ANNUAL SCIENTIFIC REPORT 2011

IDIBAPS

Institut
D'Investigacions
Biomèdiques
August Pi i Sunyer

Annual Scientific Report 2011

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.

ANNUAL SCIENTIFIC REPORT

IDIBAPS
Institut D'Investigacions Biomèdiques August Pi i Sunyer

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University of Barcelona – Faculty of Medicine

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August Pi i Sunyer

(Barcelona 1879 – Mexico 1965),
eminent doctor and politician
who changed the entire course of
biomedicine and politics in this country,
after whom this Institute is named.

The Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) is a public research centre 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 concerning the main health problems present in our society, with the final purpose of improving their prevention and treatment. Innovation and technological progress are therefore essential lines of activity at IDIBAPS. The IDIBAPS task force combines more than 460 researchers, making IDIBAPS probably one of the most powerful translational research centres in Spain.

IDIBAPS is located in a melting pot for biomedical research, Barcelona Clinic Campus. The University of Barcelona School of Medicine and Barcelona's Hospital Clínic are found in the same area. This institutional combination is ideal for creating powerful synergies and ensuring that the IDIBAPS research is efficiently transferred to the patient and included in the training of new health professionals.

The Centre's research activities are divided into five different areas which group over 59 top-level research teams and over 460 investigators. IDIBAPS' researchers are distributed into the following fields of activity: Biological Aggression and Response Mechanisms (Area 1), Respiratory, Cardiovascular and Renal Pathobiology and Bioengineering (Area 2), Liver, Digestive System and Metabolism (Area 3), Clinical and Experimental Neuroscience (Area 4), and Oncology and Haematology (Area 5).

The data presented in this Annual Scientific Report detail the ever-growing scientific output led by IDIBAPS' investigators, and their capacity for attracting public and private funding. In 2011, they reached a new record, with 906 original articles published in high-impact-factor scientific journals. This is only possible thanks to hard work, enthusiasm and infrastructures such as the recently built Esther Koplowitz Research Centre or the soon-to-be-finished CELLEX Research Centre. 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.

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

INTRODUCTION

Esther Koplowitz Research Centre (CEK) – Patronage to continue innovating

In order to guarantee financial stability and ensure continuity, IDIBAPS recognizes that the financing of R&D and research institutes should not only come from public agencies but also from private funding institutions. Therefore, fundraising is extremely important at two levels: at the researcher level to finance their own research and at the institutional level to be able to finance strategic infrastructures and interventions. The ability to obtain private funds is also a reflection of the quality and prestige of the institution and its researchers. In this aspect, IDIBAPS and its researchers also have a good track record of obtaining private funds. In recent years, around €35 million has been obtained at the institutional level, enabling the acquisition of new equipment, the construction of new lab facilities and the modernisation of the old ones.

The Esther Koplowitz Research Centre (CEK) is a wonderful example of public and private co-responsibility, since it benefits from the participation of the Catalan Autonomous Government (*Generalitat de Catalunya*), the Spanish Ministry for the Economy and Competitiveness (*Ministerio de Economía y Competitividad*), the Carlos III Health Institute (*Instituto de Salud Carlos III*) and the University of Barcelona (*Universitat de Barcelona*), as well as the support of other patrons such as the Esther Koplowitz Foundation, the Cellex Private Foundation, Sardà Farriol Action for Diabetes Research (*Acción Sardà Farriol para la Investigación en Diabetes*) and Laboratoris Esteve.

Funded with a capital contribution of €15 million from the Esther Koplowitz Foundation to the Clínic Foundation, the investment in the building exceeds €50 million. With space for more than 350 researchers, the CEK receives international scientists and PhD students, thus fostering the exchange of experience and professional cooperation. In 2011, it reached its full operating capacity.

The CEK building houses a large number of the IDIBAPS teams, covering a massive range of research lines. The biomedical progress achieved in the CEK has its grounds in the history and the top-level research developed by IDIBAPS over the years. The multitude of international researchers that combine their efforts in the new facilities allows us to look to the future with hope and enthusiasm.

Management Report

1. **Funding of IDIBAPS.** IDIBAPS funding in 2011 totalled more than €21 million. Twenty-seven percent of this amount corresponded to the contribution of the Ministry of Economy and Knowledge (*Departament d'Economia i Coneixement*) and the Ministry of Health (*Departament de Salut*) of the Catalan Autonomous Government (*Generalitat de Catalunya*). The rest of the funding executed by IDIBAPS in 2011 corresponded to calls for research funding (58%), as well as contracts and cooperation agreements with private entities (12%) and financial income sources (3%).

2. **Resource volume generated by the IDIBAPS researchers.** This is a very significant aspect. The resources generated by IDIBAPS researchers during the financial year 2011 totalled €39,325,319. These resources have been managed by different institutions: IDIBAPS itself (€12,857,082) and the Clínic Foundation (*Fundació Clínic per a la Recerca Biomèdica*) (€26,468,237). It is important to mention that 63% of the resources execured by IDIBAPS researchers in 2011 (more than €24 million) corresponded to competitive research projects or were provided on a grant basis (calls for funding). The remaining 37% was distributed as follows: contracts with private entities (21%); clinical trials managed by the Clinic Foundation (3%); donations (11%); and teaching contracts (3%).

IDIBAPS FUNDING 2011

RESOURCES EXECURED BY IDIBAPS RESEARCHERS IN 2011

Keeping our focus on translational research and innovation

IDIBAPS has a very clear mission statement that focuses all its efforts in research on achieving both a clinical and medical approach. That means that **IDIBAPS has a unique strength in clinical research and a clear mandate to orientate its basic research projects to relevant clinical questions**. Additionally, there is an increasing focus on developing capabilities to bring our biomedical and health-care knowledge to the market, in close cooperation with both local and international research and health-care centres and biotech and medtech industrial partners. All this is being developed jointly with the Direction of Innovation of Hospital Clínic de Barcelona and the Innovation Management Offices of Clinic Foundation.

There is no question that 2011 was a challenging year due to the difficult and unpredictable economic environment. In spite of that, IDIBAPS kept its focus on translational research and high-impact cooperation with relevant stakeholders, including other research and innovation centres, industrial companies and technology-driven small and medium-sized enterprises (SMEs). This was reflected in the fact that 8 additional patents were submitted (including PCT extensions) in 2011, two of them jointly with industrial partners, two with large national research organisations and one with SMEs. In addition, 4 technology transfer agreements were closed with biotech and medtech SMEs, raising the number of Hospital Clínic and IDIBAPS innovation and transfer deals in the period 2007-2011 to 66.

Organisational Chart

BOARD OF GOVERNORS

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Area 3
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Jorge Ferrer, Representative

Area 4
Anna Planas, Coordinator
Pablo Villoslada, Representative

Area 5
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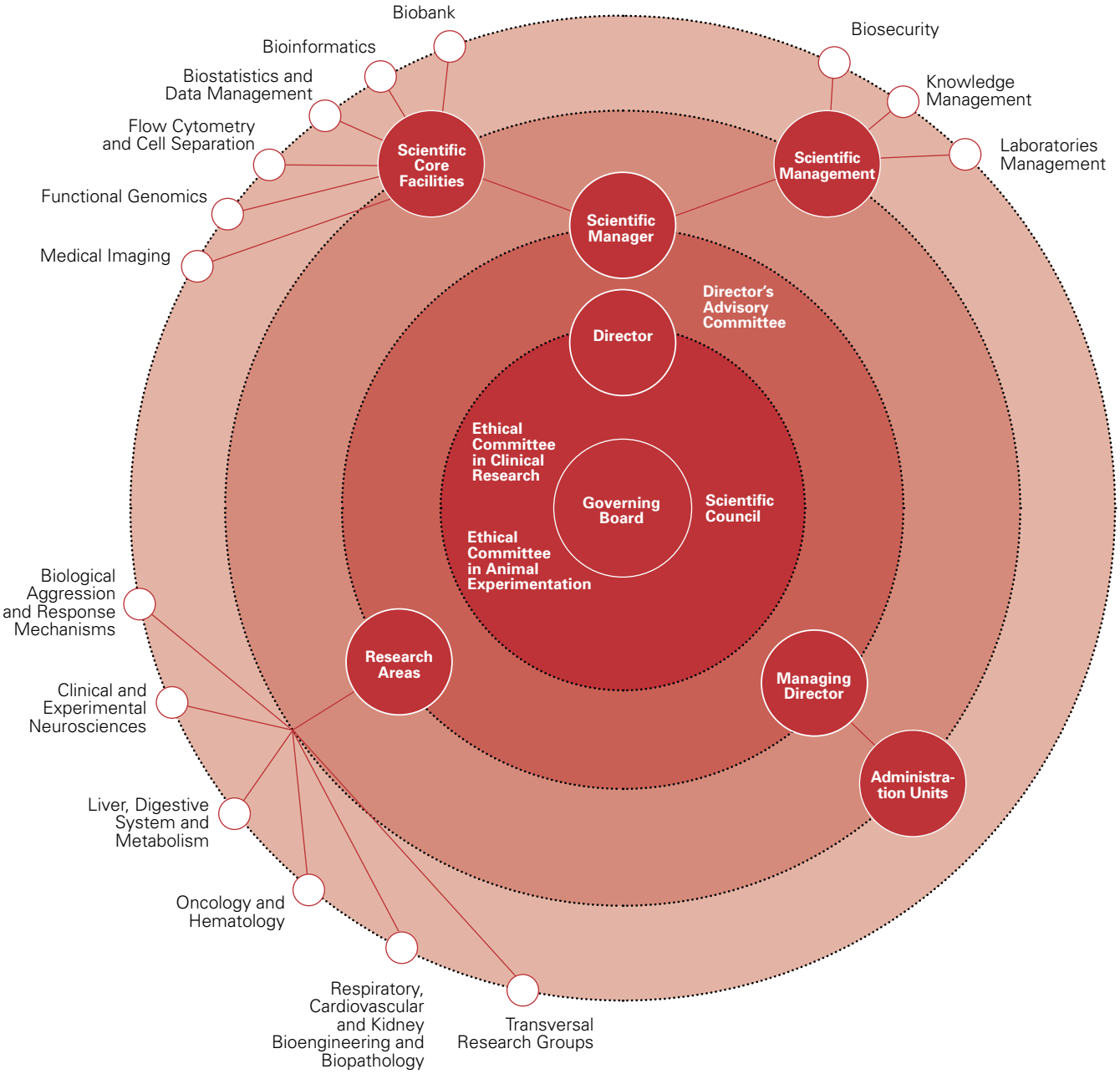
National Coordinator of the RETIC on AIDS
Àlvar Agustí,
CIBERres Scientific Director
Elías Campo
Hospital Clínic Research Director

SECRETARY

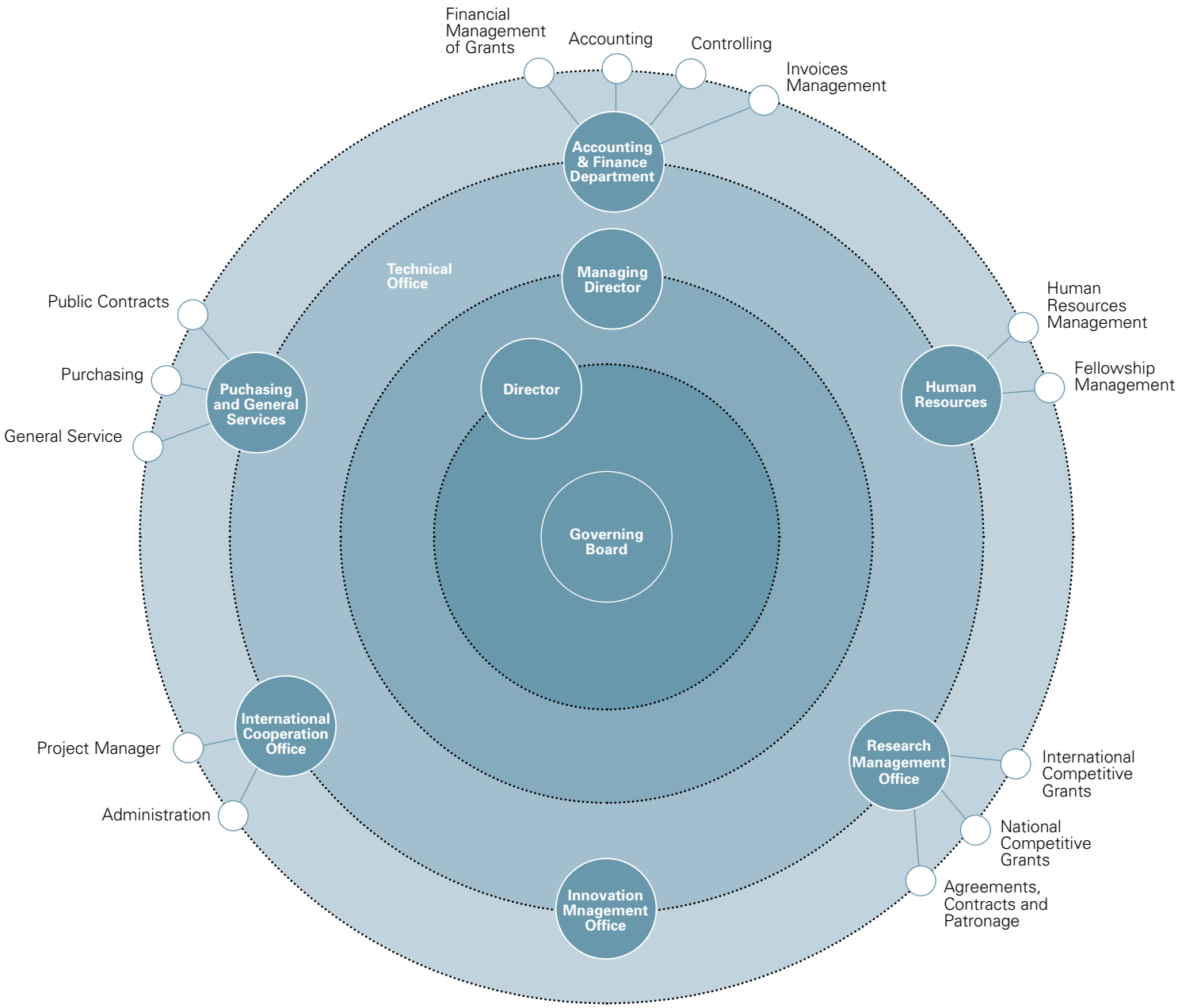
Albert Barberà,
Scientific Manager of IDIBAPS

IDIBAPS Organisational Chart

The organisational charts for IDIBAPS and the Clinic Foundation are shown in the following graphics. With a view to ensuring smooth functioning, the research structure of IDIBAPS is supported by the Management and Administration Departments offered by the Fundació Clínic.



Clinic Foundation Organisational Chart



IDIBAPS RESEARCH AND INNOVATION

Since its creation in 1996, IDIBAPS has shown constant growth of the principal quality indicators for a research centre: the number of scientific publications; the total impact factor; the financial resources; and the contracting of qualified personnel.

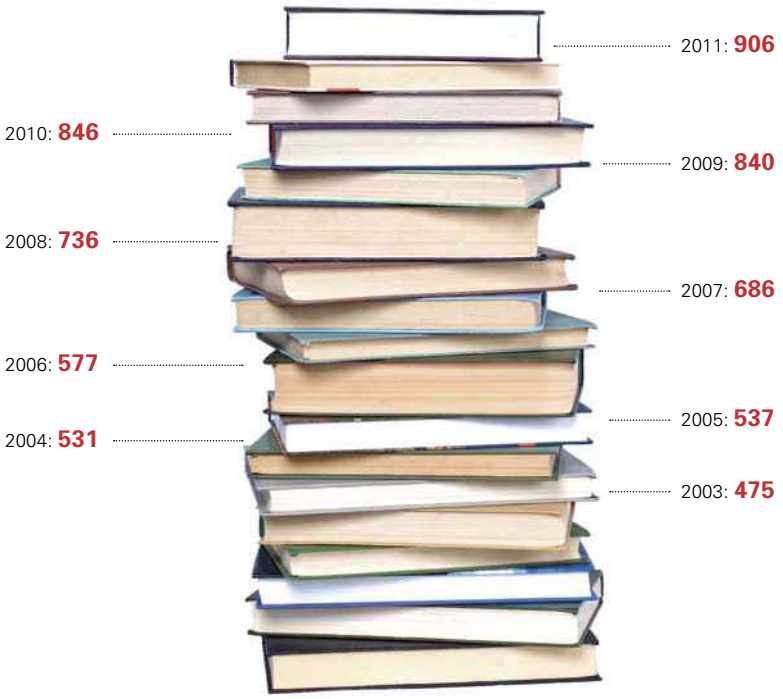
A full description of how these indicators and other success factors have evolved over time is presented below with graphs to provide clarity.

Scientific Output

The number of publications and their impact factor represent one of the most reliable indicators of the competitiveness of a research centre. Both parameters show a clear rising trend in IDIBAPS. In 2011 alone, there were **906 original publications in scientific journals with an impact factor greater than 0.5**.

An original paper is taken to be an article contributing new knowledge as a result of experiments performed by investigators of the Institute. In order to be considered as such, the article must have among its signing authors at least one member of IDIBAPS pertaining to one of the research teams reflected in this Report, with specific mention of IDIBAPS or of the entities within the IDIBAPS Consortium.

ORIGINAL ARTICLES 2003-2011



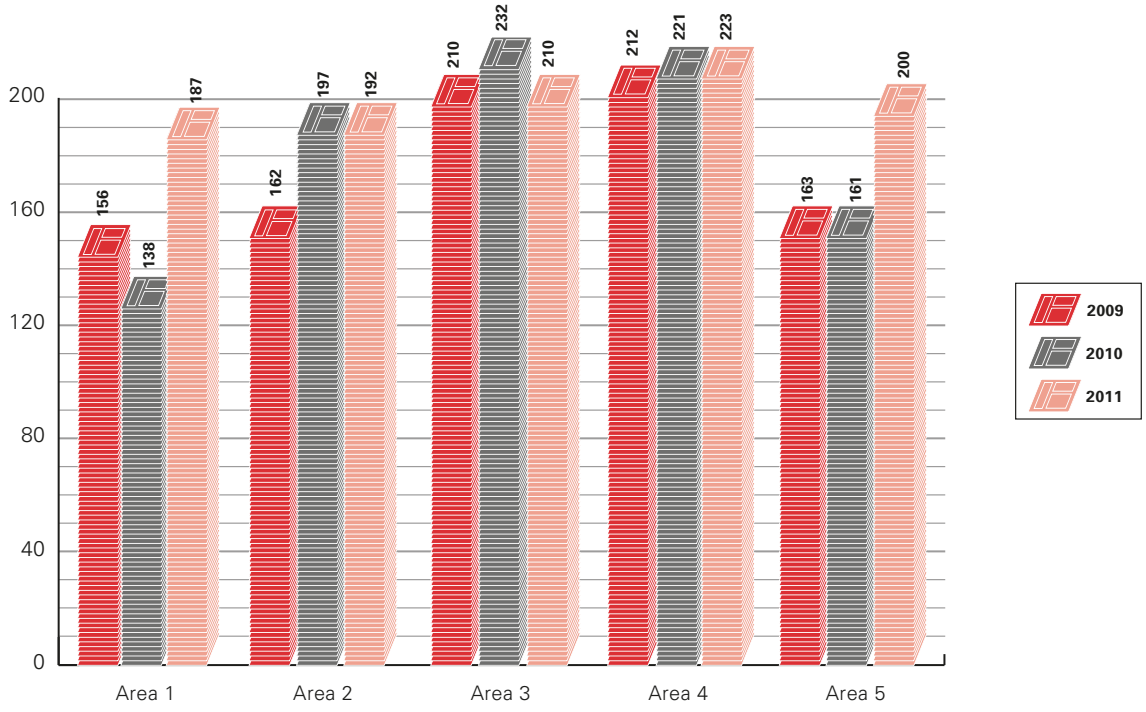
The investigators working for the different institutions that form part of IDIBAPS are distributed into **5 fields of activity**. Each area is divided into different teams that combine in-house research conducted with their own lines of research and cooperation with other teams. Apart from the 5 IDIBAPS areas, this report contains a specific section dedicated to transversal groups doing research in **Primary Care, Nursing, Pharmacology and Clinical Trials**, which also play a very important role in translational research.

The areas reported on are listed below, with graphs showing each area's scientific output – once again, original papers only.

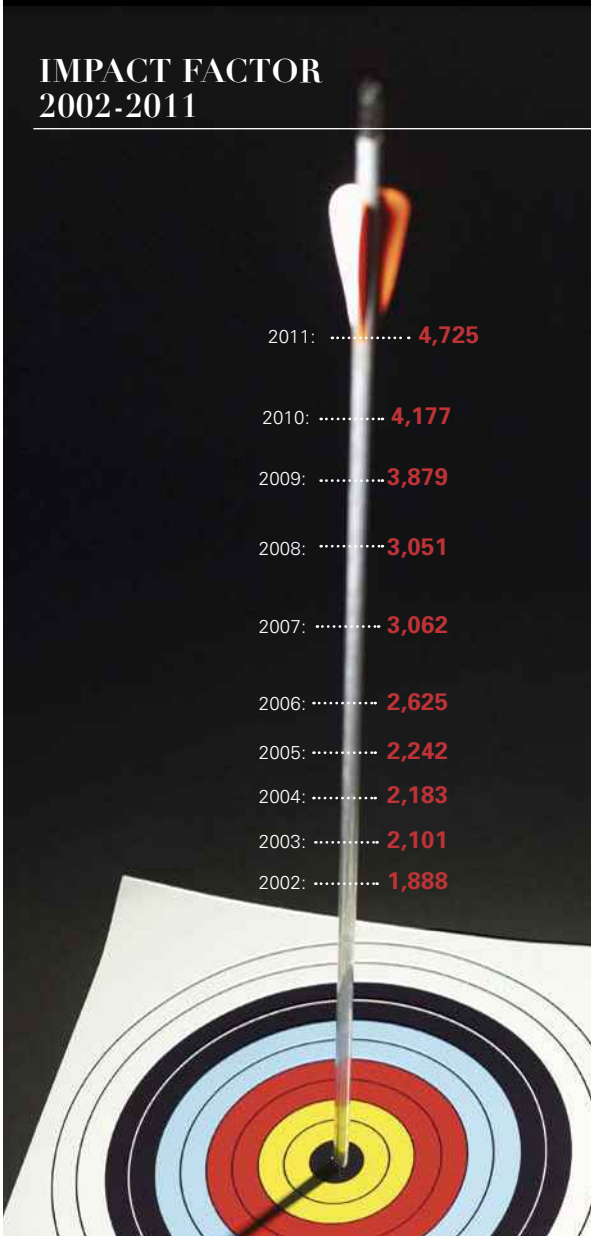
It should be noted that the sum of the articles per area is higher than the institutional total because publications resulting from collaboration between teams in two different areas have been counted once for each area. The graph shows that production in all the areas was of a very high level, and collaboration among areas increased considerably compared with the previous year.

ORIGINAL ARTICLES 2009-2011

1. Biological aggression and response mechanisms
2. Respiratory, cardiovascular and renal pathobiology and bioengineering
3. Liver, digestive system and metabolism
4. Clinical and experimental neuroscience
5. Oncology and haematology



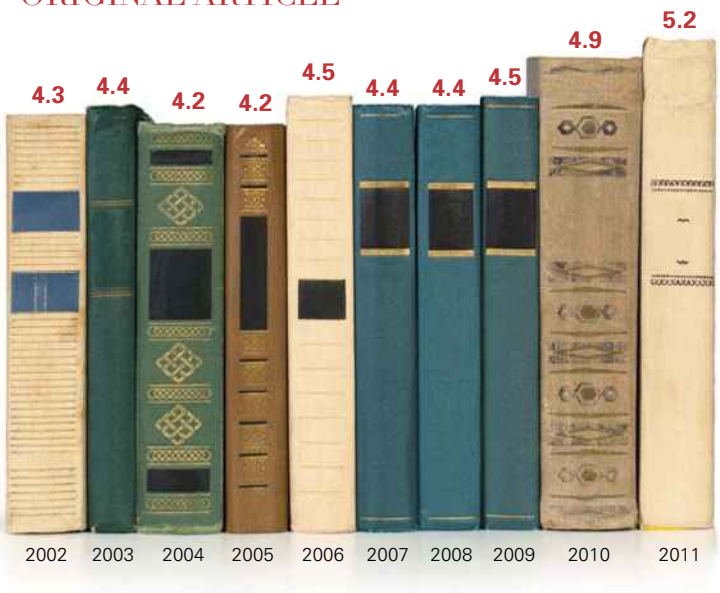
IMPACT FACTOR 2002-2011



The **impact factor** (IF) of the journals in which the articles are published provides a measure or marker of the influence of the research carried out in a given centre. It is based on statistical data from the number of times articles published in a particular journal are cited. Although there are many factors that may be just as, or even more, important in terms of analysing the work carried out by our researchers, the IF is an objective measurement that serves as a guide. In this Report, IF considered are those indicated at the Journal Citation Report 2010 (ISI Web of Knowledge).

The progress made in terms of the total IF for IDIBAPS publications in recent years is shown in the figure on the right side. In 2011, the 906 articles published by IDIBAPS investigators reached a total of **4,725.06** IF points. This means that the mean IF per article published by IDIBAPS in 2011 is **5.22** - a figure that implies a significant increase with respect to the 4.94 recorded in 2010. Added to this, close to 60% of these original papers appeared in journals in the upper quartile of impact in their field. Thus, while the number of publications increases yearly, there has been no drop in quality.

MEAN IMPACT FACTOR / ORIGINAL ARTICLE



Journals Index

This list reflects the 50 journals with the highest Impact Factors in which IDIBAPS investigators published original articles during 2011.

Journal	IF	Total Original Articles
NEW ENGL J MED	53.49	3
NAT GENET	36.38	5
NATURE	36.10	4
LANCET	33.63	2
JAMA-J AM MED ASSOC	30.01	1
LANCET NEUROL	21.66	2
J CLIN ONCOL	18.97	8
LANCET ONCOL	17.76	3
J EXP MED	14.78	2
CIRCULATION	14.43	3
J CLIN INVEST	14.15	2
BRIT MED J	13.47	1
PLOS BIOL	12.47	1
GASTROENTEROLOGY	12.03	6
AM J HUM GENET	11.68	1
HEPATOLOGY	10.89	7
ARCH GEN PSYCHIAT	10.78	1
ANN NEUROL	10.75	3
ARCH INTERN MED	10.64	1
GUT	10.61	8
BLOOD	10.56	22
AM J RESP CRIT CARE	10.19	4
EUR HEART J	10.05	5
CURR BIOL	10.03	1
P NATL ACAD SCI USA	9.77	1

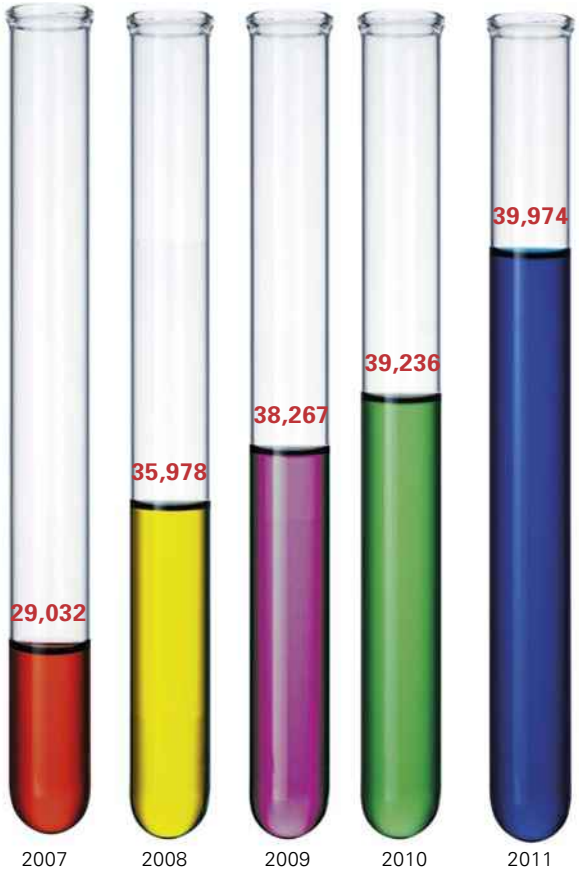
Journal	IF	Total Original Articles
PLOS GENET	9.54	1
J HEPATOL	9.33	9
J ALLERGY CLIN IMMUN	9.27	1
BRAIN	9.23	1
ANN RHEUM DIS	9.08	10
CELL DEATH DIFFER	9.05	1
LEUKEMIA	8.97	2
BIOL PSYCHIAT	8.67	3
ARTHRITIS RHEUM-US	8.44	3
SCHIZOPHRENIA BULL	8.27	3
CANCER RES	8.23	2
CLIN INFECT DIS	8.19	3
HUM MOL GENET	8.06	2
NEUROLOGY	8.02	6
ANN SURG	7.47	2
CLIN CANCER RES	7.34	6
J NEUROSCI	7.27	2
J PATHOL	7.27	2
DIABETES CARE	7.14	3
ARCH NEUROL-CHICAGO	7.11	2
J BONE MINER RES	7.06	1
DIABETOLOGIA	6.97	1
CLIN CHEM	6.89	2
EMERG INFECT DIS	6.86	1
CEREB CORTEX	6.84	1

The number of **editorials (70)** and **reviews (112)** has also been outstanding. This reflects the role of the members of IDIBAPS as opinion leaders. Moreover, also documented in this report are **51 multicentre studies** in which IDIBAPS researchers have actively participated, but without being the main signing authors. These researchers are specifically mentioned in some section or annex of the article as forming part of the study group.

906 originals	**Total IF: 4,725.06**	**Mean IF: 5.22**
112 reviews	588.94	5.26
70 editorials	442.44	6.32
17 guidelines	64.71	3.81
51 multicentre studies	715.54	14.03

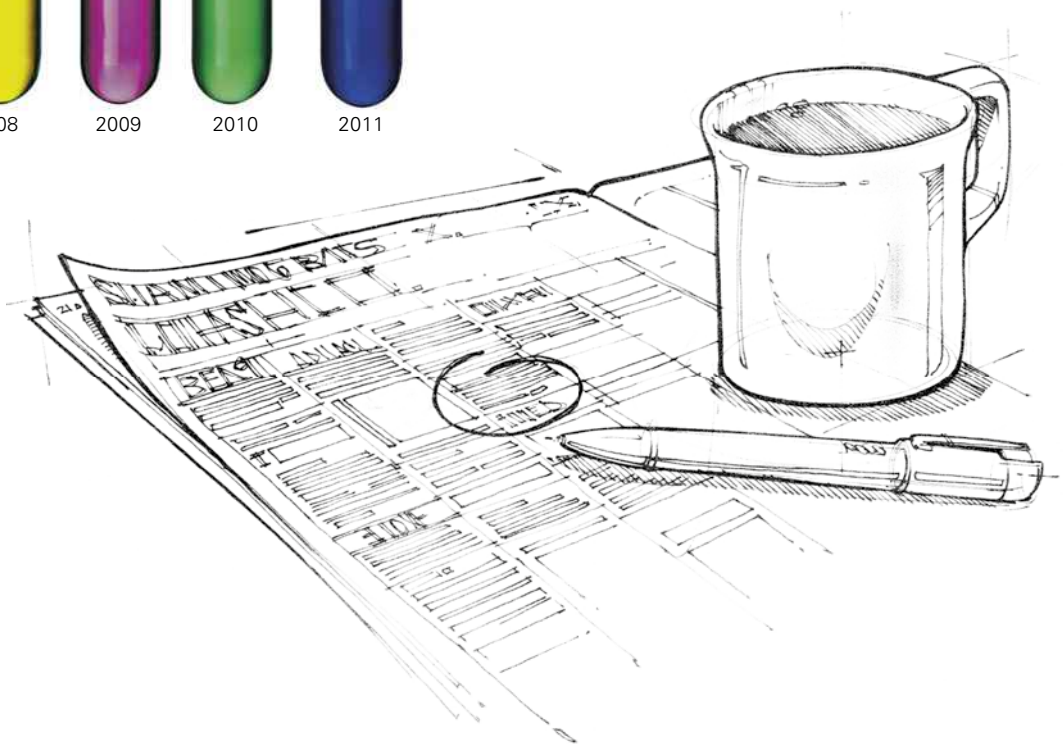
Since the impact factor (IF) refers to the journals and not specifically to the published articles, the graph below shows the number of citations received by the studies published by IDIBAPS investigators (data calculated through the *ISI Web of Knowledge)*:

CITATIONS



The total is **182,487 citations** received by IDIBAPS studies in the last five years. This figure confirms the international projection of the work carried out by this Institute.

Another important aspect to be taken into account is the type of research reflected in the original works published by our investigators. Of note is the fact that **28%** of the original publications listed in this report were the result of **collaboration between two or more IDIBAPS teams**.



Clinical Guidelines

To provide a general overview of IDIBAPS' impact on society, it is important to mention the fact that every year, our researchers participate in the elaboration of international clinical guidelines. These guidelines are not only published in high-impact peer-reviewed journals but also have a tremendous impact on patient care and on society in general. Consequently, IDIBAPS researchers are responsible for setting new trends to be followed in medical practice.

The list below reflects the participation of IDIBAPS investigators in clinical guidelines published in 2011 in international journals subject to peer review. In addition to contributing new data for improving patient treatment, the influence of the IDIBAPS investigators places them at the head of expert committees that establish the new trends to be followed in medical practice. The names of the IDIBAPS investigators are shown in capital letters under the section Authors:

Title	Associated Journal Short Text	Reference	IF	Authors
International Myeloma Working Group consensus approach to the treatment of multiple myeloma patients who are candidates for autologous stem cell transplantation	BLOOD	117 (23): 6063-6073	10.56	Cavo M; Rajkumar SV; Palumbo A; Moreau P; Orlowski R; BLADE J; Sezer O; Ludwig H; Dimopoulos MA; Attal M; Sonneveld P; Boccadoro M; Anderson KC; Richardson PG; Bensinger W; Johnsen HE; Kroeger N; Gahrton G; Bergsagel PL; Vesole DH; Einsele H; Jagannath S; Niesvizky R; Durie BGM; San Miguel J; Lonial S
ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatm	EUR HEART J	32(22):2851-906	10.05	Tendera M; Aboyans V; Bartelink ML; Baumgartner I; Collet JP; Cremonesi A; De Carlo M; Erbel R; HERAS M; Kownator S; Minar E; Ostergren J; Poldermans D; RIAMBAU V; Roffi M; Sievert H; van Sambeek M; Zeller T; Bax J; Auricchio A; Baumgartner H; Ceconi C; Dean V; Deaton C; Fagard R; Funck-Brentano C; Hasdai D; Hoes A; Knuuti J; Kolh P; McDonagh T; Moulin C; Popescu B; Reiner Z; Sechtem U; Sirnes PA; Torbicki A; Vahanian A; Windecker S
Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines	EUR UROL	59(6):1009-18	8.84	Stenzl A, Cowan NC, De Santis M, Kuczyk MA, Merseburger AS, Ribal MJ, Sherif A, Witjes JA.
Comprehensive risk reduction in patients with atrial fibrillation: Emerging diagnostic and therapeutic options Executive summary* of the report from the 3rd AFNET/EHRA consensus conference	THROMB HAEMOSTASIS	106 (6): 1012-1019	4.70	Kirchhof P; Lip GYH; Van Gelder IC; Bax J; Hylek E; Kaab S; Schotten U; Wegscheider K; Boriani G; Ezekowitz M; Diener H; Heidbuchel H; Lane D; MONT L; Willems S; Dorian P; Vardas P; Breithardt G; Camm AJ

Title	Associated Journal Short Text	Reference	IF	Authors
New treatment guidelines for acute bipolar depression: A systematic review	J AFFECT DISORDERS	129 (1-3): 14-26	3.74	Nivoli AMA; COLOM F; Murru A; Pacchiarotti I; Castro-Loli P; Gonzalez-Pinto A; Fountoulakis KN; VIETA E
Guidelines for emergency management of acute heart failure: consensus of the Acute Heart Failure Working Group of the Spanish Society of Emergency Medicine (ICA-SEMES) in 2011	EMERGENCIAS	23 (2): 119-139	3.09	Llorens P; MIRO O; Sanchez FJM; Puente PH; Rodriguez JJ; Gil V; Perello R; Aguirre A; Valero A
Comments on the 2011 ESC/EAS guidelines for the management of dyslipidemias. A report of the Task Force of the Clinical Practice Guidelines Committee of the Spanish Society of Cardiology	REV ESP CARDIOL	64 (12): 1090-1095	2.16	Anguita M; Alegria E; Barrios V; Casasnovas JA; Escobar C; Leon M; Luengo E; Llisterri JL (HERAS M)
Management of patients with palpitations: a position paper from the European Heart Rhythm Association	EUROPACE	13 (7): 920-934	1.84	Raviele A; Giada F; Bergfeldt L; Blanc JJ; Blomstrom-Lundqvist C; MONT L; Morgan JM; Raatikainen MJP; Steinbeck G; Viskin S
National consensus document by GESIDA/National Aids Plan on antiretroviral treatment in adults infected by the human immunodeficiency virus (January 2011 update)	ENFERM INFEC MICR CL	29(3):209.e1-103.	1.66	Panel de expertos de GESIDA y Plan Nacional sobre el Sida (GATELL JM, MALLOLAS J)
SEAIC-SEORL. Consensus Document on Nasal Polyposis. POLINA Project	J INVEST ALLERG CLIN	21 Suppl 1:1-58	1.49	Alobid I; Anton E; Armengot M; Chao J; Colas C; del Cuvillo A; Davila I; Dordal MT; Escobar C; Fernandez-Parra B; Gras-Cabrerizo JR; Ibanez MD; Lluch M; Mateu V; Montoro J; Gili JR; MULLOL J; Navarro AM; Pumarola F; Rondon C; Sanchez-Hernandez MC; Sarandeses A; Soler R; Valero AL; Rhinoconjunctivitis Committee; Spanish Society of Allergy and Clinical Immunology; Rhinology and Allergy Commission; Spanish Society of Otorhinolaryngology

Title	Associated Journal Short Text	Reference	IF	Authors
Multiple chemical sensitivity	MED CLIN-BARCELONA	136(15):683-7	1.41	Alobid I; Alonso JR; Barrot C; Benitez P; Canizares S; Castanyer T; Centellas S; Civeira E; Climent B; Duenas A; FERNANDEZ-SOLA J; Ferrer A; Gene M; Godas T; Gomez E; Montori E; Munne P; NOGUE S; PICADO C; Rovira E; SANZ P; Valero A
Soft tissue sarcomas: clinical practice guidelines	MED CLIN-BARCELONA	136(9):408.e1-8	1.41	Garcia Del Muro X; Martin J; MAUREL J; Cubedo R; Bague S; de Alava E; Pousa AL; Narvaez JA; Ortiz E; Pomes J; Poveda A; Romasanta LP; Tendero O; Viñals JM; Grupo Español de Investigacion en Sarcomas (GEIS)
SEOM clinical guidelines for the treatment of anal cancer	CLIN TRANSL ONCOL	13 (8): 525-527	1.25	MAUREL J; Fernandez-Martos C; Feliu J; Isla D
Hepatocellular and biliary tract carcinomas: SEOM clinical guidelines	CLIN TRANSL ONCOL	13 (8): 536-544	1.25	Feliu J; Sastre J; MAUREL J; Isla D
SEOM guidelines on thrombosis in cancer patients	CLIN TRANSL ONCOL	13 (8): 592-596	1.25	Munoz AJ; VINOLAS N; Cubedo R; Isla D
Recommendations for the treatment of invasive fungal infection caused by filamentous fungi in the hematological patient	REV ESP QUIM	24 (4): 263-270	0.67	Barberan J; MENSA J; Llamas JCV; Ramos IJ; Ruiz JCG; Marin JRC; Tello PB; Massana MB; Vidal JB; Vinas JMC; Huelva FJC; Pons EC; Mediavilla JD; Morfa MLD; Barrigon FE; Avellan PF; Lopez SG; Garcia CG; Maraver DH; de la Guia AL; JIMENEZ JL; Chacon EM; Rubio MO; de Oteyza JP; Ramirez GR; Contreras RR; Barbero AR; Tarrats MR; Felix DR; Godoy PS; Salinas AS; Alonso MA; Torroba JD; Ferreiras DV; Lopez LV; Garcia JMA; Perea JRA; Moreno RC; Cancer RC; Abete JF; Rodriguez JG; Gomez JG; de la Pedrosa EGG; Baranda JMM; Garcia FJP; Camps IR; Lleti MS; Cisneros JD
SEPAR Guidelines for Nosocomial Pneumonia	ARCH BRONCONEUMOL	47 (10): 510-520	0	Blanquer J; Aspa J; Anzueto A; FERRER M; Gallego M; Rajas O; Rello J; de Castro FR; TORRES A

Research Funding

Funding obtained from open calls for funding is one of the main driving forces of research. The table below shows the large number of projects granted in 2011 by different entities that help make the excellence of the IDIBAPS possible:

Public funding	
Funding Institutions	**Number of Projects**
Instituto de Salud Carlos III (ISCIII)	26
Ministerio de Economía y Competitividad (MINECO) - Plan Nacional I+D+i [Ministry of the Economy and Competitiveness – National R&D Plan]	24
European Commission	13
Ministerio de Sanidad, Política Social e Igualdad [Ministry of Health, Social Policy and Equality]	10
National Institute of Health (NIH)	6
Generalitat de Catalunya [Catalan Autonomous Government] - ACC10 i AGAUR	5
Agence Nationale Français de recherches sur le sida et les hépatites virales	1

Private funding	
Funding Institutions	**Number of Projects**
Fundación Mutua Madrileña	3
Asociación Española Contra el Cáncer (AECC) [Spanish Association against Cancer]	2
FIPSE	2
Fundació Marató TV3	2
La Caixa "Obra Social"	1
COIB - Col.legi Oficial Infermeria de Barcelona [Barcelona Official College of Nursing]	1
Caja Navarra	1
MAPFRE	1
Michael J. Fox Foundation for Parkinson	1
Premi Fund. Roche Transplant.	1
Lymphoma Research Foundation	1

IDIBAPS Researchers and Technical Personnel

In the area of **Human Resources**, it should be mentioned that many of the IDIBAPS professionals come from the different institutions that make up the IDIBAPS consortium. The table below shows the origin of the 461 accredited investigators:

Investigators accredited by IDIBAPS	
Hospital Clínic and University of Barcelona	142
Hospital Clínic de Barcelona	184
CSIC - IIBB	34
University of Barcelona	33
IDIBAPS	47
Fundació Clínic	16
ICREA	5
TOTAL:	**461**

Funding obtained in 2011for hiring researchers and technical personnel can come from different sources:

Sources of Funding	Type	No. of Aid Agreements and Contracts
Instituto de Salud Carlos III (ISCIII)	Pre-doctoral Research Grants (FI)	3
	Post-doctoral Research Grants (Sara Borrell)	3
	Senior Researcher Grants - ISIS	1
	Post-residency (Rio Hortega)	6
	Support Technician	1
	Extension of Studies (BAE)	2
Ministry of Science and Innovation (MICINN)	Pre-doctoral Research Grants (FPI)	5
	Pre-doctoral Research Grants (FPU)	5
	Post-doctoral Research Grants (Juan Cierva)	1
	Senior Researcher Grants (Ramon y Cajal)	1
	Support Technician	2
	Short Stays	4
Generalitat de Catalunya	Pre-doctoral Research Grants (FI)	3
	Post-doctoral Research Grants (BP)	1
	Senior Research Grants - ICREA	1
	Pre-doctoral Research Grants (FI)	1
Others	Post-doctoral Research Grants	3
IDIBAPS calls	IDIBAPS Pre-doctoral Research Grants	6
	Post-doctoral Research Grants BIOTRACK	4

Institució Catalana de Recerca i Estudis Avançats (ICREA)

The Catalan Institute for Research and Advanced Studies (Institució Catalana de Recerca i Estudis Avançats, ICREA) is a foundation supported by the Catalan Autonomous Government through the Catalan Ministry of Economy and Knowledge (Departament d'Economia i Coneixement) that aims to recruit top scientists for the Catalan R&D system. IDIBAPS has five ICREA investigators that contribute knowledge, experience and leadership to the teams into which they are incorporated:

Dr. Josep M. Llovet

Translational research group in liver oncology

Dr. Josep Dalmau

Autoimmunity against synaptic antigens

The *Translation research group in liver oncology* was created in 2006 by Dr Josep M. Llovet, ICREA Research Professor for IDIBAPS and Professor of Medicine at the *Mount Sinai School of Medicine*. The group is composed of 8 people from 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 recognised as an Outstanding Research Group by the Catalan Autonomous 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 a grant from the Spanish Association against Cancer (*Asociación Española contra el Cancer, AECC*). Finally, during this year Dr Llovet has been nominated as President of the International Liver Cancer Association (ILCA).

The following are the main contributions made by the group over these last few years:

- Definition of a molecular classification of hepatocellular carcinoma (Chang, Can Res, 2008; Hoshida, *Cancer Res* 2009; Villanueva, *Gastroenterology* 2011; Minguez, *J Hep* 2011)
- 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).
- 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.

The Autoimmunity against Synaptic Antigens team is led by Dr Josep Dalmau i Obrador, ICREA Research Professor at IDIBAPS and Professor of Neurology at the University of Pennsylvania in Philadelphia. Dr Dalmau is a clinical neuro-oncologist 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 memory, behaviour and cognition alterations, and which may cause psychosis. These processes are associated with autoimmune responses characterised by antibodies targeted at synaptic proteins and receptors, such as the glutamate receptors (NMDA, AMPA) or the GABA(B) receptors, or synaptic proteins related with epilepsy (LGI1, Caspr2). Once the antigens have been identified, Dr Dalmau's group's 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.

icrea
Institució Catalana de Recerca i Estudis Avançats

Dr. Albert Pol

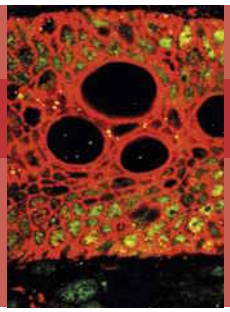
Cell proliferation and signalling

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 pathophysiological 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 particularly focused on the cost to the cell 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 IDIBAPS in 2008 and is the head of the Systems Neurosciences Group, recognised by AGAUR (Agency for Management of University and Research Grants) 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 this function has been altered. Neuron connectivity and cellular and synaptic properties make up brain activity and this, in turn, has effects upon the network. The objective of 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 recovering function. The models of diseases in genetically-modified mice allow us to carry out such studies.
Another of the group's lines of research concerns 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 an integrated project 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. Antonio Postigo

Group on Regulation of Gene Expression in Cell Differentiation and Cancer

Dr Postigo's laboratory investigates the molecular mechanisms involved in the regulation of gene expression during cell differentiation and in cancer. To that effect, our research focuses on ZEB1 (deltaEF1) and ZEB2 (SIP1) factors, key modulators of cell differentiation, stemness maintenance in normal and cancer stem cells, oncogenic transformation, and tumour invasion and metastasis.
The group uses *in vitro* and *in vivo* models to address the following two main research lines:

- Study of the mechanisms by which ZEB1 and ZEB2 regulate tumorigenesis and the epithelial-mesenchymal transition (EMT) during cancer progression.
- Role of ZEB1 and ZEB2 in the regulation of normal hematopoietic differentiation and its malignant transformation

The group's research at IDIBAPS has been funded by, among other sources, grants from the Spanish Ministry for the Economy and Competitiveness (formerly, of Science and Innovation), the European Union, Spanish Association Against Cancer (AECC), La Caixa Foundation, O. Torres Foundation and AVON Cosmetics SAU.

ISIS

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 Cristina Fillat started up at the IDIBAPS in September 2011 with the support of the Instituto de Salud Carlos III ISIS Programme. It has been recognised by the Catalan Autonomous Government as an Outstanding Research Group.

Dr Fillat's group's 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:

- To identify specific cellular pathways and molecular determinants altered in pancreatic tumours.
- Development of antitumour therapies based on oncolytic adenovirus. The main interest is devoted to the search for sensitizers of adenoviral oncolysis and to study their mechanisms of synergy. Special emphasis is also applied to engineering tumour-selective oncolytic adenoviruses.
- To explore novel non-viral experimental therapies for pancreatic tumours.

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 tumour progression and metastatic processes.

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.

Innovation and Transference

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

Taking innovation into consideration is not an additional task in the routine work of researchers, but is a philosophy that is present in all the activities they carry out. It is important for researchers, for patients and for the Institute.
A list is provided below of the patents that have been developed in 2011:

Patents applied for:

Number	Inventors	Owners	Title	Type
EP11382290.2	Elías Campo, Luis Colomo	Europath Biosciences S.L., Fundació Clínic per a la Recerca Biomèdica	Methods for prognosis of diffuse large B-cell lymphoma	Prognostic
P201131310	Raimon Sanmartí, Isabel Haro, Mª José Gómara	CSIC, Fundació Clínic per a la Recerca Biomèdica	Chimeric polypeptides derived from the protein vimentin with utility for the diagnosis of rheumatoid arthritis	Diagnostic
P201130965	Susana Puig	ISDIN, IDIBAPS, Hospital Clínic de Barcelona	Use of photolyase for the reduction or improvement of the subclinical field cancerization associated with actinic keratosis	Treatment
P201131696	Susana Puig	ISDIN, IDIBAPS, Hospital Clínic de Barcelona	Use of photolyase for the reduction or improvement of the subclinical field cancerization associated with actinic keratosis	Treatment
EP11382172	Francisco Lozano, Vanessa Martínez, Rafael Fenutria	Fundació Clínic per a la Recerca Biomèdica, Hospital Clínic de Barcelona, Universitat de Barcelona	New compounds derived from the scavenger-like lymphocyte receptors for use in immunotherapy	Treatment
EP 11382103.7	Sonsoles Sánchez-Palomino, Montserrat Plana Prades, José Alcamí Pertejo	Fundació Clínic per a la Recerca Biomèdica, IDIBAPS, Instituto de Investigaciones Sanitarias Carlos III	Non-replicative virions of the human immunodeficiency virus and their therapeutic applications	Prophylaxis
EP11382174.8	Julián Panés Díaz, Elena Ricart Gómez, Daniel Benítez Ribas	Hospital Clínic de Barcelona, CIBERehd	Tolerogenic dendritic cells and their use in cell therapy	Treatment
P201031183	Ramon Farré, Daniel Navajas, Josep M. Montserrat	Universitat de Barcelona,Hospital Clínic de Barcelona, CIBER de Enfermedades Respiratorias, IDIBAPS	Device for generating upper airway obstruction in animals	Experimental
EP11382174.8	Julián Panés Díaz, Elena Ricart Gómez, Daniel Benítez Ribas	Hospital Clínic de Barcelona, CIBER de Enfermedades Hepáticas y Digestivas	Tolerogenic dendritic cells and their use in cell therapy	Treatment
US2011/055391	Francesc Balaguer, Meritxell Gironella, Juan José Lozano, Leticia Moreira, Antoni Castells, Ajay Goel, Richard C. Boland	Baylor Research Institute, Hospital Clínic de Barcelona, CIBER de Enfermedades Hepáticas y Digestivas	MicroRNAs (miRNA) as biomarkers for the identification of familial and non-familial colorectal cancer	Diagnostic
US Application Serial Number: 13/419,744	Ajay Goel, Richard C. Boland, Francesc Balaguer	Baylor Research Institute	LINE-1 hypomethylation as a biomarker for early-onset colorectal cancer	Diagnostic
US PTO 61/604,058	Antoni Castells, Luis LaSalvia, Aurea Mira, Míriam Cuatrecasas, Christoph Petry	Hospital Clínic de Barcelona, Siemens Healthcare	Gene-expression signature of tumor recurrence in patients with stage II and III colon cancer treated with 5'fluoruracil-based adjuvant chemotherapy	Diagnostic

Number	Inventors	Owners	Title	Type
PCT/ EP2011/056270	Andrés Pablo Montefeltro, Gabriel Alvarado Urbina, Analía Bortolozzi Biassoni, Francesc Artigas Pérez, Miquel Vila Bover	Nlife Therapeutics	Compositions and methods for selective delivery of oligonucleotide molecules to specific neuron types	Treatment
US 61/550,148	Meritxell Gironella, Antoni Castells, Juan José Lozano Salvatella, Maria Dolores Giráldez	CIBER de Enfermedades Hepáticas y Digestivas, Hospital Clínic de Barcelona	Plasma microRNAs for the detection of early colorectal cancer.	Diagnostic

Patent Cooperation Treaty (PCTs):

Number	Inventors	Owners	Title	Type
PCT/ EP2011/053127	Albert Sanchez-Fueyo, Juan José Lozano, Marc Martínez Llordella, Antoni Rimola Castella, Felix Bohne	HCB, CIBERehd	Method and kit for the diagnosis of tolerance in liver transplantation using liver tissue	Diagnostic

Patents in course of transference:

Number	Inventors	Owners	Title	Type	Licence Holder
ES200902164	Miguel Morales, Xavier Gasull, Francesc Rabanal, Ángel Acebes, Alberto Ferrús, Jesús Pintor	Universitat de Barcelona, CSIC, IDIBAPS, UCM, CIBIR	Peptides for the treatment of ocular hypertension and/or glaucoma	Biotech	ProRetina
B-3774-09	Raimundo Lozano Raví	Hospital Clínic de Barcelona	OntoDDB	Software	Setting
EP11382172	Francisco Lozano, Vanessa Martínez, Rafael Fenutria.	Fundació Clínic per a la Recerca Biomèdica, Hospital Clínic de Barcelona, Universitat de Barcelona	New compounds derived from the scavenger-like lymphocyte receptors for use in immunotherapy.	Biotech	Immunovative Developments
AF0962029	Eduard Gratacós Solsona Ivan Amat Roldan	Fundació Clínic per a la Recerca Biomèdica, Hospital Clínic de Barcelona, Universitat de Barcelona	AQUA characterization software	Secreto Industrial	Transmural Biotech
US 7867475	F. Sanchez-Madrid, Carlos Martinez-A, D Sancho Madrid, P Engel, E. Esplugues Artola, J Vega Ramos, P Lauzurica Gómez	Universidad Autónoma de Madrid	Immune regulation based on the depletion of CD69+ cells	Biotech	Albor Biologics (USA)
US 20110081292	F. Sanchez-Madrid, Carlos Martinez-A, D Sancho Madrid, P Engel, E. Esplugues Artola, J Vega Ramos, P Lauzurica Gómez.	Universidad Autónoma de Madrid	Immune regulation based on the depletion of CD69+ cells. Methods of Treating Viral Hepatitis.	Biotech	Albor Biologics (USA)
US 20110165071	F. Sanchez-Madrid, Carlos Martinez-A, D Sancho Madrid, P Engel, E. Esplugues Artola, J Vega Ramos, P Lauzurica Gómez	Universidad Autónoma de Madrid	Immune regulation based on the depletion of CD69+ cells. Methods of Treating Cancer.	Biotech	Albor Biologics (USA)

SPIN-OFF COMPANIES

The knowledge generated by IDIBAPS usually completes its cycle when transferred to 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)
This spin-off company launched by Dr Francisco Lozano was created in February 2010, based on the transference of two patents pertaining to the University of Barcelona, Hospital Clínic de Barcelona and the Clínic Foundation for Biomedical Research. IND's activity focuses on the development of new biological therapies for the prevention and treatment of inflammatory disorders with an immune basis.
For further information: www.immunnovative.com

BIONURE (2009)
Spin-off from Hospital Clínic/IDIBAPS and CSIC for the development of new neuroprotective drugs for the treatment of multiple sclerosis and other neurological diseases. Bionure was launched by Dr Pablo Villoslada.
For further information: www.bionure.com

TRANSMURAL BIOTECH (2009)
Spin-off from Hospital Clínic and UB, created by Dr Eduard Gratacós, for the development and commercialization of different diagnostic devices in the gynaecology field.
For further information: www.transmuralbiotech.com

LINKCARE (2009)
Linkcare HS administers a Patient-Centred, Case-Management oriented Open Health Care model that has been designed as a joint effort of several leading medical care research centres in Europe led by Hospital Clínic. It was launched by Dr Josep Roca. Linkcare's Open Source platform 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. Linkcare application main areas are: Chronicity, Fragility, End of Life Care, Reproduction and Perinatology, Wellness and Clinical Research.
For further information: info@linkcare.es

NEUROTEC PHARMA (2006)
This R&D company founded by Dr Nicole Mahy centres its activity on 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 (MS), Amyotrophic Lateral Sclerosis (ALS), Parkinson's Disease (PD) and Alzheimer's Disease (AD).
For further information: www.neurotec-pharma.com

Clinical Trials

IDIBAPS is 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 quality specialised healthcare practice, are aspects of IDIBAPS that can be very useful for the development of drugs.

The table below summarizes the number of clinical trials approved by the Ethical Committee in Clinical Research (ECCR) in the past years. Of note is the large number of clinical trials designed and sponsored by the IDIBAPS investigators themselves:

CLINICAL TRIALS APPROVED BY THE IEC

Year	Clinical Trials presented to the ECCR	Clinical trials promoted by IDIBAPS investigators
2010	219	12
2011	232	26

Clinical trial type	Approved in 2011
Single-centre trial	16
Multicentre (reference ethics committee)	39
Multicentre (concerned ethics committee)	123
Observational/non-comparative phase IV study	32
Medical devices	20
Other	2
Total	**232**

SCIENTIFIC CORE FACILITIES

High-level biomedical research requires the use of high-cost techniques and equipment. In addition, the high complexity of many of these techniques requires the dedication of specialised personnel. In many cases a given technique is applied by different research teams without any of them requiring exclusive and permanent use of the methodology.

IDIBAPS promotes the setting up of common service 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.

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

- Biobank of Hospital Clínic – IDIBAPS (Page 30)
- Bioinformatics (Page 33)
- Biostatistics and Data Management (Page 34)
- Cytometry and Cell Sorting (Page 35)
- Functional Genomics (Page 36)
- Medical Imaging (Page 37)

Biobank of Hospital Clínic - IDIBAPS

INTRODUCTION

The Biobank is a centralised institutional support core facility for coordinating the collection, processing, storage and transfer of human biological samples to promote biomedical research of the highest standard.

With the aim of optimizing the human resources and equipment in the Biobank, this facility offers a wide range of services for the processing and analysis of the samples collected by the research groups.

All the procedures performed at the Biobank are carried out under ISO9001 certification.

When it was first set up, the Biobank had a dual mission:

- To provide the scientific community with standard, well-characterised biological samples with high added value, in order to promote, foster and develop biomedical research in accordance with current legislation
- To standardise all the Institute's research sample collections (in accordance with article 67 of Law 14/2007 and Royal Decree RD1716/2011 related to Biomedical Research with human samples)

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 cadavers 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 tumour and non-tumour 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.
Visit the web: **www.clinicbiobanc.org**

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

- Nerve tissue from cadaveric donors affected by neurologic diseases.
- Frozen and paraffin-embedded tissues representing the most common neoplasms.
- 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 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).
- Lasser microdissection.
- Tissue microarray construction (TMA).
- Histological staining.
- Definitive neuropathological diagnosis of neurological diseases.
- 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.

EQUIPMENT

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

NEUROLOGICAL TISSUE BANK

- Cubicles for obtaining the material under sterile conditions.
- Instruments for preparing samples for the microscope.
- Filing cabinets for collecting paraffined samples.
- Gas filtration cabinet.
- Automated immunostaining appliance.
- Combination refrigerator and -40ºC freezer for preserving fungibles.
- Autoclave for sterilising surgical material.

TUMOUR BANK

- Equipment for preparing tissue microarrays (TMAs): TMA Master (3Dhistech) (UB Faculty of Medicine / FEDER).
- LaserTissue microdissection microscope with laser 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).

BLOOD AND FLUID BIOBANK

- Programmable freezer with a controlled freezing ramp.
- "Chemagic MSM1®" automated device for obtaining DNA from large volumes of blood.
- "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.
- ABF500 Automated Blood Fractionation system (RTS).

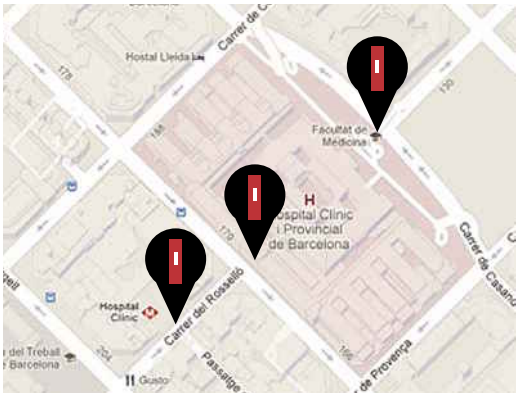
LOCATION

Neurological Tissue Bank
Faculty of Medicine UB
South wing, floor 0

Tumour Bank
CEK building
c/ Rosselló, 149-153, planta -1
Servei d'Anatomia Patològica (Hospital Clínic)
c/ Villarroel, 170. Escala 3, planta 5

Blood and Fluid Bank
CEK building
c/ Rosselló, 149-153, planta -1

Contact: **biobanc.idibaps@clinic.ub.es**



PEOPLE

SCIENTIFIC COORDINATOR

Anna Bosch Comas, PhD (IDIBAPS)

STAFF

- **Joan Albert Barberà**, MD, PhD (Hospital Clínic)
  Director
- **Meritxell Rufet** (Fundació Clínic)
  Assistant Manager
- **Ángela Martín** (Fundació Clínic)
  Informed Consent Manager
- **Esther Barnadas** (IDIBAPS)
  Lab Manager

Neurological Tissue Bank

Manager: **Ellen Gelpí**, MD, PhD (IDIBAPS)

- **Maria Jesús Rey**, MD, PhD (UB)
  Neuropathologist. Senior Technician
- **Carina Antiga** (IDIBAPS)
  Secretary
- **Sara Charif** (IDIBAPS)
  Laboratory Technician
- **Rosa Rivera** (UB)
  Specialised Technician
- **Abel Muñoz** (Fundació Clínic)
  Autopsy Assistant
- **Leire Etxarri** (Fundació Clínic)
  Autopsy Assistant

Tumour Bank

Manager: **Miriam Cuatrecasas**, MD, PhD (Hospital Clínic)

- **Laura Gelabert** (Fundació Clínic)
  Laboratory Technician
- **Mónica Marín** (Hospital Clínic)
  Laboratory Technician
- **Raquel Bermudo Gascón**, PhD (Fundació Clínic)
  Tumour Bank Manager
- **Blanca Noemí Luján**, MD,
  PhD (Hospital Clìnic - IDIBAPS)
  Pathologist and Website Manager
  for the Catalan Tumour Bank Network
  (*Xarxa de Bancs de Tumors de Catalunya*)

Blood and Fluid Bank

Manager: **Verónica Fernandez Pascual**, PhD (IDIBAPS)

- **Anna Morales** (IDIBAPS)
  Laboratory Technician
- **Regina Cañaveras** (Fundació Clínic)
  Laboratory Technician

Bioinformatics

INTRODUCTION

The Bioinformatics Unit is mainly devoted to analysis and support in the interpretation of data coming from OMICS disciplines (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.
Visit the web: bioinformatics.fcrb.es

SERVICES

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

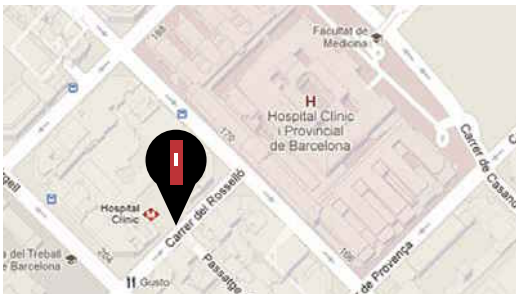
- **Consultancy and Analysis:** counselling in experimental design; low-level and quality-control analyses; orientation on biostatistical resources; assistance in tools utilisation; intensive analysis of OMICS technology data in collaborative settings; interpretation of results.
- **Administration of Bioinformatic 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:** course and seminar 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.

LOCATION

CEK building
C/ Roselló 149-153, -1 Floor.
Bioinformatics Core Facility CEK
bioinformatica.idibaps@clinic.ub.es



PEOPLE

SCIENTIFIC COORDINATOR
Susana Kalko, PhD. (IDIBAPS)

STAFF
- **Joan Protasio** (IDIBAPS) Technician

Biostatistics and Data Management

INTRODUCTION

The Biostatistics and Data Management Platform provides methodological and statistical support for research projects carried out by IDIBAPS and allied institutions. Depending on projects and availability, the platform may provide support to external public and private entities.

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:

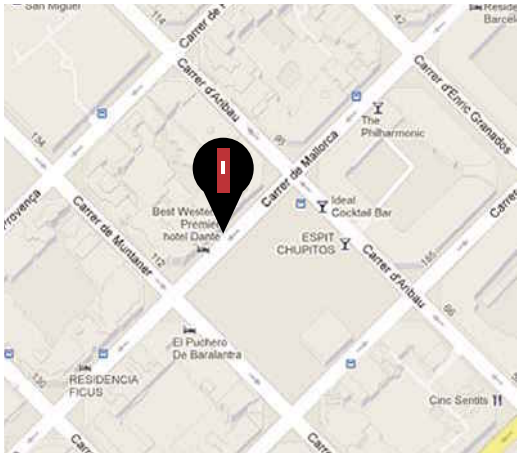
- Creation and maintenance of a clinical trial data base: (a) creation of the eCRF (electronic case report form); (b) creation and consensus of Data Management and Validation Plans with the research team; (c) traceable data export to analysis systems.
- Statistical analysis of clinical trials or other 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.

LOCATION

Biostatistics and Data Management Core Facility
IDIBAPS (Institut d'investigacions Biomèdiques August Pi i Sunyer)
Hospital Clinic Barcelona
183, Mallorca Street, floor -1, 08036 Barcelona
ftorres1@clinic.ub.es

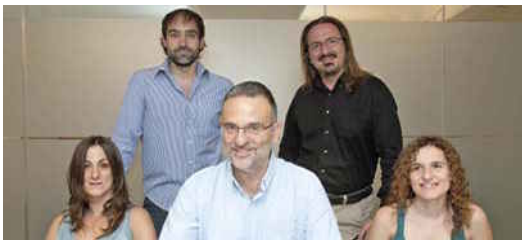


PEOPLE

SCIENTIFIC DIRECTOR:
Ferran Torres MD, PhD. (IDIBAPS)
Scientific Director

STAFF

- **José Ríos** (IDIBAPS)
  Scientific Coordinator
  Training and Consultancy Manager
- **Abiguei Torrents** (Fundació Clínic – CAIBER)
  Junior Statistician
- **José Fernández Sardiña**
  (Fundació Clínic – CAIBER)
  Data Management Manager
- **Sandra Serrano** (Fundació Clínic – CAIBER)
  Data Management



Cytometry and Cell Sorting

INTRODUCTION

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.

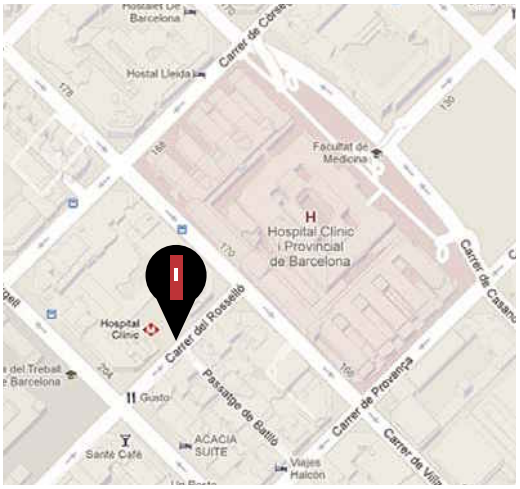
Fluorescence-activated cell sorting is a specialised type of flow cytometry. It provides a method for sorting a heterogeneous mixture of biological cells, one cell at a time, based on the specific light-scattering and fluorescent characteristics of each cell. It provides fast, objective and quantitative 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 in flow room; data analysis room; and cell sorting room.

LOCATION

CEK building
C/ Roselló 149-153, -1 Floor.
citometria.idibaps@clinic.ub.es



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

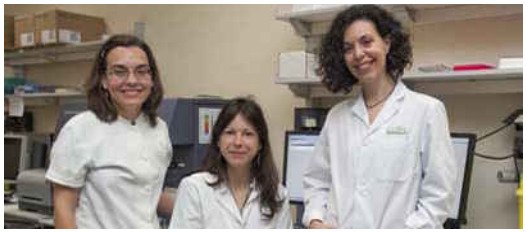
- BD FACSCalibur: 2 LASER, Up to 4 fluorescence.
- BD FACSCantol : 2 LASER, Up to 6 fluorescence.
- BD FACSCantoII: 3 LASER, Up to 8 fluorescence.
- BD LSRFortessa SORP + HTS: 4 LASER, Up to 16 fluorescence.
- BD LSRFortessa SORP: 5 LASER, Up to 18 fluorescence.
- AMNIS ISX : 2 digital cameras, Up to 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.

PEOPLE

SCIENTIFIC COORDINATOR AND HEAD OF FACILITY:
Isabel Crespo (IDIBAPS)

STAFF

- **Cristina López** (IDIBAPS)
  Specialist Technician
- **Laia Llinas** (IDIBAPS)
  Specialist Technician



Functional Genomics

INTRODUCTION

The IDIBAPS Genomic 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 and gene-dose analysis using different platforms including real-time PCR and microarrays.

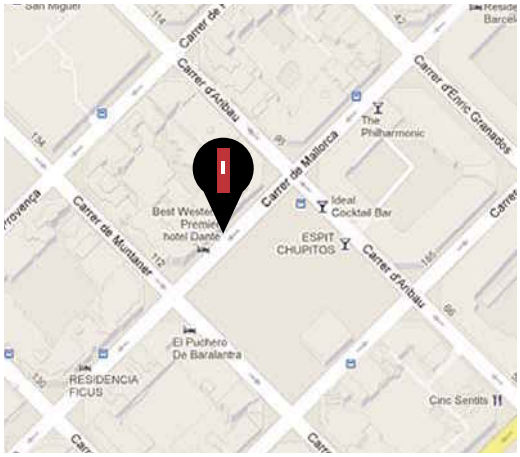
SERVICES

- Quantification of nucleic acids.
- Qualitative analysis of nucleic acids.
- Expression analysis by Real-time PCR.
- Genotyping analysis by Real-time PCR.
- 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).
- Scanner Axon 4000B.
- Pyrosequencing.
- Next-generation sequencing (Illumina).

In addition to these services, the Core Facility offers advice on experimental design for transcriptomic studies, on extracting RNA and on analysis of microarray data.

LOCATION

CEK building
C/ Roselló 149-153, -1 Floor.
genomica.idibaps@clinic.ub.es



EQUIPMENT

- NanoDrop.
- Sinergy2.
- Bioanalyzer 2100 (Agilent).
- Viia7 (Applied Biosystems).
- Fluidigim (BioMark).
- GeneChip Affymetrix genetic analysis system.
- GeneTitan Affymetrix genetic analysis system.
- Agilent platform.
- Axon 4000B scanner.
- PyroMark Q96 ID.
- GenomeAnalyzer IIx (Illumina).

PEOPLE

SCIENTIFIC COORDINATOR:
Pedro Jares, PhD. (HC-UB)

STAFF

- **Elías Campo**, MD, PhD. (HC-UB)
  Scientific Director
- **Magda Pinyol**, PhD. (IDIBAPS)
  Unit Manager
- **Montse Sánchez** (IDIBAPS)
  Technician
- **Laura Plà** (IDIBAPS)
  Technician
- **Helena Suárez**, PhD. (IDIBAPS)
  Specialist Technician
- **Anna Enjuanes**, PhD. (IDIBAPS)
  Specialist Technician

Medical Imaging

INTRODUCTION

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

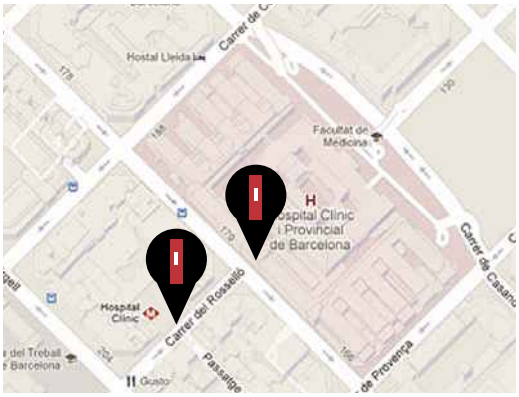
- Clinical Imaging Research (3T MRI Unit).
- Experimental Imaging Research (7T MRI Unit).
- Imaging Processing Lab.

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 post-processing
  - 10 standard PC
  - Software licences: 10 Matlab, 2 LcModel, 1 AnalyzeDirect

LOCATION

3T MRI Unit 7T MRI Unit:
Hospital Clinic de Barcelona, floor 0, 3a stairs
Mri3t.idibaps@clinic.ub.es
Mri7t.idibaps@clinic.ub.es
Post-processing Imaging Lab:
CEK building
C/ Roselló 149-153, -1 Floor.
Imatge.idibaps@clinic.ub.es



PEOPLE

SCIENTIFIC COORDINATOR
Clinical Imaging Research
(3T MRI Unit):
Núria Bargalló Alabart, MD, PhD.
(Hospital Clínic)

STAFF
Experimental Imaging Research (7T MRI Unit)

- **Guadalupe Soria Rodríguez**, PhD. (IDIBAPS)

Image Analysis Advisor

- **Raúl Tudela**, PhD. (CIBER-BBN, GIB-UB)
  CIBER-BBN, GIB-UB

Image Processing Lab

- **Carles Falcón Falcón**, PhD. (IDIBAPS)

NETWORKING

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

- **IDIBAPS participates in all nine Spanish Biomedical Research Centres of the Instituto de Salud Carlos III (ISCIII).** A total of 27 research groups from IDIBAPS participate in these national networks and 3 of them are coordinated by an IDIBAPS researcher: CIBER of Diabetes and Metabolic Diseases; CIBER of Hepatic and Gastrointestinal Diseases; and CIBER of Respiratory Diseases.
- **IDIBAPS' researchers also participate in 11 National ISCIII Networks**, 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 Consumer Protection Programme**, IDIBAPS participates in 56 projects, coordinating 14 of them.
- IDIBAPS' researchers also participate in **many international consortiums** 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 Hepatocellular Carcinoma International (HCC) Genomic Consortium.

Spanish Biomedical Networks (CIBERS, RETICS and CAIBER)

In the last few years, much of the financial support provided by the Instituto de Salud Carlos III (Spanish Ministry of the Economy and Competitiveness) has been geared towards the consolidation of the Spanish National Research Networks, an initiative that includes the Networked Biomedical Research Centres (*Centros de Investigación Biomédica en Red, CIBERs*), Cooperative Research Topic Networks (*Redes Temáticas de Investigación Cooperativa en Salud, RETICs*), and the Networked Biomedical Research Support Consortium – Spanish Clinical Trials Platform (*Consorcio de Apoyo a la Investigación Biomédica en Red - Plataforma Española de Ensayos Clínicos, CAIBER*), which represent a new way of understanding cooperative biomedical research that has given excellent results over recent years.

IDIBAPS participates in most of these virtual research structures and leads a number of them. Investigators of the IDIBAPS direct the following networks:

- Networked Biomedical Research Centre for Hepatic and Digestive Diseases (*Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, CIBERehd*).
- Spanish Biomedical Research Centre in Diabetes and Associated Metabolic Disorders (*Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas, CIBERDEM*).
- Networked Biomedical Research Centre for Respiratory Diseases (CIBERES).
- AIDS Research Network (RIS).
- Spanish Multiple Sclerosis Network (REEM).

NETWORKED BIOMEDICAL RESEARCH CENTRE FOR HEPATIC AND DIGESTIVE DISEASES

(Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, CIBERehd)

Director: Dr Jaume Bosch

www.ciberehd.org

CIBERehd was created on 29 November 2006, and is presently composed of 45 groups (and six others on *ad honorem* basis), corresponding to 31 centres in 10 Autonomous Regions throughout Spain. Its Scientific Director is Prof. Jaume Bosch, and its activities are supervised by an External Advisory Board and Scientific Committee. Its central facilities are located in Calle Córcega 180, in Barcelona.

The objectives of the CIBER for Hepatic and Digestive Diseases are:

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

CIBERehd's scientific activity is essentially focused on its research programmes and strategic actions, and is complemented by the training programme, the scientific and technological platforms and common resources. 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.

CIBERehd has 6 major research programmes:

- 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.

Its budget, totalling €5.3 million in 2011, covers the salaries of the investigators integrated in its different groups, scientific infrastructure, training programmes and strategic actions – involving the implementation of large research projects that can only be addressed through firm cooperative action.

CIBERehd's activity is reflected in its annual report, which includes the publication of over 200 articles per year in top journals (first upper quartile of the SCI) and clinical guidelines, as well as the conducting of over 50 clinical trials. Sixty-four cooperative studies are ongoing at present.

NETWORKED BIOMEDICAL RESEARCH CENTRE IN DIABETES AND ASSOCIATED METABOLIC DISORDERS

(Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas, CIBERdem)

Director: Dr Ramon Gomis

ciberdem

Centro de Investigación Biomédica en Red de
Diabetes y Enfermedades Metabólicas Asociadas

www.ciberdem.org
www.investigaladiabetes.org

The CIBER in Diabetes and Associated Metabolic Disorders is made up of 31 elite research groups in 19 associate institutions. It represents the biggest network of scientific diabetes research in Spain. Its objectives are to achieve the highest standards of research practice and to accelerate the translation of scientific results into clinical applications. With the aim of achieving pioneering biomedical advances, CIBERdem promotes the development of projects in collaboration with other national and international institutes and it has two of its own technological platforms: the Biobank and the Metabolomics Platform.

The consortium seeks to involve not only the scientific community, but also the business sector, in R&D investment. It offers companies the possibility of working together on research projects, scientific consultancy, organisation of scientific events and socially-responsible corporate actions. Furthermore, it disseminates and divulges its scientific work through multiple actions such as the periodic organisation of scientific seminars and its annual Science Open Day, always with the active collaboration of patients' associations.

In its effort to continue supporting the work of its research groups, CIBERdem has implemented a strategic fundraising plan (investigaladiabetes.org) to generate active participation from the business world and society in general, with the objective of collecting funds which will enable us to continue to promote and finance scientific activity in order to find new means of preventing, diagnosing, treating and curing diabetes. Worthy of special note in 2011 was the launch of the 'Amicus Canis' and 'Pilchardus' projects (both in collaboration with IDIBAPS) and diabetesalacarta.org (in collaboration with the Alícia Foundation).

At CIBERdem, despite the recession, researchers have battled on with their projects and have made significant achievements, even though they have been obliged to restructure or downsize their teams or be much more sparing in their use of materials. It was extraordinary and highly stimulating to see how, year after year, we were able to discuss new proposals and, in the majority of cases, give a positive answer. However, countries with a solid scientific tradition show us that now is the time to make better use of our scientific structures, to put a little extra effort into our work, be more rigorous in our priorities and sharpen our wits, in order to make the most of the results we have obtained. It is also a time to look outside our frontiers to Europe and try to obtain funding from beyond our own borders.

CIBERdem has made significant advances which are of great importance to our health system, such as the Di@bet.es Study, which provides us with accurate information on the prevalence of diabetes in the Spanish population, and the results obtained by researchers using the Metabolomics Platform. They are collective achievements, a general effort made by all our researchers.

NETWORKED BIOMEDICAL RESEARCH CENTRE FOR RESPIRATORY DISEASES

(Centro de Investigación Biomédica en Red de Enfermedades Respiratorias, CIBERES)

Director: Dr Àlvar Agustí

www.ciberes.org

The CIBER for respiratory diseases (CIBERES) is a networked, multidisciplinary and multicentre research institution integrating basic, clinical and populational research in respiratory illnesses. CIBERES is composed of 34 research groups, 60% of which belong to hospitals and 40% to universities and research centres. The Scientific director of CIBERES is Dr Alvar Agustí (Chest Institute, Hospital Clinic). The administrative centre of CIBERES is in the Fundació Caubet-Cimera in Mallorca.

CIBERES' research activity is structured on 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 addresses a relevant healthcare problem in the field of respiratory disease. At present, CIBERES has 10 active PCIs:

- 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 organised a series of research support platforms, such as: (1) Pulmonary Biobank; (2) Technological Development and Transference; (3) Training Programme; and (4) Communications Department. CIBERES organises annual scientific sessions and a number of different monographic research seminars.

AIDS RESEARCH NETWORK

(Red de Investigación en Sida, RIS)

Director:
Dr Josep Maria Gatell

www.retic-ris.net

The AIDS Research Network (Red de Investigación en SIDA - RIS) was created in 2003 and established the basis for driving original and innovative research in the field of AIDS. In its second operating period (2007-2011), the Network became consolidated and focused its activity on the creation of common platforms (Cohorts, Biobank, Laboratories and Resistance) that generate data and biological samples on which the research strategies are founded (clinico-epidemiological, clinico-therapeutic, immunopathogenesis and vaccines). The network's priorities are projects that require a network in order to be implemented, and issues that are relatively specific to Spain, or in which we are able to make high-level original contributions.

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 achieve the established objectives are based on important breakthroughs which can only be addressed through network-based efforts and the creation of different platforms. A large cohort has been defined, corresponding to different groups of patients with 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 allow for the study of particular pathologies associated with HIV infection, such as hepatitis C coinfection.

The AIDS network is composed of 19 core research groups and 17 associate clinical groups. It includes groups with different experience in virology, immunology and cellular and molecular biology that contribute complementary points of view and techniques in order to globally address complex problems relating to the pathogenesis of HIV infection, such as immune reconstitution, virus-host interactions and the mechanisms underlying cell damage.

SPANISH MULTIPLE SCLEROSIS NETWORK

(Red Española de Esclerosis Múltiple, REEM)

Director:
Dr Pablo Villoslada

www.reem.es

The Spanish Multiple Sclerosis Network (*Red Española de Esclerosis Múltiple, REEM*) 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. The Director of the network is Dr Pablo Villoslada, Head of the IDIBAPS Neuroimmunology team.

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 REEM, such as biobanks and clinical databases.
- Training of young investigators in understanding multiple sclerosis, based on courses, conferences and spells in other laboratories.

Multiple sclerosis presently affects over two million people throughout the world and our greatest challenge is to improve the quality of life of affected patients.

CIBERs and RETICs in which IDIBAPS takes part

IDIBAPS also actively participates in other CIBER and RETIC research networks through its research teams:

Networked Biomedical Research Centres (CIBERs)

CIBER	IDIBAPS Team	Principal investigator
CIBERdem - Diabetes y enfermedades metabolicas	Diabetes: metabolic and molecular networks	Anna Maria Novials Sardà
CIBERdem - Diabetes y enfermedades metabólicas	Genomic Programming of Beta Cells and Diabetes	Jorge Pedro Ferrer Marrades
CIBERdem - Diabetes y enfermedades metabólicas	Diabetes: metabolic and molecular networks	Ramon Gomis Barbarà
CIBERehd - Enfermedades hepáticas y digestivas	Physiopathology and treatment of ascites and altered renal function in liver cirrhosis	Vicente Arroyo Pérez
CIBERehd - Enfermedades hepáticas y digestivas	Liver hemodynamics and portal hypertension. Digestive bleeding secondary to ruptured esophageal varicose veins	Jaime Bosch Genover
CIBERehd - Enfermedades hepáticas y digestivas	Hepatic oncology	Jordi Bruix Tudó
CIBERehd - Enfermedades hepáticas y digestivas	Gastrointestinal and pancreatic oncology	Antoni Castells Garangou
CIBERehd - Enfermedades hepáticas y digestivas	Viral hepatitis in the immune competent host and in liver transplant patients	Xavier Forns Bernhardt
CIBERehd - Enfermedades hepáticas y digestivas	Inflammatory bowel disease (IBD)	Julián Panés Díaz
CIBERehd - Enfermedades hepáticas y digestivas	Cholestasis and bone pathology	Albert Parés Darnaculleta
CIBERehd - Enfermedades hepáticas y digestivas	Liver transplantation and graft viability	Antonio Rimola Castellà
CIBERehd - Enfermedades hepáticas y digestivas	Mitochondrial regulation of cell death and steatohepatitis	José Carlos Fernández-Checa
CIBERned - Enfermedades neurodegenerativas	Neurodegenerative diseases: Clinical and experimental research	Eduard Tolosa Sarró
CIBERned - Enfermedades neurodegenerativas	Neuropharmacology and experimental neuropathology.	Guadalupe Mengod
CIBERned - Enfermedades neurodegenerativas	Cellular biology of pathological processes	Jordi Alberch
CIBERned - Enfermedades neurodegenerativas	Neurobiology Unit	Ramon Trullas Oliva
CIBERned - Enfermedades neurodegenerativas	Neuropharmacology and experimental neuropathology.	Eduard Rodríguez Farré
CIBERer - Enfermedades raras	Secondary lesions due to chronic alcohol ingestion, muscle pathology	Francesc Cardellach López
CIBERer - Enfermedades raras	Fetal and perinatal medicine	Eduard Gratacós Solsona
CIBERer - Enfermedades raras	Genetics	Montserrat Milà Recasens
CIBERer - Enfermedades raras	Hereditary metabolic diseases	Maria Antònia Ribes Rubio
CIBERer - Rare Diseases	Gene Therapy and Cancer	Cristina Fillat
CIBERes - Enfermedades respiratorias	Physiopathological mechanisms of respiratory illnesses	Joan Albert Barberà Mir
CIBERes - Enfermedades respiratorias	Applied research in infectious respiratory diseases, critically ill patients and lung cancer	José María Montserrat Canal

CIBER	IDIBAPS Team	Principal investigator
CIBERes - Enfermedades respiratorias	Clinical and Experimental Respiratory Immunoallergy (IRCE)	César Picado Vallés
CIBERes - Enfermedades respiratorias	Applied research in infectious respiratory diseases, critically ill patients and lung cancer	Antoni Torres Martí
CIBERes - Enfermedades respiratorias	Respiratory biophysics and bioengineering	Ramón Farré
CIBEResp - Epidemiología y Salud Pública	Neuropharmacology and experimental neupathology	Eduard Rodríguez Farré
CIBERobn - Fisiopatología de la obesidad y nutrición	Hypertension, lipids and cardiovascular risk	Emili Ros Rahola
CIBERobn - Fisiotatología de la obesidad y nutrición	Secondary lesions due to chronic alcohol ingestion, muscle pathology	Ramon Estruch Riba
CIBERsam - Salud Mental	Biological bases of psychiatric disorders and nuclear psychiatry	Miguel Bernardo Arroyo
CIBERsam - Salud Mental	Biological bases of psychiatric disorders and nuclear psychiatry	Eduard Vieta Pascual
CIBERsam - Salud Mental	Neuropharmacology and experimental neuropathology	Francesc Artigas
CIBER-BBN - Bioingeniería, Biomateriales y Nanomedicina (Grupo Asociado)	Respiratory biophysics and bioengineering	Ramón Farré
CIBER-BBN - Bioingeniería, Biomateriales y Nanomedicina	Respiratory biophysics and bioengineering	Javer Pavia

Cooperative Health Research Thematic Networks (RETICs)

RETIC	IDIBAPS Team	Principal investigator
REDINSCOR - Red de Investigación en Insuficiencia Cardíaca en España	Arrhythmias, resynchronization and cardiac imaging	Josep Brugada Terradellas
RIS - Red Española de Investigación en SIDA	Infectious diseases and AIDS	Josep Maria Gatell Artigas
REIPI - Red española de investigación en patología infecciosa (REIPI)	Immune receptors of the innate and adaptive system	Francisco Lozano Soto
HERACLES - Determinantes Genéticos y Ambientales de la Disfunción Vascular en la Hipertensión y Cardiopatía Isquémica	Atherosclerosis and coronary disease	Maria Magdalena Heras Fortuny
HERACLES - Determinantes genéticos y ambientales de la disfunción vascular	Hemotherapy - hemostasis	Ginés Escolar Albaladejo
Red de Terapia Celular	Cellular biology of pathological processes	Josep Mª Canals Coll
RETICEF - Red temática de investigación cooperativa en envejecimiento y fragilidad	Neuropharmacology and experimental neuropathology	Coral Sanfeliu Pujol
RECAVA - Factores de Riesgo, Evolución y Tratamiento de las Enfermedades Cardiovasculares y sus Mecanismos	Diagnosis and therapy in oncology	Maria Àfrica Muxí Pradas
REDINREN - Red de Investigación en Enfermedades Renales	Nephro-urological diseases and kidney transplantation	Esteban Poch López de Briñas
REDINREN - Red de Investigación en Enfermedades Renales	Nephro-urological diseases and kidney transplantation	Josep Maria Campistol Plana

RETIC	IDIBAPS Team	Principal investigator
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Hematological oncology	Francisco Cervantes Requena
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Hematological oncology	Juan Bladé Creixenti
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Cell proliferation and signaling	Oriol Bachs Valldeneu
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Hematopoietic progenitor cell transplantation	Álvaro Urbano Ispizúa
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Physiopathology and molecular bases in hematology	Dolors Colomer Pujol
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Diagnosis and therapy in oncology	Francisca Eugenia Pons Pons
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Human and experimental functional oncomorphology	Elias Campo Guerri
RED DE CANCER - Red temática de investigación cooperativa de cáncer	Hematological oncology	Emili Montserrat Costa
RED DE CANCER - Red tematica de investigación cooperativa de cancer.	Molecular and translational oncology	Pedro Gascón Vilaplana
RED DE CANCER - Red tematica de investigación cooperativa de cancer	Cell proliferation and signaling	Carles Enrich
REEM - Red Española de Esclerosis Múltiple	Clinical and experimental neuroimmunology	Pablo Villoslada Díaz
REEM - Red Española de Esclerosis Múltiple	Clinical and experimental neuroimmunology	Francesc Graus Ribas
RIRAAF - Red de Investigación de Reacciones Adversas a Alérgenos y Fármacos	Clinical and Experimental Respiratory Immunoallergy (IRCE)	Joan Bartra Tomàs
RIER - Red de investigación en inflamación y enfermedades reumáticas	Inflammatory joint diseases (IJDs)	Juan de Dios Cañete Crespillo
RETIC de Biobancos	Biobank	Joan Albert Barberà Mir / Anna Bosch
RETICS INNOVACIÓN - RETICS de Innovación en Tecnologías Médicas y Sanitarias	Direction of Innovation, Hospital Clínic of Barcelona	Juan Bigorra Llosas
OFTARED - RETIC en Oftalmología	Neurophysiology and functional studies of the nervous system	Arcadi Gual

Consortium to Support Network Biomedical Research - Spanish Clinical Trials Platform (CAIBER)

The aim of CAIBER is to empower the development of both internal and network-based clinical research programmes and clinical trials. It places special focus on those with no commercial interest or which are oriented towards prevention, diagnosis, treatment and services in the subject areas reflected in the Strategic Action on Health as relevant social and public health interest groups. The objective is to facilitate and promote multi-centre clinical trials which are safe, rigorous, controlled and guaranteed to preserve the quality of the study, patient safety and the reliability of the data.

IDIBAPS, through the Clínic Foundation, is one of the nodes in the CAIBER consortium. This node is led by Dr A. Trilla and Dr X. Carné.

International Projection

International projection is one of IDIBAPS' strategic objectives, with a view both to establishing collaborative ties with entities of reference in other countries and gaining access to international calls for research funding. More and more researchers from this Institute are participating in major international projects.

A good example of this is the increasing presence of IDIBAPS investigators in research projects financed by the European Commission. At present, we are participating in 84 such projects (FPVI and FPVII), of which, we are responsible for coordinating a total of 14; in 70 we are participating as partners and we have 7 monocontract Marie Curie projects.

PROJECTS COORDINATED BY IDIBAPS RESEARCHERS

The 14 European projects coordinated by IDIBAPS researchers are presented below:

COOPERATION

NEXES - Supporting healthier and independent living for chronic patients and elderly
Dr Josep Roca
2008 - 2012
Call: CE-CIP-ICTPSP2007-1
Official code: 225025

TROCAR - Translational Research on Combating Antimicrobial Resistance
Dr Jordi Vila
2009 - 2012
Call: CE_FP7_Health_B_07
Official code: 223031

AMPHORA - Alcohol Measures for Public Health Research Alliance
Dr Antoni Gual
2009 - 2012
Call: CE_FP7_Health_B_07
Official code: 223059

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

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

PROJECTS COORDINATED BY IDIBAPS RESEARCHERS

PEOPLE

FETAL-MED - Multidisciplinary Research Training Programme in Fetal Medicine and Health
Dr Eduard Gratacós
2006 - 2011
Call: CE_Marie_C_06
Official code: MEST-CT-2005-019707

uVOLUMES - Novel Ultrasound-based Tridimensional Tools for Structural and Functional Evaluation of Volumes of Interest in Human Organs
Dr Eduard Gratacós
2008 - 2012
Call: CE_FP7_07_3_1_IAPP
Official code: 217911

ADIBET - The role of adipose tissue in obesity: beta cell crosstalk
Dr Ramon Gomis
2008 - 2012
Call: CE_FP7_07_3_1_IAPP
Official code: PIAP-GA-2008-218130

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

SANCO - EAHC

EU-LIVING-DONOR - European Living Donation and Public Health
Dr Martí Manyalich
2007 - 2012
Call: CE_SANCO05
Official code: 2006211

ELIPSY - European Living Donor Psychosocial Follow-up
Dr Martí Manyalich
2009 - 2012
Call: CE_SANCO08
Official code: 20081104

ENERCA III - European reference network of expert centres in rare anaemias
Dr Juan Luis Vives-Corrons
2009 - 2012
Call: CE_SANCO08
Official code: 20081210

Biotrack - Professional Training and Career Development in Biomedicine

IDIBAPS' institutional mobility action
www.idibaps.org/biotrack

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 Programme. This is an institutional mobility action that aims to increase scientific output and quality by strengthening and reinforcing the centre's previously-existing research programmes.

This programme comprises two different forms of life-long training and career development:

- *In-coming mobility scheme: Post-doctoral programme*
  This BIOTRACK scheme aims to recruit outstanding young researchers with a good track record in scientific publications who have acquired experience in other countries.

  IDIBAPS' Group Leaders offer the applicants the chance to find out more about the research frameworks they may work within if they are selected. This part is dynamic as, in each call, the research lines available may be modified.

  In 2011, a new timetable was introduced for this scheme. Four 3-month calls were offered instead of one annual call. This structure makes BIOTRACK more visible to the scientific community and attracts more talented researchers every time (see Figure 1).

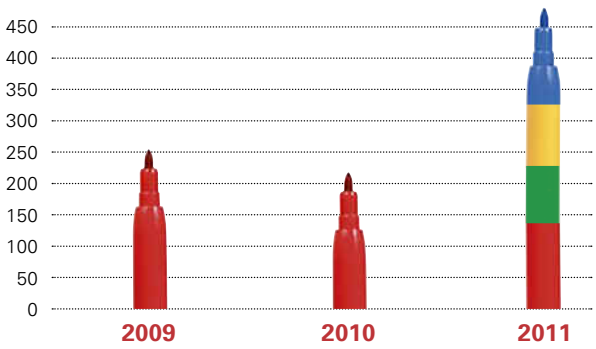


Figure 1. One call per year was opened in 2009 and 2010, receiving 156 and 116 applications respectively. In 2011, a new structure was operated, with four 3-month calls instead of one annual call. As a result, in one year, 411 applicants presented their candidatures for the post-doctoral programme. This amounted to nearly four times the number of candidatures received in previous years.

- *Reintegration schemes: Additional start-up incentive*
  IDIBAPS participates in a number of reintegration programmes directed at Senior Researchers. BIOTRACK provides accomplished scientists, who wish to reintegrate but have mobility requirements, with additional resources to increase the initial start-up funding granted within the framework of these schemes. It is hoped that this additional incentive will help to enhance their excellent research.

Present and future of the programme

In 2011, the community of BIOTRACK researchers in IDIBAPS continued to grow:

- Eight post-doctoral fellows have been working in the centre since their acceptance in the previous in-coming mobility calls: four were selected in 2010 and four in 2011.

- Three researchers were reintegrated into IDIBAPS thanks to the above Reintegration Schemes and BIOTRACK grants.

IDIBAPS has declared its commitment to the principles of *The European Charter for Researchers* and *The Code of Conduct for the Recruitment of Researchers* proposed by the European Commission. Therefore, the selection processes are transparent; there is no discrimination by gender, nationality or any other aspects.

TRAINING

Research Seminars

As well as being orientated towards the creation of networks, the research seminars organised by IDIBAPS are a clear demonstration of the institute's dedication to teaching. The speakers always offer added value that contributes to the knowledge of our investigators. The goal is to share knowledge as it becomes available, with the consolidation of alliances all over the world in order to obtain better research.

The following institutional seminars were organised by the management of IDIBAPS in 2011:

- *Brain imaging and neuropathological aspects of medial temporal lobe atrophy in aged patients*
  Monday 24th January
  Prof Alphonse Probst
  Emeritus Professor, Department of Neuropathology, University of Basel, and Memory Clinic assessor

- *Advances in endoscopic imaging; towards "endopathology"*
  Monday 14th February
  Dr Michael Wallace
  Mayo Clinic College of Medicine, Director of Research for the Department of Medicine, Director of the Gastroenterology and Hepatology Division

- *Somatic reprogramming of adult ovaries to testes*
  Monday 21st February
  Prof. Mathias Treier
  Director of the Institute for Molecular Endocrinology/ Medical Faculty, University Hospital of Cologne (Germany)

- *VEGF, HIF-1-alpha and the lung structure maintenance program*
  Monday 21st March
  Dr Norbert Voelkel
  Director, Victoria Johnson Center for Obstructive Lung Diseases/Virginia Commonwealth University, Richmond, Virginia, USA

- *Linking of the Allergic Environment to Autoimmunity: IgE and basophils as amplifiers in lupus*
  Monday 11th April
  Dr Juan Rivera
  National Institutes of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health (USA)

- *Advances in colorectal cancer genetics: fine mapping of known regions, novel variants and associations with cancer initiation*
  Monday 27th June
  Dr Luis Carvajal-Carmona
  Wellcome Trust Centre for Human Genetics, University of Oxford

- *Genetic architecture of diabetes: the present and the future*
  Monday 17th October
  Dr Valeriya Lyssenko
  Associate Professor at Lund University

- *The visual system in Multiple Sclerosis and neurodegenerative disease*
  Monday 17th October
  Prof Ari Green
  Department of Neurology, University of California, San Francisco

- *The role of telomerase in cancer and aging*
  Monday 21st November
  Dr María Blasco
  Director of the Spanish National Cancer Research Centre (CNIO), Madrid

- *Neuroprotection and Cell Therapy in Parkinson's Disease*
  Monday 19th December
  Dr José López Barneo
  Professor at Seville Biomedicine Institute (*Instituto de Biomedicina de Sevilla (IBiS)*), Hospital Universitario Virgen del Rocío/CSIC/University of Seville

In addition, two new lines of seminars were started in 2011. The **"In House" Seminars** aim to share in-house knowledge through presentations of research and challenges led by IDIBAPS investigators. The **"Core Facility" Seminars** have become a tool for introducing new techniques and services offered by the IDIBAPS Core Facilities.

Doctoral Theses

IDIBAPS' dedication to training is also reflected by the large number of doctoral theses that are directed and supported by the IDIBAPS integrated members.

A list is provided below of the **84 doctoral theses** directed by investigators from this centre in 2011:

Thesis Author	Title	Thesis Directors
Juan Manuel Abolafia Moya	Neuronal basis of auditory adaptation and temporal discrimination in the auditory cortex of the awake, freely-moving rat	Sanchez-Vives MV
Jerusa Alecrim Andrade	Evaluation of the efficacy of acupuncture in the prevention of migraine attacks	Carne X
Felicia Alexandra Hanzu	Molecular determinants of adipose tissue crosstalks	Gomis R, Parrizas M, Diaz-Ricart M
Isabel Alfany Fernández	Differential role of Angiotensin II in liver resections and liver transplant	Peralta C
Sergio Amaro Delgado	Combined therapy with uric acid and RTPA in acute ischaemic stroke: pharmacokinetics, clinical safety and biological activity of the intravenous administration of uric acid in ischaemic stroke treated with RTPA	Chamorro A, Planas A
Albert Antolín Santaliestra	Living will, chronically-ill patient and A&E	Sanchez M, Miro O
Maria Antònia Auladell Llorens	Prevalence and factors associated with non-alcoholic hepatic steatosis in the general population	Pares A
María de las Mercedes Barzi Diéguez	Involvement of G-proteins and PKA in local regulation of the sonic hedgehog pathway in the primary cilium	Bachs O
Mercedes Barzy Dieguez	Role of G i and PKA in Shh signalling	Pons S
Ana Beatriz Fagundo	Early-onset of chronic cannabis use: effects on cognitive function and brain activity	Martin R
Lluïsa Benito Serrano	Utility of early detection of atrial fibrillation	Coll-Vinent B
Jordi Berenguer de Felipe	MicroRNA regulation of neuronal proliferation	Pons S
Isabel Blanco Vich	Study of the effects of vasodilator drugs on gaseous exchange and pulmonary haemodynamics in chronic respiratory diseases	Barbera JA
Caterina del Mar Bonnin Roig	Psychosocial functioning in bipolar disorder: factors involved and follow-up at 4 years	Vieta E, Martinez A
Victor Briz	Effects of organochlorine pesticides on glutamatergic neurotransmission in primary neuronal cultures: interactions with the neuroendocrine system	Suñol C
Lucas Brunso Welker	Early biomarkers for platelet hyperactivity: characteristics of the mechanisms of contraction and secretion in horses	Diaz-Ricart M, Escolar G
Marc Campayo	Analysis of single-nucleotide polymorphisms (SNPs) as factors predictive of relapse in patients with surgically-resected non-small cell lung cancer	Vinolas N
Olga Carretón Gómez	Study of the alteration in signalling pathways involved in the neuronal dysfunction Huntington's Disease: evaluation of its application as therapy in prevention of cognitive deterioration	Alberch J
Arani Casillas Ramírez	Strategies to protect the steatotic graft in liver transplant	Peralta C
Dacia Cerdà Gabaroi	Osteoporosis in the postmenopausal woman: fracture risk in cholestatic disease and prevalence of other associated disorders	Guañabens N
Catia Cillóniz Campos	Community-acquired pneumonia: prospective study of aetiology and clinical progress in a 12-year study period	Torres A
Montserrat Comas Rovira	Cardiac dysfunction by tissue doppler in early-and late-onset fetal growth restriction	Gratacos E, Crispi F

Thesis Author	Title	Thesis Directors
Ricard Corcelles Codina	Effects of the laparoscopic "Roux-en-Y" bypass as a bariatric surgery technique in the treatment of metabolic syndrome associated with morbid obesity	Lacy A
Josep M Cots Yago	Effectiveness of two interventions in the prescribing of antibiotics in respiratory tract infections in Primary Care in Spain	Coca A
Gerardo Dambrava Rodríguez Povilas	Characterization of community-acquired pneumonia	Torres A
Elena de la Serna Gómez	Clinical and neuropsychological characteristics in children and adolescents at high risk of schizophrenia	Castro J, Baeza I
Elisenda Eixarch Roca	Brain reorganization in an experimental model of intrauterine growth restriction	Gratacos E, Figueras F
Rafael Fenutria Aumesquet	Immunomodulatory properties of the CD5 extracellular region	Lozano F
Carlos José Fernández de Larrea Rodríguez	Complete remission in multiple myeloma: prognostic impact of the oligoclonal bands, serum free light-chain ratio and residual plasma cells in bone marrow	Blade J
Elisabet Ferrer Andrés	Pulmonary vascular changes induced by exposure to cigarette smoke in an animal model of COPD	Barbera JA, Peinado VI
Míriam Aurora Font Nieves de la Vega	The inflammatory process triggered by activation of the TLR4 innate immune receptor, and natural autoregulation mechanisms in astrocytes	Planas A, Petegnief V
Juan Fortea Ormaechea	Multimodal magnetic resonance imaging and cerebrospinal fluid analysis in preclinical familial and sporadic Alzheimer's Disease	Molinuevo JL, Bartres-Faz D
Carles Gaig Ventura	Prevalence and clinical and neuropathological phenotype of Parkinsonism associated with LRRK2 gene mutations	Tolosa E
Elena Gallardo Martín	Clinical significance of the microRNAs of the p53 pathway in non-small-cell lung cancer: miR-34a and miR-16	Vinolas N
Reyes Gamo	In-vivo reflectance confocal microscopy in dermatology: application in the diagnosis of skin tumours	Puig S
Ana Isabel García Díez	Magnetic resonance imaging study of the musculoskeletal system in the assessment of Lipodystrophy Syndrome in patients infected by the human immunodeficiency virus	Oleaga L, Mallolas J
Silvia García Etelvino	Study of cardiac electromechanics by signal post-processing and cardiac imaging: application of a clinical model of cardiac resynchronization therapy	Sitges M
Clemente García Rizo	Metabolism and inflammation in first episode psychosis	Bernardo M
Sabrina Gea Sorlí	Characterization of the types of activation of different populations of macrophages during experimental acute pancreatitis and their relationship with the severity of the disease	Closa D
Thomas Gener	Modulation of spatial processing by somatosensory inputs in the rat	Sanchez-Vives MV
Elena González Moreno	Biogenesis of lipid bodies	Pol A
Immaculada Grau Corral	Analysis of the virtual communities in the ForumClinic portal forums	Siso A
Carlos Guarner Argente	Physiological and immunological changes after natural orifice transluminal endoscopic surgery (NOTES) using three different access routes versus laparoscopy: comparative study in a porcine model	Lacy A, Fernandez-Esparrach G
David Guillen Tunica	Study of the immunomodulatory effect of statins. In vitro and in vivo studies	Brunet M
Gonzalo Gutiérrez García	Biological and prognostic characterization of diffuse large-cell lymphoma during immunochemotherapy	Lopez-Guillermo A
Emily Johansson	cAMP specific-phosphodiesterases: mRNA variations and sex-related differences in mouse brain following immune response	Mengod G
Júlia Calvo Castillo	Molecular changes in metastatic transition of breast cancer	Fernandez PL, Thomson T
Adam Kassan	The study of lipid droplet biogenesis	Pol A

Thesis Author	Title	Thesis Directors
Meritxell Lluis Padierna	Study of myocardial regeneration in alcoholic cardiomyopathy and its relationship with the functional damage and myocardial structure, activation of apoptosis and myostatin activity	Fernandez-Sola J
Maria Carlota Londoño Hurtado	Utility of pretransplant MELD and sodium in the short-term prognosis for liver transplant	Gines P
Giuliana Magri	Characterization of natural killer response to human cytomegalovirus-infected dendritic cells	Angulo A, Lopez-Botet M
Anna Mané Santacana	Dopamine Transporter (DAT) and schizophrenia prognosis: prospective study of a cohort evaluated by DATSCAN, volumetric MRI and the DAT gene polymorphism -67 A/T	Bernardo M, Parellada E
Victoria Martín Yuste	Revascularization of Chronically-Occluded Coronary Arteries: Predictors of Angiographic Success and Role of the New Imaging Techniques in Patient Selection	Sabate M, Cinca J
Marcos Martínez Clemente	Participation of 5- and 12/15 - lipoxygenase in the development and progression of hepatic inflammation and steatosis	Claria J
Mª Ángeles Martínez Zamora	Analysis of fibrinolysis as a new thrombotic pathogenic mechanism in early and advanced gestational disease. Relationship with antiphospholipid antibodies	Balasch J, Carmona F, Tassies D
Mercè Masana Nadal	Modulation of the monoaminergic systems in the prefrontal cortex: implications in schizophrenia and depression	Bortolozzi A, Artigas F
Sílvia Maya Enero	Safety in resuscitation in the extremely-premature neonates ward	Botet F
Mª Carme Morales Peydró	Changes in prenatal and postnatal cytogenetic diagnosis with the implementation of new molecular biology techniques and the repercussions on genetic counselling	Sanchez A, Bachs O
Carlos Muñoz Santos	Sporadic and familial porphyria cutanea tarda: observational study of the clinical and biochemical characteristics and the risk factors	Herrero C
Norma Nardi	Clinical significance of the presence of autoantibodies in primary Sjögren's Syndrome: implications for routine practice	Siso A, Ramos-Casals M
Blanca Noemi Luján	Expression of mucines and related molecules in mucoepidermoid carcinomas of the salivary glands: diagnostic and prognostic implications	Alos L, Cardesa A
Natalia Nuño Lambarri, Universidad Autónoma Metropolitana, Mexico DF	Hepatocyte growth factor and c-Met: role of hypercholesterolaemia and signal transduction	Fernandez-Checa JC, Gomez L
J. Osorio	The combination of different pathology criteria enhances the effectiveness of node involvement as a prognostic factor in stomach cancer	Fuster J
Isabella Pacchiarotti	Treatment outcomes of antidepressant use in bipolar disorder	Vieta E, Colom F
Raffaella Pippa	P27kip1 regulates the transcription of genes involved in tumorigenesis	Bachs O
Guillermo Javier Pons-Estel Silvestre	Renal involvement in systemic lupus erythematosus and antiphospholipid syndrome: clinical/epidemiological, anatomical pathology study including predictive factors for morbidity/mortality	Cervera R
Jordi Puiguriguer Ferrando	Improvement in the clinical safety of the poisoned patient following compliance with the quality indicators in Clinical Toxicology	Nogue S
Ignacio Revuelta Vicente	Molecular characterization of neoplasms in solid-organ transplant	Campistol JM
Núria Roé Vellvé	Evaluation of Compton scattering in SPECT studies with 123-I-labelled radiotracers and quantification of small-animal neurotransmission studies	Ros D
Lucía Russo	Role of the Kruppel-like factor 2 transcription factor in hepatic endothelial dysfunction associated with portal hypertension and ischaemia- and reperfusion-related damage	Bosch J, Gracia J
Regina Sala Cassola	Prevalence, clinical correlates and factors associated with course and outcome of anxiety disorders in adolescents with bipolar disorder	Castro J
Noelia Salvador Marcos	SAPKs in the DNA replication checkpoint	Agell N

Thesis Author	Title	Thesis Directors
Cristina Sanabra Palau	cAMP and neuroinflammation: identification of proteins involved in the regulation of cAMP levels in experimental autoimmune encephalomyelitis	Mengod G
Sonia Segura	Dermatoscopic characteristics of the melonocytic lesions in atypical multiple-mole melanoma in different anatomical areas and of melanomas on trunk and lower limbs	Puig S
Sonia Segura Tigell	In-vivo reflectance confocal microscopy in dermatology: application in the diagnosis of skin tumours	Puig S
Javier Selva Sánchez	Signalling pathways and potential therapeutic agents in an in vitro model of foetal alcoholic syndrome	Egea G
Jordi Sintes Castro	Expression and functional role of CD84 and CD229 receptors in innate and adaptive immunity	Engel P
Ivonne Torres Atencio, Autònoma de Barcelona (UAB)	Regulatory role of Prostaglandin E2 in osmotic activation in mast cells	Picado C, Martin M
Francisco Javier Tovillas Morán	Left ventricular hypertrophy and prediction of cardiovascular risk in people with hypertension in our setting	Coca A
Joan Carles Trullàs Vila	Chronic kidney disease and renal replacement therapy in patients with human immunodeficiency virus infection. Prevalence and survival in renal replacement therapy and kidney transplant	Miro JM, Moreno A, Barril G
Mauricio Valencia Arango	Prevention of complications associated with mechanical ventilation	Torres A, Ferrer M
Van Arensbergen, Joris	The role of polycomb-mediated gene repression in beta-cell identity	Ferrer J
Mª Teresa Vidal-Quadras de Soto	Benefits of calmodulin binding to RAC 1: implications in clathrin-independent endocytosis	Tebar F
Pedro Zaballos Diego	Description and evaluation of the dermatoscopic parameters and patterns of non-melanocytic skin lesions and their differential diagnosis with melanoma	Puig S, Malvehy J, Estrach MT

IDIBAPS AND SOCIETY

IDIBAPS understands that new biomedical discoveries must reach the citizens not only through medical and scientific benefits, but also through high-quality information. It is our obligation to inform society of advances, of basic and healthcare novelties and of the principal research lines being pursued. The responsibility of informing society is based on the principle that a well-informed person is a healthier person.

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https://twitter.com/idibaps/

Mass media play an important role in the communication of research results. That is why IDIBAPS investigators work together with the IDIBAPS Communication Office in press releases and press meetings to provide reliable and relevant data to journalists. In 2011, over 20 press releases were launched, adding to the individual news items, where investigators from this Institute are interviewed as independent experts expressing their opinion about other issues.

Multimedia applications are also an ideal tool for stimulating learning and explaining complex concepts. With this in mind, IDIBAPS joined forces with Ambientech, an institution specialising in educational websites. The result is a virtual laboratory designed to become an educational support in the classrooms which explains scientific concepts and everyday activity in clinical and basic laboratories. This activity, which was started with a grant from the Generalitat de Catalunya (ACDC 2010) and had the support of the Obra Social "la Caixa", is now available in Spanish, Catalan and English and at **www.ambientech.org**.

Lastly, IDIBAPS is exploring the context of social networks as a channel for communication with society. The Facebook and Twitter profiles are a new way to interact with IDIBAPS and learn more about what is going on inside its laboratories:

IMMUNE
RECEPTORS OF THE
INNATE AND
ADAPTIVE
SYSTEM
MOLECULAR
AND CELLULAR
BASES
OF INFLAMMATION
BIOLOGICAL
AGGRESSION
RESPONSE
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AND REPAIR
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AREA 1

BIOLOGICAL AGGRESSION AND RESPONSE MECHANISMS

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AREA 1

Biological aggression and response mechanisms

Inflammatory joint diseases (IJDs)

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TEAM INVOLVED IN:

RIER

STRATEGIC OBJECTIVES

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

MAIN LINES OF RESEARCH

1. **Prognostic factors in initial arthritis**
   - Prognostic factors (clinical and immunogenetic) in patients with initial rheumatoid arthritis.
   - Production of new synthetic citrullinated peptides for the design of immunoassays with diagnostic and prognostic value in recent-onset rheumatoid arthritis.
   - Effect of tobacco on the phenotype of recent-onset rheumatoid arthritis
2. **Pharmacogenomics of chronic arthritis**
   - Genetic biomarkers associated to TNF antagonists response in rheumatoid arthritis and psoriatic arthritis
3. **Immunopathology of synovitis in chronic arthritis**
   - Utility in differential diagnosis and prognosis. Immunopathological changes related to biological treatments. Synovial response biomarkers.
4. **Role of autoinflammatory genes in the pathogenesis of chronic arthritis**
   - MEFV gene mutations in intermittent arthritis.

PUBLICATIONS

ORIGINALS
I.F.: 36.45

1 Haro I, Gomara MJ, Perez ML, Vinas O, Ercilla G, Gomez-Puerta JA, Sanmarti R. Antibodies against beta-fibrin synthetic peptides: A study of their association with the immunogenetic background and disease course of rheumatoid arthritis patients. EUR J MED CHEM. 46:1095-1102. I.F.: 3.19.

2 Villa MD, Jimenez-Jorquera C, Haro I, Gomara MJ, Sanmarti R, Fernandez-Sanchez C, Mendoza E. Carbon nanotube composite peptide-based biosensors as putative diagnostic tools for rheumatoid arthritis. BIOSENS BIOELECTRON. 27:113-118. I.F.: 5.36.

3 Canete JD, Albaladejo C, Hernandez MV, Lainez B, Pinto JA, Ramirez J, Lopez-Armada MJ, Rodriguez-Cros JR, Engel P, Blanco FJ, Sanmarti R. Clinical significance of high levels of soluble tumour necrosis factor-alpha receptor-2 produced by alternative splicing in rheumatoid arthritis: a longitudinal prospective cohort study. RHEUMATOLOGY. 50:721-728. I.F.: 4.17.

4 Ruiz-Esquide V, Gomez-Puerta JA, Canete JD, Graell E, Vazquez I, Ercilla MG, Vinas O, Gomez-Centeno A, Haro I, Sanmarti R. Effects of Smoking on Disease Activity and Radiographic Progression in Early Rheumatoid Arthritis. J RHEUMATOL. 38:2536-2539. I.F.: 3.55.

5 Navarro-Sarabia F, Fernandez-Sueiro JL, Torre-Alonso JC, Gratacos J, Queiro R, Gonzalez C, Loza E, Linares L, Zarco P, Juanola X, Roman-Ivorra J, Martin-Mola E, Sanmarti R, Mulero J, Diaz G, Armendariz Y, Collantes E. High-dose etanercept in ankylosing spondylitis: results of a 12-week randomized, double blind, controlled multicentre study (LOADET study). RHEUMATOLOGY. 50:1828-1837. I.F.: 4.17.

6 Narvaez J, Diaz-Torne C, Ruiz JM, Hernandez MV, Torrente-Segarra V, Ros S, DeLaSerna AR, Diaz-Lopez C, Sanmarti R, Nolla JM. Predictors of response to rituximab in patients with active rheumatoid arthritis and inadequate response to anti-TNF agents or traditional DMARDs. CLIN EXP RHEUMATOL. 29:991-997. I.F.: 2.36.

7 Izquierdo E, Canete JD, Celis R, DelRey MJ, Usategui A, Marsal S, Sanmarti R, Criado G, Pablos JL. Synovial Fibroblast Hyperplasia in Rheumatoid Arthritis Clinicopathologic Correlations and Partial Reversal by Anti-Tumor Necrosis Factor Therapy. ARTHRITIS RHEUM-US. 63:2575-2583. I.F.: 8.44.

8 Malakoutikhah M, Gomara MJ, Gomez-Puerta JA, Sanmarti R, Haro I. The Use of Chimeric Vimentin Citrullinated Peptides for the Diagnosis of Rheumatoid Arthritis. J MED CHEM. 54:7486-7492. I.F.: 5.21.

REVIEWS
I.F.: 4.74

1 Narvaez J, Diaz-Torne C, Ruiz JM, Hernandez MV, Torrente-Segarra V, Ros S, DeLaSerna AR, Diaz-Lopez C, Sanmarti R, Nolla JM. Comparative Effectiveness of Rituximab in Combination with Either Methotrexate or Leflunomide in the Treatment of Rheumatoid Arthritis. SEMIN ARTHRITIS RHEU. 41:401-405. I.F.: 4.74.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	45.44	11	6	3
2010	10.06	3	2	1
2011	36.45	8	5	3

GRANTS FOR RESEARCH IN PROGRESS

Cañete J. Red de Inflamación y Enfermedades Reumáticas. Sponsored by: Instituto de Salud Carlos III (ISCIII), RETICS RD08/0075/0006 "RIER". Duration: 01/01/2009-31/01/2012.

Cañete J. Subtipos de células T sinoviales (Th1, Th2, Th17 y Treg) y actividad y gravedad de la artritis psoriásica. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080206. Duration: 01/01/2009-31/12/2011.

Sanmarti R. Estudio comparativo fenotípico, genotípico e inmunohistológico. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080207. Duration: 01/01/2009-31/12/2011.

Cañete J. Asociación de polimorfismo de un sólo nucleótido (SNPs) de los genes de las vias de señalización intracelular NFkB, MAPK y JAK/STAT con la artritis reumatoide y con diferentes fenotipos de la enfermedad. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI041023. Duration: 01/01/2005-30/12/2011.

AREA 1

Biological aggression and response mechanisms

Systemic autoimmune diseases

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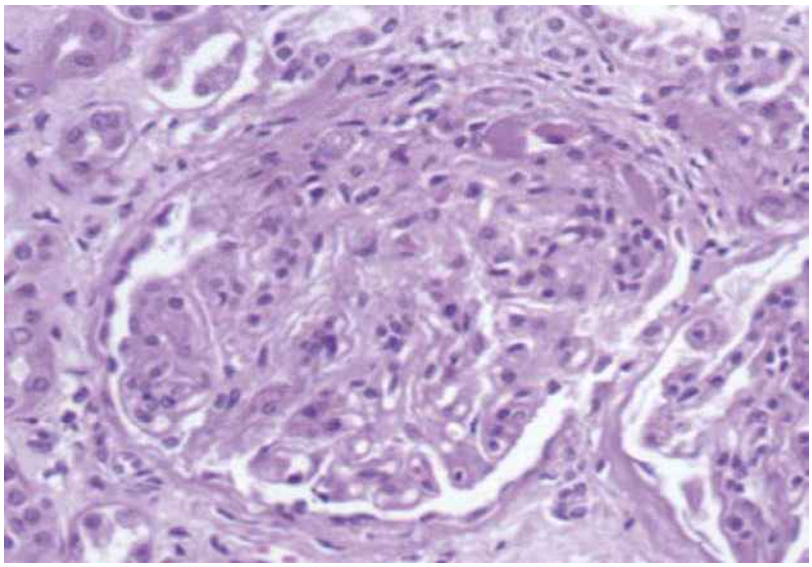
Claudia Mendoza (Puebla, México)
Horacio Berman (Tucumán, Argentina)
Verônica Vilela (Río de Jainero, Brasil)

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.



Renal thrombotic microangiopathy associated with antiphospholipid antibodies.

- 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 lymphomas associated with Sjögren's syndrome.
- Study of the cardiovascular and endothelial damage risk factors found in this syndrome.
- Clinical and basic studies in 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.
- 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.

EMERGENT GROUP
AUTOIMMUNE OPHTHALMOPATHY

Group Leader: Alfredo Manuel Adan (Hospital Clínic)

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 (Hospital Clínic)

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.: 185.01

1 Furie R, Petri M, Zamani O, Cervera R, Wallace DJ, Tegzova D, Sanchez-Guerrero J, Schwarting A, Merrill JT, Chatham WW, Stohl W, Ginzler EM, Hough DR, Zhong ZJ, Freimuth W, VanVollenhoven RF. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. ARTHRITIS RHEUM-US. 63:3918-3930. I.F.: 8.44.

2 Bossini-Castillo L, Broen JCA, Simeon CP, Beretta L, Vonk MC, Ortego-Centeno N, Espinosa G, Carreira P, Camps MT, Navarrete N, Gonzalez-Escribano MF, Vicente-Rabaneda E, Rodriguez L, Tolosa C, Roman-Ivorra JA, Gomez-Gracia I, Garcia-Hernandez FJ, Castellvi I, Gallego M, Fernandez-Nebro A, Garcia-Portales R, Egurbide MV, Fonollosa V, DeLaPena PG, Pros A, Gonzalez-Gay MA, Hesselstrand R, Riemekasten G, Witte T, Coenen MJH, Koeleman BP, Houssiau F, Smith V, DeKeyser F, Westhovens R, DeLanghe E, Voskuyl AE, Schuerwegh AJ, Chee MM, Madhok R, Shiels P, Fonseca C, Denton C, Claes K, Padykov L, Nordin A, Palm O, Lie BA, Airo P, Scorza R, VanLaar JM, Hunzelmann N, Kreuter A, Herrick A, Worthington J, Radstake TRDJ, Martin J, Rueda B. A replication study confirms the association of TNFSF4 (OX40L) polymorphisms with systemic sclerosis in a large European cohort. ANN RHEUM DIS. 70:638-641. I.F.: 9.08.

3 Casaroli-Marano R, Adan A, Gomez-Ulla F, Diaz JM. Age-related macular degeneration: Analysis of the results of ranibizumab therapy. MED CLIN-BARCELONA. 136:128-129. I.F.: 1.41.

