goldin LR, Strom SS, Lanasa MC, Spector LG, Leis JF,Cunningham JM, Weinberg JB, Morrison VA, Caporaso NE, Norman AD, Linet MS, De Roos AJ, Morton LM, Severson RK, Riboli E, Vineis P, Kaaks R, Trichopoulos D, Masala G, Weiderpass E, Chirlaque MD, Vermeulen RC, Travis RC, Giles GG, Albanes D, Virtamo J, Weinstein S, Clavel J, Zheng T, Holford TR, Offit K, Zelenetz A, Klein RJ, Spinelli JJ, Bertrand KA, Laden F, Giovannucci E, Kraft P, Kricker A, Turner J, Vajdic CM, Ennas MG, Ferri GM, Miligi L, Liang L, Sampson J, Crouch S, Park JH, North KE, Cox A, Snowden JA, Wright J, Carracedo A, Lopez-Otin C, Bea S, Salaverria I, Martin-Garcia D, Campo E, Fraumeni JF Jr, de Sanjose S, Hjalgrim H, Cerhan JR, Chanock SJ, Rothman N, Slager SL. **Genome-wide association study identifies multiple risk loci for chronic lymphocytic leukemia.** *Nat Genet* 45(8):868-876 I.F.: 35.209

3. Ramsay AJ, Quesada V, Foronda M, Conde L, Martínez-Trillos A, Villamor N, Rodríguez D, Kwarciak A, Garabaya C, Gallardo M, López-Guerra M, López-Guillermo A, Puente XS, Blasco MA, Campo E, López-Otín C. **POT1 mutations cause telomere dysfunction in chronic lymphocytic leukaemia.** *Nat Genet* 45(5):526-530 I.F.: 35.209

4. Huang X, Meng B, Iqbal J, Ding BB, Perry AM, Cao W, Smith LM, Bi C, Jiang C, Greiner TC, Weisenburger DD, Rimsza L, Rosenwald A, Ott G, De labie J, Campo E, Braziel RM, Gascoyne RD, Cook JR, Tubbs RR, Jaffe ES, Armitage JO, Vose JM,Staudt LM, McKeithan TW, Chan WC, Ye BH, Fu K. **Activation of the STAT3 Signaling Pathway Is Associated With Poor Survival in Diffuse Large B-Cell Lymphoma Treated with R-CHOP.** *J Clin Oncol* 31(36):4520-4528 I.F.: 18.038

5. Zucca E, Conconi A, Laszlo D, López-Guillermo A, Bouabdallah R, Coiffier B, Sebban C, Jardin F, Vitolo U, Morschhauser F, Pileri SA, Copie-Bergman C, Campo E, Jack A, Floriani I, Johnson P, Martelli M, Cavalli F, Martinelli G, Thieblemont C. **Addition of Rituximab to Chlorambucil Produces Superior Event-Free Survival in the Treatment of Patients With Extranodal Marginal-Zone B-Cell Lymphoma: 5-Year Analysis of the IELSG-19 Randomized Study.** *J Clin Oncol* 31(5):565-572 I.F.: 18.038

6. Bassaganyas L, Beà S, Escaramís G, Tornador C, Salaverria I, Zapata L, Drechsel O, Ferreira PG, Rodriguez-Santiago B, Tubio JM, Navarro A, Martín-García

D, López C, Martínez-Trillos A, López-Guillermo A, Gut M, Ossowski S, López-Otín C, Campo E, Estivill X. **Sporadic and reversible chromothripsis in chronic lymphocytic leukemia revealed by longitudinal genomic analysis.** *Leukemia* 27(12):2376-2379 I.F.: 10.164

7. Ramsay AJ, Rodríguez D, Villamor N, Kwarciak A, Tejedor JR, Valcárcel J, López-Guillermo A, Martínez-Trillos A, Puente XS, Campo E, López-Otín C, Quesada V. **Frequent somatic mutations in components of the RNA processing machinery in chronic lymphocytic leukemia.** *Leukemia* 27(7):1600-1603 I.F.: 10.164

8. Villamor N, Conde L, Martínez-Trillos A, Cazorla M, Navarro A, Beà S, López C, Colomer D, Pinyol M, Aymerich M, Rozman M, Abrisqueta P, Baumann T, Delgado J, Giné E, González-Díaz M, Hernández JM, Colado E, Payer AR, Rayon C, Navarro B, Terol MJ, Bosch F, Quesada V, Puente XS, López-Otín C, Jares P, Pereira A, Campo E, López-Guillermo A. **NOTCH1 mutations identify a genetic subgroup of chronic lymphocytic leukemia patients with high risk of transformation and poor outcome.** *Leukemia* 27(5):1100-1106 I.F.: 10.164

9. Liu Y, Sánchez-Tilló E, Lu X, Huang L, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A, Dean DC. **Rb1 family mutation is sufficient for sarcoma initiation.** *Nat Commun* 4:2650-2661 I.F.: 10.015

10. Beà S, Valdés-Mas R, Navarro A, Salaverria I, Martín-Garcia D, Jares P, Giné E, Pinyol M, Royo C, Nadeu F, Conde L, Juan M, Clot G, Vizán P, Di Croce L, Puente DA, López-Guerra M, Moros A, Roue G, Aymerich M, Villamor N, Colomo L, Martínez A, Valera A, Martín-Subero JI, Amador V, Hernández L, Rozman M, Enjuanes A, Forcada P, Muntañola A, Hartmann EM, Calasanz MJ, Rosenwald A, Ott G, Hernández-Rivas JM, Klapper W, Siebert R, Wiestner A, Wilson WH, Colomer D, López-Guillermo A, López-Otín C*, Puente XS*, Campo E*. **Landscape of somatic mutations and clonal evolution in mantle cell lymphoma.** *Proc Natl Acad Sci U S A* 110(45):18250-18255 I.F.: 9.373

11. Chiorazzi M, Rui L, Yang Y, Ceribelli M, Tishbi N, Maurer CW, Ranuncolo SM, Zhao H, Xu W, Chan WC, Jaffe ES, Gascoyne RD, Campo E, Rosenwald A, Ott G, Delabie J, Rimsza LM, Shaham S, Staudt LM. **Related F-box proteins control cell death in Caenorhabditis elegans and human lymphoma.** *Proc Natl Acad Sci U S A* 110(10):3943-3948 I.F.: 9.373

12. Boi M, Rinaldi A, Kwee I, Bonetti P, Todaro M, Tabbò F, Piva R, Rancoita PM, Matolcsy A, Timar B, Tousseyn T, Rodríguez-Pinilla SM, Piris MA, Beà S, Campo E, Bhagat G, Swerdlow SH, Rosenwald A, Ponzoni M, Young KH, Piccaluga PP, Dummer R, Pileri S, Zucca E, Inghirami G, Bertoni F. **PRDM1/BLIMP1 is commonly inactivated in anaplastic large T-cell lymphoma.** *Blood* 122(15):2683-2693 I.F.: 9.060

13. Bödör C, Grossmann V, Popov N, Okosun J, O'Riain C, Tan K, Marzec J, Araf S, Wang J, Lee AM, Clear A, Montoto S, Matthews J, Iqbal S, Rajnai H, Rosenwald A, Ott G, Campo E, Rimsza LM, Smeland EB, Chan WC, Braziel RM, Staudt LM, Wright G, Lister TA, Elemento O, Hills R, Gribben JG, Chelala C, Matolcsy A, Kohlmann A, Haferlach T, Gascoyne RD, Fitzgibbon J. **EZH2 mutations are frequent and represent an early event in follicular lymphoma.** *Blood* 122(18):3165-3168 I.F.: 9.060

14. Salaverria I, Royo C, Carvajal-Cuenca A, Clot G, Navarro A, Valera A, Song JY, Woroniecka R, Rymkiewicz G, Klapper W, Hartmann EM, Sujobert P, Wlodarska I, Ferry JA, Gaulard P, Ott G, Rosenwald A, Lopez-Guillermo A, Quintanilla-Martinez L, Harris NL, Jaffe ES, Siebert R, Campo E, Beà S. **CCND2 rearrangements are the most frequent genetic events in Cyclin D1-negative mantle cell lymphoma**. *Blood* 121(8):1394-1402 I.F.: 9.060

15. Vegliante MC, Palomero J, Pérez-Galán P, Roué G, Castellano G, Navarro A, Clot G, Moros A, Suárez-Cisneros H, Beà S, Hernández L, Enjuanes A, Jares P, Villamor N, Colomer D, Martín-Subero JI, Campo E, Amador V. **SOX11 regulates PAX5expression and blocks terminal B-cell differentiation in aggressive mantle cell lymphoma**. *Blood* 121(12):2175-2185 I.F.: 9.060

16. Garcia-Recio S, Fuster G, Fernandez-Nogueira P, Pastor-Arroyo EM, Park SY, Mayordomo C, Ametller E, Mancino M, Gonzalez-Farre X, Russnes HG, Engel P, Costamagna D, Fernandez PL, Gascón P, Almendro V. **Substance P Autocrine Signaling Contributes to Persistent HER2 Activation That Drives Malignant Progression and Drug Resistance in Breast Cancer.** *Cancer Res* 73:6424-6434 I.F.: 8.650

17. Navarro A, Clot G, Prieto M, Royo C, Vegliante MC, Amador V, Hartmann E, Salaverria I, Beà S, Martín-Subero JI, Rosenwald A, Ott G, Wiestner A, Wilson WH, Campo E, Hernández L. **MicroRNA expression profiles identify subtypes of mantle cell lymphoma with different clinicobiological characteristics.** *Clin Cancer Res* 19(12):3121-3129 I.F.: 7.837

18. Sanchez-Tillo E, de Barrios O, Siles L, Amendola P, Darling DS, Cuatrecasas M, Castells A, Postigo A*. **ZEB1 promotes invasiveness of colorectal carcinoma cells through regulation of uPA and PAI-1.** *Clin Cancer Res* 19:1071-1082 I.F.: 7.837

19. Xargay-Torrent S, López-Guerra M, Montraveta A, Saborit-Villarroya I, Rosich L, Navarro A, Pérez-Galán P, Roué G, Campo E, Colomer D. **Sorafenib Inhibits Cell Migration and Stroma-Mediated Bortezomib Resistance by Interfering B-cell Receptor Signaling and Protein Translation in Mantle Cell Lymphoma.** *Clin Cancer Res* 19(3):586-597 I.F.: 7.837

20. Rodríguez D, Ramsay AJ, Quesada V, Garabaya C, Campo E, Freije JMP, López-Otín C. **Functional analysis of sucrase-**

isomaltase mutations from chronic lymphocytic leukemia patients. *Hum Mol Genet* 22(11):2273-2282 I.F.: 7.692

21. Marqués N, Sesé M, Cánovas V, Valente F, Bermudo R, de Torres I, Fernández Y, Abasolo I, Fernández PL, Contreras H, Castellón E, Celià-Terrassa T, Méndez R, Ramón y Cajal S, Thomson TM, Paciucci R. **Regulation of protein translation and c-Jun expression by Prostate Tumor Overexpressed 1 (PTOV1).** *Oncogene* 33:1124-1134 I.F.: 7.357

22. Enjuanes A, Albero R, Clot G, Navarro A, Beà S, Pinyol M, Martín-Subero JI, Klapper W, Staudt LM, Jaffe ES, Rimsza L, Braziel RM, Delabie J, Cook JR, Tubbs RR, Gascoyne R, Connors JM, Weisenburger DD, Greiner TC, Chan WC, López-Guillermo A, Rosenwald A, Ott G, Campo E, Jares P. **Genome-wide methylation analyses identify a subset of mantle cell lymphoma with a high number of methylated CpGs and aggressive clinicopathological features**. *Int J Cancer* 133(12):2852-2863 I.F.: 6.198

23. Martin-Guerrero I, Salaverria I, Burkhardt B, Szczepanowski M, Baudis M, Bens S, de Leval L, Garcia-Orad A, Horn H, Lisfeld J, Pellissery S, Klapper W, Oschlies I, Siebert R. **Recurrent loss of heterozygosity in 1p36 associated with TNFRSF14 mutations in IRF4 translocation negative pediatric follicular lymphomas.** *Haematologica* 98(8):1237-1241 I.F.: 5.935

24. Rosich L, Saborit-Villarroya I, López-Guerra M, Xargay-Torrent S, Montraveta A, Aymerich M, Villamor N, Campo E, Pérez-Galán P, Roué G, Colomer D. **The phosphatidylinositol-3-kinase inhibitor NVP-BKM120 overcomes resistance signals derived from microenvironment by regulating the Akt/FoxO3a/Bim axis in chronic lymphocytic leukemia cells.** *Haematologica* 98(11):1739-1747 I.F.: 5.935

25. Valera A, López-Guillermo A, Cardesa-Salzmann T, Climent F, González-Barca E, Mercadal S, Espinosa I, Novelli S, Briones J, Mate JL, Salamero O, Sancho JM, Arenillas L, Serrano S, Erill N, Martínez D, Castillo P, Rovira J, Martínez A, Campo E, Colomo L. **MYC protein expression and genetic alterations have prognostic impact in diffuse large B-cell lymphoma treated with immunochemotherapy.** *Haematologica* 98(10):1554-1562 I.F.: 5.935

26. Perrot CY, Gilbert C, Marsaud V, Postigo A, Javelaud D, Mauviel A. **GLI2 cooperates with ZEB1 for transcriptional repression of CDH1 expression in human melanoma cells.** *Pigment Cell Melanoma Res* 26:861-873 I.F.: 5.839

27. Siles L, Sanchez-Tillo E, Lim JW, Darling DS, Kroll KL, Postigo A. **ZEB1 imposes a temporary stage-dependent inhibition of muscle gene expression and differentiation via CtBP-dependent transcriptional repression.** *Mol Cell Biol* 33:1368-1382 I.F.: 5.372

28. Valera A, Colomo L, Martinez A, de Jong D, Balague O, Matheu G, Martínez M, Taddesse-Heath L, Jaffe E, Bacchi C, Campo E. **ALK-positive large B-cell lymphomas express a terminal B-cell differentiation program and activated STAT3 but lack MYC rearrangements.** *Mod Pathol* 26(10):1329-1337 I.F.: 5.253

29. Liu Q, Salaverria I, Pittaluga S, Jegalian AG, Xi L, Siebert R, Raffeld M, Hewitt SM, Jaffe ES. **Follicular lymphomas in children and young adults: a comparison of the pediatric variant with usual follicular lymphoma.** *Am J Surg Pathol* 37(3):333-343 I.F.: 4.868

30. Martinez D, Valera A, Perez NS, Sua Villegas LF, Gonzalez-Farre B, Sole C, Gine E, Lopez-Guillermo A, Roue G, Martinez S, Sant F, Warzocha K, Robak T, Czader M, Villamor N, Colomo L, Campo E, Martinez A. **Plasmablastic Transformation of Low-grade B-cell Lymphomas: Report on 6 Cases.** *Am J Surg Pathol* 37(2):272-281 I.F.: 4.868

31. Liu Y, Sánchez-Tilló E, Lu X, Huang L, Clem B, Telang S, Jenson AB, Cuatrecasas M, Chesney J, Postigo A, Dean DC. **Sequential Inductions of the ZEB1 Transcription Factor Caused by Mutation of Rb and Then Ras Proteins Are Required for Tumor Initiation and Progression.** *J Biol Chem* 288:11572-11580 I.F.: 4.651

32. Camacho L, Meca-Cortes O, Abad JL, Garcia S, Rubio N, Diaz A, Celia-Terrassa T, Cingolani F, Bermudo R, Fernandez PL, Blanco J, Delgado A, Casas J, Fabrias G, Thomson TM. **Acid ceramidase as a therapeutic target in metastatic prostate cancer.** *J Lipid Res* 54:1207-1220 I.F.: 4.386

33. Codony-Servat J, Marín-Aguilera M, Visa L, Garcıía-Albéniz X, Pineda E, Fernández PL, Filella X, Gascón P, Mellado B. **Nuclear Factor-Kappa B and Interleukin- 6 Related Docetaxel Resistance in Castration-Resistant Prostate Cancer.** *Prostate* 73:512-521 I.F.: 3.843

34. Calvo J, Sánchez-Cid L, Muñoz M, Lozano JJ, Thomson TM, Fernández PL. **Infrequent Loss of Luminal Differentiation in Ductal Breast Cancer Metastasis.** *PLoS One* 8:1-12 e78097 I.F.: 3.730

35. Costa D, Muñoz C, Carrió A, Nomdedeu M, Calvo X, Solé F, Luño E, Cervera J, Vallespí T, Berneaga D, Gómez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardañaz MT, Hernández JM, Azaceta G, Álvarez S, Sánchez J, Martín ML, Bargay J, Gómez V, Cervero CJ, Allegue MJ, Collado R, Campo E, Nomdedeu B; Spanish Group of Myelodysplastic Syndromes (GESMD). **Reciprocal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemias: review of 5,654 patients with an evaluable karyotype.** *Gene Chromosome Canc* 52(8):753-763 I.F.: 3.546

36. López C, Delgado J, Costa D, Villamor N, Navarro A, Cazorla M, Gómez C, Arias A, Muñoz C, Cabezas S, Baumann T, Rozman M, Aymerich M, Colomer D, Pereira A, Cobo F, López-Guillermo A, Campo E, Carrió A. **Clonal evolution in chronic lymphocytic**

leukemia: Analysis of correlations with IGHV mutational status, NOTCH1 mutations and clinical significance. *Gene Chromosome Canc* 52(10):920-927 I.F.: 3.546

37. Salaverria I, Martin-Guerrero I, Burkhardt B, Kreuz M, Zenz T, Oschlies I, Arnold N, Baudis M, Bens S, García-Orad A, Lisfeld J, Schwaenen C, Szczepanowski M, Wessendorf S, Pfreundschuh M, Trümper L, Klapper W, Siebert R. **High resolution copy number analysis of IRF4 translocation-positive diffuse large B-cell and follicular lymphomas.** *Gene Chromosome Canc* 52(2):150-155 I.F.: 3.546

38. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Peguero A, Nadal A, Parra G, Gratacos E, Figueras F. **Placental findings in late-onset SGA births without Doppler signs of placental insufficiency.** *Placenta* 34(12):1136-1141 I.F.: 3.117

39. Valentino C, Kendrick S, Johnson N, Gascoyne R, Chan WC, Weisenburger D, Braziel R, Cook JR, Tubbs R, Campo E, Rosenwald A, Ott G, Delabie J, Jaffe E, Zhang W, Brunhoeber P, Nitta H, Grogan T, Rimsza L. **Colorimetric In Situ Hybridization Identifies MYC Gene Signal Clusters Correlating With Increased Copy Number, mRNA, and Protein in Diffuse Large B-Cell Lymphoma.** *Am J Clin Pathol* 139(2):242-254 I.F.: 2.881

40. Romeu C, Farré X, Cardesa A, Nadal A. **Expression of Ep-CAM, but not of E48, associates with nodal involvement in advanced squamous cell carcinomas of the larynx**. *Histopathology* 62:954-961 I.F.: 2.857

41. Wilson AL, Swerdlow SH, Przybylski GK, Surti U, Choi JK, Campo E, Trucco MM, Van Oss SB, Felgar RE. **Intestinal γδ T-cell lymphomas are most frequently of typeII enteropathy-associated T-cell type.** *Hum Pathol* 44(6):1131-1145 I.F.: 2.843

42. Miranda Rius J, Nadal A, Lahor E, Mtui B, Brunet L. **Unusual presentation of localized gingival enlargement associated with a slow-growing odontogenic myxoma.** *Int J Oral Sci* 5:172-175 I.F.: 2.719

43. Prats-Muñoz G, Galtés I, Armentano N, Cases S, Fernández PL, Malgosa A . **Human soft tissue preservation in the Cova des Pas site (Minorca Bronze Age).** *J Arch Science*. 40:4701-4710 I.F.: 1.889

44. Santamaría G, Velasco M, Farrús B, Caparrós FX, Fernández PL. **Dynamic contrast-enhanced mri reveals the extent and the microvascular pattern of breast ductal carcinoma in situ.** *Breast J* 19:402-410 I.F.: 1.831

45. Valduvieco I, Verger E, Bruna J, Caral L, Pujol T, Ribalta T, Boget T, Oleaga L, Pineda E, Graus F. **Impact of radiotherapy delay on survival in glioblastoma.** *Clin Transl Oncol* 15:278-282 I.F.: 1.276

46. Costa D, Vidal A, Carrió A, Muñoz C, Arias A, Gómez C, Berneaga D, Colomer D, Rozman M, Pratcorona M, Torrebadell M, Díaz-Beyá M, Esteve J, Campo E. **Refining the Diagnosis and Prognostic Categorization of Acute Myeloid Leukemia Patients with an Integrated Use of Cytogenetic and Molecular Studies.** *Acta Haematol* 129(2):65-71 I.F.: 0.894

Reviews / I.F.: 37.778

1. Ott G, Rosenwald A, Campo E. **Understanding MYC driven aggressive B-cell lymphomas: pathogenesis and classification.** *Blood* 122(24):3884-3891 I.F.: 9.060

2. Quesada V, Ramsay AJ, Rodríguez D, Puente XS, Campo E, López-Otín C. **The genomic landscape of chronic lymphocytic leukemia: clinical implications.** *BMC Med* 11:124 I.F.: 6.680

3. Campo E. **Whole genome profiling and other high throughput technologies in lymphoid neoplasms-current contributions and future hopes.** [Revision] *Mod Pathol* 1:S97-S110 I.F.: 5.250

4. Martín-Subero JI, López-Otín C, Campo E. **Genetic and epigenetic basis of chronic lymphocytic leukemia.** *Curr Opin Hematol* 20(4):362-368 I.F.: 4.110

5. Villamor N, López-Guillermo A, López-Otín C, Campo E. **Next-generation sequencing in chronic lymphocytic leukemia.** *Semin Hematol* 50(4):286-295 I.F.: 3.360

6. Williams ME, Bernstein SH, Jares P, Kahl BS, Witzig TE, Gordon LI. **Recent advances in mantle cell lymphoma: report of the 2012 Mantle Cell Lymphoma Consortium Workshop.** *Leukemia Lymphoma* 54(9):1882-90 I.F.: 2.300

7. Dreyling M*, Kluin-Nelemans HC, Beà S, Klapper W, Vogt N, Delfau-Larue MH, Hutter G, Cheah C, Chiappella A, Cortelazzo S, Pott C, Hess G, Visco C, Vitolo U, Klener P, Aurer I, Unterhalt M, Ribrag V, Hoster E, Hermine O for the European MCL Network. **Update on the molecular pathogenesis and clinical treatment of mantle cell lymphoma – report of the 11th annual conference of the EUROPEAN MANTLE CELL LYMPHOMA NETWORK.** *Leukemia Lymphoma* 54(4):699-707 I.F.: 2.300

8. Martínez-Trillos A, Quesada V, Villamor N, Puente XS, López-Otín C, Campo E. **Recurrent Gene Mutations in CLL.** *Adv Exp Med Biol* 792:87-107 I.F.: 1.830

9. Carvajal-Cuenca A, Campo E. **Early neoplastic lymphoid lesions.** Semin Diagn Pathol 30(2):146-155 I.F.: 1.620

10. Ramsay AJ, Martínez-Trillos A, Jares P, Rodríguez D, Kwarciak A, Quesada V. **Next-generation sequencing reveals the secrets of the chronic lymphocytic leukemia genome.** *Clin Transl Oncol* 15(1):3-8 I.F.: 1.280

Editorials / I.F.: 2.380

1. Soldini D, Campo E. **Genetic sequencing studies in Burkitt's lymphoma: what can**

we learn about tumorigenesis? *Expert Rev Hematol* 6(3):219-21 I.F.: 2.380

Clinical Guidelines / I.F.: 10.250

1. Dreyling M, Thieblemont C, Gallamini A, Arcaini L, Campo E, Hermine O, Kluin-Nelemans JC, Ladetto M, Le Gouill S, Iannitto E, Pileri S, Rodriguez J, Schmitz N, Wotherspoon A, Zinzani P, Zucca E. **ESMO Consensus conferences: guidelines on malignant lymphoma. part 2: marginal zone lymphoma, mantle cell lymphoma, peripheral T-cell lymphoma.** *Ann Oncol* 24(4).857-877 I.F.: 7.380

2. Caballero D, Campo E, López-Guillermo A, Martín A, Arranz-Sáez R, Giné E, López A, González-Barca E, Canales MA, González-Díaz M, Orfao A. **Clinical practice guidelines for diagnosis, treatment, and follow-up of patients with mantle cell lymphoma. Recommendations from the GEL/TAMO Spanish Cooperative Group.** *Ann Hematol* 92(9):1151-1179 I.F.: 2.870

GRANTS FOR RESEARCH IN PROGRESS

Alos L. **Alteraciones genéticas predictivas del desarrollo del carcinoma escamoso oral. Diseño de sondas con hibridación in situ fluorescente para el diagnóstico de lesiones preneoplásicas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01570.
Duration: 01/01/2012-31/12/2014

Alos L. **Identificación de las alteraciones genéticas en la mucosa oral predictivas del desarrollo del carcinoma escamoso.** Sponsored by: FUNDACION DE INVESTIGACION MEDICA MUTUA MADRILEÑA. AP94722011.
Duration: 03/08/2011-02/08/2014

Amador V. **Mecanismos oncogénicos regulados por SOX11 en los linfomas agresivos.** Sponsored by: Ministerio de Economía y Competitividad. BFU2012-30857.
Duration: 01/01/2013-31/12/2015

Amador V. **Papel de los factores de transcripción High-Mobility Group (HMG) en los Linformas Malignos Agresivos.** Sponsored by: Ministerio de Economía y Competitividad. BFU2009_09235.
Duration: 01/01/2010-30/06/2013

Amador V. **Characterization of the oncogenic molecular mechanisms of the SOX11 transcription factor in aggressive mantle cell lymphomas.** Fundació La Marató de TV3. TV3-Cancer_I3/20130110.
Duration: 01/04/2014-30/03/2017

Beà S. **Identificación de mutaciones, variantes estructurales y perfiles genómicos en neoplasias linfoides mediante ultrasecuenciación y microarrays.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01177.
Duration: 01/01/2012-31/12/2014

Beà S. **Comprehensive whole genome and exome sequence analysis in mantle cell lymphoma primary tumors.** Sponsored by: ASSOCIATION FOR INTERNATIONAL CANCER RESEARCH. AICR_MAY2011_001.
Duration: 01/01/2012-31/12/2014

Campo E. **Molecular Signatures to Improve Diagonosis and Outcome Prediction in NHL.** Sponsored by: National Institute of Health (NIH). 5U01CA114778-03.
Duration: 31/07/2007-31/12/2011

Campo E. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0036.
Duration: 01/01/2013-31/12/2016

Campo E. **A BLUEPRINT of Haematopoietic Epigenomes.** Sponsored by: European Commission. 282510.
Duration: 01/10/2011-31/03/2016

Campo E. **Análisis del impacto clínico de los perfiles genómicos de mutaciones somáticas en neoplasias linfoides.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-38432.
Duration: 01/01/2013-31/12/2015

Campo E. **Of DNA methylation and looping of distant regulatory elements in mantle cell lymphoma.** Sponsored by: NETHERLANDS ORGANISATION FOR SCIENTIST RESEARCH. 825.12.024.
Duration: 01/04/2013-31/03/2015

Campo E. **Estudio del Genoma de la Leucemia Linfocítica Crónica.** Instituto de Salud Carlos III.
Duración: 27/03/2009-31/12/2014

Campo E. **Caracterización genética y molecular de alta resolución de neoplasias linfoides. Implicaciones patogenéticas y clínica.** Sponsored by: Ministerio de Economía y Competitividad. SAF2008-03630.
Duration: 01/01/2009-31/12/2014

Campo **E. MOLECULAR DIAGNOSIS AND PROGNOSIS OF AGGRESSIVE LYMPHOMA – Strategic Partnering to Evaluate Cancer Signatures – SPECSII.** Sponsored by: University of Arizona .
Duration: 01/08/2011-31/07/2016

Campo E. **Oncomorfologia funcional humana i experimental.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_992.
Duration: 15/09/2009-30/04/2014

Campo E. **Data submission of collected tissue for the cancer genome atlas program.** Sponsored by: National Institute of Health (NIH). 13XS502ST.
Duration: 05/11/2013-31/03/2015

Campo E. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0039.
Duration: 01/01/2007-31/12/2013

Campo E. **Procurement of 40 paired pre- and post-chemotherapy samples of DNA derived from peripheral blood for TCGA analysis.** Sponsored by: National Institute of Health (NIH). HHSN261201000076I.