4 Diaz-Gallo L, Gourh P, Broen J, Simeon C, Fonollosa V, Ortego-Centeno N, Agarwal S, Vonk MC, Coenen M, Riemekasten G, Hunzelmann N, Hesselstrand R, Tan FK, Reveille JD, Assassi S, Garcia-Hernandez FJ, Carreira P, Camps MT, Fernandez-Nebro A, DeLaPena PG, Nearney T, Hilda D, Gonzalez-Gay MA, Airo P, Beretta L, Scorza R, Herrick A, Worthington J, Pros A, Gomez-Gracia I, Trapiella L, Espinosa G, Castellvi I, Witte T, DeKeyser F, Vanthuyne M, Mayes MD, Radstake TRDJ, Arnett FC, Martin J, Rueda B. Analysis of the influence of PTPN22 gene polymorphisms in systemic sclerosis. ANN RHEUM DIS. 70:454-462. I.F.: 9.08.

5 Carmona FD, Simeon CP, Beretta L, Carreira P, Vonk MC, Rios-Fernandez R, Espinosa G, Navarrete N, Vicente-Rabaneda E, Rodriguez-Rodriguez L, Tolosa C, Garcia-Hernandez FJ, Castellvi I, Egurbide MV, Fonollosa V, Gonzalez-Gay MA, Rodriguez-Carballeira M, Diaz-Gonzalez F, Saez-Comet L, Hesselstrand R, Riemekasten G, Witte T, Voskuyl AE, Schuerwegh AJ, Madhok R, Shiels P, Fonseca C, Denton C, Nordin A, Palm O, Hoffmann-Vold AM, Airo P, Scorza R, Lunardi C, VanLaar JM, Hunzelmann N, Kreuter A, Herrick A, Worthington J, Koeleman BPC, Radstake TRDJ, Martin J. Association of a non-synonymous functional variant of the ITGAM gene with systemic sclerosis. ANN RHEUM DIS. 70:2050-U203. I.F.: 9.08.

6 Hanly JG, Urowitz MB, Su L, Bae SC, Gordon C, Clarke A, Bernatsky S, Vasudevan A, Isenberg D, Rahman A, Wallace DJ, Fortin PR, Gladman D, Romero-Dirz J, Sanchez-Guerrero J, Dooley MA, Bruce I, Steinsson K, Khamashta M, Manzi S, Ramsey-Goldman R, Sturfelt G, Nived O, VanVollenhoven R, Ramos-Casals M, Aranow C, Mackay M, Kalunian K, Alarcon GS, Fessler BJ, Ruiz-Irastorza G, Petri M, Lim S, Kamen D, Peschken C, Farewell V, Thompson K, Theriault C, Merrill JT. Autoantibodies as biomarkers for the prediction of neuropsychiatric events in systemic lupus erythematosus. ANN RHEUM DIS. 70:1726-1732. I.F.: 9.08.

7 Ramos-Casals M, Diaz-Lagares C, Khamashta MA. B-cell-depletion therapy in systemic autoinmune diseases. Recommendations for use in clinical practice. MED CLIN-BARCELONA. 136:257-263. I.F.: 1.41.

8 Pelegrin L, Mesquida M, Adan A, Cervera C, Bosch-Mestres J, Esteban-Redondo C, Juiz-Gonzalez P, Llorenc V, Miro JM. Candida dubliniensis endophthalmitis in a HIV-infected intravenous drug abuser. MYCOSES. 54:E856-E858. I.F.: 1.67.

9 Alba MA, Espigol-Frigole G, Prieto-Gonzalez S, Tavera-Bahillo I, Garcia-Martinez A, Butjosa M, Hernandez-Rodriguez J, Cid MC. Central Nervous System Vasculitis: Still More Questions than Answers. CURR NEUROPHARMACOL. 9:437-448. I.F.: 2.78.

10 Bossini-Castillo L, Simeon CP, Beretta L, Vonk MC, Callejas-Rubio JL, Espinosa G, Carreira P, Camps MT, Rodriguez-Rodriguez L, Rodriguez-Carballeira M, Garcia-Hernandez FJ, Lopez-Longo FJ, Hernandez-Hernandez V, Saez-Comet L, Egurbide MV, Hesselstrand R, Nordin A, Hoffmann-Vold AM, Vanthuyne M, Smith V, DeLanghe E, Kreuter A, Riemekasten G, Witte T, Hunzelmann N, Voskuyl AE, Schuerwegh AJ, Lunardi C, Airo P, Scorza R, Shiels P, VanLaar JM, Fonseca C, Denton C, Herrick A, Worthington J, Koeleman BP, Rueda B, Radstake TRDJ, Martin J. Confirmation of association of the macrophage migration inhibitory factor gene with systemic sclerosis in a large European population. RHEUMATOLOGY. 50:1976-1981. I.F.: 4.17.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	134.58	34	11	15
2010	173.60	33	15	13
2011	185.01	37	19	13

11 Illei GG, Cervera R, Burt RK, Doria A, Hiepe F, Jayne D, Pavletic S, Martin T, Marmont A, Saccardi R, Voskuyl AE, Farge D. Current state and future directions of autologous hematopoietic stem cell transplantation in systemic lupus erythematosus. ANN RHEUM DIS. 70:2071-2074. I.F.: 9.08.

12 Mosca M, Tani C, Aringer M, Bombardieri S, Boumpas D, Cervera R, Doria A, Jayne D, Khamashta MA, Kuhn A, Gordon C, Petri M, Schneider M, Shoenfeld Y, Smolen JS, Talarico R, Tincani A, Ward MM, Werth VP, Carmona L. Development of quality indicators to evaluate the monitoring of SLE patients in routine clinical practice. AUTOIMMUN REV. 10:383-388. I.F.: 6.56.

13 Marcos M, Fernandez C, Soriano A, Marco F, Martinez JA, Almela M, Cervera R, Mensa J, Espinosa G. Epidemiology and clinical outcomes of bloodstream infections among lupus patients. LUPUS. 20:965-971. I.F.: 2.60.

14 VanAssen S, Agmon-Levin N, Elkayam O, Cervera R, Doran MF, Dougados M, Emery P, Geborek P, Ioannidis JPA, Jayne DRW, Kallenberg CGM, Muller-Ladner U, Shoenfeld Y, Stojanovich L, Valesini G, Wulffraat NM, Bijl M. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. ANN RHEUM DIS. 70:414-422. I.F.: 9.08.

15 Seror R, Ravaud P, Mariette X, Bootsma H, Theander E, Hansen A, Ramos-Casals M, Dorner T, Bombardieri S, Hachulla E, Brun JG, Kruize AA, Praprotnik S, Tomsic M, Gottenberg JE, Devauchelle V, Devita S, Vollenweider C, Mandl T, Tzioufas A, Carsons S, Saraux A, Sutcliffe N, Vitali C, Bowman SJ. EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI): development of a consensus patient index for primary Sjogren's syndrome. ANN RHEUM DIS. 70:968-972. I.F.: 9.08.

16 Perez-Alvarez R, Diaz-Lagares C, Garcia-Hernandez F, Lopez-Roses L, Brito-Zeron P, Perez-De-Lis M, Retamozo S, Bove A, Bosch X, Sanchez-Tapias JM, Forns X, Ramos-Casals M. Hepatitis B Virus (HBV) Reactivation in Patients Receiving Tumor Necrosis Factor (TNF)-Targeted Therapy Analysis of 257 Cases. MEDICINE. 90:359-371. I.F.: 4.26.

17 Garcia-Carrasco M, Mendoza-Pinto C, Riebeling C, Sandoval-Cruz M, Nava A, Etchegaray-Morales I, Jimenez-Hernandez M, Montiel-Jarquin A, Lopez-Colombo A, Cervera R. Influence of Prevalent Vertebral Fractures on the Quality of Life of Patients with Systemic Lupus Erythematosus. ISR MED ASSOC J. 13:333-337. I.F.: 0.95.

18 Perez-Alvarez R, Perez-De-Lis M, Diaz-Lagares C, Pego-Reigosa JM, Retamozo S, Bove A, Brito-Zeron P, Bosch X, Ramos-Casals M. Interstitial Lung Disease Induced or Exacerbated by TNF-Targeted Therapies: Analysis of 122 Cases. SEMIN ARTHRITIS RHEU. 41:256-264. I.F.: 4.74.

19 Arevalo JF, Adan A, Berrocal MH, Espinoza JV, Maia M, Wu L, Roca JA, Quiroz-Mercado H, Ruiz-Moreno JM, Serrano MA. Intravitreal bevacizumab for inflammatory choroidal neovascularization. Results from the Pan-American Collaborative Retina Study Group at 24 Months. RETINA-J RET VIT DIS. 31:353-363. I.F.: 2.77.

20 Silvarino R, Sant F, Espinosa G, Pons-Estel G, Sole M, Cervera R, Arrizabalaga P. Nephropathy associated with antiphospholipid antibodies in patients with systemic lupus erythematosus. LUPUS. 20:721-729. I.F.: 2.60.

21 Noval S, Ortiz-Perez S, Sanchez-Dalmau BF, Ruiz-Ares G, Arpa J, Adan A. Neuro-Ophthalmological Features of Primary Diffuse Leptomeningeal Gliomatosis. J NEURO-OPHTHALMOL. 31:299-305. I.F.: 1.06.

22 Carmona FD, Serrano-Lopera A, Lopez-Isac E, Simeon CP, Carreira P, Rios-Fernandez R, Espinosa G, Camps MT, Navarrete N, Gonzalez-Escribano MF, Vicente-Rabaneda E, Rodriguez-Rodriguez L, Tolosa C, Beltran E, Gomez-Garcia I, Fernandez-Castro M, Lopez-Longo FJ, Garcia-Hernandez FJ, Castellvi I, Trapiella L, Fernandez-Nebro A, Garcia-Portales R, Egurbide MV, Fonollosa V, DeLaPena PG, Pros A, Rodriguez-Carballeira M, Diaz-Gonzalez F, Saez-Comet L, Gonzalez-Gay MA, Martin J. No evidence for association between the CCR5/Delta32CCR5 polymorphism and systemic sclerosis. CLIN EXP RHEUMATOL. 29:895-896. I.F.: 2.36.

23 Llorenc V, Keller J, Pelegrin L, Adan A. Pars Plana Vitrectomy for Vitreo-Retinal Complications of Birdshot Chorioretinopathy. OCUL IMMUNOL INFLAMM. 19:346-352. I.F.: 0.95.

24 DeVita S, Soldano F, Isola M, Monti G, Gabrielli A, Tzioufas A, Ferri C, Ferraccioli GF, Quartuccio L, Corazza L, DeMarchi G, Ramos M, Voulgarelis M, Lenzi M, Saccardo F, Fraticelli P, Mascia MT, Sansonno D, Cacoub P, Tomsic M, Tavoni A, Pietrogrande M, Zignego AL, Scarpato S, Mazzaro C, Pioltelli P, Steinfeld S, Lamprecht P, Bombardieri S. Preliminary classification criteria for the cryoglobulinaemic vasculitis. ANN RHEUM DIS. 70:1183-1190. I.F.: 9.08.

25 Casaroli-Marano R, Pinero A, Adan A, Castro J, Armada F, Cervera E, Llopis MD, Abreu P, Esteban E, Arias L, Fernandez-Arias I, Kim HK, Acebes X, Acosta B, Bahaya Y, Barrios M, Blazquez A, Bueno R, Bures A, Carnota P, Castanos A, Cubillas M, Degollada N, Fernandez C, Fuste C, Garcia P, Gil MA, Graell X, Granados M, Guerra P, Hernandez A, Kalitovics N, Llorente S, Mesa JC, Molina JJ, Mones A, Montero J, Nadal E, Navarro M, Ortiz JV, Ortiz S, Otxoa I, Pereira E, Perez JR, Planas N, Prades S, Rodriguez E, Rosal F, Ruiz A, Sanchez A, Udaondo P, Vargas JC, Villota E, Zarallo J. Prevalence of age-related macular degeneration in Spain. BRIT J OPHTHALMOL. 95:931-936. I.F.: 2.93.

26 Ramos-Casals M, Perez-Alvarez R, Perez-De-Lis M, Xaubet A, Bosch X. Pulmonary Disorders Induced by Monoclonal Antibodies in Patients with Rheumatologic Autoimmune Diseases. AM J MED. 124:386-394. I.F.: 5.12.

27 Diaz-Lagares C, Perez-Alvarez R, Garcia-Hernandez FJ, Ayala-Gutierrez MM, Callejas JL, Martinez-Berriotxoa A, Rascon J, Caminal-Montero L, Selva-O'callaghan A, Oristrell J, Hidalgo C, Gomez-De-La-Torre R, Saez L, Canora-Lebrato J, Camps MT, Ortego-Centeno N, Castillo-Palma MJ, Ramos-Casals M. Rates of, and risk factors for, severe infections in patients with systemic autoimmune diseases receiving biological agents off-label. ARTHRITIS RES THER. 13:-. I.F.: 4.36.

28 Hanly JG, Urowitz MB, Jackson D, Bae SC, Gordon C, Wallace DJ, Clarke A, Bernatsky S, Vasudevan A, Isenberg D, Rahman A, Sanchez-Guerrero J, Romero-Diaz J, Merrill JT, Fortin PR, Gladman DD, Bruce IN, Steinsson K, Khamashta M, Alarcon GS, Fessler B, Petri M, Manzi S, Nived O, Sturfelt G, Ramsey-Goldman R, Dooley MA, Aranow C, VanVollenhoven R, Ramos-Casals M, Zoma A, Kalunian K, Farewell V. SF-36 summary and subscale scores are reliable outcomes of neuropsychiatric events in systemic lupus erythematosus. ANN RHEUM DIS. 70:961-967. I.F.: 9.08.

29 Cervera R, Tektonidou MG, Espinosa G, Cabral AR, Gonzalez EB, Erkan D, Vadya S, Adrogue HE, Solomon M, Zandman-Goddard G, Shoenfeld Y. Task Force on Catastrophic Antiphospholipid Syndrome (APS) and Non-criteria APS Manifestations (I): catastrophic APS, APS nephropathy and heart valve lesions. LUPUS. 20:165-173. I.F.: 2.60.

30 Cervera R, Tektonidou MG, Espinosa G, Cabral AR, Gonzalez EB, Erkan D, Vadya S, Adrogue HE, Solomon M, Zandman-Goddard G, Shoenfeld Y. Task Force on Catastrophic Antiphospholipid Syndrome (APS) and Non-criteria APS Manifestations (II): thrombocytopenia and skin manifestations. LUPUS. 20:174-181. I.F.: 2.60.

31 Mosca M, Govoni M, Tomietto P, Aringer M, Boumpas D, Cervera R, Conti F, D'cruz D, Doria A, DeLaFuente D, Galeazzi M, Houssiau F, Huizinga TWJ, Khamashta MA, Ines L, Duarte C, Couto M, Meroni P, Montecucco C, Norkuviene E, Riemekasten G, Rios V, Schneider M, Shoenfeld Y, Steup-Beekman GM, Szmyrka-Kaczmarek M, Tani C, Tincani A, Tzioufas AG, Voll R, Bencivelli W, Salaffi F, Bombardieri S. The development of a simple questionnaire to screen patients with SLE for the presence of neuropsychiatric symptoms in routine clinical practice. LUPUS. 20:485-492. I.F.: 2.60.

32 Visvanathan S, Rahman MU, Hoffman GS, Xu S, Garcia-Martinez A, Segarra M, Lozano E, Espigol-Frigole G, Hernandez-Rodriguez J, Cid MC. Tissue and serum markers of inflammation during the follow-up of patients with giant-cell arteritis-a prospective longitudinal study. RHEUMATOLOGY. 50:2061-2070. I.F.: 4.17.

33 Prieto-Gonzalez S, Cardellach F, Estruch R, Miguel R, Grau JM, Cid MC. Type 1 autoimmune hepatitis in a patient with microscopic polyangiitis: challenges in diagnosis and treatment. MED CLIN-BARCELONA. 136:345-348. I.F.: 1.41.

34 VanAssen S, Elkayam O, Agmon-Levin N, Cervera R, Doran MF, Dougados M, Emery P, Geborek P, Ioannidis JP, Jayne DR, Kallenberg CG, Müller-Ladner U, Shoenfeld Y, Stojanovich L, Valesini G, Wulffraat NM, Bijl M. Vaccination in adult patients with autoimmune inflammatory rheumatic diseases: A systematic literature review for the EULAR evidence-based recommendations for vaccination in adult patients with auto-immune inflammatory rheumatic diseases. AUTOIMMUN REV. 10:341-352. I.F.: 6.56.

35 Agmon-Levin N, Blank M, Zandman-Goddard G, Orbach H, Meroni PL, Tincani A, Doria A, Cervera R, Miesbach W, Stojanovich L, Barak V, Porat-Katz BS, Amital H, Shoenfeld Y. Vitamin D: an instrumental factor in the anti-phospholipid syndrome by inhibition of tissue factor expression. ANN RHEUM DIS. 70:145-150. I.F.: 9.08.

36 Font C, Vidal L, Espinosa G, Tassies D, Monteagudo J, Farrus B, Visa L, Cervera R, Gascon P, Reverter JC. Solid cancer, antiphospholipid antibodies, and venous thromboembolism. AUTOIMMUN REV. 10:222-227. I.F.: 6.56.

37 Pons-Estel GJ, Salerni GE, Serrano RM, Gomez-Puerta JA, Plasin MA,

Aldasoro E, Lozano M, Cid J, Cervera R, Espinosa G. Therapeutic plasma exchange for the management of refractory systemic autoimmune diseases: Report of 31 cases and review of the literature. AUTOIMMUN REV. 10:679-684. I.F.: 6.56.

REVIEWS
I.F.: 57.54

1 Bosch X, Lozano F, Cervera R, Ramos-Casals M, Min B. Basophils, IgE, and Autoantibody-Mediated Kidney Disease. J IMMUNOL. 186:6083-6090. I.F.: 5.75.

2 Pons-Estel GJ, Serrano R, Plasin MA, Espinosa G, Cervera R. Epidemiology and management of refractory lupus nephritis. AUTOIMMUN REV. 10:655-663. I.F.: 6.56.

3 Espinosa G, Berman H, Cervera R. Management of refractory cases of catastrophic antiphospholipid syndrome. AUTOIMMUN REV. 10:664-668. I.F.: 6.56.

4 Bosch X, Saiz A, Ramos-Casals M. Monoclonal antibody therapy-associated neurological disorders. NAT REV NEUROL. 7:165-172. I.F.: 6.51.

5 Ramos-Casals M, Diaz-Lagares C, Soto-Cardenas MJ, Brito-Zeron P, Cuadrado MJ, Sanna G, Bertolaccini L, Khamashta MA. Rituximab Therapy in Lupus Nephritis: Current Clinical Evidence. CLIN REV ALLERG IMMU. 40:159-169. I.F.: 3,44.

6 Garcia-Carrasco M, Jimenez-Hernandez C, Jimenez-Hernandez M, Voorduin-Ramos S, Mendoza-Pinto C, Ramos-Alvarez G, Montiel-Jarquin A, Rojas-Rodriguez J, Cervera R. Susac's syndrome: An update. AUTOIMMUN REV. 10:548-552. I.F.: 6.56.

7 O'neill S, Cervera R. Systemic lupus erythematosus. BEST PRACT RES CL RH. 24:841-855. I.F.: 3.30.

8 Engel P, Gomez-Puerta JA, Ramos-Casals M, Lozano F, Bosch X. Therapeutic Targeting of B Cells for Rheumatic Autoimmune Diseases. PHARMACOL REV. 63:127-156. I.F.: 18.86.

EDITORIALS
I.F.: 5.20

1 Vasconcelos C, Cervera R, Khamashta M. "So this is Lupus" FOREWORD. LUPUS. 20:339-339. I.F.: 2.60.

2 Cervera R. 'ASIA': a new systemic autoimmune syndrome?. LUPUS. 20:665-666. I.F.: 2.60.

MULTICENTRICS
I.F.: 65.19

1 Gorlova O, Martin JE, Rueda B, Koeleman BPC, Ying J, Teruel M, Diaz-Gallo LM, Broen JC, Vonk MC, Simeon CP, Alizadeh BZ, Coenen MJH, Voskuyl AE, Schuerwegh AJ, VanRiel PLCM, Vanthuyne M, Van'tSlot R, Italiaander A, Ophoff RA, Hunzelmann N, Fonollosa V, Ortego-Centeno N, Gonzalez-Gay MA, Garcia-Hernandez FJ, Gonzalez-Escribano MF, Airo P, VanLaar J, Worthington J, Hesselstrand R, Smith V, DeKeyser F, Houssiau F, Chee MM, Madhok R, Shiels PG, Westhovens R, Kreuter A, DeBaere E, Witte T, Padyukov L, Nordin A, Scorza R, Lunardi C, Lie BA, Hoffmann-Vold AM, Palm O, DeLaPena PG, Carreira P, Varga J, Hinchcliff M, Lee AT, Gourh P, Amos CI, Wigley FM, Hummers LK, Hummers J, Nelson JL, Riemekasten G, Herrick A, Beretta L, Fonseca C, Denton CP, Gregersen PK, Agarwal S, Assassi S, Tan FK, Arnett FC, Radstake TRDJ, Mayes MD, Martin J. Identification of Novel Genetic Markers Associated with Clinical Phenotypes of Systemic Sclerosis through a Genome-Wide Association Strategy. PLOS GENET. 7:-. I.F.: 9.54.

2 Dooley MA, Jayne D, Ginzler EM, Isenberg D, Olsen NJ, Wofsy D, Eitner F, Appel GB, Contreras G, Lisk L, Solomons N. Mycophenolate versus Azathioprine as Maintenance Therapy for Lupus Nephritis. NEW ENGL J MED. 365:1886-1895. I.F.: 53.49.

3 Pfeiffer N. Timolol versus brinzolamide added to travoprost in glaucoma or ocular hypertension. GRAEF ARCH CLIN EXP. 249:1065-1071. I.F.: 2.16.

GRANTS FOR RESEARCH IN PROGRESS

Adan AM. Estudio aleatorizado y abierto de la eficacia, seguridad y tolerabilidad de dosis repetidas de bevacizumab intravítreo en pacientes con edema macular uveítico refractario. Sponsored by: Instituto de Salud Carlos III (ISCIII), EC08/00096. Duration: 01/01/2008-31/12/2011.

Cid MC. Mecanismos implicados y consecuencias clínicas de la persistencia de la inflamación vascular en la arteritis de células gigantes. Identificación de dianas terapéuticas. Sponsored by: Ministerio de Ciencia e Innovación (Plan Nacional I+D), SAF 08/04328. Duration: 01/01/2009-31/12/2011.

Ramos M. Alteraciones genéticas del sistema inmunitario innato y estado protrombótico como factores predisponentes de arteriosclerosis subclínica y enfermedad cardiovascular en pacientes con síndrome de Sjögren primario. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080103. Duration: 01/01/2009-30/06/2012.

Casaroli R. Análisis celular y molecular de las células progenitoras mesenquimales estromales de la medula ósea humana y su potencial en la en la terapia celular para la superficie ocular. Sponsored by: Instituto de Salud Carlos III, PI09/0992. Duration: 01/01/2010-31/12/2012.

Ramos M. Multilingual Organic Information Management in the Medical Domain. Sponsored by: European Comission, Coordinador: Kentro Erevnon Notioanatolikis Evropis Astiki Mi Kerdoskopiki, 250534. Duration: 01/03/2010-31/08/2012.

Ramos M. Susceptibilitat immunogenètica i alteracions metabòliques com a factors etiopatogènics de dolor crònic en pacients amb síndrome de Sjögren en comparació amb pacients atesos a l'àmbit de l'atenció primària. Sponsored by: Fundació La Marató de TV3, 071810. Duration: 13/02/2008-12/08/2012.

Casaroli R. Medicina Regenerativa en la Superfície Ocular: Aplicación de terapia celular para la reparación de la superficie oculr mediante amplificación ex vivo de éclulas progenitoras autólogas del limbo esclerocorneal sobre membrana amniótica. Sponsored by: Ministerio de Sanidad, Politica Social e Igualdad, TRA-072. Duration: 01/01/2010-31/12/2011.

Cervera R. Grup de recerca de malalties autoimmunes sistèmiques. Sponsored by: AGAUR_SGR09, 2009_SGR_1421. Duration: 15/09/2009-31/12/2013.

Ramos M. Grup de Recerca en la Síndrome de Sjögren (GRESS). Sponsored by: AGAUR_SGR09, 2009_SGR_1357. Duration: 28/09/2009-31/12/2013.

Adan AM. Estudio de factores predictores para el desarrollo de recurrencias en la toxoplasmosis ocular. Sponsored by: Instituto de Salud Carlos III (ISCIII), 010PI10/00479. Duration: 01/01/2011-31/12/2013.

Cid MC. Grup de Recerca sobre Inflamació Vascular (vasculitis). Sponsored by: AGAUR_SGR09, 2009_SGR_1301. Duration: 15/09/2009-31/12/2013.

DOCTORAL THESES

Siso A, Ramos-Casals M. Significado clínico de la presencia de autoanticuerpos en el síndrome de Sjögren primario: implicaciones en la práctica diaria. PhD student: Norma Nardi, Universitat de Barcelona.

Cervera R. Afectación renal en el lupus eritematoso sistémico y el síndrome antifosfolipídico: Estudio clínco-epidemiológico, anátomopatológico y de factores predictivos de morbi-mortalidad. PhD student: Guillermo Javier Pons-Estel Silvestre (Universitat de Barcelona).

AREA 1

Biological aggression and response mechanisms

Infectious diseases and AIDS

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BIOLOGICAL AGGRESSION AND RESPONSE MECHANISMS

Infectious diseases and AIDS

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.
- Complications related to aging

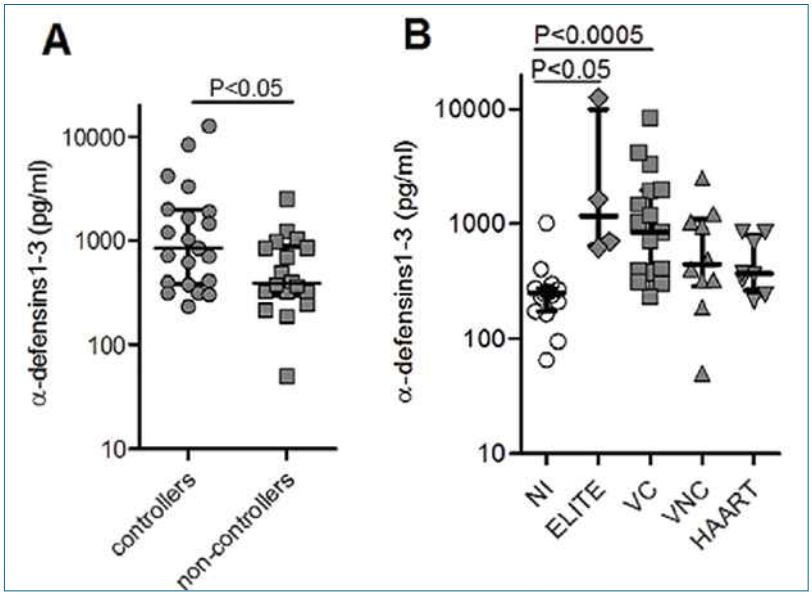
2. In the general infections field:

- Prevention and treatment support in endocarditis due to multiresistant germs, 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** is



Levels of a-defensins 1-3 produced by imMDDC from HIV-infected individuals. (A) Comparison between the secreted levels of a-defensins 1-3 by imMDDC from HIV-controllers (elite controllers and viremic controllers; n = 19) and HIV non-controllers (viremic non-controllers and patients with HAART; n = 20). (B) Secreted levels of a-defensins 1-3 by imMDDC from healthy non-infected (NI; n = 15), elite controllers (ELITE; n = 4), viremic controllers (VC; n = 15), viremic non-controllers (VNC; n = 11) and patients receiving HAART (HAART; n = 9). Dots indicate each patient, and lines represent median 6 interquartile ranges (Rodriguez-Garcia M, et al. PloS ONE 2010;5:1-10).

RESEARCH GROUP
ENDOCARDITIS. CARDIOVASCULAR INFECTIONS. EXPERIMENTAL MODEL

Group Leader:
Josep Maria Miro
(Hospital Clínic)

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.

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 the 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 administration of autologous dendritic cells *stimulated ex vivo* with the virus of the patient. The first two Phase I clinical trials have already been finished and published. The third study is now practically finished.
- We are developing different immunogens which may be potential candidates for **therapeutic or preventive vaccines**.

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. J. Mensa).
- Response to treatment, resistance and transmission of tuberculosis.
- Prognostic factors of community-acquired 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.

For further information:
www.idibaps.org/aidsresearch

RESEARCH GROUP
INFECTIONS IN SOLID-ORGAN TRANSPLANT RECIPIENTS

Group Leader:
Asuncion Moreno
(Hospital Clínic)

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 investigators specialized in Microbiology and Immunology, and with the different Transplantation Units (Institutes of Digestive, Renal and Thoracic Diseases).

RESEARCH GROUP
AIDS AND HIV INFECTION

Group Leader:
Josep Maria Gatell
(Hospital Clínic)

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 into vaccines against HIV infection.

EMERGENT GROUP
NOSOCOMIAL INFECTION STUDY GROUP

Group Leader:
Alex Soriano
(Hospital Clínic)

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. Its components are members of the REIPI (Spanish Research Network in Infectious Disease), and participate actively in multicenter projects financed by the FIS.

PUBLICATIONS

ORIGINALS
I.F.: 359.35

1 Pelegrin L, Mesquida M, Adan A, Cervera C, Bosch-Mestres J, Esteban-Redondo C, Juiz-Gonzalez P, Llorenc V, Miro JM. Candida dubliniensis endophthalmitis in a HIV-infected intravenous drug abuser. MYCOSES. 54:E856-E858. I.F.: 1.67.

2 Marcos M, Fernandez C, Soriano A, Marco F, Martinez JA, Almela M, Cervera R, Mensa J, Espinosa G. Epidemiology and clinical outcomes of bloodstream infections among lupus patients. LUPUS. 20:965-971. I.F.: 2.60.

3 Sanchez-Palomino S, Massanella M, Carrillo J, Garcia A, Garcia F, Gonzalez N, Merino A, Alcami J, Bofill M, Yuste E, Gatell JM, Clotet B, Blanco J. A cell-to-cell HIV transfer assay identifies humoral responses with broad neutralization activity. VACCINE. 29:5250-5259. I.F.: 3.57.

4 Reekie J, Reiss P, Ledergerber B, Sedlacek D, Parczewski M, Gatell J, Katlama C, Fatkenheuer G, Lundgren JD, Mocroft A. A comparison of the long-term durability of nevirapine, efavirenz and lopinavir in routine clinical practice in Europe: a Euro-SIDA study. HIV MED. 12:259-268. I.F.: 3.58.

5 Leon A, Caceres C, Fernandez E, Chausa P, Martin M, Codina C, Rousaud A, Blanch J, Mallolas J, Martinez E, Blanco JL, Laguno M, Larrousse M, Milinkovic A, Zamora L, Canal N, Miro JM, Gatell JM, Gomez EJ, Garcia F. A New Multidisciplinary Home Care Telemedicine System to Monitor Stable Chronic Human Immunodeficiency Virus-Infected Patients: A Randomized Study. PLOS ONE. 6:-. I.F.: 4.41.

6 Garcia F, Climent N, Assoumou L, Gil C, Gonzalez N, Alcami J, Leon A, Romeu J, Dalmau J, Martinez-Picado J, Lifson J, Autran B, Costagliola D, Clotet B, Gatell JM, Plana M, Gallart T. A Therapeutic Dendritic Cell-Based Vaccine for HIV-1 Infection. J INFECT DIS. 203:473-478. I.F.: 6.29.

7 Tomas X, Bori G, Garcia S, Garcia-Diez AI, Pomes J, Soriano A, Rios J, Almela M, Mensa J, Gallart X, Martinez JC, Riba J. Accuracy of CT-guided joint aspiration in patients with suspected infection status post-total hip arthroplasty. SKELETAL RADIOL. 40:57-64. I.F.: 1.39.

8 Martinez-Navio JM, Casanova V, Pacheco R, Naval-Macabuhay I, Climent N, Garcia F, Gatell JM, Mallol J, Gallart T, Lluis C, Franco R. Adenosine deaminase potentiates the generation of effector, memory, and regulatory CD4(+) T cells. J LEUKOCYTE BIOL. 89:127-136. I.F.: 4.63.

9 Freitas P, Carvalho D, Santos AC, Mesquita J, Correia F, Xerinda S, Marques R, Martinez E, Sarmento A, Medina JL. Assessment of body fat composition disturbances by bioimpedance analysis in HIV-infected adults. J ENDOCRINOL INVEST. 34:E321-E329. I.F.: 1.48.

10 Labarga P, Soriano V, Caruz A, Poveda E, DiLello F, Hernandez-Quero J, Moreno S, Bernal E, Miro JM, Leal M, Gutierrez F, Portilla J, Pineda JA. Association between IL28B gene polymorphisms and plasma HCV-RNA levels in HIV/HCV-co-infected patients. AIDS. 25:761-766. I.F.: 6.35.

11 Kiefer T, Park L, Tribouilloy C, Cortes C, Casillo R, Chu V, Delahaye F, Durante-Mangoni E, Edathodu J, Falces C, Logar M, Miro JM, Naber C, Tripodi MF, Murdoch DR, Moreillon P, Utili R, Wang A. Association Between Valvular Surgery and Mortality Among Patients With Infective Endocarditis Complicated by Heart Failure. JAMA-J AM MED ASSOC. 306:2239-2247. I.F.: 30.01.

12 Medina-Ramirez M, Sanchez-Merino V, Sanchez-Palomino S, Merino-Mansilla A, Ferreira CB, Perez I, Gonzalez N, Alvarez A, Alcocer-Gonzalez JM, Garcia F, Gatell JM, Alcami J, Yuste E. Broadly Cross-Neutralizing Antibodies in HIV-1 Patients with Undetectable Viremia. J VIROL. 85:5804-5813. I.F.: 5.19.

13 Pinilla MI, Cobos-Trigueros N, Soriano A, Martinez JA, Zboromyrska Y, Almela M, Mensa J. Burkholderia cepacia bacteremia: a prospective analysis of 33 episodes. REV ESP QUIM. 24:209-212. I.F.: 0.67.

14 Ortega M, Marco F, Soriano A, Almela M, Martinez JA, Lopez J, Pitart C, Mensa J. Candida species bloodstream infection: epidemiology and outcome in a single institution from 1991 to 2008. J HOSP INFECT. 77:157-161. I.F.: 3.08.

15 Ortega M, Marco F, Soriano A, Almela M, Martinez JA, Lopez J, Pitart C, Mensa J. Cefotaxime resistance and outcome of Klebsiella spp bloodstream infection. EUR J CLIN MICROBIOL. 30:1599-1605. I.F.: 2.63.

16 Marcos M, Soriano A, Inurrieta A, Martinez JA, Romero A, Cobos N, Hernandez C, Almela M, Marco F, Mensa J. Changing epidemiology of central venous catheter-related bloodstream infections: increasing prevalence of Gram-negative pathogens. J ANTIMICROB CHEMOTH. 66:2119-2125. I.F.: 4.66.

17 Llibre JM, Arribas JR, Domingo P, Gatell JM, Lozano F, Santos JR, Rivero A, Moreno S, Clotet B. Clinical implica-

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	299.30	60	41	10
2010	207.37	47	24	7
2011	359.35	91	37	19

tions of fixed-dose coformulations of antiretrovirals on the outcome of HIV-1 therapy. AIDS. 25:1683-1690. I.F.: 6.35.

18 Miro JM, Manzardo C, Zamora L, Pumarola T, Herreras Z, Gallart T, Gatell JM. Clinical management of acute and chronic human immunodeficiency virus infection before starting antiretroviral treatment. ENFERM INFEC MICR CL. 29:759-772. I.F.: 1.66.

19 Perello R, Calvo M, Miro O, Castaneda M, Saubi N, Camon S, Foix A, Gatell JM, Masotti M, Mallolas J, Sanchez M, Martinez E. Clinical presentation of acute coronary syndrome in HIV infected adults: A retrospective analysis of a prospectively collected cohort. EUR J INTERN MED. 22:485-488. I.F.: 1.66.

20 Marcos MA, Ramon S, Anton A, Martinez E, Vilella A, Olive V, Cilloniz C, Moreno A, Torres A, Pumarola T. Clinical relevance of mixed respiratory viral infections in adults with influenza A H1N1. EUR RESPIR J. 38:739-742. I.F.: 5.92.

21 Cervera C, Castaneda X, Pericas JM, DelRio A, DeLaMaria CG, Mestres C, Falces C, Marco F, Moreno A, Miro JM. Clinical utility of daptomycin in infective endocarditis caused by Gram-positive cocci. INT J ANTIMICROB AG. 38:365-370. I.F.: 3.79.

22 Cilloniz C, Ewig S, Ferrer M, Polverino E, Gabarrus A, DeLaBellacasa JP, Mensa J, Torres A. Community-acquired polymicrobial pneumonia in the intensive care unit: aetiology and prognosis. CRIT CARE. 15:-. I.F.: 4.60.

23 Rotger M, Dalmau J, Rauch A, Mclaren P, Bosinger SE, Martinez R, Sandler NG, Roque A, Liebner J, Battegay M, Bernasconi E, Descombes P, Erkizia I, Fellay J, Hirschel B, Miro JM, Palou E, Hoffmann M, Massanella M, Blanco J, Woods M, Gunthard HF, DeBakker P, Douek DC, Silvestri G, Martinez-Picado J, Telenti A. Comparative transcriptomics of extreme phenotypes of human HIV-1 infection and SIV infection in sooty mangabey and rhesus macaque. J CLIN INVEST. 121:2391-2400. I.F.: 14.15.

24 Munoz-Mahamud E, Garcia S, Bori G, Martinez-Pastor JC, Zumbado JA, Riba J, Mensa J, Soriano A. Comparison of a low-pressure and a high-pressure pulsatile lavage during debridement for orthopaedic implant infection. ARCH ORTHOP TRAUM SU. 131:1233-1238. I.F.: 1.20.

25 Papagno L, Alter G, Assoumou L, Murphy RL, Garcia F, Clotet B, Larsen M, Braibant M, Marcelin AG, Costagliola D, Altfeld M, Katlama C, Autran B. Comprehensive analysis of virus-specific T-cells provides clues for the failure of therapeutic immunization with ALVAC-HIV vaccine. AIDS. 25:27-36. I.F.: 6.35.

26 Blasco AJ, Arribas JR, Clotet B, Domingo P, Gonzalez-Garcia J, Lopez-Bernaldo JC, Llibre JM, Lozano F, Podzamczer D, Santamaria JM, Tuset M, Zamora L, Lazaro P, Gatell JM. Costs and cost effectiveness analysis of preferred GESIDA regimens for initial antiretroviral therapy. ENFERM INFEC MICR CL. 29:721-730. I.F.: 1.66.

27 Mothe B, Llano A, Ibarrondo J, Daniels M, Miranda C, Zamarreno J, Bach V, Zuniga R, Perez-Alvarez S, Berger CT, Puertas MC, Martinez-Picado J, Rolland M, Farfan M, Szinger JJ, Hildebrand WH, Yang OO, Sanchez-Merino V, Brumme CJ, Brumme ZL, Heckerman D, Allen TM, Mullins JI, Gomez G, Goulder PJ, Walker BD, Gatell JM, Clotet B, Korber BT, Sanchez J, Brander C. Definition of the viral targets of protective HIV-1-specific T cell responses. J TRANSL MED. 9:-. I.F.: 3.51.

28 Martinez E. Disorders of fat partitioning in treated HIV-infection. BEST PRACT RES CL EN. 25:415-427. I.F.: 4.19.

29 Berenguer J, VonWichmann MA, Quereda C, Miralles P, Mallolas J, Lopez-Aldeguer J, Alvarez-Pellicer J, DeMiguel J, Crespo M, Guardiola JM, Tellez MJ, Galindo MJ, Arponen S, Barquilla E, Bellon JM, Gonzalez-Garcia J. Effect of accompanying antiretroviral drugs on virological response to pegylated interferon and ribavirin in patients co-infected with HIV and hepatitis C virus. J ANTIMICROB CHEMOTH. 66:2843-2849. I.F.: 4.66.

30 Tural C, Sola R, Alvarez NP, Molto J, Sanchez M, Zamora AM, Ornelas A, Laguno M, Gonzalez J, VonWichmann MA, Tellez MJ, Paredes R, Clotet B. Effect of an induction period of pegylated interferon-alpha 2a and ribavirin on early virological response in HIV-HCV-coinfected patients: results from the CORAL-2 study. ANTIVIR THER. 16:833-841. I.F.: 3.77.

31 Viasus D, Pano-Pardo JR, Cordero E, Campins A, Lopez-Medrano F, Villoslada A, Farinas MC, Moreno A, Rodriguez-Bano J, Oteo JA, Martinez-Montauti J, Torre-Cisneros J, Segura F, Carratala J. Effect of immunomodulatory therapies in patients with pandemic influenza A (H1N1) 2009 complicated by pneumonia. J INFECTION. 62:193-199. I.F.: 3.81.

32 Cervera C, DelRio A, Garcia L, Sala M, Almela M, Moreno A, Falces C,

Mestres CA, Marco F, Robau M, Gatell JM, Miro JM. Efficacy and safety of outpatient parenteral antibiotic therapy for infective endocarditis: a ten-year prospective study. ENFERM INFEC MICR CL. 29:587-592. I.F.: 1.66.

33 Vilchez F, Martinez-Pastor JC, Garcia-Ramiro S, Bori G, Tornero E, Garcia E, Mensa J, Soriano A. Efficacy of debridement in hematogenous and early post-surgical prosthetic joint infections. INT J ARTIF ORGANS. 34:863-869. I.F.: 1.50.

34 Cervera C, Fernandez-Ruiz M, Valledor A, Linares L, Anton A, Marcos MA, Sanclemente G, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Pumarola T, Moreno A. Epidemiology and risk factors for late infection in solid organ transplant recipients. TRANSPL INFECT DIS. 13:598-607. I.F.: 2.04.

35 Carcelero E, Tuset M, Martin M, DeLazzari E, Codina C, Miro J, Gatell JM. Evaluation of antiretroviral-related errors and interventions by the clinical pharmacist in hospitalized HIV-infected patients. HIV MED. 12:494-499. I.F.: 3.58.

36 Gil C, Garcia MT, Garcia F, Miro JM, Aguero F, Alos L, Zamora L, Capon A, Costa J, Pumarola T, Gatell JM. Evaluation of the Roche COBAS (R) TaqMan (R) HIV-1 test for quantifying HIV-1 RNA in infected cells and lymphoid tissue. J VIROL METHODS. 174:69-76. I.F.: 2.14.

37 Gil C, Climent N, Garcia F, Hurtado C, Nieto-Marquez S, Leon A, Garcia MT, Rovira C, Miralles L, Dalmau J, Pumarola T, Almela M, Martinez-Picado J, Lifson JD, Zamora L, Miro JM, Brander C, Clotet B, Gallart T, Gatell JM. Ex vivo production of autologous whole inactivated HIV-1 for clinical use in therapeutic vaccines. VACCINE. 29:5711-5724. I.F.: 3.57.

38 Viasus D, Pano-Pardo JR, Pachon J, Campins A, Lopez-Medrano F, Villoslada A, Farinas MC, Moreno A, Rodriguez-Bano J, Oteo JA, Martinez-Montauti J, Torre-Cisneros J, Segura F, Gudiol F, Carratala J. Factors associated with severe disease in hospitalized adults with pandemic (H1N1) 2009 in Spain. CLIN MICROBIOL INFEC. 17:738-746. I.F.: 4.78.

39 Reekie J, Gatell JM, Yust I, Bakowska E, Rakhmanova A, Losso M, Krasnov M, Francioli P, Kowalska JD, Mocroft A. Fatal and nonfatal AIDS and non-AIDS events in HIV-1-positive individuals with high CD4 cell counts according to viral load strata. AIDS. 25:2259-2268. I.F.: 6.35.

40 DeLaTorre-Cisneros J, Farinas MC, Caston JJ, Aguado JM, Cantisan S, Carratala J, Cervera C, Cisneros JM, Cordero E, Crespo-Leiro MG, Fortun J, Frauca E, Gavalda J, Gil-Vernet S, Gurgui M, Len O, Lumbreras C, Marcos MA, Martin-Davila P, Monforte V, Montejo M, Moreno A, Munoz P, Navarro D, Pahissa A, Perez JL, Rodriguez-Bernot A, Rumbao J, Juan RS, Santos F, Varo E, Zurbano F. GESITRA-SEIMC/REIPI recommendations for the management of cytomegalovirus infection in solid-organ transplant patients. ENFERM INFEC MICR CL. 29:735-758. I.F.: 1.66.

41 Fortun J, Carratala J, Gavalda J, Lizasoain M, Salavert M, DeLaCamara R, Borges M, Cervera C, Garnacho J, Lassaleta A, Lumbreras C, Sanz MA, Ramos JT, Torre-Cisneros J, Aguado JM, Cuenca-Estrella M. Guidelines for the Treatment of Invasive Fungal Disease by Aspergillus spp. and Other Fungi Issued by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). 2011 Update. ENFERM INFEC MICR CL. 29:435-454. I.F.: 1.66.

42 Lee A, Chalfine A, Daikos GL, Garilli S, Jovanovic B, Lemmen S, Martinez JA, Aumatell CM, Mcewen J, Pittet D, Rubinovitch B, Sax H, Harbarth S. Hand hygiene practices and adherence determinants in surgical wards across Europe and Israel: A multicenter observational study. AM J INFECT CONTROL. 39:517-520. I.F.: 3.04.

43 Etcheverry MF, Lum PJ, Evans JL, Sanchez E, DeLazzari E, Mendez-Arancibia E, Sierra E, Gatell JM, Page K, Joseph J. HIV vaccine trial willingness among injection and non-injection drug users in two urban centres, Barcelona and San Francisco. VACCINE. 29:1991-1996. I.F.: 3.57.

44 Bohlius J, Schmidlin K, Boue F, Fatkenheuer G, May M, Caro-Murillo AM, Mocroft A, Bonnet F, Clifford G, Paparizos V, Miro JM, Obel N, Prins M, Chene G, Egger M. HIV-1-related Hodgkin lymphoma in the era of combination antiretroviral therapy: incidence and evolution of CD4(+) T-cell lymphocytes. BLOOD. 117:6100-6108. I.F.: 10.56.

45 Lopez-Medrano F, Fernandez-Ruiz M, Morales JM, San-Juan R, Cervera C, Carratala J, Torre-Cisneros J, Gavalda J, Munoz P, Len O, Martin-Davila P, Ramos A, Montejo M, Lumbreras C, Moreno A, Aguado JM. Impact of Hepatitis C Virus Infection on the Risk of Infectious Complications After Kidney Transplantation: Data From the RESITRA/REIPI Cohort. TRANSPLANTATION. 92:543-549. I.F.: 3.68.

46 Freitas P, Carvalho D, Souto S, Santos AC, Xerinda S, Marques R, Martinez E, Sarmento A, Medina JL. Impact of Lipodystrophy on the prevalence and components of metabolic syndrome in HIV-infected patients. BMC INFECT DIS. 11:-. I.F.: 2.83.

47 Ferrer E, DelRio L, Martinez E, Curto J, Domingo P, Ribera E, Negredo E, Rosales J, Saumoy M, Ordonez J, Gatell JM, Podzamczer D. Impact of Switching from Lopinavir/Ritonavir to Atazanavir/Ritonavir on Body Fat Redistribution in Virologically Suppressed HIV-Infected Adults. AIDS RES HUM RETROV. 27:1061-1065. I.F.: 2.08.

48 Letang E, Miro JM, Nhampossa T, Ayala E, Gascon J, Menendez C, Alonso PL, Naniche D. Incidence and Predictors of Immune Reconstitution Inflammatory Syndrome in a Rural Area of Mozambique. PLOS ONE. 6:-. I.F.: 4.41.

49 Linares L, Sanclemente G, Cervera C, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Marcos MA, Anton A, Pumarola T, Moreno A. Influence of Cytomegalovirus Disease in Outcome of Solid Organ Transplant Patients. TRANSPL P. 43:2145-2148. I.F.: 0.99.

50 Martinez E, Marcos MA, Hoyo-Ulloa I, Anton A, Sanchez M, Vilella A, Larrousse M, Perez I, Moreno A, Trilla A, Pumarola T, Gatell JM. Influenza A H1N1 in HIV-infected adults. HIV MED. 12:236-245. I.F.: 3.58.

51 Bori G, Munoz-Mahamud E, Garcia S, Mallofre C, Gallart X, Bosch J, Garcia E, Riba J, Mensa J, Soriano A. Interface membrane is the best sample for histological study to diagnose prosthetic joint infection. MODERN PATHOL. 24:579-584. I.F.: 4.18.

52 Garcia-Vidal C, Barba P, Arnan M, Moreno A, Ruiz-Camps I, Gudiol C, Ayats J, Orti G, Carratala J. Invasive Aspergillosis Complicating Pandemic Influenza A (H1N1) Infection in Severely Immunocompromised Patients. CLIN INFECT DIS. 53:E16-E19. I.F.: 8.19.

53 Sterzik H, Soriano A, Mohamad AM, Martinez JA, Fernandez J, Cobos N, Morata L, Mensa J. Is linezolid a risk factor for Gram-negative bacillus infections in intensive care unit patients? A comparative study with vancomycin. SCAND J INFECT DIS. 43:765-770. I.F.: 1.56.

54 Martina MN, Cofan F, Suarez A, Masso E, Trullas JC, Cervera C, Moreno A, Oppenheimer F, Miiro JM, Campistol JM. Kidney Transplantation and Waiting List for Renal Transplantation for Human Immunodeficiency Virus Patients. TRANSPL P. 43:2179-2181. I.F.: 0.99.

55 Antinori A, Coenen T, Costagiola D, Dedes N, Ellefson M, Gatell J, Girardi E, Johnson M, Kirk O, Lundgren J, Mocroft A, Monforte AD, Phillips A, Raben D, Rockstroh JK, Sabin C, Sonnerborg A, DeWolf F. Late presentation of HIV infection: a consensus definition. HIV MED. 12:61-64. I.F.: 3.58.

56 Gomez J, Canovas E, Banos V, Martinez L, Garcia E, Hernandez-Torres A, Canteras M, Ruiz J, Medina M, Martinez P, Canovas A, Soriano A, Clavel M. Linezolid plus Rifampin as a Salvage Therapy in Prosthetic Joint Infections Treated without Removing the Implant. ANTIMICROB AGENTS CH. 55:4308-4310. I.F.: 4.67.

57 Saumoy M, Ordonez-Llanos J, Martinez E, Barragan P, Ribera E, Bonet R, Knobel H, Negredo E, Lonca M, Curran A, Gatell JM, Podzamczer D. Low-density lipoprotein size and lipoprotein-associated phospholipase A2 in HIV-infected patients switching to abacavir or tenofovir. ANTIVIR THER. 16:459-468. I.F.: 3.77.

58 Diaz A, Garcia F, Mozos A, Caballero M, Leon A, Martinez A, Gil C, Plana M, Gallart T, Gatell JM, Alos L. Lymphoid Tissue Collagen Deposition in HIV-Infected Patients Correlates With the Imbalance Between Matrix Metalloproteinases and Their Inhibitors. J INFECT DIS. 203:810-813. I.F.: 6.29.

59 Cilloniz C, Ewig S, Polverino E, Marcos MA, Esquinas C, Gabarrus A, Mensa J, Torres A. Microbial aetiology of community-acquired pneumonia and its relation to severity. THORAX. 66:340-346. I.F.: 6.53.

60 Garrabou G, Lopez S, Moren C, Martinez E, Fontdevila J, Cardellach F, Gatell JM, Miro O. Mitochondrial damage in adipose tissue of untreated HIV-infected patients. AIDS. 25:165-170. I.F.: 6.35.

61 Garcia AI, Milinkovic A, Tomas X, Rios J, Perez I, Vidal-Sicart S, Pomes J, DelAmo M, Mallolas J. MRI signal changes of the bone marrow in HIV-infected patients with lipodystrophy: correlation with clinical parameters. SKELETAL RADIOL. 40:1295-1301. I.F.: 1.39.

62 Saubi N, Im EJ, Fernandez-Lloris R, Gil O, Cardona PJ, Gatell J, Hanke T, Joseph J. Newborn Mice Vaccination with BCG.HIVA(222) plus MVA.HIVA Enhances HIV-1-Specific Immune Responses: Influence of Age and Immunization Routes. CLIN DEV IMMUNOL. :-. I.F.: 2.26.

63 Ortiz M, Poloni ES, Furrer H, Kovari H, Martinez R, Arnedo M, Elzi L, Bernasconi E, Vernazza P, Hirschel B, Cavassini M, Ledergerber B, Gunthard HF, Telenti A, Tarr PE. No Longitudinal Mitochondrial DNA Sequence Changes in HIV-infected Individuals With and Without Lipoatrophy. J INFECT DIS. 203:620-624. I.F.: 6.29.

64 Cervera C, Fernandez-Aviles F, DeLaCalle-Martin O, Bosch X, Rovira

M, Plana M, Moreno A, Garcia F, Miro JM, Martinez A, Gallart T, Carreras E, Blade J, Gatell JM. Non-myeloablative hematopoietic stem cell transplantation in the treatment of severe idiopathic CD4+lymphocytopenia. EUR J HAEMATOL. 87:87-91. I.F.: 2.79.

65 Vilchez F, Martinez-Pastor JC, Garcia-Ramiro S, Bori G, Macule F, Sierra J, Font L, Mensa J, Soriano A. Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to Staphylococcus aureus treated with debridement. CLIN MICROBIOL INFEC. 17:439-444. I.F.: 4.78.

66 Trullas JC, Cofan F, Barril G, Martinez-Castelao A, Jofre R, Rivera M, Martinez-Ara J, Ros S, Perez I, Moreno A, Miro JM. Outcome and Prognostic Factors in HIV-1-Infected Patients on Dialysis in the cART Era: a GESIDA/SEN Cohort Study. JAIDS-J ACQ IMM DEF. 57:276-283. I.F.: 4.26.

67 Martinez-Rebollar M, Lonca M, Perez I, Soy D, Brunet M, Martin R, Coll O, Hernandez S, Laguno M, Milinkovic A, Larrousse M, Calvo M, Blanco JL, Martinez E, Gatell JM, Mallolas J. Pharmacokinetic Study of Saquinavir 500 mg Plus Ritonavir (1000/100 mg Twice a Day) in HIV-Positive Pregnant Women. THER DRUG MONIT. 33:772-777. I.F.: 3.13.

68 Viasus D, Pano-Pardo JR, Pachon J, Riera M, Lopez-Medrano F, Payeras A, Farinas MC, Moreno A, Rodriguez-Bano J, Oteo JA, Martinez-Montauti J, Torre-Cisneros J, Segura F, Gudiol F, Carratala J. Pneumonia Complicating Pandemic (H1N1) 2009 Risk Factors, Clinical Features, and Outcomes. MEDICINE. 90:328-336. I.F.: 4.26.

69 Pett SL, Carey C, Lin E, Wentworth D, Lazovski J, Miro JM, Gordin F, Angus B, Rodriguez-Barradas M, Rubio R, Tambussi G, Cooper DA, Emery S. Predictors of bacterial pneumonia in Evaluation of Subcutaneous Interleukin-2 in a Randomized International Trial (ESPRIT). HIV MED. 12:219-227. I.F.: 3.58.

70 Font-Vizcarra L, Lozano L, Rios J, Forga MT, Soriano A. Preoperative nutritional status and post-operative infection in total knee replacements: A prospective study of 213 patients. INT J ARTIF ORGANS. 34:876-881. I.F.: 1.50.

71 Orcau A, Cayla JA, Martinez JA. Present epidemiology of tuberculosis. Prevention and control programs. ENFERM INFEC MICR CL. 29:2-7. I.F.: 1.66.

72 Romero A, Sued O, Puig T, Esteve A, Pumarola T, Casabona J, Gonzalez V, Matas L, Tural C, Rodrigo I, Margall N, Domingo P, Casanova A, Ferrer E, Caballero E, Ribera E, Farre J, Amengual MJ, Navarro G, Prat JM, Masabeu A, Simo JM, Villaverde CA, Barrufet P, Sauca MG, Ortin X, Orti A, Navarro R, Euras JM, Vilaro J, Villa MC, Montull S, Vilanova C, Pujol F, Diaz O, Miro JM. Prevalence of Transmitted Antiretroviral Resistance and Distribution of HIV-1 Subtypes Among Patients with Recent Infection in Catalonia (Spain) between 2003 and 2005. ENFERM INFEC MICR CL. 29:482-489. I.F.: 1.66.

73 Garcia-Oltra E, Garcia-Ramiro S, Pastor JCM, Tibau R, Bori G, Bosch J, Mensa J, Soriano A. Prosthetic joint infection by Candida spp.. REV ESP QUIM. 24:37-41. I.F.: 0.67.

74 Mogollon MV, Anguita MP, Aguado JM, Tornos P, Miro JM, Galvez-Acebal J, Munoz-Sanz A, Farinas MD, Fernandez-Guerrero M, Vilacosta I, Munoz P, Montejo-Baranda JM, Hidalgo-Tenorio C, Falco V, DelRio A, Arnaiz AM, San-Feliu I, DeAlarcon A. Q fever endocarditis in Spain. Clinical characteristics and outcome. ENFERM INFEC MICR CL. 29:109-116. I.F.: 1.66.

74 Font-Vizcarra L, Zumbado A, Garcia S, Bosch J, Mensa J, Soriano A. Relationship between haematoma in femoral neck fractures contamination and early postoperative prosthetic joint infection. INJURY. 42:200-203. I.F.: 2.27.

76 Font-Vizcarra L, Tornero E, Bori G, Bosch J, Mensa J, Soriano A. Relationship between intraoperative cultures during hip arthroplasty, obesity, and the risk of early prosthetic joint infection: A prospective study of 428 patients. INT J ARTIF ORGANS. 34:870-875. I.F.: 1.50.

77 Sierra JM, Garcia S, Martinez-Pastor JC, Tomas X, Gallart X, Vila J, Bori G, Macule F, Mensa J, Riba J, Soriano A. Relationship between the degree of osteolysis and cultures obtained by sonication of the prostheses in patients with aseptic loosening of a hip or knee arthroplasty. ARCH ORTHOP TRAUM SU. 131:1357-1361. I.F.: 1.20.

78 Lejeune M, Miro JM, DeLazzari E, Garcia F, Claramonte X, Martinez E, Ribera E, Arrizabalaga J, Arribas JR, Domingo P, Ferrer E, Plana M, Valls ME, Podzamczer D, Pumarola T, Jacquet A, Mallolas J, Gatell JM, Gallart T. Restoration of T Cell Responses to Toxoplasma gondii after Successful Combined Antiretroviral Therapy in Patients with AIDS with

Previous Toxoplasmic Encephalitis. CLIN INFECT DIS. 52:662-670. I.F.: 8.19.

79 Arenas-Pinto A, Grant A, Bhaskaran K, Copas A, Carr A, Worm SW, Martinez E, Reiss P, Dunn D, Weber R, Hoy J, Weller I. Risk factors for fatality in HIV-infected patients with dideoxynucleoside-induced severe hyperlactataemia or lactic acidosis. ANTIVIR THER. 16:219-226. I.F.: 3.77.

80 Garcia F, DeQuiros JCLB, Gomez CE, Perdiguero B, Najera JL, Jimenez V, Garcia-Arriaza J, Guardo AC, Perez I, Diaz-Brito V, Conde MS, Gonzalez N, Alvarez A, Alcami J, Jimenez JL, Pich J, Arnaiz JA, Maleno MJ, Leon A, Munoz-Fernandez MA, Liljestrom P, Weber J, Pantaleo G, Gatell JM, Plana M, Esteban M. Safety and immunogenicity of a modified pox vector-based HIV/AIDS vaccine candidate expressing Env, Gag, Pot and Nef proteins of HIV-1 subtype B (MVA-B) in healthy HIV-1-uninfected volunteers: A phase I clinical trial (RISVAC02). VACCINE. 29:8309-8316. I.F.: 3.57.

81 San-Juan R, Aguado JM, Lumbreras C, Fortun J, Len O, Munoz P, Montejo M, Moreno A, Cordero E, Blanes M, Ramos A, Torre-Cisneros J, Lopez-Medrano F, Carratala J, Moreno E. Selective Intestinal Decontamination With Fluoroquinolones for the Prevention of Early Bacterial Infections After Liver Transplantation. LIVER TRANSPLANT. 17:896-904. I.F.: 3.07.

82 Miro JM, Manzardo C, Mussini C, Johnson M, Monforte AD, Antinori A, Gill MJ, Sighinolfi L, Uberti-Foppa C, Borghi V, Sabin C. Survival Outcomes and Effect of Early vs. Deferred cART Among HIV-Infected Patients Diagnosed at the Time of an AIDS-Defining Event: A Cohort Analysis. PLOS ONE. 6:-. I.F.: 4.41.

83 Gomez CE, Najera JL, Perdiguero B, Garcia-Arriaza J, Sorzano COS, Jimenez V, Gonzalez-Sanz R, Jimenez JL, Munoz-Fernandez MA, DeQuiros JCLB, Guardo AC, Garcia F, Gatell JM, Plana M, Esteban M. The HIV/AIDS Vaccine Candidate MVA-B Administered as a Single Immunogen in Humans Triggers Robust, Polyfunctional, and Selective Effector Memory T Cell Responses to HIV-1 Antigens. J VIROL. 85:11468-11478. I.F.: 5.19.

84 Viasus D, Pano-Pardo JR, Pachon J, Riera M, Lopez-Medrano F, Payeras A, Farinas MC, Moreno A, Rodriguez-Bano J, Oteo JA, Ortega L, Torre-Cisneros J, Segura F, Carratala J. Timing of Oseltamivir Administration and Outcomes in Hospitalized Adults With Pandemic 2009 Influenza A(H1N1) Virus Infection. CHEST. 140:1025-1032. I.F.: 6.52.

85 Martina MN, Cervera C, Esforzado N, Linares L, Torregrosa V, Sanclemente G, Hoyo I, Cofan F, Oppenheimer F, Miro JM, Campistol JM, Moreno A. Toxoplasma gondii primary infection in renal transplant recipients. Two case reports and literature review. TRANSPL INT. 24:e6-e12. I.F.: 3.21.

86 Garcia F, Perez-Cachafeiro S, Guillot V, Alvarez M, Perez-Romero P, Perez-Elias MJ, Viciana I, Blanco JR, Lopez-Dieguez M, DeMendoza C. Transmission of HIV drug resistance and non-B subtype distribution in the Spanish cohort of antiretroviral treatment naive HIV-infected individuals (CoRIS). ANTIVIR RES. 91:150-153. I.F.: 4.44.

87 San-Juan R, Aguado JM, Lumbreras C, Fortun J, Len O, Munoz P, Montejo M, Moreno A, Cordero E, Blanes M, Ramos A, DeLaTorre-Cisneros J, Lopez-Medrano F, Carratala J, Moreno E. Universal Prophylaxis With Fluconazole for the Prevention of Early Invasive Fungal Infection in Low-Risk Liver Transplant Recipients. TRANSPLANTATION. 92:346-350. I.F.: 3.68.

88 Perello R, Miro O, Miro JM, Masso E, Sanchez M, Camon S, DeLaBellacasa JP, Moreno A, Marcos MD. Urgent pneumococcal urinary antigen, importance in the diagnosis of acquired pneumonia in HIV-1 patients. EUR J EMERG MED. 18:50-54. I.F.: 0.90.

89 Sousa R, Lopez R, Martinez-Pastor JC, Cervera C, Bori G, Garcia-Ramiro S, Mensa J, Soriano A. Usefulness of monitoring linezolid trough serum concentration in prolonged treatments. REV ESP QUIM. 24:151-153. I.F.: 0.67.

90 Fuster D, Soriano A, Garcia S, Piera C, Suades J, Rodriguez D, Martinez JC, Mensa J, Campos F, Pons F. Usefulness of Tc-99m-ciprofloxacin scintigraphy in the diagnosis of prosthetic joint infections. NUCL MED COMMUN. 32:44-51. I.F.: 1.37.

91 Viard JP, Souberbielle JC, Kirk O, Reekie J, Knysz B, Losso M, Gatell J, Pedersen C, Bogner JR, Lundgren JD, Mocroft A. Vitamin D and clinical disease progression in HIV infection: results from the EuroSIDA study. AIDS. 25:1305-1315. I.F.: 6.35.

REVIEWS
I.F.: 27.41

1 Albert M, Benito J, Bhagani S, Boesecke C, Deterding K, Dominguez S, Fisher M, Fontanet A, Garcia D, Gilson R, Guiguet M, Hoepelman AIM, Horban A, Katla-

ma C, Mallolas J, Page E, Peters L, Pozniak A, Prins M, Puoti M, Rauch A, Rodger A, Rockstroh JK, Soriano V, Stephan C, Thibault V, Tural C, Valantin MA, VanDeLaar T, VanDerMeer J, Vella S, Vogel M, DeWit S, Autran B, Clotet B, Danta M, Journiac M, Matthews G, Meyer-Olson D, Nelson M, Schmidt R, Wedemeyer H. Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel. AIDS. 25:399-409. I.F.: 6.35.

2 Garcia F, Routy JP. Challenges in dendritic cells-based therapeutic vaccination in HIV-1 infection Workshop in dendritic cell-based vaccine clinical trials in HIV-1. VACCINE. 29:6454-6463. I.F.: 3.57.

3 Martinez-Rebollar M, Larrousse M, Calvo M, Munoz A, Gonzalez A, Lonca M, Martinez E, Blanco JL, Mallolas J, Laguno M. Current status of acute hepatitis C. ENFERM INFEC MICR CL. 29:210-215. I.F.: 1.66.

4 Vidal F, Domingo P, Vilades C, Peraire J, Arnedo M, Alcami J, Leal M, Villarroya F, Gatell JM. Pharmacogenetics of the lipodystrophy syndrome associated with HIV infection and combination antiretroviral therapy. EXPERT OPIN DRUG MET. 7:1365-1382. I.F.: 3.37.

5 Trullas JC, Cofan F, Tuset M, Ricart MJ, Brunet M, Cervera C, Manzardo C, Lopez-Dieguez M, Oppenheimer F, Moreno A, Campistol JM, Miro JM. Renal transplantation in HIV-infected patients: 2010 update. KIDNEY INT. 79:825-842. I.F.: 6.11.

6 Guaraldi G, Fontdevila J, Christensen LH, Orlando G, Stentarelli C, Carli F, Zona S, DeSantis G, Pedone A, DeFazio D, Bonucci P, Martinez E. Surgical correction of HIV-associated facial lipoatrophy. AIDS. 25:1-12. I.F.: 6.35.

EDITORIALS
I.F.: 8.19

1 Gatell JM. Antiretroviral Therapy for HIV: Do Subtypes Matter?. CLIN INFECT DIS. 53:1153-1155. I.F.: 8.19.

CLINICAL GUIDELINES
I.F.: 2.33

1 Barberan J, Mensa J, Llamas JCV, Ramos IJ, Ruiz JCG, Marin JRC, Tello PB, Massana MB, Vidal JB, Vinas JMC, Huelva FJC, Pons EC, Mediavilla JD, Morfa MLD, Barrigon FE, Avellan PF, Lopez SG, Garcia CG, Maraver DH, DeLaGuia AL, Jimenez JL, Chacon EM, Rubio MO, DeOteyza JP, Ramirez GR, Contreras RR, Barbero AR, Tarrats MR, Felix DR, Godoy PS, Salinas AS, Alonso MA, Torroba JD, Ferreiras DV, Lopez LV, Garcia JMA, Perea JRA, Moreno RC, Cancer RC, Abete JF, Rodriguez JG, Gomez JG, DeLaPedrosa EGG, Baranda JMM, Garcia FJP, Camps IR, Lleti MS, Cisneros JD. Recommendations for the treatment of invasive fungal infection caused by filamentous fungi in the hematological patient. REV ESP QUIM. 24:263-270. I.F.: 0.67.

2 PanelDeExpertosDeGesidaYPlanNacionalSobreEl SIDA. National consensus document by GESIDA/National Aids Plan on antiretroviral treatment in adults infected by the human immunodeficiency virus (January 2011 update). ENFERM INFEC MICR CL. 29:-. I.F.: 1.66.

MULTICENTRICS
I.F.: 165.68

1 Cain LE, Logan R, Robins JM, Sterne JAC, Sabin C, Bansi L, Justice A, Goulet J, VanSighem A, DeWolf F, Bucher HC, VonWyl V, Esteve A, Casabona J, DelAmo J, Moreno S, Seng R, Meyer L, Perez-Hoyos S, Muga R, Lodi S, Lanoy E, Costagliola D, Hernan MA. When to Initiate Combined Antiretroviral Therapy to Reduce Mortality and AIDS-Defining Illness in HIV-Infected Persons in Developed Countries An Observational Study. ANN INTERN MED. 154:509-W173. I.F.: 16.73.

2 Nienaber JJC, Kuinkel BKS, Clarke-Pearson M, Lamlertthon S, Park L, Rude TH, Barriere S, Woods CW, Chu VH, Marin M, Bukovski S, Garcia P, Corey GR, Korman T, Doco-Lecompte T, Murdoch DR, Reller LB, Fowler VG. Methicillin-Susceptible Staphylococcus aureus Endocarditis Isolates Are Associated With Clonal Complex 30 Genotype and a Distinct Repertoire of Enterotoxins and Adhesins. J INFECT DIS. 204:704-713. I.F.: 6.29.

3 Yuan J, Guo S, Hall D, Cammett AM, Jayadev S, Distel M, Storfer S, Huang ZM, Mootsikapun P, Ruxrungtham K, Podzamczer D, Haas DW. Toxicogenomics of nevirapine-associated cutaneous and hepatic adverse events among populations of African, Asian, and European descent. AIDS. 25:1271-1280. I.F.: 6.35.

4 English S, Katzourakis A, Bonsall D, Flanagan P, Duda A, Fidler S, Weber J, Mcclure M, Phillips R, Frater J. Phylogenetic analysis consistent with a clinical history of sexual transmission of HIV-1 from a single donor reveals transmission of highly distinct variants. RETROVIROLOGY. 8:-. I.F.: 5.24.

5 Millet JP, Orcau A, Rius C, Casals M, DeOlalla PG, Moreno A, Nelson JL, Cayla JA. Predictors of Death among Patients Who Completed Tuberculosis Treatment: A Population-Based Cohort Study. PLOS ONE. 6:-. I.F.: 4.41.

6 Trevino A, DeMendoza C, Caballero E, Rodriguez C, Parra P, Benito R, Cabezas T, Roc L, Aguilera A, Soriano V. Drug resistance mutations in patients infected with HIV-2 living in Spain. J ANTIMICROB CHEMOTH. 66:1484-1488. I.F.: 4.66.

7 Yebra G, DeMulder M, Martin L, Perez-Cachafeiro S, Rodriguez C, Labarga P, Garcia F, Tural C, Jaen A, Navarro G, Holguin A. Sensitivity of seven HIV subtyping tools differs among subtypes/recombinants in the Spanish cohort of naive HIV-infected patients (CoRIS). ANTIVIR RES. 89:19-25. I.F.: 4.44.

8 Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies D, Kerrigan A, Weis SE, Weiner M, Wing D, Conde MB, Bozeman L, Horsburgh CR, Chaisson RE. Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection. NEW ENGL J MED. 365:2155-2166. I.F.: 53.49.

9 Kruk A, Bannister W, Podlekarev DN, Chentsova NP, Rakhmanova AG, Horban A, Domingo P, Mocroft A, Lundgren JD, Kirk O. Tuberculosis among HIV-positive patients across Europe: changes over time and risk factors. AIDS. 25:1505-1513. I.F.: 6,35.

10 Sobrino-Vegas P, Gutierrez F, Berenguer J, Labarga P, Garcia F, Alejos-Ferreras B, Munoz MA, Moreno S, DelAmo J. The cohort of the spanish hiv research network (coris) and its associated biobank; organizational issues, main findings and losses to follow-up. ENFERM INFEC MICR CL. 29:645-653. I.F.: 1.66.

11 Paredes R, Puertas MC, Bannister W, Kisic M, Cozzi-Lepri A, Pou C, Bellido R, Betancor G, Bogner J, Gargalianos P, Banhegyi D, Clotet B, Lundgren J, Menendez-Arias L, Martinez-Picado J. A376S in the Connection Subdomain of HIV-1 Reverse Transcriptase Confers Increased Risk of Virological Failure to Nevirapine Therapy. J INFECT DIS. 204:741-752. I.F.: 6.29.

12 Castro H, Judd A, Gibb DM, Butler K, Lodwick RK, VanSighem A, Ramos JT, Warsawski J, Thorne C, Noguera-Julian A, Obel N, Costagliola D, Tookey PA, Colin C, Kjaer J, Grarup J, Chene G, Phillips A. Risk of triple-class virological failure in children with HIV: a retrospective cohort study. LANCET. 377:1580-1587. I.F.: 33.63.

13 Wittkop L, Gunthard HF, DeWolf F, Dunn D, Cozzi-Lepri A, DeLuca A, Kucherer C, Obel N, VonWyl V, Masquelier B, Stephan C, Torti C, Antinori A, Garcia F, Judd A, Porter K, Thiebaut R, Castro H, VanSighem AI, Colin C, Kjaer J, Lundgren JD, Paredes R, Pozniak A, Clotet B, Phillips A, Pillay D, Chene G. Effect of transmitted drug resistance on virological and immunological response to initial combination antiretroviral therapy for HIV (EuroCoord-CHAIN joint project): a European multicohort study. LANCET INFECT DIS. 11:363-371. I.F.: 16.14.

GRANTS FOR RESEARCH IN PROGRESS

Gatell JM. NoE - European AIDS Treatment Network. Sponsored by: European Commission, LSHP-CT-2006-037570. Duration: 01/02/2007-31/01/2012.

Miro JM. Tratamiento antiretroviral una vez al dia en pacientes con infecciones por el VIH-1 no tratados previamente y con cifras de linfocitos CD4+ inferiores a 100 céls/MM3. Estudio prospectivo aleatorizado, multicéntrico y abierto. Estudio advanz-3. Sponsored by: Instituto de Salud Carlos III (ISCIII), EC07/90642. Duration: 29/10/2007-30/06/2012.

Caballero M. Desarrollo de un modelo experimental en cobaya de enfermedad de vías aéreas superiores por exposición al humo de tabaco. Estudio de los cambios anatomopatológicos y de los marcadores de inflamación. Sponsored by: Ministerio Sanidad y Consumo, PI070434. Duration: 26/11/2007-30/06/2012.

Yuste E. Optimización como inmunógeno de la proteína de la envuelta del virus de la inmunodeficiencia humana tipo 1. Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE), 36780/08. Duration: 30/10/2008-31/08/2012.

Arnedo M. Factores genéticos implicados en el desarrollo de dislipemia en pacientes infectados por VIH-1 que inician tratamiento antiretroviral de gran actividad. Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE), PS09/00396. Duration: 30/10/2008-29/10/2011.

Climent N. Evaluación de la adenosina desaminasa como molécula coestimuladora de la actividad linfocitaria en una vacuna terapéutica del VIH. Sponsored by: Fundación para la Investigación y la Prevención del Sida en España (FIPSE), 36750/08. Duration: 11/12/2008-31/12/2011.

BIOLOGICAL AGGRESSION AND RESPONSE MECHANISMS

Infectious diseases and AIDS

Miro JM. Optimización farmacocinética/farmacodinámica del tratamiento con vancomicina de la endocarditis experimental por Staphylococcus aureus resistente o no a la meticilina causada por cepas con una CMI a la vancomicina de 0.5, 1 o 2 mcg/mL. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080268. Duration: 01/01/2009-30/12/2011.

Miro JM. Estudio FIPSE de trasplante hepático en pacientes infectados por el VIH en España. Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE), TOH/VIH-08. Duration: 01/01/2009-15/01/2012.

Garcia F. Desarrollo de una vacuna frente a VIH: Estudio de los cambios de la biología de células dendríticas humanas tras interacción dcon distintos inmunógenos. Sponsored by: Instituto de Salud Carlos III, PS09/01297. Duration: 01/01/2010-31/12/2012.

Arnedo M. Factores genéticos implicados en el desarrollo de dislipemia en pacientes infectados por VIH-1 que inician tratamiento antiretroviral de gran actividad. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0396. Duration: 01/01/2010-31/12/2012.

Eloisa Yuste. Desarrollo de una vacuna frente al VIH: aislamiento y caracterización de nuevos anticuerpos neutralizantes de amplio espectro. Diseño de inmunógenos capaces de generar dichos anticuerpos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/1459. Duration: 01/01/2010-31/12/2012.

Gatell JM. Evaluación del impacto de nuevos sistemas de información en el cuidado de pacientes VIH crónicos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90897. Duration: 01/01/2010-31/12/2012.

Miro JM. 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: 04/01/2010-03/01/2012.

Gatell JM. Premio Fundación Lilly de Investigación Clínica. Sponsored by: Fundación Lilly, 10/104. Duration: 01/05/2010-30/04/2012.

Caballero M. Estudio del cambio de eficacia y la seguridad de la bleomicina aplicada con electroquimioterapia en el tratamiento de neoplasias de cabeza y cuello.. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, EC10-067. Duration: 01/01/2011-31/12/2011.

Garcia F. Estudio en fase I abierto para evaluar la seguridad e inmunogenicidad de la vacuna frente a VIH-1 MVA-B en pacientes infectados por VIH crónicos en tratamiento antirretroviral (RISVAC03). Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-094. Duration: 01/01/2010-31/12/2011.

Moreno A. Evaluar la eficacia y la seguridad de la combinación 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, EC08/00190. Duration: 01/01/2009-30/06/2012.

Moreno A. Infecciones en el Trasplante de órgano sólido (INFTOS). Sponsored by: AGAUR_SGR09, 2009_SGR_1341. Duration: 15/09/2009-31/12/2013.

Gatell JM. European Network of HIV/AIDS Cohort Studies to Coordinate at European and International level Clinical. Sponsored by: European Commission, CE_FP7_Health_1st_10. 260694. Duration: 01/01/2011-31/12/2015.

Gatell JM. Red de investigación en sida. Sponsored by: Instituto de Salud Carlos III (ISCIII), RD06/0006/0000. Duration: 01/01/2007-31/12/2012.

Gatell JM. Programa HIVACAT. Sponsored by: Conveni Generalitat de Catalunya, Fundació La Caixa, Laboratorios Esteve, RD06/0006/0000. Duration: 01/01/2007-31/12/2012.

Gatell JM. Simposio internacional sobre la NucleoCápside Retroviral. Sponsored by: Ministerio de Ciencia e Innovación, SAF2011-13586-E. Duration: 20/12/2011-19/12/2012.

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: Fipse, 36-0963. Duration: 16/02/2011-15/02/2014.

Eloisa Yuste. Diseño, síntesis y estudio anti-HIV-1 de dominios peptídicos del GB virus C. Sponsored by: Fundación para la Investigación y Prevención del Sida en España (FIPSE), 36-0735-09. Duration: 09/03/2010-08/03/2013.

Garcia F. Design of multifunctional nanoparticles targeting TLR or Nod receptors for dendritic cell immune therapy. Sponsored by: Instituto de Salud Carlos III, PI10/02984 (NO-NO-MED). Duration: 01/01/2011-31/12/2013.

Gatell JM. Grup de recerca VIH/sida. Sponsored by: AGAUR_SGR09, 2009_SGR_1159. Duration: 23/09/2009-31/12/2013.

Gatell JM. 8th International Retroviral NC Symposium. Sponsored by: AGAUR_ARCS11, JG075298. Duration: 18/09/2011-21/09/2011.

Gatell JM. Nanopartículas de ácido poli-láctico (PLA) recubiertas de antígenos VIH y vectores poxvirus que expresan proteína Gag o proteínas reguladoras del ciclo del VIH como inmunógenos para una vacuna contra el SIDA: Interacción con células dendríticas. Sponsored by: Ministerio de Ciencia e Innovación (Plan Nacional I+D), SAF2008-04395. Duration: 01/01/2009-31/12/2011.

Miro JM. 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: Duke University, NIHAI2008025. Duration: 23/05/2011-30/06/2012.

DOCTORAL THESES

Miro JM, Moreno A, Barril G. Enfermedad renal crónica y terapia renal sustitutiva en pacientes con infección por el virus de la inmunodeficiencia humana. Prevalencia y supervivencia en terapia renal sustitutiva y trasplante renal. PhD student: Joan Carles Trullàs Vila.

Mallolas J. Estudio del sistema musculoesquelético mediante resonancia magnética en la valoración del síndrome de lipodistrofia en pacientes infectados por el virus de la inmunodeficiencia humana. PhD student: Ana Isabel García Díez.

AREA 1

Biological aggression and response mechanisms

Immune receptors of the innate and adaptive system

TEAM INVOLVED IN:

GROUP MEMBERS

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Vanesa G. Martínez (JdC)
Xavier Romero (IDIBAPS)
Esther Carreras Margalef (BioTrack)

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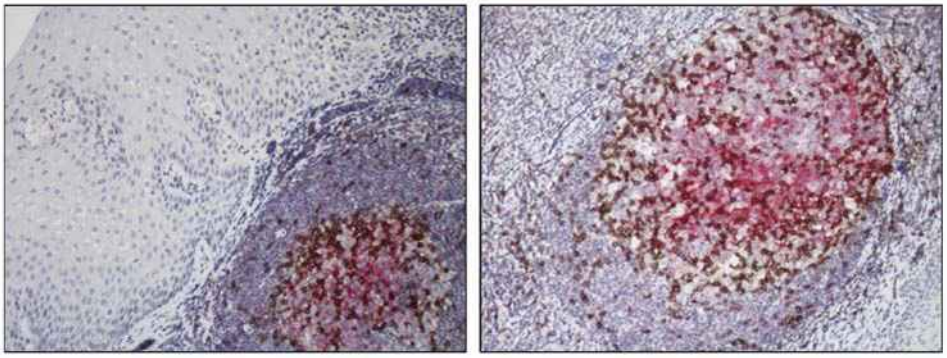
Rafael Fenutría (Fundació Clínic)
Elena Isern (IDIBAPS)
Jordi Sintes (UB)
Cristina Miró (MEC/FPU)
Cristina Escoda (MEC/FPI)
Natalia Pérez Carmona (UB)
Jose de Salort (UB)
M. Carmen Diaz-Ramos (IDIBAPS)
Marta Consuegra (AGAUR)
Marc Orta (MICINN/FPI)
Ángela Zarama (IDIBAPS)
Inês Simoês (FCyT)

TECHNICIANS:
Adriana Lázaro (Fundació Clínic)
Noelia Armiger Borràs (IDIBAPS)

STRATEGIC OBJECTIVES

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



Immunohistochemical staining of a normal tonsil specimen exhibiting secondary folicles. Brown, CD279/PD-1 (Programmed death-1) positive cells (activated T and B lymphocytes). Red, CD23 positive cells (activated B cells and Follicular Dendritic Cells).

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 CD5 and CD6 receptors in lymphocyte activation and differentiation.
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 genic regulation mechanisms of CMV and identification of functions encoded for by CMV.
7. Study of CMV mediated modulation of immune response and immune evasion strategies.

EMERGENT GROUP
MOLECULAR MECHANISMS OF THE PATHOGENESIS OF CMV DISEASE

Group Leader:
Ana Angulo (IDIBAPS)

Cytomegalovirus (CMV) is an ubiquitous pathogen that establishes latent infections for life – with serious consequences for immune-compromised individuals. The group studies different aspects of the interactions between CMV and the host, with special emphasis on the mechanisms that regulate viral genic expression, the determination of new functions encoded by the virus, and the identification of processes of interference with the immune system.

PUBLICATIONS

ORIGINALS
I.F.: 92.77

1 Canete JD, Albaladejo C, Hernandez MV, Lainez B, Pinto JA, Ramirez J, Lopez-Armada MJ, Rodriguez-Cros JR, Engel P, Blanco FJ, Sanmarti R. Clinical significance of high levels of soluble tumour necrosis factor-alpha receptor-2 produced by alternative splicing in rheumatoid arthritis: a longitudinal prospective cohort study. RHEUMATOLOGY. 50:721-728. I.F.: 4.17.

2 Bamberger M, Santos AM, Goncalves CM, Oliveira MI, James JR, Moreira A, Lozano F, Davis SJ, Carmo AM. A New Pathway of CD5 Glycoprotein-mediated T Cell Inhibition Dependent on Inhibitory Phosphorylation of Fyn Kinase. J BIOL CHEM. 286:30324-30336. I.F.: 5.33.

3 Keszei M, Detre C, Rietdijk ST, Munoz P, Romero X, Berger SB, Calpe S, Liao GX, Castro W, Julien A, Wu YY, Shin DM, Sancho J, Zubiaur M, Morse HC, Morel L, Engel P, Wang NH, Terhorst C. A novel isoform of the Ly108 gene ameliorates murine lupus. J EXP MED. 208:811-822. I.F.: 14.78.

4 DeSalort J, Sintes J, Llinas L, Matesanz-Isabel J, Engel P. Expression of SLAM (CD150) cell-surface receptors on human B-cell subsets: From pro-B to plasma cells. IMMUNOL LETT. 134:129-136. I.F.: 2.51.

5 Llinas L, Lazaro A, DeSalort J, Matesanz-Isabel J, Sintes J, Engel P. Expression profiles of novel cell surface molecules on B-cell subsets and plasma cells as analyzed by flow cytometry. IMMUNOL LETT. 134:113-121. I.F.: 2.51.

6 Blanc M, Hsieh WY, Robertson KA, Watterson S, Shui GH, Lacaze P, Khondoker M, Dickinson P, Sing G, Rodriguez-Martin S, Phelan P, Forster T, Strobl B, Muller M, Riemersma R, Osborne T, Wenk MR, Angulo A, Ghazal P. Host Defense against Viral Infection Involves Interferon Mediated Down-Regulation of Sterol Biosynthesis. PLOS BIOL. 9:-. I.F.: 12.47.

7 Engel P, Perez-Carmona N, Alba MM, Robertson K, Ghazal P, Angulo A. Human cytomegalovirus UL7, a homologue of the SLAM-family receptor CD229, impairs cytokine production. IMMUNOL CELL BIOL. 89:753-766. I.F.: 3.74.

8 Pascual-Garcia M, Carbo JM, Leon T, Matalonga J, Out R, VanBerkel T, Sarrias MR, Lozano F, Celada A, Valledor AF. Liver X Receptors Inhibit Macrophage Proliferation through Downregulation of Cyclins D1 and B1 and Cyclin-Dependent Kinases 2 and 4. J IMMUNOL. 186:4656-4667. I.F.: 5.75.

9 Miro-Julia C, Rosello S, Martinez VG, Fink DR, Escoda-Ferran C, Padilla O, Vazquez-Echeverria C, Espinal-Marin P, Pujades C, Garcia-Pardo A, Vila J, Serra-Pages C, Holmskov U, Yelamos J, Lozano F. Molecular and Functional Characterization of Mouse S5D-SRCRB: A New Group B Member of the Scavenger Receptor Cysteine-Rich Superfamily. J IMMUNOL. 186:2344-2354. I.F.: 5.75.

10 Romo N, Magri G, Muntasell A, Heredia G, Baia D, Angulo A, Guma M, Lopez-Botet M. Natural killer cell-mediated response to human cytomegalovirus-infected macrophages is modulated by their functional polarization. J LEUKOCYTE BIOL. 90:717-726. I.F.: 4.63.

11 Matesanz-Isabel J, Sintes J, Llinas L, DeSalort J, Lazaro A, Engel P. New B-cell CD molecules. IMMUNOL LETT. 134:104-112. I.F.:2.51.

12 Magri G, Muntasell A, Romo N, Saez-Borderias A, Pende D, Geraghty DE, Hengel H, Angulo A, Moretta A, Lopez-Botet M. NKp46 and DNAM-1 NK-cell receptors drive the response to human cytomegalovirus-infected myeloid dendritic cells overcoming viral immune evasion strategies. BLOOD. 117:848-856. I.F.: 10.56.

13 Kropp KA, Robertson KA, Sing G, Rodriguez-Martin S, Blanc M, Lacaze P, Hassim MF, Khondoker MR, Busche A, Dickinson P, Forster T, Strobl B, Mueller M, Jonjic S, Angulo A, Ghazal P. Reversible Inhibition of Murine Cytomegalovirus Replication by Gamma Interferon (IFN-gamma) in Primary Macrophages Involves a Primed Type I IFN-Signaling Subnetwork for Full Establishment of an Immediate-Early Antiviral State. J VIROL. 85:10286-10299. I.F.: 5.19.

14 Lacaze P, Forster T, Ross A, Kerr LE, Salvo-Chirnside E, Lisnic VJ, Lopez-Campos GH, Garcia-Ramirez JJ, Messerle M, Trgovcich J, Angulo A, Ghazal P. Temporal Profiling of the Coding and Noncoding Murine Cytomegalovirus Transcriptomes. J VIROL. 85:6065-6076. I.F.: 5.19.

15 Isern E, Gustems M, Messerle M, Borst E, Ghazal P, Angulo A. The Activator Protein 1 Binding Motifs within the Human Cytomegalovirus Major Immediate-Early Enhancer Are Functionally Redundant and Act in a Cooperative Manner with the NF-kappa B Sites during Acute Infection. J VIROL. 85:1732-1746. I.F.: 5.19.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	50.14	11	9	1
2010	55.45	11	8	1
2011	92.77	16	11	0

16 Diaz-Ramos MC, Engel P, Bastos R. Towards a comprehensive human cell-surface immunome database. IMMUNOL LETT. 134:183-187. I.F.: 2.51.

REVIEWS
I.F.: 53.61

1 Bosch X, Lozano F, Cervera R, Ramos-Casals M, Min B. Basophils, IgE, and Autoantibody-Mediated Kidney Disease. J IMMUNOL. 186:6083-6090. I.F.: 5.75.

2 Engel P, Gomez-Puerta JA, Ramos-Casals M, Lozano F, Bosch X. Therapeutic Targeting of B Cells for Rheumatic Autoimmune Diseases. PHARMACOL REV. 63:127-156. I.F.: 18.86.

3 Martinez VG, Moestrup SK, Holmskov U, Mollenhauer J, Lozano F. The Conserved Scavenger Receptor Cysteine-Rich Superfamily in Therapy and Diagnosis. PHARMACOL REV. 63:967-1000. I.F.: 18.86.

4 Soldevila G, Raman C, Lozano F. The immunomodulatory properties of the CD5 lymphocyte receptor in health and disease. CURR OPIN IMMUNOL. 23:310-318. I.F.: 10.14.

EDITORIALS
I.F.: 6.25

1 Sintes J, Engel P. Bacterial recognition SLAM (CD150) is a multitasking immunoreceptor: from cosignalling to bacterial recognition. IMMUNOL CELL BIOL. 89:161-163. I.F.: 3.74.

2 Engel P. Editorial HLDA9 special issue. IMMUNOL LETT. 134:103-103. I.F.: 2.51.

GRANTS FOR RESEARCH IN PROGRESS

Angulo A. Regulación transcripcional y funciones de los genes principales inmediatamente tempranos: implicaciones en la patogénesis viral. Sponsored by: Ministerio de Ciencia e Innovación (Plan Nacional I+D). Duration: 01/01/2008-31/12/2011.

Lozano F. Implicaciones funcionales y terapéuticas del reconocimiento de ligandos exógenos y endógenos por parte de receptores linfocitarios tipo scavenger. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-19717. Duration: 01/01/2011-31/12/2013.

Lozano F. Análisis de los factores del sistema inmunitario innato implicados en la respuesta a la infección por el Virus Influenza A/H1N1 2009 Sponsored by: Instituto de Salud Carlos III (ISCIII), Programa de investigación del MICINN ante la Gripe A/H1N1 (GR09/0013). Duration: 24/11/2009-31/10/2012.

Engel P. Estudio de las moléculas CD150/SLAM en la función efectora de los linfocitos B de tipo innato. Sponsored by: Ministerio de Ciencia e Innovación (Plan Nacional I+D) SAF2009-07071. Duration: 01/01/2010-31/12/2011.

Lozano F. Red española de investigación en patología infecciosa (REIPI). Sponsored by: Instituto de Salud Carlos III (ISCIII), RETIC07 RD06/0008/1013. Duration: 29/2/2008-31/12/2012.

Lozano F. Estudio de las propiedades inmunomoduladoras de miembros linfoides y no linfoides de la superfamilia de receptores SRCR (Scavenger Receptor Cysteine-Rich). Sponsored by: Ministerio de Ciencia e Innovación (Plan Nacional I+D), SAF2007-62197. Duration: 1/12/2007-30/4/2011.

Lozano F. Nova bioteràpia en sepsis fúngica i polimicrobiana. Sponsored by: CIDEM VALTEC08-2-0034. Duration: 31/10/2008-31/10/2011.

Lozano F. Immunoreceptores del Sistema Inmunitario Innato y Adaptativo. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), 2009/SGR/00252. Duration: 01/01/2009-31/12/2012.

Lozano F. Papel modulador de receptores linfocitarios tipo scavenger (CD5 y CD6) en la patofisiología de la infección por el virus de la inmunodeficiencia humana 1 (VIH-1). Sponsored by: FIPSE-Fundación para la Investigación y Prevención del Sida en España, 36-0773-09. Duration: 04/01/2010-03/01/2013.

DOCTORAL THESES

Lozano F. Propiedades inmunomoduladoras de la región extracelular de CD5. PhD student: Rafael Fenutria Aumesquet.

Engel P. Expression and functional role of CD84 and CD229 receptors in innate and adaptive immunity. PhD student: Jordi Sintes Castro.

Angulo A, Lopez-Botet M. Characterization of natural killer response to human cytomegalovirus infected dendritic cells. PhD student: Giuliana Magri.

AREA 1

Biological aggression and response mechanisms

Musculoskeletal repair and plasticity

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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.

Navigation and robotics applied to skeletal grafts.

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 HIV-infected patients.
15. Nervous system:
    - Tubulization repair of peripheral nervous system damage.
    - Experimental reimplantation of nerve root preganglionic avulsions.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	43.02	15	8	4
2010	27.31	11	5	3
2011	62.94	21	7	6

ORIGINALS
I.F.: 62.94

1 Marcos M, Fernandez C, Soriano A, Marco F, Martinez JA, Almela M, Cervera R, Mensa J, Espinosa G. Epidemiology and clinical outcomes of bloodstream infections among lupus patients. LUPUS. 20:965-971. I.F.: 2.60.

2 Tomas X, Bori G, Garcia S, Garcia-Diez AI, Pomes J, Soriano A, Rios J, Almela M, Mensa J, Gallart X, Martinez JC, Riba J. Accuracy of CT-guided joint aspiration in patients with suspected infection status post-total hip arthroplasty. SKELETAL RADIOL. 40:57-64. I.F.: 1.39.

3 Ortega M, Marco F, Soriano A, Almela M, Martinez JA, Lopez J, Pitart C, Mensa J. Candida species bloodstream infection: epidemiology and outcome in a single institution from 1991 to 2008. J HOSP INFECT. 77:157-161. I.F.: 3.08.

4 Marcos M, Soriano A, Inurrieta A, Martinez JA, Romero A, Cobos N, Hernandez C, Almela M, Marco F, Mensa J. Changing epidemiology of central venous catheter-related bloodstream infections: increasing prevalence of Gram-negative pathogens. J ANTIMICROB CHEMOTH. 66:2119-2125. I.F.: 4.66.

5 Munoz-Mahamud E, Garcia S, Bori G, Martinez-Pastor JC, Zumbado JA, Riba J, Mensa J, Soriano A. Comparison of a low-pressure and a high-pressure pulsatile lavage during debridement for orthopaedic implant infection. ARCH ORTHOP TRAUM SU. 131:1233-1238. I.F.: 1.20.

6 Vilchez F, Martinez-Pastor JC, Garcia-Ramiro S, Bori G, Tornero E, Garcia E, Mensa J, Soriano A. Efficacy of debridement in hematogenous and early post-surgical prosthetic joint infections. INT J ARTIF ORGANS. 34:863-869. I.F.: 1.50.

7 Bori G, Munoz-Mahamud E, Garcia S, Mallofre C, Gallart X, Bosch J, Garcia E, Riba J, Mensa J, Soriano A. Interface membrane is the best sample for histological study to diagnose prosthetic joint infection. MODERN PATHOL. 24:579-584. I.F.: 4.18.

8 Sterzik H, Soriano A, Mohamad AM, Martinez JA, Fernandez J, Cobos N, Morata L, Mensa J. Is linezolid a risk factor for Gram-negative bacillus infections in intensive care unit patients? A comparative study with vancomycin. SCAND J INFECT DIS. 43:765-770. I.F.: 1.56.

9 Vilchez F, Martinez-Pastor JC, Garcia-Ramiro S, Bori G, Macule F, Sierra J, Font L, Mensa J, Soriano A. Outcome and predictors of treatment failure in early post-surgical prosthetic joint infections due to Staphylococcus aureus treated with debridement. CLIN MICROBIOL INFEC. 17:439-444. I.F.: 4.78.

10 Garcia-Oltra E, Garcia-Ramiro S, Pastor JCM, Tibau R, Bori G, Bosch J, Mensa J, Soriano A. Prosthetic joint infection by Candida spp.. REV ESP QUIM. 24:37-41. I.F.: 0.67.

11 Font-Vizcarra L, Zumbado A, Garcia S, Bosch J, Mensa J, Soriano A. Relationship between haematoma in femoral neck fractures contamination and early postoperative prosthetic joint infection. INJURY. 42:200-203. I.F.: 2.27.

12 Sierra JM, Garcia S, Martinez-Pastor JC, Tomas X, Gallart X, Vila J, Bori G, Macule F, Mensa J, Riba J, Soriano A. Relationship between the degree of osteolysis and cultures obtained by sonication of the prostheses in patients with aseptic loosening of a hip or knee arthroplasty. ARCH ORTHOP TRAUM SU. 131:1357-1361. I.F.: 1.20.

13 Sousa R, Lopez R, Martinez-Pastor JC, Cervera C, Bori G, Garcia-Ramiro S, Mensa J, Soriano A. Usefulness of monitoring linezolid trough serum concentration in prolonged treatments. REV ESP QUIM. 24:151-153. I.F.: 0.67.

14 Fuster D, Soriano A, Garcia S, Piera C, Suades J, Rodriguez D, Martinez JC, Mensa J, Campos F, Pons F. Usefulness of Tc-99m-ciprofloxacin scintigraphy in the diagnosis of prosthetic joint infections. NUCL MED COMMUN. 32:44-51. I.F.: 1.37.

15 Penas C, Font-Nieves M, Fores J, Petegnief V, Planas A, Navarro X, Casas C. Autophagy, and BiP level decrease are early key events in retrograde degeneration of motoneurons. CELL DEATH DIFFER. 18:1617-1627. I.F.: 9.05.

16 Ruiz-Gaspa S, Martinez-Ferrer A, Guanabens N, Dubreuil M, Peris P, Enjuanes A, DeOsaba MJM, Alvarez L, Monegal A, Combalia A, Pares A. Effects of Bilirubin and Sera from Jaundiced Patients on Osteoblasts: Contribution to the Development of Osteoporosis in Liver Diseases. HEPATOLOGY. 54:2104-2113. I.F.: 10.89.

17 Nunez M, Lozano L, Nunez E, Segur JM, Sastre S. Factors Influencing Health-related Quality of Life after TKA in Patients who are Obese. CLIN ORTHOP RELAT R. 469:1148-1153. I.F.: 2.12.

18 Nunez M, Lozano L, Nunez E, Sastre S, DelVal JL, Suso S. Good Quality of Life in Severely Obese Total Knee Replacement Patients: A Case-Control Study. OBES SURG. 21:1203-1208. I.F.: 3.08.

19 Munoz-Mahamud E, Popescu D, Nunez E, Lozano LM, Nunez M, Sastre S, Torner P, Segur JM, Macule F. Secondary patellar resurfacing in the treatment of patellofemoral pain after total knee arthroplasty. KNEE SURG SPORT TR A. 19:1467-1472. I.F.: 1.86.

20 Herrera A, Carpintero P, Fernandez-Perez C, Hernandez-Vaquero D, Martinez AA, Suso S. Secondary prevention in osteoporotic fractures. The GIOS project. MED CLIN-BARCELONA. 136:50-55. I.F.: 1.41.

21 Penas C, Pascual-Font A, Mancuso R, Fores J, Casas C, Navarro X. Sigma Receptor Agonist 2-(4-Morpholinethyl) 1 Phenylcyclohexanecarboxylate (Pre084) Increases GDNF and BiP Expression and Promotes Neuroprotection after Root Avulsion Injury. J NEUROTRAUM. 28:831-840. I.F.: 3.43.

REVIEWS
I.F.: 6.35

1 Albert M, Benito J, Bhagani S, Boesecke C, Deterding K, Dominguez S, Fisher M, Fontanet A, Garcia D, Gilson R, Guiguet M, Hoepelman AIM, Horban A, Katlama C, Mallolas J, Page E, Peters L, Pozniak A, Prins M, Puoti M, Rauch A, Rodger A, Rockstroh JK, Soriano V, Stephan C, Thibault V, Tural C, Valantin MA, VanDeLaar T, VanDerMeer J, Vella S, Vogel M, DeWit S, Autran B, Clotet B, Danta M, Journiac M, Matthews G, Meyer-Olson D, Nelson M, Schmidt R, Wedemeyer H. Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel. AIDS. 25:399-409. I.F.: 6.35.

MULTICENTRICS
I.F.: 2.51

1 Kovacs FM, Seco J, Royuela A, Pena A, Muriel A. The Correlation Between Pain, Catastrophizing, and Disability in Subacute and Chronic Low Back Pain A Study in the Routine Clinical Practice of the Spanish National Health Service. SPINE. 36:339-345. I.F.: 2.51.

GRANTS FOR RESEARCH IN PROGRESS

Soriano A. Estudio aleatorizado y doble ciego para establecer el momento más apropiado de la administración de la proxilaxis antibiótica en la artroplastia total de rodilla cuando se realiza bajo isquemia. Sponsored by: Ministerio de Sanidad y Consumo, EC07/90330. Duration: 29/10/2007-30/06/2011.

Nuñez M. Calidad de vida relacionada con la salud, dependencia física y costes en pacientes con artrosis después de artroplastia total de rodilla. Estudio prospectivo. Sponsored by: Fondo de Investigacion Sanitaria (FIS) Instituto de Salud Carlos III, PS09/01148. Duration: 01/01/2010-31/12/2012.

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, EC08/00079. Duration: 01/01/2009-30/12/2011.

Garcia S. Estudio aleatorizado y abierto para determinar si la administración de un antibiótico puede reducir la incidencia de infección en pacientes con cultivos positivos durante una artroplastia de cadera. Sponsored by: Instituto de Salud Carlos III, EC08/00182. Duration: 01/01/2009-30/12/2011.

Soriano A. Estudio comparativo de la eficacia de pautas ''cortas'' y ''largas'' de la combinación rifampicina-levofloxacino en la infección estafilocócica postquirúrgica precoz y hematógena de prótesis articular. Sponsored by: Instituto de Salud Carlos III, EC08/00189. Duration: 01/01/2009-30/12/2011.

Sastre S. Determinación de los niveles plasmáticos de substancia P en pacientes afectos de patología tendinosa degenerativa del hombro tributarios de cirugía. Sponsored by: Fund_Esp_Artroscop11, AEA2011-SASTRE. Duration: 04/05/2011-03/05/2012.

Soriano A. Grup de patologia sèptica de l'aparell locomotor. Sponsored by: Generalitat de Catalunya, AGAUR, SGR09 2009_SGR_906. Duration: 15/09/2009-31/12/2013.

Soriano A. Estudio para determinar la presencia de microorganismos en la superfície de prótesis articulares retiradas por un aflojamiento aséptico. Sponsored by: Instituto de Salud Carlos III (ISCIII), FIS10 PI10/02245. Duration: 01/01/2011-31/12/2013.

AREA 1

Biological aggression and response mechanisms

Immunogenetics of the autoinflammatory response

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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

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	41.69	7	5	2
2010	19.96	4	3	1
2011	70.42	9	5	1

ORIGINALS
I.F.: 70.42

1 Pedrosa E, Carretero-Iglesia L, Boada A, Colobran R, Faner R, Pujol-Autonell I, Palou E, Esteve A, Pujol-Borrell R, Ferrandiz C, Juan M, Carrascosa JM. CCL4L Polymorphisms and CCL4/CCL4L Serum Levels Are Associated with Psoriasis Severity. J INVEST DERMATOL. 131:1830-1837. I.F.: 6.27.

2 Ferrer G, Hodgson K, Pereira A, Juan M, Elena M, Colomer D, Roue G, Aymerich M, Baumann T, Montserrat E, Moreno C. Combined analysis of levels of serum B-cell activating factor and a proliferation-inducing ligand as predictor of disease progression in patients with chronic lymphocytic leukemia. LEUKEMIA LYMPHOMA. 52:2064-2068. I.F.: 2.49.

3 DeLarrea CF, Tovar N, Cibeira MT, Arostegui JI, Rosinol L, Elena M, Filella X, Yague J, Blade J. Emergence of oligoclonal bands in patients with multiple myeloma in complete remission after induction chemotherapy: association with the use of novel agents. HAEMATOL-HEMATOL J. 96:171-173. I.F.: 6.53.

4 Tanaka N, Izawa K, Saito MK, Sakuma M, Oshima K, Ohara O, Nishikomori R, Morimoto T, Kambe N, Goldbach-Mansky R, Aksentijevich I, DeSaintBasile G, Neven B, VanGijn M, Frenkel J, Arostegui JI, Yague J, Merino R, Ibanez M, Pontillo A, Takada H, Imagawa T, Kawai T, Yasumi T, Nakahata T, Heike T. High Incidence of NLRP3 Somatic Mosaicism in Patients With Chronic Infantile Neurologic, Cutaneous, Articular Syndrome Results of an International Multicenter Collaborative Study. ARTHRITIS RHEUM-US. 63:3625-3632. I.F.: 8.44.

5 Azmanov DN, Dimitrova S, Florez L, Cherninkova S, Draganov D, Morar B, Saat R, Juan M, Arostegui JI, Ganguly S, Soodyall H, Chakrabarti S, Padh H, Lopez-Nevot MA, Chernodrinska V, Anguelov B, Majumder P, Angelova L, Kaneva R, Mackey DA, Tournev I, Kalaydjieva L. LTBP2 and CYP1B1 mutations and associated ocular phenotypes in the Roma/Gypsy founder population. EUR J HUM GENET. 19:326-333. I.F.: 4.38.

6 DeLarrea CF, Tovar N, Rozman M, Rosinol L, Arostegui JI, Cibeira MT, Rovira M, Yague J, Blade J. Multiple Myeloma in Serologic Complete Remission after Autologous Stem Cell Transplantation: Impact of Bone Marrow Plasma Cell Assessment by Conventional Morphology on Disease Progression. BIOL BLOOD MARROW TR. 17:1084-1087. I.F.: 3.28.

7 Fortea J, Llado A, Clarimon J, Lleo A, Oliva R, Peri J, Pintor L, Yague J, Blesa R, Molinuevo JL, Sanchez-Valle R. PICOGEN: Five years experience with a genetic counselling program for dementia. NEUROLOGIA. 26:143-149. I.F.: 0.59.

8 Abraira V, Alvarez-Cermeno JC, Arroyo R, Camara C, Casanova B, Cubillo S, DeAndres C, Espejo C, Fernandez O, Ferrer J, Figueredo MA, Garcia-Merino A, Garcia-Sanchez MI, Garcia-Trujillo JA, Gomez M, Gonzalez-Oria C, Gosis A, Izquierdo G, Jimenez J, Lopez-Trascasa M, Montalban X, Moreno MJ, Munoz D, Nunez V, Muriel A, Navarro J, Olascoaga J, Oreja-Guevara C, Prada A, Ramil E, Ramo-Tello C, Rodriguez C, Rodriguez E, Rodriguez-Frias F, Rodriguez-Antiguedad A, Rodriguez-Molina JJ, Ruiz E, Saiz A, Sarasola E, Simo M, Yague J, Villar LM. Utility of oligoclonal IgG band detection for MS diagnosis in daily clinical practice. J IMMUNOL METHODS. 371:170-173. I.F.: 2.34.

9 Puente XS, Pinyol M, Quesada V, Conde L, Ordonez GR, Villamor N, Escaramis G, Jares P, Bea S, Gonzalez-Diaz M, Bassaganyas L, Baumann T, Juan M, Lopez-Guerra M, Colomer D, Tubio JMC, Lopez C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernandez JM, Puente DA, Freije JMP, Velasco G, Gutierrez-Fernandez A, Costa D, Carrio A, Guijarro S, Enjuanes A, Hernandez L, Yague J, Nicolas P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, DeSanjose S, Piris MA, DeAlava E, Miguel JS, Royo R, Gelpi JL, Torrents D, Orozco M, Pisano DG, Valencia A, Guigo R, Bayes M, Heath S, Gut M, Klatt P, Marshall J, Raine K, Stebbings LA, Futreal PA, Stratton MR, Campbell PJ, Gut I, Lopez-Guillermo A, Estivill X, Montserrat E, Lopez-Otin C, Campo E. Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia. NATURE. 475:101-105. I.F.: 36.10.

GRANTS FOR RESEARCH IN PROGRESS

Yague J. Análisis de las vías de señalización TOLL/IL-1 receptor (TIR), NOD-LIKE receptor (NLR) y NF-kB en las formas hereditarias y no hereditarias de las enfermedades autoinflamatorias. Sponsored by: FIS, PS09/01182. Duration: 01/01/2010-30/12/2012.

Otero MJ. Reevaluación del papel de HLA-DRB3 (DR52) en la respuesta de los linfocitos T CD4+. Sponsored by: FIS PI10/01404. Duration: 01/01/2011-31/12/2013.

Yagüe J. Immunogenètica en la resposta autoinflamatòria. Sponsored by: AGAUR SGR09 2009_SGR_1260. Duration:23/9/2009-31/12/2013.

AREA 1

Biological aggression and response mechanisms

Emergencies: Processes and pathologies

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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.** Since 1997, the group has dedicated an important part of its research effort to exploring the fundamental functional mechanisms of a Hospital Emergency Department. In a series of studies, the group has demonstrated that the most important limiting element regarding the efficacy, effectiveness and quality of the Emergency Department is fundamented upon extrinsic rather than upon intrinsic factors (service demand). Among the intrinsic factors, those dependent upon the Hospital rather than on the Emergency Department as such are the most decisive in determining the functionality of a given Emergency Department.

2. **Clinical aspects of intoxicated patients.** This is a line of long tradition and history in our research group. The Clinic Hospital is a reference centre in Catalonia for healthcare and research in relation to intoxications of all kinds. It is a member of the SEMES-TOX group, which is the toxicology working group of the Spanish Society of Emergency Care Medicine and Urgencies, and of the STC-AETOX group of the Spanish Association of Toxicology.

3. **Treatment of arrhythmias in the emergency room.** For over 10 years the group has participated in a coordinated manner with the cardiologists of the center, with primary care physicians working in clinics in their corresponding reference areas, and with other investigators in Spain who work in Emergency Departments (the group forms part of the arrhythmias chapter of the Spanish Society of Emergency Care Medicine and Urgencies), in the investigation of disorders of this kind. The most relevant contributions of the group in this setting have been in reference to ATRIAL FIBRILLATION.

4. **Evaluation of chest pain in the Emergency Department.** The group coordinates and conducts important research work in the only structural chest pain unit currently operating in Spain, which began its activities in 2002. From the start, the group has centered its efforts on taking advantage of this fact to investigate the medical care of these patients, and to further knowledge of a subgroup of these subjects who had not been diagnosed at the time with acute coronary disease, and had therefore not been sufficiently investigated.

5. **Diffusion of the teaching of cardiopulmonary resuscitation maneuvers among the general population.** This is an interdisciplinary line of work which, from its start in the year 2000, has involved different professionals (physicians and nurses in both out- and in-hospital emergency services, with pedagogical support). Its main objective is to explore all the possibilities and difficulties for diffusing knowledge of cardiopulmonary resuscitation maneuvers among the general population. The setting in which the research activity has been most intense is among students in secondary education (14-16 years of age), where the approach is made through a specific program, the PROCES (Programa de Reanimació cardiopulmonar Orientat a Centres d'Ensenyament Secundari, or cardiopulmonary resuscitation program oriented towards secondary education centres) designed exclusively for application in the current Catalan educational model, which has been fully developed by members of the group (Òscar Miró i Andreu, Miquel Sánchez-Sánchez, and Núria Díaz-Miranda).

6. **Emergency medical care for problems caused by drug abuse.** Originally conceived as a toxicological variant, the importance and specificity of research in this field made it possible in 2001 to create this line of research. The advantages derived as a result of research from the emergency care perspective has made it possible to clearly improve our knowledge of this group of disorders. At present, the group works in collaboration with other groups in Spain and in other countries.

7. **Acute heart failure.** This research line focuses on the differential aspects (both clinical and epidemiological) of acute decompensated heart failure. Investigation of this syndrome – highly prevalent in Emergency Departments – is carried out in combination with other Emergency Departments throughout Spain, within the context of the acute heart failure working group of the Spanish Society of Emergency Care Medicine and Urgencies.

8. **Attention to infectious diseases in Emergency Departments.** This new research line brings together different approaches to infections, focusing on the clinical data and diagnostic or therapeutic actions performed during the first hours of the patients at the hospital, which use to occur in the Emergency Department. The research is focused on prevalent infections, life-threatening infections (especially sepsis) and infections associated with HIV.

9. **Dynamics of teaching and research in Emergency Medicine.** In Spain Emergency Medicine is not officially recognized as a specialty. Therefore there is a lack of teaching and research which demands a deep analysis. At the same time, it would be interesting to gain a better understanding of the characteristics that drive these activities and compare them with the results of the activity recorded in other specialties with long experience and recognition. In addition, bibliometric tools are becoming very powerful, allowing detailed examination of the research activity as well as opening new research possibilities around these tools.

PUBLICATIONS

ORIGINALS
I.F.: 49.13

1 Lopez B, Sanchez M, Bragulat E, Jimenez S, Coll-Vinent B, Ortega M, Gomez-Angelats E, Miro O. Validation of a triage flowchart to rule out acute coronary syndrome. EMERG MED J. 28:841-846. I.F.: 1.27.

2 Perello R, Calvo M, Miro O, Castaneda M, Saubi N, Camon S, Foix A, Gatell JM, Masotti M, Mallolas J, Sanchez M, Martinez E. Clinical presentation of acute coronary syndrome in HIV infected adults: A retrospective analysis of a prospectively collected cohort. EUR J INTERN MED. 22:485-488. I.F.: 1.66.

3 Garrabou G, Lopez S, Moren C, Martinez E, Fontdevila J, Cardellach F, Gatell JM, Miro O. Mitochondrial damage in adipose tissue of untreated HIV-infected patients. AIDS. 25:165-170. I.F.: 6.35.

4 Perello R, Miro O, Miro JM, Masso E, Sanchez M, Camon S, DeLaBellacasa JP, Moreno A, Marcos MD. Urgent pneumococcal urinary antigen, importance in the diagnosis of acquired pneumonia in HIV-1 patients. EUR J EMERG MED. 18:50-54. I.F.: 0.90.

5 Benito L, Hoyo J, Montroig A, Fornes B, Fluxa G, Marti D, Pedros M, Siso A, Mont L, Miro O, Coll-Vinent B. Adverse effects of antiarrhythmic drugs in patients with atrial fibrillation in Primary Care. MED CLIN-BARCELONA. 137:241-246. I.F.: 1.41.

6 Riesgo A, Miro O, Lopez-De-Sa E, Sanchez M. Comparison of the Management of Non-ST Segment Elevation Myocardial Infarction During Emergency Care According to Sex of the Patient. REV ESP CARDIOL. 64:1060-1064. I.F.: 2.16.

7 Rodriguez JJ, Puente PH, Sanchez FJM, Llorens P, Miro O, Perello R. EAHFE (Epidemiology Acute Heart Failure Emergency) study: analysis of the patients with echocardiography performed prior to an emergency visit due to an episode of acute heart failure. REV CLIN ESP. 211:329-337. I.F.: 0.76.

8 Guitian PP, Xarau SN, Guillermo JR, Tejero IN, Viladot JRA. Evaluation of acute poisonings due to chemical agents treated in an Emergency Department. MED CLIN-BARCELONA. 136:149-152. I.F.: 1.41.

9 Jimenez S, Aguilo S, Antolin A, Coll-Vinent B, Miro O, Sanchez M. Home hospitalization directly from emergency department: an efficient alternative to standard inpatient hospitalization. MED CLIN-BARCELONA. 137:587-590. I.F.: 1.41.

10 Galicia M, Nogue S, Miro O. Liquid ecstasy intoxication: clinical features of 505 consecutive emergency department patients. EMERG MED J. 28:462-466. I.F.: 1.27.

11 Sanchez M, Bauset JL, Cuervo R, Carbajosa J, Oria MC, Povar J, Santalo M. Management of non-ST-segment elevation acute coronary syndromes in emergency departments according to hospital size: cases from the Emergency Management of Acute Coronary Syndrome (MUSICA) registry. EMERGENCIAS. 23:447-454. I.F.: 3.09.

12 Moren C, Noguera-Julian A, Rovira N, Garrabou G, Nicolas M, Cardellach F, Martinez E, Sanchez E, Miro O, Fortuny C. Mitochondrial assessment in asymptomatic HIV-infected paediatric patients on HAART. ANTIVIR THER. 16:719-724. I.F.: 3.77.

13 Moren C, Noguera-Julian A, Rovira N, Corrales E, Garrabou G, Hernandez S, Nicolas M, Tobias E, Cardellach F, Miro O, Fortuny C. Mitochondrial impact of human immunodeficiency virus and antiretrovirals on infected pediatric patients with or without lipodystrophy. PEDIATR INFECT DIS J. 30:992-995. I.F.: 3.06.

14 Garrabou G, Inoriza JM, Moren C, Oliu G, Miro O, Marti MJ, Cardellach F. Mitochondrial Injury in Human Acute Carbon Monoxide Poisoning: The Effect of Oxygen Treatment. J ENVIRON SCI HEAL C. 29:32-51. I.F.: 4.84.

15 Miro O, Jacob J, Martin-Sanchez FJ, Herrero P, Pavon J, Perez-Dura MJ, Noval A, Segura F, Richard F, Gimenez A, Gil C, Alonso H, Ruiz M, Garrido M, Roman JJG, Aguirre A, Torres JM, Ruiz F, Perello R, Villena H, Gil V, Llorens P. Prognostic implications of emergency department determination of B-type natriuretic peptide in patients with acute heart failure: the PICASU-2 study. EMERGENCIAS. 23:437-446. I.F.: 3.09.

16 Jacob J, Llorens P, Martin-Sanchez FJ, Herrero P, Alvarez A, Perez-Dura MJ, Noval A, Segura F, Richard F, Gimenez A, Miro O. Prognostic value of emergency department testing for N-terminal fragment of brain natriuretic peptide in patients with acute heart failure: the PICASU-1 study. EMERGENCIAS. 23:183-192. I.F.: 3.09.

17 Côté HC, Gerschenson M, Walker UA, Miro O, Garrabou G, Hammond E, Villarroya J, Giralt M, Villarroya F, Cinque P, Garcia-Arumi E, Andreu AL, Pinti M, Cossarizza A. Quality assessment of human mitochondrial DNA quantification: MITONAUTS, an international multicentre survey. MITOCHONDRION. 11:520-527. I.F.: 3.24.

18 Salmeron JM, Jimenez L, Miro O, Sanchez M. Safety and efficacy of hospital emergency department discharge from triage by nurses accredited to use an algorithmic aid for the Spanish Triage System without physician evaluation. EMERGENCIAS. 23:346-355. I.F.: 3.09.

19 Riesgo A, Sant E, Benito L, Hoyo J, Miro O, Mont L, Bragulat E, Coll-Vinent B. Sex Differences in the Treatment of Patients With Atrial Fibrillation: Population-Based Study in a Local Health District. REV ESP CARDIOL. 64:233-236. I.F.: 2.16.

20 Antolin A, Sanchez M, Miro O. Temporal trend in understanding of and attitudes to advance directives in patients with chronic diseases. GAC SANIT. 25:412-418. I.F.: 1.11.

REVIEWS
I.F.: 3.09

1 Nogue S, Corominas N, Soy D, Cino J. Intravenous lipid emulsion: a new antidote for use in resuscitation. EMERGENCIAS. 23:378-385. I.F.: 3.09.

EDITORIALS
I.F.: 19.12

1 Miro O. 3,085 EDITORIAL. EMERGENCIAS. 23:261-263. I.F.: 3.09.

2 Miro O. Another year without recognition for emergency medical training in Spain. EMERGENCIAS. 23:421-422. I.F.: 3.09.

3 Julian-Jimenez A, Miro O. Emergencias: results of a readership opinion survey. EMERGENCIAS. 23:341-343. I.F.: 3.09.

4 Sanz-Gallen P, Nogue S, Herrera-Mozo I, Delclos GL, Valero A. Occupational contact allergy to omeprazole and fluoxetine. CONTACT DERMATITIS. 65:118-119. I.F.: 3.67.

5 Miro O. Project EMERGER: the fifth year. EMERGENCIAS. 23:1-2. I.F.: 3.09.

6 Sanchez M. Treatment of myocardial infarction with ST-segment elevation: a war between the sexes?. EMERGENCIAS. 23:83-84. I.F.: 3.09.

CLINICAL GUIDELINES
I.F.: 3.09

1 Llorens P, Miro O, Sanchez FJM, Puente PH, Rodriguez JJ, Gil V, Perello R, Aguirre A, Valero A. Guidelines for emergency management of acute heart failure: consensus of the Acute Heart Failure Working Group of the Spanish Society of Emergency Medicine (ICASEMES) in 2011. EMERGENCIAS. 23:119-139. I.F.: 3.09.

GRANTS FOR RESEARCH IN PROGRESS

Coll-Vinent B. Utilidad de la detección precoz de la fibrilación auricular. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI070278. Duration: 26/11/2007-30/06/2011.

Miro O. Grup de recerca consolidat. Sponsored by: Generalitat de Catalunya, SGR 2009-1385. Duration: 01/01/2009-31/12/2013.

Miro O. Comparación de dos metodologías diferentes para la difusión de la enseñanza de la reanimación cardiopulmonar básica durante la escolarización obligatoria. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI 07/0073. Duration: 26/11/2007-30/06/2011.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	24.46	8	3	3
2010	40.83	21	1	7
2011	49.13	20	4	5

DOCTORAL THESES

Coll-Vinent B. Utilitat de la detecció precoç de la fibril·lació auricular. PhD student: Lluïsa Benito Serrano.

Sanchez M, Miro O. Testamento vital, enfermo crónico y urgencias. PhD student: Albert Antolín Santaliestra.

Nogue S. Mejora de la seguridad clínica del paciente intoxicado a partir del cumplimiento de los indicadores de calidad en Toxicología Clínica. PhD student: Jordi Puiguriguer Ferrando.

AREA 1

Biological aggression and response mechanisms

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

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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 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.: 24.86

1 Morina D, Puig P, Rios J, Vilella A, Trilla A. A statistical model for hospital admissions caused by seasonal diseases. STAT MED. 30:3125-3136. I.F.:2.33.

2 Gea-Sorli S, Guillamat R, Serrano-Mollar A, Closa D. Activation of lung macrophage subpopulations in experimental acute pancreatitis. J PATHOL. 223:417-424. I.F.:7.27.

3 Balasa M, Gelpi E, Antonell A, Rey MJ, Sanchez-Valle R, Molinuevo JL, Llado A. Clinical features and APOE genotype of pathologically proven early-onset Alzheimer disease. NEUROLOGY. 76:1720-1725. I.F.:8.02.