Duration: 08/09/2010-30/09/2013

Campo E. **Identification of somatic mutations in mantle cell lymphoma using next generation sequencing.** Sponsored by: LYMPHOMA RESEARCH FOUNDATION. 2011 LRF MCL.
Duration: 30/09/2011-29/09/2013

Hernandez L. **Búsqueda de lncRNAs como biomarcadores relevantes en las células tumorales y del microambiente de los linfomas foliculares.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01302.
Duration: 01/01/2013-31/12/2015

Martinez A. **Diferenciación Plasmocelular y transformación secretoria en linfomas no Hodgkin de células B: Implicaciones clínicas y terapéuticas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00907.
Duration: 01/01/2012-31/12/2014

Fernandez P.L. **Biomarcadores de autorrenovación y transición epitelio-mesénquima en el pronóstico, la predicción y el diagnóstico precoz de los carcinomas de próstata y mama.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-40017-C02-02.
Duration: 01/01/2013-31/12/2015

Fernandez P.L. **Optimización de la detección molecular precoz del cáncer de próstata en material residual de biopsias prostáticas y en masajes prostáticos.** Sponsored by: Asociación Española Contra el Cáncer (AECC). AECC_CAT_11_004.
Duration: 28/03/2012-28/03/2014

Postigo A. **Regulación de la diferenciación hematopoyética y de su transformación maligna por la familia ZEB de factores de transcripción.** Sponsored by: Ministerio de Economía y Competitividad. BFU2010-15163.
Duration: 01/01/2011-31/12/2014

Postigo A. **Regulación transcripcional de la cadherina E y de la capacidad invasiva y metastática de tumores de colon.** Sponsored by: FUNDACIÓ PRIVADA OLGA TORRES (FOT). FOT_09_002.
Duration: 01/01/2010-28/06/2013

Postigo A. **Validación del bucle ZEB1-ZEB2/microRNA como factor pronóstico y diana terapéutica en la capacidad invasiva/metastásica y la respuesta al tratamiento de carcinomas colorectales.** Sponsored by: Asociación Española Contra el Cáncer (AECC). AECC_CAT_10_009.
Duration: 30/03/2011-29/03/2013.

Postigo A. **Identificación de perfiles de expresión génica regulados por la vía microRNA/ZEB1-ZEB2 y su papel en la capacidad invasiva y metastásica de carcinomas de mama y la respuesta al tratamiento.I Beca en Investigación en Cáncer de Mama.** Sponsored by: Avon Cosmetics S.A.
Duration: 01/09/2012-31/12/2013 .

Postigo A. **Caracterització de la via ZEB1/microARN com biomarcador pronòstic de la capacitat metastàtic de carcinomes colorectals i la seva resposta a quimioteràpia. Validació de ZEB1 com potencial diana terapéutica.** Sponsored by: Acadèmia Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i de Balears. Beca de Recerca Basica 2013.
Duration: 01/04/2013-31/05/2015

Salaverria I. **Comprehensive genomic and epigenomic profiling of pediatric lymphomas:. new insights into biology and treatment.** Sponsored by: Instituto Carlos III CP13/00159.
Duration: 01/02/2014-30/01/2017

DOCTORAL THESES

Amador V, Campo E. **SOX11 transcription factor functional analysis in aggressive MCL.**
PhD student: María Carmela Vegliante.

Beà S, Campo E. **Caracterización genética y molecular del linfoma de células del manto y sus implicaciones clínicas.**
PhD student: Cristina Royo Moreno.

Campo E, Colomo L. **Implicació de l'oncogen MYC en la patogènesi dels limfomes B agressius.**
PhD student: Alexandra Valera Barros.

5.3 Diagnosis and therapy in oncology

LOCATION
HCB building

KEYWORDS
1. **Oncology Molecular studies**
2. **Radiotherapy**
3. **Breast cancer diagnosis**
4. **Sentinel lymph node**
5. **Positron Emission Tomography**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	81.69	26	9	7
2012	79.96	20	12	6
2013	105.40	24	17	3

TEAM INVOLVED IN
RECAVA
RTICC

AWARDS
XXV Jornades de la Societat Catalana de Medicina. Nuclear's Best Oral Communication.
Institution: Societat Catalana de Medicina Nuclear.
Awardees: Maria Mayoral, Pilar Paredes, Aranzazu Fernández, Laura Vidal, Andrés Perissinotti, David Fuster, Marina Depetris, Francesca Pons.

TEAM LEADER
Francesca Pons (HCB)
T. 93 227 54 82
fpons@clinic.cat

RESEARCHERS
Albert Biete (HCB)
Carles Conill (HCB)
David Fuster (HCB)
Marià Monzó (UB)
Maria Africa Muxí (HCB)
Laura Oleaga (HCB)
Xavier Setoain (HCB)
Martín Velasco (HCB)
Sergi Vidal-Sicart (HCB)

COLLABORATORS
Francisco Campos (HCB)
Sebastián Capurro (HCB)
Francesc Casas (HCB)
Lluís Donoso (HCB)
Blanca Farrús (HCB)
Fernando Gómez (HCB)
Francisco Lomeña (HCB)
Mario Pagés (HCB)
Pilar Paredes (HCB)
Javier Pavía (HCB)
Teresa Pujol (HCB)
Sonia Rodríguez (HCB)
Angels Rovirosa (HCB)
Marcelo Sánchez (HCB)
Gorane Santamaría (HCB)
Eugènia Verger (HCB)

STRATEGIC OBJECTIVES

Development of techniques for improving the diagnosis, prognostic evaluation and treatment response assessment in oncological patients.

- Development and application of new therapies in oncology.

MAIN LINES OF RESEARCH

1. **Molecular studies in embryonic and tumor cells: applications to pharmacogenomics.** Two types of studies are carried out: one type analyzes and compares microRNA

patterns in embryonic and tumor tissues, and the other uses allelic discrimination to analyze polymorphic profiles (SNPs) in oncological patients, with a view to selecting more specific treatments.

2. **Effects of synchrotron radiation upon the neoplastic cell.** In this study, which is carried out jointly with Barcelona Autonomous University (UAB), comparison is made of the biological action of synchrotron radiation (currently the Grenoble system until the UAB Alba unit comes into operation) with conventional X-rays used in radiotherapy. The cell-sensitizing effectiveness of gold nanoparticles and cisplatin is also studied.

3. **Breast cancer imaging diagnosis.** Two types of studies are carried out. One type of study uses 10G needle biopsies to improve the presurgical diagnosis of breast tumors, particularly in application to those with microcalcifications. The aim is to minimize the number of surgical biopsies required for establishing the diagnosis. The other type of study assesses the response to neoadjuvant chemotherapy in breast cancer based on breast MRI evaluation.

4. **Application of functional mRI techniques in oncology.** Studies of perfusion, diffusion and spectroscopy applied to the staging and monitoring of brain and head and neck tumours treatment.

5. **Gammagraphic (scintigraphic) detection of the sentinel node.** Lymphogammagraphy and posterior use of an external detection probe during surgery serves to identify and remove the sentinel node. This technique makes it possible to avoid 75% of all unnecessary lymphadenectomies. The use of a portable gammacamera during surgery offers additional advantages.

6. **Application of positron emission tomography (PET-CT) in oncology.** PET studies are made for the staging and control of treatment response in different types of tumors, including lymphomas, breast cancer and digestive tract lesions. We plan to use an intraoperative PET probe to improve the detection of tumor lesions.

PUBLICATIONS

Originals / I.F.: 105.404

1. Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. **Enalapril and carvedilol for preventing chemotherapy-induced left ventricular systolic dysfunction in patients with malignant hemopathies: the OVERCOME trial (prevention of left Ventricular dysfunction with Enalapril and caRvedilol in patients submitted to intensive Chemotherapy for the treatment of Malignant hEmopathies).** *J Am Coll Cardiol* 61(23):2355-2362 I.F.: 14.086

2. Guañabens N, Monegal A, Cerdá D, Muxí Á, Gifre L, Peris P, Parés A. **Randomized trial comparing monthly ibandronate and weekly alendronate for osteoporosis in patients with primary biliary cirrhosis.** *Hepatology* 58(6):2070-2078 I.F.: 12.003

3. Díaz-Beyá M, Navarro A, Ferrer G, Díaz T, Gel B, Camós M, Pratcorona M, Torrebadell M, Rozman M, Colomer D, Monzo M, Esteve J. **Acute myeloid leukemia with translocation (8;16)(p11;p13) and MYST3-CREBBP rearrangement harbors a distinctive microRNA signature targeting RET proto-oncogene.** *Leukemia* 27(3):595-603 I.F.: 10.164

4. Campayo M, Navarro A, Viñolas N, Diaz T, Tejero R, Gimferrer JM, Molins L, Cabanas ML, Ramirez J, Monzo M, Marrades R. **Low miR-145 and high miR-367 are associated with unfavourable prognosis in resected nonsmall cell lung cancer.** *Eur Respir* J 41(5):1172-1178 I.F.: 6.355

5. Fuertes S, Setoain X, Lopez-Guillermo A, Carrasco JL, Rodríguez S, Rovira J, Pons F. **Interim FDG PET/CT as a prognostic factor in diffuse large B-cell lymphoma.** *Eur J Nucl Med Mol Imaging* 40(4):496-504 I.F.: 5.114

6. Grau JJ, Zanon G, Caso C, Gonzalez X, Rodriguez A, Caballero M, Biete A. **Prognosis in women with breast cancer and private extra insurance coverage.** *Ann Surg Oncol* 20(9):2822-2827 I.F.: 4.120

7. Solá M, Alberro JA, Fraile M, Santesteban P, Ramos M, Fabregas R, Moral A, Ballester B, Vidal S. **Complete axillary lymph node dissection versus clinical follow-up in breast cancer patients with sentinel node micrometastasis: final results from the multicenter clinical trial AATRM 048/13/2000.** *Ann Surg Oncol.* 20(1):120-7 I.F.: 4.120

8. Perissinotti A, Paredes P, Vidal-Sicart S, Torné A, Albela S, Navales I, Martínez-Román S, Pahisa J, Pons F. **Use of SPECT/CT for improved sentinel lymph node localization in endometrial cancer.** *Gynecol Oncol* 129(1):42-48 I.F.: 3.929

9. Torné A, Pahisa J, Vidal-Sicart S, Martínez-Roman S, Paredes P, Puerto B, Albela S, Fusté P, Perisinotti A, Ordi J. **Transvaginal ultrasound-guided myometrial injection of radiotracer (TUMIR): A new method for sentinel lymph node detection in endometrial cancer.** *Gynecol Oncol* 128:88-94 I.F.: 3.929

10. Donaire A, Capdevila A, Carreño M, Setoain X, Rumià J, Aparicio J, Campistol J, Padilla N, Sanmartí F, Vernet O, Pintor L, Boget T, Ortells J, Bargalló N. **Identifying the cortical substrates of interictal epileptiform activity in patients with extratemporal epilepsy: An EEG-fMRI sequential analysis and FDG-PET study.** *Epilepsia* 54(4):678-690 I.F.: 3.909

11. Rubí S, Costes N, Heckemann R.A, Bouvard S, Hammers A, Martí Fuster B, Ostrowsky K, Montavont A, Jung J, Setoain X, Catenoix H, Hino K, Liger F, Le Bars D, Ryvlin P. **Positron emission tomography with a-[11C]methyl-Ltryptophan in**

tuberous sclerosis complex–related epilepsy. *Epilepsia* 54: 2143–2150 I.F.: 3.909

12. Sierra-Marcos A, Maestro I, Falcón C, Donaire A, Setoain J, Aparicio J, Rumiá J, Pintor L, Boget T, Carreño M, Bargalló N. **Ictal EEG-fMRI in localization of epileptogenic area in patients with refractory neocortical focal epilepsy.** *Epilepsia* 54: 1688–1698 I.F.: 3.909

13. Navarro A, Muñoz C, Gaya A, Díaz-Beyá M, Gel B, Tejero R, Díaz T, Martinez A, Monzó M. **MiR-SNPs as markers of toxicity and clinical outcome in Hodgkin lymphoma patients.** *PLoS One* 8(5):e64716 I.F.: 3.730

14. Navarro-Otano J, Gaig C, Muxi A, Lomeña F, Compta Y, Buongiorno MT, Martí MJ, Tolosa E, Valldeoriola F. **123I-MIBG cardiac uptake, smell identification and 123I-FP-CIT SPECT in the differential diagnosis between vascular parkinsonism and Parkinson's disease.** *Parkinsonism Relat Disord* 20(2):192-197 I.F.: 3.274

15. González-Ortiz S, Oleaga L, Pujol T, Medrano S, Rumiá J, Caral L, Boget T, Capellades J, Bargalló N. **Simple fMRI postprocessing suffices for normal clinical practice.** *Am J Neuroradiol* 34(6):1188-1193 I.F.: 3.167

16. Martí Fuster B, Esteban O, Planes X, Aguiar P, Crespo C, Falcon C, Wollny G, Rubí Sureda S, Setoain X, Frangi AF, Ledesma MJ, Santos A, Pavía J, Ros D. **FocusDET, a new toolbox for SISCOM analysis. Evaluation of the registration accuracy using Monte Carlo simulation.** *Neuroinformatics* 11(1):77-89 I.F.: 3.136

17. Fuster D, Depetris M, Torregrosa JV, Squarcia M, Paschoalin RP, Mayoral M, Granados U, Colletti PM, Rubello D, Pons F. **Advantages of pinhole collimator double-phase scintigraphy with 99mTc-MIBI in secondary hyperparathyroidism.** *Clin Nucl Med* 38(11):878-881 I.F.: 2.955

18. Fernández de Larrea C, Martín-Antonio B, Cibeira MT, Navarro A, Tovar N, Díaz T, Rosiñol L, Monzó M, Urbano-Ispizua A, Bladé J. **Impact of global and gene-specific DNA methylation pattern in relapsed multiple myeloma patients treated with bortezomib.** *Leukemia Res* 37(6):641-646 I.F.: 2.764

19. Monegal A, Navasa M, Peris P, Colmenero J, Cuervo A, Muxí A, Gifre L, Guañabens N. **Bone disease in patients awaiting liver transplantation. Has the situation improved in the last two decades?** *Calcif Tissue Int* 93(6):571-576 I.F.: 2.495

20. Ferrer G, Navarro A, Hodgson K, Aymerich M, Pereira A, Baumann T, Monzo M, Moreno C, Montserrat E. **MicroRNA expression in chronic lymphocytic leukemia developing autoimmune hemolytic anemia.** *Leukemia Lymphoma* 54(9):2016-2022 I.F.: 2.301

21. Rumià J, Marmol F, Sanchez J, Giménez-Crouseilles J, Carreño M, Bargalló N, Boget T, Pintor L, Setoain X, Donaire A, Saez GT, Ribalta T, Ferrer E, Puig-Parellada P. **Oxidative stress markers in the neocortex of drug-resistant epilepsy patients submitted to epilepsy surgery.** *Epilepsy Res* 107(1-2):75-81 I.F.: 2.241

22. Santamaría G, Velasco M, Farrús B, Caparrós FX, Fernández PL. **Dynamic contrast-enhanced MRI reveals the extent and the microvascular pattern of breast ductal carcinoma in situ.** *Breast J* 19(4):402-10 I.F.: 1.831

23. Bargalló X, Velasco M, Santamaría G, Del Amo M, Arguis P, Sánchez Gómez S. **Role of computer-aided detection in very small screening detected invasive breast cancers. J Digit Imaging** 26(3):572-577 I.F.: 1.100

24. Frontado L, Brouwer OR, van den Berg N.S, Mathéron HM, Vidal-Sicart S, van Leeuwen FWB, Valdés RA. **Valor añadido del trazador híbrido verde de indocianina-99mTc-nanocoloide para la biopsia del ganglio centinela en una serie de pacientes con drenaje en diferentes territorios anatómicos.** *Rev Esp Med Nucl Imagen Mol* 32:227–233 I.F.: 0.863

Reviews / I.F.: 5.114

1. Soriano AM, Prats E, Pons F, Carreras J.L. **Nuclear medicine training and practice in Spain.** *Eur J Nucl Med Mol Imaging* 40:1949–1951 I.F.: 5.114

Clinical Guidelines / I.F.: 5.114

1. Giammarile F, Alazraki N, Aarsvold J.N, Audisio R.A, Glass E, Grant S. F, Kunikowska J, Leidenius M, Moncayo V. M, Uren R. F, Oyen W.J.G, Valdés R.A, Vidal-Sicart S. **The EANM and SNMMI practice guideline for lymphoscintigraphy and sentinel node localization in breast cancer.** *Eur J Nucl Med Mol Imaging* 40:1932–1947 I.F.: 5.114

GRANTS FOR RESEARCH IN PROGRESS

Oleaga L. **Gestión del remodelado cardiovascular mediante integración de tecnologías de monitorización ubicua y conceptos del humano fisiológico virtual.** Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI) 09/397.
Duration: 15/09/2009-31/12/2013.

Pons F. **Imatge Molecular en Medicina Nuclear.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 2009_SGR_1049.
Duration: 15/09/2009-30/04/2014.

Pons F. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII) RD06/0020/0038.
Duration: 01/01/2007-31/12/2013.

5.4 Molecular genetics

LOCATION
UB School of Medicine

KEYWORDS
1. **Spermatogenenesis**
2. **Male infertility**
3. **Proteomics**
4. **Epigenetics**
5. **Cancer**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	32.90	11	5	1
2012	4.47	1	1	-
2013	14.89	3	3	-

TEAM LEADER
Cristóbal Mezquita (UB)
T. 93 402 45 18
cmezquita@ub.edu

RESEARCHERS:
Jovita Mezquita (UB)
Rafael Oliva (HCB-UB)
Josep Oriola (HCB-UB)

POST-DOCTORAL RESEARCHERS
Alexandra Amaral (UB)
Montse Codina (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Claudio Attardo Parrinello (IDIBAPS)
Rubén Azpiazu (IDIBAPS)
Judit Castillo (FCRB)
Meritxell Jodar (FCRB)
Carla Paiva (FCRB)

TECHNICIANS
Montserrat Pau (UB)

COLLABORATORS
Josep Lluís Ballescà (HCB)
Betlem Mezquita (UB)

STRATEGIC OBJECTIVES

The research group comprises the laboratories of Gene Expression and Cancer (www.fisiologia.net) and Human Genetics (www.ub.edu/humangen). Our research work is set within the paradigm of current physiology: the study of genic expression mechanisms as a new approach to the study of the functions of the body. On one hand, our work is presently directed towards the proteomic and molecular characterization of spermatozoa in infertile patients and controls, while on the other, studies are made of the mechanisms involved in angiogenesis and in tumor cell invasion.

MAIN LINES OF RESEARCH

The group has traditionally worked on gene expression mechanisms and the differentiation of the spermatogenic germinal line, and more recently on the mechanisms involved in angiogenesis and in tumour cell invasion. One relevant aspect is the contribution towards characterisation

of the complete human sperm proteome (Amaral et al., 2013). One of the important challenges is to elucidate the basic mechanisms that opera-te in nucleus-histone nucleus-protamine transition during spermatogenesis and how alterations may lead to alterations in the sperm's epigenetic information. We are also currently undertaking the study of the sperm metabolic pathways as a complementary approach towards understanding the sperm cell functions and failure in male sterility and the identification of proteins involved in male fertility and infertility (de Mateo et al., 2013; Vilagran et al., 2013). Another challenge will be the translation of important basic observations to the clinical setting. VEGFR1 expression in different tumour cells is essential for the invasion and formation of metastases. VEGFR1 expression in tissue stromal cells is also important in the formation of metastases. Not all invasive tumour cells express VEGFR1, due to the hypermethylation of the gene promoter. In highly invasive breast carcinoma cells, with the hypermethylated VEGFR1 gene promoter, we have discovered the existence of truncated intracellular forms of VEGFR1 transcribed from intronic promoters. One of these forms is preferentially expressed in invasive breast carcinoma cells and promotes tumour invasion by activating the Src tyrosine kinase. We recently observed that this truncated form, which promotes invasion independently of VEGF and other ligands, is positively regulated by the Notch signalling pathway and negatively regulated by retinoic acid through the miR-200 microRNA family.

PUBLICATIONS

Originals / I.F.: 14.893

1. Amaral A, Castillo J, Estanyol JM, Ballescà JL, Ramalho-Santos J, Oliva R. **Human sperm tail proteome suggests new endogenous metabolic pathways.** *Mol Cell Proteomics* 12(2):330-342
I.F.: 7.251

2. Silva F, Rodriguez-Revenga L, Madrigal I, Alvarez-Mora MI, Oliva R, Milà M. **High apolipoprotein E4 allele frequency in FXTAS patients.** *Genet Med* 15(8):639-642
I.F.: 5.560

3. Vilagran I, Castillo J, Bonet S, Sancho S, Yeste M, Estanyol JM, Oliva R. **Acrosin-binding protein (ACRBP) and triosephosphate isomerase (TPI) are good markers to predict boar sperm freezing capacity.** *Theriogenology* 80(5):443-450
I.F.: 2.082

GRANTS FOR RESEARCH IN PROGRESS

Oliva R. **Identificación proteómica de biomarcadores en espermatozoides de pacientes infértiles predictores de los resultados de reproducción asistida.** Sponsored by: FUNDACIÓ SALUD 2000. SERONO13_015.
Duration: 01/06/2013-01/06/2016

Oliva R. **Reproductive Biology Early Research Training.** Sponsored by: European Commission. 289880.
Duration: 01/01/2012-31/12/2015

Oliva R. **Grup de Genètica Humana.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1440.
Duration: 29/07/2009-30/04/2014

Oliva R. **Caracterización proteómica y genómica del núcleo del espermatozoide humano normal y de sus alteraciones en pacientes infértiles.** Sponsored by: Ministerio de Economía y Competitividad. BFU2009_07118.
Duration: 01/01/2010-1/03/2013

5.5 Genetics

LOCATION
HCB building

KEYWORDS
1. **Intellectual disability**
2. **Next Generation Sequencing**
3. **Cryptic chromosomal imbalances**
4. ***FMR1* premutation associated pathologies**
5. **Porphyria**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	128.51	14	7	4
2012	48.78	16	6	3
2013	41.67	14	7	3

TEAM INVOLVED IN
CIBERER

TEAM LEADER
Montserrat Milà (HCB)
T. 93 227 54 00 (Ext.2784)
mmila@clinic.cat

RESEARCHERS
Anna Carrió (HCB)
Carmen Herrero (HCB)
Irene Madrigal (HCB)
Ester Margarit (HCB)
Laia Rodriguez Revenga (HCB)
Aurora Sánchez (HCB)
Anna Soler (HCB)
Jordi To-Figueras (HCB)

COLLABORATORS
Maria Isabel Alvarez (CIBERER)
Cèlia Badenas (HCB)
Francisca Silva (FCRB)

STRATEGIC OBJECTIVES

To clinically, cytogenetic and molecular characterize rare genetic diseases. There are four main research lines. Each line has the strategic objectives defined by the supporting research projects. In this context, the study of intellectual disability (ID) and the identification of the causal genetic factors are based on the application of high performance array CGH and Next Generation Sequencing (NGS) technologies. On the other hand, the study of fragile X–associated tremor/ataxia syndrome (FXTAS) aims to identify a biological marker that might allow FXTAS presymptomatic diagnosis. Regarding the porphyrias, the strategic objective is to advance in our knowledge of the correlation genotype – phenotype: biochemical and clinical expression.

MAIN LINES OF RESEARCH

1. **Identification of genetic bases of intellectual disability (ID), both syndromic and non-syndromic, using new technologies such as NGS.** The application of high throughput

sequencing to different groups of clinically well characterized ID patients will allow us to identify new genes and to establish new molecular causes of ID.

2. **Fragile X syndrome:** Study of the FMR1 premutation associated pathologies: FXPOI (fragile X-associated primary ovarian insufficiency), FXTAS (fragile X-associated tremor/ataxia syndrome), and fibromyalgia associated to the FMR1 premutation. Study of the microRNA and mRNA expression profiles as possible susceptibility risk factors for FXTAS.

3. **Detection of cryptic chromosomal imbalances and identification of new phenotypes based on cytogenetic - molecular techniques in a prenatal and postnatal diagnostic setting.** The aim is to characterize chromosomal imbalances in fetuses with congenital anomalies and with normal karyotype using arraysCGH.

4. **Study of the genotype-phenotype correlation and expression mechanisms of porphyria.** The research lines aim to establish the following:

- Advance in the study of the alterations in iron regulation and metabolism in skin and erythropoietic porphyria.
- Investigate the role of modifier genes that modulate the clinical expression of erythropoietic porphyria.
- Study of new serum and urine biomarkers of acute porphyria severity of use in clinical practice.

The group will remain a member of the "European Porphyria Initiative" network as a reference center for the diagnosis, investigation and treatment of porphyria.