4 Gay M, Pares A, Carrascal M, Bosch-I-Crespo P, Gorga M, Mas A, Abian J. Proteomic Analysis of Polypeptides Captured from Blood during Extracorporeal Albumin Dialysis in Patients with Cholestasis and Resistant Pruritus. PLOS ONE. 6:-. I.F.:4.41.

5 Quero C, Colome N, Rodriguez C, Eichhorn P, DeLaPaz MP, Gelpi E, Abian J. Proteomics of toxic oil syndrome in humans: Phenotype distribution in a population of patients. CHEM-BIOL INTERACT. 192:129-135. I.F.:2.83.

GRANTS FOR RESEARCH IN PROGRESS

Abian J. La activación linfocitaria a través del análisis del fosfoproteoma. Determinación de perfiles de fosforilación in vivo. Sponsored by: MICINN, BIO2009-11735. Duration: 01/01/2010-31/12/2012.

Closa D. Trasplante de macrófagos reprogramados ex vivo como terapia para la pancreatitis aguda experimental. Sponsored by: Ministerio Ciencia e Innovación, SAF2009-07605. Duration: 01/01/2010-31/12/2011.

Closa D. Derivados lipídicos como agentes moduladores de la respuesta hiperinflamatoria sistémica. Sponsored by: Ministerio Ciencia e Innovación, 201022002. Duration: 01/06/2010-01/06/2011.

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.

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.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	38.98	9	8	1
2010	51.15	9	8	0
2011	24.86	5	3	0

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.

Montserrat Carrascal. Caracterización del secretoma y fosfosecretoma del linfocito T CD4+ primario humano mediante herramientas proteómicas. Sponsored by: MICINN. Duration: 01/01/2011-31/12/2012.

Closa D. Regulació de la Inflamació Aguda i Crónica. Sponsored by: Generalitat de Catalunya, AGAUR, 2009_SGR_966. Duration: 16/09/2009-31/12/2013.

DOCTORAL THESES

Closa D. Caracterització del tipus d'activació de diferents poblacions de macròfags durant la pancreatitis aguda experimental i la seva relació amb la severitat del procés. PhD student: Sabrina Gea Sorlí, Universitat de Barcelona.

ATHEROSCLEROSIS AND ARRHYTHMIAS RESYNCHRONIZATION

CORONARY DISEASE AND CARDIAC IMAGING

NEPHRO-UROLOGICAL AND DISEASES

TRANSPLANTATION KIDNEY

RESPIRATORY AND BIOPHYSICS BIOENGINEERING

HYPERTENSION AND LIPIDS CARDIOVASCULAR RISK

AREA 2

RESPIRATORY, CARDIOVASCULAR AND RENAL PATHOBIOLOGY AND BIOENGINEERING

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AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Atherosclerosis, coronary disease and heart failure

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TEAM INVOLVED IN:

Red HERACLES de investigación cardiovascular

STRATEGIC OBJECTIVES

- To identify the pathophysiological mechanisms involved in the process of accelerated atherosclerosis. The research focuses on the area of cardiovascular biology.
- 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 in the areas of basic and clinical research, imaging techniques, biomarkers, risk factors and advances in both medical treatment and treatment with medical devices. The research focuses on patients with advanced heart failure and patients with heart failure in the community.
- To gain an increased understanding of the organisational models for the care of cardiovascular patients in the community: integration between cardiology and primary care, cardiovascular prevention and care of the chronic patient.
- To gain a more in-depth understanding of the pathophysiology, diagnostic methods and results of new treatments for acute and chronic ischaemic heart disease. The research focuses on basic in vitro studies, studies on animal models, clinical studies of the pathophysiology and safety and efficacy studies on the different treatments for coronary heart disease. The aim is to further concentrate on the effects of the risk factors on the development of ischaemic heart disease.
- To evaluate the repercussions of the new diagnostic techniques and types of treatment in structural heart disease, including valvular disease and congenital and acquired structural 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

Cardiovascular Biology:

- Study of the mechanisms of hyperplasia of the intima following coronary revascularisation procedures in murine and porcine experimental models with the aim of developing pharmacological prevention strategies.
- Study of the biocompatibility of the materials in the design of intracoronary devices.
- Study of impedance during the endothelialisation process of a coronary stent. Development of the "smart stent".
- Study of the influence of hormonal factors and aging on the regulation of the nitric oxide and superoxide systems in the healthy population and the population with cardiovascular disease.
- Determination of the mechanisms involved in the regulation of the nitric oxide and superoxide systems through steroid receptors and their role in regulating the development of cardiovascular diseases such as atherosclerosis, hypertension, diabetes and metabolic syndrome.

Cell Therapy:

- Study of the efficacy of cell therapy in patients with chronic refractory angina and non-revascularisable coronary disease and the regulation of endothelial progenitor cell activation in acute myocardial infarction. At an experimental level, we are analysing the regulatory mechanisms and the efficacy of the administration of mesenchymal stem cells on myocardial regeneration in an experimental pig model.

Ischaemic heart disease:

- Pathophysiology and improvement in the diagnosis and treatment of acute coronary syndrome. Role of the mechanisms of vascular inflammation and thrombosis. Evaluation of the circulating endothelial cells and the progenitor endothelial cells.
- Study of the impact of gender differences on ischaemic heart disease. Evaluation of the characteristics of cardiovascular disease in women and the different factors affecting the prognosis.
- Clinical studies evaluating the efficacy and safety of drug-eluting stents coated with everolimus in patients with ST-segment elevation myocardial infarction (EXAMINATION Study).
- Clinical evaluation of the fully bioresorbable coronary device (Absorb) in patients with ischaemic heart disease.
- Chronic total occlusion of coronary arteries in humans: from the pathophysiology to the clinical implications of successful recanalisation through percutaneous coronary intervention. Utility of imaging techniques in the indications and treatment of patients with chronic coronary artery occlusions and assessment of results and follow-up.

Heart failure:

- Study of neurohormonal activation and the fibrotic process associated with ventricular remodelling in idiopathic or ischaemic dilated cardiomyopathy using molecular biology and immunohistochemical techniques on myocardial tissue and through neurohormonal determinations.
- Genetic study of familial idiopathic cardiomyopathy.
- Prevention of ventricular dysfunction in chemotherapy patients. Evaluation of drugs for the prevention of ventricular dysfunction in oncology patients undergoing chemotherapy.
- Study of heart failure with normal ejection fraction: role of biomarkers and imaging techniques in the diagnosis, relationship between myocardial remodelling biomarkers in diagnosis and prognosis of outpatients and study of lung function in these patients.
- Evaluation of mechanical circulatory support devices: ventricular assist device as bridge to transplant.

Cardiovascular disease in the community:

- Study of the integrated care models between cardiology and primary care for improving clinical practice in patients with chronic heart disease.
- Outpatient characterisation of new-onset heart failure using high-resolution imaging.
- Study of interventions in chronic patients for improving prognosis and prevention of readmissions due to heart failure.

Structural heart disease

- Study of the efficacy and efficiency, and the repercussions on quality of life, 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 who have a recent history of gastrointestinal bleeding.
- Evaluation of the impact of the use of MitraClip in patients with functional mitral regurgitation in different population groups.
- Role of cardiac imaging in the indications, diagnosis, treatment and follow-up of patients with structural heart disease.
- Advances in diagnostic imaging for and treatment of heart valve diseases and complications such as infectious endocarditis.

Chagas Heart Disease

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

Pulmonary hypertension and right ventricular dysfunction

- Utility of cardiac magnetic resonance imaging in the estimation and monitoring of haemodynamic parameters in pulmonary hypertension.
- Utility of magnetic resonance imaging for the early detection of right ventricular dysfunction.
- Research into new pharmacological treatments in pulmonary hypertension.

PUBLICATIONS

ORIGINALS
I.F.: 97.59

1 Cervera C, Fernandez-Ruiz M, Valledor A, Linares L, Anton A, Marcos MA, Sanclemente G, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Pumarola T, Moreno A. Epidemiology and risk factors for late infection in solid organ transplant recipients. TRANSPL INFECT DIS. 13:598-607. I.F.: 2.04.

2 Linares L, Sanclemente G, Cervera C, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Marcos MA, Anton A, Pumarola T, Moreno A. Influence of Cytomegalovirus Disease in Outcome of Solid Organ Transplant Patients. TRANSPL P. 43:2145-2148. I.F.: 0.99.

3 Novensa L, Novella S, Medina P, Segarra G, Castillo N, Heras M, Hermenegildo C, Dantas AP. Aging Negatively Affects Estrogens-Mediated Effects on Nitric Oxide Bioavailability by Shifting ER alpha/ER beta Balance in Female Mice. PLOS ONE. 6:-. I.F.: 4.41.

4 Mohr FW, Rastan AJ, Serruys PW, Kappetein AP, Holmes DR, Pomar JL, Westaby S, Leadley K, Dawkins KD, Mack MJ. Complex coronary anatomy in coronary artery bypass graft surgery: Impact of complex coronary anatomy in modern bypass surgery? Lessons learned from the SYNTAX trial after two years. J THORAC CARDIOV SUR. 141:130-140. I.F.: 3.61.

5 Bosch D, Masia R, Sala J, Vila J, Ramos R, Elosua R, Subirana I, Heras M, Sanchis J, Grau M, Brugada R, Marrugat J. Effect of Opening a New Catheterization Laboratory on 30-Day and 2-Year Survival Rates in Myocardial Infarction Patients. REV ESP CARDIOL. 64:96-104. I.F.: 2.16.

6 Anguita M, Beiras AC, Cobo E, Coca A, DeTeresa E, Diez J, Lopez B, Cebollada J, Diaz B, Galve E, Gonzalez-Juanatey JR, Jimenez-Navarro M, Lopez I, Lupon J, Martin C, Monserrat L, Narejos S, Figal DAP, Perez-Calvo JI, Querejeta R, Ridocci F, Rodriguez A, Rodriguez M, Roig E, Roure J, Ruiz S, Sanchez PL, Terns M, Toran P, Munoz-Tuduri M. Effects of Prolonged-Release Torasemide Versus Furosemide on Myocardial Fibrosis in Hypertensive Patients with Chronic Heart Failure: A Randomized, Blinded End Point, Active-Controlled Study. CLIN THER. 33:1204-1213. I.F.: 2.55.

7 Roque M, Sitges M, Sala J, Delgado V, Morales M, Marrugat J, Vila J, Subirana I, Tassies D, Reverter JC, Castro M, Duran M. Effects of Raloxifene on Endothelial Function and Hemostasis in Women With Ischemic Heart Disease. REV ESP CARDIOL. 64:572-578. I.F.: 2.16.

8 Martin-Yuste V, Alvarez-Contreras L, Brugaletta S, Ferreira-Gonzalez I, Cola C, Garcia-Picart J, Marti V, Sabate M. Emergent Versus Elective Percutaneous Stent Implantation in the Unprotected Left Main: Long-Term Outcomes from a Single-Center Registry. J INVASIVE CARDIOL. 23:392-397. I.F.: 1.78.

9 Garcia-Alvarez A, Sitges M, Heras M, Poyatos S, Posada E, Pinazo MJ, Regueiro A, Gascon J, Sanz G. Endothelial Function and High-Sensitivity C-reactive Protein Levels in Patients With Chagas Disease Living in a Nonendemic Area. REV ESP CARDIOL. 64:891-896. I.F.: 2.16.

10 Freixa X, Masotti M, Palomo M, Diaz-Ricart M, Escolar G, Guasch E, Regueiro A, Jimenez M, Betriu A, Heras M. Endothelin-1 levels predict endothelial progenitor cell mobilization after acute myocardial infarction. MICROVASC RES. 82:177-181. I.F.: 2.39.

11 Sanchis J, Bodi V, Nunez J, Nunez E, Bosch X, Pellicer M, Heras M, Bardaji A, Marrugat J, Llacer A. Identification of very low risk chest pain using clinical data in the emergency department. INT J CARDIOL. 150:260-263. I.F.: 6.80.

12 Sabate S, Mases A, Guilera N, Canet J, Castillo J, Orrego C, Sabate A, Fita G, Parramon F, Paniagua P, Rodriguez A, Sabate M. Incidence and predictors of major perioperative adverse cardiac and cerebrovascular events in non-cardiac surgery. BRIT J ANAESTH. 107:879-890. I.F.: 4.22.

13 Sanchis J, Nunez J, Bodi V, Nunez E, Garcia-Alvarez A, Bonanad C, Regueiro A, Bosch X, Heras M, Sala J, Bielsa O, Llacer A. Influence of Comorbid Conditions on One-Year Outcomes in Non-ST-Segment Elevation Acute Coronary Syndrome. MAYO CLIN PROC. 86:291-296. I.F.: 5.71.

14 Falces C, Andrea R, Heras M, Vehi C, Sorribes M, Sanchis L, Cevallos J, Menacho I, Porcar S, Font D, Sabate M, Brugada J. Integration Between Cardiology and Primary Care: Impact on Clinical Practice. REV ESP CARDIOL. 64:564-571. I.F.: 2.16.

15 Garcia-Alvarez A, Sitges M, Regueiro A, Poyatos S, Pinazo MJ, Posada E, Bijnens B, Heras M, Gascon J, Sanz G. Myocardial Deformation Analysis in Chagas Heart Disease With the Use of Speckle Tracking Echocardiography. J CARD FAIL. 17:1028-1034. I.F.: 3.36.

16 Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ, Lopez-Sendon JL, Macaya C, Hernandez-Antolin R. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio eN Ancianos) randomized trial and pooled analysis with previous studies. EUR HEART J. 32:51-60. I.F.: 10.05.

17 Castel MA, Farrero M, Vallejos I, Cardona M, Regueiro A, Perez-Villa F. Primary Immunosuppression and Outcome Differences After Heart Transplantation: Tacrolimus Versus Cyclosporine. TRANSPL P. 43:2244-2246. I.F.: 0.99.

18 Aros F, Heras M, Vila J, Sanz H, Ferreira-Gonzalez I, Permanyer-Miralda G, Cunat J, Lopez-Bescos L, Cabades A, Loma-Osorio A, Marrugat J. Reduction in 28 Days and 6 Months of Acute Myocardial Infarction Mortality From 1995 to 2005. Data From PRIAMHO I, II and MASCARA Registries. REV ESP CARDIOL. 64:972-980. I.F.: 2.16.

19 Esteban V, Mendez-Barbero N, Jimenez-Borreguero LJ, Roque M, Novensa L, Garcia-Redondo AB, Salaices M, Vila L, Arbones ML, Campanero MR, Redondo JM. Regulator of calcineurin 1 mediates pathological vascular wall remodeling. J EXP MED. 208:2125-2139. I.F.: 14.78.

20 Gimenez M, Gilabert R, Monteagudo J, Alonso A, Casamitjana R, Pare C, Conget I. Repeated Episodes of Hypoglycemia as a Potential Aggravating Factor for Preclinical Atherosclerosis in Subjects With Type 1 Diabetes. DIABETES CARE. 34:198-203. I.F.: 7.14.

21 Delgado JF, Manito N, Almenar L, Crespo-Leiro M, Roig E, Segovia J, DePrada JAV, Lage E, Palomo J, Camprecios M, Arizon JM, Rodriguez-Lambert JL, Blasco T, DeLaFuente L, Pascual D, Rabago G. Risk factors associated with cytomegalovirus infection in heart transplant patients: a prospective, epidemiological study. TRANSPL INFECT DIS. 13:136-144. I.F.: 2.04.

22 Guasch E, Sionis A, Reverter JC, Andrea R, Loma-Osorio P, Freixa X, Heras M. Safety issues of adjunctive clopidogrel in patients discharged after percutaneous coronary intervention with stent placement and requiring oral anticoagulation. INT J CARDIOL. 146:E1-E4. I.F.: 6.80.

23 Loma-Osorio P, Peñafiel P, Doltra A, Sionis A, Bosch X. Shoshin beriberi mimicking a high-risk non-ST-segment elevation acute coronary syndrome with cardiogenic shock: when the arteries are not guilty. J EMERG MED. 41:e73-e77. I.F.: 1.55.

24 Diaz JF, DeLaTorre JM, Sabate M, Goicolea J. Spanish Cardiac Catheterization and Coronary Intervention Registry. 20th Official Report of the Spanish Society of Cardiology Working Group on Cardiac Catheterization and Interventional Cardiology (1990-2010). REV ESP CARDIOL. 64:1012-1022. I.F.: 2.16.

25 Freixa X, Heras M, Ortiz JT, Argiro S, Guasch E, Doltra A, Jimenez M, Betriu A, Masotti M. Usefulness of Endothelin-1 Assessment in Acute Myocardial Infarction. REV ESP CARDIOL. 64:105-110. I.F.: 2.16.

26 Sanchis J, Bodi V, Nunez J, Bosch X, Heras M, Bonanad C, Pellicer M, Merlos P, Minana G, Llacer A. Usefulness of pain presentation characteristics for predicting outcome in patients presenting to the hospital with chest pain of uncertain origin. EMERG MED J. 28:847-850. I.F.: 1.27.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	89.11	21	13	3
2010	131.29	33	16	9
2011	97.59	26	6	12

EDITORIALS
I.F.: 15.63

1 DiMario C, James S, Dudek D, Sabate M, Degertekin M. Commentary: The risk of over-regulation. BRIT MED J. 342:-. I.F.: 13.47.

2 Martin-Yuste V, Alvarez-Contreras L, Cola C, Brugaletta S, Picart JG, Marti V, Masotti M, Sabate M. Usefulness of the Tornus (R) Catheter in Nondilatable Coronary Chronic Total Occlusion. REV ESP CARDIOL. 64:935-938. I.F.: 2.16.

CLINICAL GUIDELINES
I.F.: 12.21

1 Anguita M, Alegria E, Barrios V, Casasnovas JA, Escobar C, Leon M, Luengo E, Llisterri JL. Comments on the 2011 ESC/EAS guidelines for the management of dyslipidemias. A report of the Task Force of the Clinical Practice Guidelines Committee of the Spanish Society of Cardiology. REV ESP CARDIOL. 64:1090-1095. I.F.: 2.16.

2 Tendera M, Aboyans V, Bartelink ML, Baumgartner I, Collet JP, Cremonesi A, DeCarlo M, Erbel R, Heras M, Kownator S, Minar E, Ostergren J, Poldermans D, Riambau V, Roffi M, Sievert H, VanSambeek M, Zeller T, Bax J, Auricchio A, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Knuuti J, Kolh P, Mcdonagh T, Moulin C, Popescu B, Reiner Z, Sechtem U, Sirnes PA, Torbicki A, Vahanian A, Windecker S. ESC Guidelines on the diagnosis

and treatment of peripheral artery diseases: Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries: the Task Force on the Diagnosis and Treatm. EUR HEART J. 32:2851-2906. I.F.: 10.05.

MULTICENTRICS
I.F.: 66.23

1 Grube E, Chevalier B, Smits P, Dzavik V, Patel TM, Mullasari AS, Wohrle J, Stuteville M, Dorange C, Kaul U. The SPIRIT V Study A Clinical Evaluation of the XIENCE V Everolimus-Eluting Coronary Stent System in the Treatment of Patients With De Novo Coronary Artery Lesions. JACC-CARDIOVASC INTE. 4:168-175. I.F.: 5.86.

2 Urban P, Abizaid A, Banning A, Bartorelli AL, Baux AC, Dzavik V, Ellis S, Gao RL, Holmes D, Jeong MH, Legrand V, Neumann FJ, Nyakern M, Spaulding C, Worthley S. Stent Thrombosis and Bleeding Complications After Implantation of Sirolimus-Eluting Coronary Stents in an Unselected Worldwide Population A Report From the e-SELECT (Multi-Center Post-Market Surveillance) Registry. J AM COLL CARDIOL. 57:1445-1454. I.F.: 14.29.

3 Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P, Budaj A, Niemela M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afzal R, Joyner CD, Chrolavicius S, Mehta SR. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. LANCET. 377:1409-1420. I.F.: 33.63.

4 Ahmed WH, Mendiz OA, Thomas MR. Usage Patterns and 1-Year Outcomes With the TAXUS Liberte Stent: Results of the TAXUS OLYMPIA Registry. CATHETER CARDIO INTE. 77:979-992. I.F.: 2.40.

5 Fraser AG, Daubert JC, VanDeWerf F, Estes NAM, Smith SC, Krucoff MW, Vardas PE, Komajda M. Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform Report of a policy conference of the European Society of Cardiology. EUR HEART J. 32:1673-1686D. I.F.: 10.05.

GRANTS FOR RESEARCH IN PROGRESS

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), RETIC06 RD06/0009/0008. Duration: 01/01/2007-31/12/2012.

Dantas AP. Regulación hormonal del perfil proteómico y la función vascular durante el envejecimiento y la evolución de enfermedades cardiovasculares. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0176. Duration: 01/01/2009-31/12/2011.

Heras M. Células endoteliales circulantes y células progenitoras endoteliales en la enfermedad cardiovascular aguda. Correlación con la función endotelial y la evolución clínica. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080272. Duration: 01/01/2008-31/12/2011.

Roque M, Heras M, Novensà L, Rigol M, Solanes N. Prevenció i tractament de la hiperplàsia de l'íntima mitjançant l'ús de bloquejants del canal Kv1.3. Sponsored by: Generalitat de Catalunya (VALTEC), VALTEC09-1-0042. Duration: 01/01/2009-31/12/2011.

Sabate M. Chronic total occlusions of human coronary arteries: from pathophysiology to long-term clinical implications of successful recanalization by means of percutaneous coronary intervention. Sponsored by: Fundació La Marató de TV3, 082130. Duration: 29/04/2010-04/03/2012.

Roque M. VALTEC09-1-0042 aportación de la Universidad de Navarra al proyecto CIDEM. Sponsored by: VALTEC09, PI040823. Duration: 30/06/2009-30/09/2011.

DOCTORAL THESES

Sabate M, Cinca J. Revascularización de las Arterias Coronarias Ocluidas Crónicamente. Predictores de éxito Angiográfico y Papel de las Nuevas Técnicas de Imagen en la Selección de los Pacientes. PhD student: Victoria Martín Yuste.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Arrhythmias, resynchronization and cardiac imaging

TEAM INVOLVED IN:

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Eduard Guasch (Rio Ortega-IDIBAPS-ISC III)
David Andreu (Fundació Clínic)
Silvia Montserrat (Hospital Clínic - Fundació Clínic)
Juan Fernández-Armenta (Fundació Clínic - cvREMOD)
Ada Doltra (Fundació Clínic - cvREMOD)
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Antonio Berruezo (Hospital Clínic)

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Malek Khatib (Beca EHRA, European Heart Rhythm Association)
Franco Merschon (Fellow Argentina)
M Emilce Trucco (Fellow Argentina)
Philippe Taghji (Fellow France)

RESPIRATORY, CARDIOVASCULAR AND RENAL PATHOBIOLOGY AND BIOENGINEERING

Arrhythmias, resynchronization and cardiac imaging

STRATEGIC OBJECTIVES

The aims for the coming year are fundamentally to go further in the six main research lines of the group: *genetic cardiovascular diseases, atrial fibrillation, cardiac resynchronization, ventricular tachycardias, and experimental models of etiological factors in atrial fibrillation, and Sports Cardiology*. Furthermore, we wish to continue promoting prospective multicenter projects allowing the obtainment of transcendental clinical results, without abandoning practical clinical research, with a view to improving patient care. On the other hand, we will keep on working with the Bioengineering team at the UPF in modeling and software development for image processing.

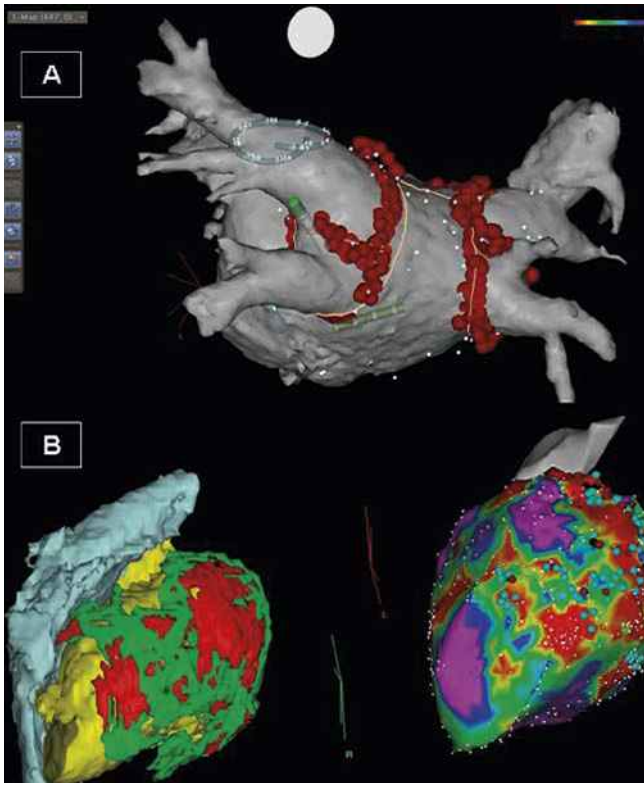
MAIN LINES OF RESEARCH

1. Cardiovascular genetic diseases:

- This year patients continue to be included in the multicenter study 'Sudden cardiac death: Translating basic science into clinical care', in collaboration with Dr. Ramon Brugada of the Cardiovascular Genetics Center UdG-IDIBGI, in Girona.

2. Experimental models for the study of etiological factors in atrial fibrillation:

- We wish to continue analyzing the mechanisms conditioning the appearance of atrial and ventricular fibrosis in the rat model of resistance exercise.
- We are continuing collaboration with the Pneumology Sleep Unit and the Department of Physical Medicine of



(A) Map of atrial fibrillation: Atrial fibrillation ablation procedure. We see the ablation scheme and integration of the 3D reconstruction of a CAT scan within the navigator. This system allows real time catheter localization within the heart of the patient.

(B) Map of ventricular tachycardia: Ventricular tachycardia ablation procedure. In this case we see an epicardial map of the left ventricle in a patient with structural heart disease (right). The 3D reconstruction derived from an MRI scan with gadolinium contrast injection allows noninvasive characterization of the tissue and planning of the intervention (left).

RESEARCH GROUP
CARDIAC IMAGING

Team Leader: Marta Sitges (Hospital Clínic)

Our group has a pluridisciplinary team of people dedicated to non-invasive cardiac imaging and its application in the knowledge of and research into cardiovascular pathophysiology and therapy within the field of cardiac mechanics and cardiac arrhythmias, as well as other 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. Application of an experimental porcine model as part of the cvREMOD project funded by the Centro para el Desarrollo Tecnológico e Industrial (CDTI) [Centre for Technological and Industrial Development].
- Study of atrial morphology and function in patients with atrial fibrillation and elite sportsmen and women. Project funded by FIS and the Spanish National Plan for R&D&i.
- Study of right ventricular morphology and function in elite athletes at rest and exercising. Project funded by the Spanish National Plan for R&D&i.
- Detection of latent ventricular dysfunction in different disorders such as Chagas disease, cirrhosis of the liver and cardiotoxicity caused by chemotherapy in blood disorders. Projects funded by the FIS.
- Analysis of post-infarction remodelling using three-dimensional echocardiography and cardiac magnetic resonance imaging. Project funded by the Spanish Cardiology Society
- Utility of multi-slice CT in the diagnosis of chest pain in Accident and Emergency. Project funded by FIS
- Non-invasive analysis of endothelial function through ultrasound of the humeral artery in myocardial infarction patients with pulmonary hypertension. Projects funded by the FIS.

the Faculty of Medicine of Barcelona University, with the purpose of studying the repercussions of obstructive apnea upon the heart, using an experimental model in rats.

- We keep working on the experimental murine model of cardiac adaptation to chronic training that we developed to study the pathophysiology of atrial fibrillation. Our research focuses specially in the adaptation of the right ventricle

3. Atrial fibrillation (AF):

- On one hand we are continuing the study of etiological factors in primary atrial fibrillation, specifically with the FUTURE study, which analyzes the role of undetected hypertension and physical exercise.

RESEARCH GROUP CARDIAC RESYNCHRONISATION

Team Leader:
Lluis Mont
(Hospital Clínic)

Our group is carrying out research into the application and results of cardiac resynchronisation techniques. Several studies are currently underway:

- Following recruitment in the SPARE III study, which is analysing the results of AV-node ablation in patients with atrial fibrillation receiving resynchronisation. Subsidy: Fondo de Investigación Sanitaria (FIS) [Health Research Fund], Instituto de Saludo Carlos III (PS09/01500).
- TRICHAMPION multicentre study on ablation and desynchronisation in patients with hypertrophic cardiomyopathy.
- Studies on optimisation of electrocardiographic resynchronisation: BEST. Subsidy: Fondo de Investigación Sanitaria (FIS) [Health Research Fund], Instituto de Saludo Carlos III (PS10/01569).
- SARA study (Spanish Atrial Fibrillation vs Antiarrhythmic Drugs). Comparative multicenter study of the efficacy of ablation versus drug treatment. Once the recruitment was completed we started analysing the results.
- Recruitment has been completed in two randomized, prospective studies designed to compare different ablation techniques.
- We are about to start several multicentric studies about new ablation techniques and new antiarrhythmic drugs: EAST, FIRE AND ICE and RAFAELLO.

4. Ventricular tachycardia (VT):

- Multicenter study of antiarrhythmic drugs versus ablation in ischemic patients with automated implantable defibrillators.
- A prospective study evaluating the ejection fraction following ventricular extrasystolia ablation in patients with ventricular extrasystoles and structural heart disease.
- 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 sysems.
- Siemens has 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.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	66.31	17	13	1
2010	93.71	27	13	4
2011	120.18	27	11	8

ORIGINALS
I.F.: 120.18

1 Benito L, Hoyo J, Montroig A, Fornes B, Fluxa G, Marti D, Pedros M, Siso A, Mont L, Miro O, Coll-Vinent B. Adverse effects of antiarrhythmic drugs in patients with atrial fibrillation in Primary Care. MED CLIN-BARCELONA. 137:241-246. I.F.: 1.41.

2 Riesgo A, Sant E, Benito L, Hoyo J, Miro O, Mont L, Bragulat E, Coll-Vinent B. Sex Differences in the Treatment of Patients With Atrial Fibrillation: Population-Based Study in a Local Health District. REV ESP CARDIOL. 64:233-236. I.F.: 2.16.

3 Roque M, Sitges M, Sala J, Delgado V, Morales M, Marrugat J, Vila J, Subirana I, Tassies D, Reverter JC, Castro M, Duran M. Effects of Raloxifene on Endothelial Function and Hemostasis in Women With Ischemic Heart Disease. REV ESP CARDIOL. 64:572-578. I.F.: 2.16.

4 Garcia-Alvarez A, Sitges M, Heras M, Poyatos S, Posada E, Pinazo MJ, Regueiro A, Gascon J, Sanz G. Endothelial Function and High-Sensitivity C-reactive Protein Levels in Patients With Chagas Disease Living in a Non-endemic Area. REV ESP CARDIOL. 64:891-896. I.F.: 2.16.

5 Falces C, Andrea R, Heras M, Vehi C, Sorribes M, Sanchis L, Cevallos J, Menacho I, Porcar S, Font D, Sabate M, Brugada J. Integration Between Cardiology and Primary Care: Impact on Clinical Practice. REV ESP CARDIOL. 64:564-571. I.F.: 2.16.

6 Garcia-Alvarez A, Sitges M, Regueiro A, Poyatos S, Pinazo MJ, Posada E, Bijnens B, Heras M, Gascon J, Sanz G. Myocardial Deformation Analysis in Chagas Heart Disease With the Use of Speckle Tracking Echocardiography. J CARD FAIL. 17:1028-1034. I.F.: 3.36.

7 Freixa X, Heras M, Ortiz JT, Argiro S, Guasch E, Doltra A, Jimenez M, Betriu A, Masotti M. Usefulness of Endothelin-1 Assessment in Acute Myocardial Infarction. REV ESP CARDIOL. 64:105-110. I.F.: 2.16.

8 Duchateau N, DeCraene M, Piella G, Silva E, Doltra A, Sitges M, Bijnens BH, Frangi AF. A spatiotemporal statistical atlas of motion for the quantification of abnormal myocardial tissue velocities. MED IMAGE ANAL. 15:316-328. I.F.: 4.36.

9 Berruezo A, DePotter T, Sitges M, Mansour F, Mont L, Brugada J. Bifocal Right Ventricular Resynchronization for the Failing Right Ventricle. PACE. 34:E78-E81. I.F.: 1.35.

10 Berruezo A, Vatasescu R, Mont L, Sitges M, Perez D, Papiashvilli G, Vidal B, Francino A, Fernandez-Armenta J, Silva E, Bijnens B, Gonzalez-Juanatey JR, Brugada J. Biventricular pacing in hypertrophic obstructive cardiomyopathy: A pilot study. HEART RHYTHM. 8:221-227. I.F.: 4.25.

11 Benito B, Gay-Jordi G, Serrano-Mollar A, Guasch E, Shi YF, Tardif JC, Brugada J, Nattel S, Mont L. Cardiac Arrhythmogenic Remodeling in a Rat Model of Long-Term Intensive Exercise Training. CIRCULATION. 123:13-U61. I.F.: 14.43.

12 Brignole M, Botto G, Mont L, Iacopino S, DeMarchi G, Oddone D, Luzi M, Tolosana JM, Navazio A, Menozzi C. Cardiac resynchronization therapy in patients undergoing atrioventricular junction ablation for permanent atrial fibrillation: a randomized trial. EUR HEART J. 32:2420-2429. I.F.: 10.05.

13 Doltra A, Vidal B, Silva E, Mont L, Tamborero D, Castel MA, Tolosana JM, Berruezo A, Brugada J, Sitges M. Comparison of Hemodynamic versus Dyssynchrony Assessment for Interventricular Delay Optimization with Echocardiography in Cardiac Resynchronization Therapy. PACE. 34:984-990. I.F.: 1.35.

14 Nagarakanti R, Ezekowitz MD, Oldgren J, Yang S, Chernick M, Aikens TH, Flaker G, Brugada J, Kamensky G, Parekh A, Reilly PA, Yusuf S, Connolly SJ. Dabigatran Versus Warfarin in Patients With Atrial Fibrillation An Analysis of Patients Undergoing Cardioversion. CIRCULATION. 123:131-136. I.F.: 14.43.

15 Lubinski A, Bissinger A, Boersma L, Leenhardt A, Merkely B, Oto A, Proclemer A, Brugada J, Vardas PE, Wolpert C. Determinants of geographic variations in implantation of cardiac defibrillators in the European Society of Cardiology member countries-data from the European Heart Rhythm Association White Book. EUROPACE. 13:654-662. I.F.: 1.84.

16 Moya A, Garcia-Civera R, Croci F, Menozzi C, Brugada J, Ammirati F, Del-Rosso A, Bellver-Navarro A, Garcia-Sacristan J, Bortnik M, Mont L, Ruiz-Granell R, Navarro X. Diagnosis, management, and outcomes of patients with syncope and bundle branch block. EUR HEART J. 32:1535-1541. I.F.: 10.05.

17 Montserrat S, Sitges M, Calvo N, Silva E, Tamborero D, Vidal B, Berruezo A, Bernado C, Mont L, Brugada J. Effect of Repeated Radiofrequency Catheter Ablation on Left Atrial Function for the Treatment of Atrial Fibrillation. AM J CARDIOL. 108:1741-1746. I.F.: 3.68.

18 Tamborero D, Vidal B, Tolosana JM, Sitges M, Berruezo A, Silva E, Castel M, Matas M, Arbelo E, Rios J, Villacastin J, Brugada J, Mont L. Electrocardiographic versus Echocardiographic Optimization of the Interventricular Pacing Delay in Patients Undergoing Cardiac Resynchronization Therapy. J CARDIOVASC ELECTR. 22:1129-1134. I.F.: 3.29.

19 Zeljko HM, Mont L, Sitges M, Tolosana JM, Nadal M, Castella M, Brugada J. Entrapment of the circular mapping catheter in the mitral valve in two patients undergoing atrial fibrillation ablation. EUROPACE. 13:132-133. I.F.: 1.84.

20 DellaBella P, Brugada J, Zeppenfeld K, Merino J, Neuzil P, Maury P, Maccabelli G, Vergara P, Baratto F, Berruezo A, Wijnmaalen AP. Epicardial Ablation for Ventricular Tachycardia A European Multicenter Study. CIRC-ARRHYTHMIA ELEC. 4:653-659. I.F.: 4.81.

21 Boriani G, Auricchio A, Klersy C, Kirchhof P, Brugada J, Morgan J, Vardas P. Healthcare personnel resource burden related to in-clinic follow-up of cardiovascular implantable electronic devices: a European Heart Rhythm Association and Eucomed joint survey. EUROPACE. 13:1166-1173. I.F.: 1.84.

22 Andreu D, Berruezo A, Ortiz-Perez JT, Silva E, Mont L, Borras R, DeCaralt TM, Perea RJ, Fernandez-Armenta J, Zeljko H, Brugada J. Integration of 3D Electroanatomic Maps and Magnetic Resonance Scar Characterization Into the Navigation System to Guide Ventricular Tachycardia Ablation. CIRC-ARRHYTHMIA ELEC. 4:674-683. I.F.: 4.81.

23 Bosch X, Esteve J, Sitges M, DeCaralt TM, Domenech A, Ortiz JT, Monzo M, Morales-Ruiz M, Perea RJ, Rovira M. Prevention of Chemotherapy-Induced Left Ventricular Dysfunction With Enalapril and Carvedilol: Rationale and Design of the OVERCOME Trial. J CARD FAIL. 17:643-648. I.F.: 3.36.

24 Macedo PG, Brugada J, Leinveber P, Benito B, Molina I, Sert-Kuniyoshi F, Adachi T, Bukartyk J, VanDerWalt C, Konecny T, Maharaj S, Kara T, Montserrat J, Somers V. Sleep-Disordered Breathing in Patients With the Brugada Syndrome. AM J CARDIOL. 107:709-713. I.F.: 3.68.

25 Sarkozy A, Sorgente A, Boussy T, Casado R, Paparella G, Capulzini L, Chierchia GB, Yazaki Y, DeAsmundis C, Coomans D, Brugada J, Brugada P. The value of a family history of sudden death in patients with diagnostic type I Brugada ECG pattern. EUR HEART J. 32:2153-2160. I.F.: 10.05.

26 Rollin A, Maury P, Guilbeau-Frugier C, Brugada J. Transient ST Elevation After Ketamine Intoxication: A New Cause of Acquired Brugada ECG Pattern. J CARDIOVASC ELECTR. 22:91-94. I.F.: 3.29.

27 Calvo N, Mont L, Vidal B, Nadal M, Montserrat S, Andreu D, Tamborero D, Pare C, Azqueta M, Berruezo A, Brugada J, Sitges M. Usefulness of transoesophageal echocardiography before circumferential pulmonary vein ablation in patients with atrial fibrillation: is it really mandatory?. EUROPACE. 13:486-491. I.F.: 1.84.

REVIEWS
I.F.: 2.49

1 VanGelder IC, Haegeli LM, Brandes A, Heidbuchel H, Aliot E, Kautzner J, Szumowski L, Mont L, Morgan J, Willems S, Themistoclakis S, Gulizia M, Elvan A, Smit MD, Kirchhof P. Rationale and current perspective for early rhythm control therapy in atrial fibrillation. EUROPACE. 13:1517-1525. I.F.: 1.84.

2 Oliva A, Brugada R, D›aloja E, Boschi I, Partemi S, Brugada J, Pascali VL. State of the Art in Forensic Investigation of Sudden Cardiac Death. AM J FOREN MED PATH. 32:1-16. I.F.: 0.65.

EDITORIALS
I.F.: 23.05

1 Arbelo E, Hindriks G, Maggioni A, Morgan J, Tavazzi L, Vardas P, Brugada J. Atrial Fibrillation Ablation Pilot Study: a new feature of the EURObservational Research Programme. EUR HEART J. 32:1173-1174. I.F.: 10.05.

2 Brugada J, Brugada R, Brugada P. Electrophysiologic testing predicts events in Brugada syndrome patients. HEART RHYTHM. 8:1595-1597. I.F.: 4.25.

3 Sitges M, Mont L. Identification of optimal candidates for heart resynchronization therapy: an ongoing search. MED CLIN-BARCELONA. 137:113-114. I.F.: 1.41.

4 Brugada J, Brugada R, Brugada P. Rebuttal to EP testing does not predict cardiac events in patients with Brugada syndrome. HEART RHYTHM. 8:1796-1796. I.F.: 4.25.

5 Brugada J. Role of emergency medicine physicians in identifying patients at risk of sudden death. EMERGENCIAS. 23:5-7. I.F.: 3.09.

CLINICAL GUIDELINES
I.F.: 6.54

1 Raviele A, Giada F, Bergfeldt L, Blanc JJ, Blomstrom-Lundqvist C, Mont L, Morgan JM, Raatikainen MJP, Steinbeck G, Viskin S. Management of patients with palpitations: a position paper from the European Heart Rhythm Association. EUROPACE. 13:920-934. I.F.: 1.84.

2 Kirchhof P, Lip GYH, VanGelder IC, Bax J, Hylek E, Kaab S, Schotten U, Wegscheider K, Boriani G, Ezekowitz M, Diener H, Heidbuchel H, Lane D, Mont L, Willems S, Dorian P, Vardas P, Breithardt G, Camm AJ. Comprehensive risk reduction in patients with atrial fibrillation: Emerging diagnostic and therapeutic options Executive summary* of the report from the 3rd AFNET/EHRA consensus conference. THROMB HAEMOSTASIS. 106:1012-1019. I.F.: 4.70.

MULTICENTRICS
I.F.: 59.84

1 Bogale N, Priori S, Gitt A, Alings M, Linde C, Dickstein K. The European cardiac resynchronization therapy survey: patient selection and implantation practice vary according to centre volume. EUROPACE. 13:1445-1453. I.F.: 1.84.

2 Bogale N, Witte K, Priori S, Cleland J, Auricchio A, Gadler F, Gitt A, Limbourg T, Linde C, Dickstein K. The European Cardiac Resynchronization Therapy Survey: comparison of outcomes between de novo cardiac resynchronization therapy implantations and upgrades. EUR J HEART FAIL. 13:974-983. I.F.: 4.51.

3 Yusuf S, Healey JS, Pogue J, Chrolavicius S, Flather M, Hart RG, Hohnloser SH, Joyner CD, Pfeffer MA, Connolly SJ. Irbesartan in Patients with Atrial Fibrillation. NEW ENGL J MED. 364:928-938. I.F.: 53.49.

GRANTS FOR RESEARCH IN PROGRESS

Brugada J. REDINSCOR - Red de Investigación en Insuficiencia Cardíaca en España. Sponsored by: Instituto de Salud Carlos III (ISCIII), RD06/0003/0008. Duration: 01/01/2007-31/12/2012.

Mont L. Estudi de la terapia de resincronització a Catalunya (TRC-CAT). Sponsored by: AATRM (Agencia d'Avaluació de Tecnología i Recerca Mèdiques, 154/4/2008. Duration: 01/01/2009-31/12/2012.

Brugada J. Mecanismos y reversibilidad de la fibrosis miocárdica asociada al ejercicio. Sponsored by: Ministerio de Ciencia e Innovación, DEP2009-12455. Duration: 01/01/2010-31/12/2012.

Brugada J. Arítmies i Estimulació Cardíaca. Sponsored by: Agència de Gestió d'Sponsored bys Universitaris i de Recerca, 2009 SGR 1104. Duration: 01/01/2009-31/12/2013.

Ortiz JT. Utilidad de la angiografía coronaria no invasiva mediante tomografía computerizada multidetector en el diagnóstico del síndrome coronario agudo en urgencias. Sponsored by: Instituto de Salud Carlos III, PI09/90513. Duration: 01/01/2010-31/12/2012.

Brugada J. iCARDEA: An Intelligent Platform for Personalized Remote Monitoring of the Cardiac Patients with Electronic Implant Devices. Sponsored by: SRDC YAZILIM ARASTIRMA VE GELISTIRME VE DANISMANLIK TICARET, Ref.: 248240. Duration: 01/02/2010-31/01/2013.

Mont L. Estudio del remodelado miocárdico en un modelo animal crónico de síndrome de apnea-hipoapnea del sueño. Sponsored by: Instituto de Salud Carlos III, PI10/00834. Duration: 01/01/2011-31/12/2013.

Brugada J. Sudden cardiac death: definig clinical algorithms for a thorough investigation. Sponsored by: CNIC, CNIC-03-2008. Duration: 21/11/2008-20/11/2012.

Sitges M. Efecto del entrenamiento crónico sobre el ventrículo derecho: Análisis por imagen. Sponsored by: Ministerio de Ciencia e Innovación, DEP2010/20565. Duration: 01/01/2010-31/12/2013.

Berruezo A. Utilidad de la resonancia magnética con realce tardío como guía para la ablación de taquicardias ventriculares. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0243. Duration: 01/01/2009-31/12/2011.

Brugada J. cvREMOD: Convergencia de tecnologías médicas para la gestión integral del remodelado vascular. Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI), CENIT09 09/370. Duration: 09/09/2009-31/12/2012.

Castel MA. 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: 01/01/2011-31/12/2013.

DOCTORAL THESES

Sitges M. Estudio de la electromecánica cardíaca mediante postprocesado de señal e imagen cardiaca: Aplicación de un modelo clínico de terapia de resincronización cardíaca. PhD student: Silvia García Etelvino.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Nephro-urological diseases and kidney transplantation

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TEAM INVOLVED IN:

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 with extensive experience in all areas of the research into the natural history of renal disease (clinical nephrology, dialysis and transplant). This creates the perfect setting for translational research, with a two-way flow of communication between bench and bedside.
Since the setting up 5 years ago of the Laboratori Experimetal en Nefrologia i Transplantament (LENIT) [Experimental Laboratory for Nephrology and Transplantation] the clinical research and the different clinical trials have moved towards focusing on more fundamental aspects and concentrating on a translational approach.
Our research focuses on the study of fibrosis mechanisms, regenerative techniques and the search for biomarkers through urinary proteomics in chronic kidney disease and interstitial fibrosis and tubular atrophy in renal transplant. We are also studying the impact of the immunosuppressive medication used in renal transplant, both in terms of the nephrotoxicity induced by calcineurin inhibitors and the beneficial and harmful effects of mTOR inhibitors on left ventricular hypertrophy and proteinuria respectively. The strategic objectives of our research group are complemented by study of the importance of cardiovascular disease and cancer in renal and solid-organ transplant patients.

RESPIRATORY, CARDIOVASCULAR AND RENAL PATHOBIOLOGY AND BIOENGINEERING

Nephro-urological diseases and kidney transplantation

MAIN LINES OF RESEARCH

1. Cardiovascular and Renal Disease

- Evaluation of cardiovascular risk and accelerated atherosclerosis in renal patients.
- Study of left ventricular hypertrophy in chronic kidney disease using an experimental model of chronic kidney disease (5/6 nephrectomy).
- Effect of the use of mTOR inhibitors on the prevention of atherosclerosis and left ventricular hypertrophy.
- Dyslipidaemia and cardiovascular risk in renal transplant. Apolipoprotein polymorphisms.
- Endothelial dysfunction and effect of the uraemic environment on endothelial cells.
- Vascular calcification according to diet and the different pharmacological strategies for the control of calcium/phosphorus metabolism and renal osteodystrophy.
- Anaemia of renal origin and erythropoiesis-stimulating proteins in uraemia.

2. Fibrosis mechanisms and the search for biomarkers in chronic kidney disease (CKD) and interstitial fibrosis and tubular atrophy (IFTA) in renal transplant.

- **Molecular mechanisms of fibrogenesis.**
- Etiopathogenic factors using a P-glycoprotein knockout mouse model and by culture of tubular epithelial cells in an attempt to define the role of P-glycoprotein in the development of calcineurin inhibitor-induced nephrotoxicity.
- **Diagnostic Approach:** Through the analysis of the urinary proteome using 2D-gel and fingerprinting techniques, we are attempting to find early markers of renal fibrosis and IFTA, as well as in primary renal diseases such as systemic lupus erythematosus and membranous nephropathy. Study of proteomics in the dialysis patient under different renal purification techniques.
- **Therapeutic Strategies.**

3. Influence of mTOR inhibition on renal function and humoral response in renal transplant patients and experimental models of renal disease.

- **The role of mTOR inhibition in the development of proteinuria and histological lesions in an experimental model of renal failure** (5/6 nephrectomy). Study of the influence of mTOR inhibition, introduced at different times, on renal function, proteinuria, histological lesions, VEGF expression and its receptors.
- Analysis of the **harmful side effects** associated with the use of mTOR inhibitors: formation of oedema, anaemia, lung involvement, testicular dystrophy, diabetes. The group has various experimental models for determining the mechanisms that lead to each of these pathophysiological situations.
- Study of the effect of mTOR inhibitors in the **humoral immune response in renal transplant** through study of the effect of a number of immunomodulating drugs, alone or in combination with rapamycin, on the B-lymphocyte and humoral rejection. In vitro and in vivo experimental models of chronic humoral rejection in rats and in an experimental model of systemic lupus erythematosus.

4. Cancer and renal transplant

- **Clinical and molecular characterisation of post-transplant cancers.** Study of tumour behaviour according to the immunosuppressive regimen used, as well as the direct oncogenic effect of the immunosuppressive drugs, using the immunohistochemical characterisation of the tumours in a renal transplant population compared to a control population. Differences between the two populations in the TGF-, VEGF and PI3K/AKT/mTOR pathways in adenocarcinoma of the colon and skin cancer and the existence of KRAS mutations in the former and alteration in p53 expression in the latter, according to treatment with calcineurin or mTOR inhibitors.
- **KO mouse experimental model for p53.**
- **Role of the dendritic cells in the development of skin cancer** induced by the immunosuppressive treatment in the renal transplant population.
- **Post-transplant Kaposi's sarcoma:** Study of expression of different oncogenic signalling pathways in tumour tissue and a virological study evaluating the relationship with oncoviruses (HV8).
- **Nanotechnology in post-transplant cancers**. Impact on tumour progression and development of metastasis.

5. Identification of new uremic toxins

- The main objective of this study is the detection of new uremic toxins and the analysis of depurative abilities of different dialytic technics. These solutes in patients with end-stage chronic kidney disease are responsible of uremic syndrome, only identified 90 of them. For identify them, we are performing proteomic analysis through 2D DIGE and mass-spectrometry.
- Evaluation of different hemodialysis technics in depurative ability of these solutes.
- **Different prospectives studies evaluation the impact of** high-flux or on-line hemodiafiltration in end-stage chronic kidney disease patient survival, the effect of nocturan, every other day on-line hemodiafiltration, or the use of bioimpedance ant the measure of plasmatic volume in the prevention of hypotension and adjust the weight on dialysis.

6. Other lines of research

- Study of **hereditary kidney diseases,** especially polycystic kidney disease, Alport syndrome and benign familial haematuria.
- **Amyloidosis** associated with dialysis or beta-2 microglobulin and other types of hereditary and non-hereditary amyloidosis with renal involvement.

Our researchers also work on research lines shared with other Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) [August Pi i Sunyer Biomedical Research Institute] teams, primarily in the fields of hypertension, endothelial dysfunction, diabetes, systemic autoimmune diseases with renal involvement and cancer.

PUBLICATIONS

ORIGINALS
I.F.: 63.97

1 Haro I, Gomara MJ, Perez ML, Vinas O, Ercilla G, Gomez-Puerta JA, Sanmarti R. Antibodies against beta-fibrin synthetic peptides: A study of their association with the immunogenetic background and disease course of rheumatoid arthritis patients. EUR J MED CHEM. 46:1095-1102. I.F.: 3.19.

2 Ruiz-Esquide V, Gomez-Puerta JA, Canete JD, Graell E, Vazquez I, Ercilla MG, Vinas O, Gomez-Centeno A, Haro I, Sanmarti R. Effects of Smoking on Disease Activity and Radiographic Progression in Early Rheumatoid Arthritis. J RHEUMATOL. 38:2536-2539. I.F.: 3.55.

3 Silvarino R, Sant F, Espinosa G, Pons-Estel G, Sole M, Cervera R, Arrizabalaga P. Nephropathy associated with antiphospholipid antibodies in patients with systemic lupus erythematosus. LUPUS. 20:721-729. I.F.: 2.60.

4 Martina MN, Cofan F, Suarez A, Masso E, Trullas JC, Cervera C, Moreno A, Oppenheimer F, Miiro JM, Campistol JM. Kidney Transplantation and Waiting List for Renal Transplantation for Human Immunodeficiency Virus Patients. TRANSPL P. 43:2179-2181. I.F.: 0.99.

5 Martina MN, Cervera C, Esforzado N, Linares L, Torregrosa V, Sanclemente G, Hoyo I, Cofan F, Oppenheimer F, Miro JM, Campistol JM, Moreno A. Toxoplasma gondii primary infection in renal transplant recipients. Two case reports and literature review. TRANSPL INT. 24:e6-e12. I.F.: 3.21.

6 Martinez-Castelao A, Gorriz JL, Portoles JM, DeAlvaro F, Cases A, Luno J, Navarro-Gonzalez JF, Montes R, DeLaCruz-Troca JJ, Natarajan A, Batlle D. Baseline characteristics of patients with chronic kidney disease stage 3 and stage 4 in spain: the MERENA observational cohort study. BMC NEPHROL. 12:-. I.F.: 2.14.

7 Grinyo JM, Saval N, Campistol JM. Clinical assessment and determinants of chronic allograft nephropathy in maintenance renal transplant patients. NEPHROL DIAL TRANSPL. 26:3750-3755. I.F.: 3.56.

8 Novoa PA, Grinyo JM, Ramos FJP, Errasti P, Franco A, Aldana G, Pefaur J, Marti-Cuadros AM, Otero AB, Saval N, Oppenheimer F. De Novo Use of Everolimus With Elimination or Minimization of Cyclosporine in Renal Transplant Recipients. TRANSPL P. 43:3331-3339. I.F.: 0.99.

9 Coto-Llerena M, Perez-Del-Pulgar S, Crespo G, Carrion JA, Martinez SM, Sanchez-Tapias JM, Martorell J, Navasa M, Forns X. Donor and Recipient IL28B Polymorphisms in HCV-Infected Patients Undergoing Antiviral Therapy before and after Liver Transplantation. AM J TRANSPLANT. 11:1051-1057. I.F.: 6.05.

10 Seron D, Moreso F, Arias M, Campistol JM, Curto J, Hernandez D, Morales JM, Sanchez-Fructuoso A, Abraira V. Estimation of renal allograft half-life: fact or fiction? (vol 26, pg 3013, 2011). NEPHROL DIAL TRANSPL. 26:-. I.F.: 3.56.

11 Alcaraz A, Musquera M, Peri L, Izquierdo L, Garcia-Cruz E, Huguet J, Alvarez-Vijande R, Campistol JM, Oppenheimer F, Ribal MJ. Feasibility of Transvaginal Natural Orifice Transluminal Endoscopic Surgery-Assisted Living Donor Nephrectomy: Is Kidney Vaginal Delivery the Approach of the Future?. EUR UROL. 59:1019-1025. I.F.: 8.84.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	80.92	23	18	1
2010	117.61	30	12	3
2011	63.97	20	7	6

12 Lloberas N, Torras J, Cruzado JM, Andreu F, Oppenheimer F, Sanchez-Plumed J, Gentil MA, Brunet M, Ekberg H, Grinyo JM. Influence of MRP2 on MPA pharmacokinetics in renal transplant recipients-results of the Pharmacogenomic Substudy within the Symphony Study. NEPHROL DIAL TRANSPL. 26:3784-3793. I.F.: 3.56.

13 Tavira B, Coto E, Diaz-Corte C, Ortega F, Arias M, Torres A, Diaz JM, Selgas R, Lopez-Larrea C, Campistol JM, Ruiz-Ortega M, Alvarez V. KCNQ1 gene variants and risk of new-onset diabetes in tacrolimus-treated renal-transplanted patients. CLIN TRANSPLANT. 25:E284-E291. I.F.: 1.75.

14 Alberu J, Pascoe MD, Campistol JM, Schena FP, Rial MD, Polinsky M, Neylan JF, Korth-Bradley J, Goldberg-Alberts R, Maller ES. Lower Malignancy Rates in Renal Allograft Recipients Converted to Sirolimus-Based, Calcineurin Inhibitor-Free Immunotherapy: 24-Month Results From the CONVERT Trial. TRANSPLANTATION. 92:303-310. I.F.: 3.68.

15 Martina MN, Sole M, Masso E, Perez N, Campistol JM, Quintana LF. Mixed cryoglobulinaemia not related to hepatitis C virus, mesangiocapillary glomerulonephritis and lymphoplasmocytic lymphoma. NEFROLOGIA. 31:743-746. I.F.: 0.74.

16 Tavira B, Garcia EC, Diaz-Corte C, Ortega F, Arias M, Torres A, Diaz JM, Selgas R, Lopez-Larrea C, Campistol JM, Alvarezca V. Pharmacogenetics of tacrolimus after renal transplantation: analysis of polymorphisms in genes encoding 16 drug metabolizing enzymes. CLIN CHEM LAB MED. 49:825-833. I.F.: 2.07.

17 Fontsere N, Blasco M, Maduell F, Vera M, Arias-Guillen M, Herranz S, Blanco T, Barrufet M, Burrel M, Montana J, Real MI, Mestres G, Riambau V, Campistol JM. Practical Utility of On-Line Clearance and Blood Temperature Monitors as Noninvasive Techniques to Measure Hemodialysis Blood Access Flow. BLOOD PURIFICAT. 31:1-8. I.F.: 1.52.

18 Vodenik B, Rovira J, Diekmann F, Revuelta I, Oppenheimer F, Campistol JM. Preemptive Use of Mammalian Target of Rapamycin Inhibitors in Living Donor Transplantation. TRANSPL P. 43:2568-2573. I.F.: 0.99.

19 Sola A, Weigert A, Jung M, Vinuesa E, Brecht K, Weis N, Brune B, Borregaard N, Hotter G. Sphingosine-1-phosphate signalling induces the production of Lcn-2 by macrophages to promote kidney regeneration. J PATHOL. 225:597-608. I.F.: 7.27.

20 Vanrenterghem Y, Bresnahan B, Campistol J, Durrbach A, Grinyó J, Neumayer HH, Lang P, Larsen CP, Mancilla-Urrea E, Pestana JM, Block A, Duan T, Glicklich A, Gujrathi S, Vincenti F. Belatacept-based regimens are associated with improved cardiovascular and metabolic risk factors compared with cyclosporine in kidney transplant recipients (BENEFIT and BENEFIT-EXT studies). TRANSPLANTATION. 91(9):976-83. I.F.: 3.68.

REVIEWS
I.F.: 12.32

1 Trullas JC, Cofan F, Tuset M, Ricart MJ, Brunet M, Cervera C, Manzardo C, Lopez-Dieguez M, Oppenheimer F, Moreno A, Campistol JM, Miro JM. Renal transplantation in HIV-infected patients: 2010 update. KIDNEY INT. 79:825-842. I.F.: 6.11.

2 Epailly E, Albanell J, Andreassen A, Bara C, Campistol JM, Delgado JF, Eisen H, Fiane AE, Mohacsi P, Schubert S, Sebbag L, Turazza FM, Valantine H, Zuckermann A, Potena L. Proliferation signal inhibitors and post-transplant malignancies in heart transplantation: practical clinical management questions. CLIN TRANSPLANT. 25:E475-E486. I.F.: 1.75.

3 Dominguez-Gil B, Andres A, Campistol JM, Morales JM. Should we be using kidneys from hepatitis C virus-infected donors?. CURR OPIN NEPHROL HY. 20:599-604. I.F.: 4.46.

MULTICENTRICS
I.F.: 3.68

1 Holdaas H, Rostaing L, Seron D, Cole E, Chapman J, Fellstrom B, Strom EH, Jardine A, Midtvedt K, Machein U, Ulbricht B, Karpov A, O'connell PJ. Conversion of Long-Term Kidney Transplant Recipients From Calcineurin Inhibitor Therapy to Everolimus: A Randomized, Multicenter, 24-Month Study. TRANSPLANTATION. 92:410-418. I.F.: 3.68.

GRANTS FOR RESEARCH IN PROGRESS

Poch E. REDINREN - Red de Investigación en Enfermedades Renales. Sponsored by: nstituto de Salud Carlos III (ISCIII), FIS_RETIC06 RD06/0016/0015. Duration: 01/01/2007-30/04/2011.

Campistol JM. Red de Investigación en Enfermedades Renales (REDINREN). Sponsored by: Instituto de Salud Carlos III (ISCIII), FIS_RETIC07 RD06/0016/1002. Duration: 29/02/2008-31/12/2012.

Brunet M. Estudio multicéntrico para la validación de los biomarcadores de elección que reflejen la respuesta individual de los pacientes trasplantados de órganos sólidos al tratamiento inmunosupresor. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080300. Duration: 01/01/2008-31/12/2011.

Poch E. Análisis de biomarcadores predictores de insuficiencia renal aguda post cirugía cardíaca. Sponsored by: Instituto de Salud Carlos III, PI08/0140. Duration: 01/01/2009-30/12/2011.

Campistol JM. 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: 01/01/2010-31/12/2012.

Campistol JM. 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, TV3_EMinoritarias_10 101430. Duration: 03/02/2011-02/02/2014.

Campistol JM. LENIT (Laboratori Experimental de Nefrologia i Transplantament). Sponsored by: AGAUR_SGR09, 2009_SGR_1125. Duration: 20/07/2009-31/12/2013.

Campistol JM. Remodelación tisular en el rechazo crónico. Sponsored by: Fundación Mutua Madrileña, AP92582011. Duration: 26/11/2011-25/11/2014.

Hotter G. Bioregeneració i micromonitorització hipóxica. Sponsored by: AGAUR_SGR09, 2009_SGR_1074. Duration: 29/07/2009-31/12/2013.

DOCTORAL THESES

Campistol JM. Caracterización molecular de las neoplasias en trasplante de órgano sólido. PhD student: Ignacio Revuelta Vicente.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Hypertension, lipids and cardiovascular risk

TEAM INVOLVED IN: ciberobn

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Miquel Camafort (Hospital Clínic)

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RESPIRATORY, CARDIOVASCULAR AND RENAL PATHOBIOLOGY AND BIOENGINEERING

Hypertension, lipids and cardiovascular risk

STRATEGIC OBJECTIVES

The general aim of our group is to gain in-depth knowledge of the epidemiology, pathogenesis, diagnosis, treatment and prevention of arterial hypertension, dyslipidemia and associated cardiovascular risk. The research lines we wish to continue consolidating are the following:

1. Mechanisms and consequences of silent lesions in target organs of hypertension.
2. Interaction of environmental determinants in cardiovascular disease, such as salt intake and the salt sensitivity phenomenon.
3. Candidate genes of hypertension and its complications.
4. Characterization of genetic dyslipidemias.
5. Detection of preclinical atherosclerosis.
6. Study of the intestinal absorption and synthesis of cholesterol.
7. Phytosterolemia as a cardiovascular risk factor.
8. Determination of the fatty acids profile in phospholipids and blood cell membranes, and their associations with diet, metabolic syndrome, cardiovascular risk phenotypes and preclinical arteriosclerosis.
9. Study of the cardiovascular functionality of foods, including the effects of foods rich in omega-3 fatty acids upon carotid atheroma plaque characteristics.
10. Effects of the Mediterraenan diet on carotid atheroma plaque vulnerability evaluated by MRI.
11. Identification of genetic variants associated with different responses to foods and nutrients (nutrigenetics).
12. Influence of the components of the Mediterranean on degenerative diseases and cognitive impairment in older people.
13. Effects of Mediterranean diet on blood pressure assessed by ambulatory and home blood pressure monitoring.

MAIN LINES OF RESEARCH

1. External arterial ultrasound of femoral and carotid arteries, coronary calcium by CT and carotid plaque MRI. Relationship between preclinical atherosclerosis and conventional and emergent risk factors and biomarkers of the usual diet, including unsaturated fatty acids and in plasma phospholipids, circulating vitamins and phytosterols. Influence of diet on carotid atheroma plaque vulnerability evaluated by sequential MRI. Correlation of plaque composition by MRI with histology.
2. Circadian patterns, arterial pressure variability and target organ damage. Sensitivity to salt in arterial hypertension. Inflammation in hypertension. Hypertension and atrial fibrillation as manifestation of hypertension-induced cardiac damage.
3. Candidate genes for cerebrovascular stroke risk in hypertensive patients. Candidate genes for the development of left ventricular hypertrophy and heart failure in hypertensive patients.
4. Functionality of dietary patterns and whole foods: influence upon arterial pressure evaluated by ambulatory and home monitoring, insulin resistance, biological markers of cholesterol absorption and synthesis and vascular risk, dietary biomarkers (unsaturated fatty acids in whole blood, carotenes and vitamin E in plasma, polyphenols in urine) and physicochemical properties of the low-density lipoproteins (LDLs) and high-density lipoproteins (HDLs).
5. Mild age-associated cognitive impairment in participants in the PREDIMED study after two years of intervention with Mediterranean diets or a low-fat diet.
6. Effect of hypercholesterolemia of different origin and severity on cognitive function as assessed by neuropsychological tests and functional brain MRI.
7. Cholesterol absorption and synthesis evaluated by the 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.
8. Influence of polyunsaturated long-chain fatty acids (plant and marine omega-3) on preclinical atherosclerosis of the carotid arteries, evaluated by high-resolution ultrasound and MRI.
9. Associations of the fatty acids profile in whole plasma, whole blood and circulating phospholipid fraction with SCD1 activity; neurodegenerative, autoinflammatory and infectious diseases; cardiometabolic risk factors and non-alcoholic liver steatosis; dietary determinants of the omega-3 index in whole blood; fatty acids composition of the "lipid rafts"; and effect upon intracellular signaling.
10. Effect of diet supplementation with nuts for 2 years on cognitive function, the integrity of the retina, the length of telomeres and different markers of inflammation, oxidation and cardiovascular risk in old people.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	70.61	22	9	11
2010	97.91	21	14	5
2011	78.21	22	9	10

ORIGINALS
I.F.: 78.21

1 Anguita M, Beiras AC, Cobo E, Coca A, DeTeresa E, Diez J, Lopez B, Cebollada J, Diaz B, Galve E, Gonzalez-Juanatey JR, Jimenez-Navarro M, Lopez I, Lupon J, Martin C, Monserrat L, Narejos S, Figal DAP, Perez-Calvo JI, Que-rejeta R, Ridocci F, Rodriguez A, Rodriguez M, Roig E, Roure J, Ruiz S, Sanchez PL, Terns M, Toran P, Munoz-Tuduri M. Effects of Prolonged-Release Torasemide Versus Furosemide on Myocardial Fibrosis in Hypertensive Patients with Chronic Heart Failure: A Randomized, Blinded End Point, Active-Controlled Study. CLIN THER. 33:1204-1213. I.F.: 2.55.

2 Cenarro A, Garcia-Otin AL, Tejedor MT, Solanas M, Jarauta E, Junquera C, Ros E, Mozas P, Puzo J, Pocovi M, Civeira F. A presumptive new locus for autosomal dominant hypercholesterolemia mapping to 8q24.22. CLIN GENET. 79:475-481. I.F.: 2.94.

3 Schroder H, Fito M, Estruch R, Martinez-Gonzalez MA, Corella D, Salas-Salvado J, Lamuela-Raventos R, Ros E, Salaverria I, Fiol M, Lapetra J, Vinyoles E, Gomez-Gracia E, Lahoz C, Serra-Majem L, Pinto X, Ruiz-Gutierrez V, Covas MI. A Short Screener Is Valid for Assessing Mediterranean Diet Adherence among Older Spanish Men and Women. J NUTR. 141:1140-1145. I.F.: 4.30.

4 Bullo M, Garcia-Aloy M, Martinez-Gonzalez MA, Corella D, Fernandez-Ballart JD, Fiol M, Gomez-Gracia E, Estruch R, Ortega-Calvo M, Francisco S, Flores-Mateo G, Serra-Majem L, Pinto X, Covas MI, Ros E, Lamuela-Raventos R, Salas-Salvado J. Association between a healthy lifestyle and general obesity and abdominal obesity in an elderly population at high cardiovascular risk. PREV MED. 53:155-161. I.F.: 3.30.

5 Cofan M, Escurriol V, Garcia-Otin AL, Moreno-Iribas C, Larranaga N, Sanchez MJ, Tormo MJ, Redondo ML, Gonzalez CA, Corella D, Pocovi M, Civeira F, Ros E. Association of plasma markers of cholesterol homeostasis with metabolic syndrome components. A cross-sectional study. NUTR METAB CARDIOVAS. 21:651-657. I.F.: 3.44.

6 Sala-Vila A, Cofan M, Nunez I, Gilabert R, Junyent M, Ros E. Carotid and femoral plaque burden is inversely associated with the alpha-linolenic acid proportion of serum phospholipids in Spanish subjects with primary dyslipidemia. ATHEROSCLEROSIS. 214:209-214. I.F.: 4.09.

7 Murie-Fernandez M, Irimia P, Toledo E, Martinez-Vila E, Buil-Cosiales P, Serrano-Martinez M, Ruiz-Gutierrez V, Ros E, Estruch R, Martinez-Gonzalez MA. Carotid intima-media thickness changes with Mediterranean diet: A randomized trial (PREDIMED-Navarra). ATHEROSCLEROSIS. 219:158-162. I.F.: 4.09.

8 Barrios V, Calderon A, Coca A, Gonzalez-Juanatey JR, Sarria A, Rodriguez-Padial L. Computerized interpretation of the electrocardiogram in the diagnosis of left ventricular hypertrophy. The ELECTROPRES project. REV CLIN ESP. 211:391-399. I.F.: 0.76.

9 Casas-Agustench P, Bullo M, Ros E, Basora J, Salas-Salvado J. Cross-sectional association of nut intake with adiposity in a Mediterranean population. NUTR METAB CARDIOVAS. 21:518-525. I.F.: 3.44.

10 Sala-Vila A, Harris WS, Cofan M, Perez-Heras AM, Pinto X, Lamuela-Raventos RM, Covas MI, Estruch R, Ros E. Determinants of the omega-3 index in a Mediterranean population at increased risk for CHD. BRIT J NUTR. 106:425-431. I.F.: 3.07.

11 Sola R, Fito M, Estruch R, Salas-Salvado J, Corella D, DeLaTorre R, Munoz MA, Lopez-Sabater MD, Martinez-Gonzalez MA, Aros F, Ruiz-Gutierrez V, Fiol M, Casals E, Warnberg J, Buil-Cosiales P, Ros E, Konstantinidou V, Lapetra J, Serra-Majem L, Covas MI. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: A randomized, controlled trial. ATHEROSCLEROSIS. 218:174-180. I.F.: 4.09.

12 Casas-Agustench P, Lopez-Uriarte P, Bullo M, Ros E, Cabre-Vila JJ, Salas-Salvado J. Effects of one serving of mixed nuts on serum lipids, insulin resistance and inflammatory markers in patients with the metabolic syndrome. NUTR METAB CARDIOVAS. 21:126-135. I.F.: 3.44.

13 Sala-Vila A, Cofan M, Mateo-Gallego R, Cenarro A, Civeira F, Ortega E, Ros E. Inverse association between serum phospholipid oleic acid and insulin resistance in subjects with primary dyslipidaemia. CLIN NUTR. 30:590-592. I.F.: 3.41.

14 Bosch X, Foix A, Jordan A, Coca A, Lopez-Soto A. Outpatient Quick Diagnosis Units for the evaluation of suspected severe diseases: an observational, descriptive study. CLINICS. 66:737-741. I.F.: 1.42.

15 Sobrino J, Domenech M, Camafort M, Vinyoles E, Coca A. Prevalence of masked hypertension in a cohort of controlled hypertensive patients in Spain. MED CLIN-BARCELONA. 136:607-612. I.F.: 1.41.

16 Ascaso JF, Millan J, Mateo-Gallego R, Ruiz A, Suarez-Tembra M, Borrallo RM, Zambon D, Gonzalez-Santos P, Peres-De-Juan M, Ros E. Prevalence of metabolic syndrome and cardiovascular disease in a hypertriglyceridemic population. EUR J INTERN MED. 22:177-181. I.F.: 1.66.

17 DeCastro-Oros I, Pampin S, Cofan M, Mozas P, Pinto X, Salas-Salvado J, Rodriguez-Rey JC, Ros E, Civeira F, Pocovi M. Promoter variant -204A > C of the cholesterol 7 alpha-hydroxylase gene: Association with response to plant sterols in humans and increased transcriptional activity in transfected HepG2 cells. CLIN NUTR. 30:239-246. I.F.: 3.41.

18 Salas-Salvado J, Bullo M, Babio N, Martinez-Gonzalez MA, Ibarrola-Jurado N, Basora J, Estruch R, Covas MI, Corella D, Aros F, Ruiz-Gutierrez V, Ros E. Reduction in the Incidence of Type 2 Diabetes With the Mediterranean Diet Results of the PREDIMED-Reus nutrition intervention randomized trial. DIABETES CARE. 34:14-19. I.F.: 7.14.

19 Corella D, Portoles O, Arriola L, Chirlaque MD, Barricarte A, Frances F, Huerta JM, Larranaga N, Martinez C, Martinez-Camblor P, Molina E, Navarro C, Quiros JR, Rodriguez L, Sanchez MJ, Ros E, Sala N, Gonzalez CA, Moreno-Iribasd C. Saturated fat intake and alcohol consumption modulate the association between the APOE polymorphism and risk of future coronary heart disease: a nested case-control study in the Spanish EPIC cohor. J NUTR BIOCHEM. 22:487-494. I.F.: 4.54.

20 Redon J, Olsen MH, Cooper RS, Zurriaga O, Martinez-Beneito MA, Laurent S, Cifkova R, Coca A, Mancia G. Stroke mortality and trends from 1990 to 2006 in 39 countries from Europe and Central Asia: implications for control of high blood pressure. EUR HEART J. 32:1424-1431. I.F.: 10.05.

21 Medina-Remon A, Zamora-Ros R, Rotches-Ribalta M, Andres-Lacueva C, Martinez-Gonzalez MA, Covas MI, Corella D, Salas-Salvado J, Gomez-Gracia E, Ruiz-Gutierrez V, DeLaCorte FJG, Fiol M, Pena MA, Saez GT, Ros E, Serra-Majem L, Pinto X, Warnberg J, Estruch R, Lamuela-Raventos RM. Total polyphenol excretion and blood pressure in subjects at high cardiovascular risk. NUTR METAB CARDIOVAS. 21:323-331. I.F.: 3.44.

22 Sierra C, Coca A, Schiffrin EL. Vascular Mechanisms in the Pathogenesis of Stroke. CURR HYPERTENS REP. 13:200-207. I.F.: 2.24.

EDITORIALS
I.F.: 2.82

1 Camafort M, Coca A. Resistant hypertension: beyond a bad control of blood pressure. MED CLIN-BARCELONA. 137:444-445. I.F.: 1.41.

2 Hernandez-Hernandez R, Coca A. The paradox of obesity in heart failure: Is more weight better?. MED CLIN-BARCELONA. 137:689-690. I.F.: 1.41.

GRANTS FOR RESEARCH IN PROGRESS

Coca A. NoE - Integrated Genomics, Clinical Research and Care in Hypertension. Sponsored by: European Commission, Istituto Auxolico Italiano, CE_FPVI06 LHSM-CT-2006-037093. Duration: 01/11/2006-31/01/2011.

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: 01/01/2010-31/12/2012.

Ros E. Subproject: Effects of a 2-year Mediterranean diet intervention on 3T MRI-monitored carotid plaque progression and vulnerability. A randomized study. Sponsored by: Centro Nacional de Investigaciones Cardiovasculares (CNIC), MSC_CNIC07-S02. Duration: 01/01/2008-31/12/2011.

DOCTORAL THESES

Coca A. Hipertrofia ventricular izquierda y prediccion del riesgo cardiovascular del hipertenso en nuestro medio. PhD student: Francisco Javier Tovillas Morán.

Coca A. Efectivitat de dues intervencions en la prescripció d'antibiòtics en infeccions del tracte respiratori en Atenció Primària a Espanya. PhD student: Josep M Cots Yago.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Respiratory biophysics and bioengineering

TEAM INVOLVED IN: ciberes & ciber-bbn

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RESPIRATORY, CARDIOVASCULAR AND RENAL PATHOBIOLOGY AND BIOENGINEERING

Respiratory biophysics and bioengineering

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 promotes 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.

De-cellularized rat lung.

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.

For further information:
www.ub.edu/biofisica

PUBLICATIONS

ORIGINALS
I.F.: 56.27

1 Mane A, Gallego J, Lomena F, Mateos JJ, Fernandez-Egea E, Horga G, Cot A, Pavia J, Bernardo M, Parellada E. A 4-year dopamine transporter (DAT) imaging study in neuroleptic-naive first episode schizophrenia patients. PSYCHIAT RES-NEUROIM. 194:79-84. I.F.: 2.06.

2 Cagido VR, Zin WA, Ramirez J, Navajas D, Farre R. Alternating ventilation in a rat model of increased abdominal pressure. RESP PHYSIOL NEUROBI. 175:310-315. I.F.: 2.38.

3 Pino F, Roe N, Orero A, Falcon C, Rojas S, Benlloch JM, Ros D, Pavia J. Development of a variable-radius pinhole SPECT system with a portable gamma camera. REV ESP MED NUCL. 30:286-291. I.F.: 0.77.

4 Horga G, Parellada E, Lomena F, Fernandez-Egea E, Mane A, Font M, Falcon C, Konova AB, Pavia J, Ros D, Bernardo M. Differential brain glucose metabolic patterns in antipsychotic-naive first-episode schizophrenia with and without auditory verbal hallucinations. J PSYCHIATR NEUROSCI. 36:312-321. I.F.: 4.89.

5 Almendros I, Farre R, Torres M, Bonsignore MR, Dalmases M, Ramirez J, Navajas D, Montserrat JM. Early and mid-term effects of obstructive apneas in myocardial injury and inflammation. SLEEP MED. 12:1037-1040. I.F.: 3.43.

6 Carreras A, Wang Y, Gozal D, Montserrat JM, Navajas D, Farre R. Non-invasive system for applying airway obstructions to model obstructive sleep apnea in mice. RESP PHYSIOL NEUROBI. 175:164-168. I.F.: 2.38.

7 Iranzo A, Valldeoriola F, Lomena F, Molinuevo JL, Serradell M, Salamero M, Cot A, Ros D, Pavia J, Santamaria J, Tolosa E. Serial dopamine transporter imaging of nigrostriatal function in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective study. LANCET NEUROL. 10:797-805. I.F.: 21.66.

8 Munoz E, Iranzo A, Rauek S, Lomena F, Gallego J, Ros D, Santamaria J, Tolosa E. Subclinical nigrostriatal dopaminergic denervation in the cerebellar subtype of multiple system atrophy (MSA-C). J NEUROL. 258:2248-2253. I.F.: 3.85.

9 Dellaca R, Montserrat JM, Govoni L, Pedotti A, Navajas D, Farre R. Telemetric CPAP titration at home in patients with sleep apnea-hypopnea syndrome. SLEEP MED. 12:153-157. I.F.: 3.43.

10 Almendros I, Farre R, Planas AM, Torres M, Bonsignore MR, Navajas D, Montserrat JM. Tissue Oxygenation in Brain, Muscle, and Fat in a Rat Model of Sleep Apnea: Differential Effect of Obstructive Apneas and Intermittent Hypoxia. SLEEP. 34:1127-1133. I.F.: 5.49.

11 Masa JF, Gonzalez MT, Pereira R, Mota M, Riesco JA, Corral J, Zamorano J, Rubio M, Teran J, Farre R. Validity of spirometry performed online. EUR RESPIR J. 37:911-918. I.F.: 5.92.

GRANTS FOR RESEARCH IN PROGRESS

Farré R. Efecto de los estímulos mecánicos en la diferenciación de células madres hacia el fenotipo epitelial alveolar. Sponsored by: Ministerio de Ciencia e Innovación, SAF2008-02991. Duration: 01/01/2009-31/12/2011.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	26.03	9	6	3
2010	48.63	11	7	3
2011	56.27	11	8	2

Ros D. Desarrollo del proyecto "Tecnologías de Imagen Molecular Avanzada (AMIT)". Sponsored by: CDTI - CETIR, CENTRE MEDIC, S.A., 10/192. Duration: 01/01/2010-01/01/2013.

Ros D. Cuantificación de estudios de SPECT cerebral utilizando ligandos del transportador de dopamina en modelos animales y en diagnóstico clínico. Sponsored by: Ministerio de Ciencia e Innovación, SAF2009-08076. Duration: 01/01/2010-31/12/2012.

Pavia J. Estudios de neuroimágen. Sponsored by: Centro para el Desarrollo Tecnológico Industrial (CDTI), CENIT10 10/157. Duration: 18/05/2010-31/12/2013.

DOCTORAL THESES

Ros D. Evaluation of Compton scattering in spect studies with 123-I-labeled rediotracers and quantification of small animal neurotransmission studies. PhD student: Núria Roé Vellvé.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Applied research in infectious respiratory diseases, critically ill patients and lung cancer

TEAM INVOLVED IN: ciberes

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Hugo Loureiro (Hospital Clínic)
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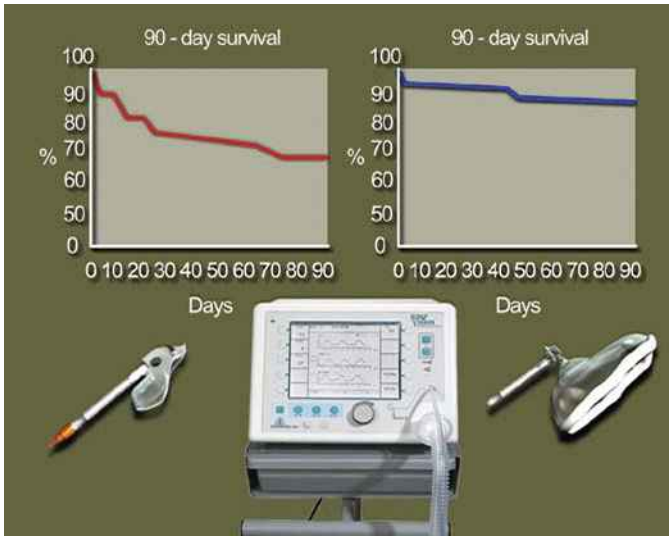
STRATEGIC OBJECTIVES

- 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.
- Human and animal model research in sleep apnea syndrome.
- Multicenter studies in relation to sleep respiratory pathology and cardiovascular disease.



Noninvasive ventilation after extubation significantly improves patient survival in relation to conventional treatment with oxygen therapy (Lancet; 374: 1082–88).

MAIN LINES OF RESEARCH

1. Epidemiology, prevention and new treatmentsof 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.

RESEARCH GROUP
BREATHING DISTURBANCES IN SLEEP

Team Leader: **Josep M. Montserrat (Hospital Clínic)**

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.

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 methicillin-resistant 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.

For further information:
www.idibapsrespiratoryresearch.org

PUBLICATIONS

ORIGINALS
I.F.: 160.67

1 Martin-Loeches I, Diaz E, Vidaur L, Torres A, Laborda C, Granada R, Bonastre J, Martin M, Insausti J, Arenzana A, Guerrero JE, Navarrete I, Bermejo-Martin J, Suarez D, Rodriguez A. Pandemic and post-pandemic Influenza A (H1N1) infection in critically ill patients. CRIT CARE. 15:-. I.F.: 4.60.

2 Marcos MA, Ramon S, Anton A, Martinez E, Vilella A, Olive V, Cilloniz C, Moreno A, Torres A, Pumarola T. Clinical relevance of mixed respiratory viral infections in adults with influenza A H1N1. EUR RESPIR J. 38:739-742. I.F.: 5.92.

3 Cilloniz C, Ewig S, Ferrer M, Polverino E, Gabarrus A, DeLaBellacasa JP, Mensa J, Torres A. Community-acquired polymicrobial pneumonia in the intensive care unit: aetiology and prognosis. CRIT CARE. 15:-. I.F.: 4.60.

4 Cilloniz C, Ewig S, Polverino E, Marcos MA, Esquinas C, Gabarrus A, Mensa J, Torres A. Microbial aetiology of community-acquired pneumonia and its relation to severity. THORAX. 66:340-346. I.F.: 6.53.

5 Martinez-Rebollar M, Lonca M, Perez I, Soy D, Brunet M, Martin R, Coll O, Hernandez S, Laguno M, Milinkovic A, Larrousse M, Calvo M, Blanco JL, Martinez E, Gatell JM, Mallolas J. Pharmacokinetic Study of Saquinavir 500 mg Plus Ritonavir (1000/100 mg Twice a Day) in HIV-Positive Pregnant Women. THER DRUG MONIT. 33:772-777. I.F.: 3.13.

6 Almendros I, Farre R, Torres M, Bonsignore MR, Dalmases M, Ramirez J, Navajas D, Montserrat JM. Early and mid-term effects of obstructive apneas in myocardial injury and inflammation. SLEEP MED. 12:1037-1040. I.F.: 3.43.

7 Carreras A, Wang Y, Gozal D, Montserrat JM, Navajas D, Farre R. Non-invasive system for applying airway obstructions to model obstructive sleep apnea in mice. RESP PHYSIOL NEUROBI. 175:164-168. I.F.: 2.38.

8 Dellaca R, Montserrat JM, Govoni L, Pedotti A, Navajas D, Farre R. Telemetric CPAP titration at home in patients with sleep apnea-hypopnea syndrome. SLEEP MED. 12:153-157. I.F.: 3.43.

9 Almendros I, Farre R, Planas AM, Torres M, Bonsignore MR, Navajas D, Montserrat JM. Tissue Oxygenation in Brain, Muscle, and Fat in a Rat Model of Sleep Apnea: Differential Effect of Obstructive Apneas and Intermittent Hypoxia. SLEEP. 34:1127-1133. I.F.: 5.49.

10 Guerrero L, Pinazo MJ, Posada E, Gascon J, Ribas J, Soy D. A high-performance liquid chromatographic method for benznidazole quantitation in plasma of patients with Chagas disease. CLIN CHEM LAB MED. 49:77-82. I.F.: 2.07.

11 Wood J, Butler CC, Hood K, Kelly MJ, Verheij T, Little P, Torres A, Blasi F, Schaberg T, Goossens H, Nuttall J, Coenen S. Antibiotic prescribing for adults with acute cough/lower respiratory tract infection: congruence with guidelines. EUR RESPIR J. 38:112-118. I.F.: 5.92.

12 Butler CC, Kelly MJ, Hood K, Schaberg T, Melbye H, Serra-Prat M, Blasi F, Little P, Verheij T, Molstad S, Godycki-Cwirko M, Edwards P, Almirall J, Torres A, Rautakorpi UM, Nuttall J, Goossens H, Coenen S. Antibiotic prescribing for discoloured sputum in acute cough/lower respiratory tract infection. EUR RESPIR J. 38:119-125. I.F.: 5.92.

13 Bordon J, Kapoor R, Martinez C, Portela D, Duvvuri P, Klochko A, Ayesu K, Peyrani P, Cilloniz C, Wiemken T, Parra A, Torres A, Rello J, Ramirez J. CD4+cell

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	212.64	34	28	3
2010	197.85	39	21	12
2011	160.67	33	22	6

counts and HIV-RNA levels do not predict outcomes of community-acquired pneumonia in hospitalized HIV-infected patients. INT J INFECT DIS. 15:E822-E827. I.F.: 2.53.

14 Miravitlles M, Izquierdo I, Herrejon A, Torres JV, Baro E, Borja J, Esfera INVESTIGATORS. COPD severity score as a predictor of failure in exacerbations of COPD. The ESFERA study. RESP MED. 105:740-747. I.F.: 2.53.

15 Alia I, DeLaCal MA, Esteban A, Abella A, Ferrer R, Molina FJ, Torres A, Gordo F, Elizalde JJ, DePablo R, Huete A, Anzueto A. Efficacy of Corticosteroid Therapy in Patients With an Acute Exacerbation of Chronic Obstructive Pulmonary Disease Receiving Ventilatory Support. ARCH INTERN MED. 171:1939-1946. I.F.: 10.64.

16 Martinez R, Menendez R, Reyes S, Polverino E, Cilloniz C, Martinez A, Esquinas C, Filella X, Ramirez P, Torres A. Factors associated with inflammatory cytokine patterns in community-acquired pneumonia. EUR RESPIR J. 37:393-399. I.F.: 5.92.

17 Ramirez P, Ferrer M, Marti V, Reyes S, Martinez R, Menendez R, Ewig S, Torres A. Inflammatory biomarkers and prediction for intensive care unit admission in severe community-acquired pneumonia. CRIT CARE MED. 39:2211-2217. I.F.: 6.25.

18 Riquelme R, Torres A, Rioseco ML, Ewig S, Cilloniz C, Riquelme M, Inzunza C, Polverino E, Gomez Y, Marcose MA, Contreras C, Gabarrus A, Fasce R. Influenza pneumonia: a comparison between seasonal influenza virus and the H1N1 pandemic. EUR RESPIR J. 38:106-111. I.F.: 5.92.

19 Casas F, Vinolas N, Ferrer F, Agusti C, Sanchez M, Gimferrer JM, Lomena F, Campayo M, Jeremic B. Long-Term Results of a Phase II Trial of Induction Paclitaxel-Carboplatin Followed by Concurrent Radiation Therapy and Weekly Paclitaxel and Consolidation Paclitaxel-Carboplatin in Stage III Non-small Cell Lung Cancer. J THORAC ONCOL. 6:79-85. I.F.: 4.04.

20 Fietze I, Penzel T, Alonderis A, Barbe F, Bonsignore MR, Calverly P, DeBacker W, Diefenbach K, Donic V, Eijsvogel MM, Franklin KA, Gislason T, Grote L, Hedner J, Jennum P, Lavie L, Lavie P, Levy P, Lombardi C, Mallin W, Marrone O, Montserrat JM, Papathanasiou ES, Parati G, Plywaczewski R, Pretl M, Riha RL, Rodenstein D, Saaresranta T, Schulz R, Sliwinski P, Steiropoulos P, Svaza J, Tomori Z, Tonnesen P, Varoneckas G, Verbraecken J, Vesely J, Vitols A, Zielinski J, Mcnicholas WT. Management of obstructive sleep apnea in Europe. SLEEP MED. 12:190-197. I.F.: 3.43.

21 Gasa M, Salord N, Fortuna AM, Mayos M, Vilarrasa N, Dorca J, Montserrat JM, Bonsignore MR, Monasterio C. Obstructive sleep apnoea and metabolic impairment in severe obesity. EUR RESPIR J. 38:1089-1097. I.F.: 5.92.

22 Garcia-Rio F, Soriano JB, Miravitlles M, Munoz L, Duran-Tauleria E, Sanchez G, Sobradillo V, Ancochea J. Overdiagnosing Subjects With COPD Using the 0.7 Fixed Ratio: Correlation With a Poor Health-Related Quality of Life. CHEST. 139:1072-1080. I.F.: 6.52.

23 Sanchez-De-La-Torre M, Barcelo A, Pierola J, Esquinas C, DeLaPena M, Duran-Cantolla J, Capote F, Masa JF, Marin JM, Vila M, Cao G, Martinez M, DeLecea L, Gozal D, Montserrat JM, Barbe F. Plasma levels of neuropeptides and metabolic hormones, and sleepiness in obstructive sleep apnea. RESP MED. 105:1954-1960. I.F.: 2.53.

24 Riquelme R, Jimenez P, Videla AJ, Lopez H, Chalmers J, Singanayagam A, Riquelme M, Peyrani P, Wiemken T, Arbo G, Benchetrit G, Rioseco ML, Ayesu K, Klotchko A, Marzoratti L, Raya M, Figueroa S, Saavedra F, Pryluka D, Inzunza C, Torres A, Alvare P, Fernandez P, Barros M, Gomez Y, Contreras C, Rello J, Bordon J, Feldman C, Arnold F, Nakamatsu R, Riquelme J, Blasi F, Aliberti S, Cosentini R, Lopardo G, Gnoni M, Welte T, Saad M, Guardiola J, Ramirez J. Predicting mortality in hospitalized patients with 2009 H1N1 influenza pneumonia. INT J TUBERC LUNG D. 15:542-546. I.F.: 2.56.

25 Sellares J, Ferrer M, Cano E, Loureiro H, Valencia M, Torres A. Predictors of prolonged weaning and survival during ventilator weaning in a respiratory ICU. INTENS CARE MED. 37:775-784. I.F.: 5.00.

26 Miravitlles M, Naberan K, Cantoni J, Azpeitia A. Socioeconomic Status and Health-Related Quality of Life of Patients with Chronic Obstructive Pulmonary Disease. RESPIRATION. 82:402-408. I.F.: 2.54.

27 Kessler R, Partridge MR, Miravitlles M, Cazzola M, Vogelmeier C, Leynaud D, Ostinelli J. Symptom variability in patients with severe COPD: a pan-European cross-sectional study. EUR RESPIR J. 37:264-272. I.F.: 5.92.

28 Rubinstein E, Lalani T, Corey GR, Kanafani ZA, Nannini EC, Rocha MG, Rahav G, Niederman MS, Kollef MH, Shorr AF, Lee PC, Lentnek AL, Luna CM, Fagon JY, Torres A, Kitt MM, Genter FC, Barriere SL, Friedland HD, Stryjewski ME. Telavancin versus Vancomycin for HospitalAcquired Pneumonia due to Gram-positive Pathogens. CLIN INFECT DIS. 52:31-40. I.F.: 8.19.

29 Miravitlles M, Sotgiu G, Dimopoulos G, Rohde G, Centis R, Ferrara G, Ewig S, Blasi F, Migliori GB. The best on infections: update from the 2010 ERS Congress. EUR RESPIR J. 38:450-455. I.F.: 5.92.

30 Hedner J, Grote L, Bonsignore M, Mcnicholas W, Lavie P, Parati G, Sliwinski P, Barbe F, DeBacker W, Escourrou P, Fietze I, Kvamme JA, Lombardi C, Marrone O, Masa JF, Montserrat JM, Penzel T, Pretl M, Riha R, Rodenstein D, Saaresranta T, Schulz R, Tkacova R, Varoneckas G, Vitols A, Vrints H, Zielinski J. The European Sleep Apnoea Database (ESADA): report from 22 European sleep laboratories. EUR RESPIR J. 38:635-642. I.F.: 5.92.

31 Masa JF, Corral J, Pereira R, Duran-Cantolla J, Cabello M, Hernandez-Blasco L, Monasterio C, Alonso A, Chiner E, Zamorano J, Aizpuru F, Montserrat JM. Therapeutic Decision-making for Sleep Apnea and Hypopnea Syndrome Using Home Respiratory Polygraphy A Large Multicentric Study. AM J RESP CRIT CARE. 184:964-971. I.F.: 10.19.

32 Masa JF, Jimenez A, Duran J, Carmona C, Monasterio C, Mayos M, Teran J, Barbe F, Rubio M, Failde I, Mota M, Montserrat JM. Visual analogical well-being scale for sleep apnea patients: validity and responsiveness A test for clinical practice. SLEEP BREATH. 15:549-559. I.F.: 1.68.

33 Ferrer M, Menendez R, Amaro R, Torres A. The Impact of Guidelines on the Outcomes of Community-acquired and Ventilator-associated Pneumonia. CLIN CHEST MED. 32:491-505. I.F.: 3.11.

REVIEWS
I.F.: 26.78

1 Nogue S, Corominas N, Soy D, Cino J. Intravenous lipid emulsion: a new antidote for use in resuscitation. EMERGENCIAS. 23:378-385. I.F.: 3.09.

2 Polverino E, Torres A. Community-acquired pneumonia. MINERVA ANESTESIOL. 77:196-211. I.F.: 2.58.

3 Ewig S, Torres A. Community-acquired pneumonia as an emergency: time for an aggressive intervention to lower mortality. EUR RESPIR J. 38:253-260. I.F.: 5.92.

4 Miravitlles M. Cough and sputum production as risk factors for poor outcomes in patients with COPD. RESP MED. 105:1118-1128. I.F.: 2.53.

5 Decramer M, Miravitlles M, Price D, Roman-Rodriguez M, Llor C, Welte T, Buhl R, Dusser D, Samara K, Siafakas N. New horizons in early stage COPD - Improving knowledge, detection and treatment. RESP MED. 105:1576-1587. I.F.: 2.53.

6 Ferrer M, Sellares J, Torres A. The use of non-invasive ventilation by Italian physicians in the clinical practice. MINERVA ANESTESIOL. 77:941-942. I.F.: 2.58.

7 Ewig S, Woodhead M, Torres A. Towards a sensible comprehension of severe community-acquired pneumonia. INTENS CARE MED. 37:214-223. I.F.: 5.00.

8 Bassi GL, Torres A. Ventilator-associated pneumonia: role of positioning. CURR OPIN CRIT CARE. 17:57-63. I.F.: 2.55.

EDITORIALS
I.F.: 13.97

1 Ewig S, Torres A. Healthcare-associated pneumonia: meeting the yeti. EUR RESPIR J. 38:755-757. I.F.: 5.92.

2 Ferrer M. Respiratory High-Dependency Care Units in Italy. RESP CARE. 56:1215-1216. I.F.: 1.53.

3 Torres A, Ewig S. The Strange Case of Community-Acquired Pneumonia in COPD. CHEST. 139:483-485. I.F.: 6.52.

MULTICENTRICS
I.F.: 3.00

1 Llaurado M, Labeau S, Vandijck D, Rello J, Rosa A, Riera A, Gallart E, Moreno R, Vandewoude K, Piner R, Benitez ML, Blot S. Southern European Intensive Care Nurses' Knowledge of Evidence-Based Guidelines for Preventing Ventilator-Associated Pneumonia. MED INTENSIVA. 35:6-12. I.F.: 1.50.

2 Rodriguez A, Martin-Loeches I, Bonastre J, Olaechea P, Alvarez-Lerma F, Zaragoza R, Guerrero J, Blanco J, Gordo F, Pozo F, Lorente J, Carratala J, Cordero M, Rello J, Esteban A, Leon C. First influenza season after the 2009 pandemic influenza: report of the first 300 ICU admissions in Spain. MED INTENSIVA. 35:208-216. I.F.: 1.50.

GRANTS FOR RESEARCH IN PROGRESS

Ferrer M. Eficacia de los glucocorticoides en la neumonía asociada a la ventilación mecánica estudio clínico aleatorizado. Sponsored by: Ministerio Sanidad y Consumo, EC07/90390. Duration: 29/10/2007-31/12/2012.

Torres A. Genomics to combat resistance against antibiotics in Community-acquired LRTI in Europe. Sponsored by: European Comission, LSHM-CT-2005-518226. Duration: 01/03/2007-28/02/2011.

Torres A. An integrated platform enabling Theranostic applications at the Point of Primary Care. Sponsored by: European Comission, FP7-ICT07-01-216027. Duration: 01/03/2008-29/02/2012.

Torres A. Health Care Associated Pneumonia (HCAP). Sponsored by: Fondo de Investigación Sanitaria, PI080240. Duration: 01/01/2009-31/12/2012.

Torres A. Fisiopatologia i tractament de les malalties respiratòries. Sponsored by: Generalitat de Catalunya, AGAUR, SGR/911. Duration: 01/01/2009-31/12/2013.

Ferrer M. Papel de la respuesta inflamatoria y el estrés oxidativo sistémico en la retirada de la ventilación mecánica invasiva. Sponsored by: Fondo de Investigación Sanitaria, PI080232. Duration: 01/01/2009-30/09/2012.

Torres A. Efectos de los flujos insipartorio-respiratorio y la presión positiva al final de la espiración en el aclaramiento de secreciones y la neumonía asociada al ventilador. Sponsored by: INSTITUTO DE SALUD CARLOS III, PI09/1249. Duration: 01/01/2010-31/12/2012.

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, EC08/00061. Duration: 01/01/2009-31/12/2012.

Montserrat JM. Efectos sistémicos del síndrome de las apneas durante el sueño. Análisis mediante modelos animales y estudios cognitivos en humanos. Sponsored by: Instituto de Salud Carlos III, PI08/0277. Duration: 31/12/2008-30/12/2011.

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, PI10/01504. Duration: 01/01/2011-31/12/2013.

Garcia C. Complicaciones pulmonares en pacientes receptores de trasplante de progenitores hematopoyéticos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI10/00507. Duration: 01/01/2011-31/12/2013.

DOCTORAL THESES

Torres A, Ferrer M. Prevención de complicaciones asociadas a la ventilación mecánica. PhD student: Mauricio Valencia Arango.

Torres A. Neumonía adquirida en la comunidad: Estudio prospectivo de etiología y evolución clínica en un período de 12 años de estudio. PhD student: Catia Cillóniz Campos.

Torres A. Caracterización de la neumonía adquirida fuera del hospital. PhD student: Gerardo Dambrava Rodríguez Povilas.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Physiopathological mechanisms of respiratory illnesses

TEAM INVOLVED IN: ciberes

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Jéssica Garcia (Fundació Clínic)
David Domínguez (Fundació Clínic)
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ADMINISTRATIVE STAFF:
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Julio Más (Fundació Clínic - CIBERES)

PHYSIOTHERAPISTS:
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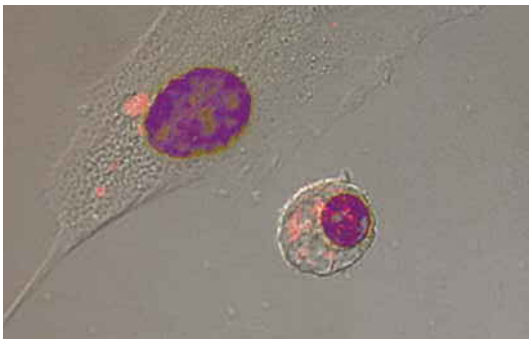
Isabel Blanco (Hospital Clínic)
Felip Burgos (Hospital Clínic)
Federico Gómez (UB)
Carme Hernández (Hospital Clínic)
Victor I. Peinado (CIBERES)
Jordi Vilaró (Fundació Clínic)
Elena Gimeno (IDIBAPS)
Marta Cascante (UB)
Eva Rivas (Hospital Clínic)

STRATEGIC OBJECTIVES

1. Investigation of the molecular and cellular bases of chronic respiratory diseases, with special emphasis on pulmonary circulatory disorders and systemic manifestations.
2. Study of the physiopathological and pathogenic mechanisms related to acute and chronic respiratory failure, focusing on chronic obstructive diseases, hepatopulmonary disorders and obesity.
3. Evaluation of the potential of cell therapy and tissue engineering applied to respiratory diseases.
4. Development of artificial and bioartificial lung models for the support of patients with acute and chronic respiratory failure.
5. Study of the determining factors of the clinical course and healthcare resource utilization in chronic respiratory diseases.

MAIN LINES OF RESEARCH

1. Biopathology and physiopathology of pulmonary circulation disorders
2. Physical activity, cell bioenergetics and systemic effects of chronic obstructive pulmonary disease (COPD)
3. Physiopathological mechanisms underlying gas exchange alterations in airway obstructive diseases
4. Interaction between systemic and pulmonary inflammation in COPD and morbid obesity
5. Tissue engineering and bioartificial lung models
6. Prognostic and determining factors of healthcare resource utilization in chronic respiratory disease
7. Analysis of inflammation and oxidative stress biomarkers in exhaled air in the study of respiratory diseases



View of two precursor vascular cells with inter-differential technology. One of the cells maintains the precursor phenotype, while the other has acquired a smooth muscle cell phenotype.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	99.63	18	12	
2010	121.18	16	11	1
2011	91.96	21	10	3

ORIGINALS
I.F.: 91.96

1 Villar J, Perez-Mendez L, Basaldua S, Blanco J, Aguilar G, Toral D, Zavala E, Romera MA, Gonzalez-Diaz G, DelNogal F, Santos-Bouza A, Ramos L, Macias S, Kacmarek RM. A Risk Tertiles Model for Predicting Mortality in Patients With Acute Respiratory Distress Syndrome: Age, Plateau Pressure, and P-aO2/F-IO2 at ARDS Onset Can Predict Mortality. RESP CARE. 56:420-428. I.F.: 1.53.

2 Turan N, Kalko S, Stincone A, Clarke K, Sabah A, Howlett K, Curnow SJ, Rodriguez DA, Cascante M, O'neill L, Egginton S, Roca J, Falciani F. A Systems Biology Approach Identifies Molecular Networks Defining Skeletal Muscle Abnormalities in Chronic Obstructive Pulmonary Disease. PLOS COMPUT BIOL. 7:-. I.F.: 5.52.

3 Moran I, Blanch L, Fernandez R, Fernandez-Mondejar E, Zavala E, Mancebo J. Acute physiologic effects of a stepwise recruitment maneuver in acute respiratory distress syndrome. MINERVA ANESTESIOL. 77:1167-1175. I.F.: 2.58.

4 Nunez B, Sauleda J, Anto JM, Julia MR, Orozco M, Monso E, Noguera A, Gomez FP, Garcia-Aymerich J, Agusti A. Anti-Tissue Antibodies Are Related to Lung Function in Chronic Obstructive Pulmonary Disease. AM J RESP CRIT CARE. 183:1025-1031. I.F.: 10.19.

5 Pepke-Zaba J, Delcroix M, Lang I, Mayer E, Jansa P, Ambroz D, Treacy C, D'armini AM, Morsolini M, Snijder R, Bresser P, Torbicki A, Kristensen B, Lewczuk J, Simkova I, Barbera JA, DePerrot M, Hoeper MM, Gaine S, Speich R, Gomez-Sanchez MA, Kovacs G, Hamid AM, Jais X, Simonneau G. Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Results From an International Prospective Registry. CIRCULATION. 124:1973-1981. I.F.: 14.43.

6 DeMas IM, Selivanov VA, Marin S, Roca J, Oresic M, Agius L, Cascante M. Compartmentation of glycogen metabolism revealed from C-13 isotopologue distributions. BMC SYST BIOL. 5:-. I.F.: 3.57.

7 Martinez-Palli G, Hirose R, Liu T, Xu FY, Dang K, Feiner J, Serkova NJ, Niemann CU. Donor pre-treatment with everolimus or cyclosporine does not reduce ischaemia-reperfusion injury in a rat kidney transplant model. NEPHROL DIAL TRANSPL. 26:1813-1820. I.F.: 3.56.

8 Otero R, Oribe M, Ballaz A, Jimenez D, Uresandi F, Nauffal D, Conget F, Rodriguez C, Elias T, Jara L, Cayuela A, Blanco I, Barbera J. Echocardiographic assessment of pulmonary arterial pressure in the follow-up of patients with pulmonary embolism. THROMB RES. 127:303-308. I.F.: 2.37.

9 Olea E, Ferrer E, Prieto-Lloret J, Gonzalez-Martin C, Vega-Agapito V, Gonzalez-Obeso E, Agapito T, Peinado V, Obeso A, Barbera JA, Gonzalez C. Effects of cigarette smoke and chronic hypoxia on airways remodeling and resistance. Clinical significance. RESP PHYSIOL NEUROBI. 179:305-313. I.F.: 2.38.

10 Ferrer E, Peinado VI, Castaneda J, Prieto-Lloret J, Olea E, Gonzalez-Martin MC, Vega-Agapito MV, Diez M, Dominguez-Fandos D, Obeso A, Gonzalez C, Barbera JA. Effects of cigarette smoke and hypoxia on pulmonary circulation in the guinea pig. EUR RESPIR J. 38:617-627. I.F.: 5.92.

11 Blanco I, Ribas J, Xaubet A, Gomez FP, Roca J, Rodriguez-Roisin R, Barbera JA. Effects of inhaled nitric oxide at rest and during exercise in idiopathic pulmonary fibrosis. J APPL PHYSIOL. 110:638-645. I.F.: 4.24.

12 Guarner-Argente C, Cordova H, Martinez-Palli G, Navarro-Ripoll R, Rodriguez-D'jesus A, DeMiguel CR, Beltran M, Fernandez-Esparrach G. Gastrotomy closure with a new tissue anchoring device: A porcine survival study. WORLD J GASTROENTERO. 17:1732-1738. I.F.: 2.24.

13 Garcia-Aymerich J, Gomez FP, Benet M, Farrero E, Basagana X, Gayete A, Pare C, Freixa X, Ferrer J, Ferrer A, Roca J, Galdiz JB, Sauleda J, Monso E, Gea J, Barbera JA, Agusti A, Anto JM. Identification and prospective validation of clinically relevant chronic obstructive pulmonary disease (COPD) subtypes. THORAX. 66:430-437. I.F.: 6.53.

14 Guarner-Argente C, Beltran M, Martinez-Palli G, Navarro-Ripoll R, Martinez-Zamora MA, Cordova H, Comas J, DeMiguel CR, Rodriguez-D'jesus A, Almela M, Hernandez-Cera C, Lacy AM, Fernandez-Esparrach G. Infection during Natural Orifice Transluminal Endoscopic Surgery Peritoneoscopy: A Randomized Comparative Study in a Survival Porcine Model. J MINIM INVAS GYN. 18:741-746. I.F.: 1.56.

15 Bader A, Lorenz K, Richter A, Scheffler K, Kern L, Ebert S, Giri S, Behrens M, Dornseifer U, Macchiarini P, Machens HG. Interactive Role of Trauma Cytokines and Erythropoietin and Their Therapeutic Potential for Acute

and Chronic Wounds. REJUV RES. 14:57-66. I.F.: 4.23.

16 Maier D, Kalus W, Wolff M, Kalko SG, Roca J, DeMas IM, Turan N, Cascante M, Falciani F, Hernandez M, Villa-Freixa J, Losko S. Knowledge management for systems biology a general and visually driven framework applied to translational medicine. BMC SYST BIOL. 5:-. I.F.: 3.57.

17 Cremona G, Barbara JA, Melgosa T, Appendini L, Roca J, Casadio C, Donner CF, Rodriguez-Roisin R, Wagner PD. Mechanisms of gas exchange response to lung volume reduction surgery in severe emphysema. J APPL PHYSIOL. 110:1036-1045. I.F.: 4.24.

18 Gambus PL, Jensen EW, Jospin M, Borrat X, Martinez-Palli G, Fernandez-Candil J, Valencia JF, Barba X, Caminal P, Troconiz IF. Modeling the Effect of Propofol and Remifentanil Combinations for Sedation-Analgesia in Endoscopic Procedures Using an Adaptive Neuro Fuzzy Inference System (ANFIS). ANESTH ANALG. 112:331-339. I.F.: 3.27.

19 Selivanov VA, Votyakova TV, Pivtoraiko VN, Zeak J, Sukhomlin T, Trucco M, Roca J, Cascante M. Reactive Oxygen Species Production by Forward and Reverse Electron Fluxes in the Mitochondrial Respiratory Chain. PLOS COMPUT BIOL. 7:-. I.F.: 5.52.

20 Llinas L, Peinado VI, Goni JR, Rabinovich R, Pizarro S, Rodriguez-Roisin R, Barbera JA, Bastos R. Similar gene expression profiles in smokers and patients with moderate COPD. PULM PHARMACOL THER. 24:32-41. I.F.: 2.09.

21 Chappell SL, Daly L, Lotya J, Alsaegh A, Guetta-Baranes T, Roca J, Rabinovich R, Morgan K, Millar AB, Donnelly SC, Keatings V, Macnee W, Stolk J, Hiemstra PS, Miniati M, Monti S, O'connor CM, Kalsheker N. The role of IREB2 and transforming growth factor beta-1 genetic variants in COPD: a replication case-control study. BMC MED GENET. 12:-. I.F.: 2.44.

REVIEWS
I.F.: 8.06

1 Martinez-Palli G, Cardenas A. Pre operative cardio pulmonary assessment of the liver transplant candidate. ANN HEPATOL. 10:421-433. I.F.: 1.87.

2 Ram FS, Rodriguez-Roisin R, Granados-Navarrete A, Garcia-Aymerich J, Barnes NC. WITHDRAWN: Antibiotics for exacerbations of chronic obstructive pulmonary disease. COCHRANE DB SYST REV. 1:-. I.F.: 6.19.

EDITORIALS
I.F.: 16.11

1 Barbera JA, Peinado VI. Disruption of the lung structure maintenance programme: a comprehensive view of emphysema development. EUR RESPIR J. 37:752-754. I.F.: 5.92.

2 Zock JP, Rodriguez-Trigo G, Pozo-Rodriguez F, Barbera JA. Health Effects of Oil Spills: Lessons from the Prestige. AM J RESP CRIT CARE. 184:1094-1096. I.F.: 10.19.

MULTICENTRICS
I.F.: 79.88

1 Leidy NK, Wilcox TK, Jones PW, Roberts L, Powers JH, Sethi S. Standardizing Measurement of Chronic Obstructive Pulmonary Disease Exacerbations Reliability and Validity of a Patient-reported Diary. AM J RESP CRIT CARE. 183:323-329. I.F.: 10.19.

2 Jones PW, Chen WH, Wilcox TK, Sethi S, Leidy NK. Characterizing and Quantifying the Symptomatic Features of COPD Exacerbations. CHEST. 139:1388-1394. I.F.: 6.52.

3 Barst RJ, Oudiz RJ, Beardsworth A, Brundage BH, Simonneau G, Ghofrani HA, Sundin DP, Galie N. Tadalafil monotherapy and as add-on to background bosentan in patients with pulmonary arterial hypertension. J HEART LUNG TRANSPL. 30:632-643. I.F.: 3.43.

4 Vogelmeier C, Hederer B, Glaab T, Schmidt H, Rutten-VanMolken MPMH, Beeh KM, Rabe KF, Fabbri LM. Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD. NEW ENGL J MED. 364:1093-1103. I.F.: 53.49.

5 Kett DH, Azoulay E, Echeverria PM, Vincent JL. Candida bloodstream infections in intensive care units: Analysis of the extended prevalence of infection in intensive care unit study. CRIT CARE MED. 39:665-670. I.F.: 6.25.

GRANTS FOR RESEARCH IN PROGRESS

Roca J. IP - Healthcare by Biosensor Measurements And Networking. Sponsored by: European Commision, CE_FPVI05. Duration: 01/11/2005-30/04/2011.

Barbera JA. Estudio de los efectos de sildenafilo sobre el intercambio gaseoso, la hemodinámica pulmonar y la tolerancia al esfuerzo en pacientes con hipertensión pulmonar asociada a

la enfermedad pulmonar obstructiva crónica. Sponsored by: Fondo de Investigación Sanitaria (FIS), EC0790049. Duration: 29/10/2007-31/12/2011.

Roca J. Supporting Healthier and Independent Living for Chronic Patients and Elderly - NEXES. Sponsored by: Unión Europea, FP7 (CIP-ICT) 225025. Duration: 01/05/2008-31/05/2011.

Peinado V. Mecanismos moleculares de la diferenciación de células progenitoras endoteliales durante la reparación del endotelio en la hipertensión pulmonar. Sponsored by: Fundació Marató TV3, 08/1310. Duration: 20/02/2009-19/12/2012.

Barbera JA. Estudio de nuevas dianas terapéuticas en el tratamiento de la hipertensión pulmonar asociada a la enfermedad pulmonar obstructiva crónica. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0536. Duration: 01/01/2010-31/12/2012.

Roca J. Servicios innovadores de atención integrada para pacientes crónicos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90634. Duration: 01/01/2010-31/12/2012.

Rodriguez R. Obesidad mórbida e inflamación sistématica y pulmonar. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0311. Duration: 31/12/2008-30/12/2011.

Roca J. Synergy – Modelling and simulation for systems medicine (COPD as a use case). Sponsored by: Unión Europea, FP7-ICT-2009-6. 270086. Duration: 28/02/2011-31/01/2014.

Gomez F. Biomarcadores inflamatorios, de estrés oxidativo y metabonómicos en el aire exhalado en la EPOC y el cáncer de pulmón. Sponsored by: Ministerio Sanidad y Consumo, PI08/0283. Duration: 01/01/2009-31/12/2011.

Bastos R. Estudio de la pérdida de masa muscular en pacientes con Enfermedad Pulmonar Obstructiva Crónica mediante técnicas de genómica y proteómica. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0320. Duration: 01/01/2009-30/06/2012.

Roca J. Desarrollo de un sistema de rehabilitación física domiciliario. Sponsored by: Ministerio de Ciencia e Innovación, IPT-2011-1193-900000. Duration: 04/05/2011-31/12/2013.

Roca J. STREP - Knowledge Sharing and Decision Support for Healthcare Professionals. Sponsored by: Unió Europea, CE_FPVI01. Duration: 01/01/2004-30/11/2011.

Roca J. Despliegue de nuevos servicios sanitarios soportados por tecnologías de la información y comunicación (DENSSA-TIC). Sponsored by: Ministerio de Ciencia e Innovación, IPT-2011-1333-900000. Duration: 05/05/2011-31/12/2014.

DOCTORAL THESES

Barbera JA. Estudio de los efectos de los agentes vasodilatadores sobre el intercambio de gases y la hemodinámica pulmonar, en las enfermedades respiratorias crónicas. PhD student: Isabel Blanco Vich.

Barbera JA, Peinado VI. Alteracions vasculars pulmonars induïdes per l'exposició a fum de tabac en un model animal de MPOC. PhD student: Elisabet Ferrer Andrés, Universitat de Barcelona.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Clinical and Experimental Respiratory Immunoallergy (IRCE)

TEAM INVOLVED IN: ciberes & RIRAAF

GROUP MEMBERS

TEAM LEADER
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Joan Bartra (Hospital Clínic)
Antonio Valero (Hospital Clínic)
Laura Pujols Tarrés (Fundació Clínic)
Isam Alobid (Hospital Clínic)

POSTDOCTORAL FELLOWS:
Josep Maria Guilemany (FIS - SEORL)
Jordi Roca-Ferrer (UB)

RESEARCH FELLOWS:
Rosa Maria Muñoz-Cano (FIS)
Francisco Garcia Garcia (FIS)
Laura Fernández-Bertolin (IDIBAPS)
Francisco de Borja Callejas (FIS)
Marta Gabasa (CIBERES)
Suha Jabr (Ministeri Assuumptes Exteriors i Cooperació)
Jaume Sánchez López (Fundació Clínic)
Maria Rueda (Fundació Clínic)
Liliana Carbalho (Erasmus Portugal)
Franklin Mariño Sánchez (Hospital Clínic)
Erola Ainsua Enrich (FPI)
Esteban Cano (Hospital Clínic)

TECHNICIANS:
Mireia Fuentes Prado (Fundació Clínic)
María Pérez Gonzalez (Fundació Clínic)

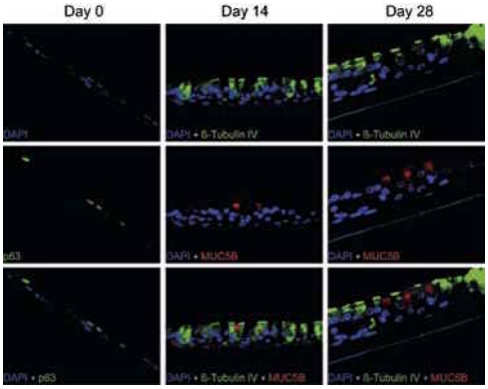
NURSING STAFF:
Sílvia Centellas (Hospital Clínic)
Sarai Sánchez Fuentes (Fundació Clínic)

ADMINISTRATIVE STAFF:
Elena Arrufat (Fundació Clínic)

COLLABORATORS:
Assumpció Martínez-Antón (CCMD NIH)
Yvonne Torres (Ministeri d'Educació, Govern de Panamà)
Rosa Torres (FIS)
María del Carmen Vennera (CIBERes)
Joaquim Ensenyat Nora (Hospital Clínic)
Margarita Martin Andorrà (Fundació Clínic)
Damiana Alvarez Errico (Juan de la Cierva)
Manuel Bernal Sprekelsen (Hospital Clínic)

STRATEGIC OBJECTIVES

1. Investigation of the mechanisms regulating inflammatory response and remodelling in bronchial asthma, rhinosinusitis and pulmonary interstitial diseases.
2. Investigation of the mechanisms underlying food allergies.
3. Investigation of the mechanisms involved in anaphylaxis of complex etiopathogenesis.
4. Investigation of the mechanisms involved in loss of smell.



Immunofluorescent analysis showing the differentiation of human nasal polyp pseudostratified epithelium from epithelial stem cells in Air Liquid Interface (ALI) culture. At day 0, epithelial cells form a monolayer of undifferentiated basal stem cells (p63+, basal stem cell marker), while at days 14 and 28 of culture, epithelial cells form a polarized and well-differentiated pseudo-stratified epithelium including ciliated cells (b-tubulin IV+, ciliated cell marker) and goblet cells (MUC5B+, goblet cell marker). DAPI (4′,6-diamidino-2-phenylindole) was used for nucleus staining. Immunofluerescence was analysed using a epifluorescence microscope (magnification ×63).

MAIN LINES OF RESEARCH

1. Molecular and cellular bases of the inflammatory response in asthma, rhinosinusitis and pulmonary interstitial diseases.
2. Role of the MUC genes in the modulation of mucosal secretion in respiratory diseases, remodeling of respiratory diseases and their regulation with glucocorticoids.
3. Role of arachidonic acid metabolites (prostaglandins and leukotrienes) in the etiopathogenesis of asthma, rhinosinusitis and pulmonary interstitial diseases.
4. Role of the angiotensin system in lung fibrosis.
5. Study of the mechanisms regulating the response to glucocorticoid treatment in inflammatory respiratory diseases.
6. Study of the mechanisms involved in severe asthma and relationship with alterations in glucocorticoid receptor function.
7. Study of the relationship between upper airway disorders (nasal and sinuses) and alterations of the lower airway (asthma, bronchiectasia, chronic obstructive pulmonary disease).
8. Study of the mechanisms regulating the response to food allergens and relationship with nonsteroidal anti-inflammatory drugs and arachidonic acid metabolism.
9. New therapeutic modalities (endothelin, proteosome and COX-2 inhibitors; prostaglandin E2 receptor 3 agonists) in asthma, rhinosinusitis and pulmonary interstitial diseases based on in vitro models and animal models of asthma and pulmonary fibrosis.
10. Study of the mechanisms of anaphylactic reactions of multiple origin (indolent mastocytosis, predisposing genetic alterations).
11. Study of quality of life in nasosinusal pathology.
12. Loss of smell: role of nasosinusal inflammation, Parkinson's disease and congenital alterations.
13. 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)

In this group we investigate different aspects of inflammatory nasosinusal disorders (allergic and non-allergic rhinitis, chronic rhinosinusitis, nasal polyposis):

- We explore the physiopathological mechanisms of nasosinusal mucosal hypersecretion and the regulation of mucins and MUC genes.
- We analyze the physiopathological and clinical association of nasosinusal disorders with asthma, atopy, NSAID intolerance and bronchiectasia, and their impact upon patient quality of life.
- We evaluate olfactory alterations and their mechanisms of action as diagnostic and severity markers. We have validated a proprietary olfactometric test (BAST-24), and have carried out an epidemiological study (OLFACAT) on olfactory function in the Catalan population.
- We use an eosinophil and epithelial cell culture model for testing and comparing the antiinflammatory action of different drugs employed in situations of respiratory inflammation, such as corticosteroids, antihistamines and antileukotrienes.

PUBLICATIONS

ORIGINALS
I.F.: 81.17

1 Alvarez-Errico D, Oliver-Vila I, Ainsua-Enrich E, Gilfillan AM, Picado C, Sayos J, Martin M. CD84 Negatively Regulates IgE High-Affinity Receptor Signaling in Human Mast Cells. J IMMUNOL. 187:5577-5586. I.F.: 5.75.

2 Ramos-Casals M, Perez-Alvarez R, Perez-De-Lis M, Xaubet A, Bosch X. Pulmonary Disorders Induced by Monoclonal Antibodies in Patients with Rheumatologic Autoimmune Diseases. AM J MED. 124:386-394. I.F.: 5.12.

3 Blanco I, Ribas J, Xaubet A, Gomez FP, Roca J, Rodriguez-Roisin R, Barbera JA. Effects of inhaled nitric oxide at rest and during exercise in idiopathic pulmonary fibrosis. J APPL PHYSIOL. 110:638-645. I.F.: 4.24.

4 Wang DY, Wardani RS, Singh K, Thanaviratananich S, Vicente G, Xu G, Zia MR, Gulati A, Fang SY, Shi L, Chan YH, Price D, Lund VJ, Mullol J, Fokkens WJ. A survey on the management of acute rhinosinusitis among Asian physicians. RHINOLOGY. 49:264-271. I.F.: 0.80.

5 Lopez-Matas MA, Ferrer A, Larramendi CH, Huertas AJ, Pagan JA, Garcia-Abujeta JL, Bartra J, Andreu C, Lavin JR, Carnes J. Acidic ribosomal protein 60S: A new tomato allergen. FOOD CHEM. 127:638-640. I.F.: 3.46.

6 Morell F, Cruz MJ, Gomez FP, Rodriguez-Jerez F, Xaubet A, Munoz X. Chacinero's lung - hypersensitivity pneumonitis due to dry sausage dust. SCAND J WORK ENV HEA. 37:349-356. I.F.: 3.54.

7 Navarro A, Valero A, Rosales MJ, Mullol J. Clinical Use of Oral Antihistamines and Intranasal Corticosteroids in Patients With Allergic Rhinitis. J INVEST ALLERG CLIN. 21:363-369. I.F.: 1.49.

8 Sanchez-Lopez J, Asturias JA, Enrique E, Suarez-Cervera M, Bartra J. Cupressus arizonica Pollen: A New Pollen Involved in the Lipid Transfer Protein Syndrome?. J INVEST ALLERG CLIN. 21:522-526. I.F.: 1.49.

9 Valero A, Chivato T, Justicia JL, Navarro AM. Diagnosis and treatment of grass pollen-induced allergic rhinitis in specialized current clinical practice in Spain. ALLERGY ASTHMA PROC. 32:384-389. I.F.: 1.74.

10 Vennera MD, Picado C, Mullol J, Alobid I, Bernal-Sprekelsen M. Efficacy of omalizumab in the treatment of nasal polyps. THORAX. 66:824-825. I.F.: 6.53.

11 Valero A, Justicia JL, Anton E, Dordal T, Fernandez-Parra B, Lluch M, Montoro J, Navarro AM. Epidemiology of allergic rhinitis caused by grass pollen or house-dust mites in Spain. AM J RHINOL ALLERGY. 25:E123-E128. I.F.: 1.88.

12 Lopez-Matas MA, Larramendi CH, Ferrer A, Huertas AJ, Pagan JA, Garcia-Abujeta JL, Bartra J, Andreu C, Lavin JR, Carnes J. Identification and quantification of tomato allergens: in vitro characterization of six different varieties. ANN ALLERG ASTHMA IM. 106:230-238. I.F.: 2.80.

13 Fernandez-Bertolin L, Mullol J, Alobid I, Roca-Ferrer J, Picado C, Pujols L. Impact of cell culture methods on the outcomes of the in vitro inflammatory response in nasal polyps. RHINOLOGY. 49:562-569. I.F.: 0.80.

14 Soria G, Aguilar E, Tudela R, Mullol J, Planas AM, Marin C. In vivo magnetic resonance imaging characterization of bilateral structural changes in experimental Parkinson's disease: a T2 relaxometry study combined with longitudinal diffusion tensor imaging and manganese-enhanced magnetic resonance imaging in the 6-. EUR J NEUROSCI. 33:1551-1560. I.F.: 3.66.

15 Alobid I, DePablo J, Mullol J, Centellas S, Parramon G, Carrasco J, Armario A, Bernal-Sprekelsen M. Increased Cardiovascular and Anxiety Outcomes but Not Endocrine Biomarkers of Stress During Performance of Endoscopic Sinus Surgery A Pilot Study Among Novice Surgeons. ARCH OTOLARYNGOL. 137:487-492. I.F.: 1.57.

16 Videler WJ, Badia L, Harvey RJ, Gane S, Georgalas C, VanDerMeulen FW, Menger DJ, Lehtonen MT, Toppila-Salmi SK, Vento SI, Hytonen M, Hellings PW, Kalogjera L, Lund VJ, Scadding G, Mullol J, Fokkens WJ. Lack of efficacy of long-term, low-dose azithromycin in chronic rhinosinusitis: a randomized controlled trial. ALLERGY. 66:1457-1468. I.F.: 6.30.

17 Pujols L, Fuentes-Prado M, Fernandez-Bertolin L, Alobid I, Roca-Ferrer J, Mullol J, Picado C. Lower sensitivity of nasal polyp fibroblasts to glucocorticoid anti-proliferative effects. RESP MED. 105:218-225. I.F.: 2.53.

18 Valero A, Mullol J, Herdman M, Rosales MJ. Measuring outcomes in allergic rhinitis: psychometric characteristics of a Spanish version of the congestion quantifier seven-item test (CQ7). HEALTH QUAL LIFE OUT. 9:-. I.F.: 1.86.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	72.62	25	11	4
2010	58.14	21	5	7
2011	81.17	28	9	11

19 Mullol J, Callejas FD, Martinez-Anton MA, Mendez-Arancibia E, Alobid I, Pujols L, Valero A, Picado C, Roca-Ferrer J. Mometasone and desloratadine additive effect on eosinophil survival and cytokine secretion from epithelial cells. RESP RES. 12:-. I.F.: 2.86.

20 Alobid I, Cardelus S, Benitez P, Guilemany JM, Roca-Ferrer J, Picado C, Bernal-Sprekelsen M, Mullol J. Persistent asthma has an accumulative impact on the loss of smell in patients with nasal polyposis. RHINOLOGY. 49:519-524. I.F.: 0.80.

21 Castillo JA, Navarro A, Quirce S, Molina J, Garcia-Marcos L, Julia B, Valero A, Mullol J. Prevalence and characteristics of rhinitis in adult asthmatic patients attending allergist, primary care and pulmonologist settings in Spain (AIR study). MED CLIN-BARCELONA. 136:284-289. I.F.: 1.41.

22 Quirce S, Plaza V, Picado C, Vennera M, Casafont J. Prevalence of Uncontrolled Severe Persistent Asthma in Pneumology and Allergy Hospital Units in Spain. J INVEST ALLERG CLIN. 21:466-471. I.F.: 1.49.

23 Roca-Ferrer J, Garcia-Garcia FJ, Pereda J, Perez-Gonzalez M, Pujols L, Alobid I, Mullol J, Picado C. Reduced expression of COXs and production of prostaglandin E-2 in patients with nasal polyps with or without aspirin-intolerant asthma. J ALLERGY CLIN IMMUN. 128:66-U110. I.F.: 9.27.

24 Valero A, Izquierdo I, Giralt J, Bartra J, DelCuvillo A, Mullol J. Rupatadine Improves Nasal Symptoms, Quality of Life (ESPRINT-15) and Severity in a Subanalysis of a Cohort of Spanish Allergic Rhinitis Patients. J INVEST ALLERG CLIN. 21:229-235. I.F.: 1.49.

25 Valero A, Sanchez-Lopez J, Bartra J, Serrano C, Munoz-Cano R, Roca J, Picado C. Safety of Parecoxib in Asthmatic Patients with Aspirin-Exacerbated Respiratory Disease. INT ARCH ALLERGY IMM. 156:221-223. I.F.: 2.24.

26 Guilemany JM, Marino-Sanchez FS, Angrill J, Alobid I, Centellas S, Pujols L, Berenguer J, Bernal-Sprekelsen M, Picado C, Mullol J. The importance of smell in patients with bronchiectasis. RESP MED. 105:44-49. I.F.: 2.53.

27 DeNotaris M, Solari D, Cavallo LM, Ensenat J, Alobid I, Soria G, Gonzalez JB, Ferrer E, Prats-Galino A. The Use of a Three-Dimensional Novel Computer-Based Model for Analysis of the Endonasal Endoscopic Approach to the Midline Skull Base. WORLD NEUROSURG. 75:106-113. I.F.: 0.68.

28 Jauregui I, Davila I, Sastre J, Bartra J, DelCuvillo A, Ferrer M, Montoro J, Mullol J, Molina X, Valero A. Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: The PEDRIAL study. PEDIAT ALLERG IMM-UK. 22:388-392. I.F.: 2.87.

REVIEWS
I.F.: 10.03

1 Dordal MT, Lluch-Bernal M, Sanchez MC, Rondon C, Navarro A, Montoro J, Matheu V, Ibanez MD, Fernandez-Parra B, Davila I, Conde J, Anton E, Colas C, Valero A. Allergen-Specific Nasal Provocation Testing: Review by the Rhinoconjunctivitis Committee of the Spanish Society of Allergy and Clinical Immunology. J INVEST ALLERG CLIN. 21:1-12. I.F.: 1.49.

2 Sahin G, Klimek L, Mullol J, Hormann K, Walther LE, Pfaar O. Nitric Oxide: A Promising Methodological Approach in Airway Diseases. INT ARCH ALLERGY IMM. 156:352-361. I.F.: 2.24.

3 Papadopoulos NG, Christodoulou I, Rohde G, Agache I, Almqvist C, Bruno A, Bonini S, Bont L, Bossios A, Bousquet J, Braido F, Brusselle G, Canonica GW, Carlsen KH, Chanez P, Fokkens WJ, Garcia-Garcia M, Gjomarkaj M, Haahtela T, Holgate ST, Johnston SL, Konstantinou G, Kowalski M, Lewandowska-Polak A, Lodrup-Carlsen K, Makela M, Malkusova I, Mullol J, Nieto A, Eller E, Ozdemir C, Panzner P, Popov T, Psarras S, Roumpedaki E, Rukhadze M, Stipic-Markovic A, Bom AT, Toskala E, VanCauwenberge P, VanDrunen C, Watelet JB, Xatzipsalti M, Xepapadaki P, Zuberbier T. Viruses and bacteria in acute asthma exacerbations - A GA2LEN-DARE* systematic review. ALLERGY. 66:458-468. I.F.: 6.30.

EDITORIALS
I.F.: 20.40

1 Sanz-Gallen P, Nogue S, Herrera-Mozo I, Delclos GL, Valero A. Occupational contact allergy to omeprazole and fluoxetine. CONTACT DERMATITIS. 65:118-119. I.F.: 3.67.

2 Mullol J, Alobid I. Combined Oral and Intranasal Corticosteroid Therapy: An Advance in the Management of Nasal Polyposis?. ANN INTERN MED. 154:365-U135. I.F.: 16.73.

CLINICAL GUIDELINES
I.F.: 2.90

1 Alobid I, Anton E, Armengot M, Chao J, Colas C, DelCuvillo A, Davila I, Dordal MT, Escobar C, Fernandez-Parra B, Gras-Cabrerizo JR, Ibanez MD, Lluch M, Mateu V, Montoro J, Gili JR, Mullol J, Navarro AM, Pumarola F, Rondon C, Sanchez-Hernandez MC, Sarandeses A, Soler R, Valero AL, Rhinoconjunctivitis Committee, Spanish Society Of Allergy And Clinical Immunology, Rhinology And Allergy Commission, Spanish Society of Otorhinolaryngology. SEAIC-SEORL. Consensus Document on Nasal Polyposis. POLINA Project. J INVEST ALLERG CLIN. 21:1-58. I.F.: 1.49.

2 Alobid I, Alonso JR, Barrot C, Benitez P, Canizares S, Castanyer T, Centellas S, Civeira E, Climent B, Duenas A, Fernandez-Sola J, Ferrer A, Gene M, Godas T, Gomez E, Montori E, Munne P, Nogue S, Picado C, Rovira E, Sanz P, Valero A. Multiple chemical sensitivity. MED CLIN-BARCELONA. 136:683-687. I.F.: 1.41.

MULTICENTRICS
I.F.: 33.63

1 Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg MK, Kardatzke D, King TE, Lancaster L, Sahn SA, Szwarcberg J, Valeyre D, DuBois RM. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. LANCET. 377:1760-1769. I.F.: 33.63.

GRANTS FOR RESEARCH IN PROGRESS

Pujols L. Papel de la prostaglandina E2 en la determinación de la sensibilidad de los glucocorticoides en enfermedades respiratorias de origen inflamatorio. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0419. Duration: 01/01/2009-30/12/2011.

Mullol J. Estudio del papel de la inflamación neurógenano alérgica en la expresión de mucinas y el proceso de remodelado de la mucosa respiratoria nasosinusal. Sponsored by: Ministerio Sanidad y Consumo, PI-0801PI08/0188. Duration: 01/01/2009-30/12/2012.

Picado C. Estudio de la regulación epigenética del gen de la COX-2 en el asama con intolerancia a los antiinflamatorios no esteroideos. Sponsored by: Ministerio Sanidad y Consumo, PI080249. Duration: 01/01/2009-30/12/2011.

Xaubet A. Implicación del sistema de la angiotensina en la etiopatogenia de la fibrosis pulmonar idiopática. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/00672. Duration: 01/01/2010-30/12/2012.

Valero AL. Efecto clínico e inflamatorio nasal tras la aplicación frl factor de agregación plaquetaria (PAF). Sponsored by: Instituto de Salud Carlos III (ISCIII), PI0901202. Duration: 01/01/2010-30/12/2012.

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: 31/12/2011-31/12/2014.

Martin M. Modulación de la activación mastocitaria por miembros de la superfamilia de receptores CD150, CD300 y moléculas adaptadoras relacionadas. Sponsored by: Ministerio de Ciencia e Innovación, SAF2009-07548. Duration: 01/01/2010-31/12/2012.

Bartra J. Red de Investigación de Reacciones Adversas a Alérgenos y Fármacos (RIRAAF). Sponsored by: Instituto de Salud Carlos III (ISCIII), FIS_RETIC07 RD07/0064/0006. Duration: 29/02/2008-31/12/2012.

Picado C. Inflamació i tractament de les malalties respiratòries. Sponsored by: AGAUR_SGR09 ,2009_SGR_954. Duration: 15/09/2009-31/12/2013.

DOCTORAL THESES

Picado C, Martin M. Paper regulador de la Prostaglandina E2 en l'activació osmòtica en mastòcits. PhD student: Ivonne Torres Atencio, Autònoma de Barcelona (UAB).

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Inflammation and repair in respiratory illnesses

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TEAM INVOLVED IN:

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.

MAIN LINES OF RESEARCH

1. Mechanisms of autoimmunity and autoinflammation that may contribute to the pathogenesis of acute outbreaks of the disease (in collaboration with the group headed by Dr. J. Yagüe, of the Department of Immunology of the Clinic Hospital).
2. Mechanisms of abnormal catabasis (resolution of the inflammation) that perpetuate the inflammatory response even after smoking cessation (a necessary yet insufficient treatment measure) (in collaboration with Dr. J. Clària, of the Clinic Hospital Biomedical Diagnostic Center) and Dra. Aina Noguera from Hospital Universitari Son Espases, Mallorca.
3. 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).
4. 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.: 115.32

1 Nunez B, Sauleda J, Anto JM, Julia MR, Orozco M, Monso E, Noguera A, Gomez FP, Garcia-Aymerich J, Agusti A. Anti-Tissue Antibodies Are Related to Lung Function in Chronic Obstructive Pulmonary Disease. AM J RESP CRIT CARE. 183:1025-1031. I.F.: 10.19.

2 Garcia-Aymerich J, Gomez FP, Benet M, Farrero E, Basagana X, Gayete A, Pare C, Freixa X, Ferrer J, Ferrer A, Roca J, Galdiz JB, Sauleda J, Monso E, Gea J, Barbera JA, Agusti A, Anto JM. Identification and prospective validation of clinically relevant chronic obstructive pulmonary disease (COPD) subtypes. THORAX. 66:430-437. I.F.: 6.53.

3 Campayo M, Navarro A, Vinolas N, Tejero R, Munoz C, Diaz T, Marrades R, Cabanas ML, Gimferrer JM, Gascon P, Ramirez J, Monzo M. A Dual Role for KRT81: A miR-SNP Associated with Recurrence in Non-Small-Cell Lung Cancer and a Novel Marker of Squamous Cell Lung Carcinoma. PLOS ONE. 6:-. I.F.: 4.41.

4 Agusti A, Sobradillo P, Celli B. Addressing the Complexity of Chronic Obstructive Pulmonary Disease From Phenotypes and Biomarkers to Scale-Free Networks, Systems Biology, and P4 Medicine. AM J RESP CRIT CARE. 183:1129-1137. I.F.: 10.19.

5 Sanchez-Lorente D, Gomez-Caro A, Jimenez MJ, Molins L. Apnoeic oxygenation on one-lung ventilation in functionally impaired patients during sleeve lobectomy. EUR J CARDIO-THORAC. 39:E77-E79. I.F.: 2.29.

6 Vestbo J, Edwards LD, Scanlon PD, Yates JC, Agusti A, Bakke P, Calverley PMA, Celli B, Coxson HO, Crim C, Lomas DA, Macnee W, Miller BE, Silverman EK, Tal-Singer R, Wouters E, Rennard SI. Changes in Forced Expiratory Volume in 1 Second over Time in COPD. NEW ENGL J MED. 365:1184-1192. I.F.: 53.49.

7 Agusti A, Vestbo J. Current Controversies and Future Perspectives in Chronic Obstructive Pulmonary Disease. AM J RESP CRIT CARE. 184:507-513. I.F.: 10.19.

8 Gomez-Caro A, Garcia S, Reguart N, Cladellas E, Arguis P, Sanchez M, Gimferrer JM. Determining the appropriate sleeve lobectomy versus pneumonectomy ratio in central non-small cell lung cancer patients: an audit of an aggressive policy of pneumonectomy avoidance. EUR J CARDIO-THORAC. 39:352-359. I.F.: 2.29.

9 Puente-Maestu L, Lazaro A, Tejedor A, Camano S, Fuentes M, Cuervo M, Navarro BO, Agusti A. Effects of exercise on mitochondrial DNA content in skeletal muscle of patients with COPD. THORAX. 66:121-127. I.F.: 6.53.

10 Jones PW, Rennard SI, Agusti A, Chanez P, Magnussen H, Fabbri L, Donohue JF, Bateman ED, Gross NJ, Lamarca R, Caracta C, Gil EG. Efficacy and safety of once-daily aclidinium in chronic obstructive pulmonary disease. RESP RES. 12:-. I.F.: 2.86.

11 Sanchez-De-La-Torre M, Pierola J, Vidal C, Barcelo A, DeLaPena M, Hussain Z, Capote F, Duran J, Agusti AGN, DeLecea L, Torres G, Esquinas C, Martinez M, Barbe F. Non-synonymous polymorphism in the neuropeptide S precursor gene and sleep apnea. SLEEP BREATH. 15:403-408. I.F.: 1.68.

12 Navarro A, Diaz T, Gallardo E, Vinolas N, Marrades RM, Gel B, Campayo M, Quera A, Bandres E, Garcia-Foncillas J, Ramirez J, Monzo M. Prognostic Implications of miR-16 Expression Levels in Resected Non-Small-Cell Lung Cancer. J SURG ONCOL. 103:411-415. I.F.: 2.43.

13 Campayo M, Vinolas N, Navarro A, Carcereny E, Casas F, Gel B, Diaz T, Gimferrer JM, Marrades RM, Ramirez J, Monzo M. Single Nucleotide Polymorphisms in Tobacco Metabolism and DNA Repair Genes and Prognosis in Resected Non-Small-Cell Lung Cancer. J SURG RES. 167:E5-E12. I.F.: 2.24.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	39.11	3	3	0
2010	99.55	14	6	5
2011	115.32	13	9	2

REVIEWS
I.F.: 2.25

1 Silverman EK, Vestbo J, Agusti A, Anderson W, Bakke PS, Barnes KC, Barr RG, Bleecker ER, Boezen HM, Burkart KM, Celli BR, Cho MH, Cookson WO, Croxton T, Daley D, Demeo DL, Gan W, Garcia-Aymerich J, Hall IP, Hansel NN, Hersh CP, Kalsheker N, Kiley JP, Kim WJ, Lambrechts D, Lee SD, Litonjua AA, Lomas DA, London SJ, Nishimura M, Nørdestgaard BG, O'donnell CJ, Postma DS, Puhan MA, Tesfaigzi Y, Tobin MD, Vogelmeier C, Wilk JB, Wouters E, Young RP, Ziegler-Heitbrock L, Macnee W, Crapo JD. Opportunities and challenges in the genetics of COPD 2010: an International COPD Genetics Conference report. COPD. 8:121-123. I.F.: 2.25.

EDITORIALS
I.F.: 12.45

1 Agusti A, Celli B. Avoiding confusion in COPD: from risk factors to phenotypes to measures of disease characterisation. EUR RESPIR J. 38:749-751. I.F.: 5.92.

2 Fabbri LM, Beghe B, Agusti A. Cardiovascular mechanisms of death in severe COPD exacerbation: time to think and act beyond guidelines. THORAX. 66:745-747. I.F.: 6.53.

MULTICENTRICS
I.F.: 2.86

1 Dickens JA, Miller BE, Edwards LD, Silverman EK, Lomas DA, Tal-Singer R. COPD association and repeatability of blood biomarkers in the ECLIPSE cohort. RESP RES. 12:-. I.F.: 2.86.

GRANTS FOR RESEARCH IN PROGRESS

Agusti A. Cohorte española de pacientes con EPOC Avanzada (CEPA): Inflamosoma, comorbilidad y curso clínico. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0629. Duration: 01/01/2010-31/12/2012.

Agustí A. Inflamasoma, enfermedades auto-inflamatorias y EPOC. Sponsored by: SEPAR, 870. Duration: 01/06/2010-30/06/2011.

Agustí A. Riboleucograma en la Enfermedad Pulmonar Obstruciva Crónica. Sponsored by: SEPAR, 133/2011. Duration: 01/06/2011-30/06/2012.

AREA 2

Respiratory, cardiovascular and renal pathobiology and bioengineering

Genetic and urological tumours

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Antoine G. Van Der Heijden (Radboud University Nijmegen Medical Center)
Juan José Lozano (Plataforma de Bioinformática, CIBEREHD)

TEAM INVOLVED IN:

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

- Study of gene expression profiles in urine for noninvasive diagnosis and prognosis of bladder tumors.
- Identification of micro-RNA in urine for the noninvasive diagnosis of bladder tumors.
- Determination of disseminated tumor disease in patients with muscle invasive bladder cancer, based on evaluation of the gene expression of bladder-specific markers in lymph nodes and peripheral blood.
- Study of the genic expression profile associated with response to neoadjuvant chemotherapy in patients with muscle invasive bladder cancer.
- Study of methylation profiles of urine cells as a method for noninvasive diagnosis of bladder cancer.
- Study of the prognostic factors in upper urinary tract tumors PCR.
- Study of gene expression and miRNA profiles in urine for noninvasive diagnosis and prognosis of prostate tumors.

PUBLICATIONS

ORIGINALS
I.F.: 28.86

1 Alcaraz A, Musquera M, Peri L, Izquierdo L, Garcia-Cruz E, Huguet J, Alvarez-Vijande R, Campistol JM, Oppenheimer F, Ribal MJ. Feasibility of Transvaginal Natural Orifice Transluminal Endoscopic Surgery-Assisted Living Donor Nephrectomy: Is Kidney Vaginal Delivery the Approach of the Future?. EUR UROL. 59:1019-1025. I.F.: 8.84.

2 Bermudo R, Abia D, Mozos A, Garcia-Cruz E, Alcaraz A, Ortiz AR, Thomson TM, Fernandez PL. Highly sensitive molecular diagnosis of prostate cancer using surplus material washed off from biopsy needles. BRIT J CANCER. 105:1600-1607. I.F.: 4.83.

3 Monsalve C, Izquierdo L, Alcaraz A. Interactions Between Hemodynamics and Pharmacology in Kidney Transplantation. TRANSPL P. 43:359-362. I.F.: 0.99.

4 Garcia-Cruz E, Romero Otero J, Martínez Salamanca JI, Leibar Tamayo A, Rodríguez Antolin A, Astobieta Odriozola A, Alcaraz A. Linguistic and Psychometric Validation of the Erection Hardness Score to Spanish. J SEX MED. 8:470-474. I.F.: 3.96.

5 Alcaraz A, Burgos FJ, Cozar JM, Gomez-Veiga F, Morote J, Solsona E, Unda M, Carballido J. Prostate cancer in Spain: from guidelines to clinical practice. BJU INT. 108:61-66. I.F.: 3.19.

6 Madersbacher S, Alcaraz A, Emberton M, Hammerer P, Ponholzer A, Schroder FH, Tubaro A. The influence of family history on prostate cancer risk: implications for clinical management. BJU INT. 107:716-721. I.F.: 3.19.

7 Leveridge M, Musquera M, Evans A, Cardella C, Pei Y, Jewett M, Robinette M, Finelli A. Renal cell carcinoma in the native allograft kidneys of renal transplant recipients. J UROL. 186(1):219-23. I.F.: 3.86

REVIEWS
I.F.: 8.84

1 Catto JWF, Alcaraz A, Bjartell AS, White RD, Evans CP, Fussel S, Hamdy FC, Kallioniemi O, Mengual L, Schlomm T, Visakorpi T. MicroRNA in Prostate, Bladder, and Kidney Cancer: A Systematic Review. EUR UROL. 59:671-681. I.F.: 8.84.

CLINICAL GUIDELINES
I.F.: 8.84

1 Stenzl A, Cowan NC, De Santis M, Kuczyk MA, Merseburger AS, Ribal MJ, Sherif A, Witjes JA. Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines. EUR UROL. 59(6):1009-18. I.F.: 8.84.

EDITORIALS
I.F.: 8.84

1 Ribal MJ. Molecular Profiling of Renal Cancer: The Journey to Clinical Application. EUR UROL. 59:731-733. I.F.: 8.84.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	19.66	7	3	3
2010	42.53	15	4	4
2011	28.86	7	3	3

GRANTS FOR RESEARCH IN PROGRESS

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.

Alcaraz A. Grup de recerca en urologia oncològica (GRUO). Sponsored by: AGAUR_SGR09, 2009_SGR_837. Duration: 20/07/2009-31/12/2013.

GYNECOLOGIC
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DIGESTIVE
BLEEDING
PATHOLOGY
SECONDARY
TRANSPLANT
TO RUPTURED
ESOPHAGEAL
GRAFT
VEINS VARICOSE
VIABILITY

AREA 3

LIVER, DIGESTIVE SYSTEM AND METABOLISM

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AREA 3

Liver, digestive system and metabolism

Gynecological endocrinology and human reproduction

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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:

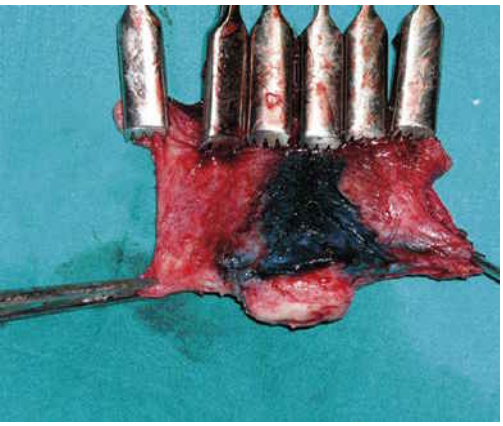
1. Determining the most relevant mechanisms in the **pathogenesis of reproductive failure** (sterility, repeated miscarriages, repeated implant failure after in vitro fertilization) **and of the principal female reproductive disease processes** (endometriosis, uterine myoma, genital cancer).
2. Optimizing 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, endocrine-metabolic 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.



Radical cervix resection piece obtained via laparoscopic surgery from a young patient with invasive cervical cancer, but with a wish to preserve fertility.

PUBLICATIONS

ORIGINALS
I.F.: 76.25

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	91.94	25	18	2
2010	89.86	26	16	3
2011	76.25	21	15	2

1 Almog B, Shehata F, Suissa S, Holzer H, Shalom-Paz E, LaMarca A, Muttukrishna S, Blazar A, Hackett R, Nelson SM, Cunha JS, Eldar-Geva T, Margalioth EJ, Raine-Fenning N, Jayaprakasan K, Mcilveen M, Wunder D, Freour T, Nardo LG, Balasch J, Penarrubia J, Smeenk J, Gnoth C, Godehardt E, Lee TH, Lee MS, Levin I, Gamzu R, Tulandi T. Age-related normograms of serum antimullerian hormone levels in a population of infertile women: a multicenter study. FERTIL STERIL. 95:2359-U280. I.F.: 3.96.

2 Del Pino M, Rodriguez-Carunchio L, Alonso I, Torne A, Rodriguez A, Fuste P, Castillo P, Nonell R, Abu-Lhiga N, Ordi J. Clinical, colposcopic and pathological characteristics of cervical and vaginal high-grade lesions negative for HPV by Hybrid Capture 2. GYNECOL ONCOL. 122:515-520. I.F.: 3.76.

3 Escudero JM, Auge JM, Filella X, Torne A, Pahisa J, Molina R. Comparison of Serum Human Epididymis Protein 4 with Cancer Antigen 125 as a Tumor Marker in Patients with Malignant and Nonmalignant Diseases. CLIN CHEM. 57:1534-1544. I.F.: 6.89.

4 Valsky DV, Martinez-Serrano MJ, Sanz M, Eixarch E, Acosta ER, Martinez JM, Puerto B, Gratacos E. Cord occlusion followed by laser cord transection in monochorionic monoamniotic discordant twins. ULTRASOUND OBST GYN. 37:684-688. I.F.: 3.16.

5 Alonso I, Fuste V, DelPino M, Castillo P, Torne A, Fuste P, Rios J, Pahisa J, Balasch J, Ordi J. Does human papillomavirus infection imply a different prognosis in vulvar squamous cell carcinoma?. GYNECOL ONCOL. 122:509-514. I.F.: 3.76.

6 Aragao FD, Abrantes CG, Gabriel RE, Sousa MF, Castelo-Branco C, Moreira MH. Effects of body composition and menopause characteristics on maximal oxygen uptake of postmenopausal women. MENOPAUSE. 18:1191-1197. I.F.: 3.32.

7 Fabregues F, Iraola A, Casals G, Creus M, Carmona F, Balasch J. Evaluation of two doses of recombinant human luteinizing hormone supplementation in down-regulated women of advanced reproductive age undergoing follicular stimulation for IVF: a randomized clinical study. EUR J OBSTET GYN R B. 158:56-61. I.F.: 1.76.

8 Castelo-Branco C, Martinez MJ, Balasch J. Further data favouring hormonal dependency of cerebral meningiomas: evidence from a patient treated with cabergoline. GYNECOL ENDOCRINOL. 27:134-137. I.F.: 1.46.

9 Comas M, Crispi F, Gomez O, Puerto B, Figueras F, Gratacos E. Gestational age- and estimated fetal weight-adjusted reference ranges for myocardial tissue Doppler indices at 24-41 weeks' gestation. ULTRASOUND OBST GYN. 37:57-64. I.F.: 3.16.

10 Molina R, Escudero JM, Auge JM, Filella X, Foj L, Torne A, Lejarcegui J, Pahisa J. HE4 a novel tumour marker for ovarian cancer: comparison with CA 125 and ROMA algorithm in patients with gynaecological diseases. TUMOR BIOL. 32:1087-1095. I.F.: 2.03.

11 Kirchner T, Munoz D, Forns M, Penarrubia J, Balasch J. Identifying by means of coping typologies and primary appraisal the likelihood of positive beta-hCG test results in women undergoing IVF treatment: a preliminary study. HUM REPROD. 26:1138-1143. I.F.: 4.36.

12 Bardaji A, Sigauque B, Sanz S, Maixenchs M, Ordi J, Aponte JJ, Mabunda S, Alonso PL, Menendez C. Impact of Malaria at the End of Pregnancy on Infant Mortality and Morbidity. J INFECT DIS. 203:691-699. I.F.: 6.29.

13 Castelo-Branco C, Hidalgo MJC. Isoflavones: effects on bone health. CLIMACTERIC. 14:204-211. I.F.: 1.94.

14 Hidalgo MJC, Castelo-Branco C. Optimizing soy isoflavones effect in postmenopausal women: the impact of timing on climacteric symptoms. GYNECOL ENDOCRINOL. 27:696-700. I.F.: 1.46.

15 Carmona F, Martinez-Zamora MA, Rabanal A, Martinez-Roman S, Balasch J. Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up. FERTIL STERIL. 96:251-254. I.F.: 3.96.

16 Serra-Casas E, Menendez C, Dobano C, Bardaji A, Quinto L, Ordi J, Sigauque B, Cistero P, Mandomando I, Alonso PL, Mayor A. Persistence of Plasmodium falciparum Parasites in Infected Pregnant Mozambican Women after Delivery. INFECT IMMUN. 79:298-304. I.F.: 4.10.

17 Martinez-Zamora MA, Creus M, Tassies D, Reverter JC, Civico S, Carmona F, Balasch J. Reduced plasma fibrinolytic potential in patients with recurrent implantation failure after IVF and embryo transfer. HUM REPROD. 26:510-516. I.F.: 4.36.

18 Martin-Jaular L, Ferrer M, Calvo M, Rosanas-Urgell A, Kalko S, Graewe S, Soria G, Cortadellas N, Ordi J, Planas A, Burns J, Heussler V, DelPortillo HA. Strain-specific spleen remodelling in Plasmodium yoelii infections in Balb/c mice facilitates adherence and spleen macrophage-clearance escape. CELL MICROBIOL. 13:109-122. I.F.: 5.63.

19 Sabria J, Barcelo-Vidal C, Arigita M, Jimenez JM, Puerto B, Borrell A. The CUSUM test applied in prospective nuchal translucency quality review. ULTRASOUND OBST GYN. 37:582-587. I.F.: 3.16.

20 Fabregues F, Castelo-Branco C, Carmona F, Guimera M, Casamitjana R, Balasch J. The effect of different hormone therapies on anti-mullerian hormone serum levels in anovulatory women of reproductive age. GYNECOL ENDOCRINOL. 27:216-224. I.F.: 1.46.

21 Rovira-Vallbona E, Dobano C, Bardaji A, Cistero P, Romagosa C, Serra-Casas E, Quinto L, Bassat Q, Sigauque B, Alonso PL, Ordi J, Menendez C, Mayor A. Transcription of var Genes Other Than var2csa in Plasmodium falciparum Parasites Infecting Mozambican Pregnant Women. J INFECT DIS. 204:27-35. I.F.: 6.29.

REVIEWS
I.F.: 1.76

1 Arjona JE, Velasco E, Cervelo P, Espejo E, Pizarro I, Carrasco S, Castelo-Branco C. Pregnancy following radical vulvectomy for carcinoma of the vulva: a case report and literature review. EUR J OBSTET GYN R B. 158:113-114. I.F.: 1.76.

EDITORIALS
I.F.: 1.94

1 Castelo-Branco C. Physical function in overweight postmenopausal women. CLIMACTERIC. 14:689-690. I.F.: 1.94.

MULTICENTRICS
I.F.: 4.72

1 Gomez-Gil E, DeAntonio IE, Almaraz MC, Sieso TG, Rabinovich IH, Escofet FS. The demand for health care services in the gender identity units of Andalusia and Catalonia during the period of 2000 to 2009. REV CLIN ESP. 211:233-239. I.F.: 0.76.

2 Nnoaham KE, Hummelshoj L, Webster P, D'hooghe T, Nardone FD, Nardone CD, Jenkinson C, Kennedy SH, Zondervan KT. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. FERTIL STERIL. 96:366-U431. I.F.: 3.96.

GRANTS FOR RESEARCH IN PROGRESS

Balasch J. Efectos de los fármacos empleados para la estimulación ovárica sobre las células foliculares. Implicaciones en el síndrome de hiperestimulación ovárica. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI070355. Duration: 26/11/2007-31/07/2011.

Balasch J. Caracterización del proteoma del epitelio y del estroma endometriales y expresión proteica diferencial en la ventana de implantación. Sponsored by: Fundación Salud 2000, PI040634. Duration: 01/01/2009-31/12/2011.

Balasch J. Grup de Fisiopatologia de la Reproducció Humana. Sponsored by: Generalitat de Catalunya, 2009 SGR 1099. Duration: 01/01/2009-31/12/2013.

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: 01/01/2010-31/12/2012.

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: 01/01/2010-31/12/2012.

DOCTORAL THESES

Balasch J, Carmona F, Tassies D. Análisis de la fibrinólisis como nuevo mecanismo patogénico trombótico en la patología gestacional precoz y avanzada. Relación con los anticuerpos antifosfolipídicos. PhD student: Mª Ángeles Martínez Zamora.

AREA 3

Liver, digestive system and metabolism

Fetal and perinatal medicine

TEAM INVOLVED IN: ciberer

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Nelly Fabiola Padilla (Fundació Clínic)
Magdalena Sanz (IDIBAPS)

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Anna González (pre-doc IDIBAPS)
Alvaro Pérez (IDIBAPS)
Dafnis Batallé (CIBER-ER)
Jesús Mª Domínguez (CIBER-ER)
Violeta Tenorio (Fundació Clínic)
Mónica Cruz-Lemini (Fundació Clínic)
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Xavier Miracle (Hospital Clínic)
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Marta García (Fundació Clínic)

VISITING SCIENTISTS:
R. Bartrons
D. Valsky
Iosefine Stergitou

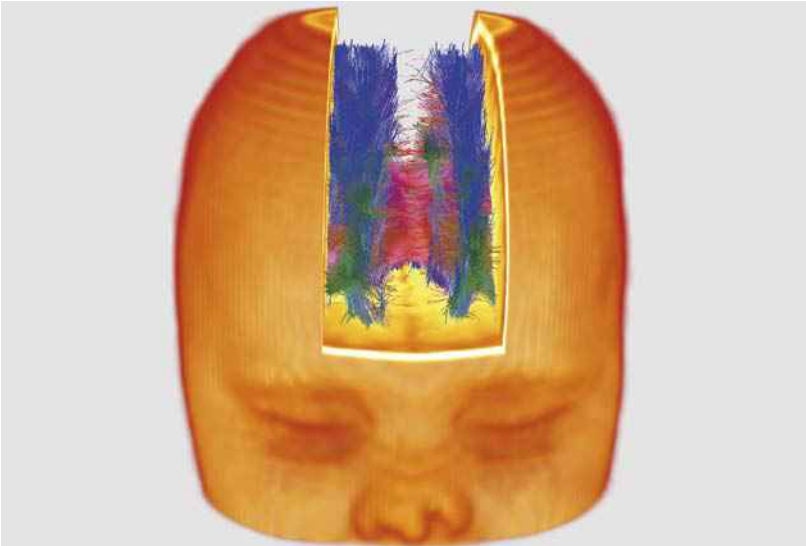
STRATEGIC OBJECTIVES

The principal strategic objective is to search for solutions to prenatal diseases, identifying the mechanisms involved in fetal brain and cardiac reprogramming, developing new technologies allowing an early diagnosis, and identifying potential therapeutic targets.

Other objectives of the team are the development and consolidation of the 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 prematureness.

MAIN LINES OF RESEARCH

1. Neurological damage of fetal and perinatal origin. Characterization of the physiopathology and development of methods for the diagnosis and treatment of prenatal brain damage, with preferential use of fetal growth retardation as a model. The group possesses an important interdisciplinary structure for the characterization and prediction of perinatal brain damage, with special attention to the fetal reprogramming mechanisms secondary to chronic hypoxia. The line is structured into major interrelated areas: fetal and neonatal brain imaging (ultrasound, moving blood fraction and MRI- DTI-RMS), neurological damage biomarkers, and follow-up of neurological development over the long term.
2. Cardiac function and cardiovascular programming in the fetus. The aim of this research line is to characterize cardiac function and develop methods for the prediction and treatment of fetal programming in the context of cardiac dysfunction in fetuses and infants. This includes new echocardiographic markers of fetal myocardial function, biochemical and genomic markers of ischemia and immune/endothelial hyperactivation.
3. Fetal therapy and surgery. As members of the European Eurofoetus group, we study the fetal surgical treatment of complications of monochorial gestation and congenital diaphragmatic herniation, and the tissue engineering repair of fetal membranes. Screening of aneuploidy and maternal disease markers.
4. Perinatal pathology. This is a mixed line that groups projects relating to prematureness (chorioamnionitis, aggressive nutrition), clinical pathology (diabetes, autoimmune diseases), preeclampsia and placental disorders (developing methods for early prediction), HIV and pregnancy, neonatal respiratory disease (study of pulmonary inflammation and prevention of bronchopulmonary dysplasia), and investigation of neonatal infection (perinatal and nosocomial infections, respiratory syncytial virus infection, etc.).



PUBLICATIONS

ORIGINALS
I.F.: 116.03

1 Sola R, Fito M, Estruch R, Salas-Salvado J, Corella D, DeLaTorre R, Munoz MA, Lopez-Sabater MD, Martinez-Gonzalez MA, Aros F, Ruiz-Gutierrez V, Fiol M, Casals E, Warnberg J, Buil-Cosiales P, Ros E, Konstantinidou V, Lapetra J, Serra-Majem L, Covas MI. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: A randomized, controlled trial. ATHEROSCLEROSIS. 218:174-180. I.F.: 4.09.

2 Valsky DV, Martinez-Serrano MJ, Sanz M, Eixarch E, Acosta ER, Martinez JM, Puerto B, Gratacos E. Cord occlusion followed by laser cord transection in monochorionic monoamniotic discordant twins. ULTRASOUND OBST GYN. 37:684-688. I.F.: 3.16.

3 Comas M, Crispi F, Gomez O, Puerto B, Figueras F, Gratacos E. Gestational age- and estimated fetal weight-adjusted reference ranges for myocardial tissue Doppler indices at 24-41 weeks' gestation. ULTRASOUND OBST GYN. 37:57-64. I.F.: 3.16.

4 Sabria J, Barcelo-Vidal C, Arigita M, Jimenez JM, Puerto B, Borrell A. The CUSUM test applied in prospective nuchal translucency quality review. ULTRASOUND OBST GYN. 37:582-587. I.F.: 3.16.

5 Benavides-Serralde A, Hernandez-Andrade E, Fernandez-Lara A, Figueras F, Moreno-Alvarez O, Camargo-Marin L, Acevedo-Gallegos S, Gallardo-Gaona J, Velazquez-Torres B. Accuracy of Different Equations for Estimating Fetal Weight. GYNECOL OBSTET INVES. 72:264-268. I.F.: 1.03.

6 Ierullo AM, Fernandez S, Palacio M, Gratacos E, Hernandez-Andrade E. Cervical blood perfusion assessed using power Doppler-derived estimation of fractional moving blood volume: a reproducibility study. ULTRASOUND OBST GYN. 38:57-61. I.F.: 3.16.

7 Benavides-Serralde A, Scheier M, Cruz-Martinez R, Crispi F, Figueras F, Gratacos E, Hernandez-Andrade E. Changes in Central and Peripheral Circulation in Intrauterine Growth-Restricted Fetuses at Different Stages of Umbilical Artery Flow Deterioration: New Fetal Cardiac and Brain Parameters. GYNECOL OBSTET INVES. 71:274-280. I.F.: 1.03.

8 Cruz-Martinez R, Moreno-Alvarez O, Hernandez-Andrade E, Castanon M, Martinez JM, Done E, Deprest J, Gratacos E. Changes in Lung Tissue Perfusion in the Prediction of Survival in Fetuses with Congenital Diaphragmatic Hernia Treated with Fetal Endoscopic Tracheal Occlusion. FETAL DIAGN THER. 29:101-107. I.F.: 0.87.

9 Cruz-Martinez R, Figueras F, Hernandez-Andrade E, Oros D, Gratacos E. Changes in myocardial performance index and aortic isthmus and ductus venosus Doppler in term, small-for-gestational age fetuses with normal umbilical artery pulsatility index. ULTRASOUND OBST GYN. 38:400-405. I.F.: 3.16.

10 Dadvand P, Basagana X, Figueras F, Sunyer J, Nieuwenhuijsen MJ. Climate and group B streptococci colonisation during pregnancy: present implications and future concerns. BJOG-INT J OBSTET GY. 118:1396-1400. I.F.: 3.35.

11 Dadvand P, Basagana X, Sartini C, Figueras F, Vrijheid M, DeNazelle A, Sunyer J, Nieuwenhuijsen MJ. Climate Extremes and the Length of Gestation. ENVIRON HEALTH PERSP. 119:1449-1453. I.F.: 6.09.

12 Cobo T, Palacio M, Eixarch E, Crispi F, Mercade I, Martinez-Crespo JM, Gratacos E. Clinical and biochemical predictors of very preterm birth in twin-to-twin transfusion syndrome treated by fetoscopy. AM J OBSTET GYNECOL. 204:-. I.F.: 3.31.

13 Cobo T, Palacio M, Martinez-Terron M, Navarro-Sastre A, Bosch J, Filella X, Gratacos E. Clinical and inflammatory markers in amniotic fluid as predictors of adverse outcomes in preterm premature rupture of membranes. AM J OBSTET GYNECOL. 205:-. I.F.: 3.31.

14 Borrell A, Robinson JN, Santolaya-Forgas J. Clinical Value of the 11- to 13(+6)-Week Sonogram for Detection of Congenital Malformations: A Review. AM J PERINAT. 28:117-123. I.F.: 1.12.

15 Scazzocchio E, Figueras F. Contemporary prediction of preeclampsia. CURR OPIN OBSTET GYN. 23:65-71. I.F.: 2.33.

16 Tenorio V, Bonet-Carne E, Botet F, Marques F, Amat-Roldan I, Gratacos E. Correlation Between a Semiautomated Method Based on Ultrasound Texture Analysis and Standard Ultrasound Diagnosis Using White Matter Damage in Preterm Neonates as a Model. J ULTRAS MED. 30:1365-1377. I.F.: 1.25.

17 Padilla N, Falcon C, Sanz-Cortes M, Figueras F, Bargallo N, Crispi F, Eixarch E, Arranz A, Botet F, Gratacos E. Differential effects of intrauterine growth restriction on brain structure and development in preterm infants: A magnetic resonance imaging study. BRAIN RES. 1382:98-108. I.F.: 2.62.

18 Salvador J, Arigita M, Carreras E, Lladonosa A, Borrell A. Evolution of prenatal detection of neural tube defects in the pregnant population of the city of Barcelona from 1992 to 2006. PRENATAL DIAG. 31:1184-1188. I.F.: 2.15.

19 Cruz-Martinez R, Figueras F, Hernandez-Andrade E, Oros D, Gratacos E. Fetal Brain Doppler to Predict Cesarean Delivery for Nonreassuring Fetal Status in Term Small-for-Gestational-Age Fetuses. OBSTET GYNECOL. 117:618-626. I.F.: 4.39.

20 DiRenzo GC, Roura LC, Facchinetti F, Antsaklis A, Breborowicz G, Gratacos E, Husslein P, Lamont R, Mikhailov A, Montenegro N, Radunovic N, Robson M, Robson SC, Sen C, Shennan A, Stamatian F, Ville Y. Guidelines for the management of spontaneous preterm labor: identification of spontaneous preterm labor, diagnosis of preterm premature rupture of membranes, and preventive tools for preterm birth. J MATERN-FETAL NEO M. 24:659-667. I.F.: 2.07.

21 Figueras-Aloy J, Salvia-Roiges MD, Rodriguez-Miguelez JM, Miracle-Echegoyen X, Botet-Mussons F, Marin-Soria JL, Carbonell-Estrany X. Impact of Chorioamnionitis on Exhaled Nitric Oxide and Endotracheal Aspirate Levels of Nitrites-Nitrates and Interleukin-8 in Mechanically Ventilated Preterm Neonates. PEDIATR PULM. 46:595-603. I.F.: 2.24.

22 Eixarch E, Hernandez-Andrade E, Crispi F, Illa M, Torre I, Figueras F, Gratacos E. Impact on fetal mortality and cardiovascular Doppler of selec-

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	91.07	34	18	5
2010	120.82	38	25	4
2011	116.03	43	21	11

tive ligature of uteroplacental vessels compared with undernutrition in a rabbit model of intrauterine growth restriction. PLACENTA. 32:304-309. I.F.: 2.99.

23 Cruz-Martinez R, VanMieghem T, Lewi L, Eixarch E, Cobo T, Martinez JM, Deprest J, Gratacos E. Incidence and clinical implications of early inadvertent septostomy after laser therapy for twin-twin transfusion syndrome. ULTRASOUND OBST GYN. 37:458-462. I.F.: 3.16.

24 Borrell A, Santolaya-Forgas J, Horbaczewski C, Henry RD, Dunn-Albanese L, Robinson JN. Is the starting section for 3D volume acquisition in the first trimester relevant in the post hoc analysis of aneuploidy screening markers and fetal anatomy?. PRENATAL DIAG. 31:1305-1310. I.F.: 2.15.

25 Cruz-Martinez R, Figueras F, Jaramillo JJ, Meler E, Mendez A, Hernandez-Andrade E, Gratacos E. Learning curve for Doppler measurement of fetal modified myocardial performance index. ULTRASOUND OBST GYN. 37:158-162. I.F.: 3.16.

26 Oros D, Figueras F, Cruz-Martinez R, Meler E, Munmany M, Gratacos E. Longitudinal changes in uterine, umbilical and fetal cerebral Doppler indices in late-onset small-for-gestational age fetuses. ULTRASOUND OBST GYN. 37:191-195. I.F.: 3.16.

27 Done E, Allegaert K, Lewi P, Jani J, Gucciardo L, VanMieghem T, Gratacos E, Devlieger R, VanSchoubroeck D, Deprest J. Maternal hyperoxygenation test in fetuses undergoing FETO for severe isolated congenital diaphragmatic hernia. ULTRASOUND OBST GYN. 37:264-271. I.F.: 3.16.

28 Estruch R, Sacanella E, Mota F, Chiva-Blanch G, Antuneza E, Casals E, Deulofeu R, Rotilio D, Andres-Lacueva C, Lamuela-Raventos RM, DeGaetano G, Urbano-Marquez A. Moderate consumption of red wine, but not gin, decreases erythrocyte superoxide dismutase activity: A randomised cross-over trial. NUTR METAB CARDIOVAS. 21:46-53. I.F.: 3.44.

29 Figueras F, Cruz-Martinez R, Sanz-Cortes M, Arranz A, Illa M, Botet F, Costas-Moragas C, Gratacos E. Neurobehavioral outcomes in preterm, growth-restricted infants with and without prenatal advanced signs of brain-sparing. ULTRASOUND OBST GYN. 38:288-294. I.F.: 3.16.

30 Cruz-Martinez R, Figueras F, Hernandez-Andrade E, Benavides-Serralde A, Gratacos E. Normal reference ranges of fetal regional cerebral blood perfusion as measured by fractional moving blood volume. ULTRASOUND OBST GYN. 37:196-201. I.F.: 3.16.

31 Roca A, Garcia-Esteve L, Imaz ML, Torres A, Hernandez S, Botet F, Gelabert E, Subira S, Plaza A, Valdes M, Martin-Santos R. Obstetrical and neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitors: The relevance of dose. J AFFECT DISORDERS. 135:208-215. I.F.: 3.74.

32 VanMieghem T, Eixarch E, Gucciardo L, Done E, Gonzales I, VanSchoubroeck D, Lewi L, Gratacos E, Deprest J. Outcome prediction in monochorionic diamniotic twin pregnancies with moderately discordant amniotic fluid. ULTRASOUND OBST GYN. 37:15-21. I.F.: 3.16.

33 Claus F, Sandaite I, Dekoninck P, Moreno O, Martinez RC, VanMieghem T, Gucciardo L, Richter J, Michielsen K, Decraene J, Devlieger R, Gratacos E, Deprest JA. Prenatal Anatomical Imaging in Fetuses with Congenital Diaphragmatic Hernia. FETAL DIAGN THER. 29:88-100. I.F.: 0.87.

34 Dekoninck P, Gratacos E, VanMieghem T, Richter J, Lewi P, Ancel AM, Allegaert K, Nicolaides K, Deprest J. Results of Fetal Endoscopic Tracheal Occlusion for congenital diaphragmatic hernia and the set up of the randomized controlled TOTAL trial. EARLY HUM DEV. 87:619-624. I.F.: 1.59.

35 Dadvand P, Basagana X, Figueras F, Amoly E, Tobias A, DeNazelle A, Querol X, Sunyer J, Nieuwenhuijsen MJ. Saharan dust episodes and pregnancy. J ENVIRON MONITOR. 13:3222-3228. I.F.: 1.81.

36 Cruz-Martinez R, Figueras F, Benavides-Serralde A, Crispi F, Hernandez-Andrade E, Gratacos E. Sequence of changes in myocardial performance index in relation to aortic isthmus and ductus venosus Doppler in fetuses with early-onset intrauterine growth restriction. ULTRASOUND OBST GYN. 38:179-184. I.F.: 3.16.

37 Deprest J, Nicolaides K, Done' E, Lewi P, Barki G, Largen E, Dekoninck P, Sandaite I, Ville Y, Benachi A, Jani J, Amat-Roldan I, Gratacos E. Technical aspects of fetal endoscopic tracheal occlusion for congenital diaphragmatic hernia. J PEDIATR SURG. 46:22-32. I.F.: 1.31.

38 Moreno R, Martinez I, Petriz J, Nadal M, Tintore X, Gonzalez JR, Gratacos E, Aran JM. The beta-Interferon Scaffold Attachment Region Confers High-Level Transgene Expression and Avoids Extinction by Epigenetic Modifications of Integrated Provirus in Adipose Tissue-Derived Human Mesenchymal Stem Cells. TISSUE ENG PART C-ME. 17:275-287. I.F.: 4.64.

39 Gardosi J, Figueras F, Clausson B, Francis A. The customised growth potential: an international research tool to study the epidemiology of fetal growth. PAEDIATR PERINAT EP. 25:2-10. I.F.: 1.93.

40 Botet F, Figueras J, Carbonell-Estrany X, Narbona E. The impact of clinical maternal chorioamnionitis on neurological and psychological sequelae in very-low-birth weight infants: a case-control study. J PERINAT MED. 39:203-208. I.F.: 1.87.

41 Comas M, Crispi F, Cruz-Martinez R, Figueras F, Gratacos E. Tissue Doppler echocardiographic markers of cardiac dysfunction in small-for-gestational age fetuses. AM J OBSTET GYNECOL. 205:-. I.F.: 3.31.

42 Baschat A, Chmait RH, Deprest J, Gratacos E, Hecher K, Kontopoulos E, Quintero R, Skupski DW, Valsky DV, Ville Y. Twin-to-twin transfusion syndrome (TTTS). J PERINAT MED. 39:107-112. I.F.: 1.87.

43 Arigita M, Borrell A, Mula R, Sanchez A, Mila M, Gratacos E. Use of fetal nuchal translucency in the first trimester to predict single-gene disorders. PRENATAL DIAG. 31:1164-1168. I.F.: 2.15.

REVIEWS
I.F.: 5.05

1 Deprest JA, Nicolaides K, Gratacos E. Fetal Surgery for Congenital Diaphragmatic Hernia Is Back from Never Gone. FETAL DIAGN THER. 29:6-17. I.F.: 0.87.

2 Figueras F, Gardosi J. Intrauterine growth restriction: new concepts in antenatal surveillance, diagnosis, and management. AM J OBSTET GYNECOL. 204:288-300. I.F.: 3.31.

3 Cruz-Martinez R, Hernandez-Andrade E, Moreno-Alvarez O, Done E, Deprest J, Gratacos E. Prognostic Value of Pulmonary Doppler to Predict Response to Tracheal Occlusion in Fetuses with Congenital Diaphragmatic Hernia. FETAL DIAGN THER. 29:18-24. I.F.: 0.87.

EDITORIALS
I.F.: 3.02

1 Gratacos E. Congenital Diaphragmatic Hernia: One Name for Various Diseases. FETAL DIAGN THER. 29:5-5. I.F.: 0.87.

2 Arigita M, Martinez D, Nadal A, Borrell A. Spina bifida in a 13-week fetus with a normal intracranial translucency. PRENATAL DIAG. 31:1104-1105. I.F.: 2.15.

GRANTS FOR RESEARCH IN PROGRESS

Gratacos E. IP- Soft tissue engineering for congenital birth defects in children: new treatment modalities for spina bifida, urogenital and abdominal wall defects (EuroSTEC). Sponsored by: European Commision, LSHB-CT-2006-037409. Duration: 01/01/2007-31/12/2011.

Gratacos E. MC - EST - Multidisciplinary Research Training Programme in Fetal Medicine and Health. Sponsored by: European Commision, MEST-CT-2005-019707. Duration: 01/06/2006-31/12/2011.

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: 29/10/2007-31/12/2012.

Gratacos E. Novel ultrasound-based tridimensional tools for structural and fucntional evaluation of interest in human organs. (Uvolumes). Sponsored by: European Commision, LSHB-CT-2006-037409. Duration: 01/08/2008-31/07/2012.

Gratacos E. A multidisciplinary research programme for the evaluation of diagnostic techniques and intervention. Measures for preantal brain damage using growth restriction as a model. Sponsored by: Cerebra Foundation, CEREBRA_07_001. Duration: 01/10/2007-30/09/2013.

Gratacos E. Clinical use of assesing reginal brain circulation perfusion to identify long term neurodevelopmental anomalies in small for gestational age fetuses (SGA). Sponsored by: Thrasher Research Fund, 02828-7. Duration: 01/04/2009-31/08/2012.

Gratacos E. eVV-endovascular vision. Sponsored by: Generalitat de Catalunya (ACC1Ó), VALTEC09-1-0048. Duration: 30/06/2009-30/06/2011.

Figueras F. Cambios hemodinámicas adaptativos a la insuficiencia placentaria crónica y relación con la lesión neurológica perinatal en modelo animal de coneja gestante. Sponsored by: FIS, PI08/0230. Duration: 01/01/2009-31/12/2011.

Gratacos E. Desarrollo de marcadores predictivos y búsqueda de mecanismos moleculares responsables de la reprogramación cardíaca en la restricción de crecimiento fetal. Sponsored by: Ministerio de Educación, SAF2009_08815. Duration: 01/01/2010-31/12/2012.

Borrell A. Aplicación clínica del genotipado RHD fetal en sangre materna en una población general de estantes RHD negativas. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90539. Duration: 01/01/2010-31/12/2011.

Figueras F. Evaluación de fracción sanguínea en movimiento como estrategia de cribado de hipoxia crónica cerebral fetal para la perdicción de alteraciones del neurodesarrollo. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90391. Duration: 01/01/2010-31/12/2011.

Gratacos E. Evaluación de la eficacia de un algoritmo combinando variables biológicas maternas, ecografía y marcadores bioquímicos para la predicción de preeclampsia y retraso de crecimiento intrauterino en primer trimestre de gestación. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90404. Duration: 01/01/2010-30/06/2011.

Gratacos E. Diagnóstico precoz en niños con daño cerebral y trastornos del aprendizaje. Sponsored by: Fundación Caja Navarra, 14802-2011. Duration: 01/01/2011-31/12/2011.

Gratacos E. eVV- endoVascularVision: new endoscopic tools for real time vascular assisted vision. Sponsored by: European Comission, 251356. Duration: 01/09/2010-30/08/2014.

Palacio M. Evaluación de la utilidad de la indometacina como tratamiento de soporte en pacientes con amenaza de parto pretérmico y alto riesgo d inflamación intra-amniótica: EUDRA-CT. Sponsored by: INDOGEST 2010-022998-33, Ministerio de Sanidad, Política Social e Igualdad, EC10-065. Duration: 01/01/2011-31/12/2011.

Palacio M. PROgesterona vaginal como tratamiento de Mantenimiento en gEStantes con Amenaza de parto pretérmino. Ensayo clínico aleatorizado, enmascarado a doble ciego y controlado con placebo.. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-096. Duration: 01/01/2010-31/12/2011.

Gratacos E. Biomarcadors quantitatius d'imatge: Nous mètodes per a la predicció del neurodesenvolupament anormal en nens amb retard de creixement fetal basats en connectòmica. Sponsored by: Caixa d'Estalvis i Pensions, 10/503. Duration: 03/12/2010-31/12/2013.

Gratacos E. CV-REMOD. Gestión del remodelado Cardiovascular mediante integración de tecnologías Monitorización ubicua y Conceptos del Humano Fisiológico Virtual. Sponsored by: MICINN - Programa CENIT (CV-REMOD), 09/398 - 10/079. Duration: 16/09/2009-31/12/2012.

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: 01/01/2011-31/12/2013.

Gratacos E. Gestión del remodelado cardiovascular mediante integración de tecnologias de monitorización ubicua y conceptos del humano fisiologico virtual. Sponsored by: MICINN - Programa CENIT (CV-REMOD), 09/371. Duration: 23/12/2009-31/12/2012.

Gratacos E. Una esperança per a families amb problemes d'origen prenatal. Sponsored by: Generalitat de Catalunya, AGAUR-ARCS2011, EG074749. Duration: 22/11/2011-22/11/2012.

DOCTORAL THESES

Gratacos E, Figueras F. Brain reorganization in an experimental model of intrauterine growth restriction. PhD student: Elisenda Eixarch Roca.

Gratacos E, Crispi F. Cardiac dysfunction by tissue doppler in early-and late-onset fetal growth restriction. PhD student: Montserrat Comas Rovira.

Botet F. Seguretat en la reanimació a la sala dels prematurs extrems. PhD student: Sílvia Maya Enero.

AREA 3

Liver, digestive system and metabolism

Viral hepatitis in the immune competent host and in liver transplant patients

TEAM INVOLVED IN: ciberehd

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STRATEGIC OBJECTIVES

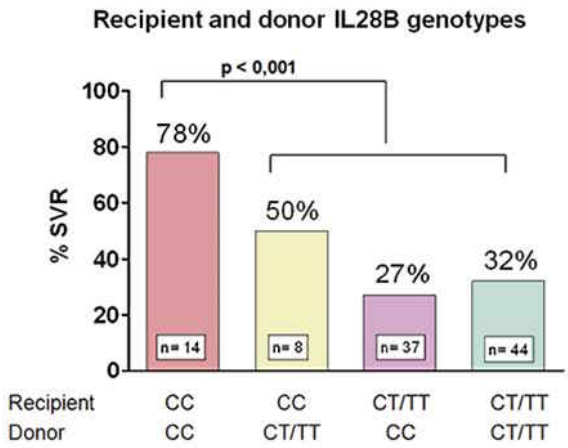
Investigation of epidemiological, pathogenic, diagnostic and therapeutic aspects of hepatitis virus infections in immune competent patients and liver transplant recipients.

MAIN LINES OF RESEARCH

1. **Study of host factors in relation to the natural history and treatment response among patients with chronic hepatitis C.** In this setting, mention should be made of the studies which the group is carrying out on the influence of polymorphisms of the IL28B gene (which encodes for interferon lambda-3) upon the natural history and antiviral treatment response of chronic hepatitis C (in immune competent individuals and liver transplant recipients). In transplant patients with hepatitis C, our group has shown that the presence of a favorable IL28B polymorphism in the recipient, if associated with the favorable polymorphism in the donor liver, significantly increases the antiviral treatment response (Fig. 1). In the coming months, evaluation will be made of the role of this polymorphism in relation to the natural history of chronic hepatitis C virus infection.
2. **Development of models for the in vitro study of the hepatitis C virus (HCV).** At present there is only a single model for studying the complete life cycle of HCV. This is a limited model, since it is based on the culture of a single cell line, in which only one viral strain grows. Over the last year we have worked on the development of new cell culture systems based on different cell lines with markers genes, allowing the detection of viral replication and the screening of biological samples with considerable rapidity. The ultimate aim of these studies is to establish one or more HCV culture systems allowing the growth and adaptation of viruses from biological samples, and which are therefore more representative of in vivo situations. It is important to note that we have established a collaboration with the Hepatic

Oncology Group led by Dr. Jordi Bruix in order to study the replication of HCV in hepatocellular carcinoma derived cell lines isolated and characterized by members of this group.

3. **Detection of HCV antigens in liver tissue.** This is a project which in a sense represents continuity of the work started in 2008 with the purpose of characterizing the expression of HCV penetration receptors (claudin-1, occludin SR-B1 and CD81). Following completion of this project, we wish to detect viral antigens in liver tissue. While this may seem an easy project, to date it has not been possible to detect these antigens in a reproducible manner. Since we have samples from transplant patients with very high viral loads, and taking advantage of the experience gained over the past years with confocal microscopy and immunohistochemistry techniques, we aim to evaluate the presence of different viral antigens in liver biopsies. Success with the project could have clinical applications in aspects as relevant as the differential diagnosis of rejection and the recurrence of hepatitis C after transplantation. One of the predoctoral fellows in our laboratory will move to to the U.S. (NIH) to initiate a collaborative study using new generation confocal microscopy.
4. **Noninvasive diagnosis of chronic hepatitis C.** In 2011 we obtained the first preliminary results of the LiverBiomark Project, funded by CIBERehd. The project applies metabolomics techniques in an attempt to secure the early identification of those patients with hepatitis C presenting a risk of developing severe forms of the disease (in both immune competent individuals and in liver transplant recipients).
5. **Treatment of chronic hepatitis C.** Our group continues to focus great effort on improving the efficacy and safety of antiviral therapy in patients with chronic HCV infection. Different aspects are included within this line of research: 1) Participation in clinical trials of new antiviral molecules (in both early stages and in pre-marketing phases); and 2) Study of the predictive factors of treatment response and designing of models allowing a reliable prediction of treatment results – particularly as regards the prediction of infection relapse in patients that have been able to achieve negative conversion of HCV during treatment. In the last year we have found that direct antiviral drug treatment (therefore not requiring interferon) is able to definitively eliminate HCV, and thus heal the chronic infection. This is an important step in the field of hepatitis, which will lead to radical changes in treatment in the next 10 years.



Influence of polymorphisms of the interleukin-28B (IL28B) gene upon antiviral treatment response in liver transplant patients with hepatitis C. Those patients with a favorable polymorphism (CC) and who receive a liver from an IL28 CC donor have a high probability of healing the infection with interferon and ribavirin.

PUBLICATIONS

ORIGINALS
I.F.: 77.73

1 Perez-Alvarez R, Diaz-Lagares C, Garcia-Hernandez F, Lopez-Roses L, Brito-Zeron P, Perez-De-Lis M, Retamozo S, Bove A, Bosch X, Sanchez-Tapias JM, Forns X, Ramos-Casals M. Hepatitis B Virus (HBV) Reactivation in Patients Receiving Tumor Necrosis Factor (TNF)-Targeted Therapy Analysis of 257 Cases. MEDICINE. 90:359-371. I.F.: 4.26.

2 Cervera C, Fernandez-Ruiz M, Valledor A, Linares L, Anton A, Marcos MA, Sanclemente G, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Pumarola T, Moreno A. Epidemiology and risk factors for late infection in solid organ transplant recipients. TRANSPL INFECT DIS. 13:598-607. I.F.: 2.04.

3 Gil C, Garcia MT, Garcia F, Miro JM, Aguero F, Alos L, Zamora L, Capon A, Costa J, Pumarola T, Gatell JM. Evaluation of the Roche COBAS (R) TaqMan (R) HIV-1 test for quantifying HIV-1 RNA in infected cells and lymphoid tissue. J VIROL METHODS. 174:69-76. I.F.: 2.14.

4 Linares L, Sanclemente G, Cervera C, Hoyo I, Cofan F, Ricart MJ, Perez-Villa F, Navasa M, Marcos MA, Anton A, Pumarola T, Moreno A. Influence of Cytomegalovirus Disease in Outcome of Solid Organ Transplant Patients. TRANSPL P. 43:2145-2148. I.F.: 0.99.

5 Coto-Llerena M, Perez-Del-Pulgar S, Crespo G, Carrion JA, Martinez SM, Sanchez-Tapias JM, Martorell J, Navasa M, Forns X. Donor and Recipient IL28B Polymorphisms in HCV-Infected

Patients Undergoing Antiviral Therapy before and after Liver Transplantation. AM J TRANSPLANT. 11:1051-1057. I.F.: 6.05.

6 Martinez SM, Fernandez-Varo G, Gonzalez P, Sampson E, Bruguera M, Navasa M, Jimenez W, Sanchez-Tapias JM, Forns X. Assessment of liver fibrosis before and after antiviral therapy by different serum marker panels in patients with chronic hepatitis C. ALIMENT PHARM THER. 33:138-148. I.F.: 3.86.

7 Koutsoudakis G, Perez-Del-Pulgar S, Coto-Llerena M, Gonzalez P, Dragun J, Mensa L, Crespo G, Navasa M, Forns X. Cell Culture Replication of a Genotype 1b Hepatitis C Virus Isolate Cloned from a Patient Who Underwent Liver Transplantation. PLOS ONE. 6:-. I.F.: 4.41.

8 Dragun J, Perez-Del-Pulgar S, Crespo G, Ramirez S, Coto-Llerena M, Mensa L, Garcia-Valdecasas JC, Navasa M, Forns X. Characterization of the Cross-Neutralizing Antibody Response Against Hepatitis C Virus in the Liver Transplantation Setting. AM J TRANSPLANT. 11:767-774. I.F.: 6.05.

9 Balderramo D, Bordas JM, Sendino O, Abraldes JG, Navasa M, Llach J, Cardenas A. Complications after ERCP in liver transplant recipients. GASTROINTEST ENDOSC. 74:285-294. I.F.: 5.65.

10 Castells L, Campos I, Bilbao I, Navasa M, Carrion J, Forns X, Berenguer M, Aguilera V, Prieto M, Fernandez I, Meneu JC, Ulloa E, Fernandez JR, Suarez MJ, Pascasio JM, Sousa JM, Casanovas T, Baliella C, Barcena R, Rodriguez M, DeLaMata M, Barrera P, Salcedo M, Banares R, Otero A, Suarez F, Banos I, Tome S, Herrero I, Guilera M. Cyclosporine A-Based Immunosuppression Reduces Relapse Rate After Antiviral Therapy in Transplanted Patients With Hepatitis C Virus Infection: A Large Multicenter Cohort Study. TRANSPLANTATION. 92:334-340. I.F.: 3.68.

11 Marino Z, Carrion JA, Bedini JL, Crespo G, Martinez SM, Sanchez-Tapias JM, Forns X, Navasa MA. Evaluation of a portable hemoglobinometer (HemoCue) to control anemia in hepatitis C liver transplant recipients undergoing antiviral therapy. EUR J GASTROEN HEPAT. 23:942-947. I.F.: 1.60.

12 Balderramo D, Prieto J, Cardenas A, Navasa M. Hepatic encephalopathy and post-transplant hyponatremia predict early calcineurin inhibitor-induced neurotoxicity after liver transplantation. TRANSPL INT. 24:812-819. I.F.: 3.21.

13 Mensa L, Crespo G, Gastinger MJ, Kabat J, Perez-Del-Pulgar S, Miquel R, Emerson SU, Purcell RH, Forns X. Hepatitis C Virus Receptors Claudin-1 and Occludin After Liver Transplantation and Influence on Early Viral Kinetics. HEPATOLOGY. 53:1436-1445. I.F.: 10.89.

14 DiMartino V, Richou C, Cervoni JP, Sanchez-Tapias JM, Jensen DM, Mangia A, Buti M, Sheppard F, Ferenci P, Thevenot T. Response-Guided Peg-Interferon Plus Ribavirin Treatment Duration in Chronic Hepatitis C: Meta-Analyses of Randomized, Controlled Trials and Implications for the Future. HEPATOLOGY. 54:789-800. I.F.: 10.89.

15 Marcellin P, Forns X, Goeser T, Ferenci P, Nevens F, Carosi G, Drenth JP, Serfaty L, DeBacker K, VanHeeswijk R, Luo DH, Picchio G, Beumont M. Telaprevir Is Effective Given Every 8 or 12 Hours With Ribavirin and Peginterferon Alfa-2a or-2b to Patients With Chronic Hepatitis C. GASTROENTEROLOGY. 140:459-U159. I.F.: 12.03.

REVIEWS
I.F.: 10.89

1 Martinez SM, Crespo G, Navasa M, Forns X. Noninvasive Assessment of Liver Fibrosis. HEPATOLOGY. 53:325-335. I.F.: 10.89.

EDITORIALS
I.F.: 6.05

1 Forns X, Navasa M. Cyclosporine A or Tacrolimus for Hepatitis C Recurrence? An Old Debate. AM J TRANSPLANT. 11:1559-1560. I.F.: 6.05.

CLINICAL GUIDELINES
I.F.: 9.33

1 [ANON]. EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. J HEPATOL. 55:245-264. I.F.: 9.33.

MULTICENTRICS
I.F.: 160.47

1 Zeuzem S, Andreone P, Pol S, Lawitz E, Diago M, Roberts S, Focaccia R, Younossi Z, Foster GR, Horban A, Ferenci P, Nevens F, Mullhaupt B, Pockros P, Terg R, Shouval D, VanHoek B, Weiland O, VanHeeswijk R, DeMeyer S, Luo D, Boogaerts G, Polo R, Picchio

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	106.96	21	12	4
2010	90.08	15	11	1
2011	77.73	15	8	2

G, Beumont M. Telaprevir for Retreatment of HCV Infection. NEW ENGL J MED. 364:2417-2428. I.F.: 53.49.

Jacobson IM, McHutchison JG, Dusheiko G, Di Bisceglie AM, Reddy KR, Bzowej NH, Marcellin P, Muir AJ, Ferenci P, Flisiak R, George J, Rizzetto M, Shouval D, Sola R, Terg RA, Yoshida EM, Adda N, Bengtsson L, Sankoh AJ, Kieffer TL, George S, Kauffman RS, Zeuzem S; ADVANCE Study Team. Telaprevir for previously untreated chronic hepatitis C virus infection. N ENGL J MED. 364(25):2405-16. I.F.: 53.49.

Poordad F, McCone J Jr, Bacon BR, Bruno S, Manns MP, Sulkowski MS, Jacobson IM, Reddy KR, Goodman ZD, Boparai N, DiNubile MJ, Sniukiene V, Brass CA, Albrecht JK, Bronowicki JP; SPRINT-2 Investigators. Boceprevir for untreated chronic HCV genotype 1 infection. N ENGL J MED. 364(13):1195-206. I.F.: 53.49.

GRANTS FOR RESEARCH IN PROGRESS

Forns X. Caracterización de la expresión hepática de los receptores de entrada del virus de la hepatitis C y su relación con la cinética de infección del injerto y la evolución clínica después del trasplante hepático. Sponsored by: Ministerio de Ciencia e Innovación, PI080239. Duration: 01/01/2009-31/12/2011.

Forns X. 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, Ministerio de Economía y Competitividad. Duration: 01/01/2010-31/12/2013.

Forns X. Early identification of severe hepatitis C recurrence after liver transplantation. Sponsored by: Roche Organ Transplantation Research Foundation (Switzerland), INT_ROTRF_11_01. Duration: 01/10/2011-30/09/2012.

Navasa M. 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: Ministerio de Ciencia e Innovación, PI10/01551. Duration: 01/01/2011-31/12/2013.

Navasa M, Forns X. Desarrollo de biomarcadores del grado de fibrosis hepática y del pronóstico de pacientes con enfermedades hepáticas avanzadas mediante el uso de herramientas metabolómicas. Sponsored by: Ministerio de Economía y Competitividad (Subprograma Innpacto 2010), IPT-010000-2010-013; LIVERBIOMARK. Duration: 01/01/2010-31/12/2012.

Forns X. Hepatitis víriques a l'hoste immunocompetent i al trasplantat hepàtic. Sponsored by: Generalitat de Catalunya, AGAUR_SGR09, 2009_SGR_1503. Duration: 23/09/2009-31/12/2013.

AREA 3

Liver, digestive system and metabolism

Pathophysiology and treatment of ascites and altered renal function in liver cirrhosis

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Marco Pavesi (CIBERehd)

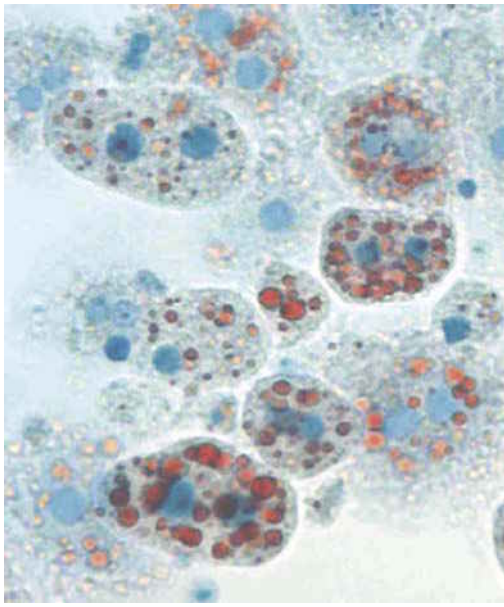
TEAM INVOLVED IN: ciberehd

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.

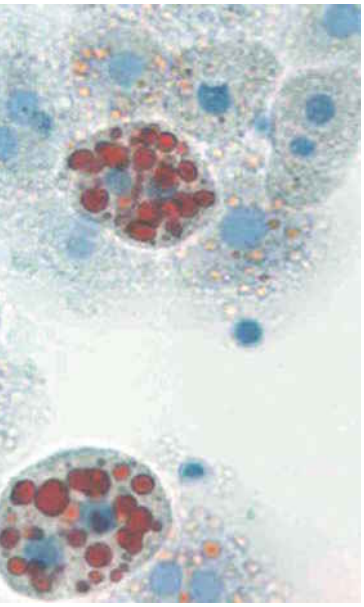
MAIN LINES OF RESEARCH

1. Molecular determinants of liver inflammation. Role of the Kupffer cells.
2. Acute bacterial infections in cirrhosis.
3. Pathophysiology and treatment of hepatorenal syndrome and renal failure associated with bacterial infections.
4. Evaluation of cirrhotic myocardiopathy.



Light microscopic view of hepatocytes from mice with steatohepatitis induced by a fat-rich diet. The interior of the liver cells show lipid vesicles stained with oil red-O.

5. Relationship between hepatic encephalopathy and alterations in renal function in cirrhosis.
6. Pathogenesis, clinical implications and treatment of hyponatremia.
7. Evaluation of different brain MRI techniques in cirrhotic patients. Relationship to hepatic encephalopathy.
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. Physiopathology and treatment of arterial vasodilatation.
13. Physiopathology and treatment of ascites.
14. Artificial liver support systems.
15. Identification of new therapeutic targets in alcoholic hepatitis.



PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	92.54	15	14	1
2010	240.97	28	23	3
2011	94.79	12	10	2

ORIGINALS
I.F.: 94.79

1 Bosch X, Esteve J, Sitges M, DeCaralt TM, Domenech A, Ortiz JT, Monzo M, Morales-Ruiz M, Perea RJ, Rovira M. Prevention of Chemotherapy-Induced Left Ventricular Dysfunction With Enalapril and Carvedilol: Rationale and Design of the OVERCOME Trial. J CARD FAIL. 17:643-648. I.F.: 3.36.

2 Martinez SM, Fernandez-Varo G, Gonzalez P, Sampson E, Bruguera M, Navasa M, Jimenez W, Sanchez-Tapias JM, Forns X. Assessment of liver fibrosis before and after antiviral therapy by different serum marker panels in patients with chronic hepatitis C. ALIMENT PHARM THER. 33:138-148. I.F.: 3.86.

3 Guevara M, Baccaro ME, Gomez-Anson B, Frisoni G, Testa C, Torre A, Molinuevo JL, Rami L, Pereira G, Sotil EU, Cordoba J, Arroyo V, Gines P. Cerebral magnetic resonance imaging reveals marked abnormalities of brain tissue density in patients with cirrhosis without overt hepatic encephalopathy. J HEPATOL. 55:564-573. I.F.: 9.33.

4 Melgar-Lesmes P, Pauta M, Reichenbach V, Casals G, Ros J, Bataller R, Morales-Ruiz M, Jimenez W. Hypoxia and proinflammatory factors upregulate apelin receptor expression in human stellate cells and hepatocytes. GUT. 60:1404-1411. I.F.: 10.61.

5 VanSteenkiste C, Ribera J, Geerts A, Pauta M, Tugues S, Casteleyn C, Libbrecht L, Olievier K, Schroyen B, Reynaert H, VanGrunsven LA, Blomme B, Coulon S, Heindryckx F, DeVos M, Stassen JM, Vinckier S, Altamirano J, Bataller R, Carmeliet P, VanVlierberghe H, Colle I, Morales-Ruiz M. Inhibition of Placental Growth Factor Activity Reduces the Severity of Fibrosis, Inflammation, and Portal Hypertension in Cirrhotic Mice. HEPATOLOGY. 53:1629-1640. I.F.: 10.89.

6 Cardenas A, Gines P. Management of patients with cirrhosis awaiting liver transplantation. GUT. 60:412-421. I.F.: 10.61.

7 Martin-Llahi M, Guevara M, Torre A, Fagundes C, Restuccia T, Gilabert R, Sola E, Pereira G, Marinelli M, Pavesi M, Fernandez J, Rodes J, Arroyo V, Gines P. Prognostic Importance of the Cause of Renal Failure in Patients With Cirrhosis. GASTROENTEROLOGY. 140:488-U192. I.F.: 12.03.

8 Titos E, Rius B, Gonzalez-Periz A, Lopez-Vicario C, Moran-Salvador E, Martinez-Clemente M, Arroyo V, Claria J. Resolvin D1 and Its Precursor Docosahexaenoic Acid Promote Resolution of Adipose Tissue Inflammation by Eliciting Macrophage Polarization toward an M2-Like Phenotype. J IMMUNOL. 187:5408-5418. I.F.: 5.75.

9 Moran-Salvador E, Lopez-Parra M, Garcia-Alonso V, Titos E, Martinez-Clemente M, Gonzalez-Periz A, Lopez-Vicario C, Barak Y, Arroyo V, Claria J. Role for PPAR gamma in

obesity-induced hepatic steatosis as determined by hepatocyte- and macrophage-specific conditional knockouts. FASEB J. 25:2538-2550. I.F.: 6.52.

10 Martinez-Clemente M, Claria J, Titos E. The 5-lipoxygenase/leukotriene pathway in obesity, insulin resistance, and fatty liver disease. CURR OPIN CLIN NUTR. 14:347-353. I.F.: 4.33.

11 Altamirano J, Higuera-DeLatijera F, Duarte-Rojo A, Martinez-Vazquez MA, Abraldes JG, Herrera-Jimenez LE, Michelena J, Zapata L, Perez-Hernandez J, Torre A, Gonzales-Gonzalez JA, Cardenas A, Dominguez M, Arroyo V, Gines P, Caballeria J, Bataller R. The Amount of Alcohol Consumption Negatively Impacts Short-Term Mortality in Mexican Patients With Alcoholic Hepatitis. AM J GASTROENTEROL. 106:1472-1480. I.F.: 6.88.

12 Wong F, Nadim MK, Kellum JA, Salerno F, Bellomo R, Gerbes A, Angeli P, Moreau R, Davenport A, Jalan R, Ronco C, Genyk Y, Arroyo V. Working Party proposal for a revised classification system of renal dysfunction in patients with cirrhosis. GUT. 60:702-709. I.F.: 10.61.

REVIEWS
I.F.: 40.82

1 Cardenas A, Gines P. Acute-on-chronic liver failure: the kidneys. CURR OPIN CRIT CARE. 17:184-189. I.F.: 2.55.

2 Altamirano J, Bataller R. Alcoholic liver disease: pathogenesis and new targets for therapy. NAT REV GASTRO HEPAT. 8:491-501. I.F.: 4.56.

3 Gao B, Bataller R. Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets. GASTROENTEROLOGY. 141:1572-1585. I.F.: 12.03.

4 Bataller R, Rombouts K, Altamirano J, Marra F. Fibrosis in alcoholic and nonalcoholic steatohepatitis. BEST PRACT RES CL GA. 25:231-244. I.F.: 2.23.

5 Guevara M, Arroyo V. Hepatorenal syndrome. EXPERT OPIN PHARMACO. 12:1405-1417. I.F.: 2.40.

6 Arroyo V, Fernandez J. Management of hepatorenal syndrome in patients with cirrhosis. NAT REV NEPHROL. 7:517-526. I.F.: 4.75.

7 Oliva R, Badenas C, Claria J, Coll MJ. Molecular genetic reports in clinical practice: Content and nomenclature of mutations. MED CLIN-BARCELONA. 136:356-361. I.F.: 1.41.

8 Olson JC, Wendon JA, Kramer DJ, Arroyo V, Jalan R, Garcia-Tsao G, Kamath PS. Intensive care care of the patient with cirrhosis. HEPATOLOGY. 54(5):1864-72. I.F.: 10.89.

EDITORIALS
I.F.: 31.06

1 Gines P. Hepatorenal Syndrome, Pharmacological Therapy, and Liver Transplantation. LIVER TRANSPLANT. 17:1244-1246. I.F.: 3.07.

2 Gines P. Pharmacological management of hepatorenal syndrome: Lessons from non-responders. J HEPATOL. 55:268-269. I.F.: 9.33.

3 Morales-Ibanez O, Bataller R. Platelet-derived chemokines: New targets to treat liver fibrosis. J HEPATOL. 54:581-583. I.F.: 9.33.

4 Affo S, Bataller R. RANTES antagonism: A promising approach to treat chronic liver diseases. J HEPATOL. 55:936-938. I.F.: 9.33.

GRANTS FOR RESEARCH IN PROGRESS

Gines P. Efecto de la administración prolongada de albúmina y midodrina 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: 29/10/2007-31/12/2012.

Guevara M. Estudio Aleatorizado y controlado sobre la eficacia de la albúmina en la prevención de las complicaciones de pacientes de cirrosis en la lista de espera de trasplante hepático. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI070443. Duration: 26/11/2007-30/06/2012.

Morales M. Función fisiopatológica de la activación de las células endoteliales hepáticas en la cirrosis. Posibles implicaciones terapéuticas. Sponsored by: Ministerio Educación, SAF2007-63069. Duration: 01/10/2007-02/03/2012.

Jimenez W. Remodelado tisular y disfunción circulatoria en modelos experimentales de enfermedad hepática. Identificación y caracterización de nuevas dianas terapéuticas. Sponsored by: Ministerio de Ciencia e Innovación, SAF2009-08839. Duration: 01/01/2010-31/12/2012.

Bataller R. Projecte TRACE 2009. Desarrollo de un test genético para predecir la progresión de la fibrosis en pacientes con hepatitis

crónica C (POLIGEN). Sponsored by: Ministerio de Ciencia e Innovación, PET2008_0304. Duration: 01/03/2009-02/03/2012.

Bataller R. Investigación traslacional en pacientes con hepatopatías crónicas: desarrollo de métodos pronósticos e identificación de nuevas dianas terapéuticas. Sponsored by: Instituto de Salud Carlos III (FIS), PI08/0237. Duration: 01/01/2009-31/12/2012.

Arroyo V. Investigació hepàtica: Recerca bàsica i experimental. Sponsored by: Generaliat de Catalunya, AGAUR, 2009_SGR_1484 . Duration: 01/01/2009-31/12/2013.

Gines P. Grup de recerca en hepatologia clínica. Sponsored by: Generalitat de Catalunya, AGAUR, 2009_SGR_1401. Duration: 01/01/2009-31/12/2013.

Gines P. Disfunción Renal en la cirrosis hepática: Investigación de nuevos métodos diagnósticos y terapéuticos. Sponsored by: Ministerio de Ciencia e Innovación Instituto de Salud Carlos III, PI 080126. Duration: 01/01/2010-31/12/2012.

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 Educación, SAF2009_08767. Duration: 01/01/2010-31/12/2012.

Bataller R. Hepatic Microfluidic Bioreactor. Sponsored by: Katholieke Universiteit Leuven, FP7-2010-TESTING_1. Duration: 01/01/2011-02/02/2015.

Jimenez W. Grupo de Investigación traslacional en nuevas estrategias de diagnóstico y tratamiento de la enfermedad hepática. Sponsored by: Generaliat de Catalunya, 2009_SGR_1496. Duration: 20/08/2009-31/12/2013.

Morales M. Implicaciones básicas y traslacionales del estudio de las alteraciones funcionales y moleculares del endotelio hepático en la cirrosis. Sponsored by: Ministerio de Economía y Competitividad, SAF 2010-19025. Duration: 01/01/2011-31/12/2013.

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, PI10/01373. Duration: 01/01/2011-31/12/2013.

Guevara M. Estudio de la fisiopatología de la encepalopatía hepática. Investigación clínica y experimental. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0108. Duration: 01/01/2009-31/12/2012.

DOCTORAL THESES

Gines P. Utilidad del MELD y el sodio pretrasplante en el pronóstico del trasplante hepático a corto plazo. PhD student: Maria Carlota Londoño Hurtado.

Claria J. Participación de la 5- y la 12/15 - lipooxigenasa en el desarrollo y progresión de la inflamación y esteatosis hepática. PhD student: Marcos Martínez Clemente.

AREA 3

Liver, digestive system and metabolism

Hepatic oncology

TEAM INVOLVED IN: ciberehd

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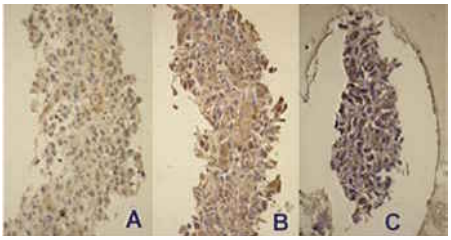
Augusto Villanueva (Ciberehd)
M. Angeles García-Criado (Hospital Clínic)

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 perfected (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, 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 capital importance.



Diagnosis of early stage HCC based on staining with GPC3 (A), HSP70 (B) and GS (C).

RESEARCH GROUP
TRANSLATIONAL RESEARCH IN HEPATIC ONCOLOGY

Group Leader:
Josep M. Llovet (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 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.

The group coordinates a European Project, FP-7-HEALTH (HEPTROMIC) with 6 academic centers and two companies, with the purpose of exploring the prognostic oncogenes and potential treatment targets in liver cancer. The group has received a 5 years grant as a stable group of the Spanish Association Against Cancer (AECC) to investigate about integrated genomic analysis of intrahepatic colangiocarcionma.

PUBLICATIONS

ORIGINALS
I.F.: 81.94

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	162.54	17	13	3
2010	62.23	11	7	1
2011	81.94	10	8	1

1 Tarocchi M, Hannivoort R, Hoshida Y, Lee UE, Vetter D, Narla G, Villanueva A, Oren M, Llovet JM, Friedman SL. Carcinogen-Induced Hepatic Tumors in KLF6+/- Mice Recapitulate Aggressive Human Hepatocellular Carcinoma Associated with p53 Pathway Deregulation. HEPATOLOGY. 54:522-531. I.F.: 10.89.

2 Villanueva A, Hoshida Y, Battiston C, Tovar V, Sia D, Alsinet C, Cornella H, Liberzon A, Kobayashi M, Kumada H, Thung SN, Bruix J, Newell P, April C, Fan JB, Roayaie S, Mazzaferro V, Schwartz M, Llovet JM. Combining clinical; pathology; and gene expression data to predict recurrence of hepatocellular carcinoma. GASTROENTEROLOGY. 140:1501-15012. I.F.: 12.03.

3 Hessheimer A, Fondevila C, Taura P, Muñoz J, Sanchez O, Fuster J, Rimola A, Garcia-Valdecasas JC. Decompression of the portal bed and twice-baseline portal inflow are necessary for the functional recovery of a small-for size graft. ANN SURG. 253:1201-1210. I.F.: 7.47.

4 Poynard T, Munteanu M, Colombo M, Bruix J, Schiff E, Terg R, Flamm S, Moreno-Otero R, Carrilho F, Schmidt W, Berg T, Mcgarrity T, Heathcote EJ, Goncales F, Diago M, Craxi A, Silva M, Boparai N, Griffel L, Burroughs M, Brass C, Albrecht J. FibroTest is an independent predictor of virologic response in chronic hepatitis C patients retreated with pegylated interferon alfa-2b and ribavirin in the EPIC3 program. J HEPATOL. 54:227-235. I.F.: 9.33.

5 Minguez B, Hoshida Y, Villanueva A, Toffanin S, Cabellos L, Thung S, Mandeli J, Sia D, April C, Fan JB, Lachenmayer A, Savic R, Roayaie S, Mazzaferro V, Bruix J, Schwartz M, Friedman SL, Llovet JM. Gene-expression signature of vascular invasion in hepatocellular carcinoma. J HEPATOL. 55:1325-1331. I.F.: 9.33.

6 Rimola J, Ordas I, Rodriguez S, Garcia-Bosch O, Aceituno M, Llach J, Ayuso C, Ricart E, Panes J. Magnetic Resonance Imaging for Evaluation of Crohn's Disease: Validation of Parameters of Severity and Quantitative Index of Activity. INFLAMM BOWEL DIS. 17:1759-1768. I.F.: 4.61.

7 Bruix J, Poynard T, Colombo M, Schiff E, Burak K, Heathcote EJ, Berg T, Poo JL, Mello CB, Guenther R, Niederau C, Terg R, Bedossa P, Boparai N, Griffel LH, Burroughs M, Brass CA, Albrecht JK, Epic3Study GROUP. Maintenance therapy with peginterferon alfa-2b does not prevent hepatocellular carcinoma in cirrhotic patients with chronic hepatitis C. GASTROENTEROLOGY. 140:1990-1999. I.F.: 12.03.

8 Toffanin S, Hoshida Y, Lachenmayer A, Villanueva A, Cabellos L, Minguez B, Savic R, Ward SC, Thung S, Chiang DY, Alsinet C, Tovar V, Roayaie S, Schwartz M, Bruix J, Waxman S, Friedman SL, Golub T, Mazzaferro V, Llovet JM. MicroRNA-based classification of hepatocellular carcinoma and oncogenic role of miR-517a. GASTROENTEROLOGY. 140:1618-1628. I.F.: 12.03.

9 Caralt M, Marti J, Cortes J, Fondevila C, Bilbao I, Fuster J, Garcia-Valdecasas JC, Sapisochin G, Balsells J, Charco R. Outcome of patients following hepatic resection for metastatic cutaneous and ocular melanoma. J HEPATO-BIL-PAN SCI. 18:268-275. I.F.: 1.96.

10 Fondevila C, Hessheimer AJ, Flores E, Vendrell M, Munoz J, Escobar B, Calatayud D, Taura P, Fuster J, Garcia-Valdecasas JC. Step-by-Step Guide for a Simplified Model of Porcine Orthotopic Liver Transplant. J SURG RES. 167:E39-E45. I.F.: 2.24.

REVIEWS
I.F.: 33.81

1 Bruix J, Reig M, Rimola J, Forner A, Burrel M, Vilana R, Ayuso C. Clinical Decision Making and Research in Hepatocellular Carcinoma: Pivotal Role of Imaging Techniques. HEPATOLOGY. 54:2238-2244. I.F.: 10.89.

2 Bruix J, Sherman M. Management of Hepatocellular Carcinoma: An Update. HEPATOLOGY. 53:1020-1022. I.F.: 10.89.

3 Villanueva A, Llovet JM. Targeted therapies for hepatocellular carcinoma. GASTROENTEROLOGY. 140:1410-1426. I.F.: 12.03.

EDITORIALS
I.F.: 49.65

1 Tremosini S, Bruix J. Diagnosis of early hepatocellular carcinoma: ideal goal, but not yet there. GASTROENTEROLOGY. 140:358-360. I.F.: 12.03.

2 Villanueva A, Hoshida Y, Llovet JM. Hepatocellular carcinoma enters the sequencing era. GASTROENTEROLOGY. 141:1943-1945. I.F.: 12.03.

3 Bruix J. Liver Cancer: Still a Long Way To Go. HEPATOLOGY. 54:1-2. I.F.: 10.89.

4 Sherman M, Llovet JM. Smoking, Hepatitis B Virus Infection, and Development of Hepatocellular Carcinoma. J NATL CANCER I. 103:1642-1643. I.F.: 14.70.

GRANTS FOR RESEARCH IN PROGRESS

Bruix J. Identificación y caracterización de la población de células madre adultas tumorales en líneas celulares derivadas de carcinoma hepatocelular humano. Sponsored by: Fondo de Investigación Sanitaria, PI080146. Duration: 01/01/2009-30/12/2012.

Bruix J. Grup de Recerca Consolidat – Oncologia Hepàtica – Barcelona Clinic Liver Cancer (BCLC). Sponsored by: Generaliat de Catalunya, AGAUR, SGR 1100. Duration: 15/09/2009-31/12/2012.

Llovet JM. Grup de Recerca Singular- Recerca Translacional en Oncologia Hepàtica. Sponsored by: Generaliat de Catalunya, AGAUR, SGR 1186. Duration: 22/07/2010-31/12/2013.

Llovet JM. AACR-Landon INNOVATION Award for International Collaborations AACR Annual Meeting, Denver, USA. Sponsored by: American Association for Cancer Research. Duration: 01/06/2009-01/06/2011.

Llovet JM. Genomic predictors and oncogenic drivers in hepatocellular carcinoma. Sponsored by: European Comission, FP7-2010 Health HEPTROMIC. Proposal nº: 259744 - 2. Duration: 01/11/2011-30/10/2013.

Llovet JM. Oncogenic addiction and gatekeepper genes in hepatocellular carcinoma. Sponsored by: American Association for Cancer Research, 09-60-27-LLOV. Duration: 01/07/2009-30/06/2011.

Llovet JM. Integrative genomic análisis of human intrahepatic cholangiocarcinoma. Sponsored by: Fundación Científica Española Contra el Cancer, GCA110347LLOV. Duration: 01/09/2011-31/08/2016.

Llovet JM. Predictores genómicos pronósticos y nuevas dianas moleculares en carcinoma hepático. Sponsored by: Ministerio de Ciencia e Innovación, SAF-2010-16055. Duration: 01/01/2011-31/12/2013.

DOCTORAL THESES

Fuster J. La combinación de diferentes criterios anatomopatológicos potencia la efectividad pronóstica de la afectación ganglionar en el cáncer gástrico. PhD student: J. Osorio, Universitat de Barcelona.

AREA 3

Clinical and experimental neuroscience

Liver hemodynamics and portal hypertension. Digestive bleeding secondary to ruptured esophageal varicose veins

TEAM INVOLVED IN: ciberehd

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Maeva Guillaume (Aide Jeunes Chercheurs)
Dinesh Mani Tripathi (ACI-COLABORA 2009-0938)
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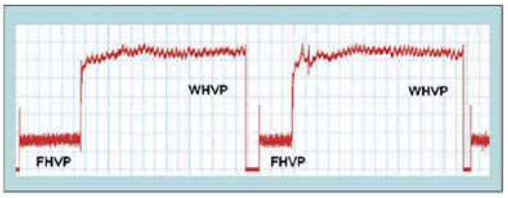
STRATEGIC OBJECTIVES

The gaining of in-depth knowledge of the mechanisms underlying portal hypertension – the main complication of liver diseases – and development of new treatments for this syndrome, and new noninvasive assessment techniques.

MAIN LINES OF RESEARCH

1. Factors regulating liver microcirculation under normal conditions and in cirrhosis, based on isolated liver perfusion studies and studies in liver sinusoid endothelial cells.
2. Post-transcriptional regulation of endothelial nitric oxide synthase (eNOS) activity. Relevance in the treatment of portal hypertension.
3. 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 cirrhosis complications.
4. Angiogenesis and portal hypertension: contribution to regulation of the development of collateral circulation, hyperdynamic circulation and liver fibrogenesis.
5. New noninvasive methods for evaluating cirrhosis.
6. Randomized clinical studies of novel treatments for portal hypertension.
7. Hepatic vascular diseases.
8. Prevention of decompensation of cirrhosis.
9. Discovery of response to treatment diagnostic biomarkers.
10. Role of sinusoidal endothelium in ischemia-reperfusion hepatic injury.



Tracing of liver venous pressure gradient.

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Liver hemodynamics and portal hypertension. Digestive bleeding secondary to ruptured esophageal varicose veins

RESEARCH GROUP
REGULATION OF LIVER MICROCIRCULATION IN CIRRHOSIS AND HEPATIC VASCULAR DISEASES

Group Leader:
Juan Carlos García-Pagán (Hospital Clínic)

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. Part of this increase is dynamic and amenable to modification by means of drugs. Therefore, improved knowledge based on experimental models in animals of the cellular, biochemical and molecular mechanisms regulating this dynamic component 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:
Mercè Fernadez Lobato (IDIBAPS)

We focus our research on the implication and regulation mechanisms of angiogenesis in the physiopathology of portal hypertension and liver cirrhosis. Our research project is also aimed to experimentally evaluate new therapeutic strategies to treat these diseases. Studies from our group in experimental models of portal hypertension and cirrhosis have shown that angiogenesis or the formation of new blood vessels is crucial to two of the most important components of the physiopathology of these diseases: the formation of portosystemic collateral vessels and the development of hyperdynamic splanchnic circulation. In addition, we found that angiogenesis is closely related to liver cirrhosis inflammation and fibrogenesis and contributes very significantly to the disease progression. These findings have turned the control of new blood vessels formation into a promising therapeutic target.
These studies may contribute valuable information with a view to improving our knowledge of the molecular and cellular mechanisms involved in the regulation of angiogenesis and implicated in the physiopathology of portal hypertension and chronic liver diseases – these being a leading cause of mortality and an important indication for liver transplantation both in this country and worldwide. Our aim is that our projects lead to the development of new therapeutic approaches designed to reduce the morbidity and mortality of patients diagnosed with these disorders.

PUBLICATIONS

ORIGINALS
I.F.: 161.36

1 Gimenez M, Gilabert R, Monteagudo J, Alonso A, Casamitjana R, Pare C, Conget I. Repeated Episodes of Hypoglycemia as a Potential Aggravating Factor for Preclinical Atherosclerosis in Subjects With Type 1 Diabetes. DIABETES CARE. 34:198-203. I.F.: 7.14.

2 Sala-Vila A, Cofan M, Nunez I, Gilabert R, Junyent M, Ros E. Carotid and femoral plaque burden is inversely associated with the alpha-linolenic acid proportion of serum phospholipids in Spanish subjects with primary dyslipidemia. ATHEROSCLEROSIS. 214:209-214. I.F.: 4.09.

3 Estruch R, Sacanella E, Mota F, Chiva-Blanch G, Antuneza E, Casals E, Deulofeu R, Rotilio D, Andres-Lacueva C, Lamuela-Raventos RM, DeGaetano G, Urbano-Marquez A. Moderate consumption of red wine, but not gin, decreases erythrocyte superoxide dismutase activity: A randomised cross-over trial. NUTR METAB CARDIOVAS. 21:46-53. I.F.: 3.44.

4 Balderramo D, Bordas JM, Sendino O, Abraldes JG, Navasa M, Llach J, Cardenas A. Complications after ERCP in liver transplant recipients. GASTROINTEST ENDOSC. 74:285-294. I.F.: 5.65.

5 Martin-Llahi M, Guevara M, Torre A, Fagundes C, Restuccia T, Gilabert R, Sola E, Pereira G, Marinelli M, Pavesi M, Fernandez J, Rodes J, Arroyo V, Gines P. Prognostic Importance of the Cause of Renal Failure

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	166.86	28	17	7
2010	211.11	30	19	4
2011	161.36	22	17	3

in Patients With Cirrhosis. GASTROENTEROLOGY. 140:488-U192. I.F.: 12.03.

6 Altamirano J, Higuera-DeLatijera F, Duarte-Rojo A, Martinez-Vazquez MA, Abraldes JG, Herrera-Jimenez LE, Michelena J, Zapata L, Perez-Hernandez J, Torre A, Gonzales-Gonzalez JA, Cardenas A, Dominguez M, Arroyo V, Gines P, Caballeria J, Bataller R. The Amount of Alcohol Consumption Negatively Impacts Short-Term Mortality in Mexican Patients With Alcoholic Hepatitis. AM J GASTROENTEROL. 106:1472-1480. I.F.: 6.88.

7 Nicolau C, Bunesch L, Peri L, Salvador R, Corral JM, Mallofre C, Sebastia C. Accuracy of contrast-enhanced ultrasound in the detection of bladder cancer. BRIT J RADIOL. 84:1091-1099. I.F.: 2.06.

8 Gracia-Sancho J, Russo L, Garcia-Caldero H, Garcia-Pagan JC, Garcia-Cardena G, Bosch J. Endothelial expression of transcription factor Kruppel-like factor 2 and its vasoprotective target genes in the normal and cirrhotic rat liver. GUT. 60:517-524. I.F.: 10.61.

9 Berzigotti A, Nicolau C, Bellot P, Abraldes JG, Gilabert R, Garcia-Pagan JC, Bosch J. Evaluation of regional hepatic perfusion (RHP) by contrast-enhanced ultrasound in patients with cirrhosis. J HEPATOL. 55:307-314. I.F.: 9.33.

10 Pasarin M, Abraldes JG, Rodriguez-Vilarrupla A, LaMura V, Garcia-Pagan JC, Bosch J. Insulin resistance and liver microcirculation in a rat model of early NAFLD. J HEPATOL. 55:1095-1102. I.F.: 9.33.

11 Berzigotti A, Ashkenazi E, Reverter E, Abraldes JG, Bosch J. Non-invasive diagnostic and prognostic evaluation of liver cirrhosis and portal hypertension. DIS MARKERS. 31:129-138. I.F.: 1.72.

12 Moize V, Deulofeu R, Torres F, DeOsaba JM, Vidal J. Nutritional Intake and Prevalence of Nutritional Deficiencies Prior to Surgery in a Spanish Morbidly Obese Population. OBES SURG. 21:1382-1388. I.F.: 3.08.

13 Berzigotti A, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Morillas R, Escorsell A, Garcia-Pagan JC, Patch D, Matloff DS, Groszmann RJ. Obesity Is an Independent Risk Factor for Clinical Decompensation in Patients with Cirrhosis. HEPATOLOGY. 54:555-561. I.F.: 10.89.

14 Pano B, Sebastia C, Bunesch L, Mestres J, Salvador R, Macias NG, Nicolau C. Pathways of Lymphatic Spread in Male Urogenital Pelvic Malignancies. RADIOGRAPHICS. 31:135-U204. I.F.: 2.76.

15 Llop E, DeJuan C, Seijo S, Garcia-Criado A, Abraldes JG, Bosch J, Garcia-Pagan JC. Portal cholangiopathy: radiological classification and natural history. GUT. 60:853-860. I.F.: 10.61.

16 Talens S, Hoekstra J, Dirkx SP, Murad SD, Trebicka J, Elias E, Primignani M, Garcia-Pagan JC, Valla DC, Janssen HL, Leebeek FW, Rijken DC, ForTheEn-VieStudy GROUP. Proteomic analysis reveals that apolipoprotein a1 levels are decreased in patients with budd-chiari syndrome. J HEPATOL. 54:908-914. I.F.: 9.33.

17 Nicolau C, Bunesch L, Sebastia C. Renal complex cysts in adults: contrast-enhanced ultrasound. ABDOM IMAGING. 36:742-752. I.F.: 1.95.

18 Bureau C, Metivier S, D'amico M, Peron JM, Otal P, Garcia-Pagan JC, Chabbert V, Chagneau-Derrode C, Procopet B, Rousseau H, Bosch J, Vinel JP. Serum bilirubin and platelet count: a simple predictive model for survival in patients with refractory ascites treated by TIPS. J HEPATOL. 54:901-907. I.F.: 9.33.

19 Luca A, Miraglia R, Caruso S, Milazzo M, Sapere C, Maruzzelli L, Vizzini G, Tuzzolino F, Gridelli B, Bosch J. Short- and long-term effects of the transjugular intrahepatic portosystemic shunt on portal vein thrombosis in patients with cirrhosis. GUT. 60:846-852. I.F.: 10.61.

20 Garcia-Caldero H, Rodriguez-Vilarrupla A, Gracia-Sancho J, Divi M, Lavina B, Bosch J, Garcia-Pagan JC. Tempol administration, a superoxide dismutase mimetic, reduces hepatic vascular resistance and portal pressure in cirrhotic rats. J HEPATOL. 54:660-665. I.F.: 9.33.

21 Smalberg JH, Koehler E, Murad SD, Plessier A, Seijo S, Trebicka J, Primignani M, DeMaat MPM, Garcia-Pagan JC, Valla DC, Janssen HLA, Leebeek FWG. The JAK2 46/1 haplotype in Budd-Chiari syndrome and portal vein thrombosis. BLOOD. 117:3968-3973. I.F.: 10.56.

22 LaMura V, Reverter JC, Flores-Arroyo A, Raffa S, Reverter E, Seijo S, Abraldes JG, Bosch J, Garcia-Pagan JC. Von Willebrand factor levels predict clinical outcome in patients with cirrhosis and portal hypertension. GUT. 60:1133-1138. I.F.: 10.61.

REVIEWS
I.F.: 11.40

1 Schouten JNL, Garcia-Pagan JC, Valla DC, Janssen HLA. Idiopathic Noncirrhotic Portal Hypertension. HEPATOLOGY. 54:1071-1081. I.F.: 10.89.

2 Escorsell A, Bosch J. Self-Expandable Metal Stents in the Treatment of Acute Esophageal Variceal Bleeding. GASTROENT RES PRACT.:-. I.F.: 0.51.

EDITORIALS
I.F.: 13.89

1 Garcia-Pagan JC. PORTAL HYPERTENSION Nonselective beta-blockers in patients with refractory ascites. NAT REV GASTRO HEPAT. 8:10-11. I.F.: 4.56.

2 Bosch J. Soft technique, hard end-points. J HEPATOL. 55:955-956. I.F.: 9.33.

GRANTS FOR RESEARCH IN PROGRESS

González-Abraldes J. Insulino resistencia y disfunción endotelial sinusoidal en las hepatopatías crónicas. Mecanismos moleculares y significación clínica. Sponsored by: FIS, PI08/0193. Duration: 01/01/2009-30/12/2011.

Mercè Fernadez Lobato. Regulación de la angiogénesis en la hipertensión portal y la cirrosis hepática. Evaluación de nuevos enfoques terapéuticos. Sponsored by: Ministerio de Ciencia e Innovación, SAF2008-02461. Duration: 01/01/2009-31/01/2012.

Mercè Fernadez Lobato. Regulació de l'angiogènesi en la hipertensió portal. Avaluació de noves estratègies terapèutiques. Sponsored by: Fundació La Marató TV3, MARATO-081210. Duration: 01/01/2009-01/01/2012.

Escorsell A. Hemorragia por varices esofágicas: optimización del tratamiento en situaciones complejas. Sponsored by: Fondo de Investigaciones Sanitarias de la Seguridad Social, FIS PI 08/0504. Duration: 01/01/2009-31/12/2011.

Bosch J. Grup de Recerca Consolidat-AGAUR: Hemodinàmica Hepàtica i Hipertensió Protal". Sponsored by: Generalitat de Catalunya, AGAUR ,2009_SGR_1108. Duration: 01/01/2009-31/12/2013.

Bosch J. Mecanismos celulares y moleculares en la hipertensión portal no cirrótica. Sponsored by: Ministerio Ciencia e Innovación (FCCI-ACI-Colabora), ACI2009-0938. Duration: 01/12/2009-30/11/2012.

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: 01/01/2010-31/12/2013.

Bosch J. Asociación de estatinas al tratamiento estándar en la prevención de la recidiva hemorrágica en pacientes con cirrosis y hemorragia por varices. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-074. Duration: 01/01/2010-31/12/2011.

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 (PREDESCI). Sponsored by: Instituto de Salud Carlos III (ISCIII), EC08/00091. Duration: 01/01/2009-30/06/2013.

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 Ciencia e Innovación, CDTI, INNPACTO 2010. Duration: 01/01/2010-31/12/2012.

Garcia-Pagan JC. Caracterización y Manipulación de Nuevas Dianas Terapéuticas Involucradas en la Fisiopatología de la Hipertensión Portal en la Cirrosis. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-17043. Duration: 01/01/2010-31/12/2013.

Garcia-Pagan JC. Estudio aleatorizado, doble ciego, controlado con placebo, sobre los efectos de la 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: 01/01/2011-31/12/2012.

Nicolau C. Evaluación funcional de riñón trasplantado mediante ecografía con contraste. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/0198. Duration: 01/01/2009-31/12/2012.

DOCTORAL THESES

Bosch J, Gracia J. Papel del factor de transcripción Kruppel-like factor 2 en la disfunción endotelial hepática asociada a la hipertensión portal y al daño por isquemia y reperfusión. PhD student: Lucía Russo.

AREA 3

Liver, digestive system and metabolism

Inflammatory bowel disease (IBD)

TEAM INVOLVED IN: ciberehd

GROUP MEMBERS

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IDIBAPS MEMBERS:
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Josep M. Piqué (Hospital Clínic)
Azucena Salas (IDIBAPS)
Elena Ricart (Hospital Clínic)
Salvadora Delgado (Hospital Clínic)
Miquel Sans (IDIBAPS)

POSTDOCTORALS FELLOWS:
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Isabella Dotti (IDIBAPS)

RESEARCH FELLOWS:
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Raquel Cabezón (Fundació Clínic)
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COLLABORATORS:
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Orlando García (Hospital Clínic)
Ingrid Ordás (Hospital Clínic)
Daniel Benítez (CIBERehd)

STRATEGIC OBJECTIVES

This IDIBAPS research team has a translational orientation, aimed at generating knowledge to provide a direct benefit to patients in the near future.
The team's schedule includes three main strategic objectives:

- The development of new treatments for Crohn's disease and ulcerative colitis, focused on cell therapy 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.

Culture of intestinal fibroblasts. Vimentin positivity.

MAIN LINES OF RESEARCH

1. Hematopoietic stem cell autotransplantation in refractory Crohn's disease in conventional treatment and biological therapies. Characterization of host related 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 the production and administration of intestinal epithelium stem cells to be applied as a regenerative therapy in severe Crohn's disease and ulcerative colitis
4. Optimization of magnetic resonance imaging and ultrasound techniques with contrast injection, for evaluation of the extent, severity and prognosis of the inflammatory lesions in Crohn's disease and ulcerative colitis.
5. Characterization of the genetic factors determining susceptibility and phenotype in Crohn's disease and ulcerative colitis. Construction of diagnostic genetic chips.
6. Study of the environmental factors influencing susceptibility and the course of inflammatory bowel disease.

PUBLICATIONS

ORIGINALS
I.F.: 110.31

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	82.29	17	8	6
2010	115.79	19	8	4
2011	110.31	19	8	6

1 Balderramo D, Bordas JM, Sendino O, Abraldes JG, Navasa M, Llach J, Cardenas A. Complications after ERCP in liver transplant recipients. GASTROINTEST ENDOSC. 74:285-294. I.F.: 5.65.

2 Rimola J, Ordas I, Rodriguez S, Garcia-Bosch O, Aceituno M, Llach J, Ayuso C, Ricart E, Panes J. Magnetic Resonance Imaging for Evaluation of Crohn's Disease: Validation of Parameters of Severity and Quantitative Index of Activity. INFLAMM BOWEL DIS. 17:1759-1768. I.F.: 4.61.

3 Abuli A, Fernandez-Rozadilla C, Giraldez MD, Munoz J, Gonzalo V, Bessa X, Bujanda L, Rene JM, Lanas A, Garcia AM, Salo J, Arguello L, Vilella A, Carreno R, Jover R, Xicola RM, Llor X, Carvajal-Carmona L, Tomlinson IPM, Kerr DJ, Houlston RS, Pique JM, Carracedo A, Castells A, Andreu M, Ruiz-Ponte C, Castellvi-Bel S. A two-phase case-control study for colorectal cancer genetic susceptibility: candidate genes from chromosomal regions 9q22 and 3q22. BRIT J CANCER. 105:870-875. I.F.: 4.83.

4 Scholin J, Buunen M, Hop W, Bonjer J, Anderberg B, Cuesta M, Delgado S, Ibarzabal A, Ivarsson ML, Janson M, Lacy A, Lange J, Pahlman L, Skullman S, Haglind E. Bowel obstruction after laparoscopic and open colon resection for cancer: Results of 5 years of follow-up in a randomized trial. SURG ENDOSC. 25:3755-3760. I.F.: 3.44.

5 Abuli A, Fernandez-Rozadilla C, Alonso-Espinaco V, Munoz J, Gonzalo V, Bessa X, Gonzalez D, Clofent J, Cubiella J, Morillas JD, Rigau J, Latorre M, Fernandez-Banares F, Pena E, Riestra S, Paya A, Jover R, Xicola RM, Llor X, Carvajal-Carmona L, Villanueva CM, Moreno V, Pique JM, Carracedo A, Castells A, Andreu M, Ruiz-Ponte C, Castellvi-Bel S. Case-control study for colorectal cancer genetic susceptibility in EPICOLON: previously identified variants and mucins. BMC CANCER. 11:-. I.F.: 3.15.

6 Montoro MA, Brandt LJ, Santolaria S, Gomollon F, Puertolas BS, Vera J, Bujanda L, Cosme A, Cabriada JL, Duran M, Mata L, Santamaria A, Cena G, Blas JM, Ponce J, Ponce M, Rodrigo L, Ortiz J, Munoz C, Arozena G, Ginard D, Lopez-Serrano A, Castro M, Sans M, Campo R, Casalots A, Orive V, Loizate A, Tito L, Portabella E, Otazua P, Calvo M, Botella MT, Thomson C, Mundi JL, Quintero E, Nicolas D, Borda F, Martinez B, Gisbert JP, Chaparro M, Bernado AJ, Gomez-Camacho F, Cerezo A, Nunez EC. Clinical patterns and outcomes of ischaemic colitis: Results of the Working Group for the Study of Ischaemic Colitis in Spain (CIE study). SCAND J GASTROENTERO. 46:236-246. I.F.: 1.97.

7 Pariente B, Cosnes J, Danese S, Sandborn WJ, Lewin M, Fletcher JG, Chowers Y, D'haens G, Feagan BG, Hibi T, Hommes DW, Irvine EJ, Kamm MA, LoftusEv JR, Louis E, Michetti P, Munkholm P, Oresland T, Panes J, Peyrin-Biroulet L, Reinisch W, Sands BE, Schoelmerich J, Schreiber S, Tilg H, Travis S, VanAssche G, Vecchi M, Mary JY, Colombel JF, Lemann M. Development of the Crohn's disease digestive damage score, the Lémann score. INFLAMM BOWEL DIS. 17:1415-1422. I.F.: 4.61.

8 Fernandez-Esparrach G, Cordova H, Bordas JM, Gomez-Molins I, Gines A, Pellise M, Sendino O, Gonzalez-Suarez B, Cardenas A, Balderramo D, Lacy AM, Delgado S, Llach J. Endoscopic management of the complications of bariatric surgery. Experience of more than 400 interventions. HEPATO-GASTROENTEROL. 34:131-136. I.F.: 0.68.

9 Fernandez-Esparrach G, Ayuso-Colella JR, Sendino O, Pages M, Cuatrecasas M, Pellise M, Maurel J, Ayuso-Colella C, Gonzalez-Suarez B, Llach J, Castells A, Gines A. EUS and magnetic resonance imaging in the staging of rectal cancer: a prospective and comparative study. GASTROINTEST ENDOSC. 74:347-354. I.F.: 5.65.

10 Chaparro M, Panes J, Garcia V, Manosa M, Esteve M, Merino O, Andreu M, Gutierrez A, Gomollon F, Cabriada JL, Montoro MA, Mendoza JL, Nos P, Gisbert JP. Long-term durability of infliximab treatment in Crohn's disease and efficacy of dose "escalation" in patients losing response. J CLIN GASTROENTEROL. 45:113-118. I.F.: 2.75.

11 Caldelari ACA, Miquel R, Bombi JA, Gines A, Fernandez-Esparrach G, Ayuso JR, Maurel J, Feu F, Castells A, Fernandez-Cruz L, Navarro S. Malignancy predictive factors in pancreatic intraductal papillary mucinous neoplasm. MED CLIN-BARCELONA. 137:631-636. I.F.: 1.41.

12 Buchanan J, Wordsworth S, Ahmad T, Perrin A, Vermeire S, Sans M, Taylor J, Jewell D. Managing the long term care of inflammatory bowel disease patients: The cost to European health care providers. J CROHNS COLITIS. 5:301-316. I.F.: 2.63.

13 Anderson CA, Boucher G, Lees CW, Franke A, D'amato M, Taylor KD, Lee JC, Goyette P, Imielinski M, Latiano A, Lagace C, Scott R, Amininejad L, Bumpstead S, Baidoo L, Baldassano RN, Barclay M, Bayless TM, Brand S, Buning C, Colombel JF, Denson LA, DeVos M, Dubinsky M, Edwards C, Ellinghaus D, Fehrmann RSN, Floyd JAB, Florin T, Franchimont D, Franke L, Georges M, Glas J, Glazer NL, Guthery SL, Haritunians T, Hayward NK, Hugot JP, Jobin G, Laukens D, Lawrance I, Lemann M, Levine A, Libioulle C, Louis E, Mcgovern DP, Milla M, Montgomery GW, Morley KI, Mowat C, Ng A, Newman W, Ophoff RA, Papi L, Palmieri O, Peyrin-Biroulet L, Panes J, Phillips A, Prescott NJ, Proctor DD, Roberts R, Russell R, Rutgeerts P, Sanderson J, Sans M, Schumm P, Seibold F, Sharma Y, Simms LA, Seielstad M, Steinhart AH, Targan SR, VanDenBerg LH, Vatn M, Verspaget H, Walters T, Wijmenga C, Wilson DC, Westra HJ, Xavier RJ, Zhao ZZ, Ponsioen CY, Andersen V, Torkvist L, Gazouli M, Anagnou NP, Karlsen TH, Kupcinskas L, Sventoraityte J, Mansfield JC, Kugathasan S, Silverberg MS, Halfvarson J, Rotter JI, Mathew CG, Griffiths AM, Gearry R, Ahmad T, Brant SR, Chamaillard M, Satsangi J, Cho JH, Schreiber S, Daly MJ, Barrett JC, Parkes M, Annese V, Hakonarson H, Radford-Smith G, Duerr RH, Vermeire S, Weersma RK, Rioux JD. Meta-analysis identifies 29 additional ulcerative colitis risk loci, increasing the number of confirmed associations to 47. NAT GENET. 43:246-U94. I.F.: 36.38.

14 Garcia-Iglesias P, Villoria A, Suarez D, Brullet E, Gallach M, Feu F, Gisbert JP, Barkun A, Calvet X. Meta-analysis: predictors of rebleeding after endoscopic treatment for bleeding peptic ulcer. ALIMENT PHARM THER. 34:888-900. I.F.: 3.86.

15 Pellise M, Lopez-Ceron M, DeMiguel CR, Jimeno M, Zabalza M, Ricart E, Aceituno M, Fernandez-Esparrach G, Gines A, Sendino O, Cuatrecasas M, Llach J, Panes J. Narrow-band imaging as an alternative to chromoendoscopy for the detection of dysplasia in long-standing inflammatory bowel disease: a prospective, randomized, crossover study. GASTROINTEST ENDOSC. 74:840-848. I.F.: 5.65.

16 Luna J, Masamunt MC, Llach J, Delgado S, Sans M. Palm oil tocotrienol rich fraction reduces extracellular matrix production by inhibiting transforming growth factor-beta 1 in human intestinal fibroblasts. CLIN NUTR. 30:858-864. I.F.: 3.41.

17 Angulo S, Morales A, Danese S, Llacuna L, Masamunt MC, Pultz N, Cifone MG, DeSimone C, Delgado S, Vila J, Panes J, Donskey C, Fernandez-Checa JC, Fiocchi C, Sans M. Probiotic sonicates selectively induce mucosal immune cells apoptosis through ceramide generation via neutral sphingomyelinase. PLOS ONE. 6:e16953-. I.F.: 4.41.

18 Vermeire S, Ghosh S, Panes J, Dahlerup JF, Luegering A, Sirotiakova J, Strauch U, Burgess G, Spanton J, Martin SW, Niezychowski W. The mucosal addressin cell adhesion molecule antibody PF-00547,659 in ulcerative colitis: a randomised study. GUT. 60:1068-1075. I.F.: 10.61.