PUBLICATIONS

Originals / I.F.: 41.670

1. Silva F, Rodriguez-Revenga L, Madrigal I, Alvarez-Mora MI, Oliva R, Milà M. **High apolipoprotein E4 allele frequency in FXTAS patients.** *Genet Med* 15(8):639-642 I.F.: 5.560

2. Puiggros A, Delgado J, Rodriguez-Vicente A, Collado R, Aventín A, Luño E, Grau J, Hernandez JÁ, Marugán I, Ardanaz M, González T, Valiente A, Osma M, Calasanz MJ, Sanzo C, Carrió A, Ortega M, Santacruz R, Abrisqueta P, Abella E, Bosch F, Carbonell F, Solé F, Hernández JM, Espinet B; Grupo Cooperativo Español de Citogenética Hematológica (GCECGH) and Grupo Español de Leucemia Linfática Crónica (GELLC). **Biallelic losses of 13q do not confer a poorer outcome in chronic lymphocytic leukaemia: analysis of 627 patients with isolated 13q deletion.** *Brit J Haematol* 163(1):47-54 I.F.: 4.942

3. Mas S, Plana MT, Castro-Fornieles J, Gassó P, Lafuente A, Moreno E, Martinez E, Milà M, Lazaro L. **Common genetic background in anorexia nervosa and obsessive compulsive disorder: preliminary results from an association study.** *J Psychiatr Res.* 47(6):747-754 I.F.: 4.066

4. Alvarez-Mora MI, Rodriguez-Revenga L, Madrigal I, Torres-Silva F, Mateu-Huertas E, Lizano E, Friedländer MR, Martí E, Estivill X, Milà M. **MicroRNA expression profiling in blood from fragile X-associated tremor/ ataxia syndrome patients.** *Genes Brain Behav* 12(6):595-603 I.F.: 3.597

5. Mademont-Soler I, Morales C, Soler A, Martínez-Crespo JM, Shen Y, Margarit E, Clusellas N, Obón M, Wu BL, Sánchez A. **Prenatal diagnosis of chromosomal abnormalities in fetuses with abnormal cardiac ultrasound findings: evaluation of chromosomal microarray-based analysis.** *Ultrasound Obstet Gynecol* 41(4): 375-382 I.F.: 3.557

6. López C, Delgado J, Costa D, Villamor N, Navarro A, Cazorla M, Gómez C, Arias A, Muñoz C, Cabezas S, Baumann T, Rozman M, Aymerich M, Colomer D, Pereira A, Cobo F, López-Guillermo A, Campo E, Carrió A. **Clonal evolution in chronic lymphocytic leukemia: analysis of correlations with IGHV mutational status, NOTCH1 mutations and clinical significance.** *Gene Chromosome* Canc 52(10):920-927 I.F.: 3.546

7. Costa D, Muñoz C, Carrió A, Nomdedeu M, Calvo X, Solé F, Luño E, Cervera J, Vallespí T, Berneaga D, Gómez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardañaz MT, Hernández JM, Azaceta G, Álvarez S, Sánchez J, Martín ML, Bargay J, Gómez V, Cervero CJ, Allegue MJ, Collado R, Campo E, Nomdedeu B; Spanish Group of Myelodysplastic Syndromes (GESMD). **Reciprocal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemias: review of 5,654 patients with an evaluable karyotype.** *Gene Chromosome Canc* 52(8):753-763 I.F.: 3.546

8. Darwich E, To-Figueras J, Molina-López RA, Deulofeu R, Olbina G, Westerman M, Sánchez-Tápias JM, Muñoz-Santos C, Herrero C. **Increased serum hepcidin levels in patients with porphyria cutanea tarda.** *J Eur Acad Dermatol Venereol* 27(1):e68-74 I.F.: 2.694

9. Casals G, Marcos J, Pozo ÓJ, Aguilera P, Herrero C, To-Figueras J. **Gas chromatography-mass spectrometry profiling of steroids in urine of patients with acute intermittent porphyria.** *Clin Biochem* 46(9):819-824 I.F.: 2.450

10. Rodriguez-Revenga L, Madrigal I, Blanch-Rubió J, Elurbe DM, Docampo E, Collado A, Vidal J, Carbonell J, Estivill X, Milà M. **Screening for the presence of FMR1 premutation alleles in women with fibromyalgia.** *Gene* 512(2):305-308 I.F.: 2.196

11. Rodríguez-Revenga L, Vallespín E, Madrigal I, Palomares M, Mur A, García-Miñaur S, Santos F, Mori MÁ, Lapunzina P, Milà M, Nevado J. **A parallel study of different array-CGH platforms in a set of Spanish patients with developmental delay and intellectual disability.** *Gene* 521(1):82-86 I.F.: 2.196

12. Pérez-Poyato MS, Marfa MP, Abizanda IF, Rodriguez-Revenga L, Sánchez VC, González MJ, Puñal JE, Pérez AV, González MM, Bermejo AM, Hernández EM, Rosell MJ, Gort L, Milà M. **Late infantile neuronal ceroid lipofuscinosis: mutations in the CLN2 gene and clinical course in Spanish patients.** *J Child Neurol* 28(4):470-478 I.F.: 1.385

13. Martinez Peinado C, Díaz de Heredia C, To-Figueras J, Arias-Santiago S, Nogueras P, Elorza I, Olivé T, Bádenas C, Moreno MJ, Tercedor J, Herrero C. **Successful treatment of congenital erythropoietic porphyria using matched unrelated hematopoietic stem cell transplantation.** *Pediatr Dermatol* 30(4):484-489 I.F.: 1.041

14. Costa D, Vidal A, Carrió A, Muñoz C, Arias A, Gómez C, Berneaga D, Colomer D, Rozman M, Pratcorona M, Torrebadell M, Díaz-Beyá M, Esteve J, Campo E. **Refining the diagnosis and prognostic categorization of acute myeloid leukemia patients with an integrated use of cytogenetic and molecular studies.** *Acta Haematol* 129(2):65-71 I.F.: 0.894

Reviews / I.F.: 2.518

1. Filella X, Foj L, Milà M, Augé JM, Molina R, Jiménez W. **PCA3 in the detection and management of early prostate cancer.** *Tumour Biol* 34(3):1337-1347 I.F.: 2.518

GRANTS FOR RESEARCH IN PROGRESS

Madrigal I. **Aplicación de la secuenciación del exoma para el diagnóstico de la discapacidad intelectual.** Sponsored by: Fundación Agrupación Mútua.
Duration 01/012013-31/12/2014

Mila M. **Estudio de la via del estrés oxidativo y disfuncional mitocondrial en pacientes FXTAS. Búsqueda de un marcador específico para el diagnóstico presintomático y pronóstico de la enfermedad.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI12/00879.
Duration: 01/01/2013-31/12/2015

Mila M. **Grup d'estudi de Malalties Rares d'Origen Genètic.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 2009_SGR_1337.
Duration: 15/09/2009-30/04/2014

Rodriguez-Revenga L. **Implicación del gen FMR1 en la etiología del trastorno del espectro autista.** Sponsored by: Fundación Alicia Koplowitz AKOPLOWITZ11_006.
Duration: 01/01/2011-31/12/2013

Sanchez A. **Alcance diagnóstico y fiabilidad de las técnicas de array-CGH en muestras de vellosidad corial. Detección de anomalías cromosómicas crípticas de posibles discrepancias feto-placentarias.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/01841.
Duration: 01/01/2012-31/12/2014

To J. **Análisis de perfiles proteicos en pacientes con porfiria aguda.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI11/00767.
Duration: 01/01/2012-31/12/2014

DOCTORAL THESES

To-Figueras J. **Estudio de los decomisos de sustancias psicoactivas en los centros penitenciarios de Catalunya (1991-2010).**
PhD student: Blanca de la Fuente Capdevila.

5.6

Melanoma: imaging, genetics and immunology

LOCATION
CEK building

KEYWORDS
1. **Melanoma**
2. **Genetics**
3. **Dermoscopy**
4. **Confocal Microscopy**
5. **Susceptibility**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	133.79	9	7	2
2012	96.70	24	14	6
2013	145.102	29	24	3

TEAM LEADER
Susana Puig (HCB)
T. 93 2275400 (Ext 5692)
spuig@clinic.cat

RESEARCHERS
Josep Malvehy (HCB)
Ramón Vilella (HCB)

PRE-DOCTORAL RESEARCHERS
Ivette Alarcon Salazar (FCRB)
Maria Alba Díaz Lorca (HCB)
Antonio Bennassar (FCRB/HCB)
Zighe Ogbah (FCRB)
Joan Anton Puig (CIBERER)
Miriam Potrony Mateu (CIBERER/FCRB)
Danielle Shitara (University of Sao Paulo)
Gemma Tell Martí (FCRB)

TECHNICIANS
Abel Caño Caño (FCRB)
Mireia Dominguez (IDIBAPS)
Dani Gabriel (FCRB)
Pablo Iglesias (FCRB)
Jordi Milà (HCB)
Luchi Millan (HCB)
Laura Martín (FCRB)

COLLABORATORS
Paula Aguilera (HCB)
Llúcia Alos (HCB)
Pedro Arguís (HCB)
Celia Badenas (HCB)
Cristina Carrera (HCB)
Carlos Conill (HCB)
Adriana García Herrera (HCB)
Ramon Rull (HCB)
Sergi Vidal (HCB)
Ramón Vilana (HCB)
Antoni Vilalta (HCB)
José Palou (HCB)

STRATEGIC OBJECTIVES

1. Development of non-invasive imaging techniques for the diagnosis of melanoma.
2. Study of the genetic bases implicated in susceptibility to melanoma and photocarcinogenesis.
3. Development of treatment study strategies in melanoma and skin cancer: specific molecular target, immunological and photoprotection therapies.
4. Application of artificial intelligence systems for evaluating complex data

in melanoma, combining imaging, epidemiological, clinical and molecular information.

5. Development of models of humanized mouse skin for the study of photoprotection and photocarcinogenesis.

MAIN LINES OF RESEARCH

Main lines of research and some of the most relevant results obtained to date:

1. Dermoscopy and digital dermoscopy.

1.1 Definition of new dermatoscopic criteria in different dermatological processes
1.2 Development of dermoscopy for introduction in primary care, pathology and dermatology. Implementation of dermoscopy in teledermatology,
1.3 Analysis of dermoscopy as a preoperative prognostic tool.
1.4 Correlation of dermoscopy with molecular signatures in tumours

2. Confocal microscopy & new photonic technologies. Description of new algorithms, study of the evolution of lesions, new classifications and the use of telemedicine.

2.1 Definition of criteria in benign and malignant tumours using in vivo reflectance confocal microscopy (RCM) and ex vivo fluorescent confocal microscopy (FCM).
2.2 Creation of diagnostic algorithm for inflammatory and infectious conditions.
2.3 Implementation of RCM in the evaluation of treatment responses and early detection of relapses.
2.4 Implementation of FCM in Mohs surgery and intraoperative diagnosis of several cancers.
2.5 Development of OCT-HD, multispectral imaging & 3D imaging of the skin

3. Genetic epidemiology.

3.1 Study of melanoma susceptibility genes in familial and sporadic melanoma (CDKN2A, CDK4, BAP1, POT1, TERT, MITF)
3.2 Identification of new genes and mechanisms of melanoma susceptibility and prognosis using Genome Wide Scan and NGS in melanoma families and in childhood melanoma.
3.3 Study of nevogenicity and pigmentation genes associated to risk in melanoma.
3.4 Study of the MC1R gene as medium penetrance gene and its implication in several types or subtypes of tumours and other pathologies.
3.5 Study of genetic background of other cutaneous pathologies: Large and Giant Congenital nevi, familial hamartoma follicularis and Phacomatosis Pigmento Vascularis.

4. Study of the mechanisms involved in carcinogenesis and photocarcinogenesis.

4.1 Analysis of topical and oral photoprotection.
4.2 Study of the UV effect in skin and melanocytic nevi using imaging techniques and high-throughput molecular technologies
4.3 Investigation of somatic mutations of NRAS, BRAF, cKIT, RAC1, STK19, genomic amplifications of different oncogenes (TERT, AURKA, CCND1), and genomic losses of 9p21 in melanoma.
4.4 DNA repair mechanisms and their therapeutic implications.

5. Development of new treatment strategies for melanoma and other skin tumours.

5.1 Research in the dermatological implications of targeted therapies in melanoma
5.2 Immunotherapy in melanoma
5.3 Development of new strategies in the treatment of the field cancerization
5.4 Inhibition of the Hedgehog pathway for the treatment of basal cell carcinomas.
5.5 Specific immunotherapy in Merkel carcinoma.
5.6 Photodynamic therapy for melanoma

6. Evaluation of immune response in melanoma.

PUBLICATIONS

Originals / I.F.: 145.102

1. The GenoMEL Consortium, Iles MM, Law MH, Stacey SN, Han J, Fang S, Pfeiffer R, Harland M, Macgregor S, Taylor JC, Aben KK, Akslen LA, Avril MF, Azizi E, Bakker B, Benediktsdottir KR, Bergman W, Scarrà GB, Brown KM, Calista D, Chaudru V, Fargnoli MC, Cust AE, Demenais F, de Waal AC, Dębniak T, Elder DE, Friedman E, Galan P, Ghiorzo P, Gillanders EM, Goldstein AM, Gruis NA, Hansson J, Helsing P, Hočevar M, Höiom V, Hopper JL, Ingvar C, Janssen M, Jenkins MA, Kanetsky PA, Kiemeney LA, Lang J, Lathrop GM, Leachman S, Lee JE, Lubiński J, Mackie RM, Mann GJ, Martin NG, Mayordomo JI, Molven A, Mulder S, Nagore E, Novaković S, Okamoto I, Olafsson JH, Olsson H, Pehamberger H, Peris K, Grasa MP, Planelles D, Puig S, Puig-Butille JA; Q-MEGA and AMFS Investigators, Randerson-Moor J, Requena C, Rivoltini L, Rodolfo M, Santinami M, Sigurgeirsson B, Snowden H, Song F, Sulem P, Thorisdottir K, Tuominen R, Van Belle P, van der Stoep N, van Rossum MM, Wei Q, Wendt J, Zelenika D, Zhang M, Landi MT, Thorleifsson G, Bishop DT, Amos CI, Hayward NK, Stefansson K, Bishop JA, Barrett JH. **A variant in FTO shows association with melanoma risk not due to BMI.** *Nat Genet* 45(4):428-32 I.F.: 35.209

2. Zebary A, Omholt K, van Doorn R, Ghiorzo P, Harbst K, Hertzman Johansson C, Höiom V, Jönsson G, Pjanova D, Puig S, Scarra GB, Harland M, Olsson H, Egyhazi Brage S, Palmer J, Kanter-Lewensohn L, Vassilaki I, Hayward NK, Newton-Bishop J, Gruis NA, Hansson J. **Somatic BRAF and NRAS Mutations in Familial Melanomas with known Germline CDKN2A Status: a GenoMEL study. J Invest Dermatol** 134(1):287-290 I.F.: 6.193

3. Bourillon A, Hu HH, Hetet G, Lacapere JJ, André J, Descamps V, Basset-Seguin N, Ogbah Z, Puig S, Saiag P, Bagot M, Bensussan A, Grandchamp B, Dumaz N, Soufir N. **Genetic variation at KIT locus may predispose to melanoma.** *Pigment Cell Melanoma Res* 26(1):88-96 I.F.: 5.839

4. Ogbah Z, Badenas C, Harland M, Puig-Butille JA, Elliot F, Bonifaci N, Guino E, Randerson-Moor J, Chan M, Iles MM, Glass D, Brown AA, Carrera C, Kolm I, Bataille V, Spector TD, Malvehy J, Newton-Bishop J, Pujana MA, Bishop T, Puig S. **Evaluation of PAX3 genetic variants and nevus number.** *Pigment Cell Melanoma Res* 26(5):666-676 I.F.: 5.839

5. Davies JR, Field S, Randerson-Moor J, Harland M, Kumar R, Anic GM, Nagore E, Hansson J, Höiom V, Jönsson G, Gruis NA, Park JY, Guan J, Sivaramakrishna Rachakonda P, Wendt J, Pjanova D, Puig S, Schadendorf D, Okamoto I, Olsson H, Affleck P, García-Casado Z, Puig-Butille JA, Stratigos AJ, Kodela E, Donina S, Sucker A, Hosen I, Egan KM, Barrett JH, van Doorn R, Bishop DT, Newton-Bishop J. **An inherited variant in the gene coding for vitamin D-binding protein and survival from cutaneous melanoma: a BioGenoMEL study.** *Pigment Cell Melanoma Res* 27(2):234-243 I.F.: 5.839

6. Pizzichetta MA, Talamini R, Marghoob AA, Soyer HP, Argenziano G, Bono R, Corradin MT, De Giorgi V, Gonzalez MA, Kolm I, Kopf AW, Malvehy J, Nami N, Oliviero M, Pellacani G, Puig S, Rabinovitz H, Rubegni P, Seidenari S, Stanganelli I, Veronesi A, Zalaudek I, Zampieri P, Menzies SW. **Negative pigment network: An additional dermoscopic feature for the diagnosis of melanoma.** *J Am Acad Dermatol* 68(4):552-559 I.F.: 4.906

7. Zalaudek I, Kittler H, Hofmann-Wellenhof R, Kreusch J, Longo C, Malvehy J, Puig S, Moscarella E, Piana S, Massone C, Cota C, Ferrara G, Fleischer M, Argenziano G. **White" network in Spitz nevi and early melanomas lacking significant pigmentation.** *J Am Acad Dermatol* 69(1):56-60 I.F.: 4.906

8. Bennàssar A, Carrera C, Puig S, Vilalta A, Malvehy J. **Fast Evaluation of 69 Basal Cell Carcinomas With Ex Vivo Fluorescence Confocal Microscopy: Criteria Description, Histopathological Correlation, and Interobserver Agreement.** *JAMA Dermatol* 149(7):839-847 I.F.: 4.906

9. Blum A, Hofmann-Wellenhof R, Marghoob AA, Argenziano G, Cabo H, Carrera C, Costa Soares de Sá B, Ehrsam E, González R, Malvehy J, Manganoni AM, Puig S, Simionescu O, Tanaka M, Thomas L, Tromme I, Zalaudek I, Kittler H. **Recurrent Melanocytic Nevi and Melanomas in Dermoscopy: Results of a Multicenter Study of the International Dermoscopy Society.** *JAMA Dermatol* 150(2):138-145 I.F.: 4.906

10. Carrera C, Puig-Butillè JA, Aguilera P, Ogbah Z, Palou J, Lecha M, Malvehy J, Puig S. **Impact of Sunscreens on Preventing UVR-Induced Effects in Nevi: In Vivo Study Comparing Protection Using a Physical Barrier vs Sunscreen.** JAMA Dermatol 149(7):803-813 I.F.: 4.906

11. Malvehy J, Aguilera P, Carrera C, Salerni G, Lovatto L, Scope A, Marghoob AA, Palou J, Alós L, Puig S. **Ex Vivo Dermoscopy for Biobank-Oriented Sampling of Melanoma.** *JAMA Dermatol* 149(9):1060-1067 I.F.: 4.906

12. Menzies SW, Moloney FJ, Byth K, Avramidis M, Argenziano G, Zalaudek I, Braun RP, Malvehy J, Puig S, Rabinovitz HS, Oliviero M, Cabo H, Bono R, Pizzichetta MA, Claeson M, Gaffney DC, Soyer HP, Stanganelli I, Scolyer RA, Guitera P, Kelly J, McCurdy O, Llambrich A, Marghoob AA, Zaballos P, Kirchesch HM, Piccolo D, Bowling J, Thomas L, Terstappen K, Tanaka M, Pellacani G, Pagnanelli G, Ghigliotti G, Ortega BC, Crafter G, Ortiz AM, Tromme I, Karaarslan IK, Ozdemir F, Tam A, Landi C, Norton P, Kaçar N, Rudnicka L, Slowinska M, Simionescu O, Di Stefani A, Coates E, Kreusch J. **Dermoscopic Evaluation of Nodular Melanoma.** *JAMA Dermatol* 149(6):699-709 I.F.: 4.906

13. Jaimes N, Chen L, Dusza SW, Carrera C, Puig S, Thomas L, Kelly JW, Dang L, Zalaudek I, Braun RP, Menzies SW, Busam KJ, Marghoob AA. **Clinical and Dermoscopic Characteristics of Desmoplastic Melanomas.** *JAMA Dermatol* 149(4):413-421 I.F.: 4.906

14. Alarcon I, Carrera C, Palou J, Alos L, Malvehy J, Puig S. **Impact of in vivo reflectance confocal microscopy on the number needed to treat melanoma in doubtful lesions.** *Br J Dermatol.* 2013. 170(4):802-808 I.F.: 3.759

15. Bennàssar A, Vilata A, Puig S, Malvehy J. **Validation Of Fluorescent Confocal Microscopy Criteria And Histopathological Correlation For The Diagnosis Of Basal Cell Carcinoma And Most Common Subtypes.** *Brit J Dermatol* 170(2):360-365 I.F.: 3.759

16. Costa J, Ortiz-Ibañez K, Salerni G, Borges V, Carrera C, Puig S, Malvehy J. **Dermoscopic patterns of Melanoma Metastases: inter-observer consistency and accuracy for metastases recognition.** *Brit J Dermatol* 169(1):91-99 I.F.: 3.759

17. Moscarella E, Rabinovitz H, Puig S, Zalaudek I, Oliviero MC, Brown L, Alarcon I, Malvehy J, Longo C, Formisano D, Carrera C, Badenas C, Piana S, Albertini G, Pellacani G, Argenziano G. **Multiple primary melanomas: do they look the same?** *Brit J Dermatol* 168(6):1267-1272 I.F.: 3.759

18. Puig-Butillé JA, Carrera C, Kumar R, Garcia-Casado Z, Badenas C, Aguilera P, Malvehy J, Nagore E, Puig S. **Distribution of MC1R variants among melanoma subtypes: p.R163Q is associated with Lentigo Maligna Melanoma in a Mediterranean population.** *Brit J Dermatol* 169(4):804-811 I.F.: 3.759

19. Puig-Butillé JA, Badenas C, Ogbah Z, Carrera C, Aguilera P, Malvehy J, Puig S. **Genetic alterations in RAS-regulated pathway in acral lentiginous melanoma.** *Exp Dermatol* 22(2):148-150 I.F.: 3.578

20. Puig-Butillé JA, Malvehy J, Potrony M, Trullas C, Garcia-García F, Dopazo J, Puig S. **Role of CPI-17 in restoring skin homoeostasis in cutaneous field of cancerization: effects of topical**

application of a film-forming medical device containing photolyase and UV filters. *Exp Dermatol* 22(7):494-496 I.F.: 3.578

21. Shitara D, Ishioka P, Alonso-Pinedo Y, Palacios-Bejarano L, Carrera C, Malvehy J, Puig S. **Shiny White Streaks: A Sign of Malignancy at Dermoscopy of Pigmented Skin Lesions.** *Acta Derm Venereol* 94(2):132-137 I.F.: 3.487

22. Carrera C, Bennassar A, Ishioka P, Dalle S, Vilalta A, Fuertes I, Alos L, Thomas L, Puig S, Malvehy J. **Desmoplastic melanoma on the nose: electrochemotherapy as an alternative treatment to local advanced disease.** *J Eur Acad Dermatol Venereol* 28(4):424-432 I.F.: 2.694

23. Grazziotin TC, Rey MC, Bica CG, Pinto LA, Bonamigo RR, Puig-Butille JA, Cuellar F, Puig S. **Genetic variations of patients with familial or multiple melanoma in Southern Brazil.** *J Eur Acad Dermatol Venereol* 27(2):e179-185 I.F.: 2.694

24. Salerni G, Terán T, Puig S, Malvehy J, Zalaudek I, Argenziano G, Kittler H. **Meta-analysis of digital dermoscopy follow-up of melanocytic skin lesions: a study on behalf of the International Dermoscopy Society.** *J Eur Acad Dermatol Venereol* 27(7):805-814 I.F.: 2.694

25. Ogbah Z, Visa L, Badenas C, Ríos J, Puig-Butille JA, Bonifaci N, Guino E, Augé JM, Kolm I, Carrera C, Pujana MA, Malvehy J, Puig S. **Serum 25-hydroxyvitamin D3 levels and vitamin D receptor variants in melanoma patients from the Mediterranean area of Barcelona: 25-hydroxyvitamin D3 levels and VDR variants in melanoma patients from Barcelona.** *BMC Med Genet* 14(1):26 I.F.: 2.536

26. Armengot-Carbo M, Abrego A, Gonzalez T, Alarcon I, Alos L, Carrera C, Malvehy J, Puig S. **Inverted Follicular Keratosis: Dermoscopic and Reflectance Confocal Microscopic Features.** *Dermatology* 227(1):62-66 I.F.: 2.024

27. Braun RP, Thomas L, Dusza SW, Gaide O, Menzies S, Dalle S, Blum A, Argenziano G, Zalaudek I, Kopf A, Rabinovitz H, Oliviero M, Perrinaud A, Cabo H, Pizzichetta M, Pozo L, Langford D, Tanaka M, Saida T, Perusquia Ortiz AM, Kreusch J, De Giorgi V, Piccolo D, Grichnik JM, Kittler H, Puig S, Malvehy J, Seidenari S, Stanganelli I, French L, Marghoob AA. **Dermoscopy of acral melanoma: a multicenter study on behalf of the international dermoscopy society.** *Dermatology* 227(4):373-380 I.F.: 2.024

28. Gamo R, Malvehy J, Puig S, Fuentes ME, Naz E, Gómez de la Fuente E, Calzado L, Sanchez-Gilo A, Vicente FJ, Lopez-Estebaranz JL. **Dermoscopic Features of Melanocytic Nevi in Seven Different Anatomical Locations in Patients With Atypical Nevi Syndrome.** *Dermatol Surg* 39(6):864-71 I.F.: 1.866

29. Jaimes N, Dusza SW, Quigley EA, Braun RP, Puig S, Malvehy J, Kittler H, Rabinovitz HS, Oliviero MC, Soyer HP, Grichnik JM, Korzenko A, Cabo H, Carlos-Ortega B, Ahlgrimm-Siess V, Kopf AW, Marghoob AA. **Influence of time on dermoscopic diagnosis and management.** *Australas J Dermatol* 54(2):96-104 I.F.: 0.965

Reviews / I.F.: 3.044

1. Argenziano G, Giacomel J, Zalaudek I, Blum A, Braun RP, Cabo H, Halpern A, Hofmann-Wellenhof R, Malvehy J, Marghoob AA, Menzies S, Moscarella E, Pellacani G, Puig S, Rabinovitz H, Saida T, Seidenari S, Soyer HP, Stolz W, Thomas L, Kittler H. **A clinico-dermoscopic approach for skin cancer screening: recommendations involving a survey of the International Dermoscopy Society. 2013.** *Dermatol Clin* 31(4):525-534 I.F.: 1.522

2. Puig S, Malvehy J. **Monitoring patients with multiple nevi.** *Dermatol Clin* 31(4):565-577 I.F.: 1.522

GRANTS FOR RESEARCH IN PROGRESS

Malvehy J. **Diagnosis of skin cancer using optics.** Sponsored by: European Commission. 621066.
Duration: 01/12/2013-30/11/2016

Puig S. **IMmune MOdulating strategies for treatment of MErkel cell Carcinoma.** Sponsored by: European Commission. 277775.
Duration: 1/1/2012-31/12/2015

Puig S. **Diagnosis of skin cancer using optics.** Sponsored by: European Commission. 621066.
Duration: 01/12/2013-30/11/2016

Puig S. **Utilización de las regiones homozigotas del genoma para la identificación de genes pronósticos en melanoma y el desarrollo de un panel molecular de pronóstico.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/00840.
Duration: 01/01/2013-31/12/2015

Puig S. **Identificación de genes implicados en desarrollo y progresión de melanoma mediante la caracterización de regiones homozigotas.** Sponsored by: Instituto de Salud Carlos III (ISCIII) PI09/1393.
Duration: 1/1/2010-30/6/2013

Vilella R. **Estudio fase II aleatorizado en pacientes con cáncer colorectal en estadio IV progresivo a dos líneas de quimioterapia, comparando el mejor tratamiento de soporte frente a tratamiento con células dendríticas y mejor tratamiento de soporte.**
Sponsored by: Ministerio de Sanidad, Política Social e Igualdad. EC11-156.
Duration: 01/01/2012-31/12/2013

DOCTORAL THESES

Puig S. **Radiación ultravioleta y lesiones melanocíticas. Implicación en prevención y diagnóstico precoz de melanoma.**
PhD Student: Cristina Carrera Álvarez.