19 Luna J, Masamunt MC, Rickmann M, Mora R, Espana C, Delgado S, Llach J, Vaquero E, Sans M. Tocotrienols Have Potent Antifibrogenic Effects in Human Intestinal Fibroblasts. INFLAMM BOWEL DIS. 17:732-741. I.F.: 4.61.

REVIEWS
I.F.: 31.78

1 Sanchez-Delgado J, Gene E, Suarez D, Garcia-Iglesias P, Brullet E, Gallach M, Feu F, Gisbert JP, Calvet X. Has H. pylori Prevalence in Bleeding Peptic Ulcer Been Underestimated? A Meta-Regression. AM J GASTROENTEROL. 106:398-405. I.F.: 6.88.

2 Jauregui-Amezaga A, Ricart E, Panes J. Lessons to Learn from Crohn's Disease Clinical Trials: Implications for Ulcerative Colitis. CURR DRUG TARGETS. 12:1467-1477. I.F.: 3.06.

3 Rieder F, Lawrance IC, Leite A, Sans M. Predictors of Fibrostenotic Crohn's Disease. INFLAMM BOWEL DIS. 17:2000-2007. I.F.: 4.61.

4 Daperno M, Castiglione F, DeRidder L, Dotan I, Farkkila M, Florholmen J, Fraser G, Fries W, Hebuterne X, Lakatos PL, Panes J, Rimola J, Louis E. Results of the 2nd part Scientific Workshop of the ECCO (II): Measures and markers of prediction to achieve, detect, and monitor intestinal healing in Inflammatory Bowel Disease. J CROHNS COLITIS. 5:484-498. I.F.: 2.63.

5 Travis SPL, Higgins PDR, Orchard T, VanDerWoude CJ, Panaccione R, Bitton A, O'morain C, Panes J, Sturm A, Reinisch W, Kamm MA, D'haens G. Review article: defining remission in ulcerative colitis. ALIMENT PHARM THER. 34:113-124. I.F.: 3.86.

6 Panes J, Bouzas R, Chaparro M, Garcia-Sanchez V, Gisbert JP, DeGuerenu BM, Mendoza JL, Paredes JM, Quiroga S, Ripolles T, Rimola J. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn›s disease. ALIMENT PHARM THER. 34:125-145. I.F.: 3.86.

7 VanAssche G, Lewis JD, Lichtenstein GR, Loftus EV, Ouyang Q, Panes J, Siegel CA, Sandborn WJ, Travis SPL, Colombel JF. The London Position Statement of the World Congress of Gastroenterology on Biological Therapy for IBD With the European Crohn›s and Colitis Organisation: Safety. AM J GASTROENTEROL. 106:1594-1602. I.F.: 6.88.

EDITORIALS
I.F.: 34.67

1 Pellise M, Panes J. Confocal endomicroscopy in celiac disease. GASTROENTEROLOGY. 140:1097-1099. I.F.: 12.03.

2 Panes J, Benitez-Ribas D, Salas A. Mesenchymal stem cell therapy of Crohn's disease: are the far-away hills getting closer?. GUT. 60:742-744. I.F.: 10.61.

3 Fernandez-Esparrach G, Panes J. Radiofrequency ablation for nondysplastic Barrett's esophagus: to treat or not to treat?. GASTROENTEROLOGY. 140:2130-2132. I.F.: 12.03.

GRANTS FOR RESEARCH IN PROGRESS

Salas A. New mediators of T effector responses and therapeutic potential of administration of tolerogenic dendritic cells in inflammatory bowel disease. Sponsored by: Ministerio de Ciencia e Innovación, BFU2008-02683/BFI . Duration: 31/12/2008-31/12/2011.

Panes J. Terapia con células dendríticas tolerogénicas en la enfermedad de Crohn refractaria. Sponsored by: Ministerio de Innovación y Ciencia, SAF2009_07272. Duration: 01/01/2010-31/12/2012.

Sans M. ECCO Fellowship 2010 Agreement. Prize awarded to Dr. Sans for ECCO's interest in supporting future research in the field of "Molecular determinations of homing of stem cells in IBD". Sponsored by: European Crohn's & Colitis Organisation ECCO, 10/311. Duration: 09/09/2010-09/09/2011.

Panes J. Tratamiento de la enfermedad de Crohn refractaria con células dendríticas reguladoras: estudio piloto. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-097. Duration: 01/01/2010-31/12/2011.

Sans M. Estudio de los principales determinantes moleculares implicados en la fibrosis intestinal en la enfermedad de Crohn. Evaluación de estrategias de tratamiento anti-fibrogénico. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-18434. Duration: 01/01/2011-31/12/2012.

Panes J. Malaltia Inflamatòria Intestinal. Sponsored by: Generalitat de Catalunya, AGAUR, 2009_SGR_1206. Duration: 15/09/2009-31/12/2013.

Salas A. Delivering nanopharmaceuticals through BIological Barriers (BIBA). Sponsored by: Ministerio de Economía y Conocimiento. ERANET, Euro Nano Med, PI10/02998. Duration: 01/01/2011-31/12/2013.

AREA 3

Liver, digestive system and metabolism

Cholestasis and bone pathology

TEAM INVOLVED IN: ciberehd

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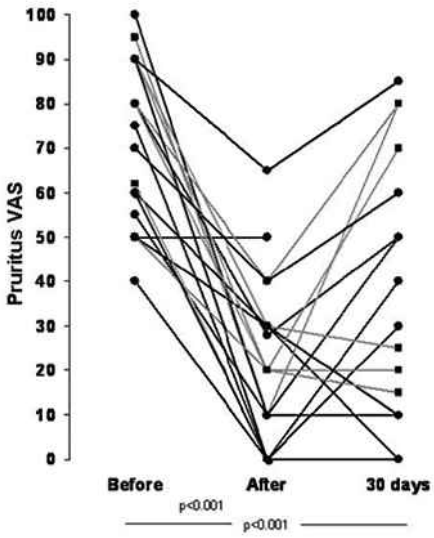
Àngels Martinez-Ferrer (Hospital Clínic)
Silvia Ruiz-Gaspá (CIBERehd)

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.



Effect of dialysis with albumin (MARS) on pruritus in patients with chronic cholestasis. VAS: visual analogue scale.

RESEARCH GROUP
CHOLESTASIS

Group Leader:
Albert Pares (Hospital Clínic)

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. Relevance of the anionic exchanger AE2.
4. Diagnosis of autoimmune hepatitis. Development of a new diagnostic procedure for autoimmune hepatitis, based on peptide mapping – a project conducted in collaboration with 6 centers in Europe and one in Israel.
5. Pruritus in chronic cholestasis and treatment response to albumin dialysis: proteomic analysis. Evaluation of treatment response based on albumin dialysis in patients with chronic cholestasis and refractory pruritus, and identification of the eliminated peptides and proteins using MARS.
6. Pathogenesis of osteoporosis and fracture development in primary biliary cirrhosis and other chronic cholestatic disorders. In collaboration with the Bone Metabolic Diseases group, evaluation of the factors underlying fractures in primary biliary cirrhosis, and the proposal of new therapeutic modalities for increasing bone mass. Likewise, investigation is conducted into the repercussion of retained bile acids and bilirubin in cholestasis upon the development of bone disease.
7. Artificial liver support. Evaluation of the safety and efficacy of different bioartificial liver and hepatic support systems in treating acute liver failure and exacerbated chronic liver failure. An open-label, prospective randomized study versus conventional treatment involving cryopreserved human hepatocytes from organs not apt for transplantation.

RESEARCH GROUP
BONE METABOLIC DISEASE

Group Leader:
Núria Guañabens (Hospital Clínic)

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 low development of bone mass and the appearance of fractures, and proposal of new therapeutic protocols. In addition, evaluation of the effect of bilirubin and bile acids upon primary osteoblasts in culture.
3. Osteoporosis in liver transplantation. Evaluation of the hormonal changes regulating bone remodeling in this pathology.
4. Analysis of the efficacy of vertebroplasty. Evaluation of the clinical usefulness and the complications of this procedure in the treatment of pain secondary to recent vertebral fracture due to osteoporosis.
5. Evaluation of bone remodeling regulators. Evaluation of the role of sclerostin and, through this protein, investigation of the influence of osteocytes upon bone loss associated with glucocorticoid treatment and immobilization.

PUBLICATIONS

ORIGINALS
I.F.: 36.73

1 Ruiz-Gaspa S, Martinez-Ferrer A, Guanabens N, Dubreuil M, Peris P, Enjuanes A, DeOsaba MJM, Alvarez L, Monegal A, Combalia A, Pares A. Effects of Bilirubin and Sera from Jaundiced Patients on Osteoblasts: Contribution to the Development of Osteoporosis in Liver Diseases. HEPATOLOGY. 54:2104-2113. I.F.: 10.89.

2 Gay M, Pares A, Carrascal M, Bosch-I-Crespo P, Gorga M, Mas A, Abian J. Proteomic Analysis of Polypeptides Captured from Blood during Extracorporeal Albumin Dialysis in Patients with Cholestasis and Resistant Pruritus. PLOS ONE. 6:-. I.F.: 4.41.

3 Cosman F, Eriksen EF, Recknor C, Miller PD, Guanabens N, Kasperk C, Papanastasiou P, Readie A, Rao H, Gasser JA, Bucci-Rechtweg C, Boonen S. Effects of intravenous zoledronic acid plus subcutaneous teriparatide [rhPTH(1-34)] in postmenopausal osteoporosis. J BONE MINER RES. 26:503-511. I.F.: 7.06.

4 Torregrosa JV, Fuster D, Monegal A, Gentil MA, Bravo J, Guirado L, Muxi A, Cubero J. Efficacy of low doses of pamidronate in osteopenic patients administered in the early post-renal transplant. OSTEOPOROSIS INT. 22:281-287. I.F.: 4.86.

5 Cerda D, Peris P, Monegal A, Albaladejo C, DeOsaba MJM, Suris X, Guanabens N. Increase of PTH in post-menopausal osteoporosis. REV CLIN ESP. 211:338-343. I.F.: 0.76.

6 Gifre L, Peris P, Monegal A, MartinezDeOsaba MJ, Alvarez L, Guañabens N. Osteomalacia revisited: a report on 28 cases. CLIN RHEUMATOL. 30:639-645. I.F.: 1.69.

7 Sabate M, Ibanez L, Perez E, Vidal X, Buti M, Xiol X, Mas A, Guarner C, Forne M, Sola R, Castellote J, Rigau J, Laporte JR. Paracetamol in therapeutic dosages and acute liver injury: causality assessment in a prospective case series. BMC GASTROENTEROL. 11:-. I.F.: 2.47.

8 Peris P, Torra M, Olivares V, Reyes R, Monegal A, Martinez-Ferrer A, Guañabens N. Prolonged bisphosphonate release after treatment in women with osteoporosis. Relationship with bone turnover. BONE. 49:706-709. I.F.: 4.60.

REVIEWS
I.F.: 3.22

1 Ruiz-Esquide V, Peris P, Gifre L, Guanabens N. Abnormalities of bone metabolism in bariatric surgery. MED CLIN-BARCELONA. 136:215-221. I.F.: 1.41.

2 Pares A. Acute Alcoholic Hepatitis. REV ESP ENFERM DIG. 103:597-597. I.F.: 1.13.

3 Guañabens N, Pares A. Management of osteoporosis in liver disease. HEPATO-GASTROENTEROL. 35:438-445. I.F.: 0.68.

GRANTS FOR RESEARCH IN PROGRESS

Pares A. Enfermedades hepáticas autoinmunes. Nuevos procedimientos diagnósticos mediante mapeo peptídico. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI07/1318E (E-RARE). Duration: 01/01/2008-30/06/2011.

Pares A. Prurito de la colestasis: fisiopatología y análisis proteómico. Sponsored by: Ministerio de Ciencia y Tecnología, SAF200804012. Duration: 01/01/2009-31/12/2011.

Guañabens N. Influencia de la bilirrubina y los ácidos biliares sobre la formación ósea. Estudio "in vitro" en osteoblastos humanos. Sponsored by: Ministerio de Sanidad y Consumo, PI080105. Duration: 01/01/2009-30/12/2011.

Peris P. Efecte de la vertebroplastia percutània en la qualitat de vida dels pacients amb dolor relacionat amb fractures vertrebals osteoporòtiques. Comparació amb el tractament conservador. Sponsored by: Fundació La Marató de TV3 ,071710. Duration: 13/02/2008-30/08/2011.

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, Marató TV3. Duration: 01/01/2011-31/12/2013.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	34.85	9	2	2
2010	59.69	13	7	1
2011	36.73	8	5	1

DOCTORAL THESES

Pares A. Prevalença i factors associats a la presència d'esteatosi hepàtica no alcohòlica en la població general. PhD student: Maria Antònia Auladell Llorens, Universitat de Barcelona.

Guañabens N. Osteoporosis en la mujer posmenopáusica. Riesgo de Fractura en la enfermedad colestásica y prevalencia de otros procesos asociados. PhD student: Dacia Cerdà Gabaroi, Universitat de Barcelona.

AREA 3

Clinical and experimental neuroscience

Mitochondrial regulation of cell death and steatohepatitis

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TEAM INVOLVED IN: ciberehd

STRATEGIC OBJECTIVES

1. Determination of intracellular signalling and the role of mitochondria in cell susceptibility in inflammation, hypoxia and chemotherapy, and their relevance in relation to (hepato) carcinogenesis.
2. Determination of the mechanisms behind cholesterol and sphingolipid participation in hepatocellular death in different disorders such as non-alcoholic steatohepatitis (NASH) or ischaemia/reperfusion damage.
3. Analysis of the role of free cholesterol in patients with non-alcoholic steatohepatitis.
4. Contribution of the physicochemical properties of the mitochondrial membrane in cell death.

MAIN LINES OF RESEARCH

1. Ischaemia-reperfusion hepatocellular damage mechanisms and their regulation based on antioxidant and anti-inflammatory strategies. (Dr Fernández-Checa).
2. Sphingolipid and mitochondrial oxidative-stress regulation of cell death (Dr Fernández-Checa).
3. Mechanisms responsible for cholesterol transport to the mitochondria (Dr Fernández-Checa).
4. Role of cholesterol in hepatocellular carcinoma response to chemotherapy (Dr Fernández-Checa).
5. Development of non-invasive diagnostic methods for diagnosis and prognosis in alcohol-induced liver disease (Dr J. Caballería).

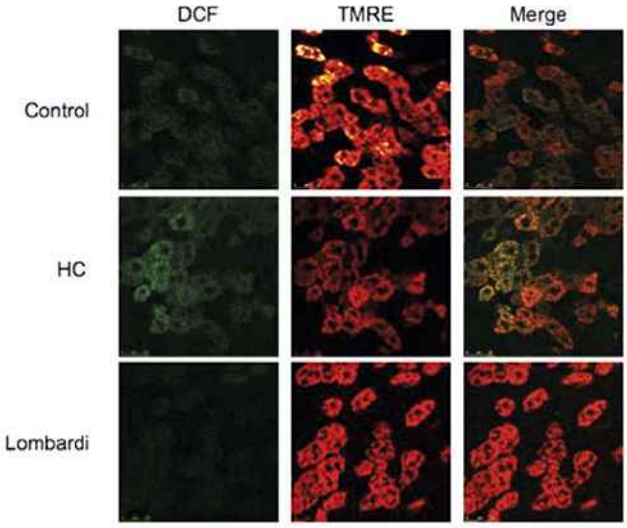

Figure 6. Von Montfort C, Matias N, unpublished observations

In vivo analysis of the liver production of reactive oxygen species (ROS) of mitochondrial origin based on two-photon confocal microscopy. The induction of nutritional liver steatosis was carried out by administering a high-cholesterol (HC) diet or a choline-deficient diet (Lombarda) during 48 hours. The administration of DCF and TMRE was carried out via the portal vein, examining the fluorescence emission of both probes in intact liver in vivo with two-photon confocal microscopy.

6. Regulation of cholesterol homeostasis in patients and experimental models of non-alcoholic steatohepatitis (Dr C. García-Ruiz).
7. Contribution of sphingolipids to non-alcoholic steatohepatitis and resistance to insulin therapy (Dr C. García-Ruiz).
8. Parenchyma-stroma interaction in cancer-related and ischaemia/reperfusion-induced liver damage: lipid therapies (Dr A. Morales)
9. Role of cholesterol and the mitochondria in Alzheimer's Disease (Dr A. Colell)
10. Contribution of the TNF and cathepsin receptors to fibrosis and inflammation of the liver (Dr M. Marí).

Three lines in which we have obtained important results are:

1. **Caveolin-1 deficiency causes cholesterol-dependent mitochondrial dysfunction and susceptibility to apoptosis.**
Our study demonstrates an unconventional function of caveolin-1 both in vivo and in vitro. Caveolins are essential components of caveolae. Caveolin-1 (CAV-1) is found on the plasma membrane as a scaffold protein organising the activity of multiple signalling molecules in caveolae. CAV-1 exhibits binding properties towards fatty acids and cholesterol and thus plays a role in regulating lipid homeostasis and transport. A lack of CAV-1 in humans and mice is associated with many disorders, including cardiovascular disease, lipodystrophy, diabetes, cancer and pulmonary fibrosis, but the underlying mechanisms behind this relationship remain unknown. In this study we have characterised an unconventional function of CAV-1, the regulation of mitochondrial function and metabolism. In the absence of CAV-1, mitochondrial function is lost due to an accumulation of cholesterol which leads to impaired oxidative phosphorylation, reduced membrane dynamics and consequently, diminished antioxidant defence due to mitochondrial GSH depletion. Under conditions of high metabolic flux requiring energy production, the failure of the mitochondria to meet the demand for energy results in high production of reactive oxygen species causing cell death. Consequently, CAV-1 deficiency leads to mitochondrial dysfunction-related conditions such as steatohepatitis and neurodegeneration.

2. **Intervention on cholesterol protects the fatty liver against ischaemia/reperfusion injury.**
Taking action against cholesterol, the accumulation of which in the mitochondria of fatty livers in humans correlates with graft failure, could be an effective way of increasing the number of organs available for transplant. Hepatic steatosis increases ischaemia/reperfusion (I/R) injury and is considered to be one of the main causes of graft failure after liver transplant. Liver transplant is an effective treatment for both end-stage chronic liver disease and acute liver failure. The reduction in the number and quality of organs available for liver transplantation is a major problem and leads to the use of grafts of suboptimal quality which can compromise the success of the transplant. Our data indicate that both cholesterol and the transport of cholesterol to the mitochondria play a critical role in the susceptibility of the fatty liver to I/R injury and that intervention on cholesterol levels could provide a unique opportunity to improve liver transplantation.

3. **Contribution of TNF receptors to fibrosis of the liver.**
Fibrosis of the liver is the excessive accumulation of extracellular matrix proteins, such as collagen, that occurs in most types of chronic liver disease. Advanced fibrosis can lead to cirrhosis, liver failure and portal hypertension and often requires liver transplantation. Activated hepatic stellate cells (HSCs) have been identified as the major collagen-producing cell-type in the damaged liver. While the inflammatory cytokine TNF has been implicated in the progression of many chronic liver diseases leading to fibrosis, its role in fibrogenesis is the subject of debate and the specific contribution of TNF receptors to HSC activation has yet to be determined. In this study, using hepatic stellate cells (HSC) from wild-type (WT), TNF-receptor-1 (TNFR1) knockout, TNF-receptor-2 (TNFR2) knockout, or TNFR1/R2 double knockout (TNFR-DKO) mice, we show that loss of both TNF receptors reduced procollagen a1(I) expression, slowed down HSC proliferation and impaired PDGF-induced promitogenic signalling in HSC. Moreover, matrix metalloproteinase-9 (MMP-9) expression in HSCs was controlled by TNF through TNFR1 and in vivo liver damage and fibrosis following bile duct ligation was reduced in TNFR-DKO and TNFR1 knockout mice compared to wild-type mice. These results are indicative of a regulatory role for TNF in extracellular matrix remodelling and liver fibrosis, suggesting that targeting TNFR1 may be of benefit to attenuate liver fibrogenesis.

PUBLICATIONS

ORIGINALS
I.F.: 46.82

1 Altamirano J, Higuera-DeLatijera F, Duarte-Rojo A, Martinez-Vazquez MA, Abraldes JG, Herrera-Jimenez LE, Michelena J, Zapata L, Perez-Hernandez J, Torre A, Gonzales-Gonzalez JA, Cardenas A, Dominguez M, Arroyo V, Gines P, Caballeria J, Bataller R. The Amount of Alcohol Consumption Negatively Impacts Short-Term Mortality in Mexican Patients With Alcoholic Hepatitis. AM J GASTROENTEROL. 106:1472-1480. I.F.: 6.88.

2 Angulo S, Morales A, Danese S, Llacuna L, Masamunt MC, Pultz N, Cifone MG, DeSimone C, Delgado S, Vila J, Panes J, Donskey C, Fernandez-Checa JC, Fiocchi C, Sans M. Probiotic sonicates selectively induce mucosal immune cells apoptosis through ceramide generation via neutral sphingomyelinase. PLOS ONE. 6:e16953-. I.F.: 4.41.

3 Bosch M, Mari M, Herms A, Fernandez A, Fajardo A, Kassan A, Giralt A, Colell A, Balgoma D, Barbero E, Gonzalez-Moreno E, Matias N, Tebar F, Balsinde J, Camps M, Enrich C, Gross SP, Garcia-Ruiz C, Perez-Navarro E, Fernandez-Checa JC, Pol A. Caveolin-1 Deficiency Causes Cholesterol-Dependent Mitochondrial Dysfunction and Apoptotic Susceptibility. CURR BIOL. 21:681-686. I.F.: 10.03.

4 Tarrats N, Moles A, Morales A, Garcia-Ruiz C, Fernandez-Checa JC, Mari M. Critical Role of Tumor Necrosis Factor Receptor 1, but not 2, in Hepatic Stellate Cell Proliferation, Extracellular Matrix Remodeling, and Liver Fibrogenesis. HEPATOLOGY. 54:319-327. I.F.: 10.89.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	56.28	9	6	3
2010	70.69	10	8	0
2011	46.82	6	5	0

5 Bosch M, Mari M, Gross SP, Fernandez-Checa JC, Pol A. Mitochondrial Cholesterol: A Connection Between Caveolin, Metabolism, and Disease. TRAFFIC. 12:1483-1489. I.F.: 5.28.

6 Llacuna L, Fernandez A, Montfort CV, Matias N, Martinez L, Caballero F, Rimola A, Elena M, Morales A, Fernandez-Checa JC, Garcia-Ruiz C. Targeting cholesterol at different levels in the mevalonate pathway protects fatty liver against ischemia-reperfusion injury. J HEPATOL. 54:1002-1010. I.F.: 9.33.

REVIEWS
I.F.: 4.77

1 Garcia-Ruiz C, Mari M, Colell A, Morales A, Fernandez-Checa JC. Metabolic Therapy: Lessons from Liver Diseases. CURR PHARM DESIGN. 17:3933-3944. I.F.: 4.77.

GRANTS FOR RESEARCH IN PROGRESS

Garcia C. Papel de los esfingolipidos en la esteatohepatitis no alcohólica y resistencia a la insulina hepática. Sponsored by: Ministerio Educación y Ciencia, SAF2008-02199. Duration: 01/01/2009-31/12/2011.

García C. Papel de la ceramida y los esfingolípidos en la estetohepatitis. Sponsored by: Fundación de Investigación Médica Mútua Madrileña. Duration: 31/12/2008-30/12/2011.

Fernández-Checa JC. Mitochondrial USC-UCLA Research Center for Alcoholic Liver and Pancreatic Injury Research Project#1. Sponsored by: National Institute of Alcohol Abuse and Alcoholism (NIAAA -NIH), 5P50AA011999. Duration: 01/01/2007-31/12/2013.

Caballeria J. Desarrollo de métodos diagnósticos no invasivos para el diagnóstico y pronóstico de las enfermedades hepáticas inducidas por el alcohol. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/1164. Duration: 01/01/2010-31/12/2012.

Fernández-Checa JC. Mitocondria y cáncer: papel del colesterol, GSH y cardiolipina en la regulación de la permeabilización de la membrana mitocondrial y muerte celular. Sponsored by: Ministerio de Ciencia e Innovación, SAF2009-11417. Duration: 01/01/2010-31/12/2012.

Morales A. Interacción parénquima-estroma en patologías hepáticas asociadas al eje inflamación-cáncer e isquemia/reperfusión: implicaciones terapéuticas. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/00056. Duration: 01/01/2010-31/12/2012.

Mari M. Catepsinas en fibrosis hepática e inflamación. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI070193. Duration: 26/11/2007-31/03/2011.

Colell A. Regulacion mitocondrial de la citotoxicidad inducida por beta-amiloide. Sponsored by: Ministerio Educación y Ciencia, SAF2010-15760. Duration: 01/01/2011-31/12/2013.

Fernández-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: 01/05/2011-01/02/2014.

Fernández-Checa JC. From gut-derived inflammation to obesity-related liver disease. Sponsored by: European Commission, JTC_META_2011_001. Duration: 07/04/2011-06/04/2014.

DOCTORAL THESES

Fernandez-Checa JC, Gomez L. Hepatocyte growth factor and c-Met: Role of hypercholesterolemia and signal transduction. PhD student: Natalia Nuño Lambarri, Universidad Autónoma Metropolitana, Mexico DF.

AREA 3

Liver, digestive system and metabolism

Liver transplantation and graft viability

TEAM INVOLVED IN: ciberehd

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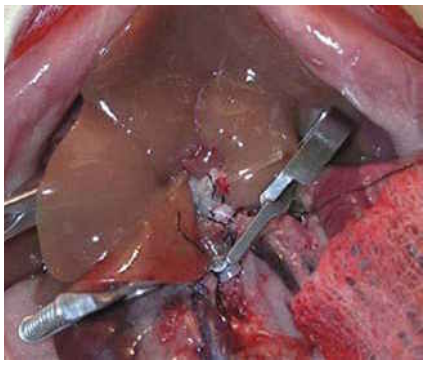
STRATEGIC OBJECTIVES

Investigation of clinical, mechanistic and therapeutic aspects of liver transplantation.

MAIN LINES OF RESEARCH

1. Ischemia-reperfusion liver damage in different models: warm ischemia; experimental liver transplantation in the rat with normal, reduced or steatosic grafts; experimental liver transplantation in the pig with whole or partial grafts, or grafts obtained from donors in asystolia; and liver transplantation in humans.
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.



Exprimental liver transplantation in the rat.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	76.07	19	14	1
2010	110.83	26	13	4
2011	69.84	16	10	2

ORIGINALS
I.F.: 69.84

1 Martinez-Rebollar M, Lonca M, Perez I, Soy D, Brunet M, Martin R, Coll O, Hernandez S, Laguno M, Milinkovic A, Larrousse M, Calvo M, Blanco JL, Martinez E, Gatell JM, Mallolas J. Pharmacokinetic Study of Saquinavir 500 mg Plus Ritonavir (1000/100 mg Twice a Day) in HIV-Positive Pregnant Women. THER DRUG MONIT. 33:772-777. I.F.: 3.13.

2 Lloberas N, Torras J, Cruzado JM, Andreu F, Oppenheimer F, Sanchez-Plumed J, Gentil MA, Brunet M, Ekberg H, Grinyo JM. Influence of MRP2 on MPA pharmacokinetics in renal transplant recipients-results of the Pharmacogenomic Substudy within the Symphony Study. NEPHROL DIAL TRANSPL. 26:3784-3793. I.F.: 3.56.

3 Dragun J, Perez-Del-Pulgar S, Crespo G, Ramirez S, Coto-Llerena M, Mensa L, Garcia-Valdecasas JC, Navasa M, Forns X. Characterization of the Cross-Neutralizing Antibody Response Against Hepatitis C Virus in the Liver Transplantation Setting. AM J TRANSPLANT. 11:767-774. I.F.: 6.05.

4 Hessheimer A, Fondevila C, Taura P, Muñoz J, Sanchez O, Fuster J, Rimola A, Garcia-Valdecasas JC. Decompression of the portal bed and twice-baseline portal inflow are necessary for the functional recovery of a small-for size graft. ANN SURG. 253:1201-1210. I.F.: 7.47.

5 Caralt M, Marti J, Cortes J, Fondevila C, Bilbao I, Fuster J, Garcia-Valdecasas JC, Sapisochin G, Balsells J, Charco R. Outcome of patients following hepatic resection for metastatic cutaneous and ocular melanoma. J HEPATO-BIL-PAN SCI. 18:268-275. I.F.: 1.96.

6 Fondevila C, Hessheimer AJ, Flores E, Vendrell M, Munoz J, Escobar B, Calatayud D, Taura P, Fuster J, Garcia-Valdecasas JC. Step-by-Step Guide for a Simplified Model of Porcine Orthotopic Liver Transplant. J SURG RES. 167:E39-E45. I.F.: 2.24.

7 Llacuna L, Fernandez A, Montfort CV, Matias N, Martinez L, Caballero F, Rimola A, Elena M, Morales A, Fernandez-Checa JC, Garcia-Ruiz C. Targeting cholesterol at different levels in the mevalonate pathway protects fatty liver against ischemia-reperfusion injury. J HEPATOL. 54:1002-1010. I.F.: 9.33.

8 Lozano JJ, Pallier A, Martinez-Llordella M, Danger R, Lopez M, Giral M, Londono MC, Rimola A, Soulillou JP, Brouard S, Sanchez-Fueyo A. Comparison of transcriptional and blood cell-phenotypic markers between operationally tolerant liver and kidney recipients. AM J TRANSPLANT. 11:1916-1926. I.F.: 6.05.

9 Jimenez-Castro MB, Casillas-Ramirez A, Massip-Salcedo M, Elias-Miro M, Serafin A, Rimola A, Rodes J, Peralta C. Cyclic Adenosine 3 ',5 '-Monophosphate in Rat Steatotic Liver Transplantation. LIVER TRANSPLANT. 17:1099-1110. I.F.: 3.07.

10 Rafael-Valdivia L, Mendoza MA, Martinez-Saldivar B, Sanchez-Fueyo A, Brunet M, Garcia-Valdecasas JC, Rimola A. How long should initiation of calcineurin inhibitors be delayed to protect renal function in liver transplantation?. TRANSPL P. 43:697-698. I.F.: 0.99.

11 Guillen D, Millan O, Brunet M. In vitro studies of the immunomodulatory effects of statins alone and in combination with immunosuppressive drugs. EUR J INFLAMM. 9:117-124. I.F.: 4.00.

12 Zaouali MA, Reiter RJ, Padrissa-Altes S, Boncompagni E, Garcia JJ, BenAbnennebi H, Freitas I, Garcia-Gil FA, Rosello-Catafau J. Melatonin protects steatotic and nonsteatotic liver grafts against cold ischemia and reperfusion injury. J PINEAL RES. 50:213-221. I.F.: 5.86.

13 Casillas-Ramirez A, Alfany-Fernandez I, Massip-Salcedo M, Juan ME, Planas JM, Serafin A, Pallas M, Rimola A, Rodes J, Peralta C. Retinol-Binding Protein 4 and Peroxisome Proliferator-Activated Receptor-gamma in Steatotic Liver Transplantation. J PHARMACOL EXP THER. 338:143-153. I.F.: 4.02.

14 Vidal O, Valentini M, Ginesta C, Espert JJ, Martinez A, Benarroch G, Anglada MT, Garcia-Valdecasas JC. Single-Incision Versus Standard Laparoscopic Cholecystectomy: Comparison of Surgical Outcomes from a Single Institution. J LAPAROENDOSC ADV S. 21:683-686. I.F.: 1.20.

15 Fondevila C, Hessheimer AJ, Maathuis MHJ, Munoz J, Taura P, Calatayud D, Leuvenink H, Rimola A, Ploeg RJ, Garcia-Valdecasas JC. Superior Preservation of DCD Livers With Continuous Normothermic Perfusion. ANN SURG. 254:1000-1007. I.F.: 7.47.

16 Vidal O, Ginesta C, Valentini M, Marti J, Benarroch G, Garcia-Valdecasas JC. Suprapubic single-incision laparoscopic appendectomy: a nonvisible-scar surgical option. SURG ENDOSC. 25:1019-1023. I.F.: 3.44.

REVIEWS
I.F.: 32.28

1 Trullas JC, Cofan F, Tuset M, Ricart MJ, Brunet M, Cervera C, Manzardo C, Lopez-Dieguez M, Oppenheimer F, Moreno A, Campistol JM, Miro JM. Renal transplantation in HIV-infected patients: 2010 update. KIDNEY INT. 79:825-842. I.F.: 6.11.

2 Elias-Miro M, Massip-Salcedo M, Jimenez-Castro M, Peralta C. Does adiponectin benefit steatotic liver transplantation?. LIVER TRANSPLANT. 17:993-1004. I.F.: 3.07.

3 Peralta C, Brenner C. Endoplasmic reticulum stress inhibition enhances liver tolerance to ischemia/reperfusion. CURR MED CHEM. 18:2016-2024. I.F.: 4.63.

4 Zaouali MA, BenAbdennebi H, Padrissa-Altes S, Alfany-Fernandez I, Rimola A, Rosello-Catafau J. How Institut Georges Lopez preservation solution protects nonsteatotic and steatotic livers against ischemia-reperfusion injury. TRANSPL P. 43:77-79. I.F.: 0.99.

5 BenAbdennebi H, Zaouali MA, Alfany-Fernandez I, Tabka D, Rosello-Catafau J. How to protect liver graft with nitric oxide. WORLD J GASTROENTERO. 17:2879-2889. I.F.: 2.24.

6 Sanchez-Fueyo A, Strom TB. Immunologic Basis of Graft Rejection and Tolerance Following Transplantation of Liver or Other Solid Organs. GASTROENTEROLOGY. 140:51-+. I.F.: 12.03.

7 Dominguez-Gil B, Delmonico FL, Shaheen FAM, Matesanz R, O'connor K, Minina M, Muller E, Young K, Manyalich M, Chapman J, Kirste G, Al-Mousawi M, Coene L, Garcia VD, Gautier S, Hasegawa T, Jha V, Kwek TK, Chen ZK, Loty B, Costa AN, Nathan HM, Ploeg R, Reznik O, Rosendale JD, Tibell A, Tsoulfas G, Vathsala A, Noel L. The critical pathway for deceased donation: reportable uniformity in the approach to deceased donation. TRANSPL INT. 24:373-378. I.F.: 3.21.

EDITORIALS
I.F.: 16.22

1 Garcia-Valdecasas JC. DCD donors: A unique source to significantly increase organ donation. J HEPATOL. 55:745-746. I.F.: 9.33.

2 Brandhorst G, Oellerich M, Brunet M, Kowalski R, Vinks A, Wallemacq P. Individually Tailored Immunosuppression: Is There a Role for Biomarkers?. CLIN CHEM. 57:376-381. I.F.: 6.89.

GRANTS FOR RESEARCH IN PROGRESS

Sanchez A. Métodos para inducir y diagnosticar la tolerancia inmunológica en el trasplante hepático. Sponsored by: Ministerio de Educación y Ciencia, SAF2008-04092. Duration: 01/01/2009-31/12/2011.

Sanchez A. Effect of rapamycin on tolerance biomarkers in liver transplantation. Sponsored by: Immune Tolerance Network (Consorcio financiado por el National Institute of Health, USA), Sirolimus Liver Tolerance, ITN10238-00SC. Duration: 01/12/2008-30/12/2011.

Fondevila C. Evaluación de la modificación farmacológica del flujo portal para prevenir la aparición del síndrome small-for-size en el transplante hepático en cerdos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080273. Duration: 01/01/2009-14/02/2012.

Brunet M. Estudio multicéntrico para la validación de los biomarcadores de elección que reflejen la respuesta individual de los pacientes trasplantados de órganos sólidos al tratamiento inmunosupresor. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080300. Duration: 01/01/2008-31/12/2011.

Peralta C. Una conservación acuosa para la conservación de órganos. Sponsored by: CIDEM, Generalitat de Catalunya, VALTEC08-2-0033. Duration: 31/10/2008-31/10/2011.

Manyalich M. European living donor psychosocial follow-up (ELIPSY). Sponsored by: Executive Agency for Health and Consumers (EAHC), European Commission, 20081104. Duration: 01/12/2009-30/11/2012.

Rimola A. Valor predictivo de parámetros inmunológicos pretrasplante del receptor y del donante en el desarrollo de rechazo e infección en el trasplante hepático. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0418. Duration: 01/01/2010-31/12/2012.

Peralta C. Regulación del RBP4 en trasplante de higados esteatósicos. Sponsored by: Ministerio de Educación, BFU2009_07410. Duration: 01/01/2010-31/12/2012.

Roselló J. Papel del proteasoma dependiente de la ubiquitina en la preservación del hígado graso frente a la lesión por isquemia-reperfusión. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI-081988. Duration: 01/01/2009-31/12/2011.

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: 01/01/2011-31/12/2013.

Peralta C. Preservació de l'empelt hepatic. Sponsored by: Generalitat de Catalunya, AGAUR, 2009_SGR_952. Duration: 22/07/2009-31/12/2013.

Sanchez A. Estudio piloto de retirada de la medicación inmunosupresora en pacientes que exhiben marcadores transcripcionales de alta probabilidad de tolerancia. Sponsored by: Fundación Mútua Madrileña, AP93762011. Duration: 16/09/2011-16/09/2013.

Sanchez A. Immunosuppression Withdrawal for Stable Pediatric Liver Transplant Recipient. Sponsored by: National Institutes of Health (NIH), 5813SC. Duration: 30/09/2009-31/08/2011.

DOCTORAL THESES

Brunet M. Estudio del efecto inmunomodulador de las estatinas. Estudios in vitro e in vivo. PhD student: David Guillen Tunica.

Peralta C. Papel diferencial de la Angiotensina II en resecciones hepáticas y trasplante de hígado. PhD student: Isabel Alfany Fernández.

Peralta C. Estrategias para proteger el injerto esteatósico en el trasplante hepático. PhD student: Arani Casillas Ramírez.

AREA 3

Liver, digestive system and metabolism

TEAM INVOLVED IN: ciberehd

Gastrointestinal and pancreatic oncology

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Laura Visa Turmo (Hospital Clínic)
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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 (IDIBAPS)

The Gene Therapy and Cancer Group led by Cristina Fillat started at the 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. Our 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:

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-modifiedmouse models and in orthotopicxenografts. Some of the animal models are specially designed to allow for the non-invasive imaging of tumor progression and metastatic processes.

PUBLICATIONS

ORIGINALS
I.F.: 206.49

1 Guarner-Argente C, Cordova H, Martinez-Palli G, Navarro-Ripoll R, Rodriguez-D'jesus A, DeMiguel CR, Beltran M, Fernandez-Esparrach G. Gastrotomy closure with a new tissue anchoring device: A porcine survival study. WORLD J GASTROENTERO. 17:1732-1738. I.F.: 2.24.

2 Guarner-Argente C, Beltran M, Martinez-Palli G, Navarro-Ripoll R, Martinez-Zamora MA, Cordova H, Comas J, DeMiguel CR, Rodriguez-D'jesus A, Almela M, Hernandez-Cera C, Lacy AM, Fernandez-Esparrach G. Infection during Natural Orifice Transluminal Endoscopic Surgery Peritoneoscopy: A Randomized Comparative Study in a Survival Porcine Model. J MINIM INVAS GYN. 18:741-746. I.F.: 1.56.

3 Abuli A, Fernandez-Rozadilla C, Giraldez MD, Munoz J, Gonzalo V, Bessa X, Bujanda L, Rene JM, Lanas A, Garcia AM, Salo J, Arguello L, Vilella A, Carreno R, Jover R, Xicola RM, Llor X, Carvajal-Carmona L, Tomlinson IPM, Kerr DJ, Houlston RS, Pique JM, Carracedo A, Castells A, Andreu M, Ruiz-Ponte C, Castellvi-Bel S. A two-phase case-control study for colorectal cancer genetic susceptibility: candidate genes from chromosomal regions 9q22 and 3q22. BRIT J CANCER. 105:870-875. I.F.: 4.83.

4 Scholin J, Buunen M, Hop W, Bonjer J, Anderberg B, Cuesta M, Delgado S, Ibarzabal A, Ivarsson ML, Janson M, Lacy A, Lange J, Pahlman L, Skullman S, Haglind E. Bowel obstruction after laparoscopic and open colon resection for cancer: Results of 5 years of follow-up in a randomi-

zed trial. SURG ENDOSC. 25:3755-3760. I.F.: 3.44.

5 Abuli A, Fernandez-Rozadilla C, Alonso-Espinaco V, Munoz J, Gonzalo V, Bessa X, Gonzalez D, Clofent J, Cubiella J, Morillas JD, Rigau J, Latorre M, Fernandez-Banares F, Pena E, Riestra S, Paya A, Jover R, Xicola RM, Llor X, Carvajal-Carmona L, Villanueva CM, Moreno V, Pique JM, Carracedo A, Castells A, Andreu M, Ruiz-Ponte C, Castellvi-Bel S. Case-control study for colorectal cancer genetic susceptibility in EPICOLON: previously identified variants and mucins. BMC CANCER. 11:-. I.F.: 3.15.

6 Fernandez-Esparrach G, Cordova H, Bordas JM, Gomez-Molins I, Gines A, Pellise M, Sendino O, Gonzalez-Suarez B, Cardenas A, Balderramo D, Lacy AM, Delgado S, Llach J. Endoscopic management of the complications of bariatric surgery. Experience of more than 400 interventions. HEPATOGASTROENTEROL. 34:131-136. I.F.: 0.68.

7 Fernandez-Esparrach G, Ayuso-Colella JR, Sendino O, Pages M, Cuatrecasas M, Pellise M, Maurel J, Ayuso-Colella C, Gonzalez-Suarez B, Llach J, Castells A, Gines A. EUS and magnetic resonance imaging in the staging of rectal cancer: a prospective and comparative study. GASTROINTEST ENDOSC. 74:347-354. I.F.: 5.65.

8 Caldelari ACA, Miquel R, Bombi JA, Gines A, Fernandez-Esparrach G, Ayuso JR, Maurel J, Feu F, Castells A, Fernandez-Cruz L, Navarro S. Malignancy predictive factors in pancreatic intraductal papillary mucinous neoplasm. MED CLIN-BARCELONA. 137:631-636. I.F.: 1.41.

9 Pellise M, Lopez-Ceron M, DeMiguel CR, Jimeno M, Zabalza M, Ricart E, Aceituno M, Fernandez-Esparrach G, Gines A, Sendino O, Cuatrecasas M, Llach J, Panes J. Narrow-band imaging as an alternative to chromoendoscopy for the detection of dysplasia in long-standing inflammatory bowel disease: a prospective, randomized, crossover study. GASTROINTEST ENDOSC. 74:840-848. I.F.: 5.65.

10 Vidal O, Valentini M, Ginesta C, Espert JJ, Martinez A, Benarroch G, Anglada MT, Garcia-Valdecasas JC. Single-Incision Versus Standard Laparoscopic Cholecystectomy: Comparison of Surgical Outcomes from a Single Institution. J LAPAROENDOSC ADV S. 21:683-686. I.F.: 1.20.

11 Jover R, Nguyen TP, Perez-Carbonell L, Zapater P, Paya A, Alenda C, Rojas E, Cubiella J, Balaguer F, Morillas JD, Clofent J, Bujanda L, Rene JM, Bessa X, Xicola RM, Nicolas-Perez D, Castells A, Andreu M, Llor X, Boland CR, Goel A. 5-Fluorouracil Adjuvant Chemotherapy Does Not Increase Survival in Patients With CpG Island Methylator Phenotype Colorectal Cancer. GASTROENTEROLOGY. 140:1174-1181. I.F.: 12.03.

12 Martinez F, Fernandez-Martos C, Quintana MJ, Castells A, Llombart A, Iniguez F, Guillem V, Dasi F. APC and KRAS mutations in distal colorectal polyps are related to smoking habits in men: results of a cross-sectional study. CLIN TRANSL ONCOL. 13:664-671. I.F.: 1.25.

13 Sanchez-Tillo E, DeBarrios O, Siles L, Cuatrecasas M, Castells A, Postigo A. beta-catenin/TCF4 complex induces the epithelial-to-mesenchymal transition (EMT)-activator ZEB1 to regulate tumor invasiveness. P NATL ACAD SCI USA. 108:19204-19209. I.F.: 9.77.

14 Perez-Torras S, Vidal-Pla A, Miquel R, Almendro V, Fernandez-Cruz L, Navarro S, Maurel J, Carbo N, Gascon P, Mazo A. Characterization of human pancreatic orthotopic tumor xenografts suitable for drug screening. CELL ONCOL. 34:511-521. I.F.: 3.18.

15 Huang K, Gutierrez LP, Bulow S, Gallinger S, Castells A, Eagle CJ, Church JM. Clinical characteristics and outcomes in familial adenomatous polyposis patients with a long-term treatment of celecoxib: a matched cohort study. FAM CANCER. 10:303-308. I.F.: 2.14.

16 Horndler C, Gallego R, Garcia-Albeniz X, Alonso-Espinaco V, Alonso V, Escudero P, Jimeno M, Ortego J, Codony-Servat J, Fernandez-Martos C, Calatrava A, Marin-Aguilera M, Munoz J, Castellvi-Bel S, Castells A, Rubini M, Gascon P, Maurel J. Co-expression of matrix metalloproteinase-7 (MMP-7) and phosphorylated insulin growth factor receptor I (pIGF-1R) correlates with poor prognosis in patients with wild-type KRAS treated with cetuximab or panitumumab A GEMCAD study. CANCER BIOL THER. 11:177-183. I.F.: 2.91.

17 Balaguer F, Moreira L, Lozano JJ, Link A, Ramirez G, Shen Y, Cuatrecasas M, Arnold M, Meltzer SJ, Syngal S, Stoffel E, Jover R, Llor X, Castells A, Boland CR, Gironella M, Goel A. Colorectal Cancers with Microsatellite Instability Display Unique miRNA Profiles. CLIN CANCER RES. 17:6239-6249. I.F.: 7.34.

18 Lluis M, Fernandez-Sola J, Castellvi-Bel S, Sacanella E, Estruch R, Urbano-Marquez A. Evaluation of Myocyte Proliferation in Alcoholic Cardiomyopathy: Telomerase Enzyme Activity (TERT) Compared with Ki-67 Expression. ALCOHOL ALCOHOLISM. 46:534-541. I.F.: 2.60.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	95.10	19	10	6
2010	132.71	26	16	4
2011	206.49	33	12	10

19 Castillejo A, Guarinos C, Martinez-Canto A, Barbera VM, Egoavil C, Castillejo MI, Perez-Carbonell L, Sanchez-Heras AB, Segura A, Ochoa E, Lazaro R, Ruiz-Ponte C, Bujanda L, Andreu M, Castells A, Carracedo A, Llor X, Clofent J, Alenda C, Paya A, Jover R, Soto JL. Evidence for classification of c.1852_1853AA > GC in MLH1 as a neutral variant for Lynch syndrome. BMC MED GENET. 12:-. I.F.: 2.44.

20 Kupfer SS, Anderson JR, Ludvik AE, Hooker S, Skol A, Kittles RA, Keku TO, Sandler RS, Ruiz-Ponte C, Castellvi-Bel S, Castells A, Carracedo A, Ellis NA. Genetic Associations in the Vitamin D Receptor and Colorectal Cancer in African Americans and Caucasians. PLOS ONE. 6:-. I.F.: 4.41.

21 Mongroo PS, Noubissi FK, Cuatrecasas M, Kalabis J, King CE, Johnstone CN, Bowser MJ, Castells A, Spiegelman VS, Rustgi AK. IMP-1 Displays Cross-Talk with K-Ras and Modulates Colon Cancer Cell Survival through the Novel Proapoptotic Protein CYFIP2. CANCER RES. 71:2172-2182. I.F.: 8.23.

22 Dumonceau JM, Polkowski M, Larghi A, Vilmann P, Giovannini M, Frossard JL, Heresbach D, Pujol B, Fernandez-Esparrach G, Vazquez-Sequeiros E, Gines A. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. ENDOSCOPY. 43:897-910. I.F.: 6.10.

23 Siegel R, Cuesta MA, Targarona E, Bader FG, Morino M, Corcelles R, Lacy AM, Pahlman L, Haglind E, Bujko K, Bruch HP, Heiss MM, Eikermann M, Neugebauer EAM. Laparoscopic extraperitoneal rectal cancer surgery: the clinical practice guidelines of the European Association for Endoscopic Surgery (EAES). SURG ENDOSC. 25:2423-2440. I.F.: 3.44.

24 King CE, Cuatrecasas M, Castells A, Sepulveda AR, Lee JS, Rustgi AK. LIN28B promotes colon cancer progression and metastasis. CANCER RES. 71:4260-4268. I.F.: 8.23.

25 Tomlinson IPM, Carvajal-Carmona LG, Dobbins SE, Tenesa A, Jones AM, Howarth K, Palles C, Broderick P, Jaeger EEM, Farrington S, Lewis A, Prendergast JGD, Pittman AM, Theodoratou E, Olver B, Walker M, Penegar S, Barclay E, Whiffin N, Martin L, Ballereau S, Lloyd A, Gorman M, Lubbe S, Howie B, Marchini J, Ruiz-Ponte C, Fernandez-Rozadilla C, Castells A, Carracedo A, Castellvi-Bel S, Duggan D, Conti D, Cazier JB, Campbell H, Sieber O, Lipton L, Gibbs P, Martin NG, Montgomery GW, Young J, Baird PN, Gallinger S, Newcomb P, Hopper J, Jenkins MA, Aaltonen LA, Kerr DJ, Cheadle J, Pharoah P, Casey G, Houlston RS, Dunlop MG. Multiple Common Susceptibility Variants near BMP Pathway Loci GREM1, BMP4, and BMP2 Explain Part of the Missing Heritability of Colorectal Cancer. PLOS GENET. 7:-. I.F.: 9.54.

26 Alonso-Espinaco V, Giraldez MD, Trujillo C, VanDerKlift H, Munoz J, Balaguer F, Ocana T, Madrigal I, Jones AM, Echeverry MM, Velez A, Tomlinson I, Mila M, Wijnen J, Carvajal-Carmona L, Castells A, Castellvi-Bel S. Novel MLH1 duplication identified in Colombian families with Lynch syndrome. GENET MED. 13:155-160. I.F.: 5.28.

27 Fernandez-Cruz L. Pancreaticojejunostomy versus pancreaticogastrostomy. J HEPATO-BILIARY-PAN. 18:762-768. I.F.: 1.96.

28 Boeckxstaens GE, Annese V, DesVarannes SB, Chaussade S, Costantini M, Cuttitta A, Elizalde JI, Fumagalli U, Gaudric M, Rohof WO, Smout AJ, Tack J, Zwinderman AH, Zaninotto G, Busch OR. Pneumatic Dilation versus Laparoscopic Heller's Myotomy for Idiopathic Achalasia. NEW ENGL J MED. 364:1807-1816. I.F.: 53.49.

29 Garcia-Albeniz X, Pericay C, Alonso-Espinaco V, Alonso V, Escudero P, Fernandez-Martos C, Gallego R, Gascon P, Castellvi-Bel S, Maurel J. Serum matrilysin correlates with poor survival independently of KRAS and BRAF status in refractory advanced colorectal cancer patients treated with irinotecan plus cetuximab. TUMOR BIOL. 32:417-424. I.F.: 2.03.

30 Diaz-Moralli S, Tarrado-Castellarnau M, Alenda C, Castells A, Cascante M. Transketolase-Like 1 Expression Is Modulated during Colorectal Cancer Progression and Metastasis Formation. PLOS ONE. 6:-. I.F.: 4.41.

31 Bessa X, Alenda C, Paya A, Alvarez C, Iglesias M, Seoane A, Dedeu JM, Abuli A, Ilzarbe L, Navarro G, Pellise M, Balaguer F, Castellvi-Bel S, Llor X, Castells A, Jover R, Andreu M. Validation Microsatellite Path Score in a Population-Based Cohort of Patients With Colorectal Cancer. J CLIN ONCOL. 29:3374-3380. I.F.: 18.97.

32 Fuster D, Ayuso JR, Poveda A, Cubedo R, Casado A, Martinez-Trufero J, Lopez-Pousa A, DelMuro

XG, Lomena F, Maurel J, Pons F. Value of FDG-PET for monitoring treatment response in patients with advanced GIST refractory to high-dose imatinib. A multicenter GEIS study. Q J NUCL MED MOL IM. 55:680-687. I.F.: 2.54.

33 Abate-Daga D, Andreu N, Camacho-Sánchez J, Alemany R, Herance R, Millán O, Fillat C. Oncolytic adenoviruses armed with thymidine kinase can be traced by PET imaging and show potent antitumoural effects by ganciclovir dosing. PLOS ONE. 6(10):e26142-e26142. I.F.: 4.41.

REVIEWS
I.F.: 4.12

1 Moreira L, Castells A. Cyclooxygenase as a Target for Colorectal Cancer Chemoprevention. CURR DRUG TARGETS. 12:1888-1894. I.F.: 3.06.

2 Fernandez-Cruz L, Belli A, Acosta M, Chavarria EJ, Adelsdorfer W, Lopez-Boado MA, Ferrer J. Which is the best technique for pancreaticoenteric reconstruction after pancreaticoduodenectomy? A critical analysis. SURG TODAY. 41:761-766. I.F.: 1.06.

EDITORIALS
I.F.: 24.06

1 Pellise M, Panes J. Confocal endomicroscopy in celiac disease. GASTROENTEROLOGY. 140:1097-1099. I.F.: 12.03.

2 Fernandez-Esparrach G, Panes J. Radiofrequency ablation for nondysplastic Barrett's esophagus: to treat or not to treat?. GASTROENTEROLOGY. 140:2130-2132. I.F.: 12.03.

GRANTS FOR RESEARCH IN PROGRESS

Castells A. Cribado del cáncer colorrectal en población de riesgo intermedio: estudio multicéntrico, aleatorizado y controlado en el que se compara la prueba de detección de sangre oculta en heces mediante método inmunológico y la colonoscopia. Sponsored by: Fundación de la Asociación Española Contra el Cáncer (AECC), AECC_07/185. Duration: 01/03/2007-30/06/2011.

Castellvi S, Castells A, Balaguer F, Gonzalo V. Genetic study of common hereditary bowel cancers in Hispania and the Americas (CHIBCHA). Sponsored by: European Commission, 7th Framework Programme, 223678. Duration: 01/06/2009-30/11/2012.

Castells A. Grup de Recerca en Oncología Gastrointestinal i Pancreàtica. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), 2009-SGR-849. Duration: 01/07/2009-30/06/2014.

Castellvi S, Pique JM, Giraldez M, Ocaña T. Componentes genéticos comunes y de baja penetrancia implicados en cáncer colorrectal: correlación genotipo-fenotipo e identificación de variantes genómicas de riesgo. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI080024. Duration: 01/01/2009-31/12/2013.

Castells A. Cribado del cáncer colorrectal en población de riesgo intermedio: estudio multicéntrico, aleatorizado y controlado en el que se compara la prueba de detección de sangre oculta. Sponsored by: Asociación Española Contra el Cáncer, 08/507. Duration: 09/10/2008-30/06/2011.

Castells A. Subproductos de la desinfección y otros determinantes ambientales, genéticos y moleculares del cáncer colorrectal. Sponsored by: Instituto de Salud Carlos III, PI080533. Duration: 01/01/2009-31/12/2012.

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, PI09/0669. Duration: 01/01/2010-31/12/2012.

Fillat C. Control transcripcional y por microRNAs de adenovirus oncolíticos portadores del gen TK: estudios de eficacia terapéutica en células troncales neoplásicas de cáncer de páncreas y en modelos animales. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), BIO2008-04692-C03-02. Duration: 15/07/2011-16/04/2012.

Fillat C. Knockdown of HAS 21-syntenic miRNAs in Ts65Dn mice by adeno-associated viral vectors. Consequences on hippocampus-dependent phenotypes. Sponsored by: Fondation Jerome Lejeune. Duration: 01/01/2009-31/12/2011.

Fillat C. Grup de Recerca Reconegut. Sponsored by: Generalitat de Catalunya, AGAUR, 2009_SGR_1527. Duration: 01/09/2009-31/12/2013.

Castells A. caracterización genómica del síndrome de Linch mediante secuenciación de nueva generación: correlación con el perfil transcriptómico y epigenómico. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-19273. Duration: 01/01/2011-31/12/2013.

Fernández-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 Ciencia e Innovacion, SAF2010-15635. Duration: 01/01/2011-31/12/2013.

Balaguer F. Implicación del metiloma en la patogénesis y diagnóstico del cáncer colorrectal. Sponsored by: Instituto de Salud Carlos III, PI10/00384. Duration: 01/01/2011-31/12/2013.

DOCTORAL THESES

Lacy A. Efectos del Bypass en "Y de Roux" por laparoscopia como técnica de cirugía bariátrica en el tratamiento del síndrome metabólico asociado a la obesidad mórbida. PhD student: Ricard Corcelles Codina.

Lacy A, Fernandez-Esparrach G. Cambios fisiológicos e inmunológicos de la cirugía endoscópica transluminal a través de orificios naturales (NOTES) utilizando diferentes vías de acceso versus la laparoscopia: estudio comparativo en un modelo porcino. PhD student: Carlos Guarner Argente.

AREA 3

Liver, digestive system and metabolism

Hereditary metabolic diseases

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Judit Garcia-Villoria (Hospital Clínic)
José Luis Marin (Hospital Clínic)

TEAM INVOLVED IN: ciberer

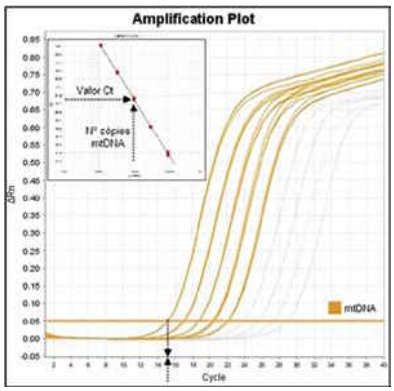
STRATEGIC OBJECTIVES

The strategic objective of our group is to investigate the genetic and biochemical bases, as well as the physiopathological mechanisms, of hereditary metabolic diseases. The ultimate aim is to develop new diagnostic and therapeutic strategies.
On the other hand, we conducttranslational research, stimulating the transfer of knowledge from basic research to the clinical practice setting, and vice versa.

MAIN LINES OF RESEARCH

Within the general line of hereditary metabolic diseases, our concrete research lines are based on the following:

1. In vitro therapeutic approaches. . This study involves the testing of chemical and peptide libraries. Selection has been made of disease stop mutations and mis-sense mutations previously identified by our group. We make use of fibroblasts IPI cells and neuron cultures as cell models.
2. CoQ10 deficiency. We are carrying out the biochemical selection of patients with CoQ10 deficiency, based on the study of the mitochondrial respiratory chain and the analysis of the metabolic pathways, using stable isotopes in fibroblasts from the previously selected patients. Posteriorly, in patients that prove negative for mutations of the genes known to date, an exome analysis will be made to identify the gene causing the disease.
3. Sanfilippo disease and CoQ10. This project is studying the relationship between CoQ10 and Mucopolysaccharidosis III or Sanfilippo disease. We aim to find out whether there is correlation between CoQ10 levels and the disease, and whether treatment of fibroblasts from patients with CoQ10 produces any effect.
4. Cerebral creatine deficiency. Our group has been a pioneer in the identification of patients with cerebral creatine deficiency. At present we are centered 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 IPI cells and HUVEC and HBMEC cells silenced with interference RNA.
5. mtDNA depletion. A nucleotide metabolic defect may give rise to mitochondrial DNA depletion. Since we have identified patients with these characteristics, without mutations of the genes known to date, our objective is to explore new genes capable of explaining the disease.
6. Type C Niemann-Pick disease. The study of patients with this disorder has been carried out in a knock-in murine model, with a view to gaining further knowledge of the underlying physiopathology. On the other hand, this model will be used to test different drugs that act upon proteosomal degradation.
7. Congenital defects of glycosylation (CDG). Our goal is to identify and characterize new cases and phenotypes of these diseases for a better understanding of their pathophysiology and finding novel therapeutic targets.



Calculation of the number of mitochondrial DNA copies, based on real-time PCR.

PUBLICATIONS

ORIGINALS
I.F.: 38.49

1 Tural C, Sola R, Alvarez NP, Molto J, Sanchez M, Zamora AM, Ornelas A, Laguno M, Gonzalez J, VonWichmann MA, Tellez MJ, Paredes R, Clotet B. Effect of an induction period of pegylated interferon-alpha 2a and ribavirin on early virological response in HIV-HCV-coinfected patients: results from the CORAL-2 study. ANTIVIR THER. 16:833-841. I.F.: 3.77.

2 Navarro-Sastre A, Tort F, Stehling O, Uzarska MA, Arranz JA, DelToro M, Labayru MT, Landa J, Font A, Garcia-Villoria J, Merinero B, Ugarte M, Gutierrez-Solana LG, Campistol J, Garcia-Cazorla A, Vaquerizo J, Riudor E, Briones P, Elpeleg O, Ribes A, Lill R. A Fatal Mitochondrial Disease Is Associated with Defective NFU1 Function in the Maturation of a Subset of Mitochondrial Fe-S Proteins. AM J HUM GENET. 89:656-667. I.F.: 11.68.

3 Alcaide P, Merinero B, Ruiz-Sala P, Richard E, Navarrete R, Arias A, Ribes A, Artuch R, Campistol J, Ugarte M, Rodriguez-Pombo P. Defining the Pathogenicity of Creatine Deficiency Syndrome. HUM MUTAT. 32:282-291. I.F.: 5.96.

4 Vega AI, Perez-Cerda C, Abia D, Gamez A, Briones P, Artuch R, Desviat LR, Ugarte M, Perez B. Expression analysis revealing destabilizing mutations in phosphomannomutase 2 deficiency (PMM2-CDG): expression analysis of PMM2-CDG mutations. J INHERIT METAB DIS. 34:929-939. I.F.: 3.81.

5 Macias-Vidal J, Rodriguez-Pascau L, Sanchez-Olle G, Lluch M, Vilageliu L, Grinberg D, Coll MJ. Molecular analysis of 30 Niemann-Pick type C patients fron Spain. CLIN GENET. 80:39-49. I.F.: 2.94.

6 Tural C, Sola R, Alvarez NP, Molto J, Sanchez M, Zamora AM, Ornelas A, Laguno M, Gonzalez J, VonWichmann MA, Tellez MJ, Paredes R, Clotet B, Coral-2Study GROUP. Population Pharmacokinetics of Lopinavir/Ritonavir (Kaletra) in HIV-Infected Patients. THER DRUG MONIT. 33:573-582. I.F.: 3.13.

7 Tort F, DelToro M, Lissens W, Montoya J, Fernandez-Burriel M, Font A, Bujan N, Navarro-Sastre A, Lopez-Gallardo E, Arranz JA, Riudor E, Briones P, Ribes A. Screening for nuclear genetic defects in the ATP synthase-associated genes TMEM70, ATP12 and ATP5E in patients with 3-methylglutaconic aciduria. CLIN GENET. 80:297-300. I.F.: 2.94.

8 Ortez C, Villar C, Fons C, Duarte ST, Perez A, Garcia-Villoria J, Ribes A, Ormazabal A, Casado M, Campistol J, Vilaseca MA, Garcia-Cazorla A. Undetectable Levels of CSF Amyloid-beta Peptide in a Patient with 17 beta-Hydroxysteroid Dehydrogenase Deficiency. J ALZHEIMERS DIS. 27:253-257. I.F.: 4.26.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	40.42	13	7	4
2010	59.95	17	3	8
2011	38.49	8	4	3

GRANTS FOR RESEARCH IN PROGRESS

Ribes A. Estudio para evaluar la efectividad del tratamiento dietético con triheptanoina en pacientes con defectos graves de la Beta-oxidación mitocondrial. Sponsored by: Instituto de Salud Carlos III (ISCIII), EC07/90552. Duration: 29/10/2007-31/12/2011.

Briones P. Estudios bioquímicos y mutacionales en pacientes con deficiencias primarias de CoQ. Selección bioquímica de pacientes y análisis de la vía metabólica mediante sustratos marcados con isótopos estables. Sponsored by: Fondo de Investigación Sanitaria, PI08/0307. Duration: 31/12/2008-30/09/2012.

Ribes A. Diagnóstico, fisiopatología y tratamiento en la deficiencia cerebral de creatina. Subproyecto 4. Estudios de captación de creatina, con distintos preparados de la misma, en neuronas derivadas de células IPS y en células HUVEC silenciadas con RNA de INTERF. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/2128. Duration: 01/01/2010-31/12/2012.

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.

Ribes A. European registry and network for Intoxication type Metabolic Diseases (E-IMD). Sponsored by: Agència Europea DG-SANCO. Coordinador: Stefan Kölker, A/100886-E-IMD. Duration: 01/01/2011-31/12/2013.

Ribes A. Automatización de métodos de diagnóstico molecular de enfermedades mitocondriales. parte 4, hospital clínic. deplecíon de MTDNA; cálculo del número de copias de mtdna y obtención de valores de referencia según edad y tejido. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/90348. Duration: 01/01/2009-30/06/2011.

AREA 3

Liver, digestive system and metabolism

Genomic Programming of Beta Cells and Diabetes

TEAM INVOLVED IN: ciberdem

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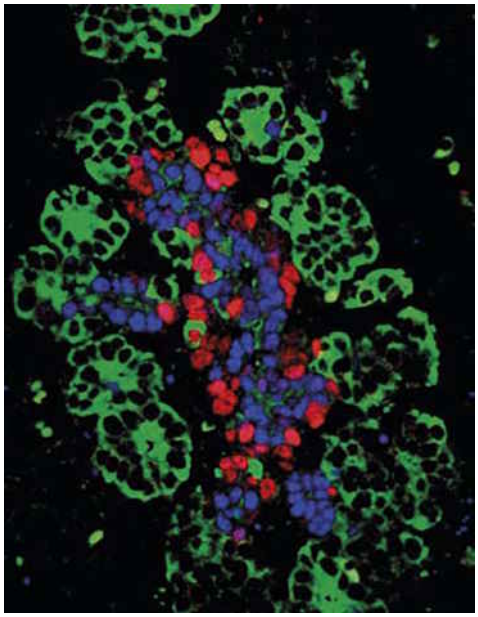
STRATEGIC OBJECTIVES

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.

MAIN LINES OF RESEARCH

1. Pancreatic regeneration and programming.
2. Epigenomic regulation of beta cells and diabetes.
3. Monogenic diabetes.

For further information:
www.betacellregulation.net



Immunofluorescence of E13.5 mouse embryonic pancreas. Nuclear staining of ductal cells, hnf1b (blue). Nuclear staining of endocrine cells, nkx2.2 (red). Cytoplasmic staining of acinar cells, CPA1 (green).

PUBLICATIONS

ORIGINALS
I.F.: 46.59

1 Allen HL, Flanagan SE, Shaw-Smith C, DeFranco E, Akerman I, Caswell R, Ferrer J, Hattersley AT, Ellard S. GATA6 haploinsufficiency causes pancreatic agenesis in humans. NAT GENET. 44:20-22. I.F.: 36.38.

2 Kirkpatrick CL, Wiederkehr A, Baquie M, Akhmedov D, Wang HY, Gauthier BR, Akerman I, Ishihara H, Ferrer J, Wollheim CB. Hepatic Nuclear Factor 1 alpha (HNF1 alpha) Dysfunction Down-regulates X-box-binding Protein 1 (XBP1) and Sensitizes beta-Cells to Endoplasmic Reticulum Stress. J BIOL CHEM. 286:32300-32312. I.F.: 5.33.

3 Hunter CS, Maestro MA, Raum JC, Guo M, ThompsonFh 3RD, Ferrer J, Stein R. Hnf1α (MODY3) regulates β-cell-enriched MafA transcription factor expression. MOL ENDOCRINOL. 25:-339. I.F.: 4.89.

EDITORIALS
I.F.: 32.16

1 Ferrer J. Glucose as a Mitogenic Hormone. CELL METAB. 13:357-358. I.F.: 18.21.

2 Akerman I, VanArensbergen J, Ferrer J. Removing the brakes on cell identity. DEV CELL. 20:411-412. I.F.: 13.95.

GRANTS FOR RESEARCH IN PROGRESS

Ferrer J. Analysis of the plasticity of pancreatic duct cells. Sponsored by: Juvenile diabetes Research Foundation, 26-2008-633. Duration: 01/08/2008-31/03/2011.

Ferrer J. Regulación epigenética y plasticidad de las células beta pancreáticas. Sponsored by: Ministerio de Ciencia e Innovación, SAF2008-03116. Duration: 01/01/2009-31/12/2011.

Ferrer J. Collaborative European Effort to Develop Diabetes Diagnosis. Sponsored by: European Commission FP7, 223211. Duration: 01/12/2008-30/11/2012.

Ferrer J. Biology of Liver and Pancreatic Development and Disease. Sponsored by: European Commission FP7, 238821. Duration: 01/09/2009-31/08/2013.

Ferrer J. Empleo de epigenomas celulares para optimizar la terapia celular a partir de células madre. Sponsored by: Ministerio de Ciencia e Innovación, PLE2009-0162. Duration: 01/11/2009-01/11/2012.

Ferrer J. Linking non-coding RNAs to beta-cell programming efforts. Sponsored by: National Institutes of Health (NIH), NIDDK. Duration: 31/01/2011-28/02/2012.

Ferrer J. Epigenetic strategies for the in vitro generation of replacement beta cells. Sponsored by: National Institute of Health, University of California/San Diego, 1U01DK089567-01. Duration: 01/07/2010-30/12/2012.

Ferrer J. Coordinating Center for Beta Cell Biology Consortium (VUMC 38271). Sponsored by: National Institutes of Health (NIH), 2U01DK072473-06. Duration: 01/03/2011-30/05/2013.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	56.28	4	4	0
2010	64.59	4	4	0
2011	46.59	3	3	0

DOCTORAL THESES

Ferrer J. The role of polycomb mediated gene repression in beta-cell indentity. PhD student: Van Arensbergen, Joris.

AREA 3

Liver, digestive system and metabolism

TEAM INVOLVED IN: ciberdem

Diabetes: metabolic and molecular networks

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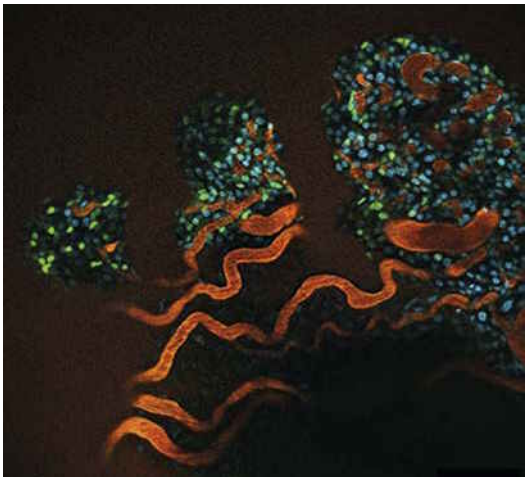
STRATEGIC OBJECTIVES

1. Molecular mechanisms regulating plasticity of the islets in diabetes and obesity.
2. Molecular determinants regulating pancreatic beta-cell function: etiopathogenic role in diabetes.
3. Diabetes andobesity as cardiovascular disease.

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.

For further information:
www.diabetes-obesity-research.org
www.ciberdem.org



Pancreatic islets transplanted into the eye anterior chamber. Confocal image. Red: vascularization; Blue: alive cells from islets; Green: dead cells from islets). (Authors: Ainhoa García, Rita Malpique; Serveis Cientifico-Tècnics Universitat de Barcelona).

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
MOLECULAR AND METABOLIC ALTERATIONS IN DIABETES

Group Leader:
Anna Novials (IDIBAPS)

The main line of research of the group headed by Dr. Novials involves the study of the molecular, genetic and environmental factors critical to pancreatic beta-cell dysfunction and destruction in type 2 diabetes.

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.

PUBLICATIONS

ORIGINALS
I.F.: 71.18

1 Gimenez M, Gilabert R, Monteagudo J, Alonso A, Casamitjana R, Pare C, Conget I. Repeated Episodes of Hypoglycemia as a Potential Aggravating Factor for Preclinical Atherosclerosis in Subjects With Type 1 Diabetes. DIABETES CARE. 34:198-203. I.F.: 7.14.

2 Fabregues F, Castelo-Branco C, Carmona F, Guimera M, Casamitjana R, Balasch J. The effect of different hormone therapies on anti-mullerian hormone serum levels in anovulatory women of reproductive age. GYNECOL ENDOCRINOL. 27:216-224. I.F.: 1.46.

3 Moize V, Deulofeu R, Torres F, DeOsaba JM, Vidal J. Nutritional Intake and Prevalence of Nutritional Deficiencies Prior to Surgery in a Spanish Morbidly Obese Population. OBES SURG. 21:1382-1388. I.F.: 3.08.

4 Moreno P, Acitores A, Gutierrez-Rojas I, Nuche-Berenguer B, ElAssar M, Rodriguez-Manas L, Gomis R, Valverde I, Visa M, Malaisse WJ, Novials A, Gonzalez N, Villanueva-Penacarrillo ML. Amylin effect in extrapancreatic tissues participating in glucose homeostasis, in normal, insulin-resistant and type 2 diabetic state. PEPTIDES. 32:2077-2085. I.F.: 2.65.

5 Conthe P, Mata M, Orozco D, Pajuelo F, Barreto CS, Anaya SF, Gomis R. Degree of control and delayed intensification of antihyperglycaemic treatment in type 2 diabetes mellitus patients in primary care in Spain. DIABETES RES CLIN PR. 91:108-114. I.F.: 2.13.

6 Mccluskey JT, Hamid M, Parke HG, Mcclenaghan NH, Gomis R, Flatt PR. Development and functional characterization of insulin-releasing human pancreatic beta cell lines produced by electrofusion. J BIOL CHEM. 286:21982-21992. I.F.: 5.33.

7 Mcneilly AM, Davison GW, Murphy MH, Nadeem N, Trinick T, Duly E, Novials A, Mceneny J. Effect of alpha-lipoic acid and exercise training on cardiovascular disease risk in obesity with impaired glucose tolerance. LIPIDS HEALTH DIS. 10:-. I.F.: 2.24.

8 Gomis R, Espadero RM, Jones R, Woerle HJ, Dugi KA. Efficacy and safety of initial combination therapy with linagliptin and pioglitazone in patients with inadequately controlled type 2 diabetes: a randomized, double-blind, placebo-controlled study. DIABETES OBES METAB. 13:653-661. I.F.: 3.42.

9 Fernandez-Novell JM, Ballester J, Altirriba J, Ramio-Lluch L, Barbera A, Gomis R, Guinovart JJ, Rodriguez-Gil JE. Glucose and fructose as functional modulators of overall dog, but not boar sperm function. REPROD FERT DEVELOP. 23:468-480. I.F.: 2.55.

10 Wen L, Green EA, Stratmann T, Panosa A, Gomis R, Eynon EE, Flavell RA, Mezquita JA, Mora C. In vivo diabetogenic action of CD4(+) T lymphocytes requires Fas expression and is independent of IL-1 and IL-18. EUR J IMMUNOL. 41:1344-1351. I.F.: 4.94.

11 Macdonald MR, Petrie MC, Home PD, Komajda M, Jones NP, Beck-Nielsen H, Gomis R, Hanefeld M, Pocock SJ, Curtis PS, Mcmurray JJ. Incidence and prevalence of unrecognized myocardial infarction in people with diabetes: a substudy of the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) study. DIABETES CARE. 34:1394-1396. I.F.: 7.14.

12 Mezghenna K, Pomies P, Chalancon A, Castex F, Leroy J, Niclauss N, Nadal B, Cambier L, Cazevieille C, Petit P, Gomis R, Berney T, Gross R, Lajoix AD. Increased neuronal nitric oxide synthase dimerisation is involved in rat and human pancreatic beta cell hyperactivity in obesity. DIABETOLOGIA. 54:2856-2866. I.F.: 6.97.

13 Soty M, Visa M, Soriano S, Carmona MD, Nadal A, Novials A. Involvement of ATP-sensitive Potassium (K-ATP) Channels in the Loss of Beta-cell Function Induced by Human Islet Amyloid Polypeptide. J BIOL CHEM. 286:40857-40866. I.F.: 5.33.

14 Vila L, Serra-Prat M, DeCastro A, Palomera E, Casamitjana R, Legaz G, Barrionuevo C, Munoz JA, Garcia AJ, Lal-Trehan S, Garcia A, Duran J, Puig-Domingo M. Iodine nutritional status in pregnant women of two historically different iodine-deficient areas of Catalonia, Spain. NUTRITION. 27:1029-1033. I.F.: 2.73.

15 Pujadas G, Felipe F, Ejarque M, Sanchez L, Cervantes S, Lynn FC, Gomis R, Gasa R. Sequence and epigenetic determinants in the regulation of the Math6 gene by Neurogenin3. DIFFERENTIATION. 82:66-76. I.F.: 3.07.

16 Amigo-Correig M, Barcelo-Batllori S, Piquer S, Soty M, Pujadas G, Gasa R, Bortolozzi A, Carmona MC, Gomis R. Sodium tungstate regulates food intake and body weight through activation of the hypothalamic leptin pathway. DIABETES OBES METAB. 13:235-242. I.F.: 3.42.

17 Conget I, Battelino T, Gimenez M, Gough H, Castaneda J, Bolinder J. The SWITCH Study (Sensing With Insulin pump Therapy to Control HbA(1c)): Design and Methods of a Randomized Controlled Crossover Trial on Sensor-Augmented Insulin Pump Efficacy in Type 1 Diabetes Suboptimally Controlled with Pump Therapy. DIABETES TECHNOL THE. 13:49-54. I.F.: 2.15.

18 Hanzu FA, Palomo M, Kalko SG, Parrizas M, Garaulet M, Escolar G, Gomis R, Diaz-Ricart M. Translational evidence of endothelial damage in obese individuals:

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	105.88	18	12	3
2010	84.13	19	13	1
2011	71.18	18	10	2

inflammatory and prothrombotic responses. J THROMB HAEMOST. 9:1236-1245. I.F.: 5.44.

GRANTS FOR RESEARCH IN PROGRESS

Servitja JM. Estudio de la respuesta del islote pancreático a la hipoxia: papel de HIF-1. Sponsored by: Ministerio de Educación y Ciencia, BFU2006-09072. Duration: 01/10/2006-30/11/2011.

Parrizas M. Regulación epigenética de la diferenciación. Sponsored by: Ministerio de Educación y Ciencia, BFU2006-14251. Duration: 01/10/2006-31/03/2012.

Esmatjes E. Efectos del by-pass gástrico sobre la presión arterial y la disfunción endotelial en personas con obesidad grave. Sponsored by: Ministerio de Sanidad y Consumo, PI070124. Duration: 01/01/2007-31/12/2011.

Gomis R. Dianas moleculares inducidas por tungstato en la obesidad. Sponsored by: Ministerio de Educación y Ciencia, SAF2006-07382. Duration: 01/10/2006-30/10/2011.

Gomis R. FOOD FOR LIFE-Supporting Healthy Lifestyles in the Mediterranean Area. Sponsored by: Marie Curie Actions - International Research Staff Exchange Scheme, FP7- PEOPLE - IRSES - 2008, 230848. Duration: 01/03/2009-28/02/2013.

Gomis R. The role of adipose tissue in obesity: beta cell crosstalk (ADIBET). Sponsored by: FP7 PEOPLE-2007-3-1-IAPP, PIAP-GA-2008-218130. Duration: 01/01/2008-31/12/2011.

Gomis R. Diabetis experimental, investigació cel·lular i molecular en models de diabetis experimental. Sponsored by: Generalitat de Catalunya, AGAUR, 2009 SGR 1426. Duration: 07/08/2009-31/12/2013.

Gasa R. Cascada transcripcional inducida por neurogenina3 en el páncreas: estudio de los factores de transcripción math6 y ebf1. Sponsored by: Ministerio de Ciencia e Innovación, BFU2008-02299/BMC. Duration: 01/01/2009-31/12/2011.

Novials A. Papel del enzima bace (beta-site amyloid precursor protein cleaving enzyme) en la funcionalidad del islote pancreático. Sponsored by: Ministerio de Sanidad, PI080088. Duration: 01/01/2009-31/12/2011.

Parrizas M. Papel de la demetilasa de histonas LSD1 en la adipogénesis. Sponsored by: Ministerio de Educación, BFU2009-09988. Duration: 01/01/2010-31/12/2012.

Servitja JM. Epigenetic control of gene expression in pancreatic islets. Sponsored by: European Foundation for the Study of Diabetes, EFSD/LILLY_10_001. Duration: 08/05/2010-07/11/2012.

Claret M. Role of hypothalamic mitochondrial fusion in appetite and body weight control: potential therapeutic target for the treatment of obesity. Sponsored by: Assoc. Cat. Universitats Públiques - ACUP, 2010ACUP_00275. Duration: 01/12/2010-30/11/2012.

Vidal J. GLP-1 y resolución tras el bypass gástrico de la diabetes tipo 2 asociada a obesidad. Sponsored by: Fundación de Investigación Médica Mútua, AP62572009. Duration: 03/08/2009-31/07/2011.

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 Mèdica, 401/17/2008. Duration: 01/12/2009-30/11/2012.

Gomis R. Determinantes moleculares de la plasticidad de la célula beta en diabetes: efectos del tungstato sódico. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-19527. Duration: 01/01/2011-31/12/2013.

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: 01/01/2011-31/12/2013.

Ceriello A. Defective antioxidant response in endothelial cells exposed to oscillating glucose: the role of Nrf2. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI10/01256. Duration: 01/01/2011-31/12/2013.

Servitja JM. Regulación y función de microRNAs en el islote pancreático. Sponsored by: Ministerio de Ciencia e Innovación, BFU2010-17639. Duration: 01/01/2011-31/12/2013.

Novials A. Seminars on Current Trends in Diabetes and Obesity Research 2011-2012. Sponsored by: Generalitat de Catalunya, AGAUR, AN076832. Duration: 06/10/2001-12/07/2012.

Lerin C. Molecular mechanisms underlying the development of insulin resistance: role of betaine supplementation. Sponsored by: European Commission, DG Research and Innovation, PCIG-GA-2011-293502. Duration: 01/09/2011-31/08/2015.

DOCTORAL THESES

Gomis R, Parrizas M. Molecular determinants of adipose tissue crosstalks. PhD student: Felicia Alexandra Hanzu.

NEUROPHARMACOLOGY
AND EXPERIMENTAL
NEUROPATHOLOGY
NEUROPHYSIOLOGY
AND FUNCTIONAL STUDIES OF THE NERVOUS SYSTEM
BRAIN ISCHEMIA
CLINICAL EXPERIMENTAL
CELLULAR BIOLOGY OF PATHOLOGICAL PROCESSES
BASIC
SYSTEMS
NEUROPSY

AREA 4

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AREA 4

Clinical and experimental neuroscience

Neuropharmacology and experimental neuropathology

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Tamara Romón (IDIBAPS)
Tony Valente (IDIBAPS)
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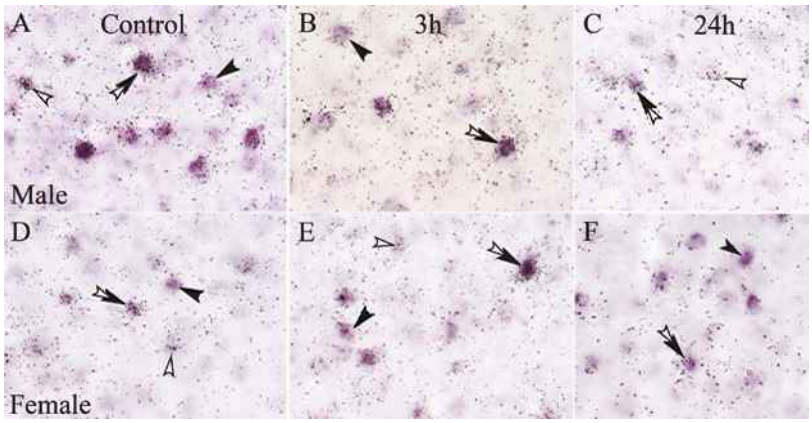

In vivo LPS treatment alters expression of PDE4B3 mRNA in oligodendrocytes. Cellular localization of PDE4B3 mRNA (cluster of dark silver grains), in oligodendrocytes (dark precipitate) in male and female mouse brain parenchyma. Black arrowheads point to oligodendrocytes, white arrowheads to radioactively-labeled cells expressing PDE4B3 and double black and white arrowheads to double-labeled cells. Bar = 20 µm.

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.

RESEARCH GROUP
NEURONAL PROLIFERATION CONTROL GROUP

Group Leader: **Sebastián Pons (IIBB-CSIC)**

The main goal of our group is to study the mechanisms controlling the proliferation of neural precursors during both normal development and in neoplastic growth. In particular, our research is focused on the molecular and cellular anomalies that contribute to Medulloblastoma formation. This posterior fosse tumor, represents the most frequent brain malignancy in children. Recently, different multicentric genomic studies succeeded to distribute Medulloblastomas into 4 different groups attending to their expression signatures. The different groups are commonly associated to a particular histologic type and prognosis. Activating mutations of molecules in Hedgehog and Wnt signaling pathways have been demonstrated to be responsible for the initiation of Meulloblastomas of Hedgehog and Wnt groups respectively. Nevertheless, the process occurring between the initial mutation and the development of the Medulloblastoma is mostly unknown. In our laboratory we use *in ovo* (chicken) and *in utero* (mouse) electroporation systems to express different oncogenic mutations of Hedgehog and Wnt pathways to study the cellular events occurring during the initial steps of Medulloblastoma formation.

RESEARCH GROUP
SYSTEMS NEUROPHARMACOLOGY GROUP

Group Leader: **Francesc Artigas (IIBB-CSIC)**

The group studies the neuronal circuits implicated 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 animal models of mental disease, with a view to identifying new therapeutic targets.

RESEARCH GROUP
NEUROTOXICITY AND NEURODEGENERATION MECHANISMS GROUP

Group Leader: **Cristina Suñol (IIBB-CSIC)**

The group carries out studies on cytotoxicity, oxidative stress, synaptic functions and proteomics, for the determination of altered targets in toxicity and aging processes of the central nervous system. It also focuses on neuroprotective strategies and the development of *in vitro* methods for predicting neurotoxicity.

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Neuropharmacology and experimental neuropathology

RESEARCH GROUP
MOLECULAR NEUROPHARMACOLOGY GROUP

Group Leader: Guadalupe Mengod (IIBB-CSIC)

The group studies neurotransmission and its anatomical, cellular and molecular aspects implicated in neurodegenerative disorders with an inflammatory component. The objective is to identify and characterize new targets for therapeutic action.

RESEARCH GROUP
CELLULAR NEUROBIOLOGY GROUP

Group Leader: Josep Saura (IIBB-CSIC)

We study the implication of C/EBP transcription factors and of neuronal-microglial communication molecules (CD200, CD200R, TREM) in glial activation and in the associated neurotoxicity. We conduct studies using experimental animals, primary cell cultures (mixed glial, astroglial and microglial-enriched, neuronal, mixed neuron-glial) and cell lines.

RESEARCH GROUP
CNEURONAL PROLIFERATION CONTROL GROUP

Group Leader: Sebastián Pons (IIBB-CSIC)

The main goal of our group is to study the mechanisms controlling the proliferation of neuronal precursors during both normal development and in neoplastic growth. In particular, our researcg is focused on the molecular and cellular anomalies that contribute to Medulloblastoma. We use *in ovo* (chicken) and *in utero* (mouse) electroporation systems to alter Hedgehog and Wnt pathways in order to study the cellular events occurring during the initial steps of Medulloblastoma formation.

PUBLICATIONS

ORIGINALS
I.F.: 68.14

1 Amigo-Correig M, Barcelo-Batllori S, Piquer S, Soty M, Pujadas G, Gasa R, Bortolozzi A, Carmona MC, Gomis R. Sodium tungstate regulates food intake and body weight through activation of the hypothalamic leptin pathway. DIABETES OBES METAB. 13:235-242. I.F.: 3.42.

2 Santana N, Troyano-Rodriguez E, Mengod G, Celada P, Artigas F. Activation of Thalamocortical Networks by the N-methyl-D-aspartate Receptor Antagonist Phencyclidine: Reversal by Clozapine. BIOL PSYCHIAT. 69:918-927. I.F.: 8.67.

3 Portella MJ, DeDiego-Adelino J, Ballesteros J, Puigdemont D, Oiler S, Santos B, Alvarez E, Artigas F, Perez V. Can We Really Accelerate and Enhance the Selective Serotonin Reuptake Inhibitor Antidepressant Effect? A Randomized Clinical Trial and a Meta-Analysis of Pindolol in Nonresistant Depression. J CLIN PSYCHIAT. 72:962-969. I.F.: 5.02.

4 Watanabe KH, Andersen ME, Basu N, Carvan MJ, Crofton KM, King KA, Sunol C, Tiffany-Castiglioni E, Schultz IR. Defining and modeling known adverse outcome pathways: Domoic acid and neuronal signaling as a case study. ENVIRON TOXICOL CHEM. 30:9-21. I.F.: 3.03.

5 Briz V, Molina-Molina JM, Sanchez-Redondo S, Fernandez MF, Grimalt JO, Olea N, Rodriguez-Farre E, Suñol C. Differential Estrogenic Effects of the Persistent Organochlorine Pesticides Dieldrin, Endosulfan, and Lindane in Primary Neuronal Cultures. TOXICOL SCI. 120:413-427. I.F.: 5.09.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	81.63	20	14	4
2010	105.96	26	16	7
2011	68.14	15	9	2

6 Romon T, Mengod G, Adell A. Expression of parvalbumin and glutamic acid decarboxylase-67 after acute administration of MK-801. Implications for the NMDA hypofunction model of schizophrenia. PSYCHOPHARMACOLOGY. 217:231-238. I.F.: 3.82.

7 Johansson EM, Sanabra C, Cortes R, Vilaro MT, Mengod G. Lipopolysaccharide Administration In Vivo Induces Differential Expression of cAMP-Specific Phosphodiesterase 4B mRNA Splice Variants in the Mouse Brain. J NEUROSCI RES. 89:1761-1772. I.F.: 2.96.

8 Hernandez RB, Farina M, Esposito BP, Souza-Pinto NC, Barbosa F, Sunol C. Mechanisms of Manganese-Induced Neurotoxicity in Primary Neuronal Cultures: The Role of Manganese Speciation and Cell Type. TOXICOL SCI. 124:414-423. I.F.: 5.09.

9 Villegas E, Estruch R, Mengod G, Cortes R. NMDA receptors in frontal cortex and hippocampus of alcohol consumers. ADDICT BIOL. 16:163-165. I.F.: 4.15.

10 Garcia-Mesa Y, Lopez-Ramos JC, Gimenez-Llort L, Revilla S, Guerra R, Gruart A, Laferla FM, Cristofol R, Delgado-Garcia JM, Sanfeliu C. Physical Exercise Protects Against Alzheimer's Disease in 3xTg-AD Mice. J ALZHEIMERS DIS. 24:421-454. I.F.: 4.26.

11 Straccia M, Gresa-Arribas N, Dentesano G, Ejarque-Ortiz A, Tusell JM, Serratosa J, Sola C, Saura J. Proinflammatory gene expression and neurotoxic effects of activated microglia are attenuated by absence of CCAAT/enhancer binding protein beta. J NEUROINFLAMM. 8:-. I.F.: 5.79.

12 Masana M, Bortolozzi A, Artigas F. Selective enhacement of mesocortical dopaminergic transmission by noradrenergic drugs: therapeutic opportunities in schizophrenia. INT J NEUROPSYCHOPH. 14:53-68. I.F.: 4.70.

13 Vazquez-Borsetti P, Celada P, Cortes R, Artigas F. Simultaneous projections from prefrontal cortex to dopaminergic and serotonergic nuclei. INT J NEUROPSYCHOPH. 14:289-302. I.F.: 4.70.

14 Barzi M, Kostrz D, Menendez A, Pons S. Sonic Hedgehog-induced Proliferation Requires Specific G alpha Inhibitory Proteins. J BIOL CHEM. 286:8067-8074. I.F.: 5.33.

15 Sanabra C, Mengod G. Neuroanatomical distribution and neurochemical characterization of cells expressing adenylyl cyclase isoforms in mouse and rat brain. J CHEM NEUROANAT. 41:43-54. I.F.: 2.12

GRANTS FOR RESEARCH IN PROGRESS

Adell A. Alteraciones de las conexiones de la corteza prefrontal en el modelo de esquizofrenia de antagonismo NMDA. Sitio de acción y mecanismo de los fármacos antipsicóticos. Sponsored by: Instituto de Salud Carlos III, PI070111. Duration: 26/11/2007-30/06/2011.

Artigas F. Modulación serotoninérgica de la corteza prefrontal: relevancia en el tratamiento de la depresión y la esquizofrenia. Sponsored by: Ministerio Educación y Ciencia, SAF2007-62378. Duration: 01/10/2007-04/10/2011.

Celada MP. Actividad cortical y alucinaciones. nuevo modelo experimental para la identificación de dianas terapeuticas en esquizofrenia. Sponsored by: Instituto de Salud Carlos III, PS09/01245. Duration: 01/01/2010-31/12/2012.

Artigas F. Estudio del mecanismo de acción de la estimulación cerebral profunda sobre la neurotransmisión serotoninérgica y dopaminérgica. Sponsored by: Ministerio de Ciencia e Innovación, 201020E046. Duration: 01/01/2010-03/06/2011.

Bortolozzi A. In vivo silencing of 5-HT2A receptor and serotonin transporter by RNA interference mechanism. Relevance to the cognitive-affective disorder in schizophrenia and depression. Sponsored by: Instituto de Salud Carlos III, P91C. Duration: 02/06/2009-02/06/2011.

Artigas F. Grup de Recerca Consolidat, Neuroquímica i Neurofarmacologia. Sponsored by: Generalitat de Catalunya, 2009SGR220. Duration: 01/01/2009-31/12/2013.

Artigas F. Novel Methods leading to New Medications in Depression and Schizophrenia (NEWMEDS). Sponsored by: IMI JU, (Comisión Europea - CE y la Federación Europea de Industrias y Asociaciones Farmacéuticas - EFPIA), Grant Agreement N° 115008. Duration: 01/09/2009-31/08/2014.

Solá C. Inhibición de la activación glial como diana terapéutica en enfermedades neurodegenerativas. Sponsored by: FIS, PI081396. Duration: 01/01/2009-31/12/2011.

Cortés R. Expresión de marcadores neuronales en demencias: enfermedad de los granos argirófilos y Alzheimer. Sponsored by: MICINN - Instituto de Salud Carlos III, PS09/01087. Duration: 01/01/2010-31/12/2012.

Sanfeliu C. Implicación de la sirtuina 1 en procesos neurodegenerativos. Sponsored by: MICINN, SAF2009-13093-C02-02. Duration: 01/01/2010-31/12/2012.

Mengod G. Fármacos innovadores para la esclerosis múltiple. Sponsored by: Fundación Española para la Ciencia y Tecnología (FECYT), INC-0367. Duration: 01/01/2010-31/12/2011.

Bortolozzi A, Artigas F. Modulación de los genes asociados al sistema serotonérgico con moléculas RNA antisentido (siRNA) y su efecto en modelo. Sponsored by: nLife Therapeutics, 10/166. Duration: 01/07/2010-31/12/2013.

Artigas F. Desarrollo y validación clínica de un modelo experimental para identificar dianas terapéuticas en el tratamiento de alucinaciones resistentes. Sponsored by: Instituto de Salud Carlos III, P82. Duration: 21/11/2008-21/11/2011.

Sanfeliu C. Disfunción cerebral durante el envejecimiento: relevancia para la enfermedad de Alzheimer (BrainAge). Sponsored by: MICINN, CSD2010-00045. Duration: 27/12/2010-26/12/2015.

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: MICINN - Instituto de Salud Carlos III, PS09/00468. Duration: 01/01/2010-31/12/2012.

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, PI10/01103. Duration: 01/01/2011-31/12/2013.

Bortolozzi A. Papel de los canales de potasio-K+ en el mecanismo de acción de los fármacos antidepresivos. Relevancia del canal TREK-1 y su relación con el receptor de serotonina 1A. Sponsored by: Instituto de Salud Carlos III, PI10/00290. Duration: 01/01/2011-31/12/2013.

Castañé A. Metabotropic glutamate receptors 2/3 (mGluR2/3) as drug targets to improve cognitive impairment in schizophrenia. Sponsored by: Instituto de Salud Carlos III, 11INT4. Duration: 01/01/2011-31/12/2012.

Pons S. Control de la proliferación de los precursores de neuronas granulares del cerebelo. Sponsored by: MICINN, BFU2008-024024BFI. Duration: 01/01/2009-31/12/2011.

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: MICINN - Instituto de Salud Carlos III, PI10/01874. Duration: 01/01/2011-31/12/2013.

Saura J. Efecto antiinflamatorio y neuroprotector de la inhibición de C/EBP y C/EBP en un modelo animal de esclerosis múltiple. Sponsored by: Instituto de Salud Carlos III, PI10/378. Duration: 01/01/2011-31/12/2013.

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: MICINN - Instituto de Salud Carlos III, PS10/00453. Duration: 01/01/2011-31/12/2013.

Rodriguez E. Grup de Recerca Consolidat, Farmacologia i Toxicologia. Sponsored by: Generalitat de Catalunya, 2009SGR214. Duration: 01/01/2009-31/12/2013.

Celada MP. Apoyo tecnológico referente al proyecto: "Caracterizar la actividad oscilatoria cortical en ratones transgénicos PKEHUM0801 y su afectación por el antipsicótico clozpina. Sponsored by: Ministerio de Economía y Competitividad, BRAINco Biopharma, CENIT10 10/156. Duration: 18/05/2010-31/12/2013.

DOCTORAL THESES

Suñol C. Efectos de los pesticidas organoclorados sobre la neurotransmisión glutamatérgica en cultivos primarios neuronales. Interacciones con el sistema neuroendocrino. PhD student: Victor Briz.

Mengod G. AMPc I neuroinflamació: Identificació de proteïnes implicades en la regulació dels nivells d'AMPc en l'encefalomielitis autoimune experimental. PhD student: Cristina Sanabra Palau.

Mengod G. cAMP specific-phosphodiesterases: mRNA variations and sex-related differences in mouse brain following immune response. PhD student: Emily Johansson.

Pons S. Papel de las G i y la PKA en la señalización de Shh. PhD student: Mercedes Barzy Dieguez.

Pons S. Control de la proliferación neuronal por microRNAs. PhD student: Jordi Berenguer de Felipe.

Bortolozzi A, Artigas F. Modulació dels sistemes monoaminèrgics a l'escorça prefrontal. Implicacions en esquizofrènia i depressió. PhD student: Mercè Masana Nadal.

AREA 4

Clinical and experimental neuroscience

Brain ischemia: Clinical and experimental studies

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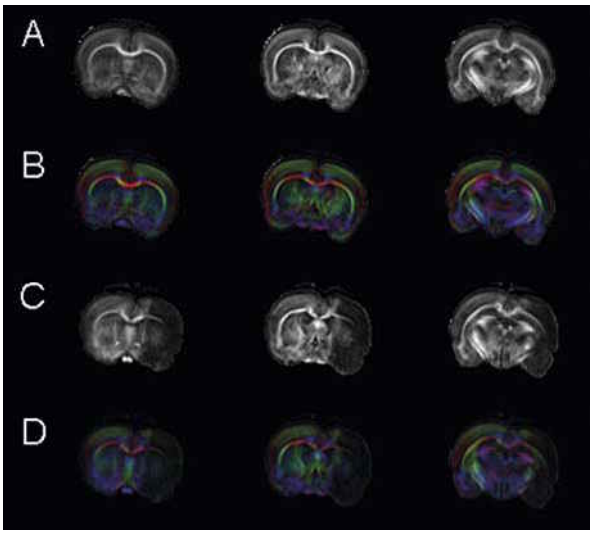
STRATEGIC OBJECTIVES

Study of cerebrovascular pathology from the clinical and basic perspective, with special emphasis on inflammation and immune response, as well as on the use of neuroimaging techniques. The ultimate aim is to develop therapeutic strategies in application to stroke.



Study of the rat brain using magnetic resonance imaging.
A) Fractional anisotropy map offering information on the magnitude of white matter fibre anisotropy, showing the anatomy of the rat brain. Control of the coronal section at three different levels of the brain.
B) The same brain sections, with a colour-code map providing information on the three-dimensional orientation of the white matter fibres using the diffusion tensor imaging (DTI) technique.
C) Coronal sections of fractional anisotropy map images of the brain of an animal 7 days after occlusion of the middle cerebral artery during 90 minutes.
D) Colour-code map of the same ischemic brain sections.

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.
- 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 IIb study involving the administration of uric acid in stroke treated with rtPA.
- Use of intraarterial rescue treatments with rtPA in patients previously treated with intravenous rtPA and selected by multimodal imaging techniques.

Magnetic Resonance

- Neuroimaging in brain ischemia: application of magnetic resonance (MR) 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

- Neurological repair and neurogenesis in brain ischemia: effect of inflammation upon neurogenesis.

Clinical trials

- Combination thrombolysis with antioxidants (uric acid).

PUBLICATIONS

ORIGINALS
I.F.: 103.37

1 Penas C, Font-Nieves M, Fores J, Petegnief V, Planas A, Navarro X, Casas C. Autophagy, and BiP level decrease are early key events in retrograde degeneration of motoneurons. CELL DEATH DIFFER. 18:1617-1627. I.F.: 9.05.

2 Bueno H, Betriu A, Heras M, Alonso JJ, Cequier A, Garcia EJ, Lopez-Sendon JL, Macaya C, Hernandez-Antolin R. Primary angioplasty vs. fibrinolysis in very old patients with acute myocardial infarction: TRIANA (TRatamiento del Infarto Agudo de miocardio en Ancianos) randomized trial and pooled analysis with previous studies. EUR HEART J. 32:51-60. I.F.: 10.05.

3 Almendros I, Farre R, Planas AM, Torres M, Bonsignore MR, Navajas D, Montserrat JM. Tissue Oxygenation in Brain, Muscle, and Fat in a Rat Model of Sleep Apnea: Differential Effect of Obstructive Apneas and Intermittent Hypoxia. SLEEP. 34:1127-1133. I.F.: 5.49.

4 Soria G, Aguilar E, Tudela R, Mullol J, Planas AM, Marin C. In vivo magnetic resonance imaging characterization of bilateral structural changes in experimental Parkinson's disease: a T2 relaxometry study combined with longitudinal diffusion tensor imaging and manganese-enhanced magnetic resonance imaging in the 6-. EUR J NEUROSCI. 33:1551-1560. I.F.: 3.66.

5 Martin-Jaular L, Ferrer M, Calvo M, Rosanas-Urgell A, Kalko S, Graewe S, Soria G, Cortadellas N, Ordi J, Planas A, Burns J, Heussler V, DelPortillo HA. Strain-specific spleen remodelling in Plasmodium yoelii infections in Balb/c mice facilitates adherence and spleen macrophage-clearance escape. CELL MICROBIOL. 13:109-122. I.F.: 5.63.

6 Gorina R, Font-Nieves M, Marquez-Kisinousky L, Santalucia T, Planas AM. Astrocyte TLR4 Activation Induces a Pro-inflammatory Environment Through the Interplay Between MyD88-Dependent NF kappa B Signaling, MAPK, and Jak1/Stat1 Pathways. GLIA. 59:242-255. I.F.: 5.19.

7 Rojas S, Herance JR, Abad S, Jimenez X, Pareto D, Ruiz A, Torrent E, Figueiras FP, Popota F, Fernandez-Soriano FJ, Planas AM, Gispert JD. Evaluation of Hypoxic Tissue Dynamics with F-18-FMISO PET in a Rat Model of Permanent Cerebral Ischemia. MOL IMAGING BIOL. 13:558-564. I.F.: 3.14.

8 Soria G, DeNotaris M, Tudela R, Blasco G, Puig J, Planas AM, Pedraza S, Prats-Galino A. Improved Assessment of Ex Vivo Brainstem Neuroanatomy with High-Resolution MRI and DTI at 7 Tesla. ANAT REC. 294:1035-1044. I.F.: 1.40.

9 Obach V, Oleaga L, Urra X, Macho J, Amaro S, Capurro S, Gomez-Choco M, SanRoman L, Cervera A, Blasco J, Vargas M, Torres F, Chamorro A. Multimodal CT-Assisted Thrombolysis in Patients With Acute Stroke A Cohort Study. STROKE. 42:1129-1131. I.F.: 5.76.

10 Domingo-Espin J, Vazquez E, Ganz J, Conchillo O, Garcia-Fruitos E, Cedano J, Unzueta U, Petegnief V, Gonzalez-Montalban N, Planas AM, Daura X, Peluffo H, Ferrer-Miralles N, Villaverde A. Nanoparticulate architecture of protein-based artificial viruses is supported by protein-DNA interactions. NANOMEDICINE-UK. 6:1047-1061. I.F.: 6.20.

11 Marco I, Valhondo M, Martin-Fontecha M, Vazquez-Villa H, DelRio J, Planas A, Sagredo O, Ramos JA, Torrecillas IR, Pardo L, Frechilla D, Benhamu B, Lopez-Rodriguez ML. New Serotonin 5-HT1A Receptor Agonists with Neuroprotective Effect against Ischemic Cell Damage. J MED CHEM. 54:7986-7999. I.F.: 5.21.

12 Abilleira S, Davalos A, Chamorro A, Alvarez-Sabin J, Ribera A, Gallofre M. Outcomes of Intravenous Thrombolysis After Dissemination of the Stroke Code and Designation of New Referral Hospitals in Catalonia The Catalan Stroke Code and Thrombolysis (Cat-SCT) Monitored Study. STROKE. 42:2001-2006. I.F.: 5.76.

13 Rojas S, Martin A, Pareto D, Herance JR, Abad S, Ruiz A, Flotats N, Gispert JD, Llop J, Gomez-Vallejo V, Planas AM. Positron emission tomography with C-11-Flumazenil in the rat shows preservation of binding sites during the acute phase after 2h-Transient Focal Ischemia. NEUROSCIENCE. 182:208-216. I.F.: 3.22.

14 Bousser MG, Amarenco P, Chamorro A, Fisher M, Ford I, Fox KM, Hennerici MG, Mattle HP, Rothwell PM, DeCordoue A, Fratacci MD. Terutroban versus aspirin in patients with cerebral ischaemic events (PERFORM): a randomised, double-blind, parallel-group trial. LANCET. 377:2013-2022. I.F.: 33.63.

REVIEWS
I.F.: 5.76

1 Amaro S, Chamorro A. Translational Stroke Research of the Combination of Thrombolysis and Antioxidant Therapy. STROKE. 42:1495-1499. I.F.: 5.76.

EDITORIALS
I.F.: 5.76

1 Planas AM, Traystman RJ. Advances in Translational Medicine 2010. STROKE. 42:283-284. I.F.: 5.76.

GRANTS FOR RESEARCH IN PROGRESS

Planas A. NoE - Diagnostic Molecular Imaging. Sponsored by: European Commission, LSHB-CT-2005-512146. Duration: 01/04/2005-30/09/2012.

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: 29/10/2007-30/12/2012.

Planas A. Affording recovery in Stroke (ARISE). Sponsored by: European Community. Seventh Framework Programme (Life Sciences), HEALTH-2007-2.2.1-1 – nº201024. Duration: 01/04/2008-01/03/2013.

Santalucía T. Efecto de la glucosa sobre la función de HIF-1alfa en neuronas y glía sometidas a isquemia y estímulos pro-inflamatorios . Sponsored by: Programa Nacional de Biomedicina (MICINN), SAF2008-04515-C02-02. Duration: 01/01/2009-31/12/2011.

Petegnief V. Mecanismos de muerte y neuroprotección en la isquemia cerebral. Efecto de la inflamación y papel de la UPR. Sponsored by: Ministerio de Ciencia e Innovación (FIS), PI081932. Duration: 01/01/2009-01/12/2011.

Justicia C. Estudio de la función cerebral por resonancia magnética de alto campo en modelos experimentales de isquemia: Degeneración y regeneración de la sustancia blanca. Sponsored by: Ministerio de Ciencia e innovación (FIS), PI081880. Duration: 01/01/2009-31/12/2012.

Planas A. Inflamación y respuesta inmune innata como dianas terapéuticas en la isquemia cerebral. Sponsored by: Programa Nacional de Biomedicina (MICINN), SAF2008-04515-C02-01. Duration: 01/01/2009-31/12/2011.

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, PI09/1313. Duration: 01/01/2010-31/12/2012.

Cervera A. Activación del complemento por la vía de la lectinas: relevancia clínica. Sponsored by: FIS, PI10/01898. Duration: 01/01/2011-31/12/2013.

Planas A. Estudios de neuroimagen. Sponsored by: Ministerio de Economía y Competitividad, CENIT10 10/157. Duration: 18/05/2010-31/12/2014.

Planas A. Grup d'investigació cerebrovascular. Sponsored by: Generalitat de Catalunya, 2009_SGR_890. Duration: 28/09/2009-31/12/2013.

Planas A. Neurogénesis endógena e inflamación en la isquemia cerebral en modelos experimentales murinos y en pacientes con ictus. Sponsored by: Instituto de Salud Carlos III, PI070917. Duration: 01/03/2009-30/09/2011.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	72.94	16	10	4
2010	90.59	14	8	2
2011	103.37	14	10	2

DOCTORAL THESES

Chamorro A, Planas A. Terapia combinada con ácido úrico y RTPA en el ictus isquémico agudo: Farmacocinética, seguridad clínica y actividad biológica de la administración endovenosa de ácido úrico en el ictus isquémico tratado con RTPA. PhD student: Sergio Amaro Delgado.

Pozas E, Petegnief V. El procés inflamatori desencadenat per l' activació del receptor de immunitat innata TLR-4, i mecanismes naturals d'autorregulació en astròcits. PhD student: Míriam Aurora Font Nieves de la Vega.

AREA 4

Clinical and experimental neuroscience

Neurodegenerative diseases: Clinical and experimental research

TEAM INVOLVED IN: CIBERNED

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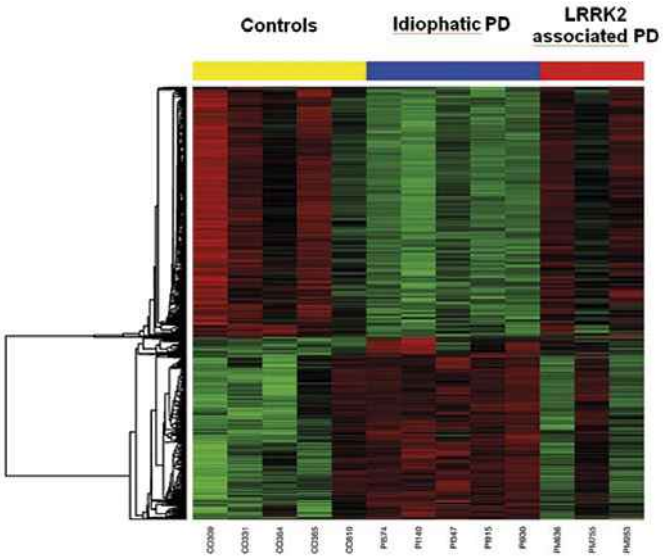
STRATEGIC OBJECTIVES

1. Development of research projects, with results that may find short term application, with a view to improving the diagnosis and treatment of degenerative neurological diseases. Many of the research lines are linked to clinical research protocols of the Clinic Hospital Department of Neurology.
2. Investigation of the molecular mechanisms implicated in dopaminergic neuron degeneration and in the physiopathology of the motor complications induced by drug treatment, in experimental models of Parkinson's disease and other movement disorders.

MAIN LINES OF RESEARCH

1. Genetic analyses, biological markers and experimental therapies in Parkinson's disease and other movement disorders. Genetic and expression studies in parkinsonisms.
2. Studies in in vivo and in vitro experimental modelsof the physiopathological mechanisms involved in Parkinson's disease and other movement disorders.
3. Genetic and diagnostic and predictive marker studies in Alzheimer's disease and other dementias. Experimental functional neuroimaging studies in healthy and in pathological aging.
4. 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.
5. Study of neurogenesis in the subventricular zone, olfactory bulb and striate nucleus in experimental models of Parkinson's disease and tardive dyskinesia.



Results of a brain transcriptomic study using Heat map analysis showed partial segregation of the expression profiles of controls, idiopathic PD (IPD) and LRRK2-associated mutation PD (MPD). IPD and controls have expression patterns that are clearly different, while MPD tissues show heterogeneous patterns - two resembling controls and one resembling IPD. This suggests the presence of different transcription processes in the putamen of MPD versus IPD.

RESEARCH GROUP
PARKINSON'S DISEASE AND MOVEMENT DISORDERS

Group Leader: Eduardo Tolosa (Hospital Clínic)

We have consolidated the line of genetics in degenerative disorders, particularly Parkinson's disease. This year we have explored or published different studies on genetic brain expression of genes potentially implicated in progressive supranuclear paralysis (isoforms of tau, CRHR1, IMP5, cdk5, GSK3 and saitohin). In addition, we have determined the frequency of the most common mutations of the LRRK2 gene in patients with Parkinson's disease seen in our Department, and in cases of parkinsonism in the Neurological Tissue Bank.

PUBLICATIONS

ORIGINALS
I.F.: 237.08

1 Fortea J, Llado A, Clarimon J, Lleo A, Oliva R, Peri J, Pintor L, Yague J, Blesa R, Molinuevo JL, Sanchez-Valle R. PICOGEN: Five years experience with a genetic counselling program for dementia. NEUROLOGIA. 26:143-149. I.F.:0. 59.

2 Balasa M, Gelpi E, Antonell A, Rey MJ, Sanchez-Valle R, Molinuevo JL, Llado A. Clinical features and APOE genotype of pathologically proven early-onset Alzheimer disease. NEUROLOGY. 76:1720-1725. I.F.: 8.02.

3 Garrabou G, Inoriza JM, Moren C, Oliu G, Miro O, Marti MJ, Cardellach F. Mitochondrial Injury in Human Acute Carbon Monoxide Poisoning: The Effect of Oxygen Treatment. J ENVIRON SCI HEAL C. 29:32-51. I.F.: 4.84.

4 Iranzo A, Valldeoriola F, Lomena F, Molinuevo JL, Serradell M, Salamero M, Cot A, Ros D, Pavia J, Santamaria J, Tolosa E. Serial dopamine transporter imaging of nigrostriatal function in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective study. LANCET NEUROL. 10:797-805. I.F.: 21.66.

5 Munoz E, Iranzo A, Rauek S, Lomena F, Gallego J, Ros D, Santamaria J, Tolosa E. Subclinical nigrostriatal dopaminergic denervation in the cerebellar subtype of multiple system atrophy (MSA-C). J NEUROL. 258:2248-2253. I.F.: 3.85.

6 Guevara M, Baccaro ME, Gomez-Anson B, Frisoni G, Testa C, Torre A, Molinuevo JL, Rami L, Pereira G, Sotil EU, Cordoba J, Arroyo V, Gines P. Cerebral magnetic resonance imaging reveals marked abnormalities of brain tissue density in patients with cirrhosis without overt hepatic encephalopathy. J HEPATOL. 55:564-573. I.F.: 9.33.

7 Rascol O, Fitzer-Attas C, Hauser R, Jankovic J, Long A, Langston JW, Melamed E, Poewe W, Stocchi F, Tolosa E, Eyal E, Weiss YM, Olanow CW. A double-blind, delayed-start trial of rasagiline in Parkinson›s disease (the ADAGIO study): prespecified and post-hoc analyses of the need for additional therapies, changes in UPDRS scores, and non-motor outcomes. LANCET NEUROL. 10:415-423. I.F.: 21.66.

8 Antonell A, Balasa M, Oliva R, Llado A, Bosch B, Fabregat N, Fortea J, Molinuevo JL, Sanchez-Valle R. A novel PSEN1 gene mutation (L235R) associated with familial early-onset Alzheimer›s disease. NEUROSCI LETT. 496:40-42. I.F.: 2.06.

9 Wachter T, Minguez-Castellanos A, Valldeoriola F, Herzog J, Stoevelaar H. A tool to improve pre-selection for deep brain stimulation in patients with Parkinson›s disease. J NEUROL. 258:641-646. I.F.: 3.85.

10 Beyer K, Ispierto L, Latorre P, Tolosa E, Ariza A. Alpha- and beta-synuclein expression in Parkinson disease with and without dementia. J NEUROL SCI. 310:112-117. I.F.: 2.17.

11 Buongiorno M, Compta Y, Marti MJ. Amyloid-beta and tau biomarkers in Parkinson's disease-dementia. J NEUROL SCI. 310:25-30. I.F.: 2.17.

12 Sole-Padulles C, Llado A, Bartres-Faz D, Fortea J, Sanchez-Valle R, Bosch B, Antonell A, Molinuevo JL, Rami L. Association between cerebrospinal fluid tau and brain atrophy is not related to clinical severity in the Alzheimer's disease continuum. PSYCHIAT RES-NEUROIM. 192:140-146. I.F.: 2.06.

13 Ibarretxe-Bilbao N, Junque C, Marti MJ, Tolosa E. Brain structural MRI correlates of cognitive dysfunctions in Parkinson's disease. J NEUROL SCI. 310:70-74. I.F.: 2.17.

14 Ibarretxe-Bilbao N, Junque C, Marti MJ, Tolosa E. Cerebral basis of visual hallucinations in Parkinson's disease: Structural and functional MRI studies. J NEUROL SCI. 310:79-81. I.F.: 2.17.

15 Rami L, Fortea J, Bosch B, Sole-Padulles C, Llado A, Iranzo A, Sanchez-Valle R, Molinuevo JL. Cerebrospinal Fluid Biomarkers and Memory Present Distinct Associations along the Continuum from Healthy Subjects to AD Patients. J ALZHEIMERS DIS. 23:1-8. I.F.: 4.26.

16 Fortea J, Llado A, Bosch B, Antonell A, Oliva R, Molinuevo JL, Sanchez-Valle R. Cerebrospinal Fluid Biomarkers in Alzheimer's Disease Families with PSEN1 Mutations. NEURODEGENER DIS. 8:202-207. I.F.: 3.79.

17 Rami L, Valls-Pedret C, Bartres-Faz D, Caprile C, Sole-Padulles C, Castellvi M, Olives J, Bosch B, Molinuevo JL. Cognitive reserve questionnaire. Scores obtained in a healthy elderly population and in one with Alzheimer's disease. REV NEUROLOGIA. 52:195-201. I.F.: 1.22.

18 Fortea J, Sala-Llonch R, Bartres-Faz D, Llado A, Sole-Padulles C, Bosch B, Antonell A, Olives J, Sanchez-Valle R, Molinuevo JL, Rami L. Cognitively Preserved Subjects with Transitional Cerebrospinal Fluid beta-Amyloid 1-42 Values Have Thicker Cortex in Alzheimer's Disease Vulnerable Areas. BIOL PSYCHIAT. 70:183-190. I.F.: 8.67.

19 Muxi A, Paredes P, Navales I, Valldeoriola F, Gaig C, Lomena F, DeLa-Cerda A, Sola O, Domenech B, Tolosa

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	196.35	43	32	7
2010	188.85	27	9	5
2011	237.08	44	24	10

E, Pons F. Diagnostic cutoff points for I-123-MIBG myocardial scintigraphy in a Caucasian population with Parkinson's disease. EUR J NUCL MED MOL I. 38:1139-1146. I.F.: 5.04.

20 Antonell A, Fortea J, Rami L, Bosch B, Balasa M, Sanchez-Valle R, Iranzo A, Molinuevo JL, Llado A. Different profiles of Alzheimer's disease cerebrospinal fluid biomarkers in controls and subjects with subjective memory complaints. J NEURAL TRANSM. 118:259-262. I.F.: 2.60.

21 Molinuevo JL, Berthier ML, Rami L. Donepezil provides greater benefits in mild compared to moderate Alzheimer's disease: Implications for early diagnosis and treatment. ARCH GERONTOL GERIAT. 52:18-22. I.F.: 1.44.

22 Ibarretxe-Bilbao N, Zarei M, Junque C, Marti MJ, Segura B, Vendrell P, Valldeoriola F, Bargallo N, Tolosa E. Dysfunctions of cerebral networks precede recognition memory deficits in early Parkinson's disease. NEUROIMAGE. 57:589-597. I.F.: 5.94.

23 Moreno-Lopez C, Santamaria J, Salamero M, DelSorbo F, Albanese A, Pellecchia MT, Barone P, Overeem S, Bloem B, Aarden W, Canesi M, Antonini A, Duerr S, Wenning GK, Poewe W, Rubino A, Meco G, Schneider SA, Bhatia KP, Djaldetti R, Coelho M, Sampaio C, Cochen V, Hellriegel H, Deuschl G, Colosimo C, Marsili L, Gasser T, Tolosa E. Excessive Daytime Sleepiness in Multiple System Atrophy (SLEEMSA Study). ARCH NEUROL-CHICAGO. 68:223-230. I.F.: 7.11.

24 Chen-Plotkin AS, Martinez-Lage M, Sleiman PMA, Hu W, Greene R, Wood EM, Bing SX, Grossman M, Schellenberg GD, Hatanpaa KJ, Weiner MF, White CL, Brooks WS, Halliday GM, Kril JJ, Gearing M, Beach TG, Graff-Radford NR, Dickson DW, Rademakers R, Boeve BF, Pickering-Brown SM, Snowden J, VanSwieten JC, Heutink P, Seelaar H, Murrell JR, Ghetti B, Spina S, Grafman J, Kaye JA, Woltjer RL, Mesulam M, Bigio E, Llado A, Miller BL, Alzualde A, Moreno F, Rohrer JD, Mackenzie IRA, Feldman HH, Hamilton RL, Cruts M, Engelborghs S, DeDeyn PP, VanBroeckhoven C, Bird TD, Cairns NJ, Goate A, Frosch MP, Riederer PF, Bogdanovic N, Lee VMY, Trojanowski JQ, VanDeerlin VM. Genetic and Clinical Features of Progranulin-Associated Frontotemporal Lobar Degeneration. ARCH NEUROL-CHICAGO. 68:488-497. I.F.: 7.11.

25 Compta Y, Ezquerra M, Munoz E, Tolosa E, Valldeoriola F, Rios J, Camara A, Fernandez M, Buongiorno MT, Marti MJ. High cerebrospinal tau levels are associated with the rs242557 tau gene variant and low cerebrospinal beta-amyloid in Parkinson disease. NEUROSCI LETT. 487:169-173. I.F.: 2.06.

26 Valldeoriola F, Gaig C, Muxi A, Navales I, Paredes P, Lomena F, DeLaCerda A, Buongiorno M, Ezquerra M, Santacruz P, Marti MJ, Tolosa E. I-123-MIBG cardiac uptake and smell identification in parkinsonian patients with LRRK2 mutations. J NEUROL. 258:1126-1132. I.F.: 3.85.

27 Hoglinger GU, Melhem NM, Dickson DW, Sleiman PMA, Wang LS, Klei L, Rademakers R, DeSilva R, Litvan I, Riley DE, VanSwieten JC, Heutink P, Wszolek ZK, Uitti RJ, Vandrovcova J, Hurtig HI, Gross RG, Maetzler W, Goldwurm S, Tolosa E, Borroni B, Pastor P, Cantwell LB, Han MR, Dillman A, VanDerBrug MP, Gibbs JR, Cookson MR, Hernandez DG, Singleton AB, Farrer MJ, Yu CE, Golbe LI, Revesz T, Hardy J, Lees AJ, Devlin B, Hakonarson H, Muller U, Schellenberg GD. Identification of common variants influencing risk of the tauopathy progressive supranuclear palsy. NAT GENET. 43:699-U125. I.F.: 36.38.

28 Marin C, Aguilar E. In vivo 6-OHDA-induced neurodegeneration and nigral autophagic markers expression. NEUROCHEM INT. 58:521-526. I.F.: 3.60.

29 Botta-Orfila T, Ezquerra M, Rios J, Fernandez-Santiago R, Cervantes S, Samaranch L, Pastor P, Marti MJ, Munoz E, Valldeoriola F, Aguilar M, Calopa M, Hernandez-Vara J, Tolosa E. Lack of interaction of SNCA and MAPT genotypes in Parkinson's disease. EUR J NEUROL. 18:E32-E32. I.F.: 3.77.

30 Valls-Pedret C, Olives J, Bosch B, Caprile C, Castellvi M, Molinuevo JL, Rami L. Landscape test for assessing visual memory in Alzheimer's disease. REV NEUROLOGIA. 53:1-7. I.F.: 1.22.

31 Costa J, Guzman J, Valldeoriola F, Rumia J, Tolosa E, Casanova-Molla J, Valls-Sole J. Modulation of the soleus H reflex by electrical subcortical stimuli in humans. EXP BRAIN RES. 212:439-448. I.F.: 2.30.

32 Molinuevo JL, Gomez-Anson B, Monte GC, Bosch B, Sanchez-Valle R, Rami L. Neuropsychological profile of prodromal Alzheimer's disease (Prd-AD) and their radiological correlates. ARCH GERONTOL GERIAT. 52:190-196. I.F.: 1.44.

33 Molinuevo JL, Hernandez B. Profile of the informal carer associated with the clinical management of the Alzheimer's disease patient refractory to symptomatic treatment of the disease. NEUROLOGIA. 26:518-527. I.F.: 0.59.

34 Tolosa E, Pont-Sunyer C. Progress in defining the premotor phase of Parkinson's disease. J NEUROL SCI. 310:4-8. I.F.: 2.17.

35 Gaig C, Valldeoriola F, Gelpi E, Ezquerra M, Llufriu S, Buongiorno M, Rey MJ, Marti MJ, Graus F, Tolosa E. Rapidly Progressive Diffuse Lewy Body Disease. MOVEMENT DISORD. 26:1316-1323. I.F.: 4.48.

36 Cavanillas ML, Fernandez O, Comabella M, Alcina A, Fedetz M, Izquierdo G, Lucas M, Cenit MC, Arroyo R, Vandenbroeck K, Alloza I, Garcia-Barcina M, Antiguedad A, Leyva L, Gomez CL, Olascoaga J, Otaegui D, Blanco Y, Saiz A, Montalban X, Matesanz F, Urcelay E. Replication of top markers of a genome-wide association study in multiple sclerosis in Spain. GENES IMMUN. 12:110-115. I.F.: 4.37.

37 Trenkwalder C, Kies B, Rudzinska M, Fine J, Nikl J, Honczarenko K, Dioszeghy P, Hill D, Anderson T, Myllyla V, Kassubek J, Steiger M, Zucconi M, Tolosa E, Poewe W, Surmann E, Whitesides J, Boroojerdi B, Chaudhuri KR. Rotigotine Effects on Early Morning Motor Function and Sleep in Parkinson's Disease: A Double-Blind, Randomized, Placebo-Controlled Study (RECOVER). MOVEMENT DISORD. 26:90-99. I.F.: 4.48.

38 Valldeoriola F, Coronell C, Pont C, Buongiorno MT, Camara A, Gaig C, Compta Y. Socio-demographic and clinical factors influencing the adherence to treatment in Parkinson's disease: the ADHESON study. EUR J NEUROL. 18:980-987. I.F.: 3.77.

39 Quintana M, Pena-Casanova J, Sanchez-Benavides G, Langohr K, Manero RM, Aguilar M, Badenes D, Molinuevo JL, Robles A, Barquero MS, Antunez C, Martinez-Parra C, Frank-Garcia A, Fernandez M, Blesa R. Spanish Multicenter Normative Studies (Neuronorma Project): Norms for the Abbreviated Barcelona Test. ARCH CLIN NEUROPSYCH. 26:144-157. I.F.: 2.30.

40 Arenaza-Urquijo EM, Bosch B, Sala-Llonch R, Sole-Padulles C, Junque C, Fernandez-Espejo D, Bargallo N, Rami L, Molinuevo JL, Bartres-Faz D. Specific Anatomic Associations Between White Matter Integrity and Cognitive Reserve in Normal and Cognitively Impaired Elders. AM J GERIAT PSYCHIAT. 19:33-42. I.F.: 3.57.

41 Mattsson N, Andreasson U, Persson S, Arai H, Batish SD, Bernardini S, Bocchio-Chiavetto L, Blankenstein MA, Carrillo MC, Chalbot S, Coart E, Chiasserini D, Cutler N, Dahlfors G, Duller S, Fagan AM, Forlenza O, Frisoni GB, Galasko D, Galimberti D, Hampel H, Handberg A, Heneka MT, Herskovits AZ, Herukka SK, Holtzman DM, Humpel C, Hyman BT, Iqbal K, Jucker M, Kaeser SA, Kaiser E, Kapaki E, Kidd D, Klivenyi P, Knudsen CS, Kummer MP, Lui J, Llado A, Lewczuk P, Li QX, Martins R, Masters C, Mcauliffe J, Mercken M, Moghekar A, Molinuevo JL, Montine TJ, Nowatzke W, O'brien R, Otto M, Paraskevas GP, Parnetti L, Petersen RC, Prvulovic D, DeReus HPM, Rissman RA, Scarpini E, Stefani A, Soininen H, Schroder J, Shaw LM, Skinningsrud A, Skrogstad B, Spreer A, Talib L, Teunissen C, Trojanowski JQ, Tumani H, Umek RM, VanBroeck B, Vanderstichele H, Vecsei L, Verbeek MM, Windisch M, Zhang J, Zetterberg H, Blennow K. The Alzheimer's Association external quality control program for cerebrospinal fluid biomarkers. ALZHEIMERS DEMENT. 7:386-395. I.F.: 5.90.

42 Marin C, Bonastre M, Aguilar E, Jimenez A. The Metabotropic Glutamate Receptor Antagonist 2-Methyl-6-(phenylethynyl) pyridine Decreases Striatal VGLUT2 Expression in Association With an Attenuation of L-Dopa-Induced Dyskinesias. SYNAPSE. 65:1080-1086. I.F.: 2.93.

43 Iranzo A, Frauscher B, Santos H, Gschliesser V, Ratti L, Falkenstetter T, Sturner C, Salamero M, Tolosa E, Poewe W, Santamaria J, Hogl B. Usefulness of the SINBAR electromyographic montage to detect the motor and vocal manifestations occurring in REM sleep behavior disorder. SLEEP MED. 12:284-288. I.F.: 3.43.

44 Scherfler C, Frauscher B, Schocke M, Iranzo A, Gschliesser V, Seppi K, Santamaria J, Tolosa E, Hogl B, Poewe W. White and Gray Matter Abnormalities in Idiopathic Rapid Eye Movement Sleep Behavior Disorder: A Diffusion-Tensor Imaging and Voxel-Based Morphometry Study. ANN NEUROL. 69:400-407. I.F.: 10.75.

REVIEWS
I.F.: 12.21

1 Bosch X, Saiz A, Ramos-Casals M. Monoclonal antibody therapy-associated neurological disorders. NAT REV NEUROL. 7:165-172. I.F.: 6.51.

2 Molinuevo JL. Memantine: the value of combined therapy. REV NEUROLOGIA. 52:95-100. I.F.: 1.22.

3 Wenning GK, Litvan I, Tolosa E. Milestones in Atypical and Secondary Parkinsonisms. MOVEMENT DISORD. 26:1083-1095. I.F.: 4.48.

MULTICENTRICS
I.F.: 4.26

1 Frolich L, Ashwood T, Nilsson J, Eckerwall G. Effects of AZD3480 on Cognition in Patients with Mild-to-Moderate Alzheimer's Disease: A Phase IIb Dose-Finding Study. J ALZHEIMERS DIS. 24:363-374. I.F.: 4.26.

GRANTS FOR RESEARCH IN PROGRESS

Tolosa E. Síntomas no-motores e integridad de la vía nigroestriatal en portadores "asintomáticos" de mutaciones en el gen LRRK2. Sponsored by: Instituto de Salud Carlos III, PI080155. Duration: 01/01/2009-30/06/2012.

Marti M. Valor predictivo y diagnóstico de demencia en la enfermedad de parkinson de los marcadores de patología tau y beta-amiloide en líquido cefalorraquídeo y tomografía de emisión de positrones. Sponsored by: Instituto de Salud Carlos III, PI080236. Duration: 01/01/2009-31/12/2011.

Tolosa E. Grup de recerca de malalties neurològiques. Sponsored by: AGAUR (Agència de Gestió d'Sponsored bys Universitaris i de Recerca -Generalitat de Catalunya), 2009 SGR1019. Duration: 01/01/2009-31/12/2013.

Marin C. Disfunción olfativa en la enfermedad de Parkinson y su relación con la neurogénesis en la zona subventricular: estudio funcional, molecular e in vitro en el parkinsonismo experimental. Sponsored by: Instituto de Salud Carlos III, PI080060. Duration: 01/01/2009-31/12/2011.

Ezquerra M. Identificación de biomarcadores de mirnas en el líquido cefalorraquídeo con interés diagnóstico para la enfermedad de Parkinson y otros parkinsonismos relacionados. Sponsored by: Instituto de Salud Carlos III, PI09/1038. Duration: 01/01/2010-31/12/2012.

Tolosa E. European Project on Mendelian Forms of Parkinson's Disease. Sponsored by: Eberhard-Karls Universitaet Tuebingen, 241791. Duration: 01/04/2010-31/03/2013.

Molinuevo JL. Disfunción cerebral durante el envejecimiento: relevancia para la enfermedad de Alzheimer. Sponsored by: Ministerio de Ciencia E Innovacion, CSD2010-00045. Duration: 27/12/2010-26/12/2015.

Sanchez R. Estudio portadores de mutaciones determinantes de demencias monogénicas en fase preclínica: valoración cognitiva, estudio por RMN de volúmenes y conectividad cerebral y de marcadores en LCR. Sponsored by: Instituto de Salud Carlos III, PI080036. Duration: 01/01/2009-30/12/2011.

Tolosa E. LRRK2 Cohort Consortium 2010 - "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 Disease (MJFF), PI08/90348. Duration: 01/01/2011-31/12/2013.

Rami L. Evolución cognitiva de un grupo de sujetos con envejecimiento saludable frente a sujetos con cognición normal a riesgo de la enfermedad de Alzheimer. Sponsored by: MSPSI_Imserso, 11 197/11. Duration: 23/12/2011-22/12/2012.

Valldeoriola F. Estudio de la enervación simpática cardíaca a través de gammagrafía con 123I-MIBG en la enfermedad de parkinson, parkinsonismo vascular y en pacientes con mutaciones del gen LRRK2. Sponsored by: Instituto de Salud Carlos III, PI070426. Duration: 26/11/2007-30/03/2011.

DOCTORAL THESES

Molinuevo JL. Estudios miltimodales de reesonancia magnética y de líquido cefalorraquídeo en la enfermedad de Alzheimer preclínica familiar y esporádica. PhD student: Juan Fortea Ormaechea.

Tolosa E. Prevalencia, fenotipo clínico y neuropatológico del Parkinsonismo asociado a mutaciones en el gen LRRK2. PhD student: Carles Gaig Ventura.

AREA 4

Clinical and experimental neuroscience

Neurophysiology and functional studies of the nervous system

TEAM INVOLVED IN:
RETIC en Oftalmología (OFTARED)

GROUP MEMBERS

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Merche Morales (IDIBAPS)
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Carles Gaig (Hospital Clínic)
Javier Aparicio (Hospital Clínic)
Jonathan Giblin (UB, Investigador Ramon y Cajal)

VISITING SCIENTISTS:
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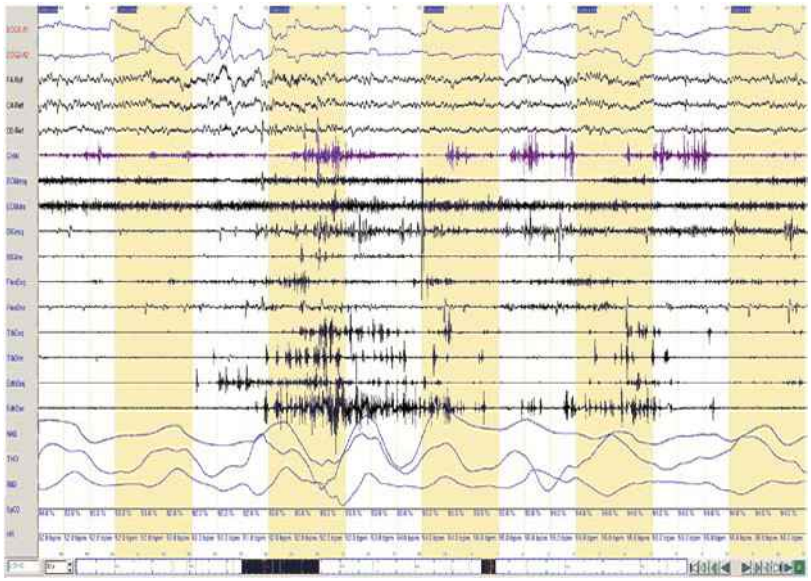
Markus Kofler (Hochzirl Neurorehabilitation Hospital, Zirl, Austria)
Juan M. Castellote (Instituto de Salud Carlos III, Madrid, España)

STRATEGIC OBJECTIVES

Expansion of scientific knowledge on functional aspects of the nervous system, with maximum integration of the 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 the regulation of intraocular pressure and glaucoma pathophysiology.



EMG hyperactivity in REM sleep behaviour disorders. Polysomnographic Study (PSG). The figure shows the recording of the electromyographic activity (EMG) of eleven muscles in a patient with REM sleep behaviour disorder (RBD). The aim of the study is to find the cut-off values for EMG activity during episodes of REM sleep which differentiate patients with RBD from the controls. In addition to carrying out a conventional PSG set-up (electro-oculogram, electroencephalogram, electrocardiogram, EMG of the mind, nasal flux, chest/abdominal effort and posture), an EMG was recorded of the surface of 5 muscle pairs: SCM (sternocleidomastoid), BIC (biceps brachii), FlexDS (flexor digitorum superficialis - fingers), TA (tibialis anterior) and ExtDB (extensor digitorum brevis - toes), right and left. Thirty seconds of REM sleep are shown with abnormal increase in EMG activity.

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. Prepulse phenomena.
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. Numbness. 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.

RESEARCH GROUP
NEUROPHYSIOLOGY

Group Leader: Xavier Gasull (UB)

Within the field of neurophysiology, the group is interested in establishing the functions of different ion channels in the regulation of different cell processes. In particular, at neuron level, we are investigating different ion channels implicated in cellular excitability in sensory neurons of the dorsal root ganglia and trigeminal ganglion, and their relationship with neuropathic pain. On the other hand, in trabecular cells that regulate aqueous humor flow in the eye, we are exploring the role of the cytoskeleton and of different ion channels in the functioning of these cells and their relationship with the physiopathology of glaucoma.

PUBLICATIONS

ORIGINALS
I.F.: 128.70

1 Iranzo A, Valldeoriola F, Lomena F, Molinuevo JL, Serradell M, Salamero M, Cot A, Ros D, Pavia J, Santamaria J, Tolosa E. Serial dopamine transporter imaging of nigrostriatal function in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective study. LANCET NEUROL. 10:797-805. I.F.: 21.66.

2 Munoz E, Iranzo A, Rauek S, Lomena F, Gallego J, Ros D, Santamaria J, Tolosa E. Subclinical nigrostriatal dopaminergic denervation in the cerebellar subtype of multiple system atrophy (MSA-C). J NEUROL. 258:2248-2253. I.F.: 3.85.

3 Rami L, Fortea J, Bosch B, Sole-Padulles C, Llado A, Iranzo A, Sanchez-Valle R, Molinuevo JL. Cerebrospinal Fluid Biomarkers and Memory Present Distinct Associations along the Continuum from Healthy Subjects to AD Patients. J ALZHEIMERS DIS. 23:1-8. I.F.: 4.26.

4 Antonell A, Fortea J, Rami L, Bosch B, Balasa M, Sanchez-Valle R, Iranzo A, Molinuevo JL, Llado A. Different profiles of Alzheimer's disease cerebrospinal fluid biomarkers in controls and subjects with subjective memory complaints. J NEURAL TRANSM. 118:259-262. I.F.: 2.60.

5 Moreno-Lopez C, Santamaria J, Salamero M, DelSorbo F, Albanese A, Pellecchia MT, Barone P, Overeem S, Bloem B, Aarden W, Canesi M, Antonini A, Duerr S, Wenning GK, Poewe W, Rubino A, Meco G, Schneider SA, Bhatia KP, Djaldetti R, Coelho M, Sampaio C, Cochen V, Hellriegel H, Deuschl G, Colosimo C, Marsili L, Gasser T, Tolosa E. Excessive Daytime Sleepiness in Multiple System Atrophy (SLEEMSA Study). ARCH NEUROL-CHICAGO. 68:223-230. I.F.: 7.11.

6 Costa J, Guzman J, Valldeoriola F, Rumia J, Tolosa E, Casanova-Molla J, Valls-Sole J. Modulation of the soleus H reflex by electrical subcortical stimuli in humans. EXP BRAIN RES. 212:439-448. I.F.: 2.30.

7 Iranzo A, Frauscher B, Santos H, Gschliesser V, Ratti L, Falkenstetter T, Sturner C, Salamero M, Tolosa E, Poewe W, Santamaria J, Hogl B. Usefulness of the SINBAR electromyographic montage to detect the motor and vocal manifestations occurring in REM sleep behavior disorder. SLEEP MED. 12:284-288. I.F.: 3.43.

8 Scherfler C, Frauscher B, Schocke M, Iranzo A, Gschliesser V, Seppi K, Santamaria J, Tolosa E, Hogl B, Poewe W. White and Gray Matter Abnormalities in Idiopathic Rapid Eye Movement Sleep Behavior Disorder: A Diffusion-Tensor Imaging and Voxel-Based Morphometry Study. ANN NEUROL. 69:400-407. I.F.: 10.75.

9 Schestatsky P, Callejas MA, Valls-Sole J. Abnormal modulation of electrodermal activity by thermoalgesic stimuli in patients with primary palmar hyperhidrosis. J NEUROL NEUROSURPS. 82:92-96. I.F.: 4.79.

10 Casanova-Molla J, Morales M, Sola-Valls N, Bosch A, Calvo M, Grau-Junyent JM, Valls-Sole J. Axonal fluorescence quantitation provides a new approach to assess cutaneous innervation. J NEUROSCI METH. 200:190-198. I.F.: 2.10.

11 Murillo N, Kumru H, Vidal-Samso J, Benito J, Medina J, Navarro X, Valls-Sole J. Decrease of spasticity with muscle vibration in patients with spinal cord injury. CLIN NEUROPHYSIOL. 122:1183-1189. I.F.: 2.79.

12 Albanese A, Asmus F, Bhatia KP, Elia AE, Elibol B, Filippini G, Gasser T, Krauss JK, Nardocci N, Newton A, Valls-Sole J. EFNS guidelines on diagnosis and treatment of primary dystonias. EUR J NEUROL. 18:5-18. I.F.: 3.77.

13 Fernandez S, Donaire A, Maestro I, Seres E, Setoain X, Bargallo N, Rumia J, Boget T, Falcon C, Carreno M. Functional neuroimaging in startle epilepsy: Involvement of a mesial frontoparietal network. EPILEPSIA. 52:1725-1732. I.F.: 3.96.

14 Sala-Blanch X, Lopez AM, Pomes J, Valls-Sole J, Garcia AI, Hadzic A. No Clinical or Electrophysiologic Evidence of Nerve Injury after Intraneural Injection during Sciatic Popliteal Block. ANESTHESIOLOGY. 115:589-595. I.F.: 5.49.

15 Casanova-Molla J, Grau-Junyent JM, Morales M, Valls-Sole J. On the relationship between nociceptive evoked potentials and intraepidermal nerve fiber density in painful sensory polyneuropathies. PAIN. 152:410-418. I.F.: 5.36.

16 Casanova-Molla J, Leon L, Castillo CD, Valls-Sole J. Reinnervation by the contralateral facial nerve in patients with peripheral facial palsy. MUSCLE NERVE. 44:923-929. I.F.: 2.30.

17 Perez-Diaz H, Iranzo A, Rye DB, Santamaria J. Restless abdomen A phenotypic variant of restless legs syndrome. NEUROLOGY. 77:1283-1286. I.F.: 8.02.

18 Carreno M, Becerra JL, Castillo J, Maestro I, Donaire A, Fernandez S, Bargallo N, Setoain X, Pintor L, Bailles E, Rumia J, Boget T, Vernet O, Fumanal S. Seizure frequency and social outcome in drug resistant epilepsy patients who do not undergo epilepsy surgery. SEIZURE-EUR J EPILEP. 20:580-582. I.F.: 1.65.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	67.12	19	11	3
2010	107.69	20	10	6
2011	128.70	26	12	7

19 Marinas A, Elices E, Gil-Nagel A, Salas-Puig J, Sanchez JC, Carreno M, Villanueva V, Rosendo J, Porcel J, Serratosa JM. Socio-occupational and employment profile of patients with epilepsy. EPILEPSY BEHAV. 21:223-227. I.F.: 1.99.

20 Cortes M, Thickbroom GW, Valls-Sole J, Pascual-Leone A, Edwards DJ. Spinal associative stimulation: A non-invasive stimulation paradigm to modulate spinal excitability. CLIN NEUROPHYSIOL. 122:2254-2259. I.F.: 2.79.

21 Leon L, Casanova-Molla J, Lauria G, Valls-Sole J. The somatosensory blink reflex in upper and lower brainstem lesions. MUSCLE NERVE. 43:196-202. I.F.: 2.30.

22 Rubi S, Setoain X, Donaire A, Bargallo N, Sanmarti F, Carreno M, Rumia J, Calvo A, Aparicio J, Campistol J, Pons F. Validation of FDG-PET/MRI coregistration in nonlesional refractory childhood epilepsy. EPILEPSIA. 52:2216-2224. I.F.: 3.96.

23 Tulleuda A, Cokic B, Callejo G, Saiani B, Serra J, Gasull X. TRESK channel contribution to nociceptive sensory neurons excitability: modulation by nerve injury. MOL PAIN. 7:30. I.F.: 4.15.

24 Deval E, Noël J, Gasull X, Delaunay A, Alloui A, Friend V, Eschalier A, Lazdunski M, Lingueglia E. Acid-sensing ion channels in postoperative pain. J NEUROSCI. 31(16):6059-66. I.F.: 7.27

25 Cuesto G, Enriquez-Barreto L, Caramés C, Cantarero M, Gasull X, Sandi C, Ferrús A, Acebes Á, Morales M. Phosphoinositide-3-kinase activation controls synaptogenesis and spinogenesis in hippocampal neurons. J NEUROSCI. 31(8):2721-33. I.F.: 7.27

26 Castany M, Jordi I, Catala J, Gual A, Morales M, Gasull X, Pintor J. Glaucoma patients present increased levels of diadenosine tetraphosphate, Ap(4)A, in the aqueous humour. EXP EYE RES. 92(3):221-6. I.F.: 2.82

REVIEWS
I.F.: 4.96

1 Valls-Sole J, Castillo CD, Casanova-Molla J, Costa J. Clinical consequences of reinnervation disorders after focal peripheral nerve lesions. CLIN NEUROPHYSIOL. 122:219-228. I.F.: 2.79.

2 Iranzo A. Sleep-wake changes in the premotor stage of Parkinson disease. J NEUROL SCI. 310:283-285. I.F.: 2.17.

GRANTS FOR RESEARCH IN PROGRESS

Valls J. Mecanismos fisiopatológicos en la cronificación del dolor neuropático y en el origen del síndrome regional complejo. Sponsored by: Instituto de Salud Carlos III, PI080266. Duration: 31/12/2008-30/12/2011.

Gual A. Patologia ocular del envejecimiento, calidad visual y calidad de vida. Redes temáticas de centros (RETIC). Sponsored by: Ministerio de Sanidad y Consumo, RD07/0062/0006. Duration: 01/01/2007-31/12/2012.

Gasull X. El canal de leak TRESK en la excitabilidad neuronal nociceptiva: implicaciones en el dolor neuropático. Sponsored by: FIS, Ministerio de Sanidad y Consumo, PI080014. Duration: 01/01/2009-31/12/2011.

Gual A. Lab. Neurofisiologia. Grup consolidat Generalitat de Catalunya. Sponsored by: Generalitat de Catalunya, SGR09_869. Duration: 01/01/2009-31/12/2013.

Valls J. Intervencions sobre els components sensorial i emocional de les respostes a estímuls de dolor en pacients amb dolor neuropàtic crònic (Interventions on emotional responses to pain stimuli in patients with chronic neuropathic pain). Sponsored by: Fundació La Marató de TV3, 071930. Duration: 25/02/2008-24/05/2011.

Gasull X. Desarrollo de un proyecto llamado "Soluciones innovadoras para acelerar la identificación y desarrollo de fármacos para patologías del Sistema Nervioso. Sponsored by: Ministerio de Economía y Competitividad, CENIT10 10/158. Duration: 01/01/2011-31/12/2012.

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. Nous compostos pel tractament de Glaucoma. Sponsored by: Generalitat de Catalunya (Centre d'Innovació i Desenvolupament Empresarial CIDEM), VALTEC09-1-0008. Duration: 01/01/2009-31/12/2011.

Valls J. Neurofisiologia del dolor, epilèpsia, son i control motor (NEDESC). Sponsored by: Generalitat de Catalunya - AGAUR, SGR09_1253. Duration: 15/09/2009-31/12/2013.

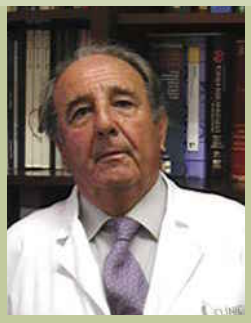
AREA 4

Clinical and experimental neuroscience

Secondary lesions due to chronic alcohol ingestion, muscle pathology

TEAM INVOLVED IN: ciberer & ciberobn

GROUP MEMBERS



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Xavier Bosch (Hospital Clínic)
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STRATEGIC OBJECTIVES

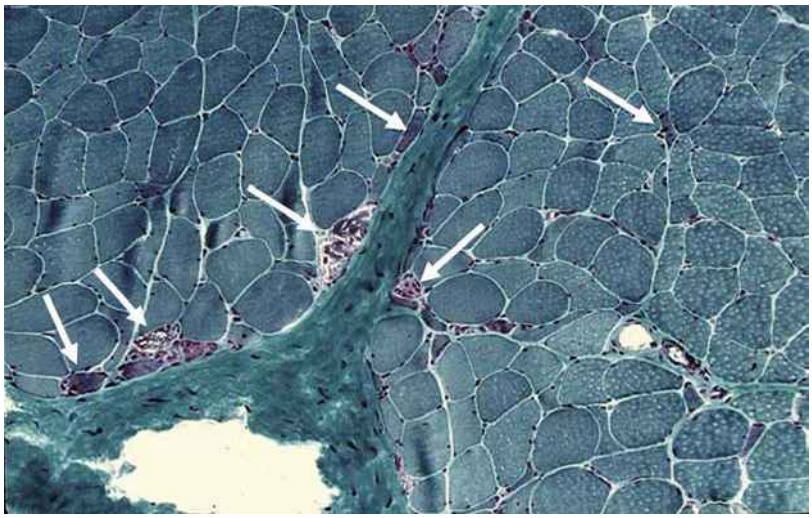
1. Study of the pathological mechanisms of alcohol upon the organ cells and its pathological effects at neurological and cardiocirculatory level.
2. Importance of alcohol in intracytosolic calcium transport.
3. Effect of food upon the prevention of chronic diseases and cancer.
4. Prognosis of alcoholic myocardiopathy and its best management options.
5. Study of muscle and myocardial apoptosis in subjects presenting chronic alcohol abuse.
6. Study of the physiopathology of muscle diseases, particularly as regards the muscle immunohistochemical, immunogenetic and angiogenic changes (prognostic factors) in inflammatory myopathies.
7. Study of metabolic myopathic disorders, particularly relating to glycogenosis and myoadenylate deaminase deficiency.
8. Study of myocardial regeneration in alcoholic myocardiopathy.
9. Clinical and functional repercussions of chronic fatigue syndrome.
10. Study of the moderate consumption of wine and the Mediterranean diet in the prevention of cardiovascular diseases.
11. Study of primary mitochondrial myopathic disorders in the adult and of secondary mitochondrial involvement in different pathological and toxic situations.
12. Study of the physiopathological mechanisms involved in the development of systemic vasculitis.

Our future challenges are:

1. Furthering of knowledge of the action of alcohol upon signals translation and the appearance of apoptosis at muscle and myocardial level, and of the impact that alterations

in mitochondrial DNA and in the mitochondrial respiratory chain may have upon degenerative diseases such as Alzheimer's disease, inflammatory myopathy and inclusion body diseases.

2. Furthering of knowledge of the prognostic factors in dermatomyositis, with a view to allowing early identification of those cases requiring stronger treatment measures (anti-TNF agents, gammaglobulins).
3. Characterization of the clinical and morphological aspects of metabolic muscle diseases (glycogenosis and MDA deficiency).
4. Study of sarcopenia in the geriatric population.
5. In-depth investigation of the mitochondrial toxicity of antiretroviral drugs and carbon monoxide (CO).
6. Evaluation of the involvement of mitochondrias in disorders such as Parkinson's disease, reduced intrauterine fetal growth or sepsis.
7. Proteomic studies to clarify the mechanisms of skeletal and cardiac muscle damage secondary to alcohol exposure.
8. Study of myocardial cell regeneration from stem cells in the myocardium of chronic alcoholic patients.
9. Study of serum and urine biomarkers in relation to food consumption and changes in cardiovascular disease risk factors.
10. In-depth study of the mechanisms involved in the development of systemic vasculitis.



Gomori trichromic staining of a muscle fibre in a patient with HIV infection showing mitochondrial toxicity due to antiretroviral treatment with zidovudine (AZT). The white arrows indicate the presence of so-called ragged-red fibres, suggestive of toxic myopathy.

MAIN LINES OF RESEARCH

I Research Group in Muscle and Mitochondrial Function:

1. Histological, histochemical and immunohistochemical study of muscle diseases.
2. Study of mitochondrial function in patients susceptible to mitochondrial disorders of genetic (primary) or toxic (secondary) origin.
3. Study of mitochondrial diseases, with special emphasis on biochemical and genetic investigations in different cell substrates.
4. Analysis of mitochondrial respiration and DNA in muscle, adipose tissue and lymphocytes of HIV-infected patients subjected to antiretroviral therapy.
5. Effect of smoking, carbon monoxide, neuroleptic drugs and antibiotics upon the mitochondrial function.
6. Mitochondrial dysfunction in Parkinson's disease, reduced intrauterine fetal growth and sepsis.

II Vascular inflammation:

1. Expressions of cytokines and growth factors in vascular inflammatory lesions and their relationship with phenotypic expression, complications and the prognosis of systemic vasculitis.
2. Study of the interactions among lymphocytes, endothelium and extracellular matrix in the development and perpetuation of vascular inflammation and in the mechanisms that participate in vascular occlusion and regeneration.
3. Development of a questionnaire for evaluating quality of life in patients with giant cell arteritis (international study).
4. Expression of angiogenic and antiangiogenic factors as prognostic data in dermatomyositis.

III Prevention and treatment of cardiovascular diseases:

1. Research is being carried out into the relationship between alcohol and arterial hypertension; the evolution of alcoholic myocardiopathy, the role of phenolic derivatives in wine, beer and alcohol as influencing factors in the development of atherosclerosis; the effect of nicotine and aging upon mitochondrial respiration; and the presence of growth factors and adhesion molecules in angiogenesis, apoptosis, myocardiopathy and alcoholic myopathy.
2. Study of the effects of moderate wine consumption, the Mediterranean diet and other polyphenol-rich products such as tomatoes in the primary prevention of cardiovascular disease and other degenerative disorders.
3. Proteomic studies of skeletal and cardiac muscle in relation to the pathogenesis of tissue damage secondary to alcohol exposure.

PUBLICATIONS

ORIGINALS
I.F.: 111.22

1 Prieto-Gonzalez S, Cardellach F, Estruch R, Miguel R, Grau JM, Cid MC. Type 1 autoimmune hepatitis in a patient with microscopic polyangiitis: challenges in diagnosis and treatment. MED CLIN-BARCELONA. 136:345-348. I.F.: 1.41.

2 Garrabou G, Lopez S, Moren C, Martinez E, Fontdevila J, Cardellach F, Gatell JM, Miro O. Mitochondrial damage in adipose tissue of untreated HIV-infected patients. AIDS. 25:165-170. I.F.: 6.35.

3 Moren C, Noguera-Julian A, Rovira N, Garrabou G, Nicolas M, Cardellach F, Martinez E, Sanchez E, Miro O, Fortuny C. Mitochondrial assessment in asymptomatic HIV-infected paediatric patients on HAART. ANTIVIR THER. 16:719-724. I.F.: 3.77.

4 Moren C, Noguera-Julian A, Rovira N, Corrales E, Garrabou G, Hernandez S, Nicolas M, Tobias E, Cardellach F, Miro O, Fortuny C. Mitochondrial impact of human imnunodeficiency virus and antiretrovirals on infected pediatric patients with or without lipodystrophy. PEDIATR INFECT DIS J. 30:992-995. I.F.: 3.06.

5 Garrabou G, Inoriza JM, Moren C, Oliu G, Miro O, Marti MJ, Cardellach F. Mitochondrial Injury in Human Acute Carbon Monoxide Poisoning: The Effect of Oxygen Treatment. J ENVIRON SCI HEAL C. 29:32-51. I.F.: 4.84.

6 Schroder H, Fito M, Estruch R, Martinez-Gonzalez MA, Corella D, Salas-Salvado J, Lamuela-Raventos R, Ros E, Salaverria I, Fiol M, Lapetra J, Vinyoles E, Gomez-Gracia E, Lahoz C, Serra-Majem L, Pinto X, Ruiz-Gutierrez V, Covas MI. A Short Screener Is Valid for Assessing Mediterranean Diet Adherence among Older Spanish Men and Women. J NUTR. 141:1140-1145. I.F.: 4.30.

7 Bullo M, Garcia-Aloy M, Martinez-Gonzalez MA, Corella D, Fernandez-Ballart JD, Fiol M, Gomez-Gracia E, Estruch R, Ortega-Calvo M, Francisco S, Flores-Mateo G, Serra-Majem L, Pinto X, Covas MI, Ros E, Lamuela-Raventos R, Salas-Salvado J. Association between a healthy lifestyle and general obesity and abdominal obesity in an elderly population at high cardiovascular risk. PREV MED. 53:155-161. I.F.: 3.30.

8 Murie-Fernandez M, Irimia P, Toledo E, Martinez-Vila E, Buil-Cosiales P, Serrano-Martinez M, Ruiz-Gutierrez V, Ros E, Estruch R, Martinez-Gonzalez MA. Carotid intima-media thickness changes with Mediterranean diet: A randomized trial (PREDIMED-Navarra). ATHEROSCLEROSIS. 219:158-162. I.F.: 4.09.

9 Sala-Vila A, Harris WS, Cofan M, Perez-Heras AM, Pinto X, Lamuela-Raventos RM, Covas MI, Estruch R, Ros E. Determinants of the omega-3 index in a Mediterranean population at increased risk for CHD. BRIT J NUTR. 106:425-431. I.F.: 3.07.

10 Sola R, Fito M, Estruch R, Salas-Salvado J, Corella D, DeLaTorre R, Munoz MA, Lopez-Sabater MD, Martinez-Gonzalez MA, Aros F, Ruiz-Gutierrez V, Fiol M, Casals E, Warnberg J, Buil-Cosiales P, Ros E, Konstantinidou V, Lapetra J, Serra-Majem L, Covas MI. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: A randomized, controlled trial. ATHEROSCLEROSIS. 218:174-180. I.F.: 4.09.

11 Salas-Salvado J, Bullo M, Babio N, Martinez-Gonzalez MA, Ibarrola-Jurado N, Basora J, Estruch R, Covas MI, Corella D, Aros F, Ruiz-Gutierrez V, Ros E. Reduction in the Incidence of Type 2 Diabetes With the Mediterranean Diet Results of the PREDIMED-Reus nutrition intervention randomized trial. DIABETES CARE. 34:14-19. I.F.: 7.14.

12 Medina-Remon A, Zamora-Ros R, Rotches-Ribalta M, Andres-Lacueva C, Martinez-Gonzalez MA, Covas MI, Corella D, Salas-Salvado J, Gomez-Gracia E, Ruiz-Gutierrez V, DeLaCorte FJG, Fiol M, Pena MA, Saez GT, Ros E, Serra-Majem L, Pinto X, Warnberg J, Estruch R, Lamuela-Raventos RM. Total polyphenol excretion and blood pressure in subjects at high cardiovascular risk. NUTR METAB CARDIOVAS. 21:323-331. I.F.: 3.44.

13 Estruch R, Sacanella E, Mota F, Chiva-Blanch G, Antuneza E, Casals E, Deulofeu R, Rotilio D, Andres-Lacueva C, Lamuela-Raventos RM, DeGaetano G, Urbano-Marquez A. Moderate consumption of red wine, but not gin, decreases erythrocyte superoxide dismutase activity: A randomised cross-over trial. NUTR METAB CARDIOVAS. 21:46-53. I.F.: 3.44.

14 Lluis M, Fernandez-Sola J, Castellvi-Bel S, Sacanella E, Estruch R, Urbano-Marquez A. Evaluation of Myocyte Proliferation in Alcoholic Cardiomyopathy: Telomerase Enzyme Activity (TERT) Compared with Ki-67 Expression. ALCOHOL ALCOHOLISM. 46:534-541. I.F.: 2.60.

15 Villegas E, Estruch R, Mengod G, Cortes R. NMDA receptors in frontal cortex and hippocampus of alcohol consumers. ADDICT BIOL. 16:163-165. I.F.: 4.15.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	119.15	23	16	6
2010	65.52	17	9	6
2011	111.22	27	9	6

16 Casanova-Molla J, Morales M, Sola-Valls N, Bosch A, Calvo M, Grau-Junyent JM, Valls-Sole J. Axonal fluorescence quantitation provides a new approach to assess cutaneous innervation. J NEUROSCI METH. 200:190-198. I.F.: 2.10.

17 Casanova-Molla J, Grau-Junyent JM, Morales M, Valls-Sole J. On the relationship between nociceptive evoked potentials and intraepidermal nerve fiber density in painful sensory polyneuropathies. PAIN. 152:410-418. I.F.: 5.36.

18 Prieto-Gonzalez S, Escoda R, Coloma E, Grau JM. Amoxicillin-induced acute aseptic meningitis. J CLIN NEUROSCI. 18:443-444. I.F.: 1.17.

19 Corella D, Tai ES, Sorli JV, Chew SK, Coltell O, Sotos-Prieto M, Garcia-Rios A, Estruch R, Ordovas JM. Association between the APOA2 promoter polymorphism and body weight in Mediterranean and Asian populations: replication of a gene-saturated fat interaction. INT J OBESITY. 35:666-675. I.F.: 5.13.

20 Chiva-Blanch G, Urpi-Sarda M, Rotches-Ribalta M, Zamora-Ros R, Llorach R, Lamuela-Raventos RM, Estruch R, Andres-Lacueva C. Determination of resveratrol and piceid in beer matrices by solid-phase extraction and liquid chromatography-tandem mass spectrometry. J CHROMATOGR A. 1218:698-705. I.F.: 4.19.

21 Bullo M, Estruch R, Salas-Salvado J. Dietary vitamin K intake is associated with bone quantitative ultrasound measurements but not with bone peripheral biochemical markers in elderly men and women. BONE. 48:1313-1318. I.F.: 4.60.

22 Cobo E, Cortes J, Ribera JM, Cardellach F, Selva-O'callaghan A, Kostov B, Garcia L, Cirugeda L, Altman DG, Gonzalez JA, Sanchez JA, Miras F, Urrutia A, Fonollosa V, Rey-Joly C, Vilardell M. Effect of using reporting guidelines during peer review on quality of final manuscripts submitted to a biomedical journal: masked randomised trial. BRIT MED J. 343:-. I.F.: 13.47.

23 Sacanella E, Perez-Castejon JM, Nicolas JM, Masanes F, Navarro M, Castro P, Lopez-Soto A. Functional status and quality of life 12 months after discharge from a medical ICU in healthy elderly patients: a prospective observational study. CRIT CARE. 15:-. I.F.: 4.60.

24 Nunez M, Fernandez-Sola J, Nunez E, Fernandez-Huerta JM, Godas-Sieso T, Gomez-Gil E. Health-related quality of life in patients with chronic fatigue syndrome: group cognitive behavioural therapy and graded exercise versus usual treatment. A randomised controlled trial with 1 year of follow-up. CLIN RHEUMATOL. 30:381-389. I.F.: 1.69.

25 Fernandez-Sola J, Lluis M, Sacanella E, Estruch R, Antunez E, Urbano-Marquez A. Increased Myostatin Activity and Decreased Myocyte Proliferation in Chronic Alcoholic Cardiomyopathy. ALCOHOL CLIN EXP RES. 35:1220-1229. I.F.: 3.47.

26 Nordmann AJ, Suter-Zimmermann K, Bucher HC, Shai I, Tuttle KR, Estruch R, Briel M. Meta-Analysis Comparing Mediterranean to Low-Fat Diets for Modification of Cardiovascular Risk Factors. AM J MED. 124:841-U100. I.F.: 5.12.

27 Sanchez-Villegas A, Galbete C, Martinez-Gonzalez MA, Martinez JA, Razquin C, Salas-Salvado J, Estruch R, Buil-Cosiales P, Marti A. The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: The PREDIMED-NAVARRA randomized trial. NUTR NEUROSCI. 14:195-201. I.F.: 1.30.

EDITORIALS
I.F.: 0.76

1 Fernandez-Sola J. Chronic fatigue syndrome: current situation. REV CLIN ESP. 211:407-409. I.F.:0.76.

CLINICAL GUIDELINES
I.F.: 1.41

1 Alobid I, Alonso JR, Barrot C, Benitez P, Canizares S, Castanyer T, Centellas S, Civeira E, Climent B, Duenas A, Fernandez-Sola J, Ferrer A, Gene M, Godas T, Gomez E, Montori E, Munne P, Nogue S, Picado C, Rovira E, Sanz P, Valero A. Multiple chemical sensitivity. MED CLIN-BARCELONA. 136:683-687. I.F.: 1.41.

GRANTS FOR RESEARCH IN PROGRESS

Urbano A. Identification and Validation of Alcohol Biomarker Signatures by Proteomics. (Subaward nº 080-04000-R82301). Sponsored by: Thomas Jefferson University, NIH06 5 R01 AA016210. Duration: 15/05/2006-30/04/2011.

Estruch R. Alimentación saludable en la prevención primaria de enfermedades crónicas: la Red PREDIMED. Sponsored by: Instituto de Salud Carlos III, RD06/0045/1003. Duration: 29/02/2008-31/12/2011.

Estruch R. Effects of a mediterranean diet intervention on atherosclerotic burden measured by imaging techniques and systemic biomarkers. PREDIMED. (Effects of a 2-year Mediterranean diet intervention on 3T MRI-monitored carotid plaque progression and vulnerability). Sponsored by: Centro Nacional de Investigaciones Cardiovasculares (CNIC), 06-2007-S01. Duration: 01/01/2008-31/12/2011.

Cardellach F, Coll JO, Hernandez AS, Garrabou G, Morén C. Toxicidad mitocondrial inducida por el consumo de tabaco en gestantes y sus recién nacidos. Sponsored by: FIS ISCIII, PI080229. Duration: 01/01/2009-31/12/2011.

Estruch R, Sacanella E, Masanes F, Chiva G, Casas R, Urpi M. Desarrollo de biomarcadores de consumo y de efecto de un patrón de alimentación Mediterranea en la prevención de la enfermedad cardiovascular. Una aproximación metabolómica. Sponsored by: Ministerio de Ciencia e Innovación, AGL2009-13906-C02-02. Duration: 01/01/2010-31/12/2012.

Grau J. Grup de Recerca Muscular. Sponsored by: Generalitat de Catalunya - AGAUR, 2009_SGR_1158. Duration: 23/09/2009-31/12/2013.

Sacanella E. Evaluación del efecto antihipertensivo y antiinflamatorio de los polifenoles, carotenos y vitamina C del tomate, según la ración dietética ingerida. Sponsored by: Ministerio de Ciencia e Innovación, AGL2010-22319-C03-02. Duration: 01/01/2011-31/12/2013.

Estruch R. Efectos de la dieta mediterránea sobre la carga arteriosclerótica medida mediante técnicas de imagen y biomarcadores vasculares. Sponsored by: MAPFRE, MAPFRE10_004. Duration: 16/02/2011-13/04/2012.

DOCTORAL THESES

Fernandez-Sola J. Estudi de la regeneració miocàrdica en la miocardiopatia alcohòlica i la seva relació amb el dany funcional i estructural miocàrdic, activació d'apoptosi i activitat miostatina. PhD student: Meritxell Lluis Padierna.

AREA 4

Clinical and experimental neuroscience

Cellular biology of pathological processes

TEAM INVOLVED IN: CIBERNED & Red de Terapia Celular

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Xavier Xifro (UG)

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

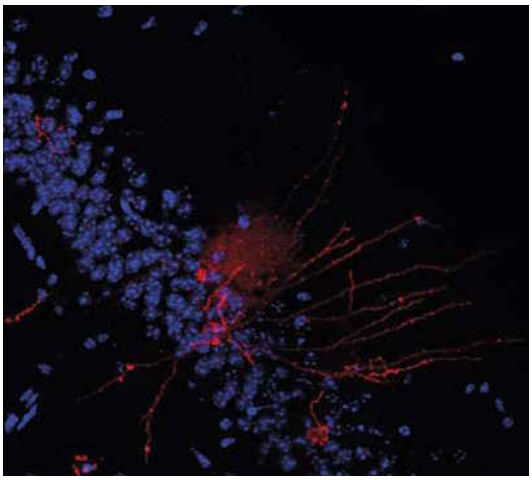
Cellular biology of pathological processes

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.
4. Exploration of the molecular mechanisms involved in the interaction of the cytoskeleton with the cell endomembrane system as structural and functional support in secretory and endocytic membrane traffic. Studies are also made of the way in which this interaction is altered in certain diseases such as alcoholism and other conditions with a strong cardiovascular base such as Marfan syndrome and Loeys-Dietz syndrome.

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 nucleus striatum.
5. Molecular bases of the interaction of actin dynamics with the Golgi apparatus and secretory traffic.
6. Role of diacylglycerol and phosphatidic acid in the formation of transport vesicles and in the structural organization of the Golgi apparatus.
7. Study of the signaling pathways that regulate the cytoskeleton and actin dynamics, altered by ethanol and other toxic agents.
8. Intracellular traffic and cytokine receptor signaling (TGF-beta).



Diolistic labeling (red) of hipocampal neuronal cells from HD mouse models. Nucleus are shown by DAPI staining (blue). Author: Verónica Brito.

RESEARCH GROUP
MEMBRANE TRAFFIC

Group Leader: **Gustavo Egea (UB)**

The objective of this group is to understand the principles that control and regulate transport of the membrane components (lipids and proteins) within the cell. In particular, we are investigating the interaction of the transport intermediaries (vesicles and tubules) with the actin cytoskeleton and its associated proteins and regulators (myosins and Rho GTPases). We are also exploring the way in which lipid homeostasis (particularly referred to diacylglycerol) participates in the organization and traffic of membranes and in the formation of transport intermediaries. Lastly, we wish to establish the physiopathological bases whereby ethanol alters nerve cell function and the mechanism underlying internalization of the receptors of cytokines such as TGF-beta in the smooth muscle cells of the coronary vessels in cardiovascular patients.

PUBLICATIONS

ORIGINALS
I.F.: 74.18

1 Rocha RA, Gimeno-Alcaniz JV, Martin-Ibanez R, Canals JM, Velez D, Devesa V. Arsenic and fluoride induce neural progenitor cell apoptosis. TOXICOL LETT. 203:237-244. I.F.: 3.58.

2 Sanchez-Gomez MV, Alberdi E, Perez-Navarro E, Alberch J, Matute C. Bax and calpain mediate excitotoxic oligodendrocyte death induced by activation of both AMPA and kainate receptors. J NEUROSCI. 31:2996-2300. I.F.: 7.27.

3 Giralt A, Carreton O, Lao-Peregrin C, Martin ED, Alberch J. Conditional BDNF release under pathological conditions improves Huntington's disease pathology by delaying neuronal dysfunction. MOL NEURODEGENER. 6:-. I.F.: 5.36.

4 Selva J, Egea G. Ethanol increases p190RhoGAP activity, leading to actin cytoskeleton rearrangements. J NEUROCHEM. 119:1306-1316. I.F.: 4.34.

5 Xifro X, Anglada-Huguet M, Rue L, Saavedra A, Perez-Navarro E, Alberch J. Increased 90-kDa ribosomal S6 kinase (Rsk) activity is protective against mutant huntingtin toxicity. MOL NEURODEGENER. 6:-. I.F.: 5.36.

6 Giralt A, Saavedra A, Carreton O, Xifro X, Alberch J, Perez-Navarro E. Increased PKA signaling disrupts recognition memory and spatial memory: role in Huntington's disease. HUM MOL GENET. 20:4232-4247. I.F.: 8.06.

7 Blazquez C, Chiarlone A, Sagredo O, Aguado T, Pazos MR, Resel E, Palazuelos J, Julien B, Salazar M, Borner C, Benito C, Carrasco C, Diez-Zaera M, Paoletti P, Diaz-Hernandez M, Ruiz C, Sendtner M, Lucas JJ, DeYebenes JG, Marsicano G, Monory K, Lutz B, Romero J, Alberch J, Gines S, Kraus J, Fernandez-Ruiz J, Galve-Roperh I, Guzman M. Loss of striatal type 1 cannabinoid receptors is a key pathogenic factor in Huntington›s disease. BRAIN. 134:119-136. I.F.: 9.23.

8 Almajano MP, Vila I, Gines S. Neuroprotective Effects of White Tea Against Oxidative Stress-Induced Toxicity in Striatal Cells. NEUROTOX RES. 20:372-378. I.F.: 3.02.

9 Sarri E, Sicart A, Lazaro-Dieguez F, Egea G. Phospholipid synthesis participates in the regulation of diacylglycerol required for membrane trafficking at the Golgi complex. J BIOL CHEM. 286:28632-28643. I.F.: 5.33.

10 Saavedra A, Giralt A, Ruee L, Xifro X, Xu J, Ortega Z, Lucas JJ, Lombroso PJ, Alberch J, Perez-Navarro E. Striatal-enriched protein tyrosine phosphatase expression and activity in Huntington's disease: a STEP in the resistance to excitotoxicity. J NEUROSCI. 31:8150-8162. I.F.: 7.27.

11 Bosch M, Mari M, Herms A, Fernandez A, Fajardo A, Kassan A, Giralt A, Colell A, Balgoma D, Barbero E, Gonzalez-Moreno E, Matias N, Tebar F, Balsinde J, Camps M, Enrich C, Gross SP, Garcia-Ruiz C, Perez-Navarro E, Fernandez-Checa JC, Pol A. Caveolin-1 Deficiency Causes Cholesterol-Dependent Mitochondrial Dysfunction and Apoptotic Susceptibility. CURR BIOL. 21:681-686. I.F.: 10.03.

12 Smith SE, Granell S, Salcedo-Sicilia L, Baldini G, Egea G, Teckman JH and Baldini G. ATF6 limits intracellular accumulation of mutant alpha-1-antitrypsin Z and mitochondrial damage in hepatoma cells. J BIOL CHEM. 286:41563-41577. I.F.: 5.33

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	24.17	5	3	2
2010	65.35	11	10	1
2011	74.18	12	9	0

GRANTS FOR RESEARCH IN PROGRESS

Canals JM. Red de Terapia Celular. Sponsored by: Ministerio Sanidad y Consumo, RD06/0010/0006. Duration: 01/01/2007-31/12/2012.

Alberch J. Generación de nuevos modelos de enfermedad de Huntington para valorar el papel del BDNF en los mecanismos patogénicos y en nuevas perspectivas terapéuticas. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), SAF2008-04360. Duration: 01/01/2009-31/12/2011.

Alberch J. Habilitación de salas GMP para el programa de terapia celular de la Facultat de Medicina. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), PLE2009-0128. Duration: 01/11/2009-31/10/2012.

Canals JM. Mejora de la supervivencia y diferenciación de células madre neurales humanas para terapia celular de la enfermedad de Huntington. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), PLE2009-0089. Duration: 01/11/2009-31/10/2012.

Gines S. Role of p75 Neurotrophin Receptor in Huntington's Disease. Sponsored by: HIGH Q FOUNDATION - INC -OFICIAL, A-3468. Duration: 01/05/2010-30/04/2012.

Gines S. Role of Cdk5 in Striatal and Hippocamapl Pathology in Huntingtons Disease. Sponsored by: HIGH Q FOUNDATION - INC -OFICIAL, A-3880. Duration: 01/11/2010-31/10/2012.

Egea G. Red Nacional sobre Integración funcional del tráfico de membranas, la señalización intracelular y la dinámica del citoesqueleto. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), BFU2008-03958-E/BMC. Duration: 01/11/2009-30/12/2012.

Egea G. La dinámica de la actina y la homeostasis del diacilglicerol en la organización del aparato de Golgi. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), BFU2009-07186(BMC). Duration: 01/01/2009-31/12/2012.

Egea G. Nanotecnologías en Biomedicina (NanoBiomed). Sponsored by: Ministerio de Ciencia e Innovación (MICINN), Programa Consolider, CSD2006-00012 . Duration: 01/01/2006-14/09/2011.

Gines S. Estudio de las cascadas de señalización asociadas a la activación dopaminérgica y glutamatérgica como estrategia terapéutica en modelos murinos de la enfermedad de Huntington: Papel de la vía de Cdk5. Sponsored by: Ministerio de Ciencia e Innovación, SAF2009-07077. Duration: 01/01/2009-31/12/2012.

Canals JM. Caracterización de nuevos factores de transcripción para la diferenciación neuronal de células madre para la enfermedad neurodegenerativa de Huntington. Sponsored by: Ministerio de Ciencia e Innovación (MICINN), SAF2009-07774. Duration: 01/01/2010-31/12/2012.

Alberch J. Fisiopatología de las enfermedades neurodegenerativas. Sponsored by: Generalitat de Catalunya, SGR2009-00326. Duration: 01/01/2009-31/12/2013.

Canals JM. Terapia Celular: Implicación de células madre adultas. Sponsored by: CMRB-Generalitat de Catalunya, PROMT-0901. Duration: 01/01/2010-31/12/2012.

Perez E. Regulación de la vía PKA como estrategia terapéutica para la enfermedad de Huntington. Sponsored by: Fondo de Investigaciones Sanitarias, Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación, PI10/0172. Duration: 10/12/2010-10/12/2013.

DOCTORAL THESES

Alberch J. Estudio de la alteración de las vias de señalización implicadas en la disfunción neuronal en la enfermedad de Huntington: Evaluación de su aplicación como terapia preventiva de las deficiencias cognitivas. PhD student: Olga Carretón Gómez.

Egea G. Vías de señalización y potenciales agentes terapéuticos en un modelo in vitro de síndrome alcohólico fetal. PhD student: Javier Selva Sánchez.

AREA 4

Clinical and experimental neuroscience

Biological bases of psychiatric disorders and nuclear psychiatry

TEAM INVOLVED IN: cibersam

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Marc Valentí (IDIBAPS)
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Brisa Solé (IDIBAPS)
Miquel Bioque (CIBERSAM)
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Carla Torrent (CIBERSAM)
Piero Castro Loli (Fundació Clinic)
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Cristina V. Oliveira (Fundació Clínic)
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Rosa Díaz (Hospital Clínic)
Enric Buisan (ForumClinic)

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Biological bases of psychiatric disorders and nuclear psychiatry

STRATEGIC OBJECTIVES

Our group studies serious psychiatric disorders from the neurobiological and therapeutic perspectives, based on the following 6 research lines: bipolar disorders, schizophrenia and depression-anxiety, pediatric psychiatry and psychology, psychiatric intervention in medical pathology and alcoholism.

MAIN LINES OF RESEARCH

The **bipolar disorders** program mainly investigates the neurobiological and anatomofunctional mechanisms implicated 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 – increasing treatment compliance and improving the efficacy of the therapeutic strategies applied to bipolar disorder. The strategic objectives are to investigate the causes and mechanisms involved in the etiopathogenesis of bipolar disorder, and to investigate new treatments with a view to improving the prognosis of the disease.

The **schizophrenia** program focuses research on the first schizophrenic episodes and on resistant and comorbid schizophrenia, through functional neuroimaging (brain perfusion and receptors SPECT, PET and functional magnetic resonance imaging). Sensory and cognitive neuroactivation studies have been made with frontal activation neuropsychological tests and dopaminergic receptor occupation studies, as well as studies of the presynaptic dopaminergic function. Likewise, plasma metabolites of dopamine have been investigated as biological indicators of relapse in a prospective longitudinal follow-up and treatment response study. We have examined the role of schizophrenia in the development of cardiovascular and metabolic diseases, and secondarily also the role of antipsychotic drugs. The pharmacogenetics of antipsychotic drugs has been studied to assess the efficacy and safety of these drugs on the basis of the individual patient genetic characteristics. Specifically, we have analyzed the pharmacogenetics of the extrapyramidal effects caused by antipsychotic drug therapy, the polymorphisms associated with the risk of schizophrenia, and new pharmacogenetic techniques for implantation at healthcare and hospital level. A psychoeducational program is adopting new knowledge transmission and exchange formulas, with the application of new technologies and offering rigorous and communicatively adequate contents. The FòrumClínic web (www.forumclinic.org) is an interactive program designed to increase patient autonomy in relation to personal health. A program has been developed for characterizing and preventing second psychotic episodes, in order to design preventive strategies allowing us to influence the course of the disease.

The **Alcohol Unit** is the reference in Catalonia for the treatment of alcohol dependency. We are one of the main research groups in Spain and consolidating our European leadership position in the setting of short interventions designed to reduce consumption among alcohol consumers at risk. This leadership allowed us to coordinate two FP7 european projects: Amphora (www.amphoraproject.net) i Odhin (www.odhinproject.eu). A number of research lines are being conducted in the context of the Alcohol Unit. The main lines are the following: Prospective longitudinal study of alcoholic disease; Follow-up of a cohort of 850 patients starting treatment in 1987 in the Catalan Drug Dependencies Network (Xarxa Catalana de Drogodependències); Screening instruments and techniques for early detection and short counselling in alcohol-consumers at risk in the hospital setting and in primary care; Evaluation and prognosis of alcoholic patients candidates for liver transplantation; treatment of smoking in alcoholic patients; and Evaluation of the European alcohol policies and their public health impact. In 2011 we started a new European project that expands the scope of the Unit towards other addictive behaviors, keeping the focus on public health from an interdisciplinary perspective. The project is called Alcie Rap (www.alicerap.eu). Finally, we must also mention the research on anticraving drugs, because we have already completed a trial with Nalmefene and about to undergo another one with oxibat with Sodium Oxibate.

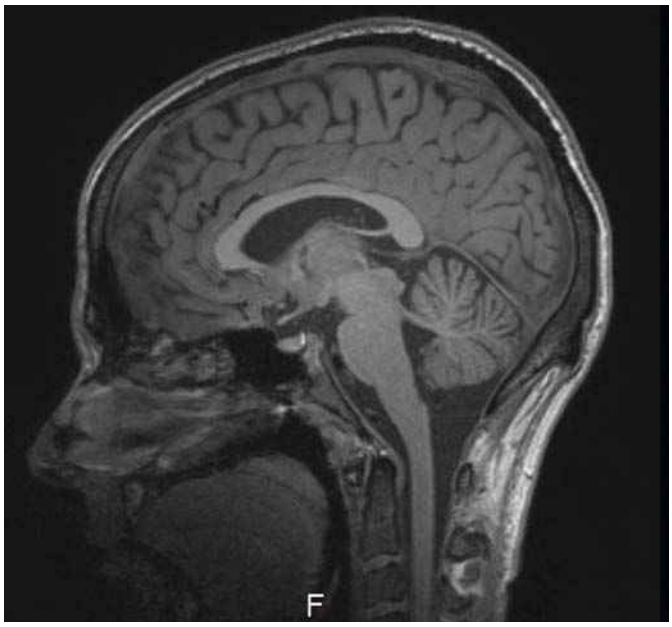
The line relating to **depression** aims to implement new psychopathological and biological endophenotypic methods in application to major depression, with the development of mechanisms for the analysis of the mechanism of action of antidepressant drugs based on the platelet model of depression (developed together with the hemostasis group led by Prof. Ginés-Escolar); the 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** of the Hospital Clínic are the following:

- Schizophrenia and bipolar disorder: Study and follow-up of the first psychotic episodes, cognitive rehabilitation of adolescent patients with schizophrenia, study of children and adolescents with a high genetic risk of developing schizophrenia and bipolar disorder (offspring of patients with such disorders), study of the prodromic manifestations of psycho-

tic disorders in children and adolescents, and study of the tolerance and safety of antidepressants in children and adolescents.

- Anorexia and bulimia nervosa, and obsessive-compulsive disorder: Study of the common and differential alterations (genetic, neuropsychological and neuroimaging) of anorexia nervosa and obsessive-compulsive disorder, study of new management approaches (psychological and pharmacological) in bulimia and anorexia nervosa, and study of autoimmune alterations in obsessive behavior and in anorexia.
- Others: mention should be made of the investigation of **addictive behaviors**, analyzing the percentages of patients seen in the Department of Pediatric Psychiatry with different disorders and who moreover consume, abuse of or show dependency of toxic substances – exploring the efficacy of new multimodal management modalities for addictive behavior in adolescents. In addition, the study line of the efficacy and safety of psychoactive drugs in children and adolescents focuses on the evaluation and follow-up of the side effects of these drugs in children and adolescents, as well as on the identification of pharmacogenetic predictors of drug response in such patients. The study line in **autistic spectrum** disorders explores the efficacy of new psychological and pharmacological treatments in these disorders, with examination of the neuropsychological profile of children with high-function autistic spectrum disorders and the correlation to clinical variables. Mention also should be made of the line for the development and validation of scales in application to different pathologies or symptoms. In turn, the line referred to attention deficit hyperactivity disorder (ADHA) involves the neuropsychological, clinical and neuroimaging assessment of predominantly inattentive children versus children with combined-type attention deficit. Lastly, the research line in autoimmune/Tourette syndrome explores the inflammatory and autoimmune processes, and their relation to serious psychiatric pathology, in children and adolescents.



MRI image of a healthy control of the study; genotype-phenotype and environment interaction. Application of a predictive model in first psychotic episodes.

The line of **psychiatric intervention in clinical pathology** has focused research on knowledge of the psychiatric alterations seen in the main neurological diseases: dementia, multiple sclerosis, epilepsy, Parkinson's disease and Huntington's disease. The study of psychiatric disease and psychological aspects associated with medical-surgical hospital processes in turn addresses: transplantation, delirium, psychiatric problems in clinical patients admitted to a general hospital, the evaluation of predictive variables and factors associated with suicide in a general hospital. Studies are also made of the biological markers and therapeutic aspects of major depression.

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.

For further information:
FòrumClínic
www.forumclinic.org
Centro de Investigación Biomédica En Red de Salud Mental (CIBERSAM)
www.cibersam.es

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Biological bases of psychiatric disorders and nuclear psychiatry

RESEARCH GROUP
BIPOLAR DISORDERS

Group Leader: Eduard Vieta (Hospital Clínic)

The bipolar disorder program has been recognized as a consolidated research group (2009 SGR 1022) by the Agency for the Management of University and Research Aids (Agència de Gestió d'Ajuts Universitaris i de Recerca, AGAUR). The bipolar disorders program fundamentally investigates the neurobiological and anatomo-functional mechanisms involved in the development of the disease and its clinical course, comorbidity with other diseases, the implicated neurocognitive mechanisms, and the search for new pharmacological, biophysical and psychosocial treatments designed to improve the prognosis and quality of life of the patients. The program is characterized by a multidiscipline approach and includes psychiatrists, psychologists, pharmacologists, biologists, nurses, social workers and personnel in training. Our group has pioneered effort in the characterization of associated neurocognitive dysfunction, in the development of new drug treatments, and in the implementation of psychoeducational techniques targeted at both patients and their relatives. As a result of such research and innovation, the main international diagnostic and treatment guides document these contributions and recommend their application in clinical practice. Our program is carried out in active collaboration with other groups of the IDIBAPS, with other groups of the CIBERSAM, and with European and other international research centers, with a view to conducting multicenter studies with a special dedication to translational and innovative investigation.

RESEARCH GROUP
SCHIZOPHRENIA

Group Leader: Miquel Bernardo (Hospital Clínic)

The Clinical Schizophrenia Group (GEC) has been recognized as a consolidated research group (2005SGR00223; 2009SGR1295) by the Agency for the Management of University and Research Aids (Agència de Gestió d'Ajuts Universitaris i de Recerca, AGAUR) since the year 2005. In 2011 we received the National Health System Best in Class Prize, to the Best Schizophrenia Unit in the Patient Care Expertise in Schizophrenia category. This grant is awarded by Gaceta Médica and the Cátedra de Innovación y Gestión Sanitaria of the Universidad Rey Juan Carlos. This is an interdisciplinary group composed of psychiatrists, psychologists, neuropsychologists, nurses, physicians specialized in nuclear medicine, physicists, pharmacologists, toxicologists and biochemists linked to the Clinic Hospital and the University of Barcelona.
Ours is a group of investigators forming part of the Clinical Schizophrenia Program (PEC) and working in disorders related to schizophrenia. This is a clinical care, research and teaching program at both hospital and outpatient level that includes different management and research protocols designed to address problems raised by schizophrenia and which integrates the different resources of the Barcelona Clinic Hospital. In the year 2007, the group became a constituting member of the Network of Mental Diseases and Affective and Psychotic Disorders (REMTAP), and in 2008 we likewise became a constituting member of the Center of Biomedical Research in Mental Health Network (CIBERSAM) (www.cibersam.es).
The Clinical Schizophrenia Group centers its research on the study of the first schizophrenic episodes, schizophrenia starting in childhood/adolescence, and resistant and comorbid schizophrenia. The main research lines are physical health, neuroimaging, psychoeducation and psychometric evaluation, genetics, neurobiology and neuropsychopharmacology in schizophrenia, with a supervisor for each of them, under the coordination of Dr. Miguel Bernardo. Another research line focuses on childhood- and adolescent-onset schizophrenia – these representing a high risk population for schizophrenia. This line is conducted in close collaboration with the Department of Childhood and Adolescent Psychiatry of the Clinic Hospital, directed by Dr. Castro, together with Drs. Baeza, Lázaro and Sánchez-Gistau (Study of high genetic risk for schizophrenia and early onset schizophrenia).

EMERGENT GROUP
CLINICAL DEPRESSION GROUP

Group Leader:
Cristobal Gasto (Hospital Clínic)

Our group is specialized in the investigation of the neurobiological bases and clinical indicators of depression associated with treatment response and the course of this disease. It has been estimated that depression affects 10% of all people at some point in their lives. Depression is currently one of the most important health problems, particularly considering its slow and sometimes incomplete resolution. This disorder significantly interferes with the normal functions of the patients and their relatives, and implies a suicide risk in more than 10% of cases. The project of the World Health Organization (WHO) for the year 2020 considers that depression will be the second cause of disability after cardiovascular disease. In Europe it has been estimated that about 30 million people suffer some form of depression, generating an annual cost of approximately 100 billion euros. Our group is actively involved in the early detection and treatment of this disease, and its comorbidities (medical and psychiatric). The genetic and neuroendocrine markers we are investigating have contributed better understanding of the physiopathological mechanisms of depression. Likewise, a number of investigators in our group are actively working on the design of new individual- and group-based pharmacological and psychotherapeutic management strategies.

RESEARCH GROUP
RESEARCH GROUP IN PEDIATRIC PSYCHIATRY AND PSYCHOLOGY

Group Leader:
Josefina Castro (Hospital Clínic)

The research group in childhood psychology and psychiatry of the Clinic Hospital forms part of the Department of Childhood and Adolescent Psychiatry, which has developed three fields: healthcare, teaching and research. These fields are all clearly interrelated with a view to affording better healthcare, with standardized protocols and evaluation and teaching at pre- and post-graduate level. Our aim is to facilitate both clinical research and collaboration with groups specialized in genetics, neuroimaging and neurobiology. The group is predominantly composed of members of the Department of Childhood Psychology and Psychiatry, and is integrated within the Biological Bases of Psychiatric Disorders group (coordinated by Dr. M. Bernardo). It also forms part of the CIBERSAM (Centro de Investigación Biomédica en Red de Salud Mental) of the Carlos III Healthcare Institute. In addition, it has established important collaboration agreements with the Department of Adult Psychiatry of the Clinic Hospital (especially as refers to schizophrenia, bipolar disorder and addictive behavior), as well as with other centers at international level, such as the Childhood Psychiatry Group of the ECNP (European College of Neuopsychopharmacology), with which relevant aspects of childhood psychopharmacology are investigated in the context of different projects, the University of Pittsburgh Medical Center, Neuroimaging Laboratory, Western Psychiatric Institute and Clinic, Pittsburgh (United States), with which studies are made in relation to bipolar disorder, and the Child and Adolescent Psychiatry Yale Child Study Center, New Haven (United States), with which aspects relating to autoimmunity are studied.
Our research objectives are the study of the manifestations, causes and treatment of the most serious and/or prevalent disorders found in these age groups: schizophrenia and bipolar disorder, anorexia and bulimia nervosa, obsessive-compulsive behavior, autistic disorders, attention deficit disorders, and addictive behaviors. In parallel, other lines have been developed related to the efficacy and safety of psychoactive drugs in children and adolescents, the development and validation of assessment scales, and the investigation of autoimmunity and psychiatric disease such as Tourette syndrome.

PUBLICATIONS

ORIGINALS
I.F.: 286.57

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	281.89	75	49	12
2010	271.16	75	50	12
2011	286.57	68	46	10

1 Fortea J, Llado A, Clarimon J, Lleo A, Oliva R, Peri J, Pintor L, Yague J, Blesa R, Molinuevo JL, Sanchez-Valle R. PICOGEN: Five years experience with a genetic counselling program for dementia. NEUROLOGIA. 26:143-149. I.F.: 0.59.

2 Mane A, Gallego J, Lomena F, Mateos JJ, Fernandez-Egea E, Horga G, Cot A, Pavia J, Bernardo M, Parellada E. A 4-year dopamine transporter (DAT) imaging study in neuroleptic-naive first episode schizophrenia patients. PSYCHIAT RES-NEUROIM. 194:79-84. I.F.: 2.06.

3 Horga G, Parellada E, Lomena F, Fernandez-Egea E, Mane A, Font M, Falcon C, Konova AB, Pavia J, Ros D, Bernardo M. Differential brain glucose metabolic patterns in antipsychotic-naive first-episode schizophrenia with and without auditory verbal hallucinations. J PSYCHIATR NEUROSCI. 36:312-321. I.F.: 4.89.

4 Roca A, Garcia-Esteve L, Imaz ML, Torres A, Hernandez S, Botet F, Gelabert E, Subira S, Plaza A, Valdes M, Martin-Santos R. Obstetrical and neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitors: The relevance of dose. J AFFECT DISORDERS. 135:208-215. I.F.: 3.74.

5 Peris P, Torra M, Olivares V, Reyes R, Monegal A, Martinez-Ferrer A, Guanabens N. Prolonged bisphosphonate release after treatment in women with osteoporosis. Relationship with bone turnover. BONE. 49:706-709. I.F.: 4.60.

6 Carreno M, Becerra JL, Castillo J, Maestro I, Donaire A, Fernandez S, Bargallo N, Setoain X, Pintor L, Bailles E, Rumia J, Boget T, Vernet O, Fumanal S. Seizure frequency and social outcome in drug resistant epilepsy patients who do not undergo epilepsy surgery. SEIZURE-EUR J EPILEP. 20:580-582. I.F.: 1.65.

7 Cobo E, Cortes J, Ribera JM, Cardellach F, Selva-O›callaghan A, Kostov B, Garcia L, Cirugeda L, Altman DG, Gonzalez JA, Sanchez JA, Miras F, Urrutia A, Fonollosa V, Rey-Joly C, Vilardell M. Effect of using reporting guidelines during peer review on quality of final manuscripts submitted to a biomedical journal: masked randomised trial. BRIT MED J. 343:-. I.F.: 13.47.

8 Haro JM, Reed C, Gonzalez-Pinto A, Novick D, Bertsch J, Vieta E. 2-year course of bipolar disorder type I patients in outpatient care: Factors associated with remission and functional recovery. EUR NEUROPSYCHOPHARM. 21:287-293. I.F.: 4.20.

9 Lazaro L, Castro-Fornieles J, Cullell C, Andres S, Falcon C, Calvo R, Bargallo N. A voxel-based morphometric MRI study of stabilized obsessive-compulsive adolescent patients. PROG NEURO-PSYCHOPH. 35:1863-1869. I.F.: 2.88.

10 Albacar G, Sans T, Martin-Santos R, Garcia-Esteve L, Guillamat R, Sanjuan J, Canellas F, Gratacos M, Cavalle P, Arija V,

Gaviria A, Gutierrez-Zotes A, Vilella E. An association between plasma ferritin concentrations measured 48 h after delivery and postpartum depression. J AFFECT DISORDERS. 131:136-142. I.F.: 3.74.

11 Valenti M, Pacchiarotti I, Rosa AR, Bonnin CM, Popovic D, Nivoli AMA, Murru A, Grande I, Colom F, Vieta E. Bipolar mixed episodes and antidepressants: a cohort study of bipolar I disorder patients. BIPOLAR DISORD. 13:145-154. I.F.: 5.22.

12 Cuesta MJ, Pino O, Guilera G, Rojo JE, Gomez-Benito J, Purdon SE, Franco M, Martinez-Aran A, Segarra N, Tabares-Seisdedos R, Vieta E, Bernardo M, Crespo-Facorro B, Mesa F, Rejas J. Brief cognitive assessment instruments in schizophrenia and bipolar patients, and healthy control subjects: A comparison study between the Brief Cognitive Assessment Tool for Schizophrenia (B-CATS) and the Screen for Cognitive Impairment in Psychiatry (SC. SCHIZOPHR RES. 130:137-142. I.F.: 4.37.

13 Gonzalez-Pinto A, DeAzua SR, Ibanez B, Otero-Cuesta S, Castro-Fornieles J, Graell-Berna M, Ugarte A, Parellada M, Moreno D, Soutullo C, Baeza I, Arango C. Can positive family factors be protective against the development of psychosis?. PSYCHIAT RES. 186:28-33. I.F.: 2.80.

14 Bergamaschi MM, Queiroz RHC, Chagas MHN, DeOliveira DCG, DeMartinis BS, Kapczinski F, Quevedo J, Roesler R, Schroder N, Nardi AE, Martin-Santos R, Hallak JEC, Zuardi AW, Crippa JAS. Cannabidiol Reduces the Anxiety Induced by Simulated Public Speaking in Treatment-Naive Social Phobia Patients. NEUROPSYCHOPHARMACOL. 36:1219-1226. I.F.: 6.69.

15 Gonzalez-Pinto A, Alberich S, Barbeito S, Gutierrez M, Vega P, Ibanez B, Haidar MK, Vieta E, Arango C. Cannabis and first-episode psychosis: different long-term outcomes depending on continued or discontinued use. SCHIZOPHRENIA BULL. 37:631-639. I.F.: 8.27.

16 Serra-Millas M, Lopez-Vilchez I, Navarro V, Galan AM, Escolar G, Penades R, Catalan R, Fananas L, Arias B, Gasto C. Changes in plasma and platelet BDNF levels induced by S-citalopram in major depression. PSYCHOPHARMACOLOGY. 216:1-8. I.F.: 3.82.

17 Alemany S, Arias B, Aguilera M, Villa H, Moya J, Ibanez MI, Vossen H, Gasto C, Ortet G, Fananas L. Childhood abuse, the BDNF-Val66Met polymorphism and adult psychotic-like experiences. BRIT J PSYCHIAT. 199:38-42. I.F.: 5.95.

18 Andres-Perpina S, Lozano-Serra E, Puig O, Lera-Miguel S, Lazaro L, Castro-Fornieles J. Clinical and biological correlates of adolescent anorexia nervosa with impaired cognitive profile. EUR CHILD ADOLES PSY. 20:541-549. I.F.: 1.62.

19 DeLaSerna E, Baeza I, Andres S, Puig O, Sanchez-Guistau V, Romero S, Bernardo M, Moreno D, Noguera A, Castro-Fornieles J. Comparison between young siblings and offspring of subjects with schizophrenia: Clinical and neuropsychological characteristics. SCHIZOPHR RES. 131:35-42. I.F.: 4.37.

20 Allamani A, Voller F, Decarli A, Casotto V, Pantzer K, Anderson P, Gual A, Matrai S, Elekes Z, Eisenbach-Stangl I, Schmied G, Knibbe RA, Nordlund S, Skjaelaaen O, Olsson B, Ornberg JC, Osterberg E, Karlsson T, Plant M, Miller P, Coghill N, Swiatkiewicz G, Wieczorek L, Annaheim B, Gmel G. Contextual Determinants of Alcohol Consumption Changes and Preventive Alcohol Policies: A 12-Country European Study in Progress. SUBST USE MISUSE. 46:1288-1303. I.F.: 1.06.

21 Mendoza L, Navines R, Crippa JA, Fagundo AB, Gutierrez F, Nardi AE, Bulbena A, Valdes M, Martin-Santos R. Depersonalization and personality in panic disorder. COMPR PSYCHIAT. 52:413-419. I.F.: 2.38.

22 Pacchiarotti I, Valenti M, Colom F, Rosa AR, Nivoli AMA, Murru A, Sanchez-Moreno J, Vieta E. Differential outcome of bipolar patients receiving antidepressant monotherapy versus combination with an antimanic drug. J AFFECT DISORDERS. 129:321-326. I.F.: 3.74.

23 Fatjo-Vilas M, Papiol S, Estrada G, Bombin I, Peralta V, Rosa A, Parellada M, Miret S, Martin M, Lazaro L, Campanera S, Munoz MJ, Lera-Miguel S, Arias B, Navarro ME, Castro-Fornieles J, Cuesta MJ, Arango C, Fananas L. Dysbindin-1 Gene Contributes Differentially to Early- and Adult-Onset Forms of Functional Psychosis. AM J MED GENET B. 156B:322-333. I.F.: 4.16.

24 Lera-Miguel S, Andres-Perpina S, Calvo R, Fatjo-Vilas M, Lourdes F, Lazaro L. Early-onset bipolar disorder: how about visual-spatial skills and executive functions?. EUR ARCH PSY CLIN N. 261:195-203. I.F.: 3.64.

25 Gonzalez-Pinto A, Vieta E, Reed C, Novick D, Barraco A, Aguado J, Haro JM. Effectiveness of olanzapine monotherapy and olanzapine combination treatment in the long term following acute mania - Results of a two year observational study in bipolar disorder (EMBLEM). J AFFECT DISORDERS. 131:320-329. I.F.: 3.74.

26 Vieta E, Gunther O, Locklear J, Ekman M, Miltenburger C, Chatterton ML, Astrom M, Paulsson B. Effectiveness of psychotropic medications in the maintenance phase of bipolar disorder: a meta-analysis of randomized controlled trials. INT J NEUROPSYCHOPH. 14:1029-1049. I.F.: 4.70.

27 Torrent C, Martinez-Aran A, Daban C, Amann B, Balanza-Martinez V, Bonnin CD, Cruz N, Franco C, Tabares-Seisdedos R, Vieta E. Effects of atypical antipsychotics on neurocognition in euthymic bipolar patients. COMPR PSYCHIAT. 52:613-622. I.F.: 2.38.

28 Yildiz A, Vieta E, Leucht S, Baldessarini RJ. Efficacy of Antimanic Treatments: Meta-analysis of Randomized, Controlled Trials. NEUROPSYCHOPHARMACOL. 36:375-389. I.F.: 6.69.

29 Yildiz A, Vieta E, Tohen M, Baldessarini RJ. Factors modifying drug and placebo responses in randomized trials for bipolar mania. INT J NEUROPSYCHOPH. 14:863-875. I.F.: 4.70.

30 Salavert J, Gasol M, Vieta E, Cervantes A, Trampal C, Gispert JD. Fronto-limbic dysfunction in borderline personality disorder: a 18F-FDG positron emission tomography study. J AFFECT DISORDERS. 131:260-267. I.F.: 3.74.

31 Nivoli AMA, Pacchiarotti I, Rosa AR, Popovic D, Murru A, Valenti M, Bonnin CM, Grande I, Sanchez-Moreno J, Vieta E, Colom F. Gender differences in a cohort study of 604 bipolar patients: The role of predominant polarity. J AFFECT DISORDERS. 133:443-449. I.F.: 3.74.

32 Miquel L, Usall J, Reed C, Bertsch J, Vieta E, Gonzalez-Pinto A, Angst J, Nolen W, VanRossum I, Haro JM. Gender differences in outcomes of acute mania: a 12-month follow-up study. ARCH WOMEN MENT HLTH. 14:107-113. I.F.: 1.81.

33 Muinos-Gimeno M, Espinosa-Parrilla Y, Guidi M, Kagerbauer B, Sipila T, Maron E, Pettai K, Kananen L, Navines R, Martin-Santos R, Gratacos M, Metspalu A, Hovatta I, Estivill X. Human microRNAs miR-22, miR-138-2, miR-148a, and miR-488 are associated with panic disorder and regulate several anxiety candidate genes and related pathways. BIOL PSYCHIAT. 69:526-533. I.F.: 8.67.

34 Vieta E, Pappadopulos E, Mandel FS, Lombardo I. Impact of geographical and cultural factors on clinical trials in acute mania: lessons from a ziprasidone and haloperidol placebo-controlled study. INT J NEUROPSYCHOPH. 14:1017-1027. I.F.: 4.70.

35 Gual A, Sabadini MBD. Implementing alcohol disorders treatment throughout the community. CURR OPIN PSYCHIATR. 24:203-207. I.F.: 3.00.

36 VanDerLoos MLM, Mulder P, Hartong EGTM, Blom MBJ, Vergouwen AC, VanNoorden MS, Timmermans MA, Vieta E, Nolen WA. Long-term outcome of bipolar depressed patients receiving lamotrigine as add-on to lithium with the possibility of the addition of paroxetine in nonresponders: a randomized, placebo-controlled trial with a novel design. BIPOLAR DISORD. 13:111-117. I.F.: 5.22.

37 Pacchiarotti I, Mazzarini L, Kotzalidis GD, Valenti M, Nivoli AMA, Sani G, Torrent C, Murru A, Sanchez-Moreno J, Patrizi B, Girardi P, Vieta E, Colom F. Mania and depression. Mixed, not stirred. J AFFECT DISORDERS. 133:105-113. I.F.: 3.74.

38 Salvatore P, Baldessarini RJ, Tohen M, Khalsa HMK, Sanchez-Toledo JP, Zarate CA, Vieta E, Maggini C. McLean-Harvard International First-Episode Project: Two-Year Stability of ICD-10 Diagnoses in 500 First-Episode Psychotic Disorder Patients. J CLIN PSYCHIAT. 72:183-193. I.F.: 5.02.

39 Fernandez-Egea E, Miller B, Garcia-Rizo C, Bernardo M, Kirkpatrick B. Metabolic Effects of Olanzapine in Patients With Newly Diagnosed Psychosis. J CLIN PSYCHOPHARM. 31:154-159. I.F.: 4.86.

40 Filho AS, Maciel BC, Romano MMD, Lascala TF, Trzesniak C, Freitas-Ferrari MC, Nardi AE, Martin-Santos R, Zuardi AW, Crippa JAS. Mitral valve prolapse and anxiety disorders. BRIT J PSYCHIAT. 199:247-248. I.F.: 5.95.

41 Winton-Brown TT, Allen P, Bhattacharyya S, Borgwardt SJ, Fusar-Poli P, Crippa JA, Seal ML, Martin-Santos R, Ffytche D, Zuardi AW, Atakan Z, Mcguire PK. Modulation of auditory and visual processing by delta-9-tetrahydrocannabinol and cannabidiol: an FMRI study. NEUROPSYCHOPHARMACOL. 36:1340-1348. I.F.: 6.69.

42 Reig S, Parellada M, Castro-Fornieles J, Janssen J, Moreno D,

Baeza I, Bargallo N, Gonzalez-Pinto A, Graell M, Ortuno F, Otero S, Arango C, Desco M. Multicenter Study of Brain Volume Abnormalities in Children and Adolescent-Onset Psychosis. SCHIZOPHRENIA BULL. 37:1270-1280. I.F.: 8.27.

43 Goldberg X, Fatjo-Vilas M, Penades R, Miret S, Munoz MJ, Vossen H, Fananas L. Neurodevelopmental liability to schizophrenia: The complex mediating role of age at onset and premorbid adjustment. SCHIZOPHR RES. 133:143-149. I.F.: 4.37.

44 Diaz R, Goti J, Garcia M, Gual A, Serrano L, Gonzalez L, Calvo R, Castro-Fornieles J. Patterns of substance use in adolescents attending a mental health department. EUR CHILD ADOLES PSY. 20:279-289. I.F.: 1.62.

45 Mas S, Gasso P, Alvarez S, Ortiz J, Sotoca JM, Francino A, Carne X, Lafuente A. Pharmacogenetic predictors of angiotensin-converting enzyme inhibitor-induced cough: the role of ACE, ABO, and BDKRB2 genes. PHARMACOGENET GENOM. 21:531-538. I.F.: 3.87.

46 Gonzalez-Pinto A, Barbeito S, Alonso M, Alberich S, Haidar MK, Vieta E, Tabares-Seisdedos R, Zorrilla I, Gonzalez-Pinto MA, Lopez P. Poor Long-Term Prognosis in Mixed Bipolar Patients: 10-Year Outcomes in the Vitoria Prospective Naturalistic Study in Spain. J CLIN PSYCHIAT. 72:671-676. I.F.: 5.02.

47 Angst J, Azorin JM, Bowden CL, Perugi G, Vieta E, Gamma A, Young AH. Prevalence and Characteristics of Undiagnosed Bipolar Disorders in Patients With a Major Depressive Episode The BRIDGE Study. ARCH GEN PSYCHIAT. 68:791-799. I.F.: 10.78.

48 Diez-Quevedo C, Masnou H, Planas R, Castellvi P, Gimenez D, Morillas RM, Martin-Santos R, Navines R, Sola R, Giner P, Ardevol M, Costa J, Diago M, Pretel J. Prophylactic treatment with escitalopram of pegylated interferon alfa-2a-induced depression in hepatitis C: a 12-week, randomized, double-blind, placebo-controlled trial. J CLIN PSYCHIAT. 72:522-528. I.F.: 5.02.

49 Grande I, Pons A, Baeza I, Torras A, Bernardo M. QTc prolongation: is clozapine safe? Study of 82 cases before and after clozapine treatment. HUM PSYCHOPHARM CLIN. 26:397-403. I.F.: 2.61.

50 Mico JA, Rojas-Corrales MO, Gibert-Rahola J, Parellada M, Moreno D, Fraguas D, Graell M, Gil J, Irazusta J, Castro-Fornieles J, Soutullo C, Arango C, Otero S, Navarro A, Baeza I, Martinez-Cengotitabengoa M, Gonzalez-Pinto A. Reduced antioxidant defense in early onset first-episode psychosis: a case-control study. BMC PSYCHIATRY. 11:-. I.F.: 2.89.

51 Gasso P, Mas S, Oliveira C, Bioque M, Parellada E, Bernardo M, Trias G, Comeche J, Lafuente A. Searching for functional SNPs or rare variants in exonic regions of DRD3 in risperidone-treated patients. EUR NEUROPSYCHOPHARM. 21:294-299. I.F.: 4.20.

52 Nieva G, Ortega LL, Mondon S, Ballbe M, Gual A. Simultaneous versus Delayed Treatment of Tobacco Dependence in Alcohol-Dependent Outpatients. EUR ADDICT RES. 17:1-9. I.F.: 1.78.

53 Rosa AR, Reinares M, Amann B, Popovic D, Franco C, Comes M, Torrent C, Bonnin CM, Sole B, Valenti M, Salamero M, Kapczinski F, Vieta E. Six-month functional outcome of a bipolar disorder cohort in the context of a specialized-care program. BIPOLAR DISORD. 13:679-686. I.F.: 5.22.

54 Segarra N, Bernardo M, Gutierrez F, Justicia A, Fernadez-Egea E, Allas M, Safont G, Contreras F, Gascon J, Soler-Insa PA, Menchon JM, Junque C, Keefe RSE. Spanish validation of the Brief Assessment in Cognition in Schizophrenia (BACS) in patients with schizophrenia and healthy controls. EUR PSYCHIAT. 26:69-73. I.F.: 3.37.

55 Vieta E, Reinares M, Rosa AR. Staging Bipolar Disorder. NEUROTOX RES. 19:279-285. I.F.: 3.02.

56 Fernandez-Egea E, Garcia-Rizo C, Miller B, Parellada E, Justicia A, Bernardo M, Kirkpatrick B. Testosterone in Newly Diagnosed, Antipsychotic-Naive Men With Nonaffective Psychosis: A Test of the Accelerated Aging Hypothesis. PSYCHOSOM MED. 73:643-647. I.F.: 3.97.

57 Nieva G, Valero S, Bruguera E, Andion O, Trasovares MV, Gual A, Casas M. The alternative five-factor model of personality, nicotine dependence and relapse after treatment for smoking cessation. ADDICT BEHAV. 36:965-971. I.F.: 2.13.

58 Forcada I, Papachristou E, Mur M, Christodoulou T, Jogia J, Reichenberg A, Vieta E, Frangou S. The impact of general intellectual ability and white matter volume on the functional outcome of patients with Bipolar Disorder and their relatives. J AFFECT DISORDERS. 130:413-420. I.F.: 3.74.

59 Cuyas E, Verdejo-Garcia A, Fagundo AB, Khymenets O, Rodriguez J, Cuenca A, Llopis SD, Langohr K, Pena-Casanova J, Torrens M, Martin-Santos R, Farre M, DeLaTorre R. The Influence of Genetic and Environmental Factors among MDMA Users in Cognitive Performance. PLOS ONE. 6:-. I.F.: 4.41.

60 Almansa J, Ayuso-Mateos JL, Garin O, Chatterji S, Kostanjsek N, Alonso J, Valderas JM, Cieza A, Raggi A, Svestkova O, Burger H, Racca V, Vieta E, Leonardi M, Ferrer M. The International Classification of Functioning, Disability and Health: development of capacity and performance scales. J CLIN EPIDEMIOL. 64:1400-1411. I.F.: 3.75.

61 Gelabert E, Subira S, Plaza A, Torres A, Navarro P, Imaz ML, Valdes M, Garcia-Esteve L, Martin-Santos R. The Vulnerable Personality Style Questionnaire: psychometric properties in Spanish postpartum women. ARCH WOMEN MENT HLTH. 14:115-124. I.F.: 1.81.

62 Vieta E, Colom F. Therapeutic options in treatment-resistant depression. ANN MED. 43:512-530. I.F.: 4.32.

63 Parellada M, Boada L, Fraguas D, Reig S, Castro-Fornieles J, Moreno D, Gonzalez-Pinto A, Otero S, Rapado-Castro M, Graell M, Baeza I, Arango C. Trait and State Attributes of Insight in First Episodes of Early-Onset Schizophrenia and Other Psychoses: A 2-Year Longitudinal Study. SCHIZOPHRENIA BULL. 37:38-51. I.F.: 8.27.

64 Otero S, Moreno-Iniguez M, Pay B, Castro-Fornieles J, Gonzalez-Pinto A, Baeza I, Mayoral M, Graell M, Arango-Lopez C. Twelve-month follow-up of family communication and psychopathology in children and adolescents with a first psychotic episode (CAFEPS study). PSYCHIAT RES. 185:72-77. I.F.: 2.80.

65 Castro-Fornieles J, Baeza I, DeLaSerna E, Gonzalez-Pinto A, Parellada M, Graell M, Moreno D, Otero S, Arango C. Two-year diagnostic stability in early-onset first-episode psychosis. J CHILD PSYCHOL PSYC. 52:1089-1098. I.F.: 4.36.

66 DeLaSerna E, Flamarique I, Castro-Fornieles J, Pons A, Puig O, Andres-Perpina S, Lazaro L, Garrido JM, Bernardo M, Baeza I. Two-Year Follow-Up of Cognitive Functions in Schizophrenia Spectrum Disorders of Adolescent Patients Treated with Electroconvulsive Therapy. J CHILD ADOL PSYCHOP. 21:611-619. I.F.: 2.48.

67 Garcia-Esteve L, Torres A, Navarro P, Ascaso C, Imaz ML, Herreras Z, Valdes M. Validation and comparison of four instruments to detect partner violence in health-care setting. MED CLIN-BARCELONA. 137:390-397. I.F.: 1.41.

68 Plaza A, Torres A, Martin-Santos R, Gelabert E, Imaz ML, Navarro P, Bremner JD, Valdes M, Garcia-Esteve L. Validation and Test-Retest Reliability of Early Trauma Inventory in Spanish Postpartum Women. J NERV MENT DIS. 199:280-285. I.F.: 1.80.

REVIEWS
I.F.: 47.56

1 Tabares-Seisdedos R, Dumont N, Baudot A, Valderas JM, Climent J, Valencia A, Crespo-Facorro B, Vieta E, Gomez-Beneyto M, Martinez S, Rubenstein JL. No paradox, no progress: inverse cancer comorbidity in people with other complex diseases. LANCET ONCOL. 12:604-608. I.F.: 17.76.

2 Sole B, Martinez-Aran A, Torrent C, Bonnin CM, Reinares M, Popovic D, Sanchez-Moreno J, Vieta E. Are bipolar II patients cognitively impaired? A systematic review. PSYCHOL MED. 41:1791-1803. I.F.: 5.20.

3 Goodwin GM, Abbar M, Schlaepfer TE, Grunze H, Licht RW, Bellivier F, Fountoulakis KN, Altamura AC, Pitchot W, Agren H, Holsboer-Trachsler E, Vieta E. Aripiprazole in patients with bipolar mania and beyond: an update of practical guidance. CURR MED RES OPIN. 27:2285-2299. I.F.: 2.61.

4 Fountoulakis KN, Vieta E, Schmidt F. Aripiprazole monotherapy in the treatment of bipolar disorder: A meta-analysis. J AFFECT DISORDERS. 133:361-370. I.F.: 3.74.

5 Rosa AR, Fountoulakis K, Siamouli M, Gonda X, Vieta E. Is anticonvulsant treatment of mania a class effect? Data from randomized clinical trials. CNS NEUROSCI THER. 17:167-177. I.F.: 3.49.

6 Montoya A, Colom S, Ferrin M. Is psychoeducation for parents and teachers of children and adolescents with ADHD efficacious? A systematic literature review. EUR PSYCHIAT. 26:166-175. I.F.: 3.37.

7 Popovic D, Reinares M, Amann B, Salamero M, Vieta E. Number needed to treat analyses of drugs used for maintenance treatment of bipolar disorder. PSYCHOPHARMACOLOGY. 213:657-667. I.F.: 3.82.

8 Murru A, Pacchiarotti I, Nivoli AMA, Grande I, Colom F, Vieta E. What we know and what we don't know about the treatment of schizoaffective disorder. EUR NEUROPSYCHOPHARM. 21:680-690. I.F.: 4.20.

9 Rosa AR, Fountoulakis K, Siamouli M, Gonda X, Vieta E. When should mood stabilizers be withdrawn due to lack of efficacy? Some methodological considerations. EUR PSYCHIAT. 26:183-186. I.F.: 3.37.

EDITORIALS
I.F.: 20.68

1 Gual A, Anderson P. A new AMPHORA: an introduction to the project Alcohol Measures for Public Health Research Alliance. ADDICTION. 106:1-3. I.F.: 4.15.

2 Vieta E. Bipolar units and programmes: are they really needed. WORLD PSYCHIATRY. 10:152-152. I.F.: 5.56.

3 Frye MA, Ha K, Kanba S, Kato T, Mcelroy SL, Ozerdem A, Vazquez G, Vieta E. International Consensus Group on Depression Prevention in Bipolar Disorder. J CLIN PSYCHIAT. 72:1295-1310. I.F.: 5.02.

4 Colom F. Keeping therapies simple: psychoeducation in the prevention of relapse in affective disorders. BRIT J PSYCHIAT. 198:338-340. I.F.: 5.95.

CLINICAL GUIDELINES
I.F.: 3.74

1 Nivoli AMA, Colom F, Murru A, Pacchiarotti I, Castro-Loli P, Gonzalez-Pinto A, Fountoulakis KN, Vieta E. New treatment guidelines for acute bipolar depression: A systematic review. J AFFECT DISORDERS. 129:14-26. I.F.: 3.74.

GRANTS FOR RESEARCH IN PROGRESS

Gasto C. Estrategias terapeuticas en trastorno depresivo mayor resistente a tratamiento con inhibidores selectivos de la recaptación de serotonina. Ensayo clínico pragmático, paralelo. Aleatorizado con evaluación enmascarada. Sponsored by: Ministerio Sanidad y Consumo, EC07/90825. Duration: 29/10/2007-30/11/2011.

Lazaro L. Estudio de la relación clínica y genética entre un subgrupo de pacientes con anorexia nerviosa y pacientes con trastorno obsesivo compulsivo en niños y adolescentes. Sponsored by: Ministerio Sanidad y Consumo, PI070350. Duration: 26/11/2007-30/06/2011.

Lazaro L. Anàlisi dels polimorfismes en gens candidats en el trastorn obsessiu-compulsiu d'inici primerenc. Relació amb alteracions cerebrals i dimensions simptomàtiques. Sponsored by: Fundació Marató TV3, 91710. Duration: 29/01/2010-28/07/2013.

Gutierrez F. Eficacia comparada de cuatro modelos diagnósticos de Trastorno de la Personalidad. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/90434. Duration: 01/01/2009-31/01/2011.

Bernardo M. Interacción genotipo-fenotipo y ambiente. Aplicación a un modelo predictivo en primeros episodios psicóticos. Sponsored by: FIS (ISCIII), PI080208. Duration: 01/01/2009-31/12/2011.

Parellada E. Apoptosis y cambios estructurales progresivos en pacientes con un primer episodio de esquizofrenia: estudio longitudinal y multimodal de neuroimagen y biología molecular. Sponsored by: FIS (ISCIII), PI080055. Duration: 01/01/2009-31/12/2011.

Catalan R. Identificación de predictores clínicos, neurohormonales, farmacogenéticos en la respuesta terapéutica a clozapina en pacientes diagnosticados de Esquizofrenia Refractaria. Sponsored by: FIS (ISCIII), EC08/00184. Duration: 01/01/2009-31/12/2012.

Bernardo M. Reconocimiento como Grupo Consolidado de Investigación. Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca, Generalitat de Catalunya, 2009SGR1295. Duration: 01/01/2009-31/12/2014.

Vieta E. Grup de Recerca Consolidat de la Generalitat de Catalunya. Sponsored by: Generalitat de Catalunya, 2009_SGR_1022. Duration: 01/01/2009-31/12/2013.

Vieta E. European Network of Bipolar Research Expert Centres (ENBREC). Sponsored by: European Union, 223102. Duration: 01/07/2009-30/06/2011.

Martinez A. Discapacidad en el trastorno bipolar e impacto funcional de una estrategia de intervención neurocognitiva. Sponsored by: FIS, PI080180. Duration: 01/01/2009-31/12/2011.

Martin-Santos R, Garcia L, Gutierrez F, Navines R, Imaz ML. Grup de Recerca en "Vulnerabilitat, psicopatologia i gènere" Modalitat Grup de recerca emergent. Sponsored by: Generalitat de Catalunya, SGR 2009/1435. Duration: 01/01/2009-31/12/2013.

Garcia L, Imaz ML, Botet F, Ascaso C, Salamero M. Estudio farmacogenético y de seguridad clínica en niños de madres tratadas con inhibidores selectivos de la recaptación de serotonina durante el embarazo: evaluación del funcionamiento cognitivo conductual a los 5 años de edad. Sponsored by: European Comission, EC08/00170. Duration: 01/01/2009-31/12/2011.

Pintor L. Análisis de los indicadores clínicos que diferencian entre crisis epilépticas y crisis no epilépticas psicógenas (CNEP): Hacia un mejor diagnóstico diferencial a través de un cuestionario de sospecha diagnóstica. Sponsored by: Fondo de Investigaciones Sanitarias (FIS), PI080111. Duration: 01/01/2009-31/12/2011.

Gual A. Alcohol Public Health Research Alliance (AMPHORA). Sponsored by: Comissió Europea, 223059. Duration: 01/01/2009-31/12/2013.

Benabarre A. Identificación de variables clínicas, sociológicas y genéticas predictoras de la respuesta al tratamiento eutimizante en el Trastorno Bipolar. Sponsored by: Instituto de Salud Carlos III, PI080247. Duration: 01/01/2009-31/12/2011.

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, PI09/1044. Duration: 01/01/2010-31/12/2012.

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, PI09/1347. Duration: 01/01/2010-31/12/2012.

Vieta E. The neural correlates of euthymic cognitive impairment in bipolar disorder. Sponsored by: Instituto de Salud Carlos III, PI09/1893. Duration: 01/01/2010-31/12/2012.

Castro J. Paediatric European Risperidone Studies. Sponsored by: European Comission, CE-FP7-HEALTH-1ST-09, 241959. Duration: 01/05/2010-30/04/2015.

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: 29/01/2010-28/01/2013.

Andres S. Trastornos de la Conducta Alimentaria, veinte años después. Estudio de estado psicopatológico y físico y su relación con el funcionamiento general. Sponsored by: Instituto de la Mujer, 234/09. Duration: 03/02/2010-02/02/2012.

Castro J. Suicidality: Treatment Occurring in Paediatrics. Sponsored by: University College London UCL, 261411. Duration: 01/11/2010-30/04/2014.

Garcia 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: 03/02/2010-02/02/2013.

Bernardo M. Antipsicóticos típicos vs. atípicos; impacto de la farmacogenética en la farmacocinética, la ocupación de receptores estriatales y la aparición se sintomatología extrapiramidal. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-065. Duration: 01/01/2010-31/12/2011.

Martin-Santos R. Estudio farmacogenético y de predicción de la depresión inducida por el tratamiento de la hepatitis C crónica con interferón alfa pegilado y rivabirina. Estudio psigen-vhc. subproyecto coordinado I. Sponsored by: IInstituto de Salud Carlos III, EC08/00201. Duration: 01/01/2009-31/05/2011.

Vieta E. Metilfenidato en el tratamiento inicial de mania aguda.. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, EC10-064. Duration: 01/01/2011-31/12/2011.

Lazaro L. Identificación de predictores farmacogenéticos en la respuesta terapéutica a fluoxetina en pacientes diagnosticados de trastorno obsesivo-compulsivo en la infancia y la adolescencia. Sponsored by: Fundación Alicia Koplowitz. Duration: 26/05/2011-26/05/2013.

Masana G. Ensayo doble ciego controlado con placebo de la eficacia de reboxetina y citalopram como tratamiento coadyuvante de los antipsicóticos de segunda generación en el tratamiento de los síntomas negativos de la esquizofrenia. Sponsored by: Instituto de Salud Carlos III (ISCIII), EC07/90553. Duration: 01/01/2008-31/12/2011.

Castro J. Caracterísitcas psicopatológicas, neuropsicológicas y de neuroimagen comunes y diferenciales en niños y adolescentes hijos de pacientes con esquizofrenia o con trastorno bipolar. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI 07/0066. Duration: 26/11/2007-30/12/2011.

Castro J. Reconocimiento como grupo consolidado de investigación. Sponsored by: Generalitat de Catalunya, AGAUR, 2009SGR1119. Duration: 03/07/2009-31/12/2013.

Morer A. Collaborative Genomic Studies of Tourette Disorders. Sponsored by: NIMH, RO1 MH092293. Duration: 01/01/2011-31/12/2012.

Morer A. European multicentre tics in children studies (EMTICS). Sponsored by: European Commission, 278367. Duration: 01/12/2011-30/05/2017.

Colom F. Development and evaluation of a multidisciplinary service for people with bipolar disorder. Sponsored by: NIHR, Programme Grants for Applied Research, RP-PG-0108-10087. Duration: 01/01/2009-31/12/2013.

Colom F. 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: 01/01/2011-31/12/2013.

Gual T. Optimizing delivery of health care interventions (Odhin). Sponsored by: European Commission, 259268. Duration: 01/01/2011-31/12/2014.

Gual T. Addictions and Lifestyles in Contemporary Europe: Reframing addictions Project (Alice Rap). Sponsored by: European Commission, 266813. Duration: 01/01/2011-31/12/2016.

Vieta E. Trastorn bipolar. Sponsored by: Generalitat de Catalunya, AGAUR, AGAUR_SGR09 2009_SGR_1022. Duration: 15/09/2009-31/12/2013.

Gasto C. Análisis de perfiles de metilación en genes involucrados en la respuesta al estrés y su correlación con morfología cerebral (MRI) en trastornos afectivos severos. Sponsored by: Ministerio de Economía y Competitividad, MEC_PN08 SAF2008-05674-C03-03. Duration: 01/01/2009-31/12/2012.

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: 01/01/2011-31/12/2013.

Gual T. European Workplace and Alcohol. Sponsored by: European Commission, CE_SANCO_09 CE_SANCO_09_01. Duration: 01/01/2011-30/06/2013.

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, MSPSI_PNSD11 2011/050. Duration: 08/11/2011-07/11/2014.

Martin-Santos R. Bases neurobiológicas de la depresión inducida por interferón en la hepatitis C crónica. Estudio PSICOCIT. Sponsored by: Instituto de Salud Carlos III (ISCIII), FIS10 PI10/02206. Duration: 01/01/2011-31/12/2013.

Vieta E. Contratos Bases biológicas del trastorno psíquico y psiquiatría nuclear. Trastornos afectivos unipolares. Colaboración con los grupos de investigación en trasplantes. Líneas de investigación en el programa de trastornos bipolares. Ministerio de Educación y Ciencia, JCI-2009-04329 Duration: 01/12/2009-30/11/2012.

DOCTORAL THESES

Castro J, Baeza I. Característiques clíniques i neuropsicològiques en nens i adolescents d'alt risc per esquizofrènia. PhD student: Elena de la Serna Gómez.

Vieta E, Colom F. Treatment outcomes of antidepressant use in bipolar disorder. PhD student: Isabella Pacchiarotti.

Vieta E, Martinez A. Funcionament psicosocial en el trastorn bipolar: Factors implicats i seguiment als 4 anys. PhD student: Caterina del Mar Bonnin Roig.

Bernardo M. Metabolism and inflammation in first episode psychosis. PhD student: Clemente García Rizo.

Castro J. Prevalence, clinical correlates and factors associated with course and outcome of anxiety disorders in youth with bipolar disorder. PhD student: Regina Sala Cassola.

Bernardo M, Parellada E. Transportador de la Dopamina (DAT) y pronóstico de la esquizofrenia: Estudio prospectivo de una cohorte evaluado mediante DATSCAN, RM volumétrica y el polimorfismo -67 A/T del gen DAT. PhD student: Anna Mané Santacana.

Martin R. Early-onset of chronic cannabis use: effects on cognitive function and brain activity. PhD student: Ana Beatriz Fagundo.

AREA 4

Clinical and experimental neuroscience

Neuropsychology

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STRATEGIC OBJECTIVES

Study of the consequences of cerebral lesions and dysfunctions in relation to 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 different high-performance workstations.

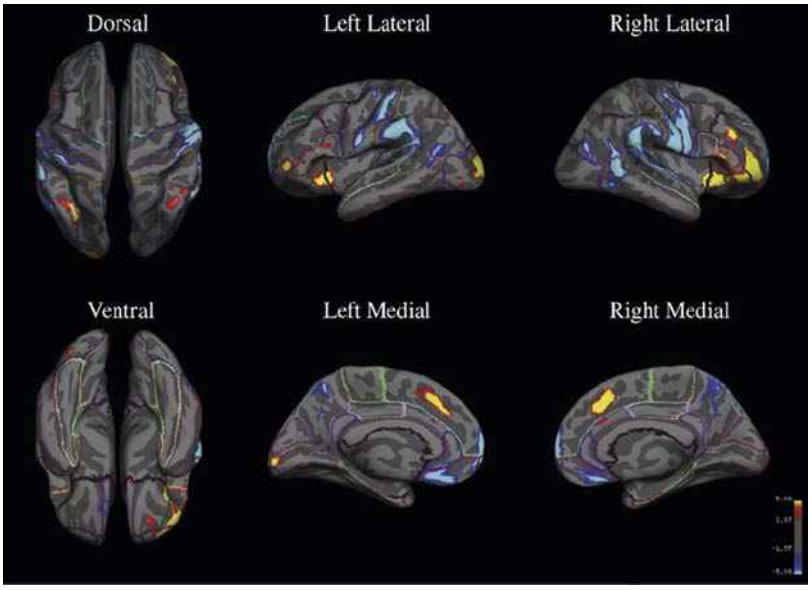
MAIN LINES OF RESEARCH

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 neuron death. Identification of the symptoms prior to actual clinical manifestations in degenerative diseases is a challenge for treatment intervention aiming to slow the neurodegenerative processes. As a subline, mention should be made of the study of the contribution of the cognitive reserve variables in the degree of cognitive deterioration 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 layer 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.



Differences between Parkinson's disease (PD) patients and healthy controls in a fMRI task of recognition memory. In yelow areas with decreased activation during the task and in blue areas with decreased deactivation . (Ibarretxe-Bilbao et al. Neuroimage 2011).

PUBLICATIONS

ORIGINALS
I.F.: 125.07

1 Iranzo A, Valldeoriola F, Lomena F, Molinuevo JL, Serradell M, Salamero M, Cot A, Ros D, Pavia J, Santamaria J, Tolosa E. Serial dopamine transporter imaging of nigrostriatal function in patients with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective study. LANCET NEUROL. 10:797-805. I.F.: 21.66.

2 Padilla N, Falcon C, Sanz-Cortes M, Figueras F, Bargallo N, Crispi F, Eixarch E, Arranz A, Botet F, Gratacos E. Differential effects of intrauterine growth restriction on brain structure and development in preterm infants: A magnetic resonance imaging study. BRAIN RES. 1382:98-108. I.F.: 2.62.

3 Sole-Padulles C, Llado A, Bartres-Faz D, Fortea J, Sanchez-Valle R, Bosch B, Antonell A, Molinuevo JL, Rami L. Association between cerebrospinal fluid tau and brain atrophy is not related to clinical severity in the Alzheimer's disease continuum. PSYCHIAT RES-NEUROIM. 192:140-146. I.F.: 2.06.

4 Ibarretxe-Bilbao N, Junque C, Marti MJ, Tolosa E. Brain structural MRI correlates of cognitive dysfunctions in Parkinson's disease. J NEUROL SCI. 310:70-74. I.F.: 2.17.

5 Ibarretxe-Bilbao N, Junque C, Marti MJ, Tolosa E. Cerebral basis of visual hallucinations in Parkinson's disease: Structural and functional MRI studies. J NEUROL SCI. 310:79-81. I.F.: 2.17.

6 Rami L, Valls-Pedret C, Bartres-Faz D, Caprile C, Sole-Padulles C, Castellvi M, Olives J, Bosch B, Molinuevo JL. Cognitive reserve questionnaire. Scores obtained in a healthy elderly population and in one with Alzheimer›s disease. REV NEUROLOGIA. 52:195-201. I.F.: 1.22.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	109.29	33	21	8
2010	100.84	23	15	5
2011	125.07	29	17	4

7 Fortea J, Sala-Llonch R, Bartres-Faz D, Llado A, Sole-Padulles C, Bosch B, Antonell A, Olives J, Sanchez-Valle R, Molinuevo JL, Rami L. Cognitively Preserved Subjects with Transitional Cerebrospinal Fluid beta-Amyloid 1-42 Values Have Thicker Cortex in Alzheimer's Disease Vulnerable Areas. BIOL PSYCHIAT. 70:183-190. I.F.: 8.67.

8 Ibarretxe-Bilbao N, Zarei M, Junque C, Marti MJ, Segura B, Vendrell P, Valldeoriola F, Bargallo N, Tolosa E. Dysfunctions of cerebral networks precede recognition memory deficits in early Parkinson›s disease. NEUROIMAGE. 57:589-597. I.F.: 5.94.

9 Moreno-Lopez C, Santamaria J, Salamero M, DelSorbo F, Albanese A, Pellecchia MT, Barone P, Overeem S, Bloem B, Aarden W, Canesi M, Antonini A, Duerr S, Wenning GK, Poewe W, Rubino A, Meco G, Schneider SA, Bhatia KP, Djaldetti R, Coelho M, Sampaio C, Cochen V, Hellriegel H, Deuschl G, Colosimo C, Marsili L, Gasser T, Tolosa E. Excessive Daytime Sleepiness in Multiple System Atrophy (SLEEMSA Study). ARCH NEUROL-CHICAGO. 68:223-230. I.F.: 7.11.

10 Arenaza-Urquijo EM, Bosch B, Sala-Llonch R, Sole-Padulles C, Junque C, Fernandez-Espejo D, Bargallo N, Rami L, Molinuevo JL, Bartres-Faz D. Specific Anatomic Associations Between White Matter Integrity and Cognitive Reserve in Normal and Cognitively Impaired Elders. AM J GERIAT PSYCHIAT. 19:33-42. I.F.: 3.57.

11 Iranzo A, Frauscher B, Santos H, Gschliesser V, Ratti L, Falkenstetter T, Sturner C, Salamero M, Tolosa E, Poewe W, Santamaria J, Hogl B. Usefulness of the SINBAR electromyographic montage to detect the motor and vocal manifestations occurring in REM sleep behavior disorder. SLEEP MED. 12:284-288. I.F.: 3.43.

12 Fernandez S, Donaire A, Maestro I, Seres E, Setoain X, Bargallo N, Rumia J, Boget T, Falcon C, Carreno M. Functional neuroimaging in startle epilepsy: Involvement of a mesial frontoparietal network. EPILEPSIA. 52:1725-1732. I.F.: 3.96.

13 Carreno M, Becerra JL, Castillo J, Maestro I, Donaire A, Fernandez S, Bargallo N, Setoain X, Pintor L, Bailles E, Rumia J, Boget T, Vernet O, Fumanal S. Seizure frequency and social outcome in drug resistant epilepsy patients who do not undergo epilepsy surgery. SEIZURE-EUR J EPILEP. 20:580-582. I.F.: 1.65.

14 Rubi S, Setoain X, Donaire A, Bargallo N, Sanmarti F, Carreno M, Rumia J, Calvo A, Aparicio J, Campistol J, Pons F. Validation of FDG-PET/MRI coregistration in nonlesional refractory childhood epilepsy. EPILEPSIA. 52:2216-2224. I.F.: 3.96.

15 Lazaro L, Castro-Fornieles J, Cullell C, Andres S, Falcon C, Calvo R, Bargallo N. A voxel-based morphometric MRI study of stabilized obsessive-compulsive adolescent patients. PROG NEURO-PSYCHOPH. 35:1863-1869. I.F.: 2.88.

16 Reig S, Parellada M, Castro-Fornieles J, Janssen J, Moreno D, Baeza I, Bargallo N, Gonzalez-Pinto A, Graell M, Ortuno F, Otero S, Arango C, Desco M. Multicenter Study of Brain Volume Abnormalities in Children and Adolescent-Onset Psychosis. SCHIZOPHRENIA BULL. 37:1270-1280. I.F.: 8.27.

17 Rosa AR, Reinares M, Amann B, Popovic D, Franco C, Comes M, Torrent C, Bonnin CM, Sole B, Valenti M, Salamero M, Kapczinski F, Vieta E. Six-month functional outcome of a bipolar disorder cohort in the context of a specialized-care program. BIPOLAR DISORD. 13:679-686. I.F.: 5.22.

18 Segarra N, Bernardo M, Gutierrez F, Justicia A, Fernadez-Egea E, Allas M, Safont G, Contreras F, Gascon J, Soler-Insa PA, Menchon JM, Junque C, Keefe RSE. Spanish validation of the Brief Assessment in Cognition in Schizophrenia (BACS) in patients with schizophrenia and healthy controls. EUR PSYCHIAT. 26:69-73. I.F.: 3.37.

19 Palacios EM, Fernandez-Espejo D, Junque C, Sanchez-Carrion R, Roig T, Tormos JM, Bargallo N, Vendrell P. Diffusion tensor imaging differences relate to memory deficits in diffuse traumatic brain injury. BMC NEUROL. 11:-. I.F.: 2.80.

20 Fernandez-Espejo D, Bekinschtein T, Monti MM, Pickard JD, Junque C, Coleman MR, Owen AM. Diffusion weighted imaging distinguishes the vegetative state from the minimally conscious state. NEUROIMAGE. 54:103-112. I.F.: 5.94.

21 Verger E, Valduvieco I, Caral L, Pujol T, Ribalta T, Vinolas N, Boget T, Oleaga L, Blanco Y, Graus F. Does gender matter in glioblastoma?. CLIN TRANSL ONCOL. 13:737-741. I.F.: 1.25.

22 Lima FPS, Lima MO, Leon D, Lucareli PRG, Falcon C, Cogo JC, Bargallo N, Vidal J, Bernabeu M, Junque C. fMRI of the sensorimotor cortex in patients with traumatic brain injury after intensive rehabilitation. NEUROL SCI. 32:633-639. I.F.: 1.22.

23 Zubiaurre-Elorza L, Soria-Pastor S, Junque C, Segarra D, Bargallo N, Mayolas N, Romano-Berindoague C, Macaya A. Gray matter volume decrements in preterm children with periventricular leukomalacia. PEDIATR RES. 69:554-560. I.F.: 2.80.

24 Pardo BM, Garolera M, Ariza M, Pareto D, Salamero M, Valles V, Delgado L, Alberni J. Improvement of cognitive flexibility and cingulate blood flow correlates after atypical antipsychotic treatment in drug-naive patients with first-episode schizophrenia. PSYCHIAT RES-NEUROIM. 194:205-211. I.F.: 2.06.

25 Salazar F, Donate M, Boget T, Bogdanovich A, Basora M, Torres F, Fabregas N. Intraoperative warming and post-operative cognitive dysfunction after total knee replacement. ACTA ANAESTH SCAND. 55:216-222. I.F.: 2.20.

26 Ortiz-Gil J, Pomarol-Clotet E, Salvador R, Canales-Rodriguez EJ, Sarro S, Gomar JJ, Guerrero A, Sans-Sansa B, Capdevila A, Junque C, Mckenna PJ. Neural correlates of cognitive impairment in schizophrenia. BRIT J PSYCHIAT. 199:202-210. I.F.: 5.95.

27 Bartres-Faz D, Arenaza-Urquijo EM. Structural and Functional Imaging Correlates of Cognitive and Brain Reserve Hypotheses in Healthy and Pathological Aging. BRAIN TOPOGR. 24:340-357. I.F.: 3.29.

28 Rametti G, Carrillo B, Gomez-Gil E, Junque C, Zubiarre-Elorza L, Segovia S, Gomez A, Guillamon A. The microstructure of white matter in male to female transsexuals before cross-sex hormonal treatment. A DTI study. J PSYCHIATR RES. 45:949-954. I.F.: 3.83.

29 Rametti G, Carrillo B, Gomez-Gil E, Junque C, Segovia S, Gomez A, Guillamon A. White matter microstructure in female to male transsexuals before cross-sex hormonal treatment. A diffusion tensor imaging study. J PSYCHIATR RES. 45:199-204. I.F.: 3.83.

REVIEWS
I.F.: 3.82

1 Popovic D, Reinares M, Amann B, Salamero M, Vieta E. Number needed to treat analyses of drugs used for maintenance treatment of bipolar disorder. PSYCHOPHARMACOLOGY. 213:657-667. I.F.: 3.82.

EDITORIALS
I.F.: 15.47

1 Valenzuela M, Bartres-Faz D, Beg F, Fornito A, Merlo-Pich E, Muller U, Ongur D, Toga AW, Yucel M. Neuroimaging as endpoints in clinical trials: Are we there yet? Perspective from the first Provence workshop. MOL PSYCHIATR. 16:1064-1066. I.F.: 15.47.

GRANTS FOR RESEARCH IN PROGRESS

Salamero M. Desarrollo y validación en una nueva escala de somnolencia de aplicación clínica. Sponsored by: Ministerio Sanidad y Consumo, PI070318. Duration: 26/11/2007-31/12/2012.

Junqué C. Ajuts de Suport als grups de Recerca. Sponsored by: DAGAUR, 2009SGR941. Duration: 01/01/2009-31/12/2013.

Marcos T. Estudio de la eficacia de la rehabilitación cognitiva en el trastorno depresivo mayor refractario al tratamiento farmacológico. Sponsored by: Instituto de Salud Carlos III, PI09/90126. Duration: 01/01/2010-31/12/2011.

Bartres D. Relación entre variables de reserva cerebral de tipo ambientales y genéticas y la función y estructura cerebrales en el envejecimiento sano y patológico. Sponsored by: Ministerio de Ciencia e Innovación, 052296. Duration: 01/01/2010-31/12/2013.

Bartres D. Prediction of cognitive properties of new drug candidates for neurodegenerative diseases in early clinical development. Sponsored by: European Commission, IMI/115009. Duration: 01/01/2010-31/12/2015.

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

Bartres-Faz D. Estudios miltimodales de reesonancia magnética y de líquido cefalorraquídeo en la enfermedad de Alzheimer preclínica familiar y esporádica. PhD student: Juan Fortea Ormaechea.

AREA 4

Clinical and experimental neuroscience

Systems neuroscience

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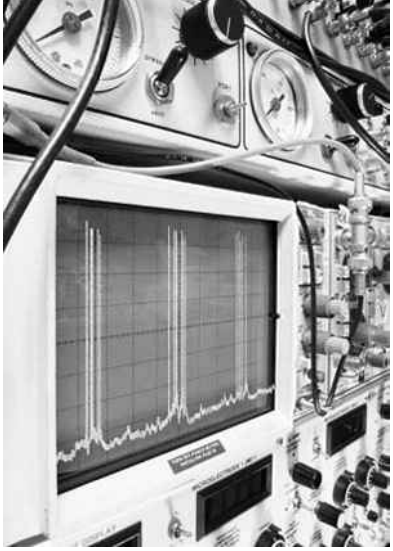
CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Systems neuroscience



STRATEGIC OBJECTIVES

Recently, 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 it 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 basal ganglia, hippocampal and cortical networks with a theoretical approach.

MAIN LINES OF RESEARCH

- Electrical activity generation and control mechanisms in neuronal networks – specifically, in the brain cortex.
- Hippocampal and subicular mechanisms of spatial processing.
- Neuronal activity synchronization mechanisms in cortical networks.
- Distributed cortical network mechanisms implicated in selective attention, working memory and executive control.
- Simple motor coding (head movement, lever activation) based on striatal clustering.
- Mechanism of information transfer between networks.
- Effect of cannabinoids on high-voltage axes.
- Use of virtual reality in neuroscience, in the context of theEVENT Lab (Virtual Environments in Neuroscience and Technology), in collaboration with Mel Slater (University of Barcelona).
- Effect of behavioral interventions on the epigenetic regulation of processes implicated in chronic diseases and related to aging.