5.7

Hematopoietic progenitor cell transplantation

LOCATION
CEK building

KEYWORDS
1. **Allogeneic transplantation**
2. **Immunotherapy**
3. **Veno-oclussive disease**
4. **Graft versus host disease**
5. **Infectious diseases**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	82.13	15	11	4
2012	54.53	13	5	6
2013	54.64	11	7	3

TEAM INVOLVED IN
RTICC

TEAM LEADER
Álvaro Urbano-Ispizua (HCB)
T. 93 227 54 75
aurbano@clinic.cat

RESEARCHERS
Enric Carreras (HCB)
Francesc Fernández-Avilés (HCB)
Pedro Marín (HCB)
Carmen Martínez Muñoz (HCB)
Montserrat Rovira (HCB)

POST-DOCTORAL RESEARCHERS
Beatriz Martin Antonio (IDIBAPS)

TECHNICIANS
Anna Mantecon (FCRB)
Nuria Montfort (HCB)

NURSING STAFF
Noemi Llobet (FCRB)

COLLABORATORS:
Josep Mensa (HCB)
Alfons Navarro (UB)
Marià Monzó (UB)
Maribel Díaz Ricart (HCB)
Maria Suarez Lledó (HCB)

STRATEGIC OBJECTIVES

In the last few years our group has developed basic and translational research lines, thanks to the collaboration with other research groups of the Clinic Hospital (Department of Immunology, Department of Hemostasis) and of the Medical School (Department of Human Anatomy). Very recently, we have established research space of our own in the CEK, and at the School of Medicine (Institute of Research Josep Carreras), and have expanded our collaboration with other research groups – particularly in reference to cell therapy. Likewise, we have started the expansion of hematopoietic precursors from umbilical cord blood based on co-cultures of mesenchymal cells and research lines in antitumor cell therapy, anti-infectious treatment and cell immune modulation. Functional studies of genetic polymorphisms have also been consolidated. Lastly, we plan to develop a line of research in the field of the

pharmacokinetics, pharmacodynamics and pharmacogenomics of immune modulators, as well as in the development of in vitro predictive models of graft-versus-host disease.

MAIN LINES OF RESEARCH

Clinical research lines

1. Assessment of new hematopoietic precursor transplantation (HPT) indications. Treatment of diseases such as amyloidosis, POEMS syndrome, scleromyxedema, autoimmune disorders (multiple sclerosis, Crohn's disease, lupus erythematosus), primary myelofibrosis or paroxysmal nocturnal hemoglobinuria – these being diseases in which our group has the most extensive experience in the country.

2. Evaluation of new progenitor sources (high-complexity hematopoietic precursor transplantation). The lack of compatible siblings for all patients amenable to hematopoietic precursor transplantation is leading to the development of transplants from non-consanguineous donors or umbilical cord blood. We are the most active group in the country in relation to these high complexity procedures, which represent 30% of our activity.

3. Evaluation of new transplant modalities.
   - Domiciliary autogenic HPT (unique in Europe, awarded on several occasions by the scientific and healthcare societies) – a modality which we aim to extend to domiciliary allogenic HPT.
   - Haploidentical transplantation with unmanipulated bone marrow.

4. Studies addressing the prevention and treatment of the main complications of HPT.
   - Prevention and treatment of graft-versus-host disease with new agents (anti-IL-2 receptor antibodies, new anti-thymocyte globulins, alemtuzumab and cell therapy using mesenchymal cells).

   Participation in different multicenter studies.

Basic and translational research lines

1. Study of the post-HPT complications originating from endothelial dysfunction. Different early complications appearing after HPT, such as veno-occlusive syndrome, capillary rupture syndrome, thrombotic microangiopathy, graft syndrome, and idiopathic pneumonia syndrome, appear to originate from endothelial dysfunction. Our project aims to characterize such dysfunction and the early diagnosis of infections then to seek effective preventive in HPT. Following the advances and treatment options. This research made in the early diagnosis of line is supported by two FIS grants fungal diseases (galactomannan and an aid from the German José antigen, high-resolution CAT) and Carreras Foundation.

2. Study of immune reconstitution following HPT. Following characterization of immune reconstitution in HPT from bone marrow, peripheral blood and in reduced intensity regimens, we plan to assess immune reconstitution in the transplantation of umbilical cord blood – this not ever having been achieved to date.

3. Study of the impact of genic polymorphisms upon the complications and outcomes of HPT.
   Following demonstration of the impact of the mannose-binding lectin variants upon the incidence of fungal infections, of the NOD2/CARD15 gene variants upon survival and the incidence of bronchiolitis obliterans and, more recently, of the impact of the NLRP2 and NLRP3 gene variants upon HPT survival, we plan to continue this line of research, assessing new polymorphisms that may affect the evolution of HPT.

4. Study of new techniques for the early diagnosis of infections in HPT. Following the advances made in the early diagnosis of fungal diseases (galactomannan antigen, high-resolution CAT) and viral infections (CMV antigenemia and PCR applied to all herpes viruses and other pathogens), which have facilitated our healthcare activities, we plan to continue evaluating new diagnostic techniques (quantitative PCR for EBV, the application of PCR to tissue samples, biological markers in bronchoalveolar lavage, and PET scan assessment of infections).

PUBLICATIONS

Originals / I.F.: 54.644

1. Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. Enalapril And Carvedilol for **Preventing Chemotherapy-Induced Left Ventricular Systolic Dysfunction in Patients with Malignant Hemopathies. The OVERCOME Trial.** *J Am Coll Cardiol* 61(23):2355-2362 I.F.: 14.086

2. Martínez C, Canals C, Sarina B, Alessandrino EP, Karakasis D, Pulsoni A, Sica S, Trneny M, Snowden JA, Kanfer E, Milpied N, Bosi A, Guidi S, de Souza CA, Willemze R, Arranz R, Jebavy L, Hellmann A, Sibon D, Oneto R, Luan JJ, Dreger P, Castagna L, Sureda A; Lymphoma Working Party of the European Group for Blood and Marrow Transplantation (EBMT) and the Gruppo Italiano Trapianto di Midollo Osseo (GITMO). **Identification of prognostic factors predicting outcome in Hodgkin's lymphoma patients relapsing after autologous stem cell transplantation.** *Ann Oncol* 24(9):2430-2434 I.F.: 7.384

3. Tovar N, Fernández de Larrea C, Aróstegui JI, Cibeira MT, Rosiñol L, Rovira M, Elena M, Filella X, Yagüe J, Bladé J. **Natural history and prognostic impact of oligoclonal humoral response in patients with multiple myeloma after autologous stem-cell transplantation: long-term results from a single institution.** *Haematologica* 98(7):1142-1146 I.F.: 5.935

4. Gerull S, Stern M, Apperley J, Beelen D, Brinch L, Bunjes D, Butler A, Ganser A, Ghavamzadeh A, Koh MB, Komarnicki M, Kröger N, Maertens J, Maschan A, Peters C, Rovira M, Sengeløv H, Socie' G, Tischer J, Oneto R, Passweg J, Marsh J. **Syngeneic transplantation in aplastic anemia: pretransplant conditioning and peripheral blood are associated with improved engraftment - an observational study on behalf of the Severe Aplastic Anemia and Pediatric Diseases Working Parties of the European Group for Blood and Marrow Transplantation.** *Haematologica* 98(11):1804-1809 I.F.: 5.935

5. Hillmen P, Muus P, Röth A, Elebute MO, Risitano AM, Schrezenmeier H, Szer J,Browne P, Maciejewski JP, Schubert J, Urbano-Ispizua A, de Castro C, Socié G,Brodsky RA. **Long-term safety and efficacy of sustained eculizumab treatment in patients with paroxysmal nocturnal haemoglobinuria.** *Brit J Haematol* 162(1):62-73 I.F.: 4.942

6. Guillem V, Hernández-Boluda JC, Gallardo D, Buño I, Bosch A, Martínez-Laperche C, de la Cámara R, Brunet S, Martin C, Nieto JB, Martínez C, Pérez A, Montoro J, Garcia-Noblejas A, Solano C; Spanish Hematopoietic Stem Cell Transplantation and Cell Therapy Group (GETH). **A polymorphism in the TYMP gene is associated with the outcome of HLA-identical sibling allogeneic stem cell transplantation.** *Am J Hematol* 88(10):883-889 I.F.: 4.138

7. Carmona A, Díaz-Ricart M, Palomo M, Molina P, Pino M, Rovira M, Escolar G,Carreras E **Distinct Deleterious Effects of Cyclosporine and Tacrolimus and Combined Tacrolimus-Sirolimus on Endothelial Cells: Protective Effect of Defibrotide.** *Biol Blood Marrow Transplant* 19(10):1439-1445 I.F.: 3.940

8. Martín-Antonio B, Suarez-Lledo M, Arroyes M, Fernández-Avilés F, Martínez C, Rovira M, Espigado I, Gallardo D, Bosch A, Buño I, Martínez-Laperche C, Jiménez-Velasco A, de la Cámara R, Brunet S, Nieto JB, Urbano-Ispizua A. **A variant in IRF3 impacts on the clinical outcome of AML patients submitted to Allo-SCT.** *Bone Marrow Transplant* 48(9):1205-1211 I.F.: 3.541

9. Fernández de Larrea C, Martín-Antonio B, Cibeira MT, Navarro A, Tovar N, Díaz T, Rosiñol L, Monzó M, Urbano-Ispizua A, Bladé J. **Impact of global and gene-specific DNA methylation pattern in relapsed multiple myeloma patients treated with bortezomib.** *Leukemia Res* 37(6):641-646 I.F.: 2.764

10. Jarque I, Tormo M, Bello JL, Rovira M, Batlle M, Julià A, Tabares S, Rivas C, Fernández-Sevilla A, García-Boyero R, Debén G, González-Campos J, Capote FJ, Sanz MA; on behalf of the Spanish Pethema Group. **Caspofungin for the treatment of invasive fungal disease in hematological patients (ProCAS Study)**. *Med Mycol* 51(2):150-154 I.F.: 1.979

Reviews / I.F.: 4.595

1. Rovira J, Cid J, Gutiérrez-García G, Pereira A, Fernández-Avilés F, Rosiñol L, Martínez C, Carreras E, Urbano A, Rovira M, Lozano M. **Fatal Immune Hemolytic Anemia Following Allogeneic Stem Cell Transplantation: Report of 2 Cases and Review of Literature.** *Transfus Med Rev* 27(3):166-170 I.F.: 3.759

2. Vallejo C, Vázquez L, Cabrera Martín JR, Carreras E, García-Rodríguez J, Ruiz-Camps I, Fortún J, Mensa J, Barberán J. Grupo Cooperativo. **Treatment of invasive fungal infections in high-risk haematological patients: What have we learnt in the past 10 years?** *Rev Esp Quimioter* 26(4):378-386 I.F.: 0.836

Editorials / I.F.: 5.935

1. Arranz L, Urbano-Ispizúa A, Méndez-Ferrer S. **Mitochondria underlie different metabolism of hematopoietic stem and progenitor cells.** *Haematologica* 98(7):993-995 I.F.: 5.935

Multicenter / I.F.: 9.060

1. Roos-Weil D, Dietrich S, Boumendil A, Polge E, Bron D, Carreras E, Iriondo Atienza A, Arcese W, Beelen DW, Cornelissen JJ, Kröger N, Milone G, Rossi G, Jardin F, Peters C, Rocha V, Sureda A, Mohty M, Dreger P; European Group for Blood and Marrow Transplantation Lymphoma, Pediatric Diseases, and Acute Leukemia Working Parties. **Stem cell transplantation can provide durable disease control in blastic plasmacytoid dendritic cell neoplasm: a retrospective study from the European Group for Blood and Marrow Transplantation.** *Blood* 121(3):440-446 I.F.: 9.060

GRANTS FOR RESEARCH IN PROGRESS

Urbano A. **Estudio de la influencia de variantes génicas en el sistema inmune innato del donate y del paciente en el pronóstico tras trasplante alogénico de progenitores hemopoyéticos.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01090. Duration: 01/01/2012-31/12/2014

Urbano A. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0012. Duration: 01/01/2007-31/08/2014

5.8 Hematological oncology

LOCATION
HCB building

KEYWORDS
1. **Lymphoid neoplasms**
2. **Genomic Profile**
3. **Multiple myeloma**
4. **Myelofibrosis**
5. **Acute myeloid leukemia**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	356.47	41	29	4
2012	441.54	44	34	6
2013	499.61	54	43	8

TEAM INVOLVED IN
RTICC

TEAM LEADER
Francisco Cervantes (HCB)
T. 93 227 54 28
fcervan@clinic.cat

GROUP LEADERS
Joan Bladé (HCB)
Francisco Cervantes (HCB)
Carlos Fernández de Larrea (IDIBAPS-HCB)
Armando López-Guillermo (HCB)

RESEARCHERS
Julio Delgado (HCB)
Jordi Esteve (HCB)
Eva Giné (HCB)
Emili Montserrat (HCB)
Benet Nomdedeu (HCB)
Laura Rosiñol (HCB)

POST-DOCTORAL RESEARCHERS
Maria Teresa Cibeira (FCRB)
Meritxell Nomdedeu (HCB)

PRE-DOCTORAL RESEARCHERS
Tycho Baumann (HCB)
Xavier Calvo (HCB)
Marina Díaz Beyá (FCRB)
Ivan Dlouhy (FCRB)
Daniel Esteban (FCRB)
Anna Gaya (HCB)
Raquel Jiménez (FCRB)
Alejandra Martínez Trillos (FCRB)
Marta Pratcorona (IDIBAPS)
Jordina Rovira (HCB)
Rodrigo Ariel Santacruz (FCRB)
Natalia Tovar (HCB)

NURSING STAFF
Mónica Blanco (HCB)
Eva Carrera (HCB)
Sonia Chaves (HCB)

ADMINISTRATIVE STAFF
Marta Bistagne (HCB)
Cristina Cerrato (FCRB)
Maria José Sánchez Melero (HCB)
Carmen Torres (HCB)

STATISTICIAN
Ester Bladé (FCRB)
Mª Carmen Pastor (FCRB)
Saudy Peláez (FCRB)
Irene Pérez (FCRB)
Montserrat Pérez (FCRB)
Antonio de la Riva (FCRB)
Llúcia Sanz (FCRB)

COLLABORATORS
Eduardo Arellano (HCB)
Ana Carrió (HCB)
Dolors Costa (HCB)
Ruth Muñoz Risueño (Institut de Recerca Josep Carreras)
Alfons Navarro (UB)
Arturo Pereira (HCB)

STRATEGIC OBJECTIVES

The main strategic objectives of our team are clinical, applied and basic research in haematological oncology. The team is structured into three study groups of three major disease categories.

MAIN LINES OF RESEARCH

1. Lymphoid neoplasms

- Mechanisms of progression and study of the clinical significance of minimal residual disease.
- Genomic profile of diffuse large cell lymphoma and its clinical significance (in collaboration with the National Cancer Institute (USA) and the Leukemia Lymphoma Molecular Profiling Project (LLMPP)).
- New prognostic models in T cell lymphomas (in collaboration in international studies, particularly the International T-cell Lymphomas Project (University of Nebraska) and follicular lymphoma.
- Mechanisms of progression of chronic lymphoid leukemia (CLL)
- Influence of the cellular microenvironment in CLL.
- Evaluation of cellular proliferation in CLL.
- Project for the Chronic Lymphocytic Leukemia (CLL) Genome, in collaboration with the Hematopathology Unit.
- Phase I/II and III clinical trials in lymphomas and CLL.

2. Multiple myeloma and other monoclonal gammopathies

- Study of molecular cytogenics, gene-expression profile of cytokines related to angiogenesis and tumors microenvironment and analysis of genes differentially expressed in bone marrow and extramedullary plasmacytomas.
- Evaluation of the immune reconstitution in patients in remission after autologous transplant or chemotherapy as compared with patients in partial response and monoclonal gammopathies of undetermined significance.
- Impact of individual genetic variability on response to treatment in multiple myeloma through analysis of single nucleotide polymorphisms (SNPs).
- Characterization of cardiac involvement in AL amyloidosis based on clinical presentation, cardiac biomarkers and imaging techniques, and influence of genetics in the predilection of light amyloidogenic chains for the heart and the severity of involvement.
- Phase I, II and III clinical trials within the Spanish PETHEMA group or pharmaceutical companies.

3. Myeloid neoplasms

- Chronic myeloid leukemia (CML): Participation in the European Registry of CML
- Philadelphia-negative myeloproliferative neoplasms: Mechanisms of thrombosis; relationship between mutational status and initial characteristics, progression and prognosis of myelofibrosis; participation in the European Registry of Myelofibrosis.
- Acute myeloid leukemia (AML): Biological prognostic factors in AML of intermediate cytogenetic risk; Analysis of biological prognostic factors in AML; Analysis of expression of non-coding RNA (microRNA&long intergenic non-coding RNA) in AML; Design of treatment protocols for the Grupo Cooperativo para el Estudio y Tratamiento de las Leucemias Agudas y Mielodisplasias.
- Myelodysplastic syndromes (MDS): Participation in the Spanish MDS Registry; cytogenetic and molecular abnormalities and prognostic implications; study of microR-NA.
- Phase I/II and III clinical trials with new drugs for CML, myelofibrosis, AML, ALL and MDS.

RESEARCH GROUP
MYELOMA AND OTHER MONOCLONAL GAMMAPATHIES

GROUP LEADER
Joan Bladé (HCB)

Multiple Myeloma and systemic AL amyloidosis. Minimal residual disease and mechanisms of disease progression studies, extramedullary involvement in myeloma, cardiac involvement in Amyloidosis, and multicentric clinical trials with novel drugs.

RESEARCH GROUP
MYELOID NEOPLASMAS

GROUP LEADER
Francisco Cervantes (HCB)

Natural history and prognosis of chronic myeloid leukemia, myeloproliferative neoplasms, acute myeloid leukemia and myelodysplastic syndromes; prognostic importance of newer molecular markers in these diseases; clinical trials with new drugs.

RESEARCH GROUP
LYMPHOID NEOPLASMS

GROUP LEADER
Armando López Guillermo (HCB)

Lymphomas, chronic lymphocytic leukemia and the other lymphoproliferative disorders: Study of progression mechanisms of the disease, genome of CLL and lymphoma, minimum residual disease and biological prognostic models.

50/50 PROGRAM
MECHANISMS OF PROGRESSION IN MONOCLONAL GAMMOPATHIES

GROUP LEADER
Carlos Fernández de Larrea Rodríguez (HCB-IDIBAPS)

Our group is focused on a comprehensive study on patients with multiple myeloma in complete remission, in order to investigate whether or not immune restoration is associated with the emergence of oligoclonal bands and to a continued response, and to search common features that these patients can share with those with long-lasting stable monoclonal gammopaties of undetermined significance (MGUS). For this purpose, a wide spectrum of biological studies in peripheral blood and bone marrow are performed in patients after transplantation or induction chemotherapy only, in comparison with patients with active myeloma.

PUBLICATIONS

Originals / I.F.: 499.61

1. Mateos MV, Hernández MT, Giraldo P, de la Rubia J, de Arriba F, López Corral L, Rosiñol L, Paiva B, Palomera L, Bargay J, Oriol A, Prosper F, López J, Olavarría E, Quintana N, García JL, Bladé J, Lahuerta JJ, San Miguel JF. **Lenalidomide plus dexamethasone for high-risk smoldering multiple myeloma.** *N Engl J Med* 369(5):438-447 I.F.:51.658

2. Ramsay AJ, Quesada V, Foronda M, Conde L, Martínez-Trillos A, Villamor N,Rodríguez D, Kwarciak A, Garabaya C, Gallardo M, López-Guerra M, López-Guillermo A, Puente XS, Blasco MA, Campo E, López-Otín C. **POT1 mutations cause telomere dysfunction in chronic lymphocytic leukemia.** *Nat Genet* 45(5):526-530 I.F.: 35.209

3. Dimopoulos M, Siegel DS, Lonial S, Qi J, Hajek R, Facon T, Rosiñol L, Williams C, Blacklock H, Goldschmidt H, Hungria V, Spencer A, Palumbo A, Graef T, Eid JE, Houp J, Sun L, Vuocolo S, Anderson KC. **Vorinostat or placebo in combination with bortezomib in patients with multiple myeloma (VANTAGE 088): a multicentre, randomised, double-blind study.** *Lancet Oncol* (11):1129-1140 I.F.: 25.117

4. Fayad L, Offner F, Smith MR, Verhoef G, Johnson P, Kaufman JL, Rohatiner A,Advani A, Foran J, Hess G, Coiffier B, Czuczman M, Giné E, Durrant S, Kneissl M, Luu KT, Hua SY, Boni J, Vandendries E, Dang NH. **Safety and clinical activity of a combination therapy comprising two antibody-based targeting agents for the treatment of non-Hodgkin lymphoma: results of a phase I/II study evaluating the immunoconjugate inotuzumab ozogamicin with rituximab.** *J Clin Oncol* 31(5):573-583 I.F.: 18.038

5. Girnius S, Seldin DC, Cibeira MT, Sanchorawala V. **New hematologic response criteria predict survival in patients with immunoglobulin light chain amyloidosis treated with high-dose melphalan and autologous stem-cell transplantation.** *J Clin Oncol* 31(21):2749-2750 I.F.: 18.038

6. San-Miguel JF, Richardson PG, Günther A, Sezer O, Siegel D, Bladé J, LeBlanc R, Sutherland H, Sopala M, Mishra KK, Mu S, Bourquelot PM, Victoria Mateos M, Anderson KC. **Phase Ib study of panobinostat and bortezomib in relapsed or relapsed and refractory multiple myeloma.** *J Clin Oncol* 31(29):3696-3703 I.F.: 18.038

7. Sonneveld P, Goldschmidt H, Rosiñol L, Bladé J, Lahuerta JJ, Cavo M, Tacchetti P, Zamagni E, Attal M, Lokhorst HM, Desai A, Cakana A, Liu K, van de Velde H, Esseltine DL, Moreau P. **Bortezomib-Based Versus Nonbortezomib-Based Induction Treatment Before Autologous Stem-Cell Transplantation in Patients With Previously Untreated Multiple Myeloma: A Meta-Analysis of Phase III Randomized, Controlled Trials.** *J Clin Oncol* 31(26):3279-3287 I.F.: 18.038

8. Valcárcel D, Ademà V, Solé F, Ortega M, Nomdedeu B, Sanz G, Luño E, Cañizo C, de la Serna J, Ardanaz M, Marco V, Collado R, Grau J, Montoro J, Mallo M, Vallespí T. **Complex, not monosomal, karyotype is the cytogenetic marker of poorest prognosis in patients with primary myelodysplastic syndrome.** *J Clin Oncol* 31(7):916-922 I.F.: 18.038.

9. Zucca E, Conconi A, Laszlo D, López-Guillermo A, Bouabdallah R, Coiffier B,Sebban C, Jardin F, Vitolo U, Morschhauser F, Pileri SA, Copie-Bergman C, Campo E, Jack A, Floriani I, Johnson P, Martelli M, Cavalli F, Martinelli G, Thieblemont C. **Addition of rituximab to chlorambucil produces superior event-free survival in the treatment of patients with extranodal marginal-zone B-cell lymphoma: 5-year analysis of the IELSG-19 Randomized Study.** *J Clin Oncol* 31(5):565-572 I.F.: 18.038

10. Bosch X, Rovira M, Sitges M, Domènech A, Ortiz-Pérez JT, de Caralt TM, Morales-Ruiz M, Perea RJ, Monzó M, Esteve J. **Enalapril And Carvedilol for Preventing Chemotherapy-Induced Left Ventricular Systolic Dysfunction in Patients with Malignant Hemopathies. The OVERCOME Trial.** *J Am Coll Cardiol* 61(23):2355-2362 I.F.: 14.156

11. Bassaganyas L, Beà S, Escaramís G, Tornador C, Salaverria I, Zapata L,Drechsel O, Ferreira PG, Rodriguez-Santiago B, Tubio JM, Navarro A, Martín-García D, López C, Martínez-Trillos A, López-Guillermo A, Gut M, Ossowski S, López-Otín C, Campo E, Estivill X. **Sporadic and reversible chromothripsis in chronic lymphocytic leukemia revealed by longitudinal genomic analysis.** *Leukemia* 27(12):2376-2379. I.F.: 10.164

12. Díaz-Beyá M, Navarro A, Ferrer G, Díaz T, Gel B, Camós M, Pratcorona M, Torrebadell M, Rozman M, Colomer D, Monzo M, Esteve J. **Acute myeloid leukemia with translocation (8;16) (p11;p13) and MYST3-CREBBP rearrangement harbors a distinctive microRNA signature targeting RET proto-oncogene.** *Leukemia* 27(3):595-603 I.F.: 10.164

13. Nomdedéu JF, Hoyos M, Carricondo M, Bussaglia E, Estivill C, Esteve J, Tormo M, Duarte R, Salamero O, de Llano MP, García A, Bargay J, Heras I, Martí-Tutusaus JM, Llorente A, Ribera JM, Gallardo D, Aventin A, Brunet S, Sierra J. **Bone marrow WT1 levels at diagnosis, post-induction and post-intensification in adult de novo AML**. *Leukemia* 27(11):2157-2164. IF:10.164

14. Paiva B, Vídriales MB, Rosiñol L, Martínez-López J, Mateos MV, Ocio EM, Montalbán MA, Cordón L, Gutiérrez NC, Corchete L, Oriol A, Terol MJ, Echeveste MA, De Paz R, De Arriba F, Palomera L, de la Rubia J, Díaz-Mediavilla J, Granell M, Gorosquieta A, Alegre A, Orfao A, Lahuerta JJ, Bladé J, San Miguel JF. **A multiparameter flow cytometry immunophenotypic algorithm for the identification of newly diagnosed symptomatic myeloma with an MGUS-like signature and long-term disease control.** *Leukemia* 27(10):2056-261.I.F.: 10.164

15. Ramsay AJ, Rodríguez D, Villamor N, Kwarciak A, Tejedor JR, Valcárcel J,López-Guillermo A, Martínez-Trillos A, Puente XS, Campo E, López-Otín C, Quesada V. **Frequent somatic mutations in components of the RNA processing machinery in chronic lymphocytic leukemia.** *Leukemia* 27(7):1600-1603. I.F.: 10.164

16. Rawstron AC, Böttcher S, Letestu R, Villamor N, Fazi C, Kartsios H, de Tute RM, Shingles J, Ritgen M, Moreno C, Lin K, Pettitt AR, Kneba M, Montserrat E, Cymbalista F, Hallek M, Hillmen P, Ghia P. **Improving efficiency and sensitivity: European Research Initiative in CLL (ERIC) update on the international harmonised approach for flow cytometric residual disease monitoring in CLL.** *Leukemia* 27(1): 142-149. I.F.: 10.164.

17. Vannucchi AM, Lasho TL, Guglielmelli P, Biamonte F, Pardanani A, Pereira A,Finke C, Score J, Gangat N, Mannarelli C, Ketterling RP, Rotunno G, Knudson RA,Chiara Susini M, Laborde RR, Spolverini A, Pancrazzi A, Pieri L, Manfredini R,Tagliafico E, Zini R, Jones A, Zoi K, Reiter A, Duncombe A, Pietra D, Rumi E,Cervantes F, Barosi G, Cazzola M, Cross NC, Tefferi A. **Mutations and prognosis in primary myelofibrosis.** *Leukemia* 27(9):1861-1869 I.F.: 10.164

18. Villamor N, Conde L, Martínez-Trillos A, Cazorla M, Navarro A, Beà S, López C, Colomer D, Pinyol M, Aymerich M, Rozman M, Abrisqueta P, Baumann T, Delgado J, Giné E, González-Díaz M, Hernández JM, Colado E, Payer AR, Rayon C, Navarro B, José Terol M, Bosch F, Quesada V, Puente XS, López-Otín C, Jares P, Pereira A, Campo E, López-Guillermo A. **NOTCH1 mutations identify a genetic subgroup of chronic lymphocytic leukemia patients with high risk of transformation and poor outcome.** *Leukemia* 27(5):1100-1106 IF:10.164

19. Beà S, Valdés-Mas R, Navarro A, Salaverria I, Martín-Garcia D, Jares P, Giné E, Pinyol M, Royo C, Nadeu F, Conde L, Juan M, Clot G, Vizán P, Di Croce L,Puente DA, López-Guerra M, Moros A, Roue G, Aymerich M, Villamor N, Colomo L,Martínez A, Valera A, Martín-Subero JI, Amador V, Hernández L, Rozman M, Enjuanes A, Forcada P, Muntañola A, Hartmann EM, Calasanz MJ, Rosenwald A, Ott G, Hernández-Rivas JM, Klapper W, Siebert R, Wiestner A, Wilson WH, Colomer D, López-Guillermo A, López-Otín C, Puente XS, Campo E. **Landscape of somatic mutations and clonal evolution in mantle cell lymphoma.** *Proc Natl Acad Sci U S A* 110(45):18250-18255. I.F: 9.737

20. Abrisqueta P, Villamor N, Terol MJ, González-Barca E, González M, Ferrà C, Abella E, Delgado J, García-Marco JA, González Y, Carbonell F, Ferrer S, Monzó E,Jarque I, Muntañola A, Constants M, Escoda L, Calvo X, Bobillo S, Montoro JB, Montserrat E, Bosch F. **Rituximab maintenance after first-line therapy with rituximab, fludarabine, cyclophosphamide, and mitoxantrone (R-FCM) for chronic lymphocytic leukemia.** *Blood* 122(24):3951-902773. I.F.: 9.060

21. Cervantes F, Vannucchi AM, Kiladjian JJ, Al-Ali HK, Sirulnik A, Stalbovskaya V, McQuitty M, Hunter DS, Levy RS, Passamonti F, Barbui T, Barosi G, Harrison CN, Knoops L, Gisslinger H; COMFORT-II investigators. **Three-year efficacy, safety, and survival findings from COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for leukemia sis.** *Blood* 122(25):4047-4053. I.F.: 9.060

22. Pratcorona M, Brunet S, Nomdedéu J, Ribera JM, Tormo M, Duarte R, Escoda L, Guàrdia R, Queipo de Llano MP, Salamero O, Bargay J, Pedro C, Martí JM, Torrebadell M, Díaz-Beyá M, Camós M, Colomer D, Hoyos M, Sierra J, Esteve J. **Favorable outcome of patients with acute myeloid leukemia harboring a low-allelic burden FLT3-ITD mutation and concomitant NPM1 mutation: relevance to post-**

remission therapy. *Blood* 121(14):2734-2738. I.F.: 9.060

23. Salaverria I, Royo C, Carvajal-Cuenca A, Clot G, Navarro A, Valera A, Song JY, Woroniecka R, Rymkiewicz G, Klapper W, Hartmann EM, Sujobert P, Wlodarska I, Ferry JA, Gaulard P, Ott G, Rosenwald A, López-Guillermo A, Quintanilla-Martinez L, Harris NL, Jaffe ES, Siebert R, Campo E, Beà S. **CCND2 rearrangements are the most frequent genetic events in cyclin D1(-) mantle cell lymphoma.** *Blood* 121(8):1394-1402. I.F.: 9.060

24. Such E, Germing U, Malcovati L, Cervera J, Kuendgen A, Della Porta MG,Nomdedeu B, Arenillas L, Luño E, Xicoy B, Amigo ML, Valcarcel D, Nachtkamp K,Ambaglio I, Hildebrandt B, Lorenzo I, Cazzola M, Sanz G. **Development and validation of a prognostic scoring system for patients with chronic myelomonocytic leukemia.** *Blood* 121(15):3005-3015 IF. 9.060

25. Cheah CY, George A, Giné E, Chiappella A, Kluin-Nelemans HC, Jurczak W,Krawczyk K, Mocikova H, Klener P, Salek D, Walewski J, Szymczyk M, Smolej L, Auer RL, Ritchie DS, Arcaini L, Williams ME, Dreyling M, Seymour JF; European Mantle Cell Lymphoma Network. **Central nervous system involvement in mantle cell lymphoma: clinical features, prognostic factors and outcomes from the European Mantle Cell Lymphoma Network.** *Ann Oncol.* 2013 Aug; 24(8):2119-23. I.F.: 7.384

26. Enjuanes A, Albero R, Clot G, Navarro A, Beà S, Pinyol M, Martín-Subero JI,Klapper W, Staudt LM, Jaffe ES, Rimsza L, Braziel RM, Delabie J, Cook JR, Tubbs RR, Gascoyne R, Connors JM, eisenburger DD, Greiner TC, Chan WC, López-Guillermo A, Rosenwald A, Ott G, Campo E, Jares P. **Genome-wide methylation analyses identify a subset of mantle cell lymphoma with a high number of methylated CpGs and aggressive clinicopathological features.** *Int J Cancer* 133(12):2852-2863 I.F.: 6.198

27. Montoto S, Corradini P, Dreyling M, Ghielmini M, Kimby E, López-Guillermo A, Mackinnon S, Marcus RE, Salles G, Schouten HC, Sureda A, Dreger P. **Indications for hematopoietic stem cell transplantation in patients with follicular lymphoma: a consensus project of the EBMT-Lymphoma Working Party.** *Haematologica* 98(7):1014-1021 I.F.: 5.935

28. Tovar N, Fernández de Larrea C, Aróstegui JI, Cibeira MT, Rosiñol L, Rovira M, Elena M, Filella X, Yagüe J, Bladé J. **Natural history and prognostic impact of oligoclonal humoral response in patients with multiple myeloma after autologous stem-cell transplantation: long-term results from a single institution.** *Haematologica* 98(7):1142-1146 I.F.: 5.935

29. Valera A, López-Guillermo A, Cardesa-Salzmann T, Climent F, González-Barca E, Mercadal S, Espinosa I, Novelli S, Briones J, Mate JL, Salamero O, Sancho JM,Arenillas L, Serrano S, Erill N, Martínez D, Castillo P, Rovira J, Martínez A,Campo E, Colomo L. **MYC protein expression and genetic alterations have prognostic impact in diffuse large B-cell lymphoma treated with immunochemotherapy.** *Haematologica* 98(10):1554-1562 I.F.: 5.935

30. Ribera JM, García O, Grande C, Esteve J, Oriol A, Bergua J, González-Campos J, Vall-Llovera F, Tormo M, Hernández-Rivas JM, García D, Brunet S, Alonso N, Barba P, Miralles P, Llorente A, Montesinos P, Moreno MJ, Hernández-Rivas JÁ, Bernal T. **Dose-intensive chemotherapy including rituximab in Burkitt's leukemia or lymphoma regardless of human immunodeficiency virus infection status: final results of a phase 2 study (Burkimab).** *Cancer.* 119(9):1660-8. I.F: 5.201

31. Fuertes S, Setoain X, López-Guillermo A, Carrasco JL, Rodríguez S, Rovira J, Pons F. **Interim FDG PET/CT as a prognostic factor in diffuse large B-cell lymphoma.** *Eur J Nucl Med Mol Imaging* 40(4):496-504 I.F.:5.114

32. Martinez-Lopez J, Fernández-Redondo E, García-Sánz R, Montalbán MA, Martínez-Sánchez P, Pavia B, Mateos MV, Rosiñol L, Martín M, Ayala R, Martínez R, Blanchard MJ, Alegre A, Besalduch J, Bargay J, Hernandez MT, Sarasquete ME, Sanchez-Godoy P, Fernández M, Bladé J, San Miguel JF, Lahuerta JJ; GEM PETHEMA cooperative study group. **Clinical applicability and prognostic significance of molecular response assessed by fluorescent-PCR of immunoglobulin genes in multiple myeloma. Results from a GEM/PETHEMA study.** *Brit J Haematol* 163(5):581-589 I.F.: 4.942

33. Alvarez-Larrán A, Pereira A, Arellano-Rodrigo E, Hernández-Boluda JC, Cervantes F. **Cytoreduction plus low-dose aspirin versus cytoreduction alone as primary prophylaxis of thrombosis in patients with high-risk essential thrombocythaemia: an observational study.** *Brit J Haematol* 161(6):865-871 I.F.: 4.942

34. Caballero-Velázquez T, López-Corral L, Encinas C, Castilla-Llorente C, Martino R, Rosiñol L, Sampol A, Caballero D, Serrano D, Heras I, San Miguel J, Pérez-Simón JA. **Phase II clinical trial for the evaluation of bortezomib within the reduced intensity conditioning regimen (RIC) and post-allogeneic transplantation for high-risk myeloma patients.** *Brit J Haematol* 162(4):474-482 I.F.: 4.942

35. Harrison CN, Mesa RA, Kiladjian JJ, Al-Ali HK, Gisslinger H, Knoops L, Squier M, Sirulnik A, Mendelson E, Zhou X, Copley-Merriman C, Hunter DS. Levy RS, Cervantes F, Passamonti F, Barbui T, Barosi G, Vannucchi AM. **Health-related quality of life and symptoms in patients with myelofibrosis treated with ruxolitinib versus best available therapy.** *Brit J Haematol* 162(2):229-239 I.F.: 4.942

36. Mallo M, Del Rey M, Ibáñez M, Calasanz MJ, Arenillas L, Larráyoz MJ, Pedro C, Jerez A, Maciejewski J, Costa D, Nomdedeu M, Diez-Campelo M, Lumbreras E, González-

Martínez T, Marugán I, Such E, Cervera J, Cigudosa JC, Alvarez S, Florensa L, Hernández JM, Solé F. **Response to lenalidomide in myelodysplastic syndromes with del(5q): influence of cytogenetics and mutations.** *Brit J Haematol* 162(1):74-86 I.F.: 4.942

37. Petrucci MT, Giraldo P, Corradini P, Teixeira A, Dimopoulos MA, Blau IW, Drach J, Angermund R, Allietta N, Broer E, Mitchell V, Bladé J. **A prospective, international phase 2 study of bortezomib retreatment in patients with relapsed multiple myeloma.** *Brit J Haematol* 160(5):649-659 I.F.: 4.942

38. Puiggros A, Delgado J, Rodriguez-Vicente A, Collado R, Aventín A, Luño E, Grau J, Hernandez JÁ, Marugán I, Ardanaz M, González T, Valiente A, Osma M, Calasanz MJ, Sanzo C, Carrió A, Ortega M, Santacruz R, Abrisqueta P, Abella E, Bosch F, Carbonell F, Solé F, Hernández JM, Espinet B; Grupo Cooperativo Español de Citogenética Hematológica (GCECGH) and Grupo Español de Leucemia Linfática Crónica (GELLC). **Biallelic losses of 13q do not confer a poorer outcome in chronic lymphocytic leukaemia: analysis of 627 patients with isolated 13q deletion.** *Brit J Haematol* 163(1):47-54 I.F.: 4.942

39. Sarasquete ME, Martínez-López J, Chillón MC, Alcoceba M, Corchete LA, Paiva B,Puig N, Sebastián E, Jiménez C, Mateos MV, Oriol A, Rosiñol L, Palomera L, Teruel AI, González Y, Lahuerta JJ, Bladé J, Gutiérrez NC, Fernández-Redondo E, González M, San Miguel JF, García-Sanz R. **Evaluating gene expression profiling by quantitative polymerase chain reaction to develop a clinically feasible test for outcome prediction in multiple myeloma.** *Brit J Haematol* 163(2):223-234 I.F.: 4.942

40. Susini MC, Guglielmelli P, Spolverini A, Biamonte F, Mannarelli C, Barosi G, Zoi K, Reiter A, Duncombe A, Cervantes F, Cazzola M, Cross N. The ERCC2 Gln/**Gln polymorphism at codon 751 isnot associated with leukaemic transformation in primary myelofibrosis.** *Brit J Haematol* 162(3):424-427 I.F.: 4.942

41. Martinez D, Valera A, Perez NS, Sua Villegas LF, Gonzalez-Farre B, Sole C, Gine E, López-Guillermo A, Roue G, Martinez S, Sant F, Warzocha K, Robak T,Czader M, Villamor N, Colomo L, Campo E, Martinez A. **Plasmablastic transformation of low-grade B-cell lymphomas: report on 6 cases.** *Am J Surg Pathol* 37(2):272-281. I.F.: 2.881

42. Blanes M,Lahuerta JJ,González JD,Ribas P,Solano C,Alegre A,Bladé J,San Miguel JF,Sanz MA,de la Rubia J. **Intravenous busulfan and melphalan as a conditioning regimen for autologous stem cell transplantation in patients with newly diagnosed multiple myeloma: a matched comparison to a melphalan-only approach.** *Biol Blood Marrow Transplant* 19(1):69-74 I.F.: 3.940

43. Gifre L, Ruiz-Gaspà S, Monegal A, Nomdedeu B, Filella X, Guañabens N, Peris P. **Effect of glucocorticoid treatment on Wnt signalling antagonists (sclerostin and Dkk-1) and their relationship with bone turnover.** *Bone* 57(1):272-276 I.F.: 3.823

44. Navarro A, Muñoz C, Gaya A, Díaz-Beyá M, Gel B, Tejero R, Díaz T, Martinez A, Monzó M. **MiR-SNPs as markers of toxicity and clinical outcome in hodgkin lymphoma patients.** *PLoS One* 8(5): e64716 I.F.: 3.730

45. Costa D, Muñoz C, Carrió A, Nomdedeu M, Calvo X, Solé F, Luño E, Cervera J, Vallespí T, Berneaga D, Gómez C, Arias A, Such E, Sanz G, Grau J, Insunza A, Calasanz MJ, Ardañaz MT, Hernández JM, Azaceta G, Álvarez S, Sánchez J, Martín ML, Bargay J, Gómez V, Cervero CJ, Allegue MJ, Collado R, Campo E, Nomdedeu B; Spanish Group of Myelodysplastic Syndromes (GESMD). **Reciprocal translocations in myelodysplastic syndromes and chronic myelomonocytic leukemias: review of 5,654 patients with an evaluable karyotype.** *Gene Chromosome Canc* 52(8):753-763 I.F.: 3.546

46. López C, Delgado J, Costa D, Villamor N, Navarro A, Cazorla M, Gómez C, Arias A, Muñoz C, Cabezas S, Baumann T, Rozman M, Aymerich M, Colomer D, Pereira A, Cobo F, López-Guillermo A, Campo E, Carrió A. **Clonal evolution in chronic lymphocytic leukemia: Analysis of correlations with IGHV mutational status, NOTCH1 mutations and clinical significance.** Gene Chromosome Canc 52(10):920-927 I.F.: 3.546

47. Sanz C, Nomdedeu M, Belkaid M, Martinez I, Nomdedeu B, Pereira A. **Red blood cell alloimmunization in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukemia.** *Transfusion* 53(4):710-715. I.F.: 3.217

48. Hernández-Boluda JC, Pereira A, Cervantes F, Gómez M, Arellano-Rodrigo E, Alvarez-Larrán A, Ferrer-Marín F, Kerguelen A, Márquez JA, Antelo ML, Besses C; on behalf of the Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas (GEMFIN). **Clinical evaluation of the European LeukemiaNet response criteria in patients with essential thrombocythemia treated with anagrelide.** *Ann Hematol* 92(6):771-775 IF 2.342

49. Fernández de Larrea C, Martín-Antonio B, Cibeira MT, Navarro A, Tovar N, Díaz T, Rosiñol L, Monzó M, Urbano-Ispizua A, Bladé J. **Impact of global and gene-specific DNA methylation pattern in relapsed multiple myeloma patients treated with bortezomib**. *Leukemia Res* 37(6):641-646 I.F.: 2.764

50. Sánchez-Castro J, Marco-Betés V, Gómez-Arbonés X, Arenillas L, Valcarcel D,Vallespí T, Costa D, Nomdedeu B, Jimenez MJ, Granada I, Grau J, Ardanaz MT, de la Serna J, Carbonell F, Cervera J, Sierra A, Luño E, Cervero CJ, Falantes J,Calasanz MJ, González-Porrás JR, Bailén A, Amigo ML, Sanz G, Solé F. **Characterization and prognostic implication of 17 chromosome abnormalities in myelodysplastic syndrome.** *Leukemia Res* 37(7):769-776. IF:2.764

51. Hoyos M, Nomdedeu JF, Esteve J, Duarte R, Ribera JM, Llorente A, Escoda L, Bueno J, Tormo M, Gallardo D, de Llano MP, Martí JM, Aventín A, Mangues R, Brunet S, Sierra J. **Core binding factor acute myeloid leukemia: The impact of age, leukocyte count, molecular findings, and minimal residual disease.** *Eur J Haematol* 91(3):209-218 I.F.: 2.548.

52. Ferrer G, Navarro A, Hodgson K, Aymerich M, Pereira A, Baumann T, Monzo M, Moreno C, Montserrat E. **MicroRNA expression in chronic lymphocytic leukemia developing autoimmune hemolytic anemia.** *Leuk Lymphoma* 54(9):2016-2022 I.F.: 2.301

53. Magnano L, Fernández de Larrea C, Cibeira MT, Rozman M, Tovar N, Rovira M, Rosiñol L, Bladé J. **Acquired Fanconi Syndrome Secondary to Monoclonal Gammopathies: A Case Series Froma Single Center.** *Clin Lymph Myelom Leuk* 13(5):614-618 IF: 1.667

54. Costa D, Vidal A, Carrió A, Muñoz C, Arias A, Gómez C, Berneaga D, Colomer D, Rozman M, Pratcorona M, Torrebadell M, Díaz-Beyá M, Esteve J, Campo E. **Refining the Diagnosis and Prognostic Categorization of Acute Myeloid Leukemia Patients with an Integrated Use of Cytogenetic and Molecular Studies**. *Acta Haematol* 129(2):65-71 I.F.: 0.894

Reviews / I.F.: 28.837

1. Burger JA, Montserrat E. **Coming full circle: 70 years of chronic lymphocytic leukemia cell redistribution, from glucocorticoids to inhibitors of B cell receptor signaling.** *Blood* 121 (9)1501-1509. I.F.: 9.060

2. Kantarjian H Cervantes F, et al. **The price of drugs for chronic myeloid leukemia (CML): Reflection of the unsustainable cancer drug prices. Perspective of CML experts.** *Blood* 121(22):4439-4442 I.F.: 9.060

3. Villamor N, López-Guillermo A, López-Otín C, Campo E. **Next-generation sequencing in chronic lymphocytic leukemia.** *Semin Hematol* 50(4):286-295 I.F.: 3.357

4. Cervantes F, Martinez-Trillos A. **Myelofibrosis: an update on current pharmacotherapy and future directions.** *Expert Opin Pharmacother* 14(7):873-884. I.F.: 2.860

5. Alvarez-Larrán A, Cervantes F, Besses C. **Treatment of essential thrombocythemia.** *Med Clin* (Barc) 141(6):260-4

6. Martínez-Trillos A, Quesada V, Villamor N, Puente XS, López-Otín C, Campo E. **Recurrent gene mutations in CLL.** *Adv Exp Med Biol* 792:87-107 I.F.: 1.825

7. Ramsay AJ, Martínez-Trillos A, Jares P, Rodríguez D, Kwarciak A, Quesada V. **Next-generation sequencing reveals the secrets of the chronic lymphocytic leukemia genome.** *Clin Transl Oncol* 15(1):3-8 I.F.: 1.276

Clinical Guidelines / I.F.: 47.594

1. Fernández de Larrea C, Kyle RA, Durie BG, Ludwig H, Usmani S, Vesole DH, Hajek R, San Miguel JF, Sezer O, Sonneveld P, Kumar SK, Mahindra A, Comenzo R, Palumbo A, Mazumber A, Anderson KC, Richardson PG, Badros AZ, Caers J, Cavo M, LeLeu X,Dimopoulos MA, Chim CS, Schots R, Noeul A, Fantl D, Mellqvist UH, Landgren O,Chanan-Khan A, Moreau P, Fonseca R, Merlini G, Lahuerta JJ, Bladé J, Orlowski RZ,Shah JJ; International Myeloma Working Group. **Plasma cell leukemia: consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group.** *Leukemia* 27(4):780-791 I.F.: 10.164

2. Baccarani M, Deininger MW, Rosti G, Hochhaus A, Soverini S, Apperley JF, Cervantes F, Clark RE, Cortes JE, Guilhot F, Hjorth-Hansen H, Hughes TP, Kantarjian HM, Kim DW, Larson RA, Lipton JH, Mahon FX, Martinelli G, Mayer J, Müller MC, Niederwieser D, Pane F, Radich JP, Rousselot P, Saglio G, Saußele S, Schiffer C, Silver R, Simonsson B, Steegmann JL, Goldman JM, Hehlmann R. **European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013.** *Blood* 122(6):872-884 I.F.: 7.837

3. Barosi G, Mesa RA, Finazzi G, Harrison C, Kiladjian JJ, Lengfelder E, Mc Mullin MF, Passamonti F, Vannucchi AM, Besses C, Gisslinger H, Samuelsson J, Verstovsek S, Hoffman R, Pardanani A, Cervantes F, Tefferi A, Barbui T. **Revised response criteria for polycythemia vera and essential thrombocythemia: a ELN and IWG-MRT consensus project.** *Blood* 121(23):4778-4781 I.F.: 9.060

4. Tefferi A, Cervantes F, Mesa RA, Passamonti F, Verstovsek S, Vannucchi AM, Gotlib J, Dupriez B, Pardanani AD, Harrison CN Hoffman R, Gisslinger H, Kroeger N, Thiele J, Barbui T, Barosi G. **Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) & European LeukemiaNet (ELN) consensus report.** *Blood* 122(8):1395-1398 I.F.: 9.060

5. Ghielmini M, Vitolo U, Kimby E, Montoto S, Walewski J, Pfreundschuh M, Federico M, Hoskin P, McNamara C, Caligaris-Cappio F, Stilgenbauer S, Marcus R, Trneny M, Dreger P, Montserrat E, Dreyling M; On behalf of the Panel Members of the 1st ESMO. **Consensus Conference on Malignant Lymphoma. ESMO Guidelines consensus conference on malignant lymphoma 2011 part 1: diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL).** *Ann Oncol* 24(3): 561-576 I.F.: 7.384

6. Caballero D, Campo E, López-Guillermo A, Martín A, Arranz-Sáez R, Giné E,López A, González-Barca E, Canales MA, González-Díaz M, Orfao A. **Clinical practice**

guidelines for diagnosis, treatment, and follow-up of patients with mantle cell lymphoma. Recommendations from the GEL/TAMO Spanish Cooperative Group. *Ann Hematol* 92(9):1151-1179. I.F.: 2.866

Multicenter / I.F.: 4.095

1. Bosly A, Grigg A, Holte H, Gisselbrecht C, Radford J, Rossi A, López-Guillermo A, Trneny M, Sebban C, Hagberg H, Leal da Costa F, Colombat P, Bron D, Coiffier B. **A randomized study of interferon α-2b versus no treatment as consolidation after high dose therapy and autologous stem cell transplantation for patients with relapsed lymphoma.** *Oncologist* 18(11):1189 I.F.: 4.095

GRANTS FOR RESEARCH IN PROGRESS

Blade J. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0046.
Duration: 01/01/2013-31/12/2016

Blade J. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0005.
Duration: 01/01/2007-31/03/2014

Cervantes F. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0010.
Duration: 01/01/2013-31/12/2016

Cervantes F. **Red Temática de Investigación Cooperativa en Cáncer**. Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0004.
Duration: 01/01/2007-31/12/2014

Cibeira MT. **Afección cardíaca en la amiloidosis primaria: estudio de biomarcadores séricos, resonancia magnética 3-Tesla y caracterización genómica de las cadenas ligeras amiloidogénicas.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01290-
Duration: 01/01/2013-31/12/2015

Cervantes F. **Estudio de la relación del haplotipo 46/1 del gen JAK2 y el estado mutacional y la carga alélica de los genes JAK2 y MPL con las características iniciales, el patrón evolutivo y el pronóstico de los pacientes con mielofibrosis.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/00236.
Duration: 01/01/2011-31/12/2014

Lopez A. **Estudio de las alteraciones de la vía inflamatoria de "toll-like receptors" (TLR-MYD88-NFkB). Significado biológico y clínica en el linfoma difuso de células grandes B.** Sponsored by Instituto de Salud Carlos III (ISCIII). PI12/01536.
Duration: 01/01/2013-31/12/2015

Lopez A. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0023.
Duration: 01/01/2013-31/12/2016

Lopez A. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0051.
Duration: 01/01/2007-30/06/2014

Montserrat E. **Grup de Recerca Consolidat: Unitat Clinico-Biologica per a l'estudi de limfomes i sindromes limproliferatives.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 2009_SGR_1008.
Duration: 23/09/2009-31/12/2013.

Rosiñol L. **Afección medular versus extramedular en el mieloma múltiple: estudio del perfil genético y de la expresión de citocinas/quemocinas relacionadas con angiogénesis y microambiente medular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01093.
Duration: 01/01/2013-31/12/2015

DOCTORAL THESES

Esteve J. **Caracterización clínica y factores pronósticos en subgrupos de pacientes pediátricos con leucemia linfoblástica aguda de alto riesgo de recaída.**
PhD student: Susana Rives Solá.

5.9 Physiopathology and molecular bases in hematology

LOCATION
CEK building

KEYWORDS
1. **Lymphoid malignancies**
2. **Targeted therapies**
3. **Clinico-biological studies**
4. **Rare anemias**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	142.13	20	12	6
2012	178.17	21	16	3
2013	175.04	23	17	1

TEAM INVOLVED IN
RTICC

TEAM LEADER
Dolors Colomer (HCB)
T. 93 227 55 72
dcolomer@clinic.cat

RESEARCHERS
Josep Lluís Aguilar (HCB)
Marta Aymerich (HCB)
Teresa Estrach (HCB)
Patricia Pérez Galán (IDIBAPS)
Gael Roue (IDIBAPS)
Maria Rozman (HCB)
Neus Villamor (HCB)
Joan Lluís Vives Corrons (HCB)

POST-DOCTORAL RESEARCHERS
Maria del Mar Mañu (IDIBAPS)
Mónica Lopez-Guerra (FCRB)
Silvia Xargay-Torrent (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Eriong Lee (FCRB)
Esther Llaudet (IDIBAPS)
Alba Matas (IDIBAPS)
Arnau Montraveta (FCRB)
Alexandra Moros (IDIBAPS)
Laura Olaya (IDIBAPS)
Laia Rosich (IDIBAPS)
Anna Vidal (IDIBAPS)

TECHNICIANS
Jessica Abad (IDIBAPS)
Sandra Cabezas (FCRB)
Laura Jiménez (FCRB)
Jocabed Roldan (IDIBAPS)
Vanina Rodriguez (IDIBAPS)

STRATEGIC OBJECTIVES

- Identification of potential points of intervention and development of new therapeutic strategies and combination approaches based on the genetic and molecular mechanisms implicated in the development and progression of lymphoid malignancies, with the idea to translate bench-to-bedside. Our aim is to perform a personalized therapy based on the optimization of treatment for

each patient, improving the benefits and avoiding the negative side effects.

- To improve the diagnosis of lymphoid malignancies using histopathological, immunophenotypic and molecular biology technologies.

- To increase the efficacy of diagnosis, treatment and follow up of patients with rare anemias to improve their quality of life.

MAIN LINES OF RESEARCH

1. To analyze the functionality and the therapeutic applicability of target drugs against recurrent alterations in chornic lymphocytic leukemia (CLL), when specific inhibitors are available

2. Characterization of molecular pathways activated by microenvironment in follicular lymphoma (FL) and mantle cell lymphoma (MCL) and CLL as a discovery tool of new therapeutic targets and resistance to treatments.

3. New targeted therapies against oncogenes and microenvironment in diffuse large B cell lymphomas (DLBCL)

4. Cytological, immunophenotypic and molecular study of malignant hematological diseases. Development of new technologies for the diagnosis and follow-up of minimum residual disease (MRD).

5. Promotion of cooperative strategies in the molecular diagnostic setting of leukemias and lymphomas.

6. Design and implementation of internal and external quality control programs.

7. Cutaneous T and B cell lymphomas. Clinical, histopathological and immunophenotypic study. Prognostic factors and epidemiology.

8. Molecular study of the congenital defects of erythrocytes and erythropoiesis, rare anaemias, and physiopathological mechanisms intervening in the production and senescence of red blood cells as a cause of anemia or erythrocytosis.

9. Genetic and epidemiological study of hemoglobinopathies,and thalassemias. Development of technologies for the newborn screening of sickle-cell disease (SCD)

PUBLICATIONS

Originals / I.F.: 175.035

1. Ramsay AJ, Quesada V, Foronda M, Conde L, Martínez-Trillos A, Villamor N, Rodríguez D, Kwarciak A, Garabaya C, Gallardo M, López-Guerra M, López-Guillermo A, Puente XS, Blasco MA, Campo E, López-Otín C. **POT1 mutations cause telomere dysfunction in chronic lymphocytic leukaemia.** *Nat Genet* 45(5):526-530 I.F.: 35.209

2. Rosich L, Colomer D, Roue G. **Autophagy controls everolimus (RAD001) activity in mantle cell lymphoma.** *Autophagy* 9(1):115-7 I.F.: 12.042

3. Díaz-Beyá M, Navarro A, Ferrer G, Díaz T, Gel B, Camós M, Pratcorona M, Torrebadell M, Rozman M, Colomer D, Monzo M, Esteve J. **Acute myeloid leukemia with translocation (8;16)(p11;p13) and MYST3-CREBBP rearrangement harbors a distinctive microRNA signature targeting RET proto-oncogene.** *Leukemia* 27(3):595-603 I.F.: 10.164

4. Herman SE, Sun X, McAuley EM, Hsieh MM, Pittaluga S, Raffeld M, Liu D, Keyvanfar K, Chapman CM, Chen J, Buggy JJ, Aue G, Tisdale JF, Pérez-Galán P,* Wiestner A.* **Modeling tumor-host interactions of chronic lymphocytic leukemia in xenografted mice to study tumor biology and evaluate targeted therapy.** *Leukemia* 27(12):2311-2321 I.F.: 10.164

5. Rawstron AC, Bottcher S, Letestu R, Villamor N, Fazi C, Kartsios H, de Tute RM, Shingles J, Ritgen M, Moreno C, Lin K, Pettitt AR, Kneba M, Montserrat E, Cymbalista F, Hallek M, Hillmen P, Ghia P. **Improving efficiency and sensitivity: European Research Initiative in CLL (ERIC) update on the international harmonised approach for flow cytometric residual disease monitoring in CLL.** *Leukemia* 27:142-149 I.F.: 10.164

6. Villamor N, Conde L, Martínez-Trillos A, Cazorla M, Navarro A, Beà S, López C, Colomer D, Pinyol M, Aymerich M, Rozman M, Abrisqueta P, Baumann T, Delgado J, Giné E, González-Díaz M, Hernández JM, Colado E, Payer AR, Rayon C, Navarro B, José Terol M, Bosch F, Quesada V, Puente XS, López-Otín C, Jares P, Pereira A, Campo E, López-Guillermo A. **NOTCH1 mutations identify a genetic subgroup ofchronic lymphocytic leukemia patients with high risk of transformation and poor outcome.** *Leukemia* 27(5):1100-1106 I.F.: 10.164

7. Beà S, Valdés-Mas R, Navarro A, Salaverria I, Martín-Garcia D, Jares P, Giné E, Pinyol M, Royo C, Nadeu F, Conde L, Juan M, Clot G, Vizán P, Di Croce L, Puente DA, López-Guerra M, Moros A, Roue G, Aymerich M, Villamor N, Colomo L, Martínez A, Valera A, Martín-Subero JI, Amador V, Hernández L, Rozman M, Enjuanes A, Forcada P, Muntañola A, Hartmann EM, Calasanz MJ, Rosenwald A, Ott G, Hernández-Rivas JM, Klapper W, Siebert R, Wiestner A, Wilson WH, Colomer D, López-Guillermo A, López-Otín C, Puente XS, Campo E. **Landscape of somatic mutations and clonal evolution in mantle cell lymphoma.** *Proc Natl Acad Sci U S A.* 110(45):18250-18255 I.F.: 9.737

8. Abrisqueta P, Villamor N, Terol MJ, Gonzalez-Barca E, Gonzalez M, Ferra C, Abella E, Delgado J, Garcia-Marco JA, Gonzalez Y, Carbonell F, Ferrer S, Monzo E, Jarque I, Muntanola A, Constants M, Escoda L, Calvo X, Bobillo S, Montoro JB, Montserrat E, Bosch F. **Rituximab maintenance after first-line therapy with rituximab, fludarabine, cyclophosphamide, and mitoxantrone (R-FCM) for chronic lymphocytic leukemia.** *Blood* 122:3951-3959 I.F.: 9.060

9. Pratcorona M, Brunet S, Nomdedéu J, Ribera JM, Tormo M, Duarte R, Escoda L, Guàrdia R, Queipo de Llano MP, Salamero O, Bargay J, Pedro C, Martí JM, Torrebadell M, Díaz-Beyá M, Camós M, Colomer D, Hoyos M, Sierra J, Esteve J; Grupo Cooperativo Para el Estudio y Tratamiento de las Leucemias Agudas Mieloblásticas. **Favorable outcome of patients with acute myeloid leukemia harboring a low-allelic burden FLT3-ITD mutation and concomitant NPM1 mutation: relevance to post-remission therapy.** *Blood* 121:2734-2738 I.F.: 9.060

10. Vegliante MC, Palomero J, Pérez-Galán P, Roué G, Castellano G, Navarro A, Clot G, Moros A, Suárez-Cisneros H, Beà S, Hernández L, Enjuanes A, Jares P, Villamor N, Colomer D, Martín-Subero JI, Campo E, Amador V. **SOX11 regulates PAX5expression and blocks terminal B-cell differentiation in aggressive mantle celllymphoma.** *Blood* 121(12):2175-8215 I.F.: 9.060

11. Xargay-Torrent S, López-Guerra M, Montraveta A, Saborit-Villarroya I, Rosich L, Navarro A, Pérez-Galán P, Roué G, Campo E, Colomer D. **Sorafenib Inhibits Cell Migration and Stroma-Mediated Bortezomib Resistance by Interfering B-cell Receptor Signaling and Protein Translation in Mantle Cell Lymphoma.** *Clin Cancer Res* 19(3):586-597 I.F.: 7.837

12. White HE, Hedges J, Bendit I, Branford S, Colomer D, Hochhaus A, Hughes T, Kamel-Reid S, Kim DW, Modur V, Müller MC, Pagnano KB, Pane F, Radich J, Cross NC, Labourier E. **Establishment and validation of analytical reference panels for the standardization of quantitative BCR-ABL1 measurements on the international scale.** *Clin Chem* 59:938-948 I.F.: 7.149

13. Fraile JM, Ordóñez GR, Quirós PM, Astudillo A, Galván JA, Colomer D, López-Otín C, Freije JM, Puente XS. **Identification of novel tumor suppressor proteases by degradome profiling of colorectal carcinomas.** *Oncotarget* 4:1919-1932 I.F.: 6.636

14. Rosich L, Saborit-Villarroya I, López-Guerra M, Xargay-Torrent S, Montraveta A, Aymerich M, Villamor N, Campo E, Pérez-Galán P, Roué G, Colomer D. **The phosphatidylinositol-3-kinase inhibitor NVP-BKM120 overcomes resistance signals derived from microenvironment by regulating the Akt/FoxO3a/Bim axis in chronic lymphocytic leukemia cells.** *Haematologica* 98(11):1739-1747 I.F.: 5.935

15. Servitje O, Muniesa C, Monsalvez V, Garcia-Muret P, Gallardo F, Domingo E, Lucas A, Benavente Y, Climent F, Rodriguez-Peralto JL, Ortiz-Romero PL, Pujol RM, Estrach T. **Primary Cutaneous Marginal Zone B-cell Lymphoma: Response to Treatment and Disease Free Survival in a series of 137 patients.** *J Am Acad Dermato.* 69:357-365 I.F.: 4.906

16. Martinez D, Valera A, Perez NS, Sua Villegas LF, Gonzalez-Farre B, Sole C, Gine E, Lopez-Guillermo A, Roue G, Martinez S, Sant F, Warzocha K, Robak T, Czader M, Villamor N, Colomo L, Campo E, Martinez A. **Plasmablastic Transformation of Low-grade B-cell Lymphomas: Report on 6 Cases.** *Am J Surg Pathol* 37(2):272-281 I.F.: 4.868

17. López C, Delgado J, Costa D, Villamor N, Navarro A, Cazorla M, Gómez C, Arias A, Muñoz C, Cabezas S, Baumann T, Rozman M, Aymerich M, Colomer D, Pereira A, Cobo F, López-Guillermo A, Campo E, Carrió A. **Clonal evolution in chronic lymphocytic leukemia: Analysis of correlations with IGHV mutational status, NOTCH1 mutations and clinical significance.** *Genes Chromosomes Cancer* 52(10):920-927 I.F.: 3.546

18. Ferrer G, Navarro A, Hodgson K, Aymerich M, Pereira A, Baumann T, Monzo M, Moreno C, Montserrat E. **MicroRNA expression in chronic lymphocytic leukemia developing autoimmune hemolytic anemia.** *Leukemia Lymphoma* 54:2016-2022 I.F.: 2.301

19. Angastiniotis M, Vives Corrons JL, Soteriades ES, Eleftheriou A. **The impact of migrations on the health services for rare diseases in Europe: the example of haemoglobin disorders.** *Sci World J* 2013:727905 I.F.: 1.730

20. Magnano L, Fernández de Larrea C, Cibeira MT, Rozman M, Tovar N, Rovira M, Rosiñol L, Bladé J. **Acquired Fanconi Syndrome Secondary to Monoclonal Gammopathies: A Case Series From a Single Center.** *Cl Lymph Myelom Leuk* 13(5):614-618 I.F.: 1.667

21. Reis-Sobreiro M, Roué G, Moros A, Gajate C, de la Iglesia-Vicente J, Colomer D, Mollinedo F. **Lipid raft-mediated Akt signaling as a therapeutic target in mantle cell lymphoma.** *Blood Cancer J* 3:e118 I.F.: 1.400

22. Fuertes I, Mascaró JM Jr, Martínez A, García-Herrera A, Estrach T. **Primary cutaneous anaplastic large cell lymphoma simulating an aggressive angiocentric T-cell lymphoma.** *Int J Dermatol* 52:1241-4 I.F.:1.342

23. Costa D, Vidal A, Carrió A, Muñoz C, Arias A, Gómez C, Berneaga D, Colomer D, Rozman M, Pratcorona M, Torrebadell M, Díaz-Beyá M, Esteve J, Campo E. **Refining the Diagnosis and Prognostic Categorization of Acute Myeloid Leukemia Patients with an Integrated Use of Cytogenetic and Molecular Studies.** *Acta Haematol* 129(2):65-71 I.F.: 0.894

Reviews / I.F.: 8.493

1. Villamor N, López-Guillermo A, López-Otín C, Campo E. **Next-generation sequencing in chronic lymphocytic leukemia.** *Semin Hematol* 50(4):286-295 I.F.: 3.357

2. Xolalpa W, Perez-Galan P, Rodríguez MS, Roué G. **Targeting the ubiquitin proteasome system: beyond proteasome inhibition.** *Curr Pharm Des* 19(22):4053-4093 I.F.: 3-311

3. Martínez-Trillos A, Quesada V, Villamor N, Puente XS, López-Otín C, Campo E. **Recurrent Gene Mutations in CLL.** *Adv Exp Med Biol* 792:87-107 I.F.: 1.825

GRANTS FOR RESEARCH IN PROGRESS

Colomer D. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0004. Duration: 01/01/2013-31/12/2016

Colomer D. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0014. Duration: 01/01/2007-31/12/2013

Colomer D. **Identificación de nuevas estrategias terapéuticas a partir de las alteraciones genéticas derivadas de la secuenciación masiva de la leucemia linfática crónica.** Sponsored by: Ministerio de Economía y Competitividad. SAF2012-31242. Duration: 01/01/2013-31/12/2015

Colomer D. **Desarrollos farmacéuticos en cánceres hematológicos catalogados como enfermedades raras mediante aproximaciones basadas en apoptosis.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2012-0673-010000. Duration: 01/01/2013-31/12/2014

Colomer D. **Dianes terapeutiques i noves tecniques diagnostiques en neoplasies limfoides.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_967. Duration: 15/09/2009-30/04/2014

Colomer D. **Utilización de terapias selectivas contra rutas de señalización desreguladas en neoplasias linfoides. Mecanismos de acción y estrategias de sensibilización.** Sponsored by: Ministerio de Economía y Competitividad. SAF2009_09503. Duration: 01/01/2010-31/01/2013

Pérez-Galán P. **Interferencia en la interacción entre la célula tumoral y su microambiente: una nueva aproximación terapéutica en el tratamiento del linfoma folicular.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-29326. Duration: 01/01/2012-31/12/2014

Roue G. **Nuevas terapias dirigidas contra oncogenes y microambiente tumoral en linfomas agresivos de células B.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01847. Duration: 01/01/2013-31/12/2015

Vives-Corrons J.L. **An integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research.** Sponsored by:European Commission. 305444. Duration: 31/01/2013-30/01/2019

Vives-Corrons J.L. **Combined Molecular Microscopy for Therapy and Personalized Medication in Rare Anaemias Treatments.** Sponsored by:European Commission. 602121-1. Duration: 01/10/2013-30/09/2018

Vives-Corrons J.L. **Platform for sharing best practices for management of rare diseases.** Sponsored by:European Commission. 305690. Duration: 31/01/2013-30/01/2017

Vives-Corrons J.L. **New e-Health services for the european reference network on rare anaemias.** Sponsored by: European Commission. 295882. Duration: 01/09/2013-31/08/2016

Vives-Corrons J.L. **Déficit congénito de piruvato cinasa. Influencia del equilibrio entre eritropoyesis y apoptosis en la intensidad del síndrome hemolítico.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI10/01460 Duration: 01/01/2011-31/12/2014

Vives-Corrons J.L. **Creation of a catalan network for the diagnosis and clinical management of rare anemias due to major haemoglobinopathies.** Sponsored by: Fundació la Marató de TV3. 101730. Duration: 14/12/2010-13/06/2014

Vives-Corrons J.L. **European reference network of expert centres in rare anaemias.** Sponsored by: European Commission. 20081210. Duration: 01/06/2009-31/01/2014

DOCTORAL THESES

Colomer D, Carrio A. **Identificación, estratificación y adquisición de nuevas alteraciones citogenéticas en el curso evolutivo de la leucemia linfática crónica.** PhD student: Cristina López González.

Estrach T, Puig S. **Efectos de la radiación ultravioleta en lesiones melanocíticas. Implicaciones en diagnóstico precoz y prevención de melanoma.** PhD student: Cristina Carrera Álvarez

5.10 Hemotherapy - hemostasis

LOCATION
HCB building

KEYWORDS
1. **Immunotrombosis**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	94.11	22	9	10
2012	97.41	19	10	8
2013	67.07	20	7	10

TEAM INVOLVED IN
Red HERACLES

TEAM LEADER
Ginés Escolar (HCB)
T. 93 227 54 48
gescolar@clinic.cat

RESEARCHERS
Joan Cid Vidal (HCB)
Maribel Díaz-Ricart (HCB)
Ana M. Galán (IDIBAPS)
Pablo García de Frutos (CSIC)
Miquel Lozano (HCB)
Anna M. Merino (HCB)
Joan Monteagudo (HCB)
Antonio Ordinas (HCB)
Arturo Pereira (HCB)
Juan Carles Reverter (HCB)
Cristina Ch. Sanz (HCB)
M. Dolors Tàssies (HCB)

POST-DOCTORAL RESEARCHER
Cristina Aresté (CSIC)
Begoña Hurtado Villarejo (FCRB)
Irene López-Vilchez (IDIBAPS)

PRE-DOCTORAL RESEARCHERS
Susana Martín Rodríguez (FCRB)

TECHNICIANS
Anhara Menéndez (CSIC)
Patricia Molina Moreno (HCB)
Marc Pino (HCB)
Verónica Sanz (FCRB)

COLLABORATORS
Eduardo Arellano Rodrigo (HCB)
Rosa Brugués (HCB)
Gabriela Gutiérrez (HCB)
M. Rosa Hernández (FCRB)
Josep M. Jou (HCB)

STRATEGIC OBJECTIVES

1. Study of the basic mechanisms regulating blood cell function and of the interactions between such cells, with the vascular wall, and with other cells.
2. Evaluation of congenital and acquired defects in hemostasis and their pharmacological and/or transfusional correction.
3. Laboratory characterization of bleeding and thrombotic phenotypes and genotypes
4. Analysis of the efficacy and safety of new strategies for sparing blood component transfusions.
5. Characterization of animal models of hemostasis, preferentially in mice.

MAIN LINES OF RESEARCH

1. Study of the mechanisms involved in the development of bleeding and thrombotic disorders. Proteomic study for determining the changes in the vascular system and in the different blood cells in thrombotic and bleeding disorders.

2. Evaluation of the physiological and pathological implications of circulating and/or intraplatelet tissue factor in atherothrombosis.

3. Characterization of endothelial dysfunction as a common factor in the development of complications associated with multiple diseases. A physiological, biochemical and proteomic approach.

4. New strategies for the treatment of combined humoral immunity in therapeutic apheresis.

5. Evaluation of the participation of serotoninergic and purinergic mechanisms in platelet function. Study of the antithrombotic potential of pharmacological inhibitors.

6. Role of the phenotype/genotype of fibrinolysis and its repercussions upon global or specific functional tests in hemorrhagic and thrombotic pathology.

7. Study of the GAS6 vitamin K-dependent protein in hemostasis and the vascular wall, using knockout mice for this gene.

8. Evaluation of the potencial of clotting factor concentrates to reverse the anticoagulant action of the new oral antithrombotic agents

PUBLICATIONS

Originals / I.F.: 67.066

1. Olivar R, Luque A, Naranjo m, Quer J, Garcia de Frutos P, Borrás FE, Rodríguez de Córdoba S, Blom JM. **The minor isoform alpha7beta0 of the soluble complement inhibitor C4BP induces a semi-mature anti-inflammatory state in dendritic cells.** *J Immunol* 190:2857-2872 I.F.: 5.520

2. Alvarez-Larrán A, Pereira A, Arellano E, Hernández-Boluda JC, Cervantes F, Besses C. **Cytoreduction plus low-dose aspirin versus cytoreduction alone as primary prophylaxis of thrombosis in patients with high-risk essential thrombocythaemia: and observational study.** *Brit J Haematol* 161:865-871 I.F.: 4.942

3. Recarte P, Tàssies D, Espinosa G, Hurtado B, Sala N, Cervera R, Reverter JC, Garcia de Frutos P. **Vitamin K-dependent proteins GAS6 and protein S and TAM receptors in patients of systemic lupus erythematosus: correlation with common genetic variants and disease activity.** *Arthritis Res Ther* 15(2):R41 I.F.: 4.302

4. Gomez-Puerta JA, Perir P, Reverter JC, Espinosa G, Martínez-Ferrer A, Monegal A, Monteagudo J, Tàssies D, Guañabens N. **High prevalence of prothrombotic abnormalities in multifocal odteosintesis: description of a series and review of the literatura.** *Medicine* 92(6):295-304 I.F.: 4.233

5. Carmona A, Díaz-Ricart M, Palomo M, Molina P, Pino M, Rovira M, Escolar G, Carreras E. **Distinct deleterious effects of cyclosporine and tacrolimus and combined tracolimius-sirollimus on andothelial cells: propective effect of defibroide.** *Biol Blood Marrow Transplant.* 19(10):1439-45 I.F.: 3.759

6. Escolar G, Fernandez-Gallego V, Arellano-Rodrigo E, Roquer J, Reverter JC, Sanz VV, Molina P, Lopez-Vilchez I, Díaz-Ricart M, Galan AM. **Reversal of apixaban induced alterations in hemostasis by different coagulation factor concentrates: significance of studies in vitro with circulating human blood.** *PLoS One* 8(11):e78696 I.F.: 3.730

7. López C, Delgado J, Costa D, Villamor N, Navarro A, Cazorla M, Gómez C, Arias A, Muñoz C, Cabezas S, Bauman T, Rozman M, Aymerich M, Colomer D, Pereira A, Cobo F, López-Guillermo A, Campo E, Carrió A. **Clonal evolution in chronic lymphocytyc leukemia: analysis of correlations with IGHV mutational status, NOTCH1 mutations and clinical significance.** *Gene Chromosome Canc* 52(10):920-927 I.F.: 3.546

8. Pereira A. **Will clinical studies elucidate the connection between the length of storage of transfused red blood cells and clinical outcomes? An analysis based on the simulation of randomized controlled trials.** *Transfusion. Jan* 53(1):34-40. I.F.:3.526

9. Cid J, Caballo C, Pino M, Galán AM, Martínez N, Escolar G, Díaz-Ricart M. **Quantitative and qualitative analysis of coagulation factors in cryoprecipitate prepared from fresh-frozen plasma inactivated with amotosalen and ultraviolet A light.** *Transfusion* 53(3):600-605 I.F.: 3.526

10. Cid J, Elena M, Diekmann F, Lozano M. **Haptoglobin is present in albumin used as a replacement solution for plasma Exchange.** *Transfusion* 53(4):757-760 I.F.: 3.526

11. Sanz C, Nomdedeu M, Belkaid M, Martínez I, Nomdedeu B, Pereira A. **Red blood cell alloimmunization in tranfused patients with myelodysplastic síndrome or chronic myelomonocytic leukemia.** *Transfusion* 53(4): 710-715 I.F.: 3.526

12. Tajes M, ILL-Raga G, Palomer E, Ramos E, Guix F, Bosch M, Guivernau B, Jiménez-Conde J, Ois A, Pérez-Asensio F, Reyes-Navarro M, Caballo C, Galán AM, Alameda F, Escolar , Opazo C, Planas A, Roquer J, Valverde MA, Muñoz FJ. **Nitro-oxidative stress after neuronal ischemia induces protein nitrotyrosination and cell death.** *Oxid Med Cell Longev* 2013:826143 I.F.: 3.393

13. González-Juanatey JR, Lobos JM, Reverter JC, Becerra V; en representación de todos los autores del artículo. **Self-management of vitamin K antagonists**

is more cost-effective tan Dabigatran for stroke prevention in non-valvular atrial fibrillation in Spain. *Rev Esp Cardiol* 66(6):511 I.F.: 3.204

14. Blasi A, Caballo C, Galán AM, Taura P, Beltrán J, Escolar G, Lozano M. **The addition of MESNA in vitro prolongs prothrombin time similar to N-acetyl cysteine.** *Clin Chem Lab Med* 51(12):e297-299 I.F.: 3.009

15. Hernández-Boluda JC, Pereira A, Cervantes F, Gómez M, Arellano E, Alvarez-Larrán A, Ferrer F, Kerguelen A, Márquez, Antelo ML, Besses C on behalf of the Grupo Español de Enfermedades Mieloproliferativas Filadelfia Negativas (GEMFIN). **Clinical evaluation of the european leukemiaNet response criteria in patients with essential thrombocythemia treated with anagrelide.** *Ann Hematol* 92:771-775 I.F.: 2.866

16. Berman H, Ugarte-Gil MF, Espinosa G, Tàssies D, Monteagudo J, Reverter JC, Cervera R. **Can inherited thrombophilia modulate the clinical phenotype of patients with antiphospholipid syndrome?** *Clin Exp Rheumatol* 31(6):926-932 I.F.: 2.655

17. Ferrer G, Navarro A, Hodgson K, Aymerich M, Pereira A, Baumann T, Monzo M, Moreno C, Montserrat E. **MicroRNA expression in chronic lymphocytic leukemia developing autoimmune hemolytic anemia.** *Leukemia Lymphoma* 54(9):2016-2022 I.F.: 2.301

18. Saibeni S, Etcheverts MJ, Tàssies D, Panés J, Reverter JC, Danese S, Piqué JM, Bruno S, Vecchi M, GAsbarrini A, Sanz M. **Assesment of anti-prothrombin antibodies in thrombosis complicating inflammatory bowel diseases.** *Int J Colorectal* 28(9):1281-1286 I.F.: 2.238

19. Caballo C, Escolar G, Díaz-Ricart M, López-ílchez I, Lozano M, Cid J, Pino M, Beltrán J, Basora M, Pereira A, Galan AM. **Impact of experimental haemodilution on platelet function, thrombin generation and clot firmness: effects of different coagulation factor concentrates.** *Blood Transfus* 11(3):391-399 I.F.: 1.858

20. Lozano M, Cid J, Areal C, Romon I, Moncunill J Spanish Apheresis Group. **Apheresis activity in Spain: a survey of the Spanish Apheresis Group.** *Transfus Apher Sci* 49(3):560-564 I.F.: 1.225

Reviews / I.F.: 13.487

1. Lozano M, Cid J. **Pathogen inactivation: coming of age.** *Curr Opin Hematol* 20(6):540-545 I.F.: 4.111

2. Lozano M, Cid J, Müller TH. **Plasma treated with methylene blue and light: clinical efficacy and safety profile.** *Transfus Med Rev* 27(4):235-240 I.F.: 3.759

3. Rovira J, Cid J, Gutiérrez-García G, Pereira A, Fernández-Avilés F, Rosiñol L, Martínez C, Carreras E, Urbano A, Rovira M, Lozano M. **Fatal immune hemolytic anemia following allogeneic stem cell transplantation: report of 2 cases and review of literatura.** *Transfus Med Rev* 27(3):166-170 I.F.: 3.759

4. Pujadas-Mestres L, Escolar G, Arellano E, Galán AM, **Apixaban in the prevention of stroke and systemic embolism in nonvalvular atrial fibrillation.** *Drug Today* 49(7):425-436 I.F.: 1.215

5. Lozano M, Cid J. **Analysis of reasons for not implementing pathogen inactivation for platelet concentrates.** *Transfus Clin Biol* 20(2):158-164 I.F.: 0.643

Multicenter/ I.F.: 3.526

1. Estcourt LJ, Heddle N, Kaufman R, McCullough J, Murphy MF, Slichter S, Wood EM, Stanworth SJ; Biomedical Excellence for Safer Transfusion Collaborative. **The challenges of measuring bleeding outcomes in clinical trials of platelet transfusions.** *Transfusion. Jul*;53(7):1531-43. I.F.: 3.526

GRANTS FOR RESEARCH IN PROGRESS

Diaz-Ricart M. **Receptores toll-like, inflamasoma NALP3 e inestabilidad epigenética en el desarrollo de disfunción endotelial en la uremia.** Sponsored by: Ministerio de Economía y Competitividad. SAF2011-28214. Duration: 01/01/2012-31/12/2014

Escolar G. **Red Cardiovascular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0042/0016. Duration: 01/01/2013-31/12/2016

Escolar G. **Red HERACLES: Determinantes genéticos y ambientales de la disfunción vascular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0009/1003. Duration: 29/02/2008-31/12/2013

Galan A.M. **El sistema serotoninérgico: una concexión entre los mecanismos de la depresión mayor, la inflamación y el riesgo cardiovascular.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/0664. Duration: 01/01/2010-30/06/2013

Tassies D. **Fenotipo procoagulante y anticoagulante de las micropartículas circulantes en la patología trombótica arterial de las enfermedades autoinmunes.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/00977. Duration: 01/01/2012-31/12/2014

DOCTORAL THESES

Tàssies D. **Sordera súbita neurosensorial idiopática. Análisis de los factores de riesgo vascular clásicos y genéticos.** PhD student: Ferran Ballesteros Alonso.