1. Cortical networks and EVENT Lab (Virtual Environments in Neuroscience and Technology). Headed by Dr. Maria Victòria Sánchez (IDIBAPS)

Neuronal connectivity and cellular and synaptic properties determine and give shape to the emergent population activity (spontaneous or invoked) generated by the neuronal networks. At the same time, 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.

The impact which the different cellular processes (e.g., ion channels activation) have upon the resultant network activity tends to be non-intuitive and unpredictable – thus making it necessary to adopt a not only theoretical but also experimental approach.

As regards the information encoded by the network activity, we have worked with different sensory modalities (visual, tactile, auditory), and are presently especially interested in the spatial processing that occurs in the hippocampal complex. Lastly, integration of the cortical information giving rise to bodily 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).

For further information:
http://www.sanchez-vives.org

2. Theoretical neurobiology of the cortical networks.Headed by Dr. 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 at all times, and technically sophisticated data-analyzing tools. We work in parallel at two levels: on 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, and on the other we study the physiological bases of cognitive capacities such as working memory and selective attention, and their dysfunction in psychiatric disorders.

For further information:
http://complab.fcrb.es

3. Physiology and basal ganglia networks and regulation with cannabinoids. Headed by Dr. David Robbe (IDIBAPS)

The principal objective of the laboratory is to understand the processing of cognitive and motor-sensory (cortical) information in the basal ganglia - a group of subcortical nuclei that are essential for motor coordination and the formation of habits, and which are implicated in Parkinson's disease and in addictions. Surprisingly, the excellent description of the anatomical characteristics of the basal ganglia (BG) has given rise to two opposed reference models of processing carried out in the BG. In the first model, the BG have been modelled as independent information processing channels, while the other model postulates that the ganglia act as cortical input integrators. In order to address this controversy, we use large-scale electrophysiological recording techniques (silica catheters, tetrodes) in the course of specific motor activities, in combination with advanced analytical tools and pharmacological perturbation (cannabinoids).

For further information:
http://neuro.fcrb.es/BasalGangLab/RobbeLab/Welcome.html

4. Neuroepigenetics lab. Headed by Perla Kaliman (IDIBAPS)

It is now accepted that brain networks and genetic information in adults are both sensitive and responsive to experience. An increasing number of studies in animal models are starting to show that behavioral interventions can induce changes in epigenetic codes in the nervous system that may be critical for synaptic plasticity and complex processes such as memory, learning and stress resistance. In this context, our research is aimed at identifying behavioral-induced molecular biomarkers associated with adaptive psychological and physiological changes. Accordingly, we investigate the effect of behavioral interventions (e.g. voluntary exercise and enriched environment in rodents and meditation-based trainings in humans) on the epigenetic regulation of processes such as oxidative stress and inflammation, which are at the root of most chronic and aging-related diseases.

5. Cortical Circuit Dynamics Group. Headed by Dr. Jaime de la Rocha (IDIBAPS)

The main focus of our research is the study of the circuit mechanisms underlying perception and decision making. In particular we are interested in the neural basis of auditory representation and its dependence on brain state and other contextual variables. We investigate the generation of ongoing cortical activity, its impact on perception and guiding decisions. We are particularly interested in the variability and co-variability observed in the sensory-evoked responses of cortical neurons, the mechanisms which generate them and their role in a neural code. We combine population cortical recordings in rats, quantitative analysis and computational modeling to address these questions.

For further information:
http://neuro.fcrb.es/delaRochaLab

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	29.99	6	3	0
2010	51.07	11	4	5
2011	16.04	4	3	1

ORIGINALS
I.F.: 16.04

1 Abolafia JM, Vergara R, Arnold MM, Reig R, Sanchez-Vives MV. Cortical Auditory Adaptation in the Awake Rat and the Role of Potassium Currents. CEREB CORTEX. 21:977-990. I.F.: 6.84.

2 Szczepanski J, Arnold M, Wajnryb E, Amigo JM, Sanchez-Vives MV. Mutual information and redundancy in spontaneous communication between cortical neurons. BIOL CYBERN. 104:161-174. I.F.: 1.67.

3 Ruiz-Mejias M, Ciria-Suarez L, Mattia M, Sanchez-Vives MV. Slow and fast rhythms generated in the cerebral cortex of the anesthetized mouse. J NEUROPHYSIOL. 106:2910-2921. I.F.: 3.11.

3 Ledberg A, Robbe D. Locomotion-related oscillatory body movements at 6-12 Hz modulate the hippocampal theta rhythm. PLoS One. 6(11):e27575. I.F.: 4.41

REVIEWS
I.F.: 9.00

1 Kaliman P, Parrizas M, Lalanza JF, Camins A, Escorihuela RM, Pallas M. Neurophysiological and epigenetic effects of physical exercise on the aging process. AGEING RES REV. 10:475-486. I.F.:9.00.

GRANTS FOR RESEARCH IN PROGRESS

Robbe D. Dynamic of neuronal network interactions in the basal ganglia. Sponsored by: European Commission, 230976. Duration: 01/09/2008-31/08/2012.

Sanchez-Vives MV. Dinámica cortical en los diferentes estados de activación de la red. Sponsored by: Ministerio de Ciencia y Tecnologia (MICINN), BFU2008-01371/BFI. Duration: 01/01/2009-31/12/2011.

Robbe D. Entendiendo los efectos de los canabinoides en los episodios epilepticos en la red talamocortical. Sponsored by: Ministerio de Educación y Ciencia, BFU2008-03946/BFI. Duration: 01/01/2009-31/12/2011.

Sanchez-Vives MV. Grups Consolidats de Recerca "Neurociencias de Sistemas". Sponsored by: AGAUR, 2009 SGR1363. Duration: 01/01/2009-31/12/2013.

Compte A. Mecanismos de redes distribuidas en memoria de trabajo y atención selectiva. Sponsored by: Ministerio de Educación, BFU2009_09537. Duration: 01/01/2010-31/12/2012.

Sanchez-Vives MV. BEAMING: Being through augmented media for natural networked gatherings. Sponsored by: European Commission, 248620. Duration: 01/01/2010-31/12/2013.

Sanchez-Vives MV. VERE: Virtual Embodiment and Robotic Re-Embodiment. Sponsored by: European Commission, 257695. Duration: 01/06/2010-31/05/2015.

Robbe D. Basal Ganglia and the control of locomotion. Sponsored by: European Commission, 253873. Duration: 01/10/2010-30/09/2012.

De La Rocha J. Network dynamics of auditory cortex and the impact of correlations on the encoding of sensory information. Sponsored by: European Commission, FP7-PEOPLE-IRG-10_01. Duration: 01/09/2010-31/08/2014.

Sanchez-Vives MV. MELOMICS: Optimización de la respuesta terapéutica a la modulación de estímulos auditivos. Sponsored by: Ministerio Ciencia e Innovación, INNPACTO IPT-300000-2010-0010. Duration: 22/06/2010-31/12/2013.

Kaliman P. Physical exercise and aging: transcriptional and epigenetic effects in and accelerated aging mouse model. Sponsored by: Ministerio de Ciencia y Tecnología, SAF2010-15050. Duration: 01/01/2010-31/12/2013.

Kaliman P. Wisconsin Center for the Neuroscience and Psychophysiology of Meditation. Sponsored by: University of Wisconsin Madison, Office of Research and Sponsored Programs, U.WISC_KALIMAN. Duration: 01/01/2011-30/06/2012.

De La Rocha J. Dinámica estocástica de los circuitos corticales y representación sensorial. Sponsored by: Ministerio de Educación y Ciencia (MICINN), SAF2010-15730. Duration: 01/01/2011-31/12/2013.

Compte A. Investigating the neural mechanisms of feature-based and spatial attention. Sponsored by: European Commission, CE-FP7-PEOPLE-IEF-10 275800. Duration: 01/06/2011-31/05/2013.

Perez E. Propiedades computacionales de las dendritas durante la actividad cortical lenta (< 1 Hz) y su modulación por los sistemas activadores colinérgicos. Sponsored by: Ministerio de Ciencia e Innovación, MICINN_PN10 SAF2010-18884. Duration: 01/01/2011-31/12/2013.

DOCTORAL THESES

Sanchez-Vives MV. Neuronal basis of auditory adaptation and temporal discrimination in the auditory cortex of the awake freely moving rat. PhD student: Juan Manuel Abolafia Moya.

Sanchez-Vives MV. Modulation of spatial processing by somatosensory inputs in the rat. PhD student: Thomas Gener.

AREA 4

Clinical and experimental neuroscience

Clinical and experimental neuroimmunology

TEAM INVOLVED IN:

redEspañolade esclerosismúltiple

GROUP MEMBERS

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Núria de la Iglesia (IDIBAPS)
Lidia Sabater (Fundació Clínic)
Albert Saiz (Hospital Clínic)
Yolanda Blanco (Hospital Clínic)
Josep Dalmau (ICREA-IDIBAPS)

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Valeria Colafrancesco (IDIBAPS)
Nuria Gresa (IDIBAPS)

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Oihana Errea (IDIBAPS)
Ion Agirrezabal (FIS)
Anna Boronat (FIS)
Sara Llufriu (IDIBAPS)
Francesco Mannara (Fundació Clínic)
Marta Moreno (FPI)
Iñigo Gabilondo (IDIBAPS)
Sara Martínez (IDIBAPS)

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Eva Caballero (Fundació Clínic)
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Eva Valero (REEM)
Laura Planas (REEM)
Maria Rodés (IDIBAPS)

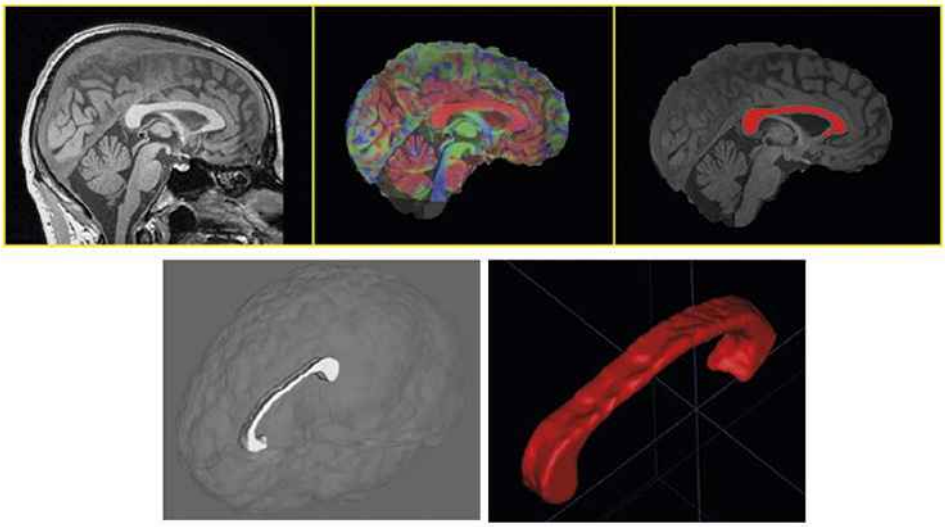
COLLABORATORS:
Myrna Rosenfeld (IDIBAPS)
Santiago Ortiz (Hospital Clínic)
Ana Catafau (IDIBAPS)
Bernardo Sanchez-Dalmau (Hospital Clínic)

CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Clinical and experimental neuroimmunology

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.



Automatic segmentation of the corpus callosum through diffusion tensor imaging and 3D-T1 imaging using FSL software. In this way it is possible to determine the volumetric characteristics of this structure, which is frequently altered in multiple sclerosis. Accepted for the 17th Annual Meeting of the Organization for Human Brain Mapping (Quebec, June 2011).

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. By late 2010 we plan to enter the clinical phase of the study of methylthioadenosine as treatment in cases of multiple sclerosis.
As the coordinating team of the RETICS REEM (Spanish Multiple Sclerosis Network - www.reem.es), 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 to cover the gap in financing existing between basic research and the clinical phase development of new drugs on the part of the biopharmaceutical industry.

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:

- 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.
- Functional characterization of the factors identified above in the initiation, maintenance and invasiveness of gliomas.
- Design of new, alternative therapies for gliomas.

RESEARCH GROUP
AUTOIMMUNITY AGAINST SYNAPTIC ANTIGENS

Group Leader: **Josep Dalmau (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. These disorders are associated with autoimmune responses characterised by antibodies against synaptic receptors and proteins, such as the glutamate receptors (NMDA, AMPA) or GABA(B) receptors, or against synaptic proteins related to epilepsy (LGI1, Caspr2). Once the antigens are identified, our studies focus on identifying the cellular and molecular mechanisms by which the antibodies alter the function of the synaptic receptors and proteins, thereby causing symptoms. The 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.

RESEARCH GROUP
IMMUNOPATHOGENESIS OF PARANEOPLASTIC NEUROLOGICAL DISORDERS

Group Leader: **Francesc Graus (Hospital Clínic)**

Paraneoplastic neurological disorders manifest in cancer patients generally in very early stages, and their correct diagnosis is essential for detecting the tumor and for preventing progression of the neurological disease. Our group has made a fundamental contribution to confirmation of the immunological cause of these disorders, and is an international reference center for the evaluation of antineuronal antibodies associated to paraneoplastic neurological disorders. The group is interested in the characterization of antineuronal antibodies and corresponding antigens of potential diagnostic or pathogenic relevance in relation to these diseases. Some of the antibodies identified by our group, such as anti-Hu, anti-Tr or anti-SOX1, are currently used on a routine basis as predictors of paraneoplastic neurological disorders.

PUBLICATIONS

ORIGINALS
I.F.: 139.97

1 Abraira V, Alvarez-Cermeno JC, Arroyo R, Camara C, Casanova B, Cubillo S, DeAndres C, Espejo C, Fernandez O, Ferrer J, Figueredo MA, Garcia-Merino A, Garcia-Sanchez MI, Garcia-Trujillo JA, Gomez M, Gonzalez-Oria C, Gosis A, Izquierdo G, Jimenez J, Lopez-Trascasa M, Montalban X, Moreno MJ, Munoz D, Nunez V, Muriel A, Navarro J, Olascoaga J, Oreja-Guevara C, Prada A, Ramil E, Ramo-Tello C, Rodriguez C, Rodriguez E, Rodriguez-Frias F, Rodriguez-Antiguedad A, Rodriguez-Molina JJ, Ruiz E, Saiz A, Sarasola E, Simo M, Yague J, Villar LM. Utility of oligoclonal IgG band detection for MS diagnosis in daily clinical practice. J IMMUNOL METHODS. 371:170-173. I.F.: 2.34.

2 Gaig C, Valldeoriola F, Gelpi E, Ezquerra M, Llufriu S, Buongiorno M, Rey MJ, Marti MJ, Graus F, Tolosa E. Rapidly Progressive Diffuse Lewy Body Disease. MOVEMENT DISORD. 26:1316-1323. I.F.: 4.48.

3 Verger E, Valduvieco I, Caral L, Pujol T, Ribalta T, Vinolas N, Boget T, Oleaga L, Blanco Y, Graus F. Does gender matter in glioblastoma?. CLIN TRANSL ONCOL. 13:737-741. I.F.: 1.25.

4 Gabilondo I, Saiz A, Galan L, Gonzalez V, Jadraque R, Sabater L, Sans A, Sempere A, Vela A, Villalobos F, Vinals M, Villoslada P, Graus F. Analysis of relapses in anti-NMDAR encephalitis. NEUROLOGY. 77:996-999. I.F.: 8.02.

5 Lancaster E, Martinez-Hernandez E, Titulaer MJ, Boulos M, Weaver S, Antoine JC, Liebers E, Kornblum C, Bien CG, Honnorat J, Wong S, Xu J, Contractor A, Balice-Gordon R, Dalmau J. Antibodies to metabotropic glutamate receptor 5 in the Ophelia syndrome. NEUROLOGY. 77:1698-1701. I.F.: 8.02.

6 Mas N, Saiz A, Leite MI, Waters P, Baron M, Castano D, Sabater L, Vincent A, Graus F. Antiglycine-receptor encephalomyelitis with rigidity. J NEUROL NEUROSUR PS. 82:1399-1401. I.F.: 4.79.

7 Vigliani MC, Honnorat J, Antoine JC, Vitaliani R, Giometto B, Psimaras D, Franchino F, Rossi C, Graus F. Chorea and related movement disorders of paraneoplastic origin: the PNS EuroNetwork experience. J NEUROL. 258:2058-2068. I.F.: 3.85.

8 Boronat A, Sabater L, Saiz A, Dalmau J, Graus F. GABA(B) receptor antibodies in limbic encephalitis and anti-GAD-associated neurologic disorders. NEUROLOGY. 76:795-800. I.F.: 8.02.

9 Oyanguren-Desez O, Rodriguez-Antiguedad A, Villoslada P, Domercq M, Alberdi E, Matute C. Gain-of-function of P2X7 receptor gene variants in multiple sclerosis. CELL CALCIUM. 50:468-472. I.F.: 3.55.

10 Sawcer S, Hellenthal G, Pirinen M, Spencer CCA, Patsopoulos NA, Moutsianas L, Dilthey A, Su Z, Freeman C, Hunt SE, Edkins S, Gray E, Booth DR, Potter SC, Goris A, Band G, Oturai AB, Strange A, Saarela J, Bellenguez C, Fontaine B, Gillman M, Hemmer B, Gwilliam R, Zipp F, Jayakumar A, Martin R, Leslie S, Hawkins S, et al. (Villoslada P) Genetic risk and a primary role for cell-mediated immune mechanisms in multiple sclerosis. NATURE. 476:214-219. I.F.: 36.10.

11 Blanco Y, Ercilla-Gonzalez G, Llufriu S, Casanova-Estruch B, Magraner MJ, Ramio-Torrenta L, Mendibe-Bilbao MD, Ucles-Sanchez AJ, Casado-Chocan JL, DeMunain AL, Ramo-Tello C, Santos-Lasaosa S, Porras RFB, Segura-Bruna N, Sepulveda-Gazguez M, Villoslada P, Graus F, Saiz A. HLA-DRB1 typing in Caucasians patients with neuromyelitis optica. REV NEUROLOGIA. 53:146-152. I.F.: 1.22.

12 Brell M, Castaner S, Pujol-Farre T, Boluda S, Ribalta T, Bruna J, Martinez M, Verger E, Villa S, Vinolas N, Gil M, Graus F, Tortosa-Moreno A. Implication of radiological pattern in the prognosis of oligodendroglial tumors: correlation with genetic profile. REV NEUROLOGIA. 52:465-471. I.F.: 1.22.

13 Lancaster E, Huijbers MGM, Bar V, Boronat A, Wong A, Martinez-Hernandez E, Wilson C, Jacobs D, Lai M, Walker RW, Graus F, Bataller L, Illa I, Markx S, Strauss KA, Peles E, Scherer SS, Dalmau J. Investigations of Caspr2, an Autoantigen of Encephalitis and Neuromyotonia. ANN NEUROL. 69:303-311. I.F.: 10.75.

14 Sepulcre J, Peraita H, Goni J, Arrondo G, Martincorena I, Duque B, DeMendizabal NV, Masdeu JC, Villoslada P. Lexical access changes in patients with multiple sclerosis: A two-year follow-up study. J CLIN EXP NEUROPSYC. 33:169-175. I.F.: 1.81.

15 DeMendizabal NV, Carneiro J, Sole RV, Goni J, Bragard J, Martinez-Forero I, Martinez-Pasamar S, Sepulcre J, Torrealdea J, Bagnato F, Garcia-Ojalvo J, Villoslada P. Modeling the effector - regulatory T cell cross-regulation reveals the

intrinsic character of relapses in Multiple Sclerosis. BMC SYST BIOL. 5:-. I.F.: 3.57.

16 Panzer J, Dalmau J. Movement disorders in paraneoplastic and autoimmune disease. CURR OPIN NEUROL. 24:346-353. I.F.: 5.02.

17 Titulaer MJ, Soffietti R, Dalmau J, Gilhus NE, Giometto B, Graus F, Grisold W, Honnorat J, Smitt PAES, Tanasescu R, Vedeler CA, Voltz R, Verschuuren JJGM. Screening for tumours in paraneoplastic syndromes: report of an EFNS Task Force. EUR J NEUROL. 18:19-E3. I.F.: 3.77.

18 Briani C, Vitaliani R, Grisold W, Honnorat J, Graus F, Antoine JC, Bertolini G, Giometto B. Spectrum of paraneoplastic disease associated with lymphoma. NEUROLOGY. 76:705-710. I.F.: 8.02.

19 Moreno B, Jukes JP, Vergara-Irigaray N, Errea O, Villoslada P, Perry VH, Newman TA. Systemic inflammation induces axon injury during brain inflammation. ANN NEUROL. 70:932-942. I.F.: 10.75.

20 Colafrancesco V, Villoslada P. Targeting NGF-pathway for developing neuroprotective therapies for multiple sclerosis and other neurological diseases. ARCH ITAL BIOL. 149:183-192. I.F.: 0.78.

21 D'intino G, Lorenzini L, Fernandez M, Taglioni A, Perretta G, DelVecchio G, Villoslada P, Giardino L, Calza L. Triiodothyronine Administration Ameliorates the Demyelination/Remyelination Ratio in a Non-Human Primate Model of Multiple Sclerosis by Correcting Tissue Hypothyroidism. J NEUROENDOCRINOL. 23:778-790. I.F.: 4.65.

22 DeMiras JR, Navas J, Villoslada P, Esteban FJ. UJA-3DFD: A program to compute the 3D fractal dimension from MRI data. COMPUT METH PROG BIO. 104:452-460. I.F.: 1.24.

23 Villa S, Weber DC, Moretones C, Manes A, Combescure C, Jove J, Puyalto P, Cuadras P, Bruna J, Verger E, Balana C, Graus F. Validation of the new graded prognostic assessment scale for brain metastases: a multicenter prospective study. RADIAT ONCOL. 6:-. I.F.: 2.41.

24 Cavanillas ML, Fernández O, Comabella M, Alcina A, Fedetz M, Izquierdo G, Lucas M, Cenit MC, Arroyo R, Vandenbroeck K, Alloza I, Garcia-Barcina M, Antiguedad A, Leyva L, Gomes CL, Olascoaga J, Otaegui D, Blanco Y, Saiz A, Montalban X, Matesanz F, Urcelay E. Replication of top markers of a genome-wide association study in multiple sclerosis in Spain. GENES INMUN. 12:110-115. I.F.: 4.37.

REVIEWS
I.F.: 6.51

1 Bosch X, Saiz A, Ramos-Casals M. Monoclonal antibody therapy-associated neurological disorders. NAT REV NEUROL. 7;165-172. I.F.: 6.51

MULTICENTRICS
I.F.: 10.75

1 Comi G, Cohen JA, Arnold DL, Wynn D, Filippi M, ForteStudy GROUP. Phase III dose-comparison study of glatiramer acetate for multiple sclerosis. ANN NEUROL. 69:75-82. I.F.: 10.75.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	31.12	6	5	1
2010	98.76	19	11	4
2011	139.97	24	12	5

GRANTS FOR RESEARCH IN PROGRESS

Villoslada P. Análisis de la respuesta al tratamiento con interferon beta en la esclerosis múltiple mediante biología de sistemas. Sponsored by: Fundación de Investigación Médica Mutua Madrileña, 08/458. Duration: 05/12/2008-04/12/2011.

Villoslada P. Red Española de Esclerosis Múltiple. Sponsored by: Instituto de Salud Carlos III - Fondo de Investigaciones Sanitarias, RD07/0060/0000. Duration: 10/02/2009-31/12/2012.

Villoslada P. United europeans for the development of pharmacogenomics in multiple sclerosis. Sponsored by: European Comisión. Marie Curie Training Network ,PITN-GA- 212877. Duration: 15/09/2008-15/09/2011.

Villoslada P. Estudio del daño axonal en esclerosis múltiple mediante estudios de neuroimagen de la vía óptica. Sponsored by: Instituto de Salud Carlos III, PS09/00259. Duration: 01/01/2010-31/12/2012.

Graus F. Anticuerpos contra de antígenos de membrana neuronal en síndormes neurológicos paraneoplásicos del sistema nervioso central. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0193. Duration: 01/01/2010-31/12/2012.

Villoslada P. Studying the relapsing dynamics of major depression through network analysis of fMRI connectivity maps:

inplications for therapy. Sponsored by: Fundació La Marató de TV3, 091430. Duration: 29/01/2010-28/01/2013.

De La Iglesia N. Factores de mantenimiento y diferenciación de células madre neurales como actores principales en la patogénesis de los gliomas. Sponsored by: Ministerio de Educación, BFU2009_14616. Duration: 01/01/2010-31/12/2012.

Villoslada P. Terapia neuroprotectora para EM mediante agonistas del Factor de Crecimiento Nervioso (NGF). Sponsored by: Ministerio de Educación, INC-0059. Duration: 01/01/2010-31/12/2011.

Villoslada P. Congreso Internacional de Neuroinmunología. Sponsored by: Ministerio de Ciencia e Innovación, SAF2010-09238-E. Duration: 01/06/2010-31/05/2011.

Graus F, Dalmau J. Clinical spectrum and cellular and synaptic mechanisms of autoimmune synaptic encephalitides. Sponsored by: Fundació La Marató de TV3, 101530. Duration: 10/12/2010-09/12/2013.

Saiz A. Analysis of new antigens in seronegative (NMO-IgG/AQP4) neuromyelitis optica (Devic disease). Sponsored by: Fundació La Marató de TV3, 101610. Duration: 10/12/2010-09/12/2013.

Mahy N, 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 Ciencia e Innovación - ADVANCELL -Advanced in vitro celltechno. IPT-010000-2010-0035. Duration: 25/06/2010-31/12/2012.

Saiz A. Trasplante autólogo de células madre mesenquimales en esclerosis múltiple: ensayo clínico fase II aleatorizado, doble-ciego y cruzado con placebo. Sponsored by: Ministerio de Sanidad, Política Social e Igualdad, TRA-066. Duration: 01/01/2010-31/12/2011.

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. 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. 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. Synaptic autoimmunity in disorders of memory behavior, cognition and psychosis. Sponsored by: NINDS/NIH ARRA Challenge Award, IRCINS068204. Duration: 30/09/2009-31/08/2012.

Villoslada P. Congress of the International Society of Neuroimmunology (ISNI). Sponsored by: Generalitat de Catalunya, AGAUR, AGAUR_ARCS10 2010 ARCS1 00329. Duration: 26/10/2010-04/05/2012.

Villoslada P. Desarrollo de terapias neuroprotectoras para Esclerosis Múltiple. Sponsored by: MICINN_INNPACTO11, IPT-2011-1312-900000. Duration: 04/05/2011-31/12/2013.

Villoslada P. STOP-ELA: Aproximación multi-tecnológica para el desarrollo de nuevas terapias y sistemas. Sponsored by: MICINN_INNPACTO11, IPT-2011-1091-900000. Duration: 20/09/2008-31/12/2012.

Villoslada P. Congreso Internacional de Neuroinmunología. Sponsored by: MICINN_AccCompl10 SAF2010-09238-E. Duration: 1/6/2010-30/4/14.

Dalmau J, Nath A. Treatment of anti-NMDA receptor encephalitis. Sponsored by: NIH Beside to Brench Program. Duration: 1/5/12-30/4/14.

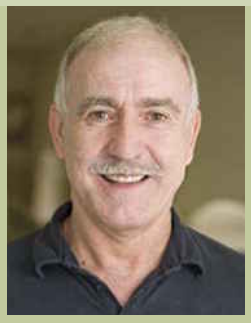
AREA 4

Clinical and experimental neuroscience

Neurobiology Unit

TEAM INVOLVED IN: cibernED

GROUP MEMBERS



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CLINICAL AND EXPERIMENTAL NEUROSCIENCE

Neurobiology Unit

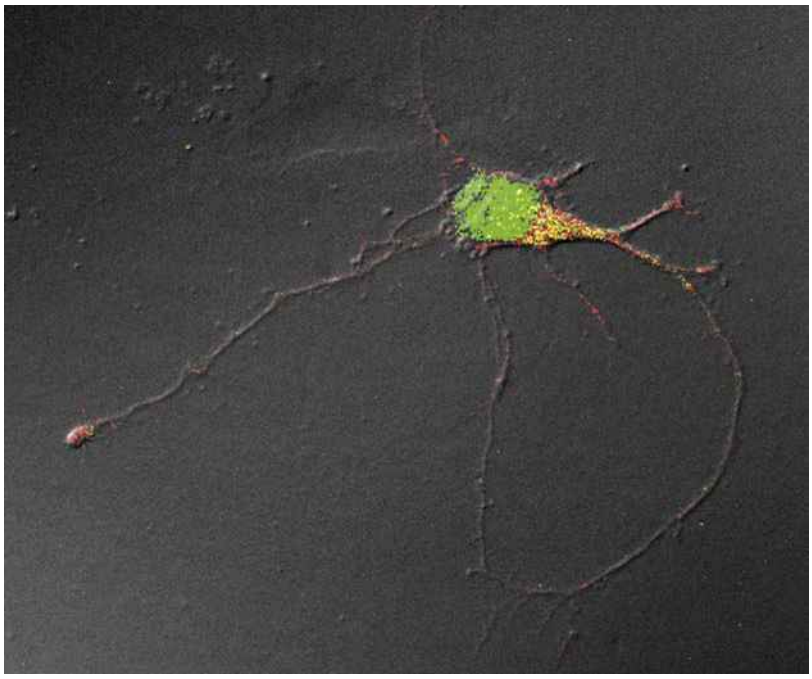
STRATEGIC OBJECTIVES

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.

Results from the first two lines of research obtained in the last year demonstrate that the mitochondrial fragmentation occurring during the neurodegenerative process is caused by NP1. We have also confirmed that NP1 regulates the transport of mitochondria to the synaptic terminals and that this effect is independent of the pro-apoptotic protein BAX. These results support the hypothesis that regulation of NP1 expression could be a target for therapeutic intervention, since it effectively halts the neurodegeneration in Alzheimer's Disease. Additionally, we have developed a new differential proteomic analysis method by which we analysed samples of cerebrospinal fluid from subjects in the preclinical stage of Alzheimer's Disease and from presymptomatic carriers of pathogenic mutations on PSEN1, and compared them with samples from patients diagnosed with Alzheimer's Disease. The aim of these studies is to establish a specific profile for protein levels in cerebrospinal fluid which would enable the preclinical diagnosis of Alzheimer's Disease.
In our studies into the role of the KATP channel in the modulation of microglia activity, using a murine model of multiple sclerosis and a rat model of excitotoxic hippocampal damage, we found that chronic activation of the microglial KATP channel reduces the pro-inflammatory activity of the microglia, with significant general inhibition of the release of inflammatory factors, such as TNF-alpha and interleukin-1 beta and NO. This ultimately means a reduction in neuronal damage and a slowing down of the neurodegenerative process started in both models. We have also demonstrated that the KATP channel plays a central role in the control of the microglial reaction which follows ischaemia in tMCAO rats and we identified the microglia as a potent regulator of neuron survival in the first phases of cerebral stroke.



Confocal microscopic image of a hippocampal neuron isolated in culture showing the neuronal pentraxin 1 (green) and the KCNQ2 potassium channel (red) in the growth cone. Joana Figueiró-Silva, Petar Podlesniy and Ramón Trullas.

PUBLICATIONS

ORIGINALS
I.F.: 11.11

1 Virgili N, Espinosa-Parrilla JF, Mancera P, Pasten-Zamorano A, Gimeno-Bayon J, Rodriguez MJ, Mahy N, Pugliese M. Oral administration of the K-ATP channel opener diazoxide ameliorates disease progression in a murine model of multiple sclerosis. J NEUROINFLAMM. 8:-. I.F.: 5.79.

2 Minano-Molina AJ, Espana J, Martin E, Barneda-Zahonero B, Fado R, Sole M, Trullas R, Saura CA, Rodriguez-Alvarez J. Soluble Oligomers of Amyloid-beta Peptide Disrupt Membrane Trafficking of alpha-Amino-3-hydroxy-5-methylisoxazole-4-propionic Acid Receptor Contributing to Early Synapse Dysfunction. J BIOL CHEM. 286:27311-27321. I.F.: 5.33.

GRANTS FOR RESEARCH IN PROGRESS

Mahy N. Grup de Neuroquímica FM. Sponsored by: AGAUR (Generalitat de Catalunya), 2009SGR1380. Duration: 01/01/2009-31/12/2012.

Mahy N, 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 Ciencia e Innovación - ADVANCELL -Advanced in vitro cell techno. IPT-010000-2010-0035. Duration: 25/06/2010-31/12/2012.

Trullas R. Potenciación de la neurogénesis mediante la modulación de la actividad microglial. Sponsored by: Ministerio de Ciencia e Innovación, SAF2008-01902. Duration: 01/01/2009-31/12/2011.

Mahy N. STOP-ELA: aproximación multi-tecnológica para el desarrollo de nuevas terapias y sistemas avanzados de administración farmacológica para la esclerosis lateral amiotrófica. Sponsored by: Ministerio de Ciencia e Innovación, IPT-2011-1091-900000. Duration: 25/06/2011-31/12/2013.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	6.61	2	1	1
2010	16.78	4	2	2
2011	11.11	2	1	0

HUMAN MELA
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AND FUNCTIONAL PHY
ONCOMORPHOLOGY
DIAGNOSIS BIOLOGI
AND IN THERAPY
ONCOLOGY IN MARKERS
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GENETICS HEMATOPOIETIC
PROGENITOR
TRANSPLANTATION
HEMATOLOGICAL
ONCOLOGY

AREA 5

ONCOLOGY AND HAEMATOLOGY

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AREA 5

Oncology and haematology

Biological markers in oncology

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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.

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. **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.

6. **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.

7. **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.

8. **Investigation of cytokine involvement in cancer development and progression.** We are consolidating research into the clinical usefulness of cytokines in cancer patients. This line is preferentially developed in hematological and urological neoplasms.

9. **Markers used in pharmacogenetics.** Study of the genetic polymorphisms implicated in metabolism and pharmacological targets. This line is particularly focused on predicting the safety and efficacy of antineoplastic drugs. During the last year we have developed high performance genotyping techniques, such as minisequencing-SBE.

PUBLICATIONS

ORIGINALS
I.F.: 26.71

1 DeLarrea CF, Tovar N, Cibeira MT, Arostegui JI, Rosinol L, Elena M, Filella X, Yague J, Blade J. Emergence of oligoclonal bands in patients with multiple myeloma in complete remission after induction chemotherapy: association with the use of novel agents. HAEMATOL-HEMATOL J. 96:171-173. I.F.: 6.53.

2 Martinez R, Menendez R, Reyes S, Polverino E, Cilloniz C, Martinez A, Esquinas C, Filella X, Ramirez P, Torres A. Factors associated with inflammatory cytokine patterns in community-acquired pneumonia. EUR RESPIR J. 37:393-399. I.F.: 5.92.

3 Escudero JM, Auge JM, Filella X, Torne A, Pahisa J, Molina R. Comparison of Serum Human Epididymis Protein 4 with Cancer Antigen 125 as a Tumor Marker in Patients with Malignant and Nonmalignant Diseases. CLIN CHEM. 57:1534-1544. I.F.: 6.89.

4 Molina R, Escudero JM, Auge JM, Filella X, Foj L, Torne A, Lejarcegui J, Pahisa J. HE4 a novel tumour marker for ovarian cancer: comparison with CA 125 and ROMA algorithm in patients with gynaecological diseases. TUMOR BIOL. 32:1087-1095. I.F.: 2.03.

5 Cobo T, Palacio M, Martinez-Terron M, Navarro-Sastre A, Bosch J, Filella X, Gratacos E. Clinical and inflammatory markers in amniotic fluid as predictors of adverse outcomes in preterm premature rupture of membranes. AM J OBSTET GYNECOL. 205:-. I.F.: 3.31.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	38.51	8	6	1
2010	20.19	4	2	1
2011	26.71	6	4	2

6 Molina R, Alvarez E, Aniel-Quiroga A, Borque M, Candas B, Leon A, Poyatos RM, Gelabert M. Evaluation of chromogranin A determined by three different procedures in patients with benign diseases, neuroendocrine tumors and other malignancies. TUMOR BIOL. 32:13-22. I.F.: 2.03.

REVIEWS
I.F.: 4.10

1 Filella X, Alcover J, Molina R. Active surveillance in prostate cancer: the need to standardize. TUMOR BIOL. 32:839-843. I.F.: 2.03.

2 Trape J, Filella X, Alsina-Donadeu M, Juan-Pereira L, Bosch-Ferrer A, Rigo-Bonnin R. Increased plasma concentrations of tumour markers in the absence of neoplasia. CLIN CHEM LAB MED. 49:1605-1620. I.F.: 2.07.

GRANTS FOR RESEARCH IN PROGRESS

Molina R. STREP - Multiparametric Quantum Dot Bioassay for Point of Care Diagnosis. Sponsored by: European Commission, LSHB-CT-2007-037933. Duration: 01/01/2007-30/06/2011.

AREA 5

Oncology and haematology

Human and experimental functional oncomorphology

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RTICC

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

Lymphoid neoplasms

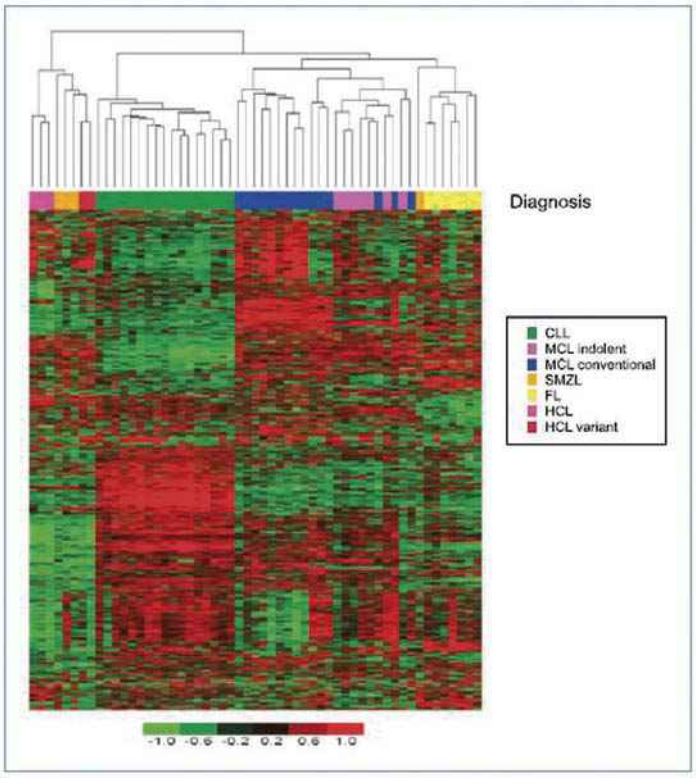
a) Study of the alterations of the molecular mechanisms related to the cell cycle, genomic instability and the transcriptional expression profiles involved in the development and progression of these tumors as biomarkers of clinicopathological relevance.

b) Functional study of molecular factors that may contribute to tumor pathogenesis, and which therefore may be candidates for the development of novel guided treatment strategies.

Solid neoplasms

a) Study of 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 (adhesion molecules) 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.

b) Study of the possible criteria of treatment response and prognosis in neurological tumors.



Microarray platforms allow the massive-scale analysis of genic expression profiles. In our group we use this technique in translation research of human lymphomas, as can be seen in the image, where cluster analysis allows us to detect new types of lymphomas at molecular level that also exhibit different clinical behaviors.

RESEARCH GROUP
MOLECULAR PATHOLOGY OF SOLID TUMORS

Group Leader: Pedro Luis Fernández (Hospital Clínic)

Our group has continued with the analysis of different types of solid tumours, in particular, urological, breast, nervous system and head and neck tumours.

An important part of the research into prostate cancer is the study of practical applications of its genetic signature through analysis of material left over from biopsies which has been shown to be clinically viable (ref. 2). We are in contact with various possible partners in the biomedical industry in order to develop a commercial kit. Our collaboration with Dr Thomson's group at the IBM-CSIC in Barcelona has made it possible to analyse prostate cancer cell models with different degrees of aggressiveness, demonstrating the importance of the mesenchymal and metastatic phenotypes, in development phase in mouse models.

In breast cancer, analysis of the microRNA profiles of primary infiltrating ductal carcinomas and their lymph node metastases has enabled us to define signatures of progression.

In nervous system cancers, studies continue in the area of confirmation and validation of the candidate genes EPHB1, BNIP3 and STAT1 obtained by analysis of glioblastoma expression in patients with unusually long survival times. These genes are involved in signalling pathways and intercellular interaction, development and function of the nervous system, cell movement and cancer.

The research into head and neck tumours includes analysis of the genetic abnormalities in premalignant lesions in the mouth, with a particular focus on those that might be predictive of the development of carcinoma, and the molecular changes that occur in carcinoma of the larynx.

RESEARCH GROUP
TRANSCRIPTIONAL REGULATION OF GENIC EXPRESSION

Group Leader: Antonio Postigo (IDIBAPS)

Regulation of Gene Expression During Cell Differentiation and in Cancer Research Group. The laboratory is investigating the molecular mechanisms involved in the regulation of gene expression during cell differentiation and in cancer. Out research is focusing on ZEB1/deltaEF1 and ZEB2/SIP1, which are key modulating factors in cell differentiation, maintenance of "stemness" in normal and cancerous stem cells, oncogenic transformation and tumour invasion and metastasis.

The group uses in vitro and in vivo models in two main lines of research:

Study of the mechanisms by which ZEB1 and ZEB2 regulate tumorigenesis and epithelial-mesenchymal transition (EMT) during the progression of the cancer.

The role of ZEB1 and ZEB2 in the regulation of normal haematopoietic differentiation and its malignant transformation.

The sources of funding for group's research include subsidies from the Spanish Ministry of Economy and Competitiveness (formerly Science and Innovation), the European Union, the *Associación Española Contra el Cáncer* (AECC) [Spanish Cancer Association], Fundació La Caixa, Fundació Olga Torres and Avon Cosmetics SAU.

PUBLICATIONS

ORIGINALS
I.F.: 322.81

1 Canete JD, Albaladejo C, Hernandez MV, Lainez B, Pinto JA, Ramirez J, Lopez-Armada MJ, Rodriguez-Cros JR, Engel P, Blanco FJ, Sanmarti R. Clinical significance of high levels of soluble tumour necrosis factor-alpha receptor-2 produced by alternative splicing in rheumatoid arthritis: a longitudinal prospective cohort study. RHEUMATOLOGY. 50:721-728. I.F.: 4.17.

2 Silvarino R, Sant F, Espinosa G, Pons-Estel G, Sole M, Cervera R, Arrizabalaga P. Nephropathy associated with antiphospholipid antibodies in patients with systemic lupus erythematosus. LUPUS. 20:721-729. I.F.: 2.60.

3 Gil C, Garcia MT, Garcia F, Miro JM, Aguero F, Alos L, Zamora L, Capon A, Costa J, Pumarola T, Gatell JM. Evaluation of the Roche COBAS (R) TaqMan (R) HIV-1 test for quantifying HIV-1 RNA in infected cells and lymphoid tissue. J VIROL METHODS. 174:69-76. I.F.: 2.14.

4 Bori G, Munoz-Mahamud E, Garcia S, Mallofre C, Gallart X, Bosch J, Garcia E, Riba J, Mensa J, Soriano A. Interface membrane is the best sample for histological study to diagnose prosthetic joint infection. MODERN PATHOL. 24:579-584. I.F.: 4.18.

5 Diaz A, Garcia F, Mozos A, Caballero M, Leon A, Martinez A, Gil C, Plana M, Gallart T, Gatell JM, Alos L. Lymphoid Tissue Collagen Deposition in HIV-Infected Patients Correlates With the Imbalance Between Matrix Metalloproteinases and Their Inhibitors. J INFECT DIS. 203:810-813. I.F.: 6.29.

6 Puente XS, Pinyol M, Quesada V, Conde L, Ordonez GR, Villamor N, Escaramis G, Jares P, Bea S, Gonzalez-Diaz M, Bassaganyas L, Baumann T, Juan M, Lopez-Guerra M, Colomer D, Tubio JMC, Lopez C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernandez JM, Puente DA, Freije JMP, Velasco G, Gutierrez-Fernandez A, Costa D, Carrio A, Guijarro S, Enjuanes A, Hernandez L, Yague J, Nicolas P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, DeSanjose S, Piris MA, DeAlava E, Miguel JS, Royo R, Gelpi JL, Torrents D, Orozco M, Pisano DG, Valencia A, Guigo R, Bayes M, Heath S, Gut M, Klatt P, Marshall J, Raine K, Stebbings LA, Futreal PA, Stratton MR, Campbell PJ, Gut I, Lopez-Guillermo A, Estivill X, Montserrat E, Lopez-Otin C, Campo E. Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia. NATURE. 475:101-105. I.F.: 36.10.

7 Martina MN, Sole M, Masso E, Perez N, Campistol JM, Quintana LF. Mixed cryoglobulinaemia not related to hepatitis C virus, mesangiocapillary glomerulonephritis and lymphoplasmocytic lymphoma. NEFROLOGIA. 31:743-746. I.F.: 0.74.

8 Cagido VR, Zin WA, Ramirez J, Navajas D, Farre R. Alternating ventilation in a rat model of increased abdominal pressure. RESP PHYSIOL NEUROBI. 175:310-315. I.F.: 2.38.

9 Almendros I, Farre R, Torres M, Bonsignore MR, Dalmases M, Ramirez J, Navajas D, Montserrat JM. Early and mid-term effects of obstructive apneas in myocardial injury and inflammation. SLEEP MED. 12:1037-1040. I.F.: 3.43.

10 Bordon J, Kapoor R, Martinez C, Portela D, Duvvuri P, Klochko A, Ayesu K, Peyrani P, Cilloniz C, Wiemken T, Parra A, Torres A, Rello J, Ramirez J. CD4+cell counts and HIV-RNA levels do not predict outcomes of community-acquired pneumonia in hospitalized HIV-infected patients. INT J INFECT DIS. 15:E822-E827. I.F.: 2.53.

11 Riquelme R, Jimenez P, Videla AJ, Lopez H, Chalmers J, Singanayagam A, Riquelme M, Peyrani P, Wiemken T, Arbo G, Benchetrit G, Rioseco ML, Ayesu K, Klotchko A, Marzoratti L, Raya M, Figueroa S, Saavedra F, Pryluka D, Inzunza C, Torres A, Alvare P, Fernandez P, Barros M, Gomez Y, Contreras C, Rello J, Bordon J, Feldman C, Arnold F, Nakamatsu R, Riquelme J, Blasi F, Aliberti S, Cosentini R, Lopardo G, Gnoni M, Welte T, Saad M, Guardiola J, Ramirez J. Predicting mortality in hospitalized patients with 2009 H1N1 influenza pneumonia. INT J TUBERC LUNG D. 15:542-546. I.F.: 2.56.

12 Campayo M, Navarro A, Vinolas N, Tejero R, Munoz C, Diaz T, Marrades R, Cabanas ML, Gimferrer JM, Gascon P, Ramirez J, Monzo M. A Dual Role for KRT81: A miR-SNP Associated with Recurrence in Non-Small-Cell Lung Cancer and a Novel Marker of Squamous Cell Lung Carcinoma. PLOS ONE. 6:-. I.F.: 4.41.

13 Navarro A, Diaz T, Gallardo E, Vinolas N, Marrades RM, Gel B, Campayo M, Quera A, Bandres E, Garcia-Foncillas J, Ramirez J, Monzo M. Prognostic Implications of miR-16 Expression Levels in Resected Non-Small-Cell Lung Cancer. J SURG ONCOL. 103:411-415. I.F.: 2.43.

14 Campayo M, Vinolas N, Navarro A, Carcereny E, Casas F, Gel B, Diaz T, Gimferrer JM, Marrades RM, Ramirez J, Monzo M. Single Nucleotide Polymorphisms in Tobacco Metabolism and DNA Repair Genes and Prognosis in Resected Non-Small-Cell Lung Cancer. J SURG RES. 167:E5-E12. I.F.: 2.24.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	241.60	45	31	8
2010	317.65	34	20	8
2011	322.81	50	31	9

15 Bermudo R, Abia D, Mozos A, Garcia-Cruz E, Alcaraz A, Ortiz AR, Thomson TM, Fernandez PL. Highly sensitive molecular diagnosis of prostate cancer using surplus material washed off from biopsy needles. BRIT J CANCER. 105:1600-1607. I.F.: 4.83.

16 Gutierrez-Garcia G, Cardesa-Salzmann T, Climent F, Gonzalez-Barca E, Mercadal S, Mate JL, Sancho JM, Arenillas L, Serrano S, Escoda L, Martinez S, Valera A, Martinez A, Jares P, Pinyol M, Garcia-Herrera A, Martinez-Trillos A, Gine E, Villamor N, Campo E, Colomo L, Lopez-Guillermo A. Gene-expression profiling and not immunophenotypic algorithms predicts prognosis in patients with diffuse large B-cell lymphoma treated with immunochemotherapy. BLOOD. 117:4836-4843. I.F.: 10.56.

17 Cardesa-Salzmann TM, Colomo L, Gutierrez G, Chan WC, Weisenburger D, Climent F, Gonzalez-Barca E, Mercadal S, Arenillas L, Serrano S, Tubbs R, Delabie J, Gascoyne RD, Connors JM, Mate JL, Rimsza L, Braziel R, Rosenwald A, Lenz G, Wright G, Jaffe ES, Staudt L, Jares P, Lopez-Guillermo A, Campo E. High microvessel density determines a poor outcome in patients with diffuse large B-cell lymphoma treated with rituximab plus chemotherapy. HAEMATOL-HEMATOL J. 96:996-1001. I.F.: 6.53.

18 Nicolau C, Bunesch L, Peri L, Salvador R, Corral JM, Mallofre C, Sebastia C. Accuracy of contrast-enhanced ultrasound in the detection of bladder cancer. BRIT J RADIOL. 84:1091-1099. I.F.: 2.06.

19 Caldelari ACA, Miquel R, Bombi JA, Gines A, Fernandez-Esparrach G, Ayuso JR, Maurel J, Feu F, Castells A, Fernandez-Cruz L, Navarro S. Malignancy predictive factors in pancreatic intraductal papillary mucinous neoplasm. MED CLIN-BARCELONA. 137:631-636. I.F.: 1.41.

20 Sanchez-Tillo E, DeBarrios O, Siles L, Cuatrecasas M, Castells A, Postigo A. beta-catenin/TCF4 complex induces the epithelial-to-mesenchymal transition (EMT)-activator ZEB1 to regulate tumor invasiveness. P NATL ACAD SCI USA. 108:19204-19209. I.F.: 9.77.

21 Soty M, Visa M, Soriano S, Carmona MD, Nadal A, Novials A. Involvement of ATP-sensitive Potassium (K-ATP) Channels in the Loss of Beta-cell Function Induced by Human Islet Amyloid Polypeptide. J BIOL CHEM. 286:40857-40866. I.F.: 5.33.

22 Verger E, Valduvieco I, Caral L, Pujol T, Ribalta T, Vinolas N, Boget T, Oleaga L, Blanco Y, Graus F. Does gender matter in glioblastoma?. CLIN TRANSL ONCOL. 13:737-741. I.F.: 1.25.

23 Brell M, Castaner S, Pujol-Farre T, Boluda S, Ribalta T, Bruna J, Martinez M, Verger E, Villa S, Vinolas N, Gil M, Graus F, Tortosa-Moreno A. Implication of radiological pattern in the prognosis of oligodendroglial tumors: correlation with genetic profile. REV NEUROLOGIA. 52:465-471. I.F.: 1.22.

24 Martin-Guerrero I, Enjuanes A, Richter J, Ammerpohl O, Colomer D, Ardanaz M, Marco F, Salas A, Campo E, Siebert R, Garcia-Orad A. A Putative «hepitype» in the ATM Gene Associated with Chronic Lymphocytic Leukemia Risk. GENE CHROMOSOME CANC. 50:887-895. I.F.: 3.99.

25 Rimsza LM, Wright G, Schwartz M, Chan WC, Jaffe ES, Gascoyne RD, Campo E, Rosenwald A, Ott G, Cook JR, Tubbs RR, Braziel RM, Delabie J, Miller TP, Staudt LM. Accurate Classification of Diffuse Large B-Cell Lymphoma into Germinal Center and Activated B-Cell Subtypes Using a Nuclease Protection Assay on Formalin-Fixed, Paraffin-Embedded Tissues. CLIN CANCER RES. 17:3727-3732. I.F.: 7.34.

26 Iqbal J, Meyer PN, Smith LM, Johnson NA, Vose JM, Greiner TC, Connors JM, Staudt LM, Rimsza L, Jaffe E, Rosenwald A, Ott G, Delabie J, Campo E, Braziel RM, Cook JR, Tubbs RR, Gascoyne RD, Armitage JO, Weisenburger DD, Chan WC. BCL2 Predicts Survival in Germinal Center B-cell-like Diffuse Large B-cell Lymphoma Treated with CHOP-like Therapy and Rituximab. CLIN CANCER RES. 17:7785-7795. I.F.: 7.34.

27 Gutierrez-Garcia G, Garcia-Herrera A, Cardesa T, Martinez A, Villamor N, Ghita G, Martinez-Trillos A, Colomo L, Setoain X, Rodriguez S, Gine E, Campo E, Lopez-Guillermo A. Comparison of four prognostic scores in peripheral T-cell lymphoma. ANN ONCOL. 22:397-404. I.F.: 6.45.

28 Zidar N, Bostjancic E, Gale N, Kojc N, Poljak M, Glavac D, Cardesa A. Down-regulation of microRNAs of the miR-200 family and miR-205, and an altered expression of classic and desmosomal cadherins in spindle cell carcinoma of the head and neck-hallmark of epithelial-mesenchymal transition. HUM PATHOL. 42:482-488. I.F.: 3.00.

29 Carrera C, Palou J, Malvehy J, Segura S, Aguilera P, Salerni G, Lovatto L, Puig-Butille JA, Alos L, Puig S. Early Stages of Melanoma on the Limbs of High-risk Patients: Clinical, Dermoscopic, Reflectance Confocal Microscopy and Histopathological Characterization for Improved Recognition. ACTA DERM-VENEREOL. 91:137-146. I.F.: 2.78.

30 Vegliante MC, Royo C, Palomero J, Salaverria I, Balint B, Martin-Guerrero I, Agirre X, Lujambio A, Richter J, Xargay-Torrent S, Bea S, Hernandez L, Enjuanes A, Calasanz MJ, Rosenwald A, Ott G, Roman-Gomez J, Prosper F, Esteller M, Jares P, Siebert R, Campo E, Martin-Subero JI, Amador V. Epigenetic Activation of SOX11 in Lymphoid Neoplasms by Histone Modifications. PLOS ONE. 6:-. I.F.: 4.41.

31 Sanz-Pamplona R, Aragues R, Driouch K, Martin B, Oliva B, Gil M, Boluda S, Fernandez PL, Martinez A, Moreno V, Acebes JJ, Lidereau R, Reyal F, VanDeVijver MJ, Sierra A. Expression of Endoplasmic Reticulum Stress Proteins Is a Candidate Marker of Brain Metastasis in both ErbB-2(+) and ErbB-2(-) Primary Breast Tumors. AM J PATHOL. 179:564-579. I.F.: 5.22.

32 Darwich E, Vicente A, Bolling MC, Gonzalez-Ensenat MA, Cusi V, Fortuny C, Bombi JA, Jonkman MF, Mascaro JM. Extensive acantholysis as the major histological feature of a severe case of Dowling Meara-epidermolysis bullosa simplex: a reappraisal of acantholysis in the newborn. EUR J DERMATOL. 21:966-971. I.F.: 2.42.

33 Espinet B, Garcia-Herrera A, Gallardo F, Baro C, Salgado R, Servitje O, Estrach T, Colomo L, Romagosa V, Barranco C, Serrano S, Campo E, Pujol RM, Sole F. FOXP1 molecular cytogenetics and protein expression analyses in primary cutaneous large B cell lymphoma, leg-type. HISTOL HISTOPATHOL. 26:213-221. I.F.: 2.50.

34 Enjuanes A, Fernandez V, Hernandez L, Navarro A, Bea S, Pinyol M, Lopez-Guillermo A, Rosenwald A, Ott G, Campo E, Jares P. Identification of Methylated Genes Associated with Aggressive Clinicopathological Features in Mantle Cell Lymphoma. PLOS ONE. 6:-. I.F.: 4.41.

35 Meyer PN, Fu K, Greiner TC, Smith LM, Delabie J, Gascoyne RD, Ott G, Rosenwald A, Braziel RM, Campo E, Vose JM, Lenz G, Staudt LM, Chan WC, Weisenburger DD. Immunohistochemical Methods for Predicting Cell of Origin and Survival in Patients With Diffuse Large B-Cell Lymphoma Treated With Rituximab. J CLIN ONCOL. 29:200-207. I.F.: 18.97.

36 DeLarrea CF, Martinez-Pozo A, Mercadal S, Garcia A, Gutierrez-Garcia G, Valera A, Ghita G, Colomo L, Gainza E, Villamor N, Nomdedeu B, Estrach T, Montserrat E, Campo E, Lopez-Guillermo A. Initial features and outcome of cutaneous and non-cutaneous primary extranodal follicular lymphoma. BRIT J HAEMATOL. 153:334-340. I.F.: 4.94.

37 Hadzidimitriou A, Agathangelidis A, Darzentas N, Murray F, Delfau-Larue MH, Pedersen LB, Lopez AN, Dagklis A, Rombout P, Beldjord K, Kolstad A, Dreyling MH, Anagnostopoulos A, Tsaftaris A, Mavragani-Tsipidou P, Rosenwald A, Ponzoni M, Groenen P, Ghia P, Sander B, Papadaki T, Campo E, Geisler C, Rosenquist R, Davi F, Pott C, Stamatopoulos K. Is there a role for antigen selection in mantle cell lymphoma? Immunogenetic support from a series of 807 cases. BLOOD. 118:3088-3095. I.F.: 10.56.

38 Leich E, Zamo A, Horn H, Haralambieva E, Puppe B, Gascoyne RD, Chan WC, Braziel RM, Rimsza LM, Weisenburger DD, Delabie J, Jaffe ES, Fitzgibbon J, Staudt LM, Mueller-Hermelink HK, Calaminici M, Campo E, Ott G, Hernandez L, Rosenwald A. MicroRNA profiles of t(14;18)-negative follicular lymphoma support a late germinal center B-cell phenotype. BLOOD. 118:5550-5558. I.F.: 10.56.

39 Visco C, Hoeller S, Malik JT, Xu-Monette ZY, Wiggins ML, Liu JS, Sanger WG, Liu ZF, Chang JL, Ranheim EA, Gradowski JF, Serrano S, Wang HY, Liu QQ, Dave S, Olsen B, Gascoyne RD, Campo E, Swerdlow SH, Chan WC, Tzankov A, Young KH. Molecular Characteristics of Mantle Cell Lymphoma Presenting With Clonal Plasma Cell Component. AM J SURG PATHOL. 35:177-189. I.F.: 4.11.

40 Navarro A, Royo C, Hernandez L, Jares P, Campo E. Molecular Pathogenesis of Mantle Cell Lymphoma: New Perspectives and Challenges With Clinical Implications. SEMIN HEMATOL. 48:155-165. I.F.: 3.04.

41 Garcia-Herrera A, Song JY, Chuang SS, Villamor N, Colomo L, Pittaluga S, Alvaro T, Rozman M, Gonzalez JD, Arrunategui AM, Fernandez E, Gonzalvo E, Estrach T, Colomer D, Raffeld M, Gaulard P, Campo E, Jaffe ES, Martinez A. Nonhepatosplenic gamma delta T-cell Lymphomas Represent a Spectrum of Aggressive Cytotoxic T-cell Lymphomas With a Mainly Extranodal Presentation. AM J SURG PATHOL. 35:1214-1225. I.F.: 4.11.

42 Ngo VN, Young RM, Schmitz R, Jhavar S, Xiao WM, Lim KH, Kohlhammer H, Xu WH, Yang YD, Zhao H, Shaffer AL, Romesser P, Wright G, Powell J, Rosenwald A, Muller-Hermelink HK, Ott G, Gascoyne RD, Connors JM, Rimsza LM, Campo E, Jaffe ES, Delabie J, Smeland EB, Fisher RI, Braziel RM, Tubbs RR, Cook JR, Weisenburger DD, Chan WC, Staudt LM. Oncogenically active MYD88 mutations in human lymphoma. NATURE. 470:115-U133. I.F.: 36.10.

43 Weisenburger DD, Savage KJ, Harris NL, Gascoyne RD, Jaffe ES, Maclennan KA, Rudiger T, Pileri S, Nakamura S, Nathwani B, Campo E, Berger F, Coiffier B, Kim WS, Holte H, Federico M, Au WY, Tobinai K, Armitage JO, Vose JM. Peripheral T-cell lymphoma, not otherwise specified: a report of 340 cases from the International Peripheral T-cell Lymphoma Project. BLOOD. 117:3402-3408. I.F.: 10.56.

44 Diaz A, Valera A, Carrera C, Hakim S, Aguilera P, Garcia A, Palou J, Puig S, Malvehy J, Alos L. Pigmented Spindle Cell Nevus: Clues for Differentiating It From Spindle Cell Malignant Melanoma. A Comprehensive Survey Including Clinicopathologic, Immunohistochemical, and FISH Studies. AM J SURG PATHOL. 35:1733-1742. I.F.: 4.11.

45 Salles G, DeJong D, Xie WL, Rosenwald A, Chhanabhai M, Gaulard P, Klapper W, Calaminici M, Sander B, Thorns C, Campo E, Molina T, Lee A, Pfreundschuh M, Horning S, Lister A, Sehn LH, Raemaekers J, Hagenbeek A, Gascoyne RD, Weller E. Prognostic significance of immunohistochemical biomarkers in diffuse large B-cell lymphoma: a study from the Lunenburg Lymphoma Biomarker Consortium. BLOOD. 117:7070-7078. I.F.: 10.56.

46 Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. BLOOD. 117:5019-5032. I.F.: 10.56.

47 Mozos A, Roue G, Lopez-Guillermo A, Jares P, Campo E, Colomer D, Martinez A. The Expression of the Endoplasmic Reticulum Stress Sensor BiP/GRP78 Predicts Response to Chemotherapy and Determines the Efficacy of Proteasome Inhibitors in Diffuse Large B-Cell Lymphoma. AM J PATHOL. 179:2601-2610. I.F.: 5.22.

48 Roue G, Perez-Galan P, Mozos A, Lopez-Guerra M, Xargay-Torrent S, Rosich L, Saborit-Villarroya I, Normant E, Campo E, Colomer D. The Hsp90 inhibitor IPI-504 overcomes bortezomib resistance in mantle cell lymphoma in vitro and in vivo by down-regulation of the prosurvival ER chaperone BiP/Grp78. BLOOD. 117:1270-1279. I.F.: 10.56.

49 Meyer PN, Fu K, Greiner T, Smith L, Delabie J, Gascoyne R, Ott G, Rosenwald A, Braziel R, Campo E, Vose J, Lenz G, Staudt L, Chan W, Weisenburger DD. The Stromal Cell Marker SPARC Predicts for Survival in Patients With Diffuse Large B-Cell Lymphoma Treated With Rituximab. AM J CLIN PATHOL. 135:54-61. I.F.: 2.51.

50 Xargay-Torrent S, Lopez-Guerra M, Saborit-Villarroya I, Rosich L, Campo E, Roue G, Colomer D. Vorinostat-Induced Apoptosis in Mantle Cell Lymphoma Is Mediated by Acetylation of Proapoptotic BH3-Only Gene Promoters. CLIN CANCER RES. 17:3956-3968. I.F.: 7.34.

REVIEWS
I.F.: 13.82

1 Franchi A, Palomba A, Cardesa A. Current diagnostic strategies for undifferentiated tumours of the nasal cavities and paranasal sinuses. HISTOPATHOLOGY. 59:1034-1045. I.F.: 3.57.

2 Royo C, Salaverria I, Hartmann EM, Rosenwald A, Campo E, Bea S. The complex landscape of genetic alterations in mantle cell lymphoma. SEMIN CANCER BIOL. 21:322-334. I.F.: 7.76.

3 Dreyling M, Kluin-Nelemans HC, Bea S, Hartmann E, Salaverria I, Hutter G, Perez-Galan P, Roue G, Pott C, Le-Gouill S, Cortelazzo S, Rule S, Hess G, Zaja F, Vitolo U, Szymczyk M, Walewski J, Ribrag V, Unterhalt M, Hermine O, Hoster E. Update on the molecular pathogenesis and clinical treatment of mantle cell lymphoma: report of the 10th annual conference of the European Mantle Cell Lymphoma Network. LEUKEMIA LYMPHOMA. 52:2226-2236. I.F.: 2.49.

EDITORIALS
I.F.: 12.27

1 Arigita M, Martinez D, Nadal A, Borrell A. Spina bifida in a 13-week fetus with a normal intracranial translucency. PRENATAL DIAG. 31:1104-1105. I.F.: 2.15.

2 Salerni G, Lovatto L, Carrera C, Palou J, Alos L, Puig-Butille JA, Badenas C, Malvehy J, Puig S. Correlation among Dermoscopy, Confocal Reflectance Microscopy, and Histologic Features of Melanoma and Basal Cell Carcinoma Collision Tumor. DERMATOL SURG. 37:275-279. I.F.: 2.26.

3 Navarro A, Campo E. New perspectives and challenges in the understanding of mantle cell lymphoma. ANN ONCOL. 22:32-35. I.F.: 6.45.

4 Molina M, Sanchez M, Ramirez J. Recurrent respiratory infections, pneumonia and pulmonary interstitial infiltrates in a 81 year old man. MED CLIN-BARCELONA. 137:311-316. I.F.: 1.41.

GRANTS FOR RESEARCH IN PROGRESS

Jares P. Identification of Tumor Supressor Genes, Epigenetic Portrait, and Genotyping of Mantle Cell Lymphomas. Sponsored by: Lymphoma Research Foundation, 07/168. Duration: 01/05/2007-31/12/2012.

Campo E. Red temática de investigación cooperativa de cáncer. Sponsored by: Ministerio Sanidad y Consumo, RD06/0020/0039. Duration: 01/01/2007-31/12/2012.

Martinez A. Estudio de la activación de las vías de supervivencia y apoptosis en respuesta al estrés secretor dependiente del retículo endoplasmítico en linfomas de células grandes como una nueva diana terapéutica. Sponsored by: Ministerio Sanidad y Consumo, PI080095. Duration: 01/01/2008-01/12/2012.

Bea S. Estudio de las Alteraciones Genómicas y los Perfiles de Expresión de Neoplasias Linfoides. Identificación de genes diana implicados en el desarrollo y progresión de estas neoplasias y definición de su impacto clínico. Sponsored by: Instituto de Salud Carlos III, PI080077. Duration: 31/12/2008-30/12/2011.

Campo E. Caracterización Genética y Molecular de Alta Resolución de Neoplasias Linfoides. Implicaciones patogenéticas y clínicas. Sponsored by: Ministerio de Ciencia e Innovación, SAF2008-03630. Duration: 01/01/2009-31/12/2013.

Campo E. Estudio de la Genómica de la Leucemia Linfocítica Crónica. Sponsored by: Instituto de Salud Carlos III, 0000. Duration: 27/03/2009-31/12/2012.

Campo E. Ajuts per donar suport a les activitats dels grups de recerca. Sponsored by: Generalitat de Catalunya, 2009, SGR_992. Duration: 30/06/2009-31/12/2013.

Jares P. Identificación de potenciales genes supresores de tumores en neoplasias linfoides y análisis de su implicación en el desarrollo y progresión de estas neoplasias. Sponsored by: Asociación Española contra el cáncer, AECC_CAT_PI08 08/004. Duration: 22/01/2009-21/01/2011.

Fernandez PL. Análisis de los fenotipos CSC y EMT y su potencial modulación por miRNA en la progresión de los tumores mamarios y próstáticos. Sponsored by: Ministerio de Ciencia e Innovación FIS, PI080274. Duration: 01/01/2009-31/12/2011.

Amador V. Papel de los factores de transcripción High-Mobility Group (HMG) en los Linformas Malignos Agresivos. Sponsored by: Ministerio de Educación, BFU2009_09235. Duration: 01/01/2010-31/12/2012.

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: 01/01/2010-31/12/2012.

Campo E. Procurem t of 40 paired pre- and post-chemotherapy samples of DNA derived from peripheral blood for TCGA analysis. Sponsored by: National Institutes of Health, HHSN261201000076I. Duration: 08/09/2010-07/09/2012.

Campo E. SPECS II - Strategic Partnering to Evaluate Cancer Signatures. Sponsored by: National Institutes of Health, USA, University of Arizona, SPECS II. Duration: 01/08/2011-31/07/2016.

Campo E. Identification of somatic mutations in mantle cell lymphoma using next generation sequencing. Sponsored by: Lymphoma Research Foundation, USA. Duration: 30/09/2011-29/11/2013.

Postigo A. Regulación de la diferenciación hematopoyetica y de su transformación maligna por la familia ZEB de factores de transcripción. Sponsored by: Ministerio de Economía y Competitividad, BFU-2010-15163. Duration: 01/01/2011-31/12/2013.

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. Duration: 01/04/2011-31/03/2013.

Alos L. Identificación de las alteraciones genéticas en la mucosa oral predictivas del desarrollo del carcinoma escamoso. Sponsored by: Fundación de Investigación Médica Mutua Madrileña, FundMM_11 AP94722011. Duration: 03/08/2011-02/08/2014.

Campo E. A BLUEPRINT of Haematopoietic Epigenomes. Sponsored by: European Commission, CE-FP7-HEALTH-1ST-11 282510. Duration: 01/10/2011-31/03/2016.

DOCTORAL THESES

Alos L, Cardesa A. Expresion de mucinas y moléculas relacionadas en los carcinomas mucoepidermoides de glándulas salivales: Implicaciones diagnósticas y pronósticas. PhD student: Blanca Noemi Luján.

Fernandez PL, Thomson T. Alteraciones moleculares en la transición metastásica del carcinoma mamario. PhD student: Júlia Calvo Castillo.

AREA 5

Oncology and haematology

Diagnosis and therapy in oncology

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TEAM INVOLVED IN:

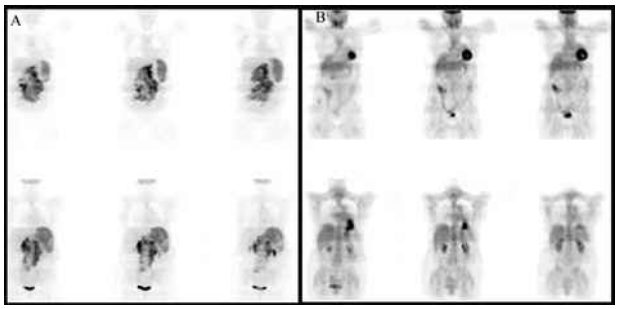
Red RECAVA & Ricc

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. **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.
5. **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.



Coronal Positron Emission Tomography (PET) images of a patient with diffuse large cell lymphoma (DLCL).
A) Initial staging showing pathological uptake of 18F-FDG in the spleen and celiac, mesenteric and retroperitoneal lymph nodes.
B) The PET performed at the end of the chemotherapy shows a normal uptake of 18F-FDG in the abdomen, without pathological uptake, suggesting a complete response to treatment.

PUBLICATIONS

ORIGINALS
I.F.: 81.69

1 Garcia AI, Milinkovic A, Tomas X, Rios J, Perez I, Vidal-Sicart S, Pomes J, DelAmo M, Mallolas J. MRI signal changes of the bone marrow in HIV-infected patients with lipodystrophy: correlation with clinical parameters. SKELETAL RADIOL. 40:1295-1301. I.F.: 1.39.

2 Fuster D, Soriano A, Garcia S, Piera C, Suades J, Rodriguez D, Martinez JC, Mensa J, Campos F, Pons F. Usefulness of Tc-99m-ciprofloxacin scintigraphy in the diagnosis of prosthetic joint infections. NUCL MED COMMUN. 32:44-51. I.F.: 1.37.

3 Bosch X, Esteve J, Sitges M, DeCaralt TM, Domenech A, Ortiz JT, Monzo M, Morales-Ruiz M, Perea RJ, Rovira M. Prevention of Chemotherapy-Induced Left Ventricular Dysfunction With Enalapril and Carvedilol: Rationale and Design of the OVERCOME Trial. J CARD FAIL. 17:643-648. I.F.: 3.36.

4 Campayo M, Navarro A, Vinolas N, Tejero R, Munoz C, Diaz T, Marrades R, Cabanas ML, Gimferrer JM, Gascon P, Ramirez J, Monzo M. A Dual Role for KRT81: A miR-SNP Associated with Recurrence in Non-Small-Cell Lung Cancer and a Novel Marker of Squamous Cell Lung Carcinoma. PLOS ONE. 6:-. I.F.: 4.41.

5 Navarro A, Diaz T, Gallardo E, Vinolas N, Marrades RM, Gel B, Campayo M, Quera A, Bandres E, Garcia-Foncillas J, Ramirez J, Monzo M. Prognostic Implications of miR-16 Expression Levels in Resected Non-Small-Cell Lung Cancer. J SURG ONCOL. 103:411-415. I.F.: 2.43.

6 Campayo M, Vinolas N, Navarro A, Carcereny E, Casas F, Gel B, Diaz T, Gimferrer JM, Marrades RM, Ramirez J, Monzo M. Single Nucleotide Polymorphisms in Tobacco Metabolism and DNA Repair Genes and Prognosis in Resected Non-Small-Cell Lung Cancer. J SURG RES. 167:E5-E12. I.F.: 2.24.

7 Torregrosa JV, Fuster D, Monegal A, Gentil MA, Bravo J, Guirado L, Muxi A, Cubero J. Efficacy of low doses of pamidronate in osteopenic patients administered in the early post-renal transplant. OSTEOPOROSIS INT. 22:281-287. I.F.: 4.86.

8 Fuster D, Ayuso JR, Poveda A, Cubedo R, Casado A, Martinez-Trufero J, Lopez-Pousa A, DelMuro XG, Lomena F, Maurel J, Pons F. Value of FDG-PET for monitoring treatment response in patients with advanced GIST refractory to high-dose imatinib. A multicenter GEIS study. Q J NUCL MED MOL IM. 55:680-687. I.F.: 2.54.

9 Obach V, Oleaga L, Urra X, Macho J, Amaro S, Capurro S, Gomez-Choco M, SanRoman L, Cervera A, Blasco J, Vargas M, Torres F, Chamorro A. Multimodal CT-Assisted Thrombolysis in Patients With Acute Stroke A Cohort Study. STROKE. 42:1129-1131. I.F.: 5.76.

10 Muxi A, Paredes P, Navales I, Valldeoriola F, Gaig C, Lomena F, DeLaCerda A, Sola O, Domenech B, Tolosa E, Pons F. Diagnostic cutoff points for I-123-MIBG myocardial scintigraphy in a Caucasian population with Parkinson's disease. EUR J NUCL MED MOL I. 38:1139-1146. I.F.: 5.04.

11 Valldeoriola F, Gaig C, Muxi A, Navales I, Paredes P, Lomena F, DeLaCerda A, Buongiorno M, Ezquerra M, Santacruz P, Marti MJ, Tolosa E. I-123-MIBG cardiac uptake and smell identification in parkinsonian patients with LRRK2 mutations. J NEUROL. 258:1126-1132. I.F.: 3.85.

12 Fernandez S, Donaire A, Maestro I, Seres E, Setoain X, Bargallo N, Rumia J, Boget T, Falcon C, Carreno M. Functional neuroimaging in startle epilepsy: Involvement of a mesial frontoparietal network. EPILEPSIA. 52:1725-1732. I.F.: 3.96.

13 Carreno M, Becerra JL, Castillo J, Maestro I, Donaire A, Fernandez S, Bargallo N, Setoain X, Pintor L, Bailles E, Rumia J, Boget T, Vernet O, Fumanal S. Seizure frequency and social outcome in drug resistant epilepsy patients who do not undergo epilepsy surgery. SEIZURE-EUR J EPILEP. 20:580-582. I.F.: 1.65.

14 Rubi S, Setoain X, Donaire A, Bargallo N, Sanmarti F, Carreno M, Rumia J, Calvo A, Aparicio J, Campistol J, Pons F. Validation of FDG-PET/MRI coregistration in nonlesional refractory childhood epilepsy. EPILEPSIA. 52:2216-2224. I.F.: 3.96.

15 Verger E, Valduvieco I, Caral L, Pujol T, Ribalta T, Vinolas N, Boget T, Oleaga L, Blanco Y, Graus F. Does gender matter in glioblastoma?. CLIN TRANSL ONCOL. 13:737-741. I.F.: 1.25.

16 Gutierrez-Garcia G, Garcia-Herrera A, Cardesa T, Martinez A, Villamor N, Ghita G, Martinez-Trillos A, Colomo L, Setoain X, Rodriguez S, Gine E, Campo E, Lopez-Guillermo A. Comparison of four prognostic scores in peripheral T-cell lymphoma. ANN ONCOL. 22:397-404. I.F.: 6.45.

17 Artells R, Navarro A, Diaz T, Monzo M. Ultrastructural and Immunohistochemical Analysis of Intestinal Myofibroblasts During the Early Organogenesis of the Human Small Intestine. ANAT REC. 294:462-471. I.F.: 1.40.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	67.93	21	8	4
2010	67.05	22	6	7
2011	81.69	26	9	7

18 Vidal-Sicart S, Brouwer OR, Valdes-Olmos RA. Evaluation of the sentinel lymph node combining SPECT/CT with the planar image and its importance for the surgical act. REV ESP MED NUCL. 30:331-337. I.F.: 0.77.

19 Cibeira MT, DeLarrea CF, Navarro A, Diaz T, Fuster D, Tovar N, Rosinol L, Monzo M, Blade J. Impact on response and survival of DNA repair single nucleotide polymorphisms in relapsed or refractory multiple myeloma patients treated with thalidomide. LEUKEMIA RES. 35:1178-1183. I.F.: 2.56.

20 Diaz T, Navarro A, Ferrer G, Gel B, Gaya A, Artells R, Bellosillo B, Garcia-Garcia M, Serrano S, Martinez A, Monzo M. Lestaurtinib Inhibition of the JAK/STAT Signaling Pathway in Hodgkin Lymphoma Inhibits Proliferation and Induces Apoptosis. PLOS ONE. 6:-. I.F.: 4.41.

21 SamperOts PM, Munoz J, Biete A, Ortiz MJ, Acuna M, Cabrera J, LopezCarrizosa C, Bayo E, Herruzo I, Perez MM, Dominguez MA, MorilloMacias V, Mira M, PerezCasas AM, Sevillano MM, GarciaRios I, Andreu F, Sotoca A, Alvarez A, Lopez E, PerezEscutia MA, LoayzaVillaroel A. PITASOR epidemiological study: prevalence, incidence and treatment of anaemia in radiation therapy oncology departments in Spain. CLIN TRANSL ONCOL. 13:322-327. I.F.: 1.25.

22 Balleyguier C, Sala E, DaCunha T, Bergman A, Brkljacic B, Danza F, Forstner R, Hamm B, Kubik-Huch R, Lopez C, Manfredi R, Mchugo J, Oleaga L, Togashi K, Kinkel K. Staging of uterine cervical cancer with MRI: guidelines of the European Society of Urogenital Radiology. EUR RADIOL. 21:1102-1110. I.F.: 3.59.

23 Gil S, Sarun S, Biete A, Prezado Y, Sabes M. Survival analysis of F98 glioma rat cells following minibeam or broad-beam synchrotron radiation therapy. RADIAT ONCOL. 6:37-37. I.F.: 2.41.

24 Gil S, Fernandez M, Prezado Y, Biete A, Bravin A, Sabes M. Synchrotron radiation in cancer treatments and diagnostics: an overview. CLIN TRANSL ONCOL. 13:715-720. I.F.: 1.25.

25 Vidal-Sicart S, Vermeeren L, Sola O, Paredes P, Valdes-Olmos RA. The use of a portable gamma camera for preoperative lymphatic mapping: a comparison with a conventional gamma camera. EUR J NUCL MED MOL I. 38:636-641. I.F.: 5.04.

26 Rovirosa A, Ascaso C, Sanchez-Reyes A, Herreros A, Abellana R, Pahisa J, Lejarcegui JA, Biete A. Three or four fractions of 4-5 GY per week in postoperative High-Dose-Rate brachytherapy for endometrial carcinoma. INT J RADIAT ONCOL. 81:418-423. I.F.: 4.50.

EDITORIALS
I.F.: 2.18

1 Fuertes J, Mestre-Fusco A, Suarez M, Plancarte F, Munne-Collado J, Vidal-Sicart S. False positive of intramammary sentinel node. REV ESP MED NUCL. 30:112-113. I.F.: 0.77.

2 Setoain X, Lopez-Guillermo A. Non-Hodgkin's lymphoma staging with PET-CT scan. MED CLIN-BARCELONA. 137:402-404. I.F.: 1.41.

GRANTS FOR RESEARCH IN PROGRESS

Pons F. Red temática de investigación cooperativa de cáncer. Sponsored by: Ministerio Sanidad y Consumo, RD06/0020/0038. Duration: 01/01/2007-31/12/2012.

Monzó M. Utilidad clínica de biomarcadores tumorales mediante análisis de microarrays de microRNAs en sangre periférica de pacientes con cáncer colorrectal. Sponsored by: Ministerio de Sanidad y Consumo, PS09/00547. Duration: 01/01/2009-31/12/2012.

Vidal S. Utilidad clínica del SPECT-CT y una gammacamara portátil para la detección del ganglio centinela en el cáncer de cérvix y endometrio. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/1108. Duration: 01/01/2010-31/12/2012.

Pons F. Imatge Molecular en Medicina Nuclear. Sponsored by: Generalitat de Catalunya, 2009_SGR_1049. Duration: 15/09/2009-31/12/2013.

Monzó M. Oncologia i embriologia molecular. Sponsored by: AGAUR_SGR09, 2009_SGR_1339. Duration: 23/09/2009-31/12/2013.

Oleaga L. Gestión del remodelado cardiovascular mediante integración de tecnologías de monitorización ubicua y conceptos del humano fisiológico virtual. Sponsored by: CENIT09 09/397. Duration: 15/9/2009-31/12/2012.

DOCTORAL THESES

Oleaga L. Estudio del sistema musculoesquelético mediamnte resonancia magnética en la valoración del Síndrome de Lipodistrofia en pacientes infectados por el virus de la inmunodeficiencia humana. PhD student: García Díez Ana Isabel.

AREA 5

Oncology and haematology

Molecular genetics

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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 identification of numerous new proteins of the sperm nucleus and the approach regarding potential transmission to the oocyte and potential epigenetic function (Mateo et al., 2011; Oliva and Castillo, 2011). We have also contributed to the identification of alterations in the ratio of protamines in the sperm nucleus, which predict assisted reproduction outcomes and are associated with alterations in sperm DNA integrity in infertile patients (Mateo et al., 2011; Castillo et al., 2011). In another line of research, we completed a study on mutations of the genes of protamines 1 and 2 in infertile patients, identifying several new mutations, polymorphisms and haplotypes (Jodar et al. 2011). One of the important challenges is to elucidate the basic mechanisms that operate in nucleus-histone nucleus-protamine transition during spermatogenesis and how alterations may lead to alterations in the sperm's epigenetic information. 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.: 32.90

1 Fortea J, Llado A, Clarimon J, Lleo A, Oliva R, Peri J, Pintor L, Yague J, Blesa R, Molinuevo JL, Sanchez-Valle R. PICOGEN: Five years experience with a genetic counselling program for dementia. NEUROLOGIA. 26:143-149. I.F.: 0.59.

2 Wen L, Green EA, Stratmann T, Panosa A, Gomis R, Eynon EE, Flavell RA, Mezquita JA, Mora C. In vivo diabetogenic action of CD4(+) T lymphocytes requires Fas expression and is independent of IL-1 and IL-18. EUR J IMMUNOL. 41:1344-1351. I.F.: 4.94.

3 Antonell A, Balasa M, Oliva R, Llado A, Bosch B, Fabregat N, Fortea J, Molinuevo JL, Sanchez-Valle R. A novel PSEN1 gene mutation (L235R) associated with familial early-onset Alzheimer's disease. NEUROSCI LETT. 496:40-42. I.F.: 2.06.

4 Fortea J, Llado A, Bosch B, Antonell A, Oliva R, Molinuevo JL, Sanchez-Valle R. Cerebrospinal Fluid Biomarkers in Alzheimer's Disease Families with PSEN1 Mutations. NEURODEGENER DIS. 8:202-207. I.F.: 3.79.

5 Mora M, Perales MJ, Serra-Prat M, Palomera E, Buquet X, Oriola J, Puig-Domingo M. Aging phenotype and its relationship with IGF-I gene promoter polymorphisms in elderly people living in Catalonia. GROWTH HORM IGF RES. 21:174-180. I.F.: 2.23.

6 DeMateo S, Ramos L, VanDerVlag J, DeBoer P, Oliva R. Improvement in chromatin maturity of human spermatozoa selected through density gradient centrifugation. INT J ANDROL. 34:256-267. I.F.: 3.60.

7 Jodar M, Oriola J, Mestre G, Castillo J, Giwercman A, Vidal-Taboada JM, Ballesca JL, Oliva R. Polymorphisms, haplotypes and mutations in the protamine 1 and 2 genes. INT J ANDROL. 34:470-485. I.F.: 3.60.

8 DeMateo S, Ramos L, DeBoer P, Meistrich M, Oliva R. Protamine 2 Precursors and Processing. PROTEIN PEPTIDE LETT. 18:778-785. I.F.: 1.85.

9 Castillo J, Simon L, DeMateo S, Lewis S, Oliva R. Protamine/DNA Ratios and DNA Damage in Native and Density Gradient Centrifuged Sperm From Infertile Patients. J ANDROL. 32:324-332. I.F.: 3.14.

10 DeMateo S, Castillo J, Estanyol JM, Ballesca JL, Oliva R. Proteomic characterization of the human sperm nucleus. PROTEOMICS. 11:2714-2726. I.F.: 4.82.

11 Simon L, Castillo J, Oliva R, Lewis SEM. Relationships between human sperm protamines, DNA damage and assisted reproduction outcomes. REPROD BIOMED ONLINE. 23:724-734. I.F.: 2.29.

REVIEWS
I.F.: 2.96

1 Oliva R, Badenas C, Claria J, Coll MJ. Molecular genetic reports in clinical practice: Content and nomenclature of mutations. MED CLIN-BARCELONA. 136:356-361. I.F.: 1.41.

2 Oliva R, Castillo J. Proteomics and the genetics of sperm chromatin condensation. ASIAN J ANDROL. 13:24-30. I.F.: 1.55.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	12.97	4	3	0
2010	2.94	1	0	1
2011	32.90	11	5	1

GRANTS FOR RESEARCH IN PROGRESS

Oliva R. Caracterización proteómica y genómica del núcleo del espermatozoide humano normal y de sus alteraciones en pacientes infértiles. Sponsored by: Ministerio de Ciencia e Innovación, BFU2009-07118. Duration: 31/12/2009-30/12/2012.

Oliva R. Grup de Genètica Humana. Sponsored by: Generalitat de Catalunya, AGAUR_SGR09, 2009_SGR_1440. Duration: 29/07/2009-31/12/2013.

AREA 5

Oncology and haematology

Genetics

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Maria Isabel Alvarez (CIBERER)
Francisca Silva

TEAM INVOLVED IN: ciberer

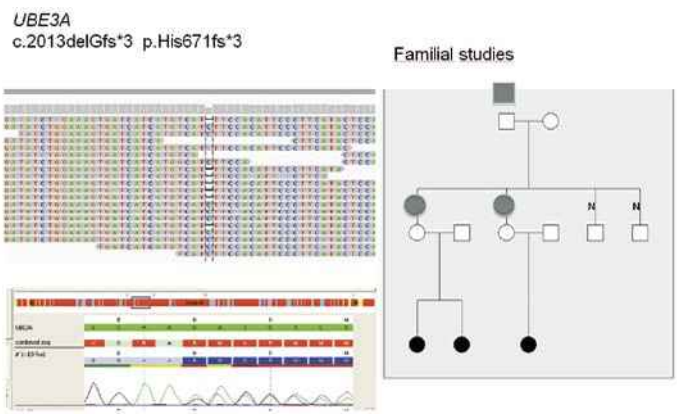
STRATEGIC OBJECTIVES

Characterization of rare hereditary diseases in the clinical, cytogenetic and molecular contexts.
There are four main lines of research. Each line has the strategic objectives defined by the supporting research projects. In this context, the study of mental retardation (MR) and identification of the causal genetic factors are fundamented upon the application of high performance *array* CGH and *Next Sequencing Generation* (NSG) technologies. On the other hand, the study of fragile X–associated tremor/ataxia syndrome (FXTAS) aims to identify a biological marker allowing us to establish a presymptomatic diagnosis of FXTAS in carriers of the premutation in the FMR1 gene, based on study of the miRNA profile. 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 the **genetic bases of intellectual disability (ID) of genetic origin**, both syndromic and non-syndromic, using the new NSG technologies.
   Application of massive sequencing to different groups of clinically well characterized ID will allow us to identify new genes and establish new molecular bases in ID. Application is also planned to the study of familial mental retardation and to sporadic cases of non-syndromic ID.

2. **Fragile X syndrome:** Study of the pathologies associated with premutation of the *FMR1* gene: FXPOI (Premature ovarian insufficienciy), FXTAS (Fragile X Tremor Ataxia Syndrome), and fibromyalgia associated with the *FMR1* gene. Study of the microRNA and ASFMR1 gene expression profiles as possible susceptibility factors for FXTAS.



c.2013delG mutation detected through Next Generation Sequencing in a family suffering an intellectual disability. The mutation was confirmed with Sanger sequencing, proven to be pathogenic with Poliphen2 software and analyzed in a family segregation study.

3. Detection of **cryptic chromosomal imbalances** and the identification of **new phenotypes**, based on cytogenetic - molecular techniques. One is conducted in the prenatal and postnatal diagnostic setting. The aim is to characterize chromosomal imbalances in fetuses with congenital anomalies and a normal karyotype, based on the use of CGH arrays.

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

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	49.78	13	5	5
2010	78.70	22	10	4
2011	128.51	14	7	4

ORIGINALS
I.F.: 128.51

1 Puente XS, Pinyol M, Quesada V, Conde L, Ordonez GR, Villamor N, Escaramis G, Jares P, Bea S, Gonzalez-Diaz M, Bassaganyas L, Baumann T, Juan M, Lopez-Guerra M, Colomer D, Tubio JMC, Lopez C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernandez JM, Puente DA, Freije JMP, Velasco G, Gutierrez-Fernandez A, Costa D, Carrio A, Guijarro S, Enjuanes A, Hernandez L, Yague J, Nicolas P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, DeSanjose S, Piris MA, DeAlava E, Miguel JS, Royo R, Gelpi JL, Torrents D, Orozco M, Pisano DG, Valencia A, Guigo R, Bayes M, Heath S, Gut M, Klatt P, Marshall J, Raine K, Stebbings LA, Futreal PA, Stratton MR, Campbell PJ, Gut I, Lopez-Guillermo A, Estivill X, Montserrat E, Lopez-Otin C, Campo E. Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia. NATURE. 475:101-105. I.F.: 36.10.

2 Arigita M, Borrell A, Mula R, Sanchez A, Mila M, Gratacos E. Use of fetal nuchal translucency in the first trimester to predict single-gene disorders. PRENATAL DIAG. 31:1164-1168. I.F.: 2.15.

3 Alonso-Espinaco V, Giraldez MD, Trujillo C, VanDerKlift H, Munoz J, Balaguer F, Ocana T, Madrigal I, Jones AM, Echeverry MM, Velez A, Tomlinson I, Mila M, Wijnen J, Carvajal-Carmona L, Castells A, Castellvi-Bel S. Novel MLH1 duplication identified in Colombian families with Lynch syndrome. GENET MED. 13:155-160. I.F.: 5.28.

4 To-Figueras J, Ducamp S, Clayton J, Badenas C, Delaby C, Ged C, Lyoumi S, Gouya L, DeVerneuil H, Beaumont C, Ferreira GC, Deybach JC, Herrero C, Puy H. ALAS2 acts as a modifier gene in patients with congenital erythropoietic porphyria. BLOOD. 118:1443-1451. I.F.: 10.56.

5 Aarsand AK, Villanger JH, Stole E, Deybach JC, Marsden J, To-Figueras J, Badminton M, Elder GH, Sandberg S. European Specialist Porphyria Laboratories: Diagnostic Strategies, Analytical Quality, Clinical Interpretation, and Reporting As Assessed by an External Quality Assurance Program. CLIN CHEM. 57:1514-1523. I.F.: 6.89.

6 Barrett JH, Iles MM, Harland M, Taylor JC, Aitken JF, Andresen PA, Akslen LA, Armstrong BK, Avril MF, Azizi E, Bakker B, Bergman W, Bianchi-Scarra G, Bressac-DePaillerets B, Calista D, Cannon-Albright LA, Corda E, Cust AE, Debniak T, Duffy D, Dunning AM, Easton DF, Friedman E, Galan P, Ghiorzo P, Giles GG, Hansson J, Hocevar M, Hoiom V, Hopper JL, Ingvar C, Janssen B, Jenkins MA, Jonsson G, Kefford RF, Landi G, Landi MT, Lang J, Lubinski J, Mackie R, Malvehy J, Martin NG, Molven A, Montgomery GW, VanNieuwpoort FA, Novakovic S, Olsson H, Pastorino L, Puig S, Puig-Butille JA, Randerson-Moor J, Snowden H, Tuominen R, Vanbelle P, VanDerStoep N, Whiteman DC, Zelenika D, Han JL, Fang SY, Lee JE, Wei QY, Lathrop GM, Gillanders EM, Brown KM, Goldstein AM, Kanetsky PA, Mann GJ, Macgregor S, Elder DE, Amos CI, Hayward NK, Gruis NA, Demenais F, Bishop JAN, Bishop DT. Genome-wide association study identifies three new melanoma susceptibility loci. NAT GENET. 43:1108-U98. I.F.: 36.38.

7 To-Figueras J, Phillips JD, Gonzalez-Lopez JM, Badenas C, Madrigal I, Gonzalez-Romaris EM, Ramos C, Aguirre JM, Herrero C. Hepatoerythropoietic porphyria due to a novel mutation in the uroporphyrinogen decarboxylase gene. BRIT J DERMATOL. 165:499-505. I.F.: 4.35.

8 Madrigal I, Xuncla M, Tejada MI, Martinez F, Fernandez-Carvajal I, Perez-Jurado LA, Rodriguez-Revenga L, Mila M. Intermediate FMR1 alleles and cognitive and/or behavioural phenotypes. EUR J HUM GENET. 19:921-923. I.F.: 4.38.

9 Nakabayashi K, Trujillo AM, Tayama C, Camprubi C, Yoshida W, Lapunzina P, Sanchez A, Soejima H, Aburatani H, Nagae G, Ogata T, Hata K, Monk D. Methylation screening of reciprocal genome-wide UPDs identifies novel human-specific imprinted genes. HUM MOL GENET. 20:3188-3197. I.F.: 8.06.

10 Bennassar A, Mas A, Guilabert A, Julia M, Mascaro-Galy JM, Herrero C. Multicentric reticulohistiocytosis with elevated cytokine serum levels. J DERMATOL. 38:905-910. I.F.: 1.36.

11 Segura S, Puig S, Carrera C, Lecha M, Borges V, Malvehy J. Non-invasive management of non-melanoma skin cancer in patients with cancer predisposition genodermatosis: a role for confocal microscopy and photodynamic therapy. J EUR ACAD DERMATOL. 25:819-827. I.F.: 3.31.

12 Mademont-Soler I, Morales C, Clusellas N, Soler A, Sanchez A. Prenatal cytogenetic diagnosis in Spain: analysis and evaluation of the results obtained from amniotic fluid samples during the last decade. EUR J OBSTET GYN R B. 157:156-160. I.F.: 1.76.

13 Munoz-Santos C, Guilabert A, Moreno N, Gimenez M, Darwich E, To-Figueras J, Herrero C. The association between porphyria cutanea tarda and diabetes mellitus: analysis of a long-term follow-up cohort. BRIT J DERMATOL. 165:486-491. I.F.: 4.35.

14 Pereira A, Nomdedeu M, Aguilar JL, Belkaid M, Carrio A, Cobo F, Costa D, Rozman M, Sanz C, Nomdedeu B. Transfusion intensity, not the cumulative red blood cell transfusion burden, determines the prognosis of patients with myelodysplastic syndrome on chronic transfusion support. AM J HEMATOL. 86:245-250. I.F.: 3.58.

REVIEWS
I.F.: 1.41

1 Oliva R, Badenas C, Claria J, Coll MJ. Molecular genetic reports in clinical practice: Content and nomenclature of mutations. MED CLIN-BARCELONA. 136:356-361. I.F.: 1.41.

MULTICENTRICS
I.F.: 12.47

1 Amos CI, Wang LE, Lee JE, Gershenwald JE, Chen WV, Fang SY, Kosoy R, Zhang MF, Qureshi AA, Vattathil S, Schacherer CW, Gardner JM, Wang YL, Bishop DT, Barrett JH, Macgregor S, Hayward NK, Martin NG, Duffy DL, Mann GJ, Cust A, Hopper J, Brown KM, Grimm EA, Xu YJ, Han YH, Jing KY, Mchugh C, Laurie CC, Doheny KF, Pugh EW, Seldin MF, Han JL, Wei QY. Genome-wide association study identifies novel loci predisposing to cutaneous melanoma. HUM MOL GENET. 20:5012-5023. I.F.:8.06.

2 Schoof N, Iles MM, Bishop DT, Newton-Bishop JA, Barrett JH. Pathway-Based Analysis of a Melanoma Genome-Wide Association Study: Analysis of Genes Related to Tumour-Immunosuppression. PLOS ONE. 6:-. I.F.: 4.41.

GRANTS FOR RESEARCH IN PROGRESS

Mila M. Estudio de los perfiles de expresión de microRNAS y del gen ASFMR1 como factores de susceptibilidad para el desarrollo del síndrome FXTAS. Sponsored by: INSTITUTO DE SALUD CARLOS III, PIO9/0413. Duration: 01/01/2010-31/12/2012.

Mila M. European Sequencing and Genotyping Infrastructure (ESGI). Whole Exome Sequencing in Intelectual Disability (WESID). Sponsored by: European Commission, 7th Framework Programme, 262055. Duration: 01/01/2011-31/12/2012.

Mila M. Grupo de excelencia reconocido y financiado. Sponsored by: Generalitat de Catalunya, AGAUR, SGR1337. Duration: 01/01/2009-31/12/2013.

DOCTORAL THESES

Sanchez A. Evolució del diagnòstic citogenètic prenatal i postnatal amb la implementació de noves tècniques de biologia molecular i la seva repercussió en el consell genètic. PhD student: Mª Carme Morales Peydró.

Herrero C. Porfiria cutánea tarda esporádica y familiar: Estudio observacional de las características clínicas, bioquímicas y de los factores de riesgo. PhD student: Carlos Muñoz Santos.

AREA 5

Oncology and haematology

Melanoma: imaging, genetics and immunology

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STRATEGIC OBJECTIVES

1. Development of noninvasive 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: target-specific molecular, 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

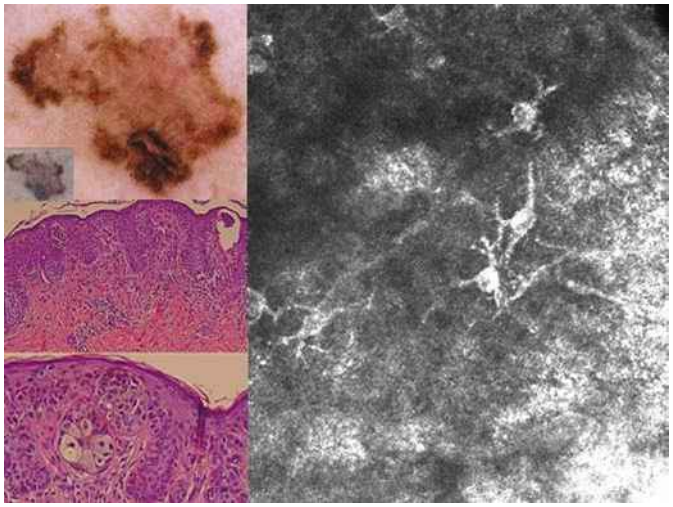
Our main lines of research, and some of the most relevant results obtained to date, are the following:

1. **Dermatoscopy and digital dermatoscopy.** In dermatoscopy studies are being made of the diagnostic criteria of different disorders that have still not been well characterized, the correlations with other imaging techniques, the impact upon the management of patients at risk, and the relationship between dermatoscopy and the genetic profile of the patients. In digital dermatoscopy we are examining the use of full body maps and digital dermatoscopy in the follow-up of patients at risk.
   - **1.1** Definition of new dermatoscopic criteria in different dermatological processes (dermatofibromas, angiokeratomas, botryomycosis, blue nevus, xanthogranuloma,

leishmaniasis, lichenoid keratosis, collision tumors).

1.2 Development of dermatoscopy for introduction in primary care, in pathology and dermatology (development of combined clinical dermatoscopic algorithms for the identification of melanomas that are difficult to diagnose).

1.3 Combined dermatoscopic and ultrasound protocol of the primary tumor for preoperative Breslow score estimation.



2. **Confocal microscopy *in vivo*.** Description of new algorithms, study of the evolution of lesions, new classifications and the use of telemedicine.
   - **2.1** Definition of criteria in nodular melanoma.
   - **2.2** Creation of a differential diagnostic algorithm for melanocytic and non-melanocytic lesions.
   - **2.3** Characterization of pigmented basal cell carcinomas, squamous carcinomas and actinic keratosis.
   - **2.4** Study of the use of confocal microscopy for the correct treatment of achromatic or poorly delimited lesions (delimitation of surgical margins or control of relapses).
   - **2.5** Use of *ex vivo* confocal microscopy for application to Mohs surgery.

3. **Genetic epidemiology.** Study of melanoma susceptibility genes in familial melanoma and in sporadic melanoma. Study of nevogenicity and risk genes in melanoma. Study of pigmentation and risk genes in melanoma. Identification of new genes and new mechanisms of melanoma susceptibility using Genome Wide Scan.
   - **3.1** Penetrance and phenotypic expression studies in patients and families carrying known CDKN2A and p14arf mutations.
   - **3.2** Study of the effect of polymorphisms of the MC1R gene as modifier gene and low penetrance gene in relation to melanoma risk, and in reference to the clinical and dermatoscopic aspects of melanomas.
   - **3.3** Identification of new melanoma and nevogenicity susceptibility genes based on the study of homozygous genome regions.
   - **3.4** Susceptibility genes involved in melanoma prognosis

4. **Study of the mechanisms involved in carcinogenesis and photocarcinogenesis.**
   - **4.1** Analysis of oral photoprotection. Study of genetic (CDKN2A, MC1R)/environmental interaction (UVR) in melanoma risk. Study of the influence of ultraviolet radiation (UVR) (UVA; UVB; UVA/UVB) in the dermatoscopic, histological and immunohistochemical characteristics of melanocytic nevi.
   - **4.2** Dermatoscopic and genetic characterization of the different Clark nevi in dysplastic nevus syndrome, in relation to genetic polymorphisms.
   - **4.3** Investigation of somatic mutations of NRAS, BRAF, cKIT, genomic amplifications of different oncogenes, and genomic losses of 9p21 (MLPA) in melanoma
   - **4.4** Expression studies (MAGE and others) in melanoma.
   - **4.5** Development of experimental models of gene/gene, gene/environment interactions between CDKN2A and MC1R. Expression studies in keratinocytes, melanocytes and fibroblasts according to their genetic profile.
   - **4.6** DNA repair mechanisms and their therapeutic implications.

5. **Development of new treatment strategies for melanoma and other skin tumors.**
   - **5.1** Hyperthermal perfusion of extremities
   - **5.2** Vaccines and new therapeutic targets in melanoma.
   - **5.3** Electrochemotherapy in melanoma.
   - **5.4** Inhibition of the Hedgehog pathway for the treatment of basal cell carcinomas.
   - **5.5** Specific immunotherapy in Merkel carcinoma.

6. **Evaluation of immune response in melanoma.**
   - **6.1** Genetic expression arrays and studies of SNPs associated with prognosis and treatment response.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	57.94	11	6	2
2010	62.31	15	9	2
2011	133.79	9	7	2

ORIGINALS
I.F.: 133.79

1 Carrera C, Palou J, Malvehy J, Segura S, Aguilera P, Salerni G, Lovatto L, Puig-Butille JA, Alos L, Puig S. Early Stages of Melanoma on the Limbs of High-risk Patients: Clinical, Dermoscopic, Reflectance Confocal Microscopy and Histopathological Characterization for Improved Recognition. ACTA DERM-VENEREOL. 91:137-146. I.F.: 2.78.

2 Diaz A, Valera A, Carrera C, Hakim S, Aguilera P, Garcia A, Palou J, Puig S, Malvehy J, Alos L. Pigmented Spindle Cell Nevus: Clues for Differentiating It From Spindle Cell Malignant Melanoma. A Comprehensive Survey Including Clinicopathologic, Immunohistochemical, and FISH Studies. AM J SURG PATHOL. 35:1733-1742. I.F.: 4.11.

3 Barrett JH, Iles MM, Harland M, Taylor JC, Aitken JF, Andresen PA, Akslen LA, Armstrong BK, Avril MF, Azizi E, Bakker B, Bergman W, Bianchi-Scarra G, Bressac-DePaillerets B, Calista D, Cannon-Albright LA, Corda E, Cust AE, Debniak T, Duffy D, Dunning AM, Easton DF, Friedman E, Galan P, Ghiorzo P, Giles GG, Hansson J, Hocevar M, Hoiom V, Hopper JL, Ingvar C, Janssen B, Jenkins MA, Jonsson G, Kefford RF, Landi G, Landi MT, Lang J, Lubinski J, Mackie R, Malvehy J, Martin NG, Molven A, Montgomery GW, VanNieuwpoort FA, Novakovic S, Olsson H, Pastorino L, Puig S, Puig-Butille JA, Randerson-Moor J, Snowden H, Tuominen R, Vanbelle P, VanDerStoep N, Whiteman DC, Zelenika D, Han JL, Fang SY, Lee JE, Wei QY, Lathrop GM, Gillanders EM, Brown KM, Goldstein AM, Kanetsky PA, Mann GJ, Macgregor S, Elder DE, Amos CI, Hayward NK, Gruis NA, Demenais F, Bishop JAN, Bishop DT. Genome-wide association study identifies three new melanoma susceptibility loci. NAT GENET. 43:1108-U98. I.F.: 36.38.

4 Segura S, Puig S, Carrera C, Lecha M, Borges V, Malvehy J. Non-invasive management of non-melanoma skin cancer in patients with cancer predisposition genodermatosis: a role for confocal microscopy and photodynamic therapy. J EUR ACAD DERMATOL. 25:819-827. I.F.: 3.31.

5 Lang JM, Shennan M, Njauw JCN, Luo S, Bishop JN, Harland M, Hayward NK, Tucker MA, Goldstein AM, Landi MT, Puig S, Gruis NA, Bergman W, Bianchi-Scarra G, Ghiorzo P, Hogg D, Tsao H. A Flexible Multiplex Bead-Based Assay for Detecting Germline CDKN2A and CDK4 Variants in Melanoma-Prone Kindreds. J INVEST DERMATOL. 131:480-486. I.F.: 6.27.

6 Bertolotto C, Lesueur F, Giuliano S, Strub T, DeLichy M, Bille K, Dessen P, D'hayer B, Mohamdi H, Remenieras A, Maubec E, DeLaFouchardiere A, Molinie V, Vabres P, Dalle S, Poulalhon N, Martin-Denavit T, Thomas L, Andry-Benzaquen P, Dupin N, Boitier F, Rossi A, Perrot JL, Labeille B, Robert C, Escudier B, Caron O, Brugieres L, Saule S, Gardie B, Gad S, Richard S, Couturier J, Teh BT, Ghiorzo P, Pastorino L, Puig S, Badenas C, Olsson H, Ingvar C, Rouleau E, Lidereau R, Bahadoran P, Vielh P, Corda E, Blanche H, Zelenika D, Galan P, Chaudru V, Lenoir GM, Lathrop M, Davidson I, Avril MF, Demenais F, Ballotti R, Bressac-DePaillerets B. A SUMOylation-defective MITF germline mutation predisposes to melanoma and renal carcinoma. NATURE. 480:94-U259. I.F.: 36.10.

7 Goulart JM, Malvehy J, Puig S, Martin G, Marghoob AA. Dermoscopy in Skin Self-examination A Useful Tool for Select Patients. ARCH DERMATOL. 147:53-58. I.F.: 4.23.

8 Macgregor S, Montgomery GW, Liu JZ, Zhao ZZ, Henders AK, Stark M, Schmid H, Holland EA, Duffy DL, Zhang M, Painter JN, Nyholt DR, Maskiell JA, Jetann J, Ferguson M, Cust AE, Jenkins MA, Whiteman DC, Olsson H, Puig S, Bianchi-Scarra G, Hansson J, Demenais F, Landi MT, Debniak T, Mackie R, Azizi E, Bressac-DePaillerets B, Goldstein AM, Kanetsky PA, Gruis NA, Elder DE, Newton-Bishop JA, Bishop DT, Iles MM, Helsing P, Amos CI, Wei QY, Wang LE, Lee JE, Qureshi AA, Kefford RF, Giles GG, Armstrong BK, Aitken JF, Han JL, Hopper JL, Trent JM, Brown KM, Martin NG, Mann GJ, Hayward NK. Genome-wide association study identifies a new melanoma susceptibility locus at 1q21.3. NAT GENET. 43:1114-U104. I.F.: 36.38.

9 Salerni G, Lovatto L, Carrera C, Puig S, Malvehy J. Melanomas Detected in a Follow-up Program Compared With Melanomas Referred to a Melanoma Unit. ARCH DERMATOL. 147:-. I.F.: 4.23.

EDITORIALS
I.F.: 2.26

1 Salerni G, Lovatto L, Carrera C, Palou J, Alos L, Puig-Butille JA, Badenas C, Malvehy J, Puig S. Correlation among Dermoscopy, Confocal Reflectance Microscopy, and Histologic Features of Melanoma and Basal Cell Carcinoma Collision Tumor. DERMATOL SURG. 37:275-279. I.F.: 2.26.

MULTICENTRICS
I.F.: 12.47

1 Amos CI, Wang LE, Lee JE, Gershenwald JE, Chen WV, Fang SY, Kosoy R, Zhang MF, Qureshi AA, Vattathil S, Schacherer CW, Gardner JM, Wang YL, Bishop DT, Barrett JH, Macgregor S, Hayward NK, Martin NG, Duffy DL, Mann GJ, Cust A, Hopper J, Brown KM, Grimm EA, Xu YJ, Han YH, Jing KY, Mchugh C, Laurie CC, Doheny KF, Pugh EW, Seldin MF, Han JL, Wei QY. Genome-wide association study identifies novel loci predisposing to cutaneous melanoma. HUM MOL GENET. 20:5012-5023. I.F.: 8.06.

2 Schoof N, Iles MM, Bishop DT, Newton-Bishop JA, Barrett JH. Pathway-Based Analysis of a Melanoma Genome-Wide Association Study: Analysis of Genes Related to Tumour-Immunosuppression. PLOS ONE. 6:-. I.F.: 4.41.

GRANTS FOR RESEARCH IN PROGRESS

Puig S. NoE - Genetic and environmental risk factors for melanoma: translation into behavioural change. Sponsored by: European Commission, LSHM-CT-2006-018702. Duration: 01/12/2005-31/05/2011.

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: 01/01/2010-31/12/2012.

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, TRA-082. Duration: 01/01/2010-30/12/2011.

DOCTORAL THESES

Puig S. Microscopía confocal de reflectancia in vivo en dermatología: Aplicación en el diagnóstico de tumores cutáneos. PhD student: Reyes Gamo.

Puig S. Características dermatoscópicas de las lesiones melanocíticas en el síndrome del nevus con atipia en diferentes áreas antómcas y de los melanomas en tronco y extremidades inferiores. PhD student: Sonia Segura.

Puig S, Malvehy J. Descripción y evaluación de los parámetros y patrones dermatoscópicos de las lesiones cutáneas no melanocíticas y su diagnóstico diferencial con el melanoma. PhD student: Pedro Zaballos Diego.

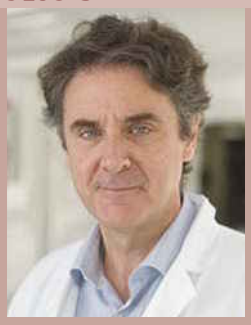
Puig S. Microscopía confocal de reflectancia in vivo en dermatología: Aplicación en el diagnóstico de tumores cutáneos. PhD student: Sonia Segura Tigell.

AREA 5

Oncology and haematology

Hematopoietic progenitor cell transplantation

GROUP MEMBERS



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TEAM INVOLVED IN:

STRATEGIC OBJECTIVES

In the last few years our group has developed basic and translational research lines, thanks to 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 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 genic polymorphisms have also been started. Lastly, we plan to develop an important 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

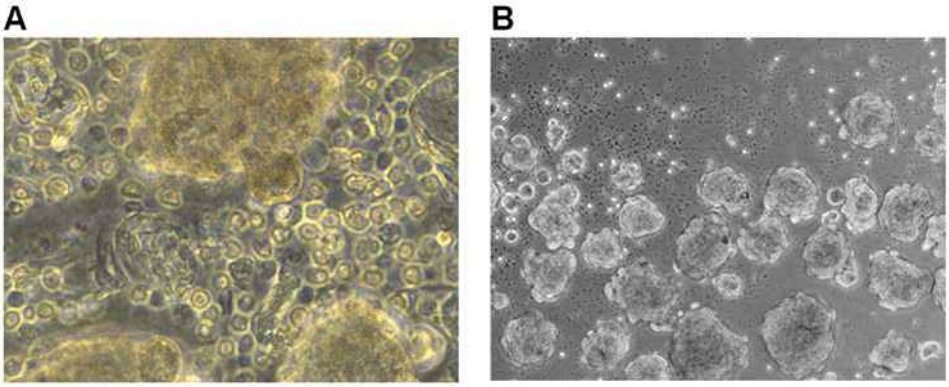
CLINICAL RESEARCH LINES

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 (the only such program in Europe, awarded on several occasions by the scientific and healthcare societies) – a modality which we aim to extend to domiciliary allogenic HPT.
   - Umbilical cord blood cell transplantation administered via the intraosseous route – an innovating modality which we and another European center are analyzing.

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.



A. Sphere obtained after one week of bone marrow isolated nestin-positive mesenchymal cell culture.

B. Sphere expansion after four weeks of culture.

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 then to seek effective preventive and treatment options. This research line is supported by two FIS grants and an aid from the German José 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.: 82.13

1 Cervera C, Fernandez-Aviles F, DeLaCalle-Martin O, Bosch X, Rovira M, Plana M, Moreno A, Garcia F, Miro JM, Martinez A, Gallart T, Carreras E, Blade J, Gatell JM. Non-myeloablative hematopoietic stem cell transplantation in the treatment of severe idiopathic CD4+lymphocytopenia. EUR J HAEMATOL. 87:87-91. I.F.: 2.79.

2 DeLarrea CF, Tovar N, Rozman M, Rosinol L, Arostegui JI, Cibeira MT, Rovira M, Yague J, Blade J. Multiple Myeloma in Serologic Complete Remission after Autologous Stem Cell Transplantation: Impact of Bone Marrow Plasma Cell Assessment by Conventional Morphology on Disease Progression. BIOL BLOOD MARROW TR. 17:1084-1087. I.F.: 3.28.

3 Bosch X, Esteve J, Sitges M, DeCaralt TM, Domenech A, Ortiz JT, Monzo M, Morales-Ruiz M, Perea RJ, Rovira M. Prevention of Chemotherapy-Induced Left Ventricular Dysfunction With Enalapril and Carvedilol: Rationale and Design of the OVERCOME Trial. J CARD FAIL. 17:643-648. I.F.: 3.36.

4 Arora M, Klein JP, Weisdorf DJ, Hassebroek A, Flowers MED, Cutler CS, Urbano-Ispizua A, Antin JH, Bolwell BJ, Boyiadzis M, Cahn JY, Cairo MS, Isola L, Jacobsohn DA, Jagasia M, Klumpp TR, Lee SJ, Petersdorf EW, Santarone S, Gale RP, Schouten HC, Spellman S, Wingard JR, Horowitz MM, Pavletic SZ. Chronic GVHD risk score: a Center for International Blood and Marrow Transplant Research analysis. BLOOD. 117:6714-6720. I.F.: 10.56.

5 Palomo M, Diaz-Ricart M, Rovira M, Escolar G, Carreras E. Defibrotide Prevents the Activation of Macrovascular and Microvascular Endothelia Caused by Soluble Factors Released to Blood by Autologous Hematopoietic Stem Cell Transplantation. BIOL BLOOD MARROW TR. 17:497-506. I.F.: 3.28.

6 Martin-Antonio B, Carmona M, Falantes J, Gil E, Baez A, Suarez M, Marin P, Espigado I, Urbano-Ispizua A. Impact of constitutional polymorphisms in VCAM1 and CD44 on CD34(+) cell collection yield after administration of granulocyte colony-stimulating factor to healthy donors. HAEMATOL-HEMATOL J. 96:102-109. I.F.: 6.53.

7 Perez-Simon JA, Lopez-Villar O, Andreu EJ, Rifon J, Muntion S, Campelo MD, Sanchez-Guijo FM, Martinez C, Valcarcel D, DelCanizo C. Mesenchymal stem cells expanded in vitro with human serum for the treatment of acute and chronic graft-versus-host disease: results of a phase I/II clinical trial. HAEMATOL-HEMATOL J. 96:1072-1076. I.F.: 6.53.

8 Duarte RF, Shaw BE, Marin P, Kottaridis P, Ortiz M, Morante C, Delgado J, Gayoso J, Goterriz R, Martinez-Chamorro C, Mateos-Mazon JJ, Ramirez C, DeLaRubia J, Achtereekte H, Gandhi PJ, Douglas KW, Russell NH. Plerixafor plus granulocyte CSF can mobilize hematopoietic stem cells from multiple myeloma and lymphoma patients failing previous mobilization attempts: EU compassionate use data. BONE MARROW TRANSPL. 46:52-58. I.F.: 3.66.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	55.38	8	7	0
2010	43.66	12	6	3
2011	82.13	15	11	4

9 Aguilar-Guisado M, Jimenez-Jambrina M, Espigado I, Rovira M, Martino R, Oriol A, Borrell N, Ruiz I, Martin-Davila P, DeLaCamara R, Salavert M, DeLaTorre J, Cisneros JM. Pneumonia in allogeneic stem cell transplantation recipients: a multicenter prospective study. CLIN TRANSPLANT. 25:E629-E638. I.F.: 1.75.

10 Barba P, Pinana JL, Fernandez-Aviles F, Perez-Simon JA, Martino R, Lopez-Guerrero E, Valcarcel D, Rovira M, Novelli S, Campos-Varela I, Lopez-Anglada L, Vidal X, Corral LL, Carreras E, Sierra J. Pretransplantation Liver Function Impacts on the Outcome of Allogeneic Hematopoietic Stem Cell Transplantation: A Study of 455 Patients. BIOL BLOOD MARROW TR. 17:1653-1661. I.F.: 3.28.

11 Jacobsohn DA, Arora M, Klein JP, Hassebroek A, Flowers ME, Cutler CS, Urbano-Ispizua A, Bolwell BJ, Antin JH, Boyiadzis M, Cahn JY, Cairo MS, Herzig RH, Isola LM, Klumpp TR, Lee SJ, Petersdorf EW, Santarone S, Gale RP, Schouten HC, Spellman SR, Weisdorf DJ, Wingard JR, Horowitz MM, Pavletic SZ. Risk factors associated with increased nonrelapse mortality and with poor overall survival in children with chronic graft-versus-host disease. BLOOD. 118:4472-4479. I.F.: 10.56.

12 Daikeler T, Labopin M, DiGioia M, Abinun M, Alexander T, Miniati I, Gualandi F, Fassas A, Martin T, Schwarze CP, Wulffraat N, Buch M, Sampol A, Carreras E, Dubois B, Gruhn B, Gungor T, Pohlreich D, Schuerwegh A, Snarski E, Snowden J, Veys P, Fasth A, Lenhoff S, Messina C, Voswinkel J, Badoglio M, Henes J, Launay D, Tyndall A, Gluckman E, Farge D. Secondary autoimmune diseases occurring after HSCT for an autoimmune disease: a retrospective study of the EBMT Autoimmune Disease Working Party. BLOOD. 118:1693-1698. I.F.: 10.56.

13 Carreras E, Diaz-Beya M, Rosinol L, Martinez C, Fernandez-Aviles F, Rovira M. The Incidence of Veno-Occlusive Disease Following Allogeneic Hematopoietic Stem Cell Transplantation Has Diminished and the Outcome Improved over the Last Decade. BIOL BLOOD MARROW TR. 17:1713-1720. I.F.: 3.28.

14 Robin M, Sanz GF, Ionescu I, Rio B, Sirvent A, Renaud M, Carreras E, Milpied N, Mohty M, Beguin Y, Bordigoni P, DeWitte T, Picardi A, Purtill D, Gluckman E, Kroger N, Rocha V. Unrelated cord blood transplantation in adults with myelodysplasia or secondary acute myeloblastic leukemia: a survey on behalf of Eurocord and CLWP of EBMT. LEUKEMIA. 25:75-81. I.F.: 8.97.

15 Ruiz-Camps I, Len O, DeLaCamara R, Gurgui M, Martino R, Jarque I, Barrenetxea C, DeHeredia CD, Batlle M, Rovira M, DeLaTorre J, Torres A, Aguilar M, Espigado I, Martin-Davila P, Bou G, Borrell N, Aguado JM, Pahissa A. Valganciclovir as pre-emptive therapy for cytomegalovirus infection in allogeneic haematopoietic stem cell transplant recipients. ANTIVIR THER. 16:951-957. I.F.: 3.77.

REVIEWS
I.F.: 3.66

1 Carreras E, Diaz-Ricart M. The role of the endothelium in the short-term complications of hematopoietic SCT. BONE MARROW TRANSPL. 46:1495-1502. I.F.: 3.66.

EDITORIALS
I.F.: 7.20

1 Martinez C, Urbano-Ispizua A. Graft-versus-host disease therapy: something else beyond glucocorticoids?. HAEMATOL-HEMATOL J. 96:1249-1251. I.F.: 6.53.

2 Novo A, Llorente A, Cladera A, Rubio D, Valcarcel D, Amutio E, Conde E, Martin E, Diaz-Mediavilla J, Rifon JJ, Diez JL, Cabrera JR, Serrano J, Besalduch J, Ruiz JCG, Zueco JCG, Vallejo JC, Vazquez L, Cuesta MA, Diaz ML, Batlle M, Rovira M, Abellan PF, Rojas R, Tabares S, Olave T, Gomez V. Invasive fungal infections in onco-haematology: a Spanish perspective. REV ESP QUIM. 24:168-172. I.F.: 0.67.