5.11

Molecular and translational oncology

LOCATION
CEK building
CELLEX building

KEYWORDS
1. **Chemotherapy Resistance**
2. **Epigenetic Plasticity**
3. **Inflammation and Neuropeptides**
4. **Tumoral Microenvironment**
5. **Tumoral Heterogeneity**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	236.85	31	19	6
2012	114.67	18	16	2
2013	102.388	23	14	3

TEAM LEADER
Pere Gascón Vilaplana (HCB)
T. 93 227 54 02
gascon@clinic.cat

RESEARCHERS
Vanessa Almendro (IDIBAPS)
Juan José Grau (HCB)
Joan Maurel (HCB)
Begoña Mellado (HCB)
Montserrat Muñoz (HCB)
Cristina Nadal (HCB)
Noemí Reguart (HCB)
Núria Viñolas (HCB)

POST-DOCTORAL RESEARCHERS
Anna Vidal (FCRB)

TECHNICIANS
Estel Enreig (FCRB)
Natalia Jiménez (FCRB)
Anna Lopez (IDIBAPS)

NURSING STAFF
Àngels Olivera (HCB)

ADMINISTRATIVE STAFF
Marta Digón (HCB)

COLLABORATORS
Jordi Alcaraz (UB)
Elisabet Ametller (IDIBAPS)
Ana Arance (HCB)
Patricia Fernandez Nogueira (UB)
Gemma Fuster (FCRB)
Susana Garcia Recio (FCRB)
Xavier Gonzalez Farre (FCRB)
Mario Mancino (FCRB)
Mercedes Marin (FCRB)
Estela Pineda (HCB,)
Oscar Reig (HCB)
Laura Vidal (HCB)
Laura Visa (HCB)
Arantzazu Zubeldia (FCRB)

STRATEGIC OBJECTIVES

The strategic objectives of the laboratory are centered in three fields:

1. A purely scientific area corresponding to the consolidation of the investigational lines and groups that work in each of them.

2. A second area corresponding to the obtainment of aids and funding for research, in order to ensure the good functioning of the laboratory.
3. A third objective is to formalize and strengthen existing international partnerships with institutions from Boston, Manchester and Oslo.

The first of the mentioned areas (scientific) comprises a qualitative and quantitative increase in scientific production. In particular, the colorectal and breast cancer stem cell lines.

Both the subject and the quality of research can attract investigators interested in a stay, in preparing a doctoral thesis, or in becoming part of the laboratory personnel. In this sense in 2011 we have incorporated two new biologists into the group. As regards the second area (funding of research), we must continue with the same criterion established years ago in order to ensure the continuity of all the research lines and facilitate the recruitment/contracting of new personnel members. At present, the laboratory has one FISS grant (2012), one Networks funding from the Carlos III Institute, one grant from the Spanish Association Against Cancer (2009), and several research grants from the CELLEX Foundation.

MAIN LINES OF RESEARCH

1. Tumor chemoresistance mechanisms:

1.1 Resistance mechanisms in colorectal cancer linked to the extrinsic apoptotic pathway, in vitro and in vivo (Joan Maurel).
1.2 Mechanisms of epigenetic adaptation and cellular plasticity during the adquisition of chemoresistance (Vanessa Almendros, Elisabet Ametller).
1.3 Epithelial-mesenchymal transition and resistance to chemotherapy (Elisabet Ametller; Vanessa Almendro).
1.4 Resistance to antitumor drugs in head and neck cancer (Juan J. Grau).
1.5 Electrochemotherapy in solid tumors. Study of electroporation. (Juan J. Grau).
1.6 Implication of IGF-1R and MMP-7 in the mechanisms of resistance to chemotherapy and antibodies against tyrosine kinase receptors. Therapeutic strategies for the reversal of chemoresistance (Joan Maurel; Mercedes Marín).
1.7 Characterization of the role of MMP-7 in resistance to bevacizumab in colon cancer (Joan Maurel; Estela Pineda; Mercedes Marín; Cristobal Mezquita; Jovita Mezquita; Betlem Mezquita).
1.8 Platform in orthotopic murine platforms characterized by the study of new drugs in pancreatic cancer (Joan Maurel; Pere Gascón; Salvador Navarro; David Fuster; Rosa Miquel).
1.9 Mechanisms of tumor progression in breast cancer HER2+ induced by the adquisition of resistance to Trastuzumab and Lapatinib (Patricia Fernández, Vanessa Almendro).

2. Stem cells, microenvironment and mechanisms of metastasis.

2.1 Neural control of breast cancer progression (Vanessa Almendro, Mario Manzino, Elisabet Ametller, Pere Gascón).
2.2 Interaction between GPCRs and RTKs (Vanessa Almendro; Elisabet Ametller; Susana Garcia).
23 Role of the PPT-I gene in the metastatic process (Pere Gascón; Vanessa Almendro; Elisabet Ametller).
2.4 Pre-angiogenic micrometastases of circulating cells (Cristina Nadal).
2.5 Mechanisms of liver metastasis in colorectal cancer (Cristina Nadal).
2.6 Neuronal influence in breast cancer progession of the phenotypy of the tumoral stem cell (Gemma Fuster, Vanessa Almendro).

3. Pharmacodynamic studies and prediction of therapeutic response

3.1 Predictive and pharmacodynamic study of the response to neoadjuvant chemotherapy in prostate cancer. (Begoña Mellado).
3.2 Mechanisms and markers of chemoresistance in prostate cancer. Therapeutic strategies for the reversal of chemoresistance. (Begoña Mellado; Mercedes Marín).

4. Study on the determination and characterization of circulating tumor cells

4.1 In prostate cancer (Begoña Mellado).
4.2 Kidney cancer
4.3 In breast cancer (Montse Muñoz; Xavier González).

5. Micro-RNAs in the development and prognosis of non-small cell lung cancer. (Nuria Viñolas).

6. Study of the tumor and stroma interactions in non-small cell lung cancer (NSCLC): role of fibroblasts associated with cancer in NSCLC (N. Reguart; J. Alcaraz; Marta Puig).

7. Effect of anomalous hardening of tumor tissue in NSCLC (J. Alcaraz; N. Reguart; Marta Puig).

8. Study of sensitivity to trastuzumab in relation to the expression of topoisomerase I (Xavi González; Montse Muñoz; Ana Arance).

9. Characterization of the metastatic profile of malignant melanoma in circulating cells and primary tumors (Ana Arance; Laura Visa).

10. Lung cancer

10.1 To Identify the mechanisms by which the most abundant stromal cell type (i.e. the fibroblast) contributes to the progression of each tumor lung cancer subtype.
10.2 To determine the predictive value of myofibroblast overactivation in the progression of NSCLC, to identify the main causes of such overactivation, and to examine its pathological consequences in terms of cancer cell invasion.
10.3 To obtain the epigenetic profile of myofibroblast from different NSCLC subtype.

PUBLICATIONS

Originals / I.F.: 102.39

1. Martín M, Ruiz A, Ruiz Borrego M, Barnadas A, González S, Calvo L, Margelí M, Antón A, Rodríguez-Lescure A, Seguí MA, Muñoz M, Dorca J, López-Vega JM, Jara C, Espinosa E, Mendiola C, Andrés R, Ribelles N, Plazaola A, Sánchez-Rovira P, Salvador J, Crespo C, Carabantes F, Servitja S, Chacón JI, Rodríguez CA, Hernando B, Álvarez I, Carrasco E, Lluch A. **Fluorouracil, Doxorubicin, and Cyclophosphamide (FAC) Versus FAC Followed by Weekly Paclitaxel As Adjuvant Therapy for High-Risk, Node-Negative Breast Cancer: Results From the GEICAM/2003-02 Study.** *Clin Oncol* 31(20):2593-2599 I.F.: 18.038

2. Garcia-Recio S, Fuster G, Fernandez-Nogueira P, Pastor-Arroyo EM, Park SY, Mayordomo C, Ametller E, Mancino M, Gonzalez-Farre X, Russnes H, Engel P, Costamagna D, Fernandez PL, Gascon P, Almendro V. **Substance P autocrine signaling contributes to persistent HER2 activation that drives malignant progression and drug resistance in breast cancer.** *Cancer Res* 73(21):6424-6434 I.F.: 8.650

3. Cohn AL, Tabernero J, Maurel J, Nowara E, Sastre J, Chuah BY, Kopp MV, Sakaeva DD, Mitchell EP, Dubey S, Suzuki S, Hei YJ, Galimi F, McCaffery I, Pan Y, Loberg R, Cottrell S, Choo SP. **A randomized, placebo-controlled phase 2 study of ganitumab or conatumumab in combination with FOLFIRI for second-line treatment of mutant KRAS metastatic colorectal cancer.** *Ann Oncol* 24(7):1777-1785 I.F.: 7.384

4. Custodio A, Moreno-Rubio J, Aparicio J, Gallego-Plazas J, Yaya R, Maurel J, Higuera O, Burgos E, Ramos D, Calatrava A, Andrada E, López R, Moreno V,Madero R, Cejas P, Feliu J. **Pharmacogenetic predictors of severe peripheral neuropathy in colon cancer patients treated with oxaliplatin-based adjuvant chemotherapy: a GEMCAD group study.** *Ann Oncol* 25(2):398-403 I.F.: 7.384

5. Garcia-Donas J, Leandro-García LJ, González Del Alba A, Morente M, Alemany I, Esteban E, Arranz JA, Climent MA, Gallardo E, Castellano DE, Bellmunt J, Mellado B, Puente J, Moreno F, Font A, Hernando S, Robledo M, Rodríguez-Antona C. **Prospective study assessing hypoxia-related proteins as markers for the outcome of treatment with sunitinib in advanced clear-cell renal cell carcinoma.** *Ann Oncol* 24(9):2409-14 I.F.: 7.384

6. Campayo M, Navarro A, Viñolas N, Diaz T, Tejero R, Gimferrer JM, Molins L, Cabanas ML, Ramirez J, Monzo M, Marrades R. **Low miR-145 and high miR-367 are associated with unfavorable prognosis in resected NSCLC.** *Eur Respir* J 41(5):1172-1178 I.F.: 6.355

7. Giráldez MD, Lozano JJ, Cuatrecasas M, Alonso-Espinaco V, Maurel J, Mármol M, Hörndler C, Ortego J, Alonso V, Escudero P, Ramírez G, Petry C, Lasalvia L, Bohmann K, Wirtz R, Mira A, Castells A. **Gene-expression signature of tumor recurrence in patients with stage II and III colon cancer treated with 5'fluoruracil-based adjuvant chemotherapy**. *Int J Cancer* 132(5): 1090-1097 I.F.: 6.198

8. Alcaraz A, González-López R, Morote J, de la Piedra C, Meseguer C, Esteban E, Climent M, González-Gragera B, Alvarez-Ossorio JL, Chirivella I, Mellado B, Lara PC, Vázquez F, Contreras JA, Carles J, Murias A, Calderero V, Comet-Batlle J, González-Del Alba A, León-Mateos L, Mañas A, Segarra J, Lassa A, González-Enguita C, Méndez MJ, Samper P, Unda M, Mahillo-Fernández I, Bellmunt J; TUGAMO GROUP. **Biochemical markers of bone turnover and clinical outcome in patients with renal cell and bladder carcinoma with bone metastases following treatment with zoledronic acid: The TUGAMO study.** *Brit J Cancer* 109(1):121-130 I.F.: 5.082

9. Grau JJ, Zanon G, Caso C, Gonzalez X, Rodriguez A, Caballero M, Biete A. **Prognosis in Women with Breast Cancer and Private Extra Insurance Coverage.** *Ann Surg Oncol* 20(9):2822-2827 I.F.: 4.120

10. Codony J, Marin-Aguilera M, Visa L, Garcia-Albeniz X, Pineda E, Fernandez PL, Filella X, Gascon P, Mellado B. **Nuclear factor-kappa B and Interleukin-6 related docetaxel resistance in castration-resistant prostate cancer.** *Prostate* 73(5): 512-521 I.F.: 3.843

11. Calvo J, Sánchez-Cid L, Muñoz M, Lozano JJ, Thomson T, Fernández PL. **Infrequent Loss of Luminal Differentiation in Ductal Breast Cancer Metastasis.** *Plos One.* 8(10): e78097, 2013 I.F.: 3.730

12 Martin-Richard M, Gallego R, Pericay C, Foncillas JG, Queralt B, Casado E, Barriuso J, Iranzo V, Juez I, Visa L, Saigi E, Barnadas A, Garcia-Albeniz X, Maurel J. **Multicenter phase II study of oxaliplatin and sorafenib in advanced gastric adenocarcinoma after failure of cisplatin and fluoropyrimidine treatment. A gemcad study.** *Invest New Drugs* 31(6):1573-1579 I.F.: 3.498

13. Caballero M, E Sosa A, Tagliapietra A, Grau JJ. **Metastatic adenoid cystic carcinoma of the salivary gland responding to cetuximab plus weekly paclitaxel after no response to weekly paclitaxel alone.** *Head Neck* 35(2):E52-54 I.F.: 2.833

14. Paño B, Sebastià C, Buñesch L, Salvador R , Mellado B, Nicolau C. **Metastatic Renal Cell Carci¬noma: Radiologic Findings and Assessment of Response to Tar¬geted Antiangiogenic Therapy by Using Multidetector CT.** *Radiographics.* 33: 1691-1716 I.F.: 2.791

15. Gascón P, Rodríguez CA, Valentin V, Garcia-Mata J, Carulla J, Cassinello J, Colomer R, Baró E. **Usefulness of the PERFORM questionnaire to measure fatigue in cancer patients with anemia: a prospective, observational study.** *Support Care Cancer* 21(11):3039-49 I.F.: 2.649

16. Codony-Servat J, Garcia-Albeniz X, Pericay C, Alonso V, Escudero P, Fernández-Martos C, Gallego R, Martínez-Cardús A, Martinez-Balibrea E, Maurel J. **Soluble FAS in the prediction of benefit from cetuximab and irinotecan for patients with advanced colorectal cancer.** *Med Oncol* 30(1):428 I.F.: 2.147

17. Yang JC, Reguart N, Barinoff J, Köhler J, Uttenreuther-Fischer M, Stammberger U, O'Brien D, Wolf J, Cohen EE. **Diarrhea associated with afatinib: an oral ErbB family blocker.** *Expert Rev Anticancer Ther* 13(6):729-736 I.F.: 2.066

18. Alba E, Ciruelos E, Lopez R, López-Vega JM, Lluch A, Martin M, Muñoz M, Sánchez-Rovira P, Seguí MA, COSTABRA X Working Group, rubio M, Pérez-Alcántara F. **Cost utility analysis of nab-paclitaxel versus paclitaxel in monotherapy in pretreated metastatic breast cancer in Spain.** *Expert Rev Pharmacoecon Outcomes Res* 13 (3): 381-391 I.F.: 1.674

19. Sosa AE, Grau JJ, Feliz L, Pereira V, Alcaraz D, Muñoz-García C, Caballero M. **Outcome of patients treated with palliative weekly Paclitaxel plus Cetuximab in recurrent head and neck cancer after failure of platinum-based therapy.** *Eur Arch Otorhinolaryngol* 271(2):373-378 I.F.: 1.458

20. Caballero C, Jantus-Lewintre E, Carrato A, Garcia-Foncillas J, Gascón P, Blasco A, Moreno-Nogueira JA, Guillem V, López R, Codes M, Antón A, Díaz-Rubio E, Camps C. **Oncological translational research in the Spanish national health system: the INTRO study.** *Clin Transl Oncol* 16(8):686-695 I.F.: 1.276

21. Carrato A, Gómez A, Escudero P, Chaves M, Rivera F, Marcuello E, González E, Grávalos C, Constenla M, Manzano JL, Losa F, Maurel J, Dueñas R, Massuti B, Gallego J, Aparicio J, Antón A, Aranda E. **Panitumumab and irinotecan every 3 weeks is an active and convenient regimen for second-line treatment of patients with wild-type K-RAS metastatic colorectal cancer.** *Clin Transl Oncol.* 15(9):705-711 I.F.: 1.276

22. Maroto JP, Del Muro XG, Mellado B, Perez-Gracia JL, Andrés R, Cruz J, Gallardo E, Domenech M, Arranz JA, Meana JA. **Phase II trial of sequential subcutaneous interleukin-2 plus interferon alpha followed by sorafenib in renal cell carcinoma (RCC).** *Clin Transl Oncol* 15(9):698-704 I.F.: 1.276

23. Provencio M, Sánchez A, Artal A, Sánchez Torres JM, de Castro J, Dómine M, Viñolas N, Sánchez A, Pérez FJ. **Cisplatin plus oral vinorelbine as first-line treatment for advanced non-small-cell lung cancer: a prospective study confirming that the day-8 hemogram is unnecessary.** *Clin Transl Oncol.* 15(8):670 I.F.: 1.276

Reviews / I.F.: 13.310

1. Estévez L, Alvarez I, Tusquets I, Seguí MA, Muñoz M, Fernández Y, Lluch A. **Finding the right dose of fulvestrant in breast cancer.** *Cancer Treat Rev.* 39(2):136-141 I.F.: 7.384

2. Tuca A, Jiménez-Fonseca P, Gascón P. **Clinical evaluation and optimal management of cancer cachexia.** *Crit Rev Oncol/Hematol* 88(3):625-636 I.F.: 4.637

3. Gascon P, Tesch H, Verpoort K, Rosati MS, Salesi N, Agrawal S, Wilking N, Barker H, Muenzberg M, Turner M. **Clinical experience with Zarzio® in Europe: what have we learned?** *Support Care Cancer* 21(10):2925-2932 I.F.: 2.649

Clinical Guidelines / I.F.: 2.552

1. Mesía R, Pastor M, Grau JJ, Del Barco E. **SEOM clinical guidelines for the treatment of head and neck cancer (HNC) 2013.** *Clin Transl Oncol* 15(12):1018-1024 I.F.: 1.276

2. Maurel J, Grávalos C, Rivera F, Vera R, González Flores E. **SEOM clinical guidelines for the adjuvant treatment of colorectal cancer 2013.** *Clin Transl Oncol* 15(12):991-995 I.F.: 1.276

Multicenter / I.F.: 51.658

1. Parker C, Nilsson S, Heinrich D, Helle SI, O'Sullivan JM, Fosså SD, Chodacki A, Wiechno P, Logue J, Seke M, Widmark A, Johannessen DC, Hoskin P, Bottomley D, James ND, Solberg A, Syndikus I, Kliment J, Wedel S, Boehmer S, Dall'Oglio M, Franzén L, Coleman R, Vogelzang NJ, O'Bryan-Tear CG, Staudacher K, Garcia-Vargas J, Shan M, Bruland ØS, Sartor O; ALSYMPCA Investigators. **Alpha emitter radium-223 and survival in metastatic prostate cancer.** *N Engl J Med* 369(3):213-223 I.F.: 51.658

GRANTS FOR RESEARCH IN PROGRESS

Gascon P. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0055.
Duration: 01/01/2013-31/12/2016

Gascon P. **Inflamación y cáncer de mama: Influencia neuronal y de neuropéptidos pro-inflamatorios en la progresión tumoral a través de la modulación del fenotipo de la célula madre.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01706.
Duration: 01/01/2013-31/12/2015

Gascon P. **Nuevas aproximaciones terapéuticas basadas en derivados de ácidos grasos esenciales dirigidos a enfermedades oncológicas y neurológicas no cubiertas.** Sponsored by: Ministerio de Economía y Competitividad. IPT-2012-0614-010000.
Duration: 01/01/2013-31/12/2015

Gascon P. **Red tematica de investigación cooperativa de cancer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD07/0020/2014.
Duration: 23/02/2009-31/12/2014

Mellado B. **Estudio de mecanismos moleculares asociados a la resistencia a la quimioterápia en el cáncer de próstata resistente a la castración: validación clínica y funcional**. Sponsored by: Instituto de Salud Carlos III (ISCIII). PI12/01226. Duration: 01/01/2013-31/12/2015

Nadal C. **Plasticidad epigenética durante la adquisición de quimioresistencia en cáncer de colon.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI11/01231. Duration: 01/01/2012-31/12/2014

Reguart N. **Papel de los fibroblastos asociados a tumores (CAFS) en el carcinoma broncogénico de pulmón: mecanismos de interacción de modelos de cultivo celular 3D.** Sponsored by: Instituto de Salud Carlos III (ISCIII). PI09/1377. Duration: 01/01/2010-30/06/2013

DOCTORAL THESES

Reguart N., Alcaraz J. **Study of the diffusive properties of extracellular matrix gels used in 3D cultures.** PhD student: Roland Galgoczy

5.12 Cell proliferation and signaling

LOCATION
CELLEX building

FOR FURTHER INFORMATION
www.celltrafficbcn.cat

KEYWORDS
1. **Cell cycle**
2. **Signaling**
3. **Endocytosis**
4. **Annexin A6**
5. **Lipid trafficking**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	50.95	10	9	-
2012	66.55	10	10	-
2013	45.66	7	7	-

TEAM INVOLVED IN
RTICC

TEAM LEADER
Oriol Bachs (UB)
T. 93 403 52 86
obachs@ub.edu

RESEARCHERS
Neus Agell (UB)
Rosa Aligué (UB)
Carles Enrich (UB)
Montserrat Jaumot (UB)
Albert Pol (ICREA-IDIBAPS)
Maria Jesús Pujol (UB)
Francesc Tebar (UB)

POST- RESEARCHERS
Marta Bosch (IDIBAPS)
Edurne Gallastegui (UB)
Carles Rentero (IDIBAPS)
Ignasi Salaet (UB)
Neus Serrat (IDIBAPS)
Miriam Vidal
Sandra Vilà de Muga (UB)

PRE-DOCTORAL RESEARCHERS
Anna Alvarez-Guaita (UB)
Carles Barceló (UB)
Atilla Biçer (UB)
Eugenia Cisneros (UB)
Amaia Ercilla (UB)
Andrea Fernández (IDIBAPS)
Ana García-Melero (UB)
Eduard Garrido (UB)
Mariona Gelabert (IDIBAPS/UB)
Martina Guerrero (IDIBAPS)
Albert Herms (IDIBAPS)
Alba Llopis (UB)
Ramon Marques(UB)
Serena Orlando (IDIBAPS)
Noelia Paco (UB)
Anna Perearnau (UB)
Meritxell Reverter (UB)
David Soriano (UB)
Tula Yance (UB)

TECHNICIANS
Sara Abelló (UB)
Sonia Brun (UB)
Alba Fajardo (IDIBAPS)
David Gimenez (UB)
María Molinos (UB)
Eulalia Rius (UB)

COLLABORATORS
Teresa Royo (IDIBAPS)

STRATEGIC OBJECTIVES

The general goal of the group is the analysis of the mechanisms involved in cell cycle progression and signalling in health and disease.

MAIN LINES OF RESEARCH

1. **Cell proliferation and Cancer:** The objective of this line of research is the analysis of the mechanisms in-volved in cell cycle regulation and its alterations during tumorigenesis:

- Role of the CKI p27(Kip1) on the regulation of transcription, splicing and translation of genes involved in tumorigenesis.
- Cell cycle regulation by protein acetylation.
- Role of calmodulin in nuclear functions.

2. **Cell cycle: signal transduction and checkpoints:** The main topics in this research line are the analysis of: the regulation of the functionality of K-Ras by Calmodulin-binding and by phosphorylation; the regulation of p21CIP1 localization and the relevance of its binding to calmodulin and its phosphorylation; and, the DNA replication checkpoint in not transformed versus transformed cell lines.

3. **Signaling and regulation of the cell cycle:** In eukaryotic organisms, the response to stress insults is through the activation of the MAP kinases pathway, Progression through the cell cycle is dependent on external stimuli and failure to correctly integrate the induced signals can lead to accumulation of genetic damage contributing to cancer development. Understanding how signaling networks and the cellular responses are regulated is one of the most crucial objectives in biomedical research. The aim of this research focuses on identifying the molecular mechanisms by which cell cycle is regulated by stress-activated protein kinases.

4. **Endocytosis, membrane trafficking and signaling:** This line of research includes the following activities:

- Study of endocytosis and membrane trafficking in polarized cells, such as hepatocytes and in nonpolarized cells.
- Study the role of calmodulin in the regulation of trafficking and signalling of EGFR.
- Study the role of Annexin A6 in the transport of caveolin, the formation of caveolae, homeostasis of cholesterol and signaling of Ras/ MAPK.

5. **Lipid trafficking and storage:** The aim of our project is to characterize in health and disease, the cellularprocesses regulated or deregulated by the accumulation of lipids within cells. With a special attention to the cellular cost of accumulation of cholesterol in the organelles and the role of the caveolin protein in the regulation of these mechanisms.

PUBLICATIONS

Originals / I.F.: 45.661

1. Kassan A, Herms A, Fernández-Vidal A, Bosch M, Schieber NL, Reddy BJ, Fajardo A, Gelabert-Baldrich M, Tebar F, Enrich C, Gross SP, Parton RG, Pol A. **Acyl-CoA synthetase 3 promotes lipid droplet biogenesis in ER microdomains.** *J Cell Biol* 203(6):985-1001 I.F.: 10.822

2. Herms A, Bosch M, Ariotti N, Reddy BJ, Fajardo A, Fernández-Vidal A, Alvarez-Guaita A, Fernández-Rojo MA, Rentero C, Tebar F, Enrich C, Geli MI, Parton RG, Gross SP, Pol A. **Cell-to-cell heterogeneity in lipid droplets suggests a mechanism to reduce lipotoxicity.** *Curr Biol* 23(15):1489-1496 I.F.: 9.494

3. Koese M, Rentero C, Vilà de Muga S, Kota BP, Wood P, Reverter M, Alvarez-Guaita A, Monastyrskaya K, Hughes WE, Tebar F, Daly RJ, Enrich C, Grewal T. **Annexin A6 is a scaffold for PKC to promote EGFR inactivation.** *Oncogene* 32:2858-2872 I.F.: 7.357

4. Barceló C, Paco N, Beckett AJ, Alvarez-Moya B, Garrido E, Gelabert M, Tebar F, Jaumot M, Prior I, Agell N. **Oncogenic K-ras segregates at spatially distinct plasma membrane signaling platforms according to its phosphorylation status.** *Journal of Cell Science* 126(20):4553-4559 I.F.: 5.877

5. Vidal-Laliena M, Gallastegui E, Mateo F, Martínez-Balbás M, Pujol MJ, Bachs O. **Histone deacetylase 3 regulates cyclin A stability.** *J Biol Chem* 288(29):21096-21104 I.F.: 4.561

6. Mulay V, Wood P, Manetsch M, Darabi M, Cairns R, Hoque M, Cecilia Chan K, Reverter M, Alvarez-Guaita A, Rye K-A, Rentero C, Heeren J, Enrich C, Grewal T. **Inhibition of mitogen-activated protein kinase Erk1/2 promotes protein degradation of ATP binding cassette transporters A1 and G1 in CHO and HuH7 cells.** *PLoS One* 8(4):e62667 I.F.: 3.730

7. Panosa C, Tebar F, Ferrer-Batallé M, Fonge H, Seno M, Reilly RM, Massaguer A, de Llorens R. **Development of an Epidermal Growth Factor Derivative with EGFR Blocking Activity.** *PLoS One* 8(7):e69325 I.F.: 3.730

GRANTS FOR RESEARCH IN PROGRESS

Agell N. **Relevancia de la fosforilacion de K-Ras y de las alteraciones del checkpoint de replicacion del DNA en la oncogenesis.** Sponsored by Ministerio de Ciencia e Innovación. SAF2010-20712. Duratión: 01/01/2010-31/12/2013.

N. Agell. **Collaborator in the el Group of del Dr. G. Tomas en la Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0049. Duration: 01/01/2013-31/12/2016

Aligué R. **The family calmodulin dependent kinases in stress response signaling and cell cycle control.** Sponsored by: Ministerio de Economía y Competitividad. BFU2012-31220. Duration: 01/01/2013-31/12/2015

Bachs O. **Red Temática de Investigación Cooperativa en Cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD12/0036/0054. Duration: 01/01/2013-31/12/2016

Bachs O. **Red temática de investigación cooperativa de cáncer.** Sponsored by: Instituto de Salud Carlos III (ISCIII). RD06/0020/0010. Duration: 01/01/2007-31/12/2013

Enrich C. **Annexin A6 is necessary for liver regeneration.** Sponsored by: Fundació la Marató de TV3. 120710. Duration: 11/01/2013-10/01/2016

Enrich C. **Mecanismo de la secreción de proteínas y de la organización de los compartimentos celulares implicados.** Sponsored by: Ministerio de Economía y Competitividad. CSD2009-00016. Duration: 17/12/2009-16/12/2014.

Enrich C. **Consecuencias fisiológicas de la expresión de la Annexina A6 (AnxA6) en el compartimiento endocítico y en la exocitosis: Estudio en ratones AnxA6-ko's.** Sponsored by: Ministerio de Economía y Competitividad. BFU2012-36272. Duration: 01/01/2013-31/12/2015.

Marques R. **Design and development of an improved enzyme for animal nutrition.** Sponsored by: Ministerio de Ciencia e innovación (CDTI) IDI2011-0192 Duration: 01/06/2010-31/05/2013.

Pol A. **Consecuencias metabólicas, celulares y sistémicas de mutaciones en las caveolinas y NPC1 humanas.** Sponsored by: Ministerio de Economía y Competitividad. BFU2011-23745. Duration: 01/01/2012-31/12/2014

Pol A. **Mecanismo de la secreción de proteínas y de la organización de los compartimentos celulares implicados.** Sponsored by: Ministerio de Economía y Competitividad. CSD2009-00016. Duration: 17/12/2009-16/12/2014

Pol A. **Hepatic and brain mitochondrial cholesterol/glycosphingolipids and altered metabolism contribute to the pathology of Niemann Pick type C disease and caveolinopathies.** Sponsored by: Fundació La Marató de TV3. 100531. Duration: 03/02/2011-29/05/2014

Tebar F. **Endosomas como plataformas de señalización. Papel de las GTPasas Rac1, H- y K-Ras en endocitosis y su regulación por CaM y EGFR.** Sponsored by Ministerio de Economía y Competitividad. BFU2012-38259. Duration: 01/01/2013-31/12/2014

DOCTORAL THESES

Agell N. **Reguladores del checkpoint de replicación en células no transformadas.** PhD student: Alba Llopis Gómez.

Bachs O. **Analysys of the role of p27 kip1 in the recruitment of cyclins and cdks on the promoters of the target genes.** PhD student: Serena Orlando.

Transversal research groups

T.1 Transversal group for research in primary care 302
Antoni Sisó

T.2 Research in nursing 305
Adelaida Zabalegui

T.3 Clinical pharmacology 307
Xavier Carné

T.1

Transversal group for research in primary care

LOCATION
EAP Les Corts
EAP Comte Borrell
EAP Casanova

KEYWORDS
1. **Primary Healthcare**
2. **Chronic diseases**
3. **Cardiovascular diseases & cardiovascular risk factors**
4. **Health technology assessment**
5. **Autoimmune & rheumatic diseases**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	23.06	5	2	3
2012	21.11	8	2	4
2013	21.02	8	2	6

AWARDS
Ajut a la Recerca en Educació Terapèutica en Diabetis ACD 2013
Institution: Associació Catalana de Diabetis
Awardee: Cristina Colungo

TEAM LEADER
Antoni Sisó Almirall (EAP Les Corts)
T. 93 227 99 24
asiso@clinic.cat

RESEARCHERS
Lluisa Benito Serrano (EAP Les Corts)
Marta Catalán Adell (EAP Casanova)
Zoe Herreras Pérez (EAP Comte Borrell)
Imma Garrell Lluís (EAP Comte Borrell)
Joan Gené Badia (EAP Casanova)
Lluís González de Paz (EAP Les Corts)
Ignacio Menacho Pascual (EAP Les Corts)
Pilar Navarrete Duran (EAP Comte Borrell)
Marta Navarro González (EAP Comte Borrell)
Jacinto Ortiz Molina (EAP Les Corts)
Montserrat Pinyol Martínez (EAP Les Corts)
Marina Rovira (Farmacia)
Rafael Ruiz Riera (CAPSE)
Antoni Salvà Riquer (Pediatria - Casanova)
Núria Sánchez Ruano (EAP Comte Borrell)
Elisenda Sant Arderiu (EAP Casanova)
Ethel Sequeira Aymar (EAP Casanova)
Josep Miquel Sotoca Momblona (Farmacia)

PRE-DOCTORAL RESEARCHERS
Mireia López Poyato (EAP Les Corts)
Emma Marianela Morales Espinoza (AP – Consorci Hospital Terrassa)

NURSING STAFF
Mª Carmen Alvira Balada (EAP Comte Borrell)
Esther Blat (EAP Les Corts)
Cristina Colungo Francia (EAP Comte Borrell)
Noemí García (EAP Comte Borrell)
Rosa Segarra (EAP Casanova)

STATISTICIAN
Belchin Adriyanov Kostov (IDIBAPS)

COLLABORATORS
Jaume Benavent Àreu (Institut Català de la Salut)
Sílvia Canivell Fusté (IDIBAPS)
Imma Grau Corral (HCB)

STRATEGIC OBJECTIVES

Primary care is the point of patient entry to the healthcare system, and the primary care centers are where most of the population health problems are dealt with. It is in this setting where the relationship between the patient and reference primary care physician and nurse is a key factor in preventing and healing diseases, and in promoting healthy habits. In the research

context, the multidisciplinary and transverse nature of the activities of the primary care professional favors a biological, psychological and social approach to the patients and their illnesses, in both the consulting office and in the home. The integral approach to the individual and longitudinal care over the full course of the life of the patient makes it possible to conduct proprietary and/or collaborative studies targeted at knowledge of the characteristics of the population, people and their illnesses.

MAIN LINES OF RESEARCH

Primary care aims to carry out research inherent to its nature, integrating within the existing investigational networks and groups, and working in a coordinated manner with other consolidated research teams from different perspectives:

- Conduction of population-based studies (both descriptive and evaluating interventions and follow-up), in an accessible and well defined population of subjects, taking advantage of the computer-based filing of clinical data.
- Conduction of research into healthcare results or outcomes.
- Description of the natural history of the patient and disease from a biological, psychological and social perspective.
- Conduction of studies of risk factors and preventive medicine.
- Analysis of the morbidity and mortality of the most prevalent disorders.
- Development of collaborative studies with the administration and research entities or groups allowing the implementation of transversal research.

The main lines of research include:

- Healthcare continuity and management of chronic diseases.
- Use of healthcare services.
- The fragility – geriatrics – dependency – home care axis.
- Use of medicines.
- Primary care and autoimmunity.
- Atherogenesis, risk factors and cardiovascular diseases.
- Chronic pain.
- Mental health, smoking and other addictions.
- Respiratory diseases.
- Digestive and liver diseases.
- HIV infection – AIDS and other infectious diseases.
- 2.0. Health.

PUBLICATIONS

Originals / I.F.: 21.018

1. Reyes C, Formiga F, Coderch M, Hoyo J, Ferriz G, Casanovas J, Monteserín R, Brotons C, Rojas M, Moral I. **Use of proton pump inhibitors and risk of fragility hip fracture in a Mediterranean region.** *Bone* 52:557-561 I.F.: 3.823

2. Canivell S, Ruano EG, Sisó-Almirall A, Kostov B, González-de Paz L, Fernandez-Rebollo E, Hanzu F, Párrizas M, Novials A, Gomis R. **Gastric inhibitory polypeptide receptor methylation in newly diagnosed, drug-naïve patients with type 2 diabetes: a case-control study.** *PLoS One* 8(9):e75474 I.F.: 3.730

3. Menacho I, Sequeira E, Muns M, Barba O, Leal L, Clusa T, Fernandez E, Moreno L, Raben D, Lundgren J, Gatell JM, Garcia F, Cayuelas L, Aragunde V, Vergara M, Catalan M, Moreno MA, Hormigo G, Sisó A, Herreras Z, Sebastian L, Benito L, Picas A, Hoyo J, Giner MJ, Cararach D, Moles E, Moro ML, Arrabal P, Roca D, Prego S, Ferrer X, Egido A, Ventosa C, García S, Muñoz S, Massana A, Solé J, Curiel M, Heras F, León A. **Comparison of two HIV testing strategies in primary care centres: indicador-conditionguided testing vs. testing of those with non-indicator conditions.** *HIV Med 14 Suppl* 3:33-37 I.F.: 3.155

4. Belenguer-Prieto R, Morales-Espinoza EM, Martín-González RM, Brito-Zerón P, Pastor-Oliver JF, Kostov B, Buss D, Gómez-Gálvez C, Salazar-Cifre A, Sisó-Almirall A, Ramos-Casals M. **Specificity and sensitivity of objective tests to detect possible malingering in fibromyalgia: a case-control study in 211 Spanish patients.** *Clin Exp Rheumatol* 31(6 Suppl 79):S86-93 I.F.: 2.655

5. Brito-Zerón P, Akasbi M, Bosch X, Bové A, Pérez-De-Lis M, Diaz-Lagares C, Retamozo S, Gandía M, Pérez-Alvarez R, Soto-Cárdenas MJ, Sisó A, Valls-Solé J, Graus F, Ramos-Casals M. **Classification and characterisation of peripheral neuropathies in 102 patients with primary Sjögren's syndrome.** *Clin Exp Rheumatol* 31(1):103-10 I.F.: 2.655

6. González-de Paz L, Devant-Altimir M, Kostov B, Mitjavila-López J, Navarro-Rubio MD, Sisó-Almirall A. **A new questionnaire to assess endorsement of normative ethics in primary health care: development, reliability and validity study.** *Fam Pract* 30(6):724-733 I.F.: 1.828

7. Gené Badia J, Borràs Santos A, Contel Segura JC, Terén CA, González LC, Ramírez EL, Gallo de Puelles P; HC>65 Research Team. **Predictors of mortality among elderly dependent home care patients**. *BMC Health Serv Res* 13:316 I.F.: 1.773

8. Sisó-Almirall A, Gilabert Solé R, Bru Saumell C, Kostov B, Mas Heredia M, González-de Paz L, Sebastián Montal L, Benavent Àreu J. **Utilidad de la ecografía portátil en el cribado del aneurisma de aorta abdominal y de la ateromatosis de aorta abdominal.** *Med Clin* (Barc) 141(10):417-22 I.F.: 1.399

Reviews / I.F.: 4.410

1. BritoZerón P, SisóAlmirall A, Bové A, Kostov BA, RamosCasals M. **Primary Sjögren syndrome: an update on current pharmacotherapy options and future directions.** *Expert Opin Pharmacother* 14(3):279289 I.F.: 2.860

2. Gallo P, Gené-Badia J. **Cuts drive health system reforms in Spain.** *Health Policy* 113(1-2):1-7 I.F.: 1.550

GRANTS FOR RESEARCH IN PROGRESS

Sisó A. **Screening programme for abdominal aortic aneurysm by hand-held-ultrasonography in primary health care.** Sponsored by: Medtronic Vascular Inc.
Duration: 01/03/2013-31/10/2014

Colungo C. **Programa d'Atenció i Educació Terapèutica per el Debut de Diabetis Mellitus Tipus 2.** Sponsored by: Associació Catalana de Diabetis.
Duration: 01/02/2012-01/02/2014

T.2

Research in nursing

LOCATION
HCB building

KEYWORDS
1. **Older people**
2. **Chronic–care /Long-term care**
3. **Dementia**
4. **Nursing Practice**
5. **Interventions**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	33.91	9	5	2
2012	15.72	5	3	2
2013	3.14	2	2	-

AWARDS
11th edition Profesor Barea Awards. Secondary prize from the category: Modalidad 2. Proyectos Multientidad
Institution: Fundación Signo
Awardee :Zabalegui A.

Best nursing publication from an International level
Institution: Col·legi Oficial d'Infermeres i Infermers de Barcelona
Awardee: de Cabrera E, Blanco I, Yague C & Zabalegui A

TEAM LEADER
Adelaida Zabalegui (HCB)
T. 93 227 54 24
azabaleg@clinic.cat

NURSE RESEARCH COORDINATOR
Ester Risco (HCB)

COLLABORATORS
Ana Alonso (HCB)
Montserrat Amigó (HCB)
Angela Arranz (HCB)
Lourdes Corominas (HCB)
Marta Farré (HCB)
Lluís González (HCB)
Teresa Peix (HCB)
Marta Quintanela (HCB)
Ester Risco (HCB)
Dolors Robles (HCB)
Victoria Ruiz (HCB)
Carmen Sánchez (HCB)

STRATEGIC OBJECTIVES

Research in nursing is essential for responding to the healing demands of the current healthcare system. Its complexity in the hospital setting is derived from the associated increase in patient severity upon admission, the reduction in hospital stay, the incorporation of new technologies, the aging of the population, patient requests for information, social change, and the global crisis.

HCB Nursing needs new crossover research areas in order to address new health challenges, adapting new professional skills to new health care goals. Multidisciplinary approach is essential to improve patient care, so new collaboration strategies within different health care professionals need to be established.

MAIN LINES OF RESEARCH

The main lines of research in nursing in our institution are:

Empowerment: The main target is to increase the patient empowerment and develop assessment tools in order to learn about the educational interventions

through experiences. For instance, the implementation of empowerment for patients who suffer from osteoarthritis aims to foster the patients´ and families´ participation in the improvement of their bio-physiological, functional and social wellbeing. They take part in the solution to problems and also gain specific skills that may enable them to handle their health problems, optimize the surgical results through getting the patients´ satisfaction while cutting down on expenses. The empowerment is also aimed at cancer patients. In this case, the objective is to develop a tool for health care professionals to help cancer patients make decisions
Chronicity: Information, training and emotional support for dependent elderly has been design and evaluated in order to enhance older dependent people living at home. Educational material composed of leaflets informative, educational books and CDs was designed to be used by informal caregivers. Main topics are: hygiene, feeding, postural changes and communication. This material is currently being of use to the acute units with family caregivers of the Hospital Clinic of Barcelona.
Original clinical and experimental research in hypertension, incontinence, diabetes and obesity has been also developed from a national and international level during the last years from nursing leadership.

Dementia: Best practice strategies' development for transition from formal professional home care to institutional long-term nursing care facilities. The main target is to improve health service for people with dementia through careful development of best practice strategies using various data collection methods including extensive literature review, focus groups and clinical assessments in different long-term nursing settings.

Innovation: As an instrument to improve the efficiency and quality of care processes. The Committee is a multidisciplinary team involving cardiac and respiratory diseases, as well as different areas of research and innovation. In this regard, the Commission encourages coordination between the ICT Commission ICT Research and Innovation Directorate of Hospital.

Professional Competencies:
To determine how hospital nurse staffing, skill mix, educational composition, and quality of the nurse work environment impact on different hospital outcomes such as mortality, failure to rescue, quality of care, and patient satisfaction. These findings will allow researchers to refine existing nurse workforce.

PUBLICATIONS

Originals / I.F.: 3.139

1. Hallberg I, Leino-Kilpi H, Meyer G, Raamat K, Soto-Martin M, Sutcliffe C, Zabalegui A, Zwakhalen S, Karlsson S. **Dementia carein eight European Countries; Developing a mapping system to explore systems.**
J Nurs Scholarsh 45(4):412-424
I.F.: 1.612

2. Gallart A, Cruz F, Zabalegui A. **Factors influencing burden among non-professional immigrant caregivers: a case-control study.**
J Adv Nurs 69(3):642–654
I.F.: 1.527

GRANTS FOR RESEARCH IN PROGRESS

Zabalegui A. **Improving health services for European citizens with dementia: Development of best practice strategies for the transition from ambulatory to institutional long-trem care facilities (RightTimePlaceCare).**
Sponsored by: European Commission of Research, 2421153 (FP7-Health-2009).
Duration: 01/03/2013 - 31/10/2014.

Zabalegui A. **Estudio experimental sobre la eficacia de una intervención innovadora de información, formación y apoyo social "INFOSA" a cuidadores principales de personas mayores dependientes.** Sponsored by: Instituto de Salud Carlos III, Fondo de Investigaciones Sanitarias. Expediente PI09/00111.
Duration: 2009-2014.

T.3

Clinical pharmacology

LOCATION
HCB building

KEYWORDS
1. **Clinical trials, design and methodology**
2. **Ethics in clinical research**
3. **Drug regulation**
4. **Pharmacoepidemiology**

Original publications from 2011 to 2013

YEAR	I.F.	TOTAL	Q1	Q2
2011	76.89	29	10	4
2012	13.24	5	1	4
2013	6.62	3	1	1

TEAM INVOLVED IN
CAIBER

TEAM LEADER
Xavier Carné (HCB)
T. 93 227 91 68
xcarne@clinic.cat

RESEARCHERS
Joan Albert Arnaiz (HCB)
Gonzalo Calvo (HCB)

COLLABORATORS
Ana Cruceta (FCRB)
Judit Pich (FCRB)
Neus Riba (HCB)
José Ríos (IDIBAPS)
Núria Sanz (FCRB)
Ferran Torres (IDIBAPS)
Sara Varea (FCRB)

STRATEGIC OBJECTIVES

The team carries out clinical research support activities with different Departments:

1. The Clinical Trials Agency, together with the Department of Pharmacy, provides support of all technical and administrative aspects related to clinical trials carried out in the Clinic Hospital - IDIBAPS. The Agency serves as a single window for sponsors and investigators, and as secretary to the CREC of the HCB (Clinical Research Ethics Committee).

2. The CTU (Clinical Trials Unit) provides support for the conduction of clinical trials on the part of the investigators of the institution that act as sponsors, in aspects related to study design, implementation and monitorization.

3. The Pharmacoepidemiology and Therapeutic Evaluation Unit, offers support of activities in pharmacovigilance, epidemiology and the evaluation of drugs in our setting.

4. The team collaborates with Dr. Amàlia Lafuente of the Pharmacology Unit of the UB, who conducts studies relating

genetics to drug substance activity and response.

5. Lastly, the team participates in the trial follow-up committees known as DSMB (Data and Safety Monitoring Boards), in charge of external supervision of the course of the clinical trials, and of deciding the pertinence of their continuity over time.

MAIN LINES OF RESEARCH

- Ethics in clinical research
- Clinical trials, design and methodology.
- Statistical support of clinical research.
- Pharmacovigilance and pharmacoepidemiology.
- Pharmacogenetics and pharmacogenomics.

PUBLICATIONS

Originals / I.F.: 6.621

1. Gassó P, Papagianni K, Mas S, de Bobadilla RF, Arnaiz JA, Bernardo M, Lafuente A. **Relationship between CYP2D6 genotype and haloperidol pharmacokinetics and extrapyramidal symptoms in healthy volunteers.** *Pharmacogenomics* 14:1551-1563 IF: 3.857

2. Mas S, Gassó P, Fernández de Bobadilla R, Arnaiz JA, Bernardo M, Lafuente A. **Secondary nonmotor negative symptoms in healthy volunteers after single doses of haloperidol and risperidone: a double-blind, crossover, placebo-controlled trial.** *Hum Psychopharmacol* 28:586-593 IF:2.097

3. Pons i Villanueva A, Romero A, Goti J, Fernandez-Egea E, Undurraga J, Carne X, Bernardo M. **Should obesity be a limiting factor for clozapine treatment?** *Rev Psiquiatr Salud Ment* 6(2):75-79 IF 0.667

Reviews / I.F.: 3.730

1. Dwan K, Gamble C, Williamson PR, Kirkham JJ; Reporting Bias Group. **Systematic review of the empirical evidence of study publication bias and outcome reporting bias - an updated review.** *PLoS One* 8:e66844 IF 3.730

Multicenter / I.F.: 67.452

1. SPARTAC Trial Investigators. **Short-course antiretroviral therapy in primary HIV infection.** *N Engl J Med* 368:207-217 IF 51.658

2. Yager N, Robinson N, Brown H, Flanagan P, Frater J, Fidler S, Weber J, Phillips R; SPARTAC Trial Investigators. **Longitudinal analysis of an HLA-B*51-restricted epitope in integrase reveals immune escape in early HIV-1 infection.** *AIDS* 27:313-323 IF:6.407

3. Gall A, Kaye S, Hué S, Bonsall D, Rance R, Baillie GJ, Fidler SJ, Weber JN, McClure MO, Kellam P; SPARTAC Trial Investigators. **Restriction of V3 region sequence divergence in the HIV-1 envelope gene during antiretroviral treatment in a cohort of recent seroconverters.** *Retrovirology* 10:8 IF:5.657

4. Bjerk SM, Baker JV, Emery S, Neuhaus J, Angus B, Gordin FM, Pett SL, Stephan C, Kunisaki KM; INSIGHT SMART Study Group. **Biomarkers and bacterial pneumonia risk in patients with treated HIV infection: a case-control study.** *PLoS One* 8(2):e56249 IF 3.730

GRANTS FOR RESEARCH IN PROGRESS

Arnaiz J.A. **Fixed Dose Combination drugs for Secondary Cardiovascular Prevention.** Sponsored by: European Commission. 241559. Duration: 01/07/2010-30/06/2014

Carne X. **European Clinical Research Infrastructures Network - Integrating Activity.** Sponsored by: European Commission. 284395. Duration: 01/01/2012-31/12/2015

Carne X. **Consorcio de Apoyo a la Investigación Biomédica en Red.** Sponsored by: Instituto de Salud Carlos III (ISCIII). CAI08/01/0013. Duration: 01/01/2009-30/09/2014

Carne X. **Farmacologia clínica i farmacogènetica.** Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). 2009_SGR_1501. Duration: 16/09/2009-30/04/2014

Team and Group Leaders Index

A Alvar Agustí 127
Alfredo Manuel Adán 59
Jordi Alberch 220
Antonio Alcaraz 130
Vicente Arroyo 148
Francesc Artigas 199

B Oriol Bachs 297
Juan Balasch 136
Joan Albert Barberà 117
Miquel Bernardo 223
Joan Bladé 278
Isabel Blanco 118
Jaume Bosch 156
Josep Brugada 92
Jordi Bruix 152

C Josep Maria Campistol 99
Elías Campo 254, 255
Xavier Carné 307
Antoni Castells 175
Josefina Castro 225
Francisco Cervantes 277, 278
Ricard Cervera 58
Ángel Chamorro 203
Maria Cinta Cid 60
Daniel Closa 81
Dolors Colomer 285
Albert Compte 239

D Josep Dalmau 243

E Gustavo Egea 94
Ginés Escolar 289

F Ramon Farré 108
Pedro Luis Fernández 255
José Carlos Fernández-Checa 168
Carlos Fernández de Larrea 279
Mercedes Fernández Lobato 157
Jorge Ferrer 185
Cristina Fillat 176
Joaquim Forés 74
Xavier Forns 145

G Juan Carlos García-Pagán 157
Xavier Gasull 214
Josep Maria Gatell 65, 67
Pere Gascón 292
Cristobal Gastó 225
Ramon Gomis 188
Eduard Gratacós 139
Josep Maria Grau 217
Francesc Graus 242
Núria Guañabens 165, 166

H Felicia Hanzu 189

I Nuria de la Iglesia 243

J Carme Junqué 234

L Armando López Guillermo 279
Josep M. Llovet 153
Francisco Lozano 72

M Guadalupe Mengod 198, 199
Cristóbal Mezquita 265
Montserrat Milà 267
Josep Maria Miro 67
Oscar Miró 78
Rafael Molina 252
Lluis Mont 93
Josep M. Montserrat 112
Asuncion Moreno 67
Joaquim Mullol 121, 122

N Anna Novials 192

P Julià Panés 161
Albert Parés 165, 166
Carmen Peralta 172
Francesca Pons 262
Sebastián Pons 200
Susana Puig 270

R Ignacio Revuelta 100
Antonia Ribes 182
Antoni Rimola 171
Emili Ros 103

S Manel Sabaté 86
Maria Victoria Sánchez Vives 238
Raimon Sanmartí 56
Pere Santamaria 188
Josep Saura 200
Antoni Sisó 302
Marta Sitges 93
Alex Soriano 67
Gisela Sugranyes 225
Cristina Suñol 199

T Eduardo Tolosa 207, 208
Antoni Torres 111
Ramon Trullàs 248

U Álvaro Urbano-Ispizua 274

V Josep Valls 213
Josep Vidal 187, 188
Eduard Vieta 224
Pablo Villoslada 243

Y Jordi Yagüe 76

Z Adelaida Zabalegui 305

IDIBAPS

www.idibaps.org

The mission of IDIBAPS is to combine high-quality clinical research with high-level basic research in order to achieve a more effective transfer of scientific results in the prevention and treatment of the most common health issues in our country.

Generalitat de Catalunya

CLÍNIC BARCELONA Hospital Universitari

Universitat de Barcelona

CSIC Consejo Superior de Investigaciones Científicas