CLINICAL GUIDELINES
I.F.: 0.67

1 Barberan J, Mensa J, Llamas JCV, Ramos IJ, Ruiz JCG, Marin JRC, Tello PB, Massana MB, Vidal JB, Vinas JMC, Huelva FJC, Pons EC, Mediavilla JD, Morfa MLD, Barrigon FE, Avellan PF, Lopez SG, Garcia CG, Maraver DH, DeLaGuia AL, Jimenez JL, Chacon EM, Rubio MO, DeOteyza JP, Ramirez GR, Contreras RR, Barbero AR, Tarrats MR, Felix DR, Godoy PS, Salinas AS, Alonso MA, Torroba JD, Ferreiras DV, Lopez LV, Garcia JMA, Perea JRA, Moreno RC, Cancer RC, Abete JF, Rodriguez JG, Gomez JG, DeLaPedrosa EGG, Baranda JMM, Garcia FJP, Camps IR, Lleti MS, Cisneros JD. Recommendations for the treatment of invasive fungal infection caused by filamentous fungi in the hematological patient. REV ESP QUIM. 24:263-270. I.F.: 0.67.

MULTICENTRICS
I.F.: 4.94

1 Marks DI, Pagliuca A, Kibbler CC, Glasmacher A, Heussel CP, Kantecki M, Miller PJS, Ribaud P, Schlamm HT, Solano C, Cook G. Voriconazole versus itraconazole for antifungal prophylaxis following allogeneic haematopoietic stem-cell transplantation. BRIT J HAEMATOL. 155:318-327. I.F.: 4.94.

GRANTS FOR RESEARCH IN PROGRESS

Carreras E. Disfunción endotelial post-trasplante hematopoyético. Impacto de los agentes empleados en el régimen de acondicionamiento y análisis de posibles agentes protectores. Sponsored by: Ministerio de Sanidad y Consumo, PI080156. Duration: 01/01/2009-31/12/2011.

Martinez Munoz C. Estudio de la farmacogenómica y la farmacodinámica de los inmunosupresores en el trasplante alogénico de progenitores hemopoyéticos y su implicación en las reacciones injerto contra huésped e injerto-contra-tumor. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/1043. Duration: 01/01/2010-31/12/2012.

Urbano A. Papel de los factores inducidos por hipoxia (HIFs), Notch, Oct4 y de microRNAs en la patogenia y transformación de los síndromes mielodisplásicos a leucemia aguda. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI08/1137. Duration: 29/07/2010-30/12/2011.

Urbano A. Trasplante de progenitores hemopoyéticos en neoplasias hematológicas. Sponsored by: Fondo de Investigaciones Sanitarias, Instituto de Salud Carlos III, RD06/0020/0012. Duration: 01/01/2007-31/12/2012.

AREA 5

Oncology and haematology

Hematological oncology

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TEAM INVOLVED IN:

STRATEGIC OBJECTIVES

The main strategic objectives of our team are clinical, applied and basic research in hematological oncology. The team is structured into three study groups of three major disease categories.

MAIN LINES OF RESEARCH

1. **Study of lymphoid neoplasms.**
2. **Multiple myeloma and other monoclonal gammapathies.**
3. **Study of myeloid neoplasms.**

RESEARCH GROUP
LYMPHOID NEOPLASMS

Group Leader: Armando López (Hospital Clínic)

1. Lymphomas
- Investigation of the progression mechanisms of the disease.
- Study of minimum residual disease and its clinical significance.
- Genomic profile of the 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 (collaboration in international studies, particularly the International T-cell Lymphomas Project. University of Nebraska) and follicular lymphoma.
- Utility of PET in evaluating the response of lymphomas and chronic lymphocytic leukemia (CLL).
- Genic profile of Hodgkin lymphoma.
- Phase I-II clinical trials with new drugs (bortezomib, anti-CD40, anti-CD22, aplidin, GA101, etc.), and international phase III trials to establish new indications in lymphomas (PRIMA and ZAR studies).

2. Chronic lymphocytic leukemia
- Mechanisms of progression of the disease.
- Biology of ZAP-70 in relation to BCR
- Analysis of transforming CLL.
- Influence of the cellular microenvironment upon the disease.
- Study of the immunological alterations and immune reconstitution in chronic lymphocytic leukemia (CLL Global Research Foundation project).
- Evaluation of cellular proliferation in CLL.
- Study of autoimmune phenomena.
- Multiparametric analysis of prognostic factors in CLL.
- Phase I/II and III clinical trials.
- Project for the Chronic Lymphocytic Leukemia (CLL) Genome, in collaboration with the Hematopatology Unit

RESEARCH GROUP
MYELOMA AND OTHER MONOCLONAL GAMMAPATHIES

Group Leader: Joan Blade (Hospital Clínic)

1. Study of molecular cytogenics, gene-expression profile of cytokines related to angiogenesis and the tumour micro-environment and analysis of genes differentially expressed in bone marrow and in extramedullary plasmacytomas in patients with multiple myoma.

2. Evaluation of immune reconstitution in patients in complete remission after autologous transplant and after chemotherapy and the possible relationship with disease progression, compared to patients with partial response and monoclonal gammopathies of undetermined significance (leucocyte subpopulations in peripheral blood and bone marrow, minimal residual disease measured by cytometry, levels of free light chains and heavy chains, miRNA in serum and bone marrow, functional analysis of the innate response by TLR and NK cell repertoire, mRNA microarrays in the bone marrow microenvironment, PET/CT).

3. Impact of individual genetic variability on the response to treatment in multiple myoma through the analysis of single nucleotide polymorphisms (SNPs).

4. Characterisation of cardiac involvement in AL amyloidosis based on clinical presentation, cardiac biomarker levels and imaging techniques, and the influence of genetics in the predilection of the light amyloidogenic chains for the heart and the severity of the cardiac involvement.

5. Clinical trials for the treatment of multiple myoma and primary amyloidosis. Phases I, II and III. Sponsored by PETHEMA and by the industry.

RESEARCH GROUP
MYELOID NEOPLASMS

Group Leader:
Francisco Cervantes (Hospital Clínic)

1. Chronic myeloid leukaemia: Updating of the Spanish protocol for the treatment of chronic myeloid leukaemia with escalating doses of imatinib versus imatinib in combination with interferon (CML/PETHEMA). Participation in the European Chronic Myeloid Leukaemia Registry. Drawing up of new criteria for response of CML to treatment with tyrosine kinase inhibitors, within the European LeukemiaNet expert panel. Clinical trials for treatment of CML with new tyrosine kinase inhibitors.

2. Philadelphia chromosome-negative chronic myeloproliferative disease: Study of the thrombosis mechanisms. Leadership of the international study into predictive factors for the progression of primary myelofibrosis to acute leukaemia, in collaboration with the main groups in Europe and the United States. Analysis of the relationship between mutational status and JAK2 and MPL allele burden, haplotype 46/1 of the JAK2 gene and the initial characteristics, the progression pattern and the prognosis of myelofibrosis. Clinical trials for the treatment of myelofibrosis with JAK2 inhibitors and other new drugs.

3. Acute myeloid leukaemia: Study of the biological prognostic factors in AML of intermediate cytogenic risk: genetic mutations, gene expression profile, microRNA expression pattern. Analysis of the microRNA expression pattern in AML with translocation (8;16)/MYST3-CREBBP, AML with t(6;9)/DEK-NUP214 and AML with multilineage dysplasia. Prognostic value of molecular markers of AML in the results of haematopoietic stem cell transplantation (within the Acute Leukemia Working Party for the European Group for Blood and Bone Marrow Transplantation, EBMT). Design of AML treatment protocols for the *Grupo Cooperativo para el Estudio y Tratamiento de las Leucemias Agudas y Mielodisplasias* (CETLAM) [Cooperative Group for the Study and Treatment of Acute Leukaemia and Myelodysplasia] (sequential protocol, AML-2012). Phase II and III clinical trials with new drugs for the treatment of AML and ALL: FLT3 inhibitors, azacitidine, blinatumomab.

4. Myelodysplastic Syndromes: Natural history and prognosis. Participation in the Spanish MDS Registry. Prognostic importance of transfusion requirements. Study of sensitisation to transfusion. Cytogenetic and molecular abnormalities in MDS and the implications for prognosis. Study of microRNA in MDS. Clinical trials with new drugs for the treatment of MDS.

PUBLICATIONS

ORIGINALS
I.F.: 356.47

1 Cervera C, Fernandez-Aviles F, DeLaCalle-Martin O, Bosch X, Rovira M, Plana M, Moreno A, Garcia F, Miro JM, Martinez A, Gallart T, Carreras E, Blade J, Gatell JM. Non-myeloablative hematopoietic stem cell transplantation in the treatment of severe idiopathic CD4+lymphocytopenia. EUR J HAEMATOL. 87:87-91. I.F.: 2.79.

2 Ferrer G, Hodgson K, Pereira A, Juan M, Elena M, Colomer D, Roue G, Aymerich M, Baumann T, Montserrat E, Moreno C. Combined analysis of levels of serum B-cell activating factor and a proliferation-inducing ligand as predictor of disease progression in patients with chronic lymphocytic leukemia. LEUKEMIA LYMPHOMA. 52:2064-2068. I.F.: 2.49.

3 DeLarrea CF, Tovar N, Cibeira MT, Arostegui JI, Rosinol L, Elena M, Filella X, Yague J, Blade J. Emergence of oligoclonal bands in patients with multiple myeloma in complete remission after induction chemotherapy: association with the use of novel agents. HAEMATOL-HEMATOL J. 96:171-173. I.F.: 6.53.

4 DeLarrea CF, Tovar N, Rozman M, Rosinol L, Arostegui JI, Cibeira MT, Rovira M, Yague J, Blade J. Multiple Myeloma in Serologic Complete Remission after Autologous Stem Cell Transplantation: Impact of Bone Marrow Plasma Cell Assessment by Conventional Morphology on Disease Progression. BIOL BLOOD MARROW TR. 17:1084-1087. I.F.: 3.28.

5 Puente XS, Pinyol M, Quesada V, Conde L, Ordonez GR, Villamor N, Escaramis G, Jares P, Bea S, Gonzalez-Diaz M, Bassaganyas L, Baumann T, Juan M, Lopez-Guerra M, Colomer D, Tubio JMC, Lopez C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernandez JM, Puente DA, Freije JMP, Velasco G, Gutierrez-Fernandez A, Costa D, Carrio A, Guijarro S, Enjuanes A, Hernandez L, Yague J, Nicolas P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, DeSanjose S, Piris MA, DeAlava E, Miguel JS, Royo R, Gelpi JL, Torrents D, Orozco M, Pisano DG, Valencia A, Guigo R, Bayes M, Heath S, Gut M, Klatt P, Marshall J, Raine K, Stebbings LA, Futreal PA, Stratton MR, Campbell PJ, Gut I, Lopez-Guillermo A, Estivill X, Montserrat E, Lopez-Otin C, Campo E. Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia. NATURE. 475:101-105. I.F.: 36.10.

6 Bosch X, Esteve J, Sitges M, DeCaralt TM, Domenech A, Ortiz JT, Monzo M, Morales-Ruiz M, Perea RJ, Rovira M. Prevention of Chemotherapy-Induced Left Ventricular Dysfunction With Enalapril and Carvedilol: Rationale and Design of the OVERCOME Trial. J CARD FAIL. 17:643-648. I.F.: 3.36.

7 Gutierrez-Garcia G, Cardesa-Salzmann T, Climent F, Gonzalez-Barca E, Mercadal S, Mate JL, Sancho JM, Arenillas L, Serrano S, Escoda L, Martinez S, Valera A, Martinez A, Jares P, Pinyol M, Garcia-Herrera A, Martinez-Trillos A, Gine E, Villamor N, Campo E, Colomo L, Lopez-Guillermo A. Gene-expression profiling and not immunophenotypic algorithms predicts prognosis in patients with diffuse large B-cell lymphoma treated with immunochemotherapy. BLOOD. 117:4836-4843. I.F.: 10.56.

8 Cardesa-Salzmann TM, Colomo L, Gutierrez G, Chan WC, Weisenburger D, Climent F, Gonzalez-Barca E, Mercadal S, Arenillas L, Serrano S, Tubbs R, Delabie J, Gascoyne RD, Connors JM, Mate JL, Rimsza L, Braziel R, Rosenwald A, Lenz G, Wright G, Jaffe ES, Staudt L, Jares P, Lopez-Guillermo A, Campo E. High microvessel density determines a poor outcome in patients with diffuse large B-cell lymphoma treated with rituximab plus chemotherapy. HAEMATOL-HEMATOL J. 96:996-1001. I.F.: 6.53.

9 Gutierrez-Garcia G, Garcia-Herrera A, Cardesa T, Martinez A, Villamor N, Ghita G, Martinez-Trillos A, Colomo L, Setoain X, Rodriguez S, Gine E, Campo E, Lopez-Guillermo A. Comparison of four prognostic scores in peripheral T-cell lymphoma. ANN ONCOL. 22:397-404. I.F.: 6.45.

10 Enjuanes A, Fernandez V, Hernandez L, Navarro A, Bea S, Pinyol M, Lopez-Guillermo A, Rosenwald A, Ott G, Campo E, Jares P. Identification of Methylated Genes Associated with Aggressive Clinicopathological Features in Mantle Cell Lymphoma. PLOS ONE. 6:-. I.F.: 4.41.

11 DeLarrea CF, Martinez-Pozo A, Mercadal S, Garcia A, Gutierrez-Garcia G, Valera A, Ghita G, Colomo L, Gainza E, Villamor N, Nomdedeu B, Estrach T, Montserrat E, Campo E, Lopez-Guillermo A. Initial features and outcome of cutaneous and non-cutaneous primary extranodal follicular lymphoma. BRIT J HAEMATOL. 153:334-340. I.F.: 4.94.

12 Mozos A, Roue G, Lopez-Guillermo A, Jares P, Campo E, Colomer D, Martinez A. The Expression of the Endoplasmic Reticulum Stress Sensor BiP/GRP78

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	191.76	24	18	3
2010	243.89	26	19	1
2011	356.47	41	29	4

Predicts Response to Chemotherapy and Determines the Efficacy of Proteasome Inhibitors in Diffuse Large B-Cell Lymphoma. AM J PATHOL. 179:2601-2610. I.F.: 5.22.

13 Cibeira MT, DeLarrea CF, Navarro A, Diaz T, Fuster D, Tovar N, Rosinol L, Monzo M, Blade J. Impact on response and survival of DNA repair single nucleotide polymorphisms in relapsed or refractory multiple myeloma patients treated with thalidomide. LEUKEMIA RES. 35:1178-1183. I.F.: 2.56.

14 Diaz T, Navarro A, Ferrer G, Gel B, Gaya A, Artells R, Bellosillo B, Garcia-Garcia M, Serrano S, Martinez A, Monzo M. Lestaurtinib Inhibition of the JAK/STAT Signaling Pathway in Hodgkin Lymphoma Inhibits Proliferation and Induces Apoptosis. PLOS ONE. 6:-. I.F.: 4.41.

15 Pereira A, Nomdedeu M, Aguilar JL, Belkaid M, Carrio A, Cobo F, Costa D, Rozman M, Sanz C, Nomdedeu B. Transfusion intensity, not the cumulative red blood cell transfusion burden, determines the prognosis of patients with myelodysplastic syndrome on chronic transfusion support. AM J HEMATOL. 86:245-250. I.F.: 3.58.

16 Nomdedeu J, Bussaglia E, Villamor N, Martinez C, Esteve J, Tormo M, Estivill C, Queipo MP, Guardia R, Carricondo M, Hoyos M, Llorente A, Junca J, Gallart M, Domingo A, Bargay J, Mascaro M, Moraleda JM, Florensa L, Ribera JM, Gallardo D, Brunet S, Aventin A, Sierra J. Immunophenotype of acute myeloid leukemia with NPM mutations: Prognostic impact of the leukemic compartment size. LEUKEMIA RES. 35:163-168. I.F.: 2.56.

17 Dubrey SW, Reece DE, Sanchorawala V, Hegenbart U, Merlini G, Palladini G, Fermand JP, Vescio RA, Blade J, Heffner LT, Hassoun H, Liu X, Enny C, Ramaswami P, Elsayed Y, VanDeVelde H, Mortimer S, Cakana A, Comenzo RL. Bortezomib in a phase 1 trial for patients with relapsed AL amyloidosis: cardiac responses and overall effects. QJM-INT J MED. 104:957-970. I.F.: 2.15.

18 Pfreundschuh M, Kuhnt E, Trumper L, Osterborg A, Trneny M, Shepherd L, Gill DS, Walewski J, Pettengell R, Jaeger U, Zinzani PL, Shpilberg O, Kvaloy S, Brown PD, Stahel R, Milpied N, Lopez-Guillermo A, Poeschel V, Grass S, Loeffler M, Murawski N. CHOP-like chemotherapy with or without rituximab in young patients with good-prognosis diffuse large-B-cell lymphoma: 6-year results of an open-label randomised study of the MabThera International Trial (MInT) Group. LANCET ONCOL. 12:1013-1022. I.F.: 17.76.

19 Conconi A, Martinelli G, Lopez-Guillermo A, Zinzani PL, Ferreri AJM, Rigacci L, Devizzi L, Vitolo U, Luminari S, Cavalli F, Zucca E. Clinical activity of bortezomib in relapsed/refractory MALT lymphomas: results of a phase II study of the International Extranodal Lymphoma Study Group (IELSG). ANN ONCOL. 22:689-695. I.F.: 6.45.

20 Montesinos P, Rayon C, Vellenga E, Brunet S, Gonzalez J, Gonzalez M, Holowiecka A, Esteve J, Bergua J, Gonzalez JD, Rivas C, Tormo M, Rubio V, Bueno J, Manso F, Milone G, DeLaSerna J, Perez I, Perez-Encinas M, Krsnik I, Ribera JM, Escoda L, Lowenberg B, Sanz MA. Clinical significance of CD56 expression in patients with acute promyelocytic leukemia treated with all-trans retinoic acid and anthracycline-based regimens. BLOOD. 117:1799-1805. I.F.: 10.56.

21 Paiva B, Martinez-Lopez J, Vidriales MB, Mateos MV, Montalban MA, Fernandez-Redondo E, Alonso L, Oriol A, Teruel AI, DePaz R, Larana JG, Bengoechea E, Martin A, Mediavilla JD, Palomera L, DeArriba F, Blade J, Orfao A, Lahuerta JJ, Miguel JF. Comparison of Immunofixation, Serum Free Light Chain, and Immunophenotyping for Response Evaluation and Prognostication in Multiple Myeloma. J CLIN ONCOL. 29:1627-1633. I.F.: 18.97.

22 Paiva B, Perez-Andres M, Vidriales MB, Almeida J, DeLasHeras N, Mateos MV, Lopez-Corral L, Gutierrez NC, Blanco J, Oriol A, Hernandez MT, DeArriba F, DeCoca AG, Terol MJ, DeLaRubia J, Gonzalez Y, Martin A, Sureda A, Schmidt-Hieber M, Schmitz A, Johnsen HE, Lahuerta JJ, Blade J, San-Miguel JF, Orfao A. Competition between clonal plasma cells and normal cells for potentially overlapping bone marrow niches is associated with a progressively altered cellular distribution in MGUS vs myeloma. LEUKEMIA. 25:697-706. I.F.: 8.97.

23 Maffioli M, Camos M, Gaya A, Hernandez-Boluda JC, Alvarez-Larran A, Domingo A, Granell M, Guillem V, Vallansot R, Costa D, Bellosillo B, Colomer D, Cervantes F. Correlation between genetic polymorphisms of the hOCT1 and MDR1 genes and the

response to imatinib in patients newly diagnosed with chronic-phase chronic myeloid leukemia. LEUKEMIA RES. 35:1014-1019. I.F.: 2.56.

24 Such E, Cervera J, Costa D, Sole F, Vallespi T, Luno E, Collado R, Calasanz MJ, Hernandez-Rivas JM, Cigudosa JC, Nomdedeu B, Mallo M, Carbonell F, Bueno J, Ardanaz MT, Ramos F, Tormo M, Sancho-Tello R, DelCanizo C, Gomez V, Marco V, Xicoy B, Bonanad S, Pedro C, Bernal T, Sanz GF. Cytogenetic risk stratification in chronic myelo-monocytic leukemia. HAEMATOL-HEMATOL J. 96:375-383. I.F.: 6.53.

25 Merino A, DeLarrea CF, Blade J. Cytoplasmic inclusions in leukocytes associated to cryoglobulinemia and IgG-kappa monoclonal gammapathy of undetermined significance. EUR J HAEMATOL. 86:550-550. I.F.: 2.79.

26 Gangat N, Caramazza D, Vaidya R, George G, Begna K, Schwager S, VanDyke D, Hanson C, Wu WT, Pardanani A, Cervantes F, Passamonti F, Tefferi A. DIPSS Plus: A Refined Dynamic International Prognostic Scoring System for Primary Myelofibrosis That Incorporates Prognostic Information From Karyotype, Platelet Count, and Transfusion Status. J CLIN ONCOL. 29:392-397. I.F.: 18.97.

27 Reece DE, Hegenbart U, Sanchorawala V, Merlini G, Palladini G, Blade J, Fermand JP, Hassoun H, Heffner L, Vescio RA, Liu K, Enny C, Esseltine DL, VanDeVelde H, Cakana A, Comenzo RL. Efficacy and safety of once-weekly and twice-weekly bortezomib in patients with relapsed systemic AL amyloidosis: results of a phase 1/2 study. BLOOD. 118:865-873. I.F.: 10.56.

28 Blade J, Sonneveld P, SanMiguel JF, Sutherland HJ, Hajek R, Nagler A, Spencer A, Robak T, Lantz KC, Zhuang SH, Harousseau JL, Orlowski RZ. Efficacy and Safety of Pegylated Liposomal Doxorubicin in Combination With Bortezomib for Multiple Myeloma: Effects of Adverse Prognostic Factors on Outcome. CL LYMPH MYELOM LEUK. 11:44-49. I.F.: 1.99.

29 Delabie J, Holte H, Vose JM, Ullrich F, Jaffe ES, Savage KJ, Connors JM, Rimsza L, Harris NL, Muller-Hermelink K, Rudiger T, Coiffier B, Gascoyne RD, Berger F, Tobinai K, Au WY, Liang R, Montserrat E, Hochberg EP, Pileri S, Federico M, Nathwani B, Armitage JO, Weisenburger DD. Enteropathy-associated T-cell lymphoma: clinical and histological findings from the International Peripheral T-Cell Lymphoma Project. BLOOD. 118:148-155. I.F.: 10.56.

30 Guglielmelli P, Biamonte F, Score J, Hidalgo-Curtis C, Cervantes F, Maffioli M, Fanelli T, Ernst T, Winkelman N, Jones AV, Zoi K, Reiter A, Duncombe A, Villani L, Bosi A, Barosi G, Cross NCP, Vannucchi AM. EZH2 mutational status predicts poor survival in myelofibrosis. BLOOD. 118:5227-5234. I.F.: 10.56.

31 Vitolo U, Chiappella A, Ferreri AJM, Martelli M, Baldi I, Balzarotti M, Bottelli C, Conconi A, Gomez H, Lopez-Guillermo A, Martinelli G, Merli F, Novero D, Orsucci L, Pavone V, Ricardi U, Storti S, Gospodarowicz MK, Cavalli F, Sarris AH, Zucca E. First-Line Treatment for Primary Testicular Diffuse Large B-Cell Lymphoma With Rituximab-CHOP, CNS Prophylaxis, and Contralateral Testis Irradiation: Final Results of an International Phase II Trial. J CLIN ONCOL. 29:2766-2772. I.F.: 18.97.

32 Mian M, Gaidano G, Conconi A, Tsang R, Gospodarowicz MK, Rambaldi A, Rossi A, Oldani E, Federico M, Luminari S, Bellei M, Pogliani EM, Rossini F, Cabrera ME, Martelli M, Lopez-Guillermo A, Busetto M, Cavalli F, Zucca E, Cortelazzo S. High response rate and improvement of long-term survival with combined treatment modalities in patients with poor-risk primary thyroid diffuse large B-cell lymphoma: an International Extranodal Lymphoma Study Group and Intergruppo Italiano Linfomi study. LEUKEMIA LYMPHO-MA. 52:823-832. I.F.: 2.49.

33 Martinez-Lopez J, Blade J, Mateos MV, Grande C, Alegre A, Garcia-Larana J, Sureda A, DeLaRubia J, Conde E, Martinez R, DeArriba F, Viguria MC, Besalduch J, Cabrera R, Gonzalez-SanMiguel JD, Guzman-Zamudio JL, DelCastillo MCG, Moraleda JM, Garcia-Ruiz JC, SanMiguel J, Lahuerta JJ. Long-term prognostic significance of response in multiple myeloma after stem cell transplantation. BLOOD. 118:529-534. I.F.: 10.56.

34 Ludwig H, Beksac M, Blade J, Cavenagh J, Cavo M, Delforge M, Dimopoulos M, Drach J, Einsele H, Facon T, Goldschmidt H, Harousseau JL, Hess U, Kropff M, DaCosta FL, Louw V, Magen-Nativ H, Mendeleeva L, Nahi H, Plesner T, San-Miguel J, Sonneveld P, Udvardy M, Sondergeld P, Palumbo A. Multiple Myeloma Treatment Strategies with Novel Agents in 2011: A European Perspective. ONCOLOGIST. 16:388-403. I.F.: 5.83.

35 Mateos MV, Gutierrez NC, Martin-Ramos ML, Paiva B, Montalban MA, Oriol A, Martinez-Lopez J, Teruel AI, Bengoechea E, Martin A, Diaz-Mediavilla J, DeArriba F, Palomera L, Hernandez JM, Sureda A, Bargay J, Penalver FJ, Ribera JM, Martin-Mateos ML, Fernandez M, Garcia-Sanz R, Vidriales MB, Blade J, Lahuerta JJ, SanMiguel JF. Outcome according to cytogenetic abnormalities and DNA ploidy in myeloma patients receiving short induction with weekly bortezomib followed by maintenance. BLOOD. 118:4547-4553. I.F.: 10.56.

36 Cibeira MT, Sanchorawala V, Seldin DC, Quillen K, Berk JL, Dember LM, Segal A, Ruberg F, Meier-Ewert H, Andrea NT, Sloan JM, Finn KT, Doros G, Blade J, Skinner M. Outcome of AL amyloidosis after high-dose melphalan and autologous stem cell transplantation: long-term results in a series of 421 patients. BLOOD. 118:4346-4352. I.F.: 10.56.

37 Ammatuna E, Montesinos P, Hasan SK, Ramadan SM, Esteve J, Hubmann M, Pagoni M, Grimwade D, Sanz MA, Lo-Coco F. Presenting features and treatment outcome of acute promyelocytic leukemia arising after multiple sclerosis. HAEMATOL-HEMATOL J. 96:621-625. I.F.: 6.53.

38 Barragan E, Montesinos P, Camos M, Gonzalez M, Calasanz MJ, Roman-Gomez J, Gomez-Casares MT, Ayala R, Lopez J, Fuster O, Colomer D, Chillon C, Larrayoz MJ, Sanchez-Godoy P, Gonzalez-Campos J, Manso F, Amador ML, Vellenga E, Lowenberg B, Sanz MA. Prognostic value of FLT3 mutations in patients with acute promyelocytic leukemia treated with all-trans retinoic acid and anthracycline monochemotherapy. HAEMATOL-HEMATOL J. 96:1470-1477. I.F.: 6.53.

39 Shah J, Blade J, Sonneveld P, Harousseau JL, Lantz K, Londhe A, Lowery C, Orlowski RZ. Rapid Early Monoclonal Protein Reduction After Therapy With Bortezomib or Bortezomib and Pegylated Liposomal Doxorubicin in Relapsed/Refractory Myeloma Is Associated With a Longer Time to Progression. CANCER-AM CANCER SOC. 117:3758-3762. I.F.: 5.13.

40 Salles G, Seymour JF, Offner F, Lopez-Guillermo A, Belada D, Xerri L, Feugier P, Bouabdallah R, Catalano JV, Brice P, Caballero D, Haioun C, Pedersen LM, Delmer A, Simpson D, Leppa S, Soubeyran P, Hagenbeek A, Casasnovas O, Intragumtornchai T, Ferme C, DaSilva MG, Sebban C, Lister A, Estell JA, Milone G, Sonet A, Mendila M, Coiffier B, Tilly H. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial. LANCET. 377:42-51. I.F.: 33.63.

41 Calpe E, Codony C, Baptista MJ, Abrisqueta P, Carpio C, Purroy N, Bosch F, Crespo M. ZAP-70 enhances migration of malignant B lymphocytes toward CCL21 by inducing CCR7 expression via IgM-ERK1/2 activation. BLOOD. 118:4401-4410. I.F.: 10.56.

REVIEWS
I.F.: 95.83

1 Cervantes F, Pereira A. Advances in the understanding and management of primary myelofibrosis. CURR OPIN ONCOL. 23:665-671. I.F.: 4.39.

2 Hodgson K, Ferrer G, Pereira A, Moreno C, Montserrat E. Autoimmune cytopenia in chronic lymphocytic leukaemia: diagnosis and treatment. BRIT J HAEMATOL. 154:14-22. I.F.: 4.94.

3 Hodgson K, Ferrer G, Montserrat E, Moreno C. Chronic lymphocytic leukemia and autoimmunity: a systematic review. HAEMATOL-HEMATOL J. 96:752-761. I.F.: 6.53.

4 Rajkumar SV, Harousseau JL, Durie B, Anderson KC, Dimopoulos M, Kyle R, Blade J, Richardson P, Orlowski R, Siegel D, Jagannath S, Facon T, Avet-Loiseau H, Lonial S, Palumbo A, Zonder J, Ludwig H, Vesole D, Sezer O, Munshi NC, SanMiguel J. Consensus recommendations for the uniform reporting of clinical trials: report of the International Myeloma Workshop Consensus Panel 1. BLOOD. 117:4691-4695. I.F.: 10.56.

5 Pardanani A, Vannucchi AM, Passamonti F, Cervantes F, Barbui T, Tefferi A. JAK inhibitor therapy for myelofibrosis: critical assessment of value and limitations. LEUKEMIA. 25:218-225. I.F.: 8.97.

6 Palumbo A, Bringhen S, Ludwig H, Dimopoulos MA, Blade J, Mateos MV, Rosinol L, Boccadoro M, Cavo M, Lokhorst H, Zweegman S, Terpos E, Davies F, Driessen C, Gimsing P, Gramatzki M, Hajek R, Johnsen HE, DaCosta FL, Sezer O, Spencer A, Beksac M, Morgan G, Einsele H, Miguel JFS, Sonneveld P. Personalized therapy in multiple myeloma according to patient age and vulnerability: a report of the European Myeloma Network (EMN). BLOOD. 118:4519-4529. I.F.: 10.56.

7 Barbui T, Barosi G, Birgegard G, Cervantes F, Finazzi G, Griesshammer M, Harrison C, Hasselbalch HC, Hehlmann R, Hoffman R, Kiladjian JJ, Kroger N, Mesa R, Mcmullin MF, Pardanani A, Passamonti F, Vannucchi AM, Reiter A, Silver RT, Verstovsek S, Tefferi A. Philadelphia-Negative Classical Myeloproliferative Neoplasms:

Critical Concepts and Management Recommendations From European LeukemiaNet. J CLIN ONCOL. 29:761-770. I.F.: 18.97.

8 Cervantes F, Mauro M. Practical Management of Patients With Chronic Myeloid Leukemia. CANCER-AM CANCER SOC. 117:4343-4354. I.F.: 5.13.

9 Blade J, DeLarrea CF, Rosinol L, Cibeira MT, Jimenez R, Powles R. Soft-Tissue Plasmacytomas in Multiple Myeloma: Incidence, Mechanisms of Extramedullary Spread, and Treatment Approach. J CLIN ONCOL. 29:3805-3812. I.F.: 18.97.

10 VanDeDonk NWCJ, Lokhorst HM, Dimopoulos M, Cavo M, Morgan G, Einsele H, Kropff M, Schey S, Avet-Loiseau H, Ludwig H, Goldschmidt H, Sonneveld P, Johnsen HE, Blade J, San-Miguel JF, Palumbo A. Treatment of relapsed and refractory multiple myeloma in the era of novel agents. CANCER TREAT REV. 37:266-283. I.F.: 6.81.

EDITORIALS
I.F.: 17.09

1 Setoain X, Lopez-Guillermo A. Non-Hodgkin's lymphoma staging with PET-CT scan. MED CLIN-BARCELONA. 137:402-404. I.F.: 1.41.

2 Montserrat E, Gribben JG. Autografting CLL: the game is over!. BLOOD. 117:6057-6058. I.F.: 10.56.

3 Nomdedeu M, Maffioli M, Calvo X, Martinez-Trillos A, Baumann T, Diaz-Beya M, Aguilar JL, Rozman M, Costa D, Esteve J, Cervantes F, Colomer D, Nomdedeu B. Efficacy of lenalidomide in a patient with myelodysplastic syndrome with isolated del(5q) and JAK2(V617F) mutation. LEUKEMIA RES. 35:1276-1278. I.F.: 2.56.

4 Blade J, DeLarrea CF. Toward deeper response in MM. BLOOD. 117:2986-+. I.F.: 10.56.

5 Gale RP, Barosi G, Barbui T, Cervantes F, Dohner K, Dupriez B, Gupta V, Harrison C, Hoffman R, Kiladjian JJ, Mesa R, McMullin MF, Passamonti F, Ribrag V, Roboz G, Saglio G, Vannucchi A, Verstovsek S. What are RBC-transfusion-dependence and -independence?. LEUKEMIA RES. 35:8-11. I.F.: 2.56.

CLINICAL GUIDELINES
I.F.: 10.56

1 Cavo M, Rajkumar SV, Palumbo A, Moreau P, Orlowski R, Blade J, Sezer O, Ludwig H, Dimopoulos MA, Attal M, Sonneveld P, Boccadoro M, Anderson KC, Richardson PG, Bensinger W, Johnsen HE, Kroeger N, Gahrton G, Bergsagel PL, Vesole DH, Einsele H, Jagannath S, Niesvizky R, Durie BGM, SanMiguel J, Lonial S. International Myeloma Working Group consensus approach to the treatment of multiple myeloma patients who are candidates for autologous stem cell transplantation. BLOOD. 117:6063-6073. I.F.: 10.56.

MULTICENTRICS
I.F.: 15.69

1 Gonzalez-Porras JR, Cordoba I, Such E, Nomdedeu B, Vallespi T, Carbonell F, Luno E, Ardanaz M, Ramos F, Pedro C, Gomez V, DePaz R, Sanchez-Barba M, Sanz GF, DelCanizo C. Prognostic impact of severe thrombocytopenia in low-risk myelodysplastic syndrome. CANCER-AM CANCER SOC. 117:5529-5537. I.F.: 5.13.

2 Dimopoulos M, Kyle R, Fermand JP, Rajkumar SV, SanMiguel J, Chanan-Khan A, Ludwig H, Joshua D, Mehta J, Gertz M, Avet-Loiseau H, Beksac M, Anderson KC, Moreau P, Singhal S, Goldschmidt H, Boccadoro M, Kumar S, Giralt S, Munshi NC, Jagannath S. Consensus recommendations for standard investigative workup: report of the International Myeloma Workshop Consensus Panel 3. BLOOD. 117:4701-4705. I.F.: 10.56.

GRANTS FOR RESEARCH IN PROGRESS

Cervantes F. Red temática de investigación cooperativa de cáncer. Sponsored by: Ministerio Sanidad y Consumo, RD06/0020/0004. Duration: 01/01/2007-31/12/2012.

Montserrat E. Diseño de un sistema clínico-biológico para el pronóstico de los pacientes con leucemia linfática crónica (LLC). Sponsored by: Instituto Carlos III- Ministerio de Ciencia e Innovación, PI080304. Duration: 01/01/2009-31/12/2011.

Montserrat E. Grup de Recerca Consolidat: Unitat Clínico-Biològica per a l'estudi de limfomes i síndromes limproliferatives. Sponsored by: Generalitat de Catalunya, 2009_SGR_1008. Duration: 23/09/2009-31/12/2013.

Blade J. Impacto de la variabilidad genética individual mediante el análisis de single neucleotide polymorphisms (SNPS) en la respuesta al tratamiento en el mieloma múltiple. Sponsored by: Instituto Carlos III- Ministerio de Ciencia e Innovación, PI080147. Duration: 01/01/2009-31/12/2011.

Esteve J. Generación de un índice pronóstico molecular en los enfermos con LMA de riego citogenético intermedio:

análisis de mutaciones, nivel de expresión génico y patrón de expresión microRNA. Sponsored by: Instituto Carlos III- Ministerio de Ciencia e Innovación, PI080158. Duration: 01/01/2009-31/12/2011.

Lopez A. Estudio de la expresión de las citoquinas y receptores de citoquinas en los diferentes tipos de linfomas T periféricos. Correlación con los perfiles genotípicos y significado clínico-biológico. Sponsored by: Instituto Carlos III. Ministerio de Ciencia e Innovación, PI070409. Duration: 01/01/2008-30/09/2011.

Montserrat E. Estudio de las características biológicas (alteraciones genéticas, inmunofeno-típicas y moleculares) y su impacto clínico en los síndromes linfoproliferativos crónicos. Sponsored by: Red temática de investigación cooperativa de cáncer. Ministerio Sanidad y Consumo, RD06/0020/0051. Duration: 01/01/2007-31/12/2011.

Blade J. Gammapatías monoclonales: de la génesis a la terapéutica. Sponsored by: Red Temática de Investigación Cooperativa Sanitaria (RTICS). Instituto de Salud Carlos III, RD06/0020/0005. Duration: 01/01/2007-31/12/2012.

Cervantes F. Estudio de la relación entre el estado mutacional y la carga alélica de JAK2 y MPL, el haplotipo 46/1 del gen JAK2 y las características iniciales, el patrón evolutivo y el pronóstico de los pacientes con mielofibrosis. Sponsored by: Instituto de Salud Carlos III (ISCIII), Ministerio de Ciencia e Innovación, PI10/00236. Duration: 01/01/2011-31/12/2013.

Cervantes F. An European network for myelofibrosis. Consensus on definition of disease improvement and study of tyrosine kinase inhibitors. Sponsored by: European Commission, QLG1-CT-2002-01123. Duration: 28/10/2002-28/11/2020.

Montserrat E. NoE-Strengthen and develop scientific and technological excellence in research and therapy of leukemia (CML, AML, ALL, CLL, MDS, CMPD) by integration of the leading national leukemia networks and their interdisciplinary partner groups in Europe. Sponsored by: European Commission, LSHC-CT-2004-503216. Duration: 01/01/2004-31/05/2012.

DOCTORAL THESES

Blade J. Remisión completa en el mieloma múltiple: Impacto pronóstico de las bandas oligoclonales, cociente de cadenas ligeras libres en suero y células plasmáticas residuales en médula ósea. PhD student: Carlos José Fernández de Larrea Rodríguez.

Lopez-Guillermo A. Caracterización biológica y pronóstica del linfoma difuso de células grandes en la era de la immunoquimioterapia. PhD student: Gonzalo Gutiérrez García.

AREA 5

Oncology and haematology

Physiopathology and molecular bases in hematology

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TEAM INVOLVED IN:

STRATEGIC OBJECTIVES

Epidemiological, genetic, molecular and physiopathological study of malignant hematological diseases and erythrocyte pathology.

MAIN LINES OF RESEARCH

1. Molecular bases of apoptosis regulation induced by drugs in lymphoid neoplasms. Evaluation of new strategies for the treatment of these disorders. Search for selective therapies against disregulated signaling pathways in lymphoid malignancies. Mechanisms of action and awareness-raising strategies.
2. Cytological, immunophenotypic and molecular study of malignant hematological diseases. Development of new technologies for the diagnosis and follow-up of minimum residual disease.
3. Promotion of cooperative strategies in the molecular diagnostic setting of leukemias and lymphomas.
4. Design and implementation of internal and external quality control programs.
5. Cutaneous T and B cell lymphomas. Clinical, histopathological and immunophenotypic study. Prognostic factors and epidemiology.
6. Molecular study of the congenital alterations of erythrocytes and of the physiopathological mechanisms intervening in the production and destruction of erythrocytes as a cause of anemia or erythrocytosis.
7. Genetic and epidemiological study of hemoglobin diseases and thalassemias.

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	101.35	15	10	3
2010	78.59	14	10	1
2011	142.13	20	12	6

ORIGINALS
I.F.: 142.13

1 Ferrer G, Hodgson K, Pereira A, Juan M, Elena M, Colomer D, Roue G, Aymerich M, Baumann T, Montserrat E, Moreno C. Combined analysis of levels of serum B-cell activating factor and a proliferation-inducing ligand as predictor of disease progression in patients with chronic lymphocytic leukemia. LEUKEMIA LYMPHOMA. 52:2064-2068. I.F.: 2.49.

2 DeLarrea CF, Tovar N, Rozman M, Rosinol L, Arostegui JI, Cibeira MT, Rovira M, Yague J, Blade J. Multiple Myeloma in Serologic Complete Remission after Autologous Stem Cell Transplantation: Impact of Bone Marrow Plasma Cell Assessment by Conventional Morphology on Disease Progression. BIOL BLOOD MARROW TR. 17:1084-1087. I.F.: 3.28.

3 Puente XS, Pinyol M, Quesada V, Conde L, Ordonez GR, Villamor N, Escaramis G, Jares P, Bea S, Gonzalez-Diaz M, Bassaganyas L, Baumann T, Juan M, Lopez-Guerra M, Colomer D, Tubio JMC, Lopez C, Navarro A, Tornador C, Aymerich M, Rozman M, Hernandez JM, Puente DA, Freije JMP, Velasco G, Gutierrez-Fernandez A, Costa D, Carrio A, Guijarro S, Enjuanes A, Hernandez L, Yague J, Nicolas P, Romeo-Casabona CM, Himmelbauer H, Castillo E, Dohm JC, DeSanjose S, Piris MA, DeAlava E, Miguel JS, Royo R, Gelpi JL, Torrents D, Orozco M, Pisano DG, Valencia A, Guigo R, Bayes M, Heath S, Gut M, Klatt P, Marshall J, Raine K, Stebbings LA, Futreal PA, Stratton MR, Campbell PJ, Gut I, Lopez-Guillermo A, Estivill X, Montserrat E, Lopez-Otin C, Campo E. Whole-genome sequencing identifies recurrent mutations in chronic lymphocytic leukaemia. NATURE. 475:101-105. I.F.: 36.10.

4 Ramirez-Bajo MJ, Repiso A, DeLaOssa PP, Banon-Maneus E, DeAtauri P, Climent F, Corrons JLV, Cascante M, Carreras J. Enzymatic and metabolic characterization of the phosphoglycerate kinase deficiency associated with chronic hemolytic anemia caused by the PGK-Barcelona mutation. BLOOD CELL MOL DIS. 46:206-211. I.F.: 2.72.

5 Gutierrez-Garcia G, Cardesa-Salzmann T, Climent F, Gonzalez-Barca E, Mercadal S, Mate JL, Sancho JM, Arenillas L, Serrano S, Escoda L, Martinez S, Valera A, Martinez A, Jares P, Pinyol M, Garcia-Herrera A, Martinez-Trillos A, Gine E, Villamor N, Campo E, Colomo L, Lopez-Guillermo A. Gene-expression profiling and not immunophenotypic algorithms predicts prognosis in patients with diffuse large B-cell lymphoma treated with immunochemotherapy. BLOOD. 117:4836-4843. I.F.: 10.56.

6 Sanchez-Schmidt JM, Salgado R, Servitje O, Gallardo F, Ortiz-Romero PL, Karpova MB, Zipser MC, Garcia-Muret MP, Estrach T, Rodriguez-Pinilla SM, Climent F, Suela J, Ferreira BI, Cigudosa JC, Salido M, Barranco C, Serrano S, Dummer R, Sole F, Pujol RM, Espinet B. Primary Cutaneous CD30+ Anaplastic Large-Cell Lymphomas Show a Heterogeneous Genomic Profile: An Oligonucleotide ArrayCGH Approach. J INVEST DERMATOL. 131:269-271. I.F.: 6.27.

7 Martin-Guerrero I, Enjuanes A, Richter J, Ammerpohl O, Colomer D, Ardanaz M, Marco F, Salas A, Campo E, Siebert R, Garcia-Orad A. A Putative «hepitype» in the ATM Gene Associated with Chronic Lymphocytic Leukemia Risk. GENE CHROMOSOME CANC. 50:887-895. I.F.: 3.99.

8 Gutierrez-Garcia G, Garcia-Herrera A, Cardesa T, Martinez A, Villamor N, Ghita G, Martinez-Trillos A, Colomo L, Setoain X, Rodriguez S, Gine E, Campo E, Lopez-Guillermo A. Comparison of four prognostic scores in peripheral T-cell lymphoma. ANN ONCOL. 22:397-404. I.F.: 6.45.

9 Espinet B, Garcia-Herrera A, Gallardo F, Baro C, Salgado R, Servitje O, Estrach T, Colomo L, Romagosa V, Barranco C, Serrano S, Campo E, Pujol RM, Sole F. FOXP1 molecular cytogenetics and protein expression analyses in primary cutaneous large B cell lymphoma, leg-type. HISTOL HISTOPATHOL. 26:213-221. I.F.: 2.50.

10 DeLarrea CF, Martinez-Pozo A, Mercadal S, Garcia A, Gutierrez-Garcia G, Valera A, Ghita G, Colomo L, Gainza E, Villamor N, Nomdedeu B, Estrach T, Montserrat E, Campo E, Lopez-Guillermo A. Initial features and outcome of cutaneous and non-cutaneous primary extranodal follicular lymphoma. BRIT J HAEMATOL. 153:334-340. I.F.: 4.94.

11 Garcia-Herrera A, Song JY, Chuang SS, Villamor N, Colomo L, Pittaluga S, Alvaro T, Rozman M, Gonzalez JD, Arrunategui AM, Fernandez E, Gonzalvo E, Estrach T, Colomer D, Raffeld M, Gaulard P, Campo E, Jaffe ES, Martinez A. Nonhepatosplenic gamma delta T-cell Lymphomas Represent a Spectrum of Aggressive Cytotoxic T-cell Lymphomas With a Mainly Extranodal Presentation. AM J SURG PATHOL. 35:1214-1225. I.F.: 4.11.

12 Mozos A, Roue G, Lopez-Guillermo A, Jares P, Campo E, Colomer D, Martinez A. The Expression of the Endoplasmic Reticulum Stress Sensor BiP/GRP78 Predicts Response to Chemotherapy and Determines the Efficacy of Proteasome Inhibitors in Diffuse Large B-Cell Lymphoma. AM J PATHOL. 179:2601-2610. I.F.: 5.22.

13 Roue G, Perez-Galan P, Mozos A, Lopez-Guerra M, Xargay-Torrent S, Rosich L, Saborit-Villarroya I, Normant E, Campo E, Colomer D. The Hsp90 inhibitor IPI-504 overcomes bortezomib resistance in mantle cell lymphoma in vitro and in vivo by down-regulation of the prosurvival ER chaperone BiP/Grp78. BLOOD. 117:1270-1279. I.F.: 10.56.

14 Xargay-Torrent S, Lopez-Guerra M, Saborit-Villarroya I, Rosich L, Campo E, Roue G, Colomer D. Vorinostat-Induced Apoptosis in Mantle Cell Lymphoma Is Mediated by Acetylation of Proapoptotic BH3-Only Gene Promoters. CLIN CANCER RES. 17:3956-3968. I.F.: 7.34.

15 Pereira A, Nomdedeu M, Aguilar JL, Belkaid M, Carrio A, Cobo F, Costa D, Rozman M, Sanz C, Nomdedeu B. Transfusion intensity, not the cumulative red blood cell transfusion burden, determines the prognosis of patients with myelodysplastic syndrome on chronic transfusion support. AM J HEMATOL. 86:245-250. I.F.: 3.58.

16 Nomdedeu J, Bussaglia E, Villamor N, Martinez C, Esteve J, Tormo M, Estivill C, Queipo MP, Guardia R, Carricondo M, Hoyos M, Llorente A, Junca J, Gallart M, Domingo A, Bargay J, Mascaro M, Moraleda JM, Florensa L, Ribera JM, Gallardo D, Brunet S, Aventin A, Sierra J. Immunophenotype of acute myeloid leukemia with NPM mutations: Prognostic impact of the leukemic compartment size. LEUKEMIA RES. 35:163-168. I.F.: 2.56.

17 Maffioli M, Camos M, Gaya A, Hernandez-Boluda JC, Alvarez-Larran A, Domingo A, Granell M, Guillem V, Vallansot R, Costa D, Bellosillo B, Colomer D, Cervantes F. Correlation between genetic polymorphisms of the hOCT1 and MDR1 genes and the response to imatinib in patients newly diagnosed with chronic-phase chronic myeloid leukemia. LEUKEMIA RES. 35:1014-1019. I.F.: 2.56.

18 Barragan E, Montesinos P, Camos M, Gonzalez M, Calasanz MJ, Roman-Gomez J, Gomez-Casares MT, Ayala R, Lopez J, Fuster O, Colomer D, Chillon C, Larrayoz MJ, Sanchez-Godoy P, Gonzalez-Campos J, Manso F, Amador ML, Vellenga E, Lowenberg B, Sanz MA. Prognostic value of FLT3 mutations in patients with acute promyelocytic leukemia treated with all-trans retinoic acid and anthracycline monochemotherapy. HAEMATOL-HEMATOL J. 96:1470-1477. I.F.: 6.53.

19 Olsen EA, Whittaker S, Kim YH, Duvic M, Prince HM, Lessin SR, Wood GS, Willemze R, Demierre MF, Pimpinelli N, Bernengo MG, Ortiz-Romero PL, Bagot M, Estrach T, Guitart J, Knobler R, Sanches JA, Iwatsuki K, Sugaya M, Dummer R, Pittelkow M, Hoppe R, Parker S, Geskin L, Pinter-Brown L, Girardi M, Burg G, Ranki A, Vermeer M, Horwitz S, Heald P, Rosen S, Cerroni L, Dreno B, Vonderheid EC. Clinical End Points and Response Criteria in Mycosis Fungoides and Sezary Syndrome: A Consensus Statement of the International Society for Cutaneous Lymphomas, the United States Cutaneous Lymphoma Consortium, and the Cutaneous Lymphoma Task Force. J CLIN ONCOL. 29:2598-2560. I.F.: 18.97.

20 Florensa L, Navarro JT, Vila MEP, Domingo A, DeLaBanda E, Rozman M, Camos M, Milla F, Perea G, Alonso E, Ayats R, Aventin A, Cabezudo E, Espinet B, Merino A, Romero P, Sanchez C, Tuset E, Sole F, Feliu E, Fernandez C, Gallart M, Vallespi T, Woessner S. Persistent polyclonal B-cell lymphocytosis: study of 35 cases. MED CLIN-BARCELONA. 136:565-573. I.F.: 1.41.

REVIEWS
I.F.: 14.18

1 Dreyling M, Kluin-Nelemans HC, Bea S, Hartmann E, Salaverria I, Hutter G, Perez-Galan P, Roue G, Pott C, LeGouill S, Cortelazzo S, Rule S, Hess G, Zaja F, Vitolo U, Szymczyk M, Walewski J, Ribrag V, Unterhalt M, Hermine O, Hoster E. Update on the molecular pathogenesis and clinical treatment of mantle cell lymphoma: report of the 10th annual conference of the European Mantle Cell Lymphoma Network. LEUKEMIA LYMPHOMA. 52:2226-2236. I.F.: 2.49.

2 Kempf W, Pfaltz K, Vermeer MH, Cozzio A, Ortiz-Romero PL, Bagot M, Olsen E, Kim YH, Dummer R, Pimpinelli N, Whittaker S, Hodak E, Cerroni L, Berti E, Horwitz S, Prince HM, Guitart J, Estrach T, Sanches JA, Duvic M, Ranki A, Dreno B, Ostheeren-Michaelis S, Knobler R, Wood G, Willemze R. EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma. BLOOD. 118:4024-4035. I.F.: 10.56.

3 Fernandez-Calotti PX, Colomer D, Pastor-Anglada M. Translocation of nucleoside analogs across the plasma membrane in hematologic malignancies. NUCLEOS NUCLEOT NUCL. 30:1324-1340. I.F.: 1.13.

EDITORIALS
I.F.: 2.56

1 Nomdedeu M, Maffioli M, Calvo X, Martinez-Trillos A, Baumann T, Diaz-Beya M, Aguilar JL, Rozman M, Costa D, Esteve J, Cervantes F, Colomer D, Nomdedeu B. Efficacy of lenalidomide in a patient with myelodysplastic syndrome with isolated del(5q) and JAK2(V617F) mutation. LEUKEMIA RES. 35:1276-1278. I.F.: 2.56.

GRANTS FOR RESEARCH IN PROGRESS

Colomer D. Red temática de investigación cooperativa de cáncer. Sponsored by: Ministerio Sanidad y Consumo, RD06/0020/0014. Duration: 01/01/2007-31/12/2012.

Vives J. European Reference Network of Expert Centres in Rare Anaemias. Sponsored by: European Commission- Executive Agency for Health and Consumers, 2008 12 10. Duration: 01/06/2009-04/07/2012.

Colomer D. Dianes terapèutiques i noves tècniques diagnòstiques en neoplasies limfoides. Sponsored by: Generalitat de Catalunya, 2009_SGR_967. Duration: 15/09/2009-31/12/2013.

Roue G. Identificación de nuevas dianas terapéuticas para mejorar la actividad del velcade en el linfoma de células del manto. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0060. Duration: 01/01/2010-31/12/2012.

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 Educación, SAF2009_09503. Duration: 01/01/2010-31/12/2012.

Vives J. 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: 14/12/2010-13/12/2013.

Vives J. 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: 01/01/2011-31/12/2013.

DOCTORAL THESES

Estrach MT. Descripción y evaluación de los parámetros y patrones dermatoscópicos ede las lesiones cutáneas no melanocíticas y su diagnóstico diferencial con el melanoma. PhD student: Pedro Zaballos Diego.

AREA 5

Oncology and haematology

Hemotherapy - hemostasis

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Antonio Ordinas (Hospital Clínic)
Arturo Pereira (Hospital Clínic)
Juan Carles Reverter (Hospital Clínic)
Cristina Ch. Sanz (Hospital Clínic)
M. Dolors Tàssies (Hospital Clínic)
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Cristina Aresté (JAEDOC-CSIC)
Eduardo Arellano Rodrigo (Hospital Clínic)

TEAM INVOLVED IN:

Red HERACLES de investigación cardiovascular

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. Development and evaluation of the efficacy of synthetic platelet substitutes.
6. 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 clotting factor concentrates potential to reverse the anticoagulant action of the new oral antithrombotic agents

PUBLICATIONS

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	84.32	20	10	4
2010	93.91	22	8	6
2011	94.11	22	9	10

ORIGINALS
I.F.: 94.11

1 Cid J, Carbasse G, Pereira A, Sanz C, Mazzara R, Escolar G, Lozano M. Platelet transfusions from D+ donors to D-patients: a 10-year follow-up study of 1014 patients. TRANSFUSION. 51:1163-1169. I.F.: 3.30.

2 Sanchez-Palomino S, Massanella M, Carrillo J, Garcia A, Garcia F, Gonzalez N, Merino A, Alcami J, Bofill M, Yuste E, Gatell JM, Clotet B, Blanco J. A cell-to-cell HIV transfer assay identifies humoral responses with broad neutralization activity. VACCINE. 29:5250-5259. I.F.: 3.57.

3 Ferrer G, Hodgson K, Pereira A, Juan M, Elena M, Colomer D, Roue G, Aymerich M, Baumann T, Montserrat E, Moreno C. Combined analysis of levels of serum B-cell activating factor and a proliferation-inducing ligand as predictor of disease progression in patients with chronic lymphocytic leukemia. LEUKEMIA LYMPHOMA. 52:2064-2068. I.F.: 2.49.

4 Roque M, Sitges M, Sala J, Delgado V, Morales M, Marrugat J, Vila J, Subirana I, Tassies D, Reverter JC, Castro M, Duran M. Effects of Raloxifene on Endothelial Function and Hemostasis in Women With Ischemic Heart Disease. REV ESP CARDIOL. 64:572-578. I.F.: 2.16.

5 Freixa X, Masotti M, Palomo M, Diaz-Ricart M, Escolar G, Guasch E, Regueiro A, Jimenez M, Betriu A, Heras M. Endothelin-1 levels predict endothelial progenitor cell mobilization after acute myocardial infarction. MICROVASC RES. 82:177-181. I.F.: 2.39.

6 Gimenez M, Gilabert R, Monteagudo J, Alonso A, Casamitjana R, Pare C, Conget I. Repeated Episodes of Hypoglycemia as a Potential Aggravating Factor for Preclinical Atherosclerosis in Subjects With Type 1 Diabetes. DIABETES CARE. 34:198-203. I.F.: 7.14.

7 Guasch E, Sionis A, Reverter JC, Andrea R, Loma-Osorio P, Freixa X, Heras M. Safety issues of adjunctive clopidogrel in patients discharged after percutaneous coronary intervention with stent placement and requiring oral anticoagulation. INT J CARDIOL. 146:E1-E4. I.F.: 6.80.

8 Martinez-Zamora MA, Creus M, Tassies D, Reverter JC, Civico S, Carmona F, Balasch J. Reduced plasma fibrinolytic potential in patients with recurrent implantation failure after IVF and embryo transfer. HUM REPROD. 26:510-516. I.F.: 4.36.

9 LaMura V, Reverter JC, Flores-Arroyo A, Raffa S, Reverter E, Seijo S, Abraldes JG, Bosch J, Garcia-Pagan JC. Von Willebrand factor levels predict clinical outcome in patients with cirrhosis and portal hypertension. GUT. 60:1133-1138. I.F.: 10.61.

10 Hanzu FA, Palomo M, Kalko SG, Parrizas M, Garaulet M, Escolar G, Gomis R, Diaz-Ricart M. Translational evidence of endothelial damage in obese individuals: inflammatory and prothrombotic responses. J THROMB HAEMOST. 9:1236-1245. I.F.: 5.44.

11 Serra-Millas M, Lopez-Vilchez I, Navarro V, Galan AM, Escolar G, Penades R, Catalan R, Fananas L, Arias B, Gasto C. Changes in plasma and platelet BDNF levels induced by S-citalopram in major depression. PSYCHOPHARMACOLOGY. 216:1-8. I.F.: 3.82.

12 Pereira A, Nomdedeu M, Aguilar JL, Belkaid M, Carrio A, Cobo F, Costa D, Rozman M, Sanz C, Nomdedeu B. Transfusion intensity, not the cumulative red blood cell transfusion burden, determines the prognosis of patients with myelodysplastic syndrome on chronic transfusion support. AM J HEMATOL. 86:245-250. I.F.: 3.58.

13 Palomo M, Diaz-Ricart M, Rovira M, Escolar G, Carreras E. Defibrotide Prevents the Activation of Macrovascular and Microvascular Endothelia Caused by Soluble Factors Released to Blood by Autologous Hematopoietic Stem Cell Transplantation. BIOL BLOOD MARROW TR. 17:497-506. I.F.: 3.28.

14 Merino A, DeLarrea CF, Blade J. Cytoplasmic inclusions in leukocytes associated to cryoglobulinemia and IgG-kappa monoclonal gammapathy of undetermined significance. EUR J HAEMATOL. 86:550-550. I.F.: 2.79.

15 Florensa L, Navarro JT, Vila MEP, Domingo A, DeLaBanda E, Rozman M, Camos M, Milla F, Perea G, Alonso E, Ayats R, Aventin A, Cabezudo E, Espinet B, Merino A, Romero P, Sanchez C, Tuset E, Sole F, Feliu E, Fernandez C, Gallart M, Vallespi T, Woessner S. Persistent polyclonal B-cell lymphocytosis: study of 35 cases. MED CLIN-BARCELONA. 136:565-573. I.F.: 1.41.

16 Heddle NM, Wu C, Vassallo R, Carey P, Arnold D, Lozano M, Pavenski K, Sweeney J, Stanworth S, Liu Y, Traore A, Barty R, Tinmouth A. Adjudicating bleeding events in a platelet dose study: impact on outcome results and challenges. TRANSFUSION. 51:2304-2310. I.F.: 3.30.

17 Hurtado B, Munoz X, Recarte-Pelz P, Garcia N, Luque A, Krupinski J, Sala N, DeFrutos PG. Expression of the vitamin K-dependent proteins GAS6 and protein S and the TAM receptor tyrosine kinases in human atherosclerotic carotid plaques. THROMB HAEMOSTASIS. 105:873-882. I.F.: 4.70.

18 Pinazo MJ, Tassies D, Munoz J, Fisa R, Posada ED, Monteagudo J, Ayala E, Gallego M, Reverter JC, Gascon J. Hypercoagulability biomarkers in Trypanosoma cruzi-infected patients. THROMB HAEMOSTASIS. 106:617-623. I.F.: 4.70.

19 Galan A, Lozano M, Molina P, Navalon F, Marschner S, Goodrich R, Escolar G. Impact of pathogen reduction technology and storage in platelet additive solutions on platelet function. TRANSFUSION. 51:808-815. I.F.: 3.30.

20 Font C, Farrus B, Vidal L, Caralt TM, Visa L, Mellado B, Tassies D, Monteagudo J, Reverter JC, Gascon P. Incidental versus symptomatic venous thrombosis in cancer: a prospective observational study of 340 consecutive patients. ANN ONCOL. 22:2101-2106. I.F.: 6.45.

21 Lopez-Vilchez I, Hedner U, Altisent C, Diaz-Ricart M, Escolar G, Galan AM. Redistribution and Hemostatic Action of Recombinant Activated Factor VII Associated with Platelets. AM J PATHOL. 178:2938-2948. I.F.: 5.22.

22 Bosch MA, Contreras E, Madoz P, Ortiz P, Pereira A, Pujol MM. The epidemiology of blood component transfusion in Catalonia, Northeastern Spain. TRANSFUSION. 51:105-116. I.F.: 3.30.

REVIEWS
I.F.: 26.11

1 Font C, Vidal L, Espinosa G, Tassies D, Monteagudo J, Farrus B, Visa L, Cervera R, Gascon P, Reverter JC. Solid cancer, antiphospholipid antibodies, and venous thromboembolism. AUTOIMMUN REV. 10:222-227. I.F.: 6.56.

2 Pons-Estel GJ, Salerni GE, Serrano RM, Gomez-Puerta JA, Plasin MA, Aldasoro E, Lozano M, Cid J, Cervera R, Espinosa G. Therapeutic plasma exchange for the management of refractory systemic autoimmune diseases: Report of 31 cases and review of the literature. AUTOIMMUN REV. 10:679-684. I.F.: 6.56.

3 Carreras E, Diaz-Ricart M. The role of the endothelium in the short-term complications of hematopoietic SCT. BONE MARROW TRANSPL. 46:1495-1502. I.F.: 3.66.

4 Cervantes F, Pereira A. Advances in the understanding and management of primary myelofibrosis. CURR OPIN ONCOL. 23:665-671. I.F.: 4.39.

5 Hodgson K, Ferrer G, Pereira A, Moreno C, Montserrat E. Autoimmune cytopenia in chronic lymphocytic leukaemia: diagnosis and treatment. BRIT J HAEMATOL. 154:14-22. I.F.: 4.94.

GRANTS FOR RESEARCH IN PROGRESS

Reverter JC. Cáncer y Tromboembolismo: Importancia de la generación de trombina relacionada con las micropartículas procoagulantes circulantes y los polimorfirmos de las mismas en el desarrollo de trombosis en los pacientes de cáncer. Sponsored by: Ministerio Sanidad y Consumo, PI070387. Duration: 26/11/2007-31/10/2011.

Galan A. Desarrollo de preparaciones con actividad hemostática como alternativa a la transfusión plaquetaria y al tratamiento procoagulante. Sponsored by: Ministerio de Educación y Ciencia, PET2007-0169. Duration: 12/09/2008-28/02/2011.

Escolar G. Red HERACLES: Determinantes genéticos y ambientales de la disfunción vascular. Sponsored by: Instituto de Salud Carlos III, RD06/0009/1003. Duration: 29/02/2008-31/12/2012.

Escolar G. Desarrollo de modelos de coagulopatía dilucional y evaluación comparativa de eficacia correctora con distintos concentrados de factores de la coagulación. Sponsored by: Ministerio de Ciencia e Innovación, PET2008-0231. Duration: 01/03/2009-28/02/2011.

García P. Thrombus stabilization as therapeutic target: from in vitro studies to animal models. Sponsored by: Fundació Marató de TV3. Duration: 01/01/2009-31/12/2011.

Galan A. El sistema serotoninérgico: una conexión entre los mecanismos de la depresión mayor, la inflamación y el riesgo cardiovascular. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/0664. Duration: 01/01/2010-31/12/2012.

Escolar G. Papel de Los receptores ligados a proteína G y los mecanismos de señalización mediados por kinasas en la internalización y expresión del factor tisular por plaquetas: Implicaciones en la trombogénesis. Sponsored by: Ministerio de Educación, SAF2009_10365. Duration: 01/01/2010-31/12/2012.

García P. Papel regulador del sistema GAS6-PROS/TAM en la respuesta a la inflamación de linfocitos y plaquetas. Sponsored by: Plan Nacional, BFU2010-22185. Duration: 01/01/2011-30/06/2012.

DOCTORAL THESES

Diaz-Ricart M. Molecular determinants of adipose tissue crosstalks. PhD student: Felicia Alexandra Hanzu.

Diaz-Ricart M, Escolar G. Biomarcadores precoces de la hiperactividad plaquetaria: particularidades de los mecanismos de contracción y secreción en équidos. PhD student: Lucas Brunso Welker.

AREA 5

Oncology and haematology

Molecular and translational oncology

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TEAM INVOLVED IN:

STRATEGIC OBJECTIVES

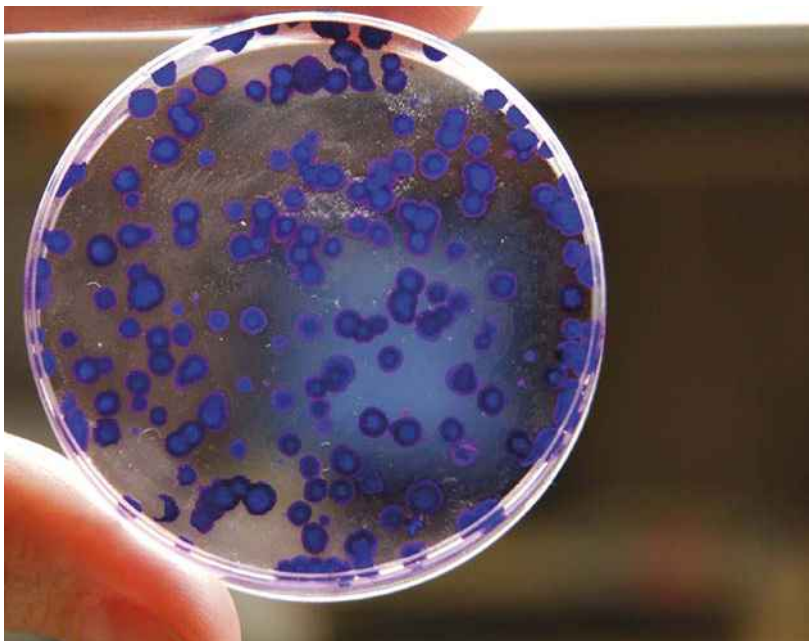
The strategic objectives of the laboratory are centered in three fields:

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 (Principal investigator: Juan J. Grau. Collaborators: Carmen Muñoz; Miguel Caballero; Mariano Monzó).
   - **1.5.** Electrochemotherapy in solid tumors. Study of electroporation. (Principal investigator: Juan J. Grau. Collaborators: Carmen Muñoz; Miguel Caballero.
   - **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 (IDIBAPS: Joan Maurel; Mercedes Marín. Germans Trias i Pujol Hospital: Albert Abad; Eva Martínez; Anna Martínez).
   - **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 (IDIBAPS: Joan Maurel; Pere Gascón; Salvador Navarro; David Fuster; Rosa Miquel. University of Barcelona: Adela Mazo. CETIR: Yolanda González; Ignasi Carrió).
   - **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 (Dra. Vanessa Almendro, Mario Manzino, Elisabet Ametller, Pere Gascón).
   - **2.2.** Interaction between GPCRs and RTKs (Vanessa Almendro; Elisabet Ametller; Susana Garcia).
   - **2.3.** 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.** 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).



PUBLICATIONS

ORIGINALS
I.F.: 263.85

1 Casas F, Vinolas N, Ferrer F, Agusti C, Sanchez M, Gimferrer JM, Lomena F, Campayo M, Jeremic B. Long-Term Results of a Phase II Trial of Induction Paclitaxel-Carboplatin Followed by Concurrent Radiation Therapy and Weekly Paclitaxel and Consolidation Paclitaxel-Carboplatin in Stage III Non-small Cell Lung Cancer. J THORAC ONCOL. 6:79-85. I.F.: 4.04.

2 Campayo M, Navarro A, Vinolas N, Tejero R, Munoz C, Diaz T, Marrades R, Cabanas ML, Gimferrer JM, Gascon P, Ramirez J, Monzo M. A Dual Role for KRT81: A miR-SNP Associated with Recurrence in Non-Small-Cell Lung Cancer and a Novel Marker of Squamous Cell Lung Carcinoma. PLOS ONE. 6:-. I.F.: 4.41.

3 Gomez-Caro A, Garcia S, Reguart N, Cladellas E, Arguis P, Sanchez M, Gimferrer JM. Determining the appropriate sleeve lobectomy versus pneumonectomy ratio in central non-small cell lung cancer patients: an audit of an aggressive policy of pneumonectomy avoidance. EUR J CARDIO-THORAC. 39:352-359. I.F.: 2.29.

4 Navarro A, Diaz T, Gallardo E, Vinolas N, Marrades RM, Gel B, Campayo M, Quera A, Bandres E, Garcia-Foncillas J, Ramirez J, Monzo M. Prognostic Implications of miR-16 Expression Levels in Resected Non-Small-Cell Lung Cancer. J SURG ONCOL. 103:411-415. I.F.: 2.43.

5 Campayo M, Vinolas N, Navarro A, Carcereny E, Casas F, Gel B, Diaz T, Gimferrer JM, Marrades RM, Ramirez J, Monzo M. Single Nucleotide Polymorphisms in Tobacco Metabolism and DNA Repair Genes and Prognosis in Resected Non-Small-Cell Lung Cancer. J SURG RES. 167:E5-E12. I.F.: 2.24.

6 Fernandez-Esparrach G, Ayuso-Colella JR, Sendino O, Pages M, Cuatrecasas M, Pellise M, Maurel J, Ayuso-Colella C, Gonzalez-Suarez B, Llach J, Castells A, Gines A. EUS and magnetic resonance imaging in the staging of rectal cancer: a prospective and comparative study. GASTROINTEST ENDOSC. 74:347-354. I.F.: 5.65.

7 Caldelari ACA, Miquel R, Bombi JA, Gines A, Fernandez-Esparrach G, Ayuso JR, Maurel J, Feu F, Castells A, Fernandez-Cruz L, Navarro S. Malignancy predictive factors in pancreatic intraductal papillary mucinous neoplasm. MED CLIN-BARCELONA. 137:631-636. I.F.: 1.41.

8 Perez-Torras S, Vidal-Pla A, Miquel R, Almendro V, Fernandez-Cruz L, Navarro S, Maurel J, Carbo N, Gascon P, Mazo A. Characterization of human pancreatic orthotopic tumor xenografts suitable for drug screening. CELL ONCOL. 34:511-521. I.F.: 3.18.

9 Horndler C, Gallego R, Garcia-Albeniz X, Alonso-Espinaco V, Alonso V, Escudero P, Jimeno M, Ortego J, Codony-Servat J, Fernandez-Martos C, Calatrava A, Marin-Aguilera M, Munoz J, Castellvi-Bel S, Castells A, Rubini M, Gascon P, Maurel J. Co-expression of matrix metalloproteinase-7 (MMP-7) and phosphorylated insulin growth factor receptor I (pIGF-1R) correlates with poor prognosis in patients with wild-type KRAS treated with cetuximab or panitumumab A GEMCAD study. CANCER BIOL THER. 11:177-183. I.F.: 2.91.

10 Garcia-Albeniz X, Pericay C, Alonso-Espinaco V, Alonso V, Escudero P, Fernandez-Martos C, Gallego R, Gascon P, Castellvi-Bel S, Maurel J. Serum matrilysin correlates with poor survival independently of KRAS and BRAF status in refractory advanced colorectal cancer patients treated with irinotecan plus cetuximab. TUMOR BIOL. 32:417-424. I.F.: 2.03.

11 Fuster D, Ayuso JR, Poveda A, Cubedo R, Casado A, Martinez-Trufero J, Lopez-Pousa A, DelMuro XG, Lomena F, Maurel J, Pons F. Value of FDG-PET for monitoring treatment response in patients with advanced GIST refractory to high-dose imatinib. A multicenter GEIS study. Q J NUCL MED MOL IM. 55:680-687. I.F.: 2.54.

12 Verger E, Valduvieco I, Caral L, Pujol T, Ribalta T, Vinolas N, Boget T, Oleaga L, Blanco Y, Graus F. Does gender matter in glioblastoma?. CLIN TRANSL ONCOL. 13:737-741. I.F.: 1.25.

13 Brell M, Castaner S, Pujol-Farre T, Boluda S, Ribalta T, Bruna J, Martinez M, Verger E, Villa S, Vinolas N, Gil M, Graus F, Tortosa-Moreno A. Implication of radiological pattern in the prognosis of oligodendroglial tumors: correlation with genetic profile. REV NEUROLOGIA. 52:465-471. I.F.: 1.22.

14 Barrett JH, Iles MM, Harland M, Taylor JC, Aitken JF, Andresen PA, Akslen LA, Armstrong BK, Avril MF, Azizi E, Bakker B, Bergman W, Bianchi-Scarra G, Bressac-DePaillerets B, Calista D, Cannon-Albright LA, Corda E, Cust AE, Debniak T, Duffy D, Dunning AM, Easton DF, Friedman E, Galan P, Ghiorzo P, Giles GG, Hansson J, Hocevar M, Hoiom V, Hopper JL, Ingvar C, Janssen B, Jenkins MA, Jonsson G, Kefford RF, Landi G, Landi MT, Lang J, Lubinski J, Mackie R, Malvehy J, Martin NG, Molven A,

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	190.89	27	18	6
2010	131.60	15	10	2
2011	236.85	31	19	6

Montgomery GW, VanNieuwpoort FA, Novakovic S, Olsson H, Pastorino L, Puig S, Puig-Butille JA, Randerson-Moor J, Snowden H, Tuominen R, Vanbelle P, VanDerStoep N, Whiteman DC, Zelenika D, Han JL, Fang SY, Lee JE, Wei QY, Lathrop GM, Gillanders EM, Brown KM, Goldstein AM, Kanetsky PA, Mann GJ, Macgregor S, Elder DE, Amos CI, Hayward NK, Gruis NA, Demenais F, Bishop JAN, Bishop DT. Genome-wide association study identifies three new melanoma susceptibility loci. NAT GENET. 43:1108-U98. I.F.: 36.38.

15 Font C, Farrus B, Vidal L, Caralt TM, Visa L, Mellado B, Tassies D, Monteagudo J, Reverter JC, Gascon P. Incidental versus symptomatic venous thrombosis in cancer: a prospective observational study of 340 consecutive patients. ANN ONCOL. 22:2101-2106. I.F.: 6.45.

16 Casado E, Garcia VM, Sanchez JJ, Blanco M, Maurel J, Feliu J, Fernandez-Martos C, DeCastro J, Castelo B, Belda-Iniesta C, Sereno M, Sanchez-Llamas B, Burgos E, Garcia-Cabezas MA, Mancenido N, Miquel R, Garcia-Olmo D, Gonzalez-Baron M, Cejas P. A Combined Strategy of SAGE and Quantitative PCR Provides a 13-Gene Signature that Predicts Preoperative Chemoradiotherapy Response and Outcome in Rectal Cancer. CLIN CANCER RES. 17:4145-4154. I.F.: 7.34.

17 Porta R, Sanchez-Torres JM, Paz-Ares L, Massuti B, Reguart N, Mayo C, Lianes P, Queralt C, Guillem V, Salinas P, Catot S, Isla D, Pradas A, Gurpide A, DeCastro J, Polo E, Puig T, Taron M, Colomer R, Rosell R. Brain metastases from lung cancer responding to erlotinib: the importance of EGFR mutation. EUR RESPIR J. 37:624-631. I.F.: 5.92.

18 VanCutsem E, Kohne CH, Lang I, Folprecht G, Nowacki MP, Cascinu S, Shchepotin I, Maurel J, Cunningham D, Tejpar S, Schlichting M, Zubel A, Celik I, Rougier P, Ciardiello F. Cetuximab Plus Irinotecan, Fluorouracil, and Leucovorin As First-Line Treatment for Metastatic Colorectal Cancer: Updated Analysis of Overall Survival According to Tumor KRAS and BRAF Mutation Status. J CLIN ONCOL. 29:2011-2019. I.F.: 18.97.

19 Ametller E, Garcia-Recio S, Pastor-Arroyo EM, Callejo G, Carbo N, Gascon P, Almendro V. Differential regulation of MMP7 in colon cancer cells resistant and sensitive to oxaliplatin-induced cell death. CANCER BIOL THER. 11:4-13. I.F.: 2.91.

20 Almendro V, Fuster G. Heterogeneity of breast cancer: etiology and clinical relevance. CLIN TRANSL ONCOL. 13:767-773. I.F.: 1.25.

21 Robert C, Thomas L, Bondarenko I, O'day S, Weber J, Garbe C, Lebbe C, Baurain JF, Testori A, Grob JJ, Davidson N, Richards J, Maio M, Hauschild A, Miller WH, Gascon P, Lotem M, Harmankaya K, Ibrahim R, Francis S, Chen TT, Humphrey R, Hoos A, Wolchok JD. Ipilimumab plus Dacarbazine for Previously Untreated Metastatic Melanoma. NEW ENGL J MED. 364:2517-2526. I.F.: 53.49.

22 Gascon P, Almenarez J, Artal A, Camps C, Firvida JL, Garrido P, Larriba JLG, Montalar J. Management of lung cancer-associated anaemia: the Spanish Lung Cancer Anaemia Survey (SLCAS). CLIN TRANSL ONCOL. 13:328-334. I.F.: 1.25.

23 Martin M, Roche H, Pinter T, Crown J, Kennedy MJ, Provencher L, Priou F, Eiermann W, Adrover E, Lang I, Ramos M, Latreille J, Jagiello-Gruszfeld A, Pienkowski T, Alba E, Snyder R, Almel S, Rolski J, Munoz M, Moroose R, Hurvitz S, Banos A, Adewoye H, Hei YJ, Lindsay MA, Rupin M, Cabaribere D, Lemmerick Y, Mackey JR. Motesanib, or open-label bevacizumab, in combination with paclitaxel, as first-line treatment for HER2-negative locally recurrent or metastatic breast cancer: a phase 2, randomised, double-blind, placebo-controlled study. LANCET ONCOL. 12:369-376. I.F.: 17.76.

24 Martin M, Sanchez-Rovira P, Munoz M, Baena-Canada JM, Mel JR, Margeli M, Ramos M, Martinez E, Garcia-Saenz JA, Casado A, Jaen AM, Gonzalez-Farre X, Escudero MJ, Rodriguez-Martin C, Carrasco E. Pegylated liposomal doxorubicin in combination with cyclophosphamide and trastuzumab in HER2-positive metastatic breast cancer patients: efficacy and cardiac safety from the GEICAM/2004-05 study. ANN ONCOL. 22:2591-2596. I.F.: 6.45.

25 Bellmunt J, Gonzalez-Larriba JL, Prior C, Maroto P, Carles J, Castellano D, Mellado B, Gallardo E, Perez-Gracia JL, Aguilar G, Villanueva X, Albanell J, Calvo A. Phase II study of sunitinib as first-line treatment of urothelial cancer patients ineligible to receive cisplatin-based chemotherapy: baseline interleukin-8 and tumor contrast enhancement as potential predictive factors of activity. ANN ONCOL. 22:2646-2653. I.F.: 6.45.

26 Rosell R, Molina MA, Costa C, Simonetti S, Gimenez-Capitan A, Bertran-Alamillo J, Mayo C, Moran T, Mendez P, Cardenal F, Isla D, Provencio M, Cobo M, Insa A, Garcia-Campelo R, Reguart N, Majem M, Viteri S, Carcereny E, Porta R, Massuti B, Queralt C, DeAguirre I, Sanchez

JM, Sanchez-Ronco M, Mate JL, Ariza A, Benlloch S, Sanchez JJ, Bivona TG, Sawyers CL, Taron M. Pretreatment EGFR T790M Mutation and BRCA1 mRNA Expression in Erlotinib-Treated Advanced Non-Small-Cell Lung Cancer Patients with EGFR Mutations. CLIN CANCER RES. 17:1160-1168. I.F.: 7.34.

27 Baro E, Carulla J, Cassinello J, Colomer R, Mata JG, Gascon P, Gasquet JA, Rodriguez CA, Valentin V. Psychometric properties of the Perform Questionnaire: a brief scale for assessing patient perceptions of fatigue in cancer. SUPPORT CARE CANCER. 19:657-666. I.F.: 2.06.

28 Garcia-Del-Muro X, Lopez-Pousa A, Maurel J, Martin J, Martinez-Trufero J, Casado A, Gomez-Espana A, Fra J, Cruz J, Poveda A, Meana A, Pericay C, Cubedo R, Rubio J, DeJuan A, Lainez N, Carrasco JA, DeAndres R, Buesa JM. Randomized Phase II Study Comparing Gemcitabine Plus Dacarbazine Versus Dacarbazine Alone in Patients With Previously Treated Soft Tissue Sarcoma: A Spanish Group for Research on Sarcomas Study. J CLIN ONCOL. 29:2528-2533. I.F.: 18.97.

29 Garcia-Donas J, Esteban E, Leandro-Garcia LJ, Castellano DE, DelAlba AG, Climent MA, Arranz JA, Gallardo E, Puente J, Bellmunt J, Mellado B, Martinez E, Moreno F, Font A, Robledo M, Rodriguez-Antona C. Single nucleotide polymorphism associations with response and toxic effects in patients with advanced renal-cell carcinoma treated with first-line sunitinib: a multicentre, observational, prospective study. LANCET ONCOL. 12:1143-1150. I.F.: 17.76.

30 Vinolas N, Provencio M, Reguart N, Cardenal F, Alberola V, Sanchez-Torres JM, Baron FJ, Cobo M, Maestu I, Moreno I, Mesia C, Izquierdo A, Felip E, Lopez-Brea M, Marquez A, Sanchez-Ronco M, Taron M, Santarpia MC, Rosell R. Single nucleotide polymorphisms in MDR1 gen correlates with outcome in advanced non-small-cell lung cancer patients treated with cisplatin plus vinorelbine. LUNG CANCER. 71:191-198. I.F.: 3.36.

31 Marotta LLC, Almendro V, Marusyk A, Shipitsin M, Schemme J, Walker SR, Bloushtain-Qimron N, Kim JJ, Choudhury SA, Maruyama R, Wu Z, Gonen M, Mulvey LA, Bessarabova MO, Huh SJ, Silver SJ, Kim SY, Park SY, Lee HE, Anderson KS, Richardson AL, Nikolskaya T, Nikolsky Y, Liu XS, Root DE, Hahn WC, Frank DA, Polyak K. The JAK2/STAT3 signaling pathway is required for growth of CD44(+)CD24(-) stem cell-like breast cancer cells in human tumors. J CLIN INVEST. 121:2723-2735. I.F.: 14.15.

REVIEWS
I.F.: 25.83

1 Font C, Vidal L, Espinosa G, Tassies D, Monteagudo J, Farrus B, Visa L, Cervera R, Gascon P, Reverter JC. Solid cancer, antiphospholipid antibodies, and venous thromboembolism. AUTOIMMUN REV. 10:222-227. I.F.: 6.56.

2 Gascon P, Aapro M, Ludwig H, Rosencher N, Turner M, Song MK, Macdonald K, Lee C, Muenzberg M, Abraham I. Background and methodology of MONITOR-GCSF, a pharmaco-epidemiological study of the multi-level determinants, predictors, and clinical outcomes of febrile neutropenia prophylaxis with biosimilar granulocyte-colony stimulating factor filgrastim. CRIT REV ONCOL HEMAT. 77:184-197. I.F.: 4.69.

3 Mancino M, Ametller E, Gascon P, Almendro V. The neuronal influence on tumor progression. BBA-REV CANCER. 1816:105-118. I.F.: 9.89.

4 Gascon P, Aapro M, Ludwig H, Rosencher N, Boccadoro M, Turner M, Macdonald K, Muenzberg M, Abraham I. Update on the MONITOR-GCSF study of biosimilar filgrastim to reduce the incidence of chemotherapy-induced febrile neutropenia in cancer patients: Protocol amendments. CRIT REV ONCOL HEMAT. 77:198-200. I.F.: 4.69.

EDITORIALS
I.F.: 1.41

1 Grau JJ, Caballero M, Tagliapetra A. New antitarget antineoplastic drugs. Clinical indications in the treatment of cancer. MED CLIN-BARCELONA. 137:370-376. I.F.: 1.41.

CLINICAL GUIDELINES
I.F.: 5.16

1 Maurel J, Fernandez-Martos C, Feliu J, Isla D. SEOM clinical guidelines for the treatment of anal cancer. CLIN TRANSL ONCOL. 13:525-527. I.F.: 1.25.

2 Feliu J, Sastre J, Maurel J, Isla D. Hepatocellular and biliary tract carcinomas: SEOM clinical guidelines. CLIN TRANSL ONCOL. 13:536-544. I.F.: 1.25.

3 Munoz AJ, Vinolas N, Cubedo R, Isla D. SEOM guidelines on thrombosis in cancer patients. CLIN TRANSL ONCOL. 13:592-596. I.F.: 1.25.

4 GarciaDelMuro X, Martin J, Maurel J, Cubedo R, Bague S, DeAlava E, Pousa AL, Narvaez JA, Ortiz E, Pomes J, Poveda A, Romasanta LP, Tendero O, Viñals JM, GrupoEspañolDeInvestigacionEnSarcomas (GEIS). Soft tissue sarcomas: clinical practice guidelines. MED CLIN-BARCELONA:-. I.F.: 1.41.

MULTICENTRICS
I.F.: 12.10

1 Arrieta O, Cardona AF, Bramuglia GF, Gallo A, Campos-Parra AD, Serrano S, Castro M, Aviles A, Amorin E, Kirchuk R, Cuello M, Borbolla J, Riemersma O, Becerra H, Rosell R. Genotyping Non-small Cell Lung Cancer (NSCLC) in Latin America. J THORAC ONCOL. 6:1955-1959. I.F.: 4.04.

2 Amos CI, Wang LE, Lee JE, Gershenwald JE, Chen WV, Fang SY, Kosoy R, Zhang MF, Qureshi AA, Vattathil S, Schacherer CW, Gardner JM, Wang YL, Bishop DT, Barrett JH, Macgregor S, Hayward NK, Martin NG, Duffy DL, Mann GJ, Cust A, Hopper J, Brown KM, Grimm EA, Xu YJ, Han YH, Jing KY, Mchugh C, Laurie CC, Doheny KF, Pugh EW, Seldin MF, Han JL, Wei QY. Genome-wide association study identifies novel loci predisposing to cutaneous melanoma. HUM MOL GENET. 20:5012-5023. I.F.: 8.06.

GRANTS FOR RESEARCH IN PROGRESS

Gascon P. Mecanismos de transactivación de los miembros de la familia ERB-B en cáncer de mama: importancia de las neuroquininas y la neurogénesis. Sponsored by: Fondo de Investigaciones Sanitarias de la Seguridad Social (FISS), PI080022. Duration: 01/01/2009-31/12/2011.

Gascon P. Red temática de investigación cooperativa de Cáncer. Sponsored by: Instituto de Salud Carlos III, RED07/0020/2014. Duration: 23/02/2009-31/12/2012.

Grau JJ. Efectividad y seguridad de la electroquimioterapia en el tratamiento de tumores sólidos. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI09/90664. Duration: 01/01/2010-31/12/2011.

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: 01/01/2010-31/12/2012.

Reguart N. Contribución de los fibroblastos asociados a tumores (CAFs) al cáncer de pulmón estudiado con modelos de cultivo celular tridimensionales. Sponsored by: Asociación Española Contra el Cáncer, 10/103. Duration: 22/02/2010-21/02/2012.

Maurel J. Papel de MMP-7 en la transactivación IGF-1R-EGFR y la resistencia intrínseca a los inhibidores de Epidermal Growth Factor Receptor (EGFR) en cáncer colorectal. Sponsored by: Fundación de Investigación Médica Mútua Madrileña, AP75002010. Duration: 17/09/2010-16/09/2011.

DOCTORAL THESES

Vinolas N. Anàlisi de polimorfismes d'una sola base (SNPs) com a factors predictius de recaiguda en pacients amb càncer de pulmó de cèl·lula no petita quirúrgic. PhD student: Marc Campayo.

Vinolas N. Importancia clínica de los microRNAs de la vía de p53 en cáncer de pulmón no microcítico: miR-34ª y miR-16. PhD student: Elena Gallardo Martín.

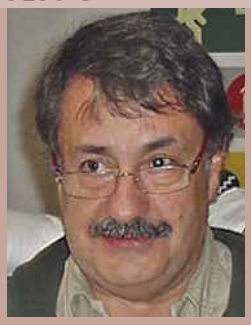
AREA 5

Oncology and haematology

Cell proliferation and signaling

TEAM INVOLVED IN: RTICC

GROUP MEMBERS



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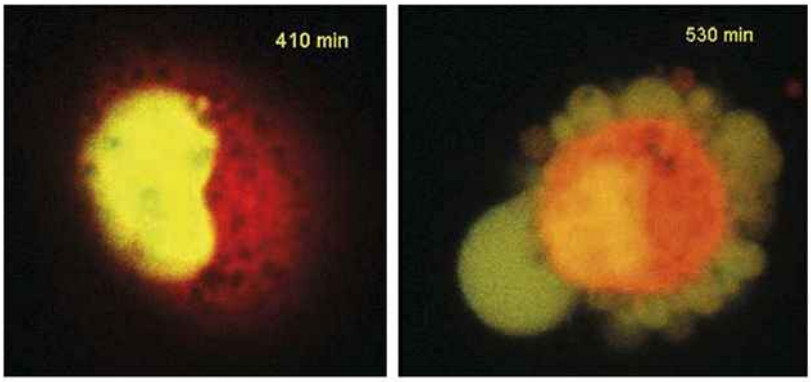

Co-localitzation of p27 (green) and PCAF (red) during apoptosis.

STRATEGIC OBJECTIVES

The general goal of the group is the analysis of the mechanisms involved in cell cycle progression and signaling 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 involved 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 non-polarized 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 cellular processes 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.

For further information:
www.celltrafficbcn.cat

PUBLICATIONS

ORIGINALS
I.F.: 50.95

1 Bosch M, Mari M, Herms A, Fernandez A, Fajardo A, Kassan A, Giralt A, Colell A, Balgoma D, Barbero E, Gonzalez-Moreno E, Matias N, Tebar F, Balsinde J, Camps M, Enrich C, Gross SP, Garcia-Ruiz C, Perez-Navarro E, Fernandez-Checa JC, Pol A. Caveolin-1 Deficiency Causes Cholesterol-Dependent Mitochondrial Dysfunction and Apoptotic Susceptibility. CURR BIOL. 21:681-686. I.F.: 10.03.

2 Bosch M, Mari M, Gross SP, Fernandez-Checa JC, Pol A. Mitochondrial Cholesterol: A Connection Between Caveolin, Metabolism, and Disease. TRAFFIC. 12:1483-1489. I.F.: 5.28.

3 Custodio L, Fernandes E, Escapa AL, Fajardo A, Aligue R, Albericio F, Neng NR, Nogueira JMF, Romano A. Antioxidant and Cytotoxic Activities of Carob Tree Fruit Pulps Are Strongly Influenced by Gender and Cultivar. J AGR FOOD CHEM. 59:7005-7012. I.F.: 2.82.

4 Millour J, DeOlano N, Horimoto Y, Monteiro LJ, Langer JK, Aligue R, Hajji N, Lam EWF. ATM and p53 Regulate FOXM1 Expression via E2F in Breast Cancer Epirubicin Treatment and Resistance. MOL CANCER THER. 10:1046-1058. I.F.: 5.23.

5 Reverter M, Rentero C, DeMuga SV, Alvarez-Guaita A, Mulay V, Cairns R, Wood P, Monastyrskaya K, Pol A, Tebar F, Blasi J, Grewal T, Enrich C. Cholesterol transport from late endosomes to the Golgi regulates t-SNARE trafficking, assembly, and function. MOL BIOL CELL. 22:4108-4123. I.F.: 5.86.

6 Aranda JF, Reglero-Real N, Kremer L, Marcos-Ramiro B, Ruiz-Saenz A, Calvo M, Enrich C, Correas I, Millan J, Alonso MA. MYADM regulates Rac1 targeting to ordered membranes required for cell spreading and migration. MOL BIOL CELL. 22:1252-1262. I.F.: 5.86.

7 Custodio L, Escapa AL, Fernandes E, Fajardo A, Aligue R, Albericio F, Neng N, Nogueira JMF, Romano A. Phytochemical Profile, Antioxidant and Cytotoxic Activities of the Carob Tree (Ceratonia siliqua L.) Germ Flour Extracts. PLANT FOOD HUM NUTR. 66:78-84. I.F.: 2.46.

8 Matito C, Agell N, Sanchez-Tena S, Torres JL, Cascante M. Protective Effect of Structurally Diverse Grape Procyanidin Fractions against UV-Induced Cell Damage and Death. J AGR FOOD CHEM. 59:4489-4495. I.F.: 2.82.

9 Vidal-Quadras M, Gelabert-Baldrich M, Soriano-Castell D, Llado A, Rentero C, Calvo M, Pol A, Enrich C, Tebar F. Rac1 and Calmodulin Interactions Modulate Dynamics of ARF6-Dependent Endocytosis. TRAFFIC. 12:1879-1896. I.F.: 5.28.

10 Wood P, Mulay V, Darabi M, Chan KC, Heeren J, Pol A, Lambert G, Rye KA, Enrich C, Grewal T. Ras/Mitogen-activated Protein Kinase (MAPK) Signaling Modulates Protein Stability and Cell Surface Expression of Scavenger Receptor SR-BI. J BIOL CHEM. 286:23077-23092. I.F.: 5.33.

REVIEWS
I.F.: 8.98

1 Cornely R, Rentero C, Enrich C, Grewal T, Gaus K. Annexin A6 is an Organizer of Membrane Microdomains to Regulate Receptor Localization and Signalling. IUBMB LIFE. 63:1009-1017. I.F.: 4.25.

2 Enrich C, Rentero C, DeMuga SV, Reverter M, Mulay V, Wood P, Koese M, Grewal T. Annexin A6-Linking Ca2+ signaling with cholesterol transport. BBA-MOL CELL RES. 1813:935-947. I.F.: 4.73.

GRANTS FOR RESEARCH IN PROGRESS

Bachs O. Red temática de investigación cooperativa de cáncer. Sponsored by: Ministerio Sanidad y Consumo, RD06/0020/0010. Duration: 01/01/2006-31/12/2011.

Agell N. Relevancia de la fosforilación de K-Ras y de las alteraciones en el Checkpoint de replicación del DNA en la oncogénesis. Sponsored by: Ministerio de Educación, SAF2010-20712. Duration: 01/01/2011-31/12/2013.

Aligué R. La MAP quinasa p38 y la MAPKAP en la señalización de respuesta a estrés y el control del ciclo celular. Sponsored by: Ministerio de Educación, BFU-2009-10778/BMC. Duration: 01/01/2009-31/12/2011.

Bachs O. Papel del regulador del ciclo celular p27Kip1 en la oncogénesis. Sponsored by: Ministerio de Educación, SAF2009- 07769 (GEN). Duration: 01/01/2009-31/12/2012.

Bachs O. Proteored. Sponsored by: Genoma España, SAF2009- 07769 (GEN). Duration: 01/01/2005-31/12/2011.

Bachs O. Proliferació Cel·lular. Sponsored by: Grups de Recerca de la Generalitat de Catalunya, 2009 SGR 1382. Duration: 01/01/2009-31/12/2013.

Enrich C. Ras/MAPK signaling regulates cholesterol efflux. Sponsored by: Fundació la Marató de TV3 ,81110. Duration: 01/01/2009-31/12/2011.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	56.36	10	8	1
2010	41.72	7	7	0
2011	50.95	10	9	0

Enrich C. Endocitosi, tràfic i senyalització. Sponsored by: Grups de Recerca de la Generalitat de Catalunya, 2009 SGR 1526. Duration: 01/01/2009-31/12/2013.

Enrich C. Estudio de l tráfico intracelular de la caveolina, formación de caveolas y la señalización: papel de la annexin A6. Sponsored by: MCINN, BFU2009-10335. Duration: 01/01/2010-31/12/2012.

Enrich C. Ayuda para la organización de la Conferencia Internacional sobre Annexinas. Sponsored by: MICINN, BFU2010-11196-E. Duration: 01/01/2011-31/12/2011.

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 Marató de TV3, PI041315. Duration: 01/01/2010-31/12/2014.

Pol A. Mechanism of Lipid Droplet formation. Sponsored by: MICINN, CONSOLIDER-INGENIO 2010, CSD2009.00016. Duration: 01/01/2009-31/12/2014.

Pol A. Intracellular accumulation of lipids: Role of CAV1, molecular mechanisms and implications on cell proliferation. Sponsored by: MICINN, BFU2008-00345. Duration: 01/01/2008-31/12/2011.

Tebar F. Función de PKCdelta y calmodulina en la regulación de la dinámica del citoesqueleto de actina y del tráfico intracelular del factor de crecimiento epidérmico. Sponsored by: MICINN, BFU2009-13526/BMC. Duration: 01/01/2010-31/12/2012.

Tebar F. Integración funcional del tráfico de membranas, la señalización intracelular y la dinámica del citoesqueleto. Sponsored by: MICINN, BFU2006-26075-E/BMC. Duration: 01/01/2009-31/12/2011.

Enrich C. Creación de la Red Española de Microscopia óptica (REMOA). Sponsored by: Ministerio de Ciencia e Innovación, BIO2010-12435-E. Duration: 01/01/2011-31/12/2012.

Enrich C. Ras signalling and cholesterol efflux from late endosomes. Sponsored by: National Health Medical Research Council of Australia (NHMRC), Project Grant 510294. Duration: 01/01/2008-31/12/2011.

Enrich C. Regulation of EGF receptor signalling. Sponsored by: National Health Medical Research Council of Australia (NHMRC), Project Grant 510293. Duration: 01/01/2008-31/12/2011.

Enrich C. Mechanism of protein secretion and compartment organization. Sponsored by: Consolider -INGENIO 2010, CSD2009-00016. Investigador coordinador: Dr. Vivek Malhotra. Investigador principal Grupo 7: Carlos Enrich. Duration 01/01/2009- 31/12/2013.

DOCTORAL THESES

Bachs O. Evolució del diagnòstic citogenètic prenatal i postnatal amb la implementació de noves tècniques de biologia molecular i la seva repercussió en el consell genètic. PhD student: Mª Carme Morales Peydró.

Bachs O. Implicación de proteinas G y de PKA en la regulación local de la vía de sonic hedgehog en el cilio promario. PhD student: María de las Mercedes Barzi Diéguez.

Pol A. The study of lipid droplets biogenesis. PhD student: Adam Kassan

Bachs O. P27kip1 regula la transcripción de genes implicados en la tumorigénesis. PhD student: Raffaella Pippa.

Agell N. SAPKs en el checkpoint de replicación del DNA. PhD student: Noelia Salvador Marcos.

Pol A. Biogénesis de los cuerpos Lipídicos. PhD student: Elena González Moreno.

Tebar F. Funcionalidad de la unión de calmodulina a RAC 1: Implicaciones en la endocitosis independiente de clatrina. PhD student: Mª Teresa Vidal-Quadras de Soto.

TRANSVERSAL

GROUP FOR RESEARCH IN PRIMARY CARE

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Transversal group for research in primary care

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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. 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 translation research.

In the year 2011, Research in Primary Care has been organized around the CAPSE-GESCLINIC Research Unit, integrated by Dr. Antoni Sisó (Director of the CAPSE_GESCLINIC Unit), Dr. Laura Sebastián (Manager of CAPSE-GESCLINIC), Lluís González (DUE-GESCLINIC), Elena Mañes (DUE-CAPSE), and Narly Benachi (DUE-Clinical Trials-CAPSE).

MAIN LINES OF RESEARCH

- 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

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	6.41	2	0	1
2010	49.85	7	4	2
2011	23.06	5	2	3

ORIGINALS
I.F.: 23.06

1 Benito L, Hoyo J, Montroig A, Fornes B, Fluxa G, Marti D, Pedros M, Siso A, Mont L, Miro O, Coll-Vinent B. Adverse effects of antiarrhythmic drugs in patients with atrial fibrillation in Primary Care. MED CLIN-BARCELONA. 137:241-246. I.F.: 1.41.

2 Riesgo A, Sant E, Benito L, Hoyo J, Miro O, Mont L, Bragulat E, Coll-Vinent B. Sex Differences in the Treatment of Patients With Atrial Fibrillation: Population-Based Study in a Local Health District. REV ESP CARDIOL. 64:233-236. I.F.: 2.16.

3 Falces C, Andrea R, Heras M, Vehi C, Sorribes M, Sanchis L, Cevallos J, Menacho I, Porcar S, Font D, Sabate M, Brugada J. Integration Between Cardiology and Primary Care: Impact on Clinical Practice. REV ESP CARDIOL. 64:564-571. I.F.: 2.16.

4 Cobo E, Cortes J, Ribera JM, Cardellach F, Selva-O'callaghan A, Kostov B, Garcia L, Cirugeda L, Altman DG, Gonzalez JA, Sanchez JA, Miras F, Urrutia A, Fonollosa V, Rey-Joly C, Vilardell M. Effect of using reporting guidelines during peer review on quality of final manuscripts submitted to a biomedical journal: masked randomised trial. BRIT MED J. 343:-. I.F.: 13.47.

5 Mas S, Gasso P, Alvarez S, Ortiz J, Sotoca JM, Francino A, Carne X, Lafuente A. Pharmacogenetic predictors of angiotensin-converting enzyme inhibitor-induced cough: the role of ACE, ABO, and BDKRB2 genes. PHARMACOGENET GENOM. 21:531-538. I.F.: 3.87.

GRANTS FOR RESEARCH IN PROGRESS

Grau I. Desarrollo y coorganización del proyecto ForumClinic. Programa interactiu per a pacients adreçat a què aquests augmentin el seu grau d'autonomia respecte a la seva salut utilitzant les oportunitats de les noves tecnologies. Sponsored by: Fundación BBVA. Duration: 01/01/2009-31/12/2012.

Siso A. Multilingual OrganiK Information management in the medical domain (Projecte MORMED). Sponsored by: Comission Europea, 250534. Duration: 01/03/2010-31/08/2012.

Ortega E, Catalan M, Herreras Z. Riesgo cardiovascular en sujetos con diabetes tipo 2 (DM2) de reciente diagnóstico: grosor de intima media (GIMC) y presencia de placa carotídea (PC) como discriminador de riesgo cardiovascular al diagnóstico y tras tratamiento de la enfermedad. Sponsored by: Instituto de Salud Carlos III (ISCIII), PI11/01723. Duration: 01/01/2011-31/12/2012.

DOCTORAL THESES

Siso A, Ramos-Casals M. Significado clínico de la presencia de autoanticuerpos en el síndrome de Sjögren primario: implicaciones en la práctica diaria. PhD student: Norma Nardi, Universitat de Barcelona.

Siso A. Anàlisis de les comunitats virtuals en els fòrums del portal ForumClinic. PhD student: Immaculada Grau Corral.

Research in nursing

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Luis González de Paz (Gesclínic)

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.

MAIN LINES OF RESEARCH

Internationally, research activity in nursing is improving thanks to the definition of priorities, the identification of groups and the focusing of their research lines, increased funding, and integration of the results obtained in the clinical practice setting. Accordingly, an increase is being observed in the number of publications in international journals, documented in the Cumulative Index to Nursing and Allied Health Literature (CINAH) and the Medline database, affording credibility and acknowledgement to our research activities. This improved scientific production has been achieved through the competitive funding of projects and the development of research training programs on the part of the professional and government organizations, and the generalized application of anonymous and rigorous peer review of the results of the investigations made.

Research in nursing presents differential paradigmatic elements with respect to other types of research in the health sciences, such as its particular patient focus (rather than disease-based focus), and the study of physiological, psychological, sociocultural and/or spiritual aspects

of the individual, with a view to improving healing. The effort to secure this unique approach has resulted in the definition of priority research areas in nursing, which in this country comprise the following: evaluation of the efficacy of nursing interventions; the promotion of health and the development of strategies designed to implicate patients in their own healing; healing based on evidence; the implementation and evaluation of results in clinical practice; and measurement of the quality of nursing care.

In Spain, research in nursing is still an emergent activity. Its consolidation will be facilitated by the recent introduction of degree programs, masters and doctorate courses specifically targeted at nursing, with the participation of professionals accredited for teaching in research. For the first time, nurses following a doctorate program will be able to access extensive and rigorous training in the scientific method, to ensure the quality of their scientific production in the field of nursing care. Our present challenge is application to the healthcare setting: nurses should understand research as a driving force in their professional development and in the improvement of their care of patients and their families – incorporating it into their daily clinical practice.

We are aware of the enormous task awaiting us. In this context, we are inspired by the brilliant trajectory of research in nursing in the United States or Europe (United kingdom, Sweden, Finland, the Netherlands, etc.) – countries where nursing has been capable of attracting financial support, gaining access to mentors, and consolidating its lines of research. Nursing in the Clinic Hospital can lead the process of incorporating research to clinical practice, based on a solid institutional reference and a strongly-rooted scientific culture. The recent creation of the Nursing Research Committee aims to visualize and reinforce this activity. We already have competitive projects financed by national and European agencies, and have ambitious plans for improvement that should result in an increase in the number and relevance of our publications. In sum, our hospital has the motivation and scientific leadership needed to face the challenge of research in nursing.

PUBLICATIONS

ORIGINALS
I.F.: 33.91

1 Nunez M, Lozano L, Nunez E, Sastre S, DelVal JL, Suso S. Good Quality of Life in Severely Obese Total Knee Replacement Patients: A Case-Control Study. OBES SURG. 21:1203-1208. I.F.: 3.08.

2 Moize V, Deulofeu R, Torres F, DeOsaba JM, Vidal J. Nutritional Intake and Prevalence of Nutritional Deficiencies Prior to Surgery in a Spanish Morbidly Obese Population. OBES SURG. 21:1382-1388. I.F.: 3.08.

3 Compta Y, Ezquerra M, Munoz E, Tolosa E, Valldeoriola F, Rios J, Camara A, Fernandez M, Buongiorno MT, Marti MJ. High cerebrospinal tau levels are associated with the rs242557 tau gene variant and low cerebrospinal beta-amyloid in Parkinson disease. NEUROSCI LETT. 487:169-173. I.F.: 2.06.

4 Valldeoriola F, Coronell C, Pont C, Buongiorno MT, Camara A, Gaig C, Compta Y. Socio-demographic and clinical factors influencing the adherence to treatment in Parkinson's disease: the ADHESON study. EUR J NEUROL. 18:980-987. I.F.: 3.77.

5 Nunez M, Fernandez-Sola J, Nunez E, Fernandez-Huerta JM, Godas-Sieso T, Gomez-Gil E. Health-related quality of life in patients with chronic fatigue syndrome: group cognitive behavioural therapy and graded exercise versus usual treatment. A randomised controlled trial with 1 year of follow-up. CLIN RHEUMATOL. 30:381-389. I.F.: 1.69.

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	10.27	6	1	1
2010	22.63	9	3	3
2011	33.91	9	5	2

6 Rosa AR, Reinares M, Amann B, Popovic D, Franco C, Comes M, Torrent C, Bonnin CM, Sole B, Valenti M, Salamero M, Kapczinski F, Vieta E. Six-month functional outcome of a bipolar disorder cohort in the context of a specialized-care program. BIPOLAR DISORD. 13:679-686. I.F.: 5.22.

7 Vizcaya D, Mirabelli MC, Anto JM, Orriols R, Burgos F, Arjona L, Zock JP. A workforce-based study of occupational exposures and asthma symptoms in cleaning workers. OCCUP ENVIRON MED. 68:914-919. I.F.: 3.49.

8 Guiral E, Mendez-Arancibia E, Soto SM, Salvador P, Fabrega A, Gascon J, Vila J. CTX-M-15-producing Enteroaggregative Escherichia coli as Cause of Travelers' Diarrhea. EMERG INFECT DIS. 17:1950-1953. I.F.: 6.86.

9 Sole M, Pitart C, Roca I, Fabrega A, Salvador P, Munoz L, Oliveira I, Gascon J, Marco F, Vila J. First Description of an Escherichia coli Strain Producing NDM-1 Carbapenemase in Spain. ANTIMICROB AGENTS CH. 55:4402-4404. I.F.: 4.67.

GRANTS FOR RESEARCH IN PROGRESS

Burgos F. Estudio Europeo de Salud Respiratoria: Seguimiento de la población española a los 18 años de su inicio. Sponsored by: FIS, 2009 ECRHS III. Duration: 01/01/2009-31/12/2011.

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, 2421153. Duration: 01/01/2010-30/06/2013.

Zabalegui A. Grup de recerca reconegut com consolidat de Catalunya al "Grup de Cures a la Gent Gran Dependent". Sponsored by: Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR), 2009 SGR 916. Duration: 03/07/2009-31/12/2012.

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 (ISCIII), PI09/0111. Duration: 17/02/2010-31/12/2012.

Comes M. Impacte d'un programa d'intervenció multidisciplinari sobre l'estil de vida en la millora del funcionament psicosocial i la qualitat de vida dels pacients bipolars d'inici precoç. Sponsored by: COIB, PR-5385-11. Duration: 01/01/2011-31/12/2011.

Nuñez M. Programa educatiu per a pacients amb artrosi de genoll i obesitat tipus I i tipus II, un estudi aleatoritzat i d'aplicació pràctica. Sponsored by: COIB, PR- 5383-11. Duration: 01/01/2011-31/12/2011.

Ocaña T. Avaluació de l'impacte de la realització de reunions informatives a famílies amb síndrome de Lynch en la prevenció del càncer colorectal. Sponsored by: COIB, PR- 5382-11. Duration: 01/01/2011-31/12/2011.

Moreno C. Empowerment del paciente a través de la información-educació dels pacients programats a intervención quirúrgicas de prótesis de maluc o de genoll. Sponsored by: Colegio Oficial de Enfermería de Barcelona. Duration: 01/01/2010-31/12/2013.

Rodriguez E. Disseny d'un instrument d'avaluació de competencias per al laboratorio de simulación d'infermeria. Sponsored by: Colegio Oficial de Enfermería de Barcelona. Duration: 01/01/2011-31/12/2011.

Zabalegui A. Reflection. projecte europeu en intervencions complexes d'infermeria. Sponsored by: European Science Foundation - European Union. Duration: 01/01/2011-31/12/2014.

Transversal research groups

Clinical pharmacology

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TEAM INVOLVED IN:

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PLATAFORMA ESPAÑOLA DE ENSAYOS CLÍNICOS

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 Clinic Hospital (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 **Statistical and Methodological Support Unit (USEM)** offers counselling in trial data analysis and planning.

4. The **Pharmacoepidemiology and Therapeutic Evaluation Unit**, offers support of activities in pharmacovigilance, epidemiology and the evaluation of drugs in our setting.

5. The team collaborates with Dr. Amàlia Lafuente (UB) of the **Pharmacology Unit of the University of Barcelona**, who conducts studies relating genetics to drug substance activity and response.

6. 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

Original publications from 2009 to 2011

Year	IF	Total	Q 1	Q 2
2009	41.47	15	7	6
2010	78.15	23	9	8
2011	76.89	29	10	4

ORIGINALS
I.F.: 76.89

1 Canovas M, Torres F, Domenech G, Cebrecos J, Pelagio P, Manriquez M, Martinez G, Arcabell M, Cabre F. Bioequivalence evaluation of two dosage forms of olanzapine 10 mg formulations in healthy volunteers. ARZNEIMITTEL-FORSCH. 61:75-79. I.F.: 0.63.

2 Ohmann C, Kuchinke W, Canham S, Lauritsen J, Salas N, Schade-Brittinger C, Wittenberg M, Mcpherson G, Mccourt J, Gueyffier F, Lorimer A, Torres F. Standard requirements for GCP-compliant data management in multinational clinical trials. TRIALS. 12:-. I.F.: 2.08.

3 Lopez CC, Marti T, Catala V, Torres F, Mateu S, Castan JB, Balcells RT. Effects of rapamycin on angiomyolipomas in patients with tuberous sclerosis. NEFROLOGIA. 31:292-298. I.F.: 0.74.

4 Domingo P, Cabeza MC, Pruvost A, Torres F, Salazar J, Gutierrez MD, Mateo MG, Fontanet A, Fernandez I, Domingo JC, Villarroya F, Vidal F, Baiget M. Association of Thymidylate Synthase Gene Polymorphisms with Stavudine Triphosphate Intracellular Levels and Lipodystrophy. ANTIMICROB AGENTS CH. 55:1428-1435. I.F.: 4.67.

5 Masclans JR, Roca O, Munoz X, Pallisa E, Torres F, Rello J, Morell F. Quality of Life, Pulmonary Function, and Tomographic Scan Abnormalities After ARDS. CHEST. 139:1340-1346. I.F.: 6.52.

6 Canovas M, Torres F, Domenech G, Cebrecos J, Pelagio P, Martinez G, Polonio F, Cabre F. Bioequivalence evaluation of two oral formulations of quetiapine fumarate in healthy volunteers. ARZNEIMITTEL-FORSCH. 61:489-493. I.F.: 0.63.

7 Matt P, VanZwieten-Boot B, CalvoRojas G, TerHofstede H, Garcia-Carbonero R, Camarero J, Abadie E, Pignatti F. The European Medicines Agency review of Tegafur/Gimeracil/Oteracil (Teysuno™) for the treatment of advanced gastric cancer when given in combination with cisplatin: summary of the Scientific Assessment of the Committee for medicinal products for human use. ONCOLOGIST. 16:1451-1457. I.F.: 5.83.

8 Description of sexual assaults treated in the emergency department of a referral hospital. GAC SANIT. 25:166-169. I.F.: 1.11.

9 Obach V, Oleaga L, Urra X, Macho J, Amaro S, Capurro S, Gomez-Choco M, SanRoman L, Cervera A, Blasco J, Vargas M, Torres F, Chamorro A. Multimodal CT-assisted thrombolysis in patients with acute stroke: a cohort study. STROKE. 42:1129-1131. I.F.: 5.76.

10 Ribera T, Monreal L, Armengou L, Rios J, Prades M. Synovial fluid D-dimer concentration in foals with septic joint disease. J VET INTERN MED. 25:1113-1117. I.F.: 2.28.

11 Leon A, Caceres C, Fernandez E, Chausa P, Martin M, Codina C, Rousaud A, Blanch J, Mallolas J, Martinez E, Blanco JL, Laguno M, Larrousse M, Milinkovic A, Zamora L, Canal N, Miro JM, Gatell JM, Gomez

EJ, Garcia F. A New Multidisciplinary Home Care Telemedicine System to Monitor Stable Chronic Human Immunodeficiency Virus-Infected Patients: A Randomized Study. PLOS ONE. 6:-. I.F.: 4.41.

12 Tomas X, Bori G, Garcia S, Garcia-Diez AI, Pomes J, Soriano A, Rios J, Almela M, Mensa J, Gallart X, Martinez JC, Riba J. Accuracy of CT-guided joint aspiration in patients with suspected infection status post-total hip arthroplasty. SKELETAL RADIOL. 40:57-64. I.F.: 1.39.

13 Carcelero E, Tuset M, Martin M, DeLazzari E, Codina C, Miro J, Gatell JM. Evaluation of antiretroviral-related errors and interventions by the clinical pharmacist in hospitalized HIV-infected patients. HIV MED. 12:494-499. I.F.: 3.58.

14 Garcia AI, Milinkovic A, Tomas X, Rios J, Perez I, Vidal-Sicart S, Pomes J, DelAmo M, Mallolas J. MRI signal changes of the bone marrow in HIV-infected patients with lipodystrophy: correlation with clinical parameters. SKELETAL RADIOL. 40:1295-1301. I.F.: 1.39.

15 Font-Vizcarra L, Lozano L, Rios J, Forga MT, Soriano A. Preoperative nutritional status and post-operative infection in total knee replacements: A prospective study of 213 patients. INT J ARTIF ORGANS. 34:876-881. I.F.: 1.50.

16 Garcia F, DeQuiros JCLB, Gomez CE, Perdiguero B, Najera JL, Jimenez V, Garcia-Arriaza J, Guardo AC, Perez I, Diaz-Brito V, Conde MS, Gonzalez N, Alvarez A, Alcami J, Jimenez JL, Pich J, Arnaiz JA, Maleno MJ, Leon A, Munoz-Fernandez MA, Liljestrom P, Weber J, Pantaleo G, Gatell JM, Plana M, Esteban M. Safety and immunogenicity of a modified pox vector-based HIV/AIDS vaccine candidate expressing Env, Gag, Pot and Nef proteins of HIV-1 subtype B (MVA-B) in healthy HIV-1-uninfected volunteers: A phase I clinical trial (RISVAC02). VACCINE. 29:8309-8316. I.F.: 3.57.

17 Morina D, Puig P, Rios J, Vilella A, Trilla A. A statistical model for hospital admissions caused by seasonal diseases. STAT MED. 30:3125-3136. I.F.: 2.33.

18 Guitian PP, Xarau SN, Guillermo JR, Tejero IN, Viladot JRA. Evaluation of acute poisonings due to chemical agents treated in an Emergency Department. MED CLIN-BARCELONA. 136:149-152. I.F.: 1.41.

19 Tamborero D, Vidal B, Tolosana JM, Sitges M, Berruezo A, Silva E, Castel M, Matas M, Arbelo E, Rios J, Villacastin J, Brugada J, Mont L. Electrocardiographic versus Echocardiographic Optimization of the Interventricular Pacing Delay in Patients Undergoing Cardiac Resynchronization Therapy. J CARDIOVASC ELECTR. 22:1129-1134. I.F.: 3.29.

20 Alonso I, Fuste V, DelPino M, Castillo P, Torne A, Fuste P, Rios J, Pahisa J, Balasch J, Ordi J. Does human papillomavirus infection imply a different prognosis in vulvar squamous cell carcinoma?. GYNECOL ONCOL. 122:509-514. I.F.: 3.76.

21 Moize V, Deulofeu R, Torres F, DeOsaba JM, Vidal J. Nutritional Intake and Prevalence of Nutritional Deficiencies Prior to Surgery in a Spanish Morbidly Obese Population. OBES SURG. 21:1382-1388. I.F.: 3.08.

22 Compta Y, Ezquerra M, Munoz E, Tolosa E, Valldeoriola F, Rios J, Camara A, Fernandez M, Buongiorno MT, Marti MJ. High cerebrospinal tau levels are associated with the rs242557 tau gene variant and low cerebrospinal beta-amyloid in Parkinson disease. NEUROSCI LETT. 487:169-173. I.F.: 2.06.

23 Botta-Orfila T, Ezquerra M, Rios J, Fernandez-Santiago R, Cervantes S, Samaranch L, Pastor P, Marti MJ, Munoz E, Valldeoriola F, Aguilar M, Calopa M, Hernandez-Vara J, Tolosa E. Lack of interaction of SNCA and MAPT genotypes in Parkinson's disease. EUR J NEUROL. 18:E32-E32. I.F.: 3.77.

24 Mas S, Gasso P, Alvarez S, Ortiz J, Sotoca JM, Francino A, Carne X, Lafuente A. Pharmacogenetic predictors of angiotensin-converting enzyme inhibitor-induced cough: the role of ACE, ABO, and BDKRB2 genes. PHARMACOGENET GENOM. 21:531-538. I.F.: 3.87.

25 Salazar F, Donate M, Boget T, Bogdanovich A, Basora M, Torres F, Fabregas N. Intraoperative warming and post-operative cognitive dysfunction after total knee replacement. ACTA ANAESTH SCAND. 55:216-222. I.F.: 2.20.

26 Sanz G, Fuster V, Guzman L, Guglietta A, Arnaiz JA, Martinez F, Sarria A, Roncaglioni MC, Taubert K. The Fixed-dose Combination Drug for Secondary Cardiovascular Prevention project: Improving equitable access and adherence to secondary cardiovascular prevention with a fixed-dose combination drug. Study design and objectives. AM HEART J. 162:-. I.F.: 5.05.

EDITORIALS
I.F.: 15.62

1 Dal-Re R, Moher D, Gluud C, Treweek S, Demotes-Mainard J, Carne X. Disclosure of Investigators' Recruitment Performance in Multicenter Clinical Trials: A Further Step for Research Transparency. PLOS MED. 8:-. I.F.: 15.62.

MULTICENTRICS
I.F.: 15.74

1 Petoumenos K, Worm S, Reiss P, DeWit S, Monforte AD, Sabin C, Friis-Moller N, Weber R, Mercie P, Pradier C, El-Sadr W, Kirk O, Lundgren J, Law MG. Rates of cardiovascular disease following smoking cessation in patients with HIV infection: results from the D:A:D study. HIV MED. 12:412-421. I.F.: 3.58.

2 Kowalska JD, Friis-Moller N, Kirk O, Bannister W, Mocroft A, Sabin C, Reiss P, Gill J, Lewden C, Phillips A, Monforte AD, Law M, Sterne J, DeWit S, Lundgren JD. The Coding Causes of Death in HIV (CoDe) Project Initial Results and Evaluation of Methodology. EPIDEMIOLOGY. 22:516-523. I.F.: 5.87.

3 DataCollectionOnAdverseEvents OfAnti-HivDrugs(d:a:d) STUDY. The impact of fasting on the interpretation of triglyceride levels for predicting myocardial infarction risk in HIV-positive individuals: the D:A:D study. J INFECT DIS. 204:521-525. I.F.: 6.29.

GRANTS FOR RESEARCH IN PROGRESS

Carne X. European Clinical Research Infrastructures Network and biotherapy facilities: Preparation Phase for the Infrastructure: INSERM. Sponsored by: IEuropean Commission, FP7. Duration: 01/03/2008-28/02/2011.

Arnaiz JA. Fixed Dose Combination drugs for Secondary Cardiovascular Prevention. Sponsored by: CNIC-Centro Nacional de Investigaciones Cardiovasculares Carlos III, 241559. Duration: 01/07/2010-30/06/2013.

Calvo G. Estudio de cohortes para evaluar la seguridad y la efectividad del programa de vacunación frente a la gripe A (H1N1) en el área de cobertura sanitaria de un hospital de tercer nivel. Sponsored by: Ministerio de Sanidad, Politica Social e Igualdad, TRA-063. Duration: 01/01/2010-31/12/2011.

Calvo G. Estudio prospectivo multicéntrico de la incidencia, relevancia clínica, factores de riesgo y preventibilidad del ingreso hospitalario por fracaso renal agudo asociado al uso de fármacos inhibidores del sistema renina-angiotensina. Sponsored by: Instituto de Salud Carlos III, EC08/00173. Duration: 01/01/2009-30/12/2011.

Calvo G. Evaluación de la utilidad clínica de un protocolo estandarizado de disminución de dosis en pacientes con espondilartritis axiales (EA) en remisión clínica persistente en tratamiento con terapia anti-TNFalfa. Sponsored by: Instituto de Salud Carlos III (ISCIII) ,Investigación independiente FIS. Duration: 01/01/2011-31/12/2012.

